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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, DC 20549

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**FORM 10-K**

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(Mark One)

**ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended September 30, 2011.

**TRANSITION REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number 000-21898

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**ARROWHEAD RESEARCH CORPORATION**

(Exact name of registrant as specified in its charter)

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Delaware  
(State of incorporation)

46-0408024  
(I.R.S. Employer Identification No.)

225 S. Lake Avenue, Suite 300  
Pasadena, California 91101  
(626) 304-3400  
(Address and telephone number of principal executive offices)

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**Securities registered under Section 12(b) of the Exchange Act:**

Title of each class	Name of each exchange on which registered
Common Stock, \$0.001 par value	The NASDAQ Capital Market

**Securities registered pursuant to Section 12(g) of the Exchange Act:**

None

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Indicate by a check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by a check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act.

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller Reporting Company

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes  No

The aggregate market value of issuer's outstanding Common Stock held by non-affiliates was approximately \$53 million based upon the bid price of issuer's Common Stock on March 31, 2011.

As of December 15, 2011, 10,525,941 shares of the issuer's Common Stock were outstanding.

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## FORWARD-LOOKING STATEMENTS

*This Annual Report on Form 10-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, and we intend that such forward-looking statements be subject to the safe harbors created thereby. For this purpose, any statements contained in this Annual Report on Form 10-K except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as “may,” “will,” “expect,” “believe,” “anticipate,” “intend,” “could,” “estimate,” or “continue” or the negative or other variations thereof or comparable terminology are intended to identify forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our businesses, or other characterizations of future events or circumstances are forward-looking statements.*

*The forward-looking statements included herein are based on current expectations of our management based on available information and involve a number of risks and uncertainties, all of which are difficult or impossible to predict accurately and many of which are beyond our control. As such, our actual results may differ significantly from those expressed in any forward-looking statements. Factors that may cause or contribute to such differences include, but are not limited to, those discussed in more detail in Item 1 (Business) and Item 1A (Risk Factors) of Part I and Item 7 (Management’s Discussion and Analysis of Financial Condition and Results of Operations) of Part II of this Annual Report on Form 10-K. Readers should carefully review these risks, as well as the additional risks described in other documents we file from time to time with the Securities and Exchange Commission. In light of the significant risks and uncertainties inherent in the forward-looking information included herein, the inclusion of such information should not be regarded as a representation by us or any other person that such results will be achieved, and readers are cautioned not to place undue reliance on such forward-looking information. Except as may be required by law, we undertake no obligation to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.*

## PART I

### ITEM 1. BUSINESS

#### *Description of Business*

Unless otherwise noted, (1) the term “Arrowhead” refers to Arrowhead Research Corporation, a Delaware corporation, (2) the terms the “Company,” “we,” “us,” and “our,” refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term “Subsidiaries” refers collectively to Arrowhead Madison Inc. (“Madison”), Calando Pharmaceuticals, Inc. (“Calando”), Ablaris Therapeutics, Inc. (“Ablaris”), Agonn Systems, Inc. (“Agonn”) and Tego Biosciences Corporation (“Tego”) as well as our former subsidiary, Unidym, Inc. (“Unidym”), which was divested in January 2011, (4) the term “Minority Investments” refers collectively to Nanotope, Inc. (“Nanotope”) and Leonardo Biosystems, Inc. (“Leonardo”) in which the company holds a less than majority ownership position, and (5) the term “Common Stock” refers to Arrowhead’s Common Stock and the term “stockholder(s)” refers to the holders of Arrowhead Common Stock.

#### *Overview*

Arrowhead Research Corporation is a clinical stage nanomedicine company developing innovative therapies at the interface of biology and nanoengineering. Arrowhead’s world-class capabilities and intellectual property covering nucleic acid delivery, siRNA chemistry, and tissue targeting allow it to design and develop therapeutic agents for a wide range of diseases. The company’s lead products include CALAA-01, an oncology drug candidate based on the gene silencing RNA interference (RNAi) mechanism, and Adipotide™, an anti-obesity peptide that targets and kills the blood vessels that feed white adipose tissue. Arrowhead is leveraging its proprietary Dynamic Polyconjugate™ (DPC), Liposomal Nanoparticle (LNP), and RONDEL™ delivery platforms to support its own pipeline of preclinical and clinical candidates and to secure external partnerships and collaborations with biotech and pharmaceutical companies.

Arrowhead was originally incorporated in South Dakota in 1989, and was reincorporated in Delaware in 2000. The Company’s principal executive offices are located at 225 South Lake Avenue, Suite 300, Pasadena, California 91101, and its telephone number is (626) 304-3400. As of September 30, 2011, Arrowhead had 11 full-time employees at the corporate office and seven full-time employees at its Subsidiaries. On October 21, 2011, as a result of an acquisition of Roche’s RNAi business, 39 full-time employees were added at Arrowhead’s newly acquired Madison, Wisconsin research facility.

#### *Our Strategy*

Partnerships with other pharmaceutical and biotech companies to drive revenue are the primary focus of our business development efforts. Given the array of our siRNA delivery platforms, we expect to enter disease specific siRNA therapeutic collaborations and siRNA delivery collaborations with large pharmaceutical and biotechnology companies which we believe will provide the opportunity to generate revenue in the near term. Using our experience, disease specific collaborations will seek to develop and optimize siRNA lead candidates based on disease targets supplied by the partner. The siRNA therapeutics will be optimized to operate efficiently using the delivery system that best addresses the disease indication. Arrowhead will seek to generate revenue through upfront technology access fees, research funding, research milestones, licensing fees, clinical milestone payments and royalties. The company also plans to continue development of its internal preclinical and clinical pipeline including ongoing RONDEL-enabled siRNA drug candidates, DPC-enabled drug candidate development, and the non-siRNA-based anti-obesity drug candidate, Adipotide. If these efforts are successful, these candidates may be sold or out-licensed in the future.

#### *Recent Event—Acquisition of Roche Facility and Intellectual Property*

In October 2011, Arrowhead acquired Roche’s RNAi business, including its RNA therapeutic assets, related intellectual property and research facility in Madison, Wisconsin. Over the last year, we have been implementing our transition from a diversified nanotechnology company to a pure play nanomedicine company. This strategic acquisition serves as the cornerstone of this transition. We are now a full-service, fully-enabled nanomedicine company with new R&D capabilities that can support the development of our existing and new programs. Our recently acquired scientific leaders, licensed technology, and development operations are expected to accelerate both our RNAi and non-RNAi programs synergistically.

The addition of these assets to Arrowhead’s existing RNAi technologies solidifies our position as one of the most advanced and broadest RNAi therapeutics companies in the world. With completion of the Roche acquisition, Arrowhead now possesses the following siRNA assets:

- Non-exclusive license from Alnylam providing license to use canonical siRNAs in oncology, respiratory diseases, metabolic diseases and certain liver diseases. This includes a sub-license from Isis Pharmaceuticals giving Arrowhead license for siRNA chemical modifications for these specific disease areas.
- Non-exclusive license from City of Hope Comprehensive Cancer Center to Dicer substrate and Meroduplex siRNAs. The Dicer technology may provide advantages over canonical siRNAs in certain circumstances. In addition, different siRNA formats may trigger RNAi more or less efficiently on a target-by-target basis.
- Ownership of the former Mirus Bio, including lab facilities, and the entire patent estate covering the Dynamic Polyconjugate (DPC) siRNA delivery system.
- Access to certain patents on targeting siRNA drugs with antibodies and small molecules from Roche.
- State of the art laboratory facilities in Madison, Wisconsin, managed by long term leaders in oligonucleotide therapeutics and delivery, including an onsite state-of-the-art small animal research facility and an offsite primate colony.
- Intellectual property covering Roche’s internally developed liposomal nanoparticle drug delivery technology.
- RONDEL siRNA delivery system which has demonstrated gene knockdown in humans in the CALAA01 clinical trial.
- Minority ownership position in Leonardo Biosystem’s multi-stage silicon-based delivery system.
- CALAA-01 Phase I oncology drug candidate

We believe this represents one of the broadest siRNA drug technology and delivery portfolios in the world. We have extensive know how and expertise in the siRNA therapeutic space, and importantly, we have extensive delivery capabilities.

### ***About RNA Interference & the Promise of siRNA Therapeutics***

RNA interference (RNAi) is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a protein of interest. Deemed to be one of the most important recent discoveries in life science with the potential to transform medicine, the discoverers of RNAi were awarded the Nobel Prize for Physiology or Medicine in 2006. Mediated by small interfering RNAs (siRNA), a class of ribonucleic acid (RNA) molecules, 20-25 nucleotides in length, RNAi-based therapeutics can leverage this natural pathway of gene silencing to potentially target and shut down specific disease causing genes.

Small molecule or antibody drugs have proven effective at inhibiting certain cell surface, intracellular, and extracellular targets. However, certain drug targets such as intranuclear genes and some proteins have proven difficult to inhibit with traditional drug-based and biologic therapeutics. Developing effective drugs for these targets would have the potential to address a very large underserved market for the treatment of many diseases. Using its potential to specifically target and silence any gene target, siRNA therapeutics may be able to address previously “undruggable” targets, unlocking the market potential of such targets.

Several classes of RNA molecules have been utilized to generate RNAi mediated gene knockdown. Canonical siRNAs are the traditionally used 20-25 nucleotide long RNA molecules that interfere with post-transcription gene expression. Meroduplex siRNAs are three stranded RNA constructs also capable of interfering with post transcription gene expression. Dicer substrates are synthetic RNA duplexes that are approximately 27 nucleotides long, and have been shown in some studies to be more potent than 21-mer siRNA with less immune stimulation. Through licenses, Arrowhead has access to all three of these technologies collectively covering a broad range of potential targets.

### ***Addressing the siRNA Delivery Challenge***

To date, the primary challenge to siRNA therapeutics has been delivering the fragile, often immunogenic and otherwise rapidly cleared siRNA molecules, into the cytoplasm of the cell, where RNAi activity occurs. To date, the hurdle of delivery has prevented siRNA therapeutics from reaching their full potential. Many companies have attempted to overcome the delivery challenge. Most early systems involved cholesterol conjugates or traditional liposomes. These have not yet proven optimal due to toxicity and immunogenicity when studied in clinical trials.

To address the delivery challenge, Arrowhead has assembled a leading team of researchers with extensive siRNA therapeutic know how and one of the broadest portfolios of siRNA delivery technologies available, with the potential to unlock siRNA as a therapeutic class through superior delivery, including:

- The Dynamic Polyconjugate (DPC) system is an amphipathic polymer to which shielding agents such as polyethylene glycol, as well as targeting ligands are reversibly attached, thus protecting the fragile siRNA therapeutic and specifying tissue specific delivery.
- The RONDEL™ delivery system utilizes targeted cyclodextrin polymers to deliver siRNA and other oligonucleotides to tumors. Human *in vivo* gene knockdown has been demonstrated in a Phase I cancer trial, establishing proof of concept for the RONDEL system.
- Affiliate Leonardo Biosystems is developing a multi-stage delivery technology, initially for oncology applications. The first stage of the system consists of biodegradable silicon nanoparticles that are rationally designed to circumvent the multiple biological barriers en route to the target site. The first stage silicon particle is loaded with second stage delivery vectors such as liposomes or polymeric particles carrying a therapeutic agent, such as siRNA or a small molecule drug.
- Stable Nucleic Acid Lipid Nanoparticles (SNALP) through a license agreement with Tekmira.

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- Roche's internally developed liposomal nanoparticles which have shown efficacy in vivo at knocking down targets in various animal disease models including models of human diseases such as cancer and chronic obstructive pulmonary disease (COPD).

No single method of delivery will be optimal for all disease areas, targets, and tissue types throughout the body. However, Arrowhead believes that these five technology platforms together represent the most comprehensive portfolio of solutions for effective delivery of therapeutic siRNA against a broad range of disease indications. We see this as transformational for Arrowhead and potentially for RNAi as a new therapeutic class of drugs. The ability to optimize delivery on a target-by-target basis is a critical tool, and we believe it positions Arrowhead as a powerful partner for biotech and pharmaceutical companies interested in developing candidates against multiple targets which may be "undruggable" by small molecule inhibitors or antibodies. We intend to use this leadership position to negotiate partnerships and collaborations as well as support our own internal pipeline of drug candidates.

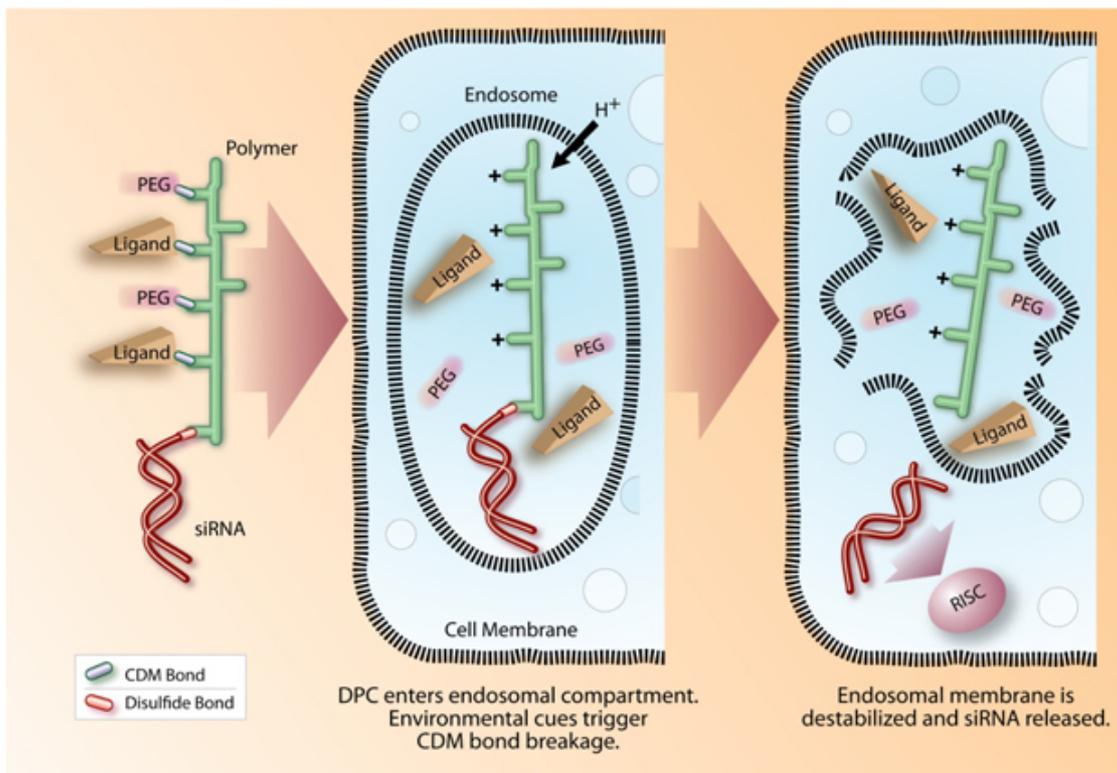
### The Dynamic Polyconjugate siRNA Delivery System

The DPC delivery system represents an elegant solution to the siRNA delivery problem, specifically designed to overcome barriers to systemic administration of siRNA. First developed by our scientists in Madison, Wisconsin, the inspiration for DPC technology came from the physical characteristics of viruses, nature's own nanoparticles for nucleic acid delivery. Viruses are efficient at finding their target cells and delivering their nucleic acid payload to the proper cellular compartment. Key features of viruses are their small size, their overall negative surface charge, their specificity for particular cell types based on receptors unique to that cell, and their ability to disassemble and release their nucleic acid cargo to the proper cell compartment in response to cellular triggers. All of these features are incorporated into DPC technology.

DPCs are small nanoparticles, 5-20 nanometers (nm) in size, composed of an amphipathic polymer to which shielding agents such as polyethylene glycol, as well as targeting ligands are reversibly attached. In some constructs, the siRNA payload is attached to the DPC, while in other constructs, the siRNA circulates attached to a different carrier. When attached, the DPC construct protects the siRNA payload while allowing the polymer to circulate in the blood without creating undue toxicity. The targeting ligand guides the nanoparticles to the cell of interest where, together with the siRNA, it is taken up into a membrane-enclosed cellular compartment known as an endosome. The polymer is selected for its ability to lyse the endosomal membrane which releases the siRNA into the cytoplasm. There, it engages the cell's RNAi machinery, ultimately resulting in knockdown of target gene expression. The lytic chemistry of the DPC polymeric backbone is modified, or "masked", using proprietary chemistry. Masking of the polymer's lytic chemistry accomplishes two interrelated objectives that are critical to in vivo siRNA delivery:

- Reduction of toxicity by controlling when the membrane lytic property of the polymer is activated.
- Inhibition of non-specific interactions with blood components and non-targeted cell types.

Dynamic Polyconjugate system and mechanism of siRNA delivery:



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We believe our DPC technology is radically different from standard liposomal or lipid nanoparticle siRNA delivery systems used by the majority of RNAi therapeutics companies. DPCs are smaller than lipid-based systems, enabling more efficient distribution from the vasculature to the target tissue. DPCs can use targeting ligands for cell-type specific delivery, which has yet to be achieved with the lipid-based systems used in clinical development programs. The modular nature of DPCs allows each component to be optimized for higher efficacy and lower toxicity. As a polymer-based system, DPCs are fundamentally different from lipid-based systems. This has the potential to open up an entirely new class of macromolecules to enable siRNA delivery.

Hepatocytes, the key parenchymal cells of the liver, are a particularly attractive target cell type for siRNA delivery given their central role in several infectious and metabolic diseases. Latest generation DPCs have shown high effectiveness in rats and non-human primates with ED80 (dose producing 80% knockdown of the gene of interest) values of ~0.1 mg/kg siRNA after a single dose. Increasing the dose two-fold in non-human primates results in >99% knockdown with a duration of effect of nearly 7 weeks. DPCs are also well tolerated and have single-dose therapeutic indices of >10 in non-human primates, indicating that there is a ten-fold safety margin between the effective dose and the toxic dose. The magnitude of the safety margin and efficiency of gene knockdown in non-human primates is, to our knowledge, unprecedented in the therapeutic RNAi field as compared to available data generated with competing delivery systems, and position DPC technology as a leading technology for siRNA delivery to liver.

Our DPC cancer delivery program is developing the optimal components for targeting DPCs to tumors. This includes identifying ligands for efficient targeting, screening polymer libraries for the most potent polymer for a given cancer cell type and enhancing tumor uptake by modulating the pharmacokinetic properties of the DPC. DPCs for several types of tumors are currently under development. Hepatocellular carcinoma (HCC) has been one of our focus areas. Gene knockdown of 40-50% has been achieved with a single dose of tumor-directed DPCs in a mouse orthotopic HCC tumor model. These results equal or surpass those published with other best-in-class siRNA delivery platforms and validate our overall strategy for tumor targeted DPC delivery. Our current focus is on further improving delivery to tumors, gene knockdown efficacy and therapeutic index by optimizing individual DPC components in animal models.

### ***Calando Pharmaceuticals, Inc.***

#### **Overview**

Founded by Arrowhead in 2005, Calando is a clinical stage nano-biotechnology company focused on RNAi therapeutics developing RONDEL, a nanoparticle-based drug delivery system, for siRNA. In August 2011, we completed enrollment in the Phase I trial of its lead siRNA candidate in oncology, CALAA-01. Initial proof of concept data showed systemic delivery of siRNA and the successful “silencing” of a widely recognized cancer gene via RNA interference (RNAi) in humans. A Phase Ib trial has been initiated to determine if a modified dosing schedule will increase patient tolerability and to gather additional data.

RONDEL is based on pioneering technology invented in the Chemical Engineering department of the California Institute of Technology by Dr. Mark Davis. Our proprietary molecules are designed to safely and effectively deliver small RNAs to target cells. Currently focused on oncology applications, Our flexible platform has the potential to be applied to a wide range of diseases beyond cancer, as well as to therapeutic classes beyond siRNA therapeutics.

We are focused on the clinical development of RONDEL™, and CALAA-01, the associated drug candidate. Interim clinical results show preliminary proof of RNAi activity in patients treated with the highest doses. These results represent several notable “firsts” in the field of RNAi, including first to demonstrate definitive RNAi delivery after systemic administration and first to show dose dependent accumulation in target cells. In addition, CALAA-01 has been shown to mediate specific gene inhibition in humans as evidenced by mRNA knockdown and protein knockdown in tumor biopsies.

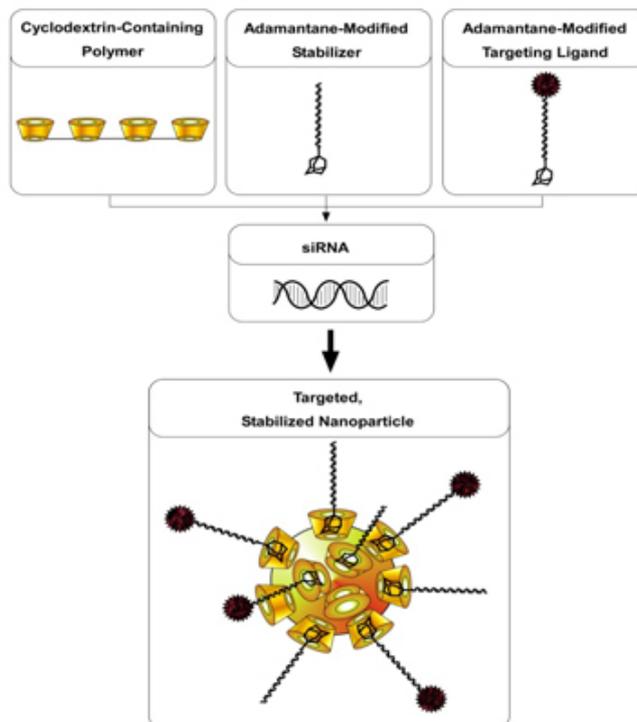
In addition, in December 2008, we concluded a Phase I trial with CRLX101 (formerly IT-101) using a drug candidate consisting of its delivery system and a small molecule anti cancer agent. Patients from this clinical trial reported fewer and less serious side effects with several cases of stable disease over many months of treatment. One patient with pancreatic cancer had stabilized disease for 17 months. The further development of the small molecule delivery platform and IT-101, the associated drug candidate, was licensed to Cerulean Pharma, Inc., (“Cerulean”) a private biotech company in Boston, Massachusetts in June 2009. Cerulean has since advanced CRLX101 to a Phase II clinical trial in non-small cell lung cancer.

#### **Platform Technology**

Based on a novel polymeric sugar (linear cyclodextrin) molecule, RONDEL has been applied thus far to the delivery of two classes of therapeutics: siRNA and other oligonucleotides and small molecule drugs. The polymer is combined with the drug molecule to form a drug containing nanoparticle sized larger than 10 nanometers and smaller than 100 nanometers. We believe that this particle size is important: drug molecules below 10 nanometers are quickly cleared from the body in the urine and nanoparticles larger than 100 nanometers are not able to escape leaky blood vessels that feed tumors. Nanoparticles between 10 and 100 nanometers can lead to preferential accumulation in tumor tissue, where the drug can take effect, leaving other tissues less affected. The drug delivery system has the added benefits of increasing solubility, allowing targeting of the nanoparticles, and having a low immune stimulatory potential.

*RONDEL™ Technology*

One of the key challenges to using RNAi therapy has been the inability to systemically deliver siRNA in humans. “Naked” siRNA is degraded and destroyed by nucleases in the bloodstream and is not taken up by cells. The RONDEL system is providing new hope that effective siRNA delivery can be achieved safely and economically. Our polymers form the foundation for a three-part RNAi/Oligonucleotide Nanoparticle Delivery (RONDEL) technology. The first component is the positively charged polymer that, when mixed with siRNA, binds to the negatively charged “backbone” of the siRNA. The polymer and siRNA self-assemble into nanoparticles less than 100 nm diameter that fully protect the siRNA from nuclease degradation in serum. The cyclodextrin in the polymer enables the surface of the particles to be decorated by stabilizing agents and targeting ligands. These surface modifications are formed by proprietary methods involving the cyclodextrins.



The surface-modifying agents have terminal adamantane groups that form inclusion complexes with the cyclodextrin and contain polyethylene glycol (PEG) to endow the particles with properties that prevent aggregation, enhance stability and enable systemic administration. Targeting molecules can be covalently attached to the adamantane-PEG modifier, enabling the siRNA-containing particles to be targeted to tissues of interest.

RONDEL technology offers the following advantages:

- Generalized delivery system – Binds to and self-assembles with the siRNA to form uniform colloidal-sized particles. Analysis has shown that these particles are spherical and between 10 nm and 100 nm in diameter.
- Ease of Administration – The RONDEL system has been designed for use as part of a two-vial system: one vial contains the delivery components, and the second vial contains the therapeutic siRNA payload. When mixed pursuant to a simple protocol, the particles self-assemble into siRNA containing nanoparticles.
- Any siRNA sequence can be easily substituted – Because RONDEL binds to the siRNA backbone, theoretically, any siRNA therapeutic could be in the second vial.

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- Stealthy delivery to the immune system – The sugar-based delivery vehicle allows for repeat dosing with reduced risk of immune reactions. Unlike lipid delivery vehicles, the cyclodextrin-based RONDEL™ delivery system is expected to have a low immune-stimulatory potential.
- Safety – The RONDEL technology has been shown to be non-toxic in *in vitro* testing with human cell cultures, and the fully formulated polymer/siRNA particles exhibit a significant therapeutic window of safety in animals, even when repeated doses (up to eight doses over a four week period) are used.
- Effective targeted delivery – Calando and its partners have demonstrated successful delivery of functional siRNA therapeutics to tumor cells and to hepatocytes by systemic administration and confirmed sequence-specific gene inhibition in humans.

### *CALAA-01*

CALAA-01 is a combination of RONDEL and a patented siRNA targeting the M2 subunit of ribonucleotide reductase, a clinically-validated cancer target. Ribonucleotide reductase catalyzes the conversion of ribonucleosides to deoxyribonucleosides and is necessary for DNA synthesis and replication, and thus tumor growth. The internally developed siRNA demonstrates potent anti-proliferative activity across multiple types of cancer cells. We believe the use of CALAA-01 in our Phase I trial, initiated in June 2008, was the first siRNA therapeutic candidate to target cancer in a human clinical study and also the first systemic delivery of an siRNA therapeutic candidate.

Interim clinical results were presented at the 2010 American Society of Clinical Oncology meeting (ASCO). Data from a total of 15 patients accrued to 5 dose levels (3, 9, 18, 24, 30 mg/m<sup>2</sup>) showed that treatment-related adverse events were mostly mild to moderate with fatigue, fever/chills, allergic, or gastrointestinal-related adverse events most frequently observed. Importantly, no changes in coagulation, liver function tests, or kidney function were observed.

Analysis of tumor biopsies from three melanoma patients showed the presence of intracellular nanoparticles in amounts that correlated with dose. Additionally, a reduction was found in both the RRM2 messenger RNA and protein levels when compared to pre-dosing tissue. Furthermore, the presence of siRNA-mediated mRNA cleavage products was confirmed by 5'-RACE, demonstrating that siRNA-mediated mRNA cleavage occurs specifically at the site predicted for an RNAi mechanism. These results were published in March 2010 in the scientific journal *Nature*, citing these interim data from our Phase I trial as the first evidence of systemic delivery of siRNA, and the successful “silencing” of a widely recognized cancer gene via RNA interference in humans.

In August 2011 enrollment into the Phase I clinical trial was completed. Adverse events observed coincided with an increase in certain cytokine levels. Elevation in cytokines is consistent with an acute immune response to the natural siRNA used in CALAA-01. These reactions also appeared to be transient, such that if a patient stayed on CALAA-01, the cytokine responses often subsided. Based on these results, a Phase Ib trial was initiated using a modified dosing schedule in which patients are pretreated with a lower dose to assess whether this strategy can increase patient safety and further increase the maximum tolerated dose. Patient accrual is ongoing and additional safety and pharmacodynamic data will be forthcoming.

We were encouraged that the adverse events observed to date did not appear to be related to the RONDEL delivery system but were consistent with an innate immune response to the natural, unmodified siRNA inside. This opens the pathway to potentially overcome these symptoms by introducing strategic chemical modifications in the siRNA component in future product candidates, a strategy that has been proven in the literature to significantly suppress these types of immune responses.

### *Cycloset™ Technology & CRLX101 (formerly IT-101)*

The other polymeric drug delivery technology, Cycloset, was designed by Calando's scientists for the delivery of small molecule drugs. Cycloset provides many of the same benefits as the RONDEL system. In December 2008, Calando completed a Phase I trial with IT-101, comprised of Calando's polymer and Camptothecin, a potent anti-cancer drug, with a positive safety profile and indications of efficacy. On June 23, 2009, Calando entered into agreements to license Cycloset and IT-101 to Cerulean. Under the terms of the agreements, Calando granted Cerulean an exclusive royalty-bearing worldwide license to certain patent rights and know-how and transferred to Cerulean certain intellectual property related to the linear-cyclodextrin drug delivery platform and IT-101 in exchange for an initial payment of \$2.4 million. Cerulean also will pay development milestone payments of up to \$2.75 million if IT-101 progresses through clinical trials and receives marketing approval. If approved, Calando is also entitled to receive up to an additional \$30 million in sales milestone payments, plus royalties on net sales. Under the agreements, Calando retained the rights to use the linear-cyclodextrin drug delivery platform to deliver any kind of nucleic acid including siRNA. As such, Calando retains the rights to its RONDEL platform, as well as the CALAA-01 and CALAA-02 lead drugs.

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### **Intellectual Property**

We control an intellectual property portfolio of patents covering certain linear cyclodextrin polymers and related technology (the “linear cyclodextrin system”). The portfolio covers both RONDEL and Cyclosert. In June 2009, Calando sold and assigned to Cerulean certain patents for linear cyclodextrin polymers conjugated to drugs. Additionally, Calando granted Cerulean an exclusive license under its rights to the linear cyclodextrin system to develop certain drug products. We retain rights to use the linear cyclodextrin system to develop drugs in which the therapeutic agent is a nucleic acid (e.g., siRNA), a second generation epothilone, tubulysin or cytolysin.

We also own an issued patent covering the siRNA active ingredient in CALAA-01 and has filed a patent application to cover the siRNA active ingredient of CALAA-02. We have licensed patents from Alnylam relevant to siRNA therapeutics for CALAA-01 and CALAA-02. We have out licensed to R&D Biopharmaceuticals the use of the linear cyclodextrin system for delivering tubulysin and cytolysin as well as second generation synthetic epothilone drugs. The RNAi and nanoparticle drug delivery patent landscape is complex and rapidly evolving. As such, we may need to obtain additional patent licenses prior to commercialization of its lead drug candidates.

### **The Drug Delivery and Oncology Markets**

Despite advances in drug discovery, pharmaceutical firms remain challenged by getting the right compound to the right place in the human body, where it can maximize its effect while minimizing side effects.

According to the American Cancer Society, cancer is the second leading cause of death in the United States and accounts for approximately one in every four deaths. The National Institutes of Health has estimated the direct medical cost of cancer to be in excess of \$74 billion per year. Dose limiting toxicity, poor tissue specificity, and large effective distribution are major restrictive factors in effective cancer chemotherapy. Consequently, complete tumor response is not often achieved in patients receiving chemotherapy alone. We believe that this offers a potentially significant opportunity for firms developing technologies to more effectively deliver anti-cancer agents to malignant cells. According to Decision Resources, the global market for oncology therapeutics is expected to grow from \$57 billion in 2007 to \$85 billion in 2013, which is approximately twice the pace of the broader market for pharmaceuticals with a CAGR of 10.8% through 2013 versus 4.6% for all pharmaceuticals. This growth is driven by high unmet medical need for new cancer therapeutics, a high price premium generated by novel drugs to treat conditions with few other available options, and insurers willing to reimburse at high prices for novel therapies due to lack of alternative therapies. Additionally, the shift towards transforming cancer into a chronic illness by management with long term suppressive therapies bodes well for oncology companies developing drugs that will require lifelong maintenance therapy versus the old line chemotherapy cyclic therapy. There is ample opportunity for novel therapeutics in cancer. siRNA may provide new therapeutics through the ability to knockdown targets previously “undruggable” by monoclonal antibodies or small molecule drugs.

### **Key Personnel**

Christopher Anzalone, Ph.D., is the CEO of Calando. Thomas Schlupe, Sc.D., is the Chief Scientific Officer (CSO) of Calando.

Calando’s Board of Directors consists of R. Bruce Stewart, Executive Chairman of Arrowhead, Christopher Anzalone, CEO and director of Arrowhead, Nanotope and Leonardo, Dr. Bruce Given, COO of Arrowhead, and Edward W. Frykman, a member of the Arrowhead Board. Dr. Mostafa Analoui is an independent Board member.

As of September 30, 2011, Arrowhead owned approximately 79% of Calando’s outstanding common stock and 74% on a fully diluted basis.

### ***Ablaris Therapeutics, Inc.***

#### **Obesity Market Overview**

We founded Ablaris, a nanomedicine company, to commercialize a new class of fat-targeting drugs for the obesity and diabetes markets. Obesity is a prevalent metabolic disorder associated with an increased risk of type 2 diabetes, hypertension, cardiovascular diseases, stroke and cancers. Additionally, obese individuals suffer from associated psychological effects such as anxiety and

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depression. Non-pharmacological management of obesity, including diet changes and exercise, is first line treatment; gastrointestinal bypass or gastric banding procedures offer alternative options for treatment of severe obesity after less drastic options have failed. These surgical procedures have significant associated risks, including death. Additionally, with the exception of the gastric bypass operation, diet and exercise are often insufficient to normalize body weight and prevent the diseases associated with obesity, due to the difficulty experienced by most adhering to a strict dietary and exercise regimen. Thus, safe and effective drugs are needed for the treatment of obesity and related disorders.

Seventy two million Americans are classified as obese, over one-third of the U.S. adult population, according to the Centers for Disease Control (CDC). US healthcare costs for obesity were estimated to be \$147 billion in 2009 and are accelerating rapidly (Finkelstein, et al. *Health Affairs* 2009, 28(5), w822). An industry forecaster, Global Data, estimates that the \$1.1 billion worldwide market (2009) for anti-obesity drugs could double to \$2 billion by 2017, with projected annual growth rate of 7 percent. “The increasing patient population and high unmet need in terms of safety and efficacy will be the primary drivers of this growth.” (GlobalData, “Anti-Obesity Therapeutics - Pipeline Assessment and Market Forecasts to 2017”).

Despite the size of the potential market, obesity remains a large and growing unmet medical need. It has been over a decade since the FDA has approved a new weight loss drug. In 2010, the FDA declined to approve three new drugs for weight loss indications, Orexigen Therapeutics Inc.’s Contrave™, Arena Pharmaceuticals Inc.’s lorcaserin and Vivus Inc.’s Qnexa™, due to various safety concerns. Theratechnologies Inc.’s drug tesamorelin was approved in 2010 to reduce visceral adipose tissue, but only for a narrow indication in HIV-infected patients with lipodystrophy, not as a broad weight-loss drug. Arrowhead has been keenly interested in the obesity market, but has been careful to identify a platform and target indications where we believe we can deliver a balance of patient benefit and a safety profile that would be acceptable to the FDA and other regulatory authorities.

### **Our Approach to the Treatment of Obesity**

Ablaris’ lead compound, Adipotide™, targets a receptor expressed by the endothelial cells lining the blood vessels of white adipose (fat) tissue. This targeting ligand was discovered using *in vivo* phage display, a technique in which a randomly generated library of peptides was injected into an animal, and sequences that homed to white fat were isolated and amplified. The targeting ligand was then fused to an antimicrobial agent designed to cause cell death (apoptosis). This apoptosis-inducing peptidomimetic has not been shown to have an effect on mammalian cells in systemic circulation, but it induces cell death once internalized by selectively targeted cells by disrupting their mitochondrial membranes. Because fat requires a continuous turnover of new capillaries to supply oxygen and maintain its storage capacity, targeted destruction of these blood vessels leads to the gradual resorption of fat and correspondingly dramatic weight loss in treated animals. This technology was developed by Drs. Wadih Arap and Renata Pasqualini at the MD Anderson Cancer Center in Houston, Texas. In December 2010, we obtained an exclusive world-wide license for its use in weight-loss and obesity-related metabolic conditions, including diabetes.

### **Preclinical Studies**

Preclinical studies of the drug in rodent models were first reported in the highly respected, peer-reviewed journal *Nature Medicine* in 2004. These studies showed obese mice lost over 30% of their body weight after only one month of daily, subcutaneous injection of the Adipotide™ treatment. These results were confirmed by an independent laboratory and reported in the journal *Diabetes* in 2010. However, a major hurdle in the development of weight-loss drugs is the significant differences in the physiological and metabolic regulation of food intake and energy expenditure between rodents and primates. To address this challenge, Drs. Arap and Pasqualini, in collaboration with Ablaris, carried out extensive studies of adipotide therapy in three species of non-human primates. These studies were reported in the journal *Science Translational Medicine* in November 2011. In spontaneously obese rhesus monkeys, a 28-day course of Adipotide™ treatment caused a 7-15% total body weight loss with a corresponding 27% average reduction in abdominal fat. Importantly, weight loss was shown to be primarily in the form of fat loss and not fluid loss or muscle wasting. Insulin resistance, a key risk factor for diabetes, rapidly improved in the obese monkeys during Adipotide™ treatment. Lean monkeys treated with Adipotide™ did not lose weight, indicating that the mechanism of action may be selective for obese animals. The drug was well-tolerated in monkeys, with minimal side-effects at the therapeutic dose. Recently, researchers at MD Anderson have validated the existence and function of the receptor targeted by Adipotide™ in humans—a result which was published in the *Proceedings of the National Academy of Sciences* in October 2011, which we believe bodes well for clinical translation of this therapeutic strategy.

### **Clinical Development**

Most weight loss drugs in clinical development target the central nervous system (CNS), acting on the brain to increase metabolic energy expenditure and/or decrease food intake through regulatory pathways for appetite and satiety. Because these pathways can have other wide-ranging functions, many weight-loss drugs have failed due to psychological or cardiovascular

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side-effects. By targeting the fat vasculature directly, rather than indirectly through the CNS, we believe that Adipotide™ may avoid these negative side effects. Along with our collaborators at MD Anderson, we have focused initially on narrower indications where a rapid reduction of abdominal fat may elicit a near-term benefit in reduction of morbidity and mortality. We believe that this approach may offer a more rapid and cost-effective path to market, if the drug is shown in human clinical trials to be safe and effective.

MD Anderson has filed an Investigational New Drug (IND) application for a first-in-man, Phase I evaluation of Adipotide™ (also known as Prohibitin TP-01) in obese men with castrate-resistant prostate cancer. White adipose tissue is known to produce hormones that promote prostate cancer growth. The goal of the Phase I clinical trial is to determine the maximum tolerated dose (MTD) and assess the safety of Adipotide™ in humans. Follow-on studies will determine if decreasing fat can slow the growth of prostate cancer. Responding to a response from the FDA, MD Anderson has submitted additional information, and pending a favorable response the study will begin enrollment soon thereafter. The study is being sponsored and funded by MD Anderson, and Ablaris is not responsible for any of the associated direct costs.

### **Pipeline**

In addition to our lead compound, Adipotide™ the company is actively pursuing development of novel follow-on compounds in the adipotide-class. Given that the dosing regimen used in preclinical studies (daily subcutaneous injection for 28 days) may not be optimal in the clinical setting, our efforts are focused on altering the pharmacokinetics of the drug to enable other formulations and treatment regimes, such as a sustained release formulation for once-weekly injection or long-term sub-dermal implant. Moreover, because long-term use needs to be anticipated for regulatory approval of a weight-loss drug, our pipeline development is also focused on broadening the therapeutic index of Adipotide™, through both enhanced ligand-receptor interactions (increased potency) and altered renal clearance (decreased toxicity). These efforts have already identified several new lead candidates, which have shown similar efficacy to the original compound with reduced renal toxicity. These compounds are covered by pending patents applications and intellectual property developed by Ablaris independently, as well as, with our collaborators at MD Anderson. Efforts will continue to optimize these pipeline candidates in 2012. Ablaris anticipates filing an IND application on a selected lead candidate in 2013. Additional candidates focused on diabetes-related indications are in also in development.

### **Clinical, Manufacturing and R&D Operations**

Good Manufacturing Practices (GMP) production of our lead compound, Adipotide™, has been carried out on a multi-gram scale by a leading manufacturer of pharmaceutical-grade peptides. The production and packaging of a sufficient quantity of material for the planned Phase I clinical study is complete. The site for the study and Institutional Review Board (IRB) approval of the clinical protocol are in place. Process development, stability studies and GLP bioanalytical assay development work are completed and ready for scale-up which would allow transfer to a commercial manufacturer if Adipotide progresses into late stage trials. Given the similarity in design of Ablaris' pipeline candidates, additional manufacturing process development needs for these compounds are not anticipated to be significant.

To date, our R&D efforts have been carried out by academic laboratories through sponsored research agreements and by contract research organizations (CROs), with management oversight by Arrowhead personnel. This has enabled us to maintain a lean operation with no dedicated laboratory personnel. The initial clinical trial of Adipotide™ in prostate cancer is being sponsored and will be run entirely by MD Anderson Cancer Center, with no direct management responsibilities for Ablaris. As we move toward clinical testing of Ablaris' pipeline compounds in 2012 and 2013, the company may develop a management plan to enable in house sponsorship and oversight of these studies.

### **Key Personnel**

Christopher Anzalone, Ph.D., is the CEO of Ablaris. James Hulvat, Ph.D. is Director, Research and Development. Ablaris' Board of Directors consists of Christopher Anzalone, CEO of Arrowhead, R. Bruce Stewart, Executive Chairman of Arrowhead, Edward Frykman and Charles McKenney. Each director of Ablaris is also a director of Arrowhead.

As of September 30, 2011, Arrowhead owned approximately 64% of the common stock of Ablaris on a primary and fully diluted basis.

### **Nanotope, Inc.**

#### **Overview**

Nanotope is a regenerative medicine company developing a suite of nanotechnology-based products customized to regenerate specific tissues: including neuronal, bone and cartilaginous tissues. Arrowhead has an approximately 23% ownership interest in Nanotope.

Nanotope's product candidates are based on a platform technology licensed from Northwestern University. The company continued its successful efforts in 2011 to expand intellectual property protection on compounds of interest, with 20 issued patents and more than 60 pending patent applications in the U.S., E.U., Japan, and select other countries in key markets worldwide.

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Nanotope operates a small research facility at the Illinois Science & Technology Park in Skokie, Illinois, employing three full-time scientists on its R&D efforts. In addition, Nanotope researchers collaborate with multiple academic laboratories and commercial research organizations to advance the company's lead and pipeline compounds.

Nanotope's first lead clinical candidate is directed to regenerating neurons and inhibiting scar tissue formation following traumatic spinal cord injury (SCI). This product is based on a peptide-amphiphile nanofiber scaffold developed by Dr. Samuel Stupp (Materials Science) and Dr. Jack Kessler (Neurology) at Northwestern University. This scaffold is designed to elicit a biological response from neural progenitor cells, suppressing scar-forming astrogliosis and promoting neurite extension and neuron regeneration. Efficacy has been demonstrated in vitro and in vivo in published studies using rodent models of spinal cord injury. Nanotope continues its manufacturing process and formulation development efforts, and selection of optimal candidates from a series of new lead compounds screened in 2011. This screening culminated in additional rodent studies, to be completed in 2012. If these studies are successful, Nanotope anticipates selecting a single SCI candidate to take forward into GLP toxicology studies to support an IND application in late 2012 or 2013.

Nanotope's second lead clinical candidate is directed to restoring cartilage in joints damaged due to injury or osteoarthritis. The company's therapeutic platform consists of a synthetic, fully degradable, customizable gel scaffold that does not involve the use of embryonic stem cells. Instead, the product works with endogenous cells in the patient's bone marrow to spur hyaline-like regeneration. Nanotope and its partners at Northwestern University, Dr. Ramille Shah (Orthopedics) and Dr. Samuel Stupp (Materials Science) have demonstrated the efficacy of the cartilage repair scaffold in a rabbit model. Nanotope's cartilage regeneration technology is currently under a license to Smith & Nephew, a global medical technology company with leadership positions in Orthopedics; including Reconstruction, Trauma and Clinical therapies; Endoscopy; including Sports Medicine; and Advanced Wound Management. This represents Nanotope's first commercial transaction and demonstrates the company's commitment to bring technological innovations in regenerative medicine to the clinical market. Further small animal in vivo studies are ongoing at Nanotope and Northwestern to develop a robust manufacturing process and optimize formulation and stability of these peptide-amphiphile compounds in support of further clinical development. This work is anticipated to continue into 2012.

In addition to these lead therapeutic candidates, Nanotope maintains an active pipeline of peptide-based compounds of interest for other areas. In 2011, Dr. Stupp's laboratory at Northwestern published 11 peer-reviewed papers reporting discovery efforts related to peptide amphiphiles. Two new candidates were in-licensed by Nanotope and will undergo further development efforts in 2012: a VEGF-mimetic peptide amphiphile for ischemic tissue revascularization, and a group of compounds for bone regeneration, where efforts have focused in particular on spinal fusion indications.

### **Related Party Interests**

Nanotope was co-founded by Arrowhead's Chief Executive Officer, Dr. Christopher Anzalone, who owns approximately 14.2% of Nanotope's outstanding voting securities. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Nanotope. Dr. Anzalone has the right to appoint a representative to the Board of Directors of Nanotope. Dr. Anzalone currently serves on the Nanotope Board in a seat reserved for Nanotope's CEO and another individual holds the seat designated by Dr. Anzalone. Dr. Anzalone has served as President and Chief Executive Officer of Nanotope since its formation and continues to serve in these capacities. Dr. Anzalone has not received any compensation for his work on behalf of Nanotope since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Nanotope before he joined the Company. Arrowhead allocates a small portion of Dr. Anzalone's salary, as well as a small portion of other administrative and finance personnel costs, to Nanotope.

### ***Leonardo Biosystems, Inc.***

#### **Overview**

Leonardo is a drug delivery company that employs a novel multi-stage drug delivery mechanism aimed at dramatically increasing targeting efficiency of pharmaceuticals. Arrowhead has an approximately 5% ownership interest in Leonardo. Leonardo's silicon microparticulate technology involves transporting a therapeutic agent past multiple biological barriers using multiple carriers, each optimized for a specific barrier. Leonardo's proprietary primary vehicles are designed to preferentially accumulate at tumor vasculature. Secondary carriers are then released from the primary carriers that are designed to accumulate around tumor cells and release their therapeutic payloads. Animal testing suggests that Leonardo's platform enables significantly increased targeting and also provides sustained release. During 2011, Leonardo received the second tranche of \$1.25 million of an overall \$2.5 million award from the State of Texas Emerging Technology Fund. Leonardo is currently focused on scaling up a commercializable manufacturing process and broadening the demonstrated areas where the technology delivers value. Arrowhead is interested in increasing its stake in Leonardo if the opportunity arises, Arrowhead has the capital resources, and Leonardo's technology development continues to move forward.

## **Related Party Interests**

Like Nanotope, Leonardo was co-founded by the Company's Chief Executive Officer, Dr. Christopher Anzalone. Dr. Anzalone owns approximately 16% of the outstanding stock of Leonardo. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Leonardo. Dr. Anzalone has the right to appoint a representative to the Board of Directors of Leonardo and Dr. Anzalone currently serves on the Leonardo Board. Dr. Anzalone has served as President and Chief Executive Officer of Leonardo since its formation until February 2010 when a new CEO, Dr. Bruce Given, was hired. Dr. Anzalone has not received any compensation for his work on behalf of Leonardo since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Leonardo before he joined the Company.

Dr. Mauro Ferrari, who joined Arrowhead's Board of Directors in August 2010, is also a co-founder of Leonardo and personally or in family trust owns approximately 23% of the outstanding stock of Leonardo and serves on the Leonardo Board of Directors. Dr. Bruce Given joined Arrowhead as Chief Operating Officer in October 2011. He continues to serve as Leonardo's CEO. While he no longer receives direct compensation from Leonardo, Arrowhead is reimbursed as part of a services agreement, which includes other general and administrative services. Dr. Given was granted 200,000 shares of Leonardo common stock upon joining as CEO in 2010. Arrowhead allocates a small portion of Dr. Anzalone's salary, as well as a small portion of other administrative and finance personnel costs, to Leonardo.

## **Competition**

Arrowhead is focused in the rapidly changing business of developing treatments for human disease through the regulation of gene expression and delivery of proprietary novel cancer therapies. Competition in these fields is intense as other companies are developing therapies similar to our nanoparticle drug delivery systems, and targeting patient populations that are similar to the patient populations that we are targeting. A number of companies are pursuing research and development programs relating to the emerging area of cancer therapies using nanoparticle conjugates and RNA interference. A number of these companies have filed patent applications in these areas. It is difficult to predict whether any of these companies will be successful in obtaining patent protection, whether the patent protection sought will address important aspects of the technology and to what extent these companies will be successful in their RNA interference efforts. New competitors may arise and we may not be aware of all competitors in this space. A number of our competitors are more established and have greater resources than we do. Furthermore, even if we are successful in developing commercial products, it is possible that competitors will achieve greater market acceptance.

Systemic delivery of siRNA and other oligonucleotide therapeutics has proven critical for the success of all nucleic acid therapeutics. Naturally, multiple firms have recognized the problem of systemic siRNA delivery as a significant opportunity and other firms are developing products in this space. Some of the most significant companies developing siRNA delivery products include Alnylam Pharmaceuticals, Inc., Marina Biotech, Inc., Tacere Therapeutics, Inc., Benitec Limited, OPKO Health, Inc., Silence Therapeutics plc, Quark Pharmaceuticals, Inc., Rosetta Genomics Ltd., Lorus Therapeutics, Inc., Tekmira Pharmaceuticals Corporation, Regulus Therapeutics Inc., and Santaris Pharma A/S, as well as a number of large pharmaceutical companies such as Merck & Co. Inc. and Novartis AG. Additionally, many academic groups are developing and may seek to commercialize siRNA delivery technologies.

## **Research and Development Expenses**

Research and development expenses consist of costs incurred in identifying, developing and testing our product programs. These expenses consist primarily of salaries and related expenses for personnel, license fees, consulting fees, contract research and manufacturing, and the costs of laboratory equipment and facilities. Research and development expense for 2011 was \$3.2 million, compared with \$0.5 million in 2010.

## **Government Regulation**

Governmental authorities in the U.S. and other countries extensively regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing, among other things, of drugs and biologic products. All of our foreseeable product candidates are expected to be regulated as drug products.

In the U.S., the FDA regulates drug products under the Federal Food, Drug and Cosmetic Act (the "FDCA"), and other laws within the Public Health Service Act. Failure to comply with applicable U.S. requirements, both before and after approval, may subject us to administrative and judicial sanctions, such as a delay in approving or refusal by the FDA to approve pending applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecutions. Before our drug products are marketed they must be approved by the FDA. The steps required before a novel drug product is approved by the FDA include: (1) pre-clinical laboratory, animal, and formulation tests; (2) submission to the

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FDA of an Investigational New Drug Application (“IND”) for human clinical testing, which must become effective before human clinical trials may begin; (3) adequate and well-controlled clinical trials to establish the safety and effectiveness of the product for each indication for which approval is sought; (4) submission to the FDA of a New Drug Application (“NDA”); (5) satisfactory completion of a FDA inspection of the manufacturing facility or facilities at which the drug product is produced to assess compliance with cGMP; and FDA review and finally (6) approval of an NDA.

Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions, such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. There can be no assurance that submission of an IND will result in FDA authorization to commence clinical trials. Once an IND is in effect, each clinical trial to be conducted under the IND must be submitted to the FDA, which may or may not allow the trial to proceed.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified physician-investigators and healthcare personnel. Clinical trials are typically conducted in three defined phases, but the phases may overlap or be combined. Phase 1 usually involves the initial administration of the investigational drug or biologic product to healthy individuals to evaluate its safety, dosage tolerance and pharmacodynamics. Phase 2 usually involves trials in a limited patient population, with the disease or condition for which the test material is being developed, to evaluate dosage tolerance and appropriate dosage; identify possible adverse side effects and safety risks; and preliminarily evaluate the effectiveness of the drug or biologic for specific indications. Phase 3 trials usually further evaluate effectiveness and test further for safety by administering the drug or biologic candidate in its final form in an expanded patient population. Our product development partners, the FDA, or we may suspend clinical trials at any time on various grounds, including any situation where we believe that patients are being exposed to an unacceptable health risk or are obtaining no medical benefit from the test material.

Assuming successful completion of the required clinical testing, the results of the pre-clinical trials and the clinical trials, together with other detailed information, including information on the manufacture and composition of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. Before approving an application, the FDA will usually inspect the facilities where the product is manufactured, and will not approve the product unless cGMP compliance is satisfactory. If the FDA determines the NDA is not acceptable, the FDA may outline the deficiencies in the NDA and often will request additional information. If the FDA approves the NDA, certain changes to the approved product, such as adding new indications, manufacturing changes or additional labeling claims are subject to further FDA review and approval. The testing and approval process requires substantial time, effort and financial resources, and we cannot be sure that any approval will be granted on a timely basis, if at all. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for this type of disease or condition will be recovered from sales in the U.S. for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other application to market the same drug for the same indication, except in very limited circumstances, for seven years.

In addition, regardless of the type of approval, we and our partners are required to comply with a number of FDA requirements both before and after approval. For example, we are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain requirements concerning advertising and promotion for our products. In addition, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in all areas of regulatory compliance, including production and quality control to comply with cGMP. In addition, discovery of problems, such as safety problems, may result in changes in labeling or restrictions on a product manufacturer or NDA holder, including removal of the product from the market.

### **ITEM 1A. RISK FACTORS**

*You should carefully consider the risks discussed below and all of the other information contained in this report in evaluating us and an investment in our securities. If any of the following risks and uncertainties should occur, they could have a material adverse effect on our business, financial condition or results of operations. In that case, the trading price of our Common Stock could decline. Additionally, we note that we are a development stage company and we have accrued net losses annually since inception. We urge you to consider our likelihood of success and prospects in light of the risks, expenses and difficulties frequently encountered by entities at similar stages of development.*

## **Risks Related to Our Financial Condition**

***We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability.***

We have incurred net losses since our inception, including net losses of \$3.5 million for the year ended September 30, 2011 and a cumulative net loss since inception of approximately \$131.5 million. We expect that our operating losses will continue as we fund our drug development and discovery efforts. To achieve profitability, we must, either directly or through licensing and/or partnering relationships, successfully develop and obtain regulatory approval for a drug candidate and effectively manufacture, market and sell any drugs we successfully develop. Even if we successfully commercialize drug candidates that receive regulatory approval, we may not be able to realize revenues at a level that would allow us to achieve or sustain profitability. Accordingly, we may never generate significant revenue and, even if we do generate significant revenue, we may never achieve profitability.

***We have limited cash resources.***

Our plan of operations is to provide substantial amounts of development funding and financial support to our subsidiaries over an extended period of time. With the recent acquisition of Roche's RNAi business, including a research facility in Madison, Wisconsin and new employees, our use of cash is expected to substantially increase compared to recent historical periods. We will need to obtain additional capital to further our development efforts, and we intend to seek additional capital by out-licensing technology, securing funded partnerships, conducting one or more private or public offerings of equity securities of the Company or our subsidiaries, or through a combination of one or more of such financing alternatives. However, there can be no assurance that we will be successful in any of these endeavors or, if we are successful, that such transactions will be accomplished on favorable terms. If we are unable to obtain additional capital, we will need to curtail our operations in order to preserve working capital, which could materially harm our business and our ability to achieve cash flow in the future, including delaying or reducing implementation of certain aspects of our plan of operations. Even if we are successful in obtaining additional capital, because we and each subsidiary are separate entities, it could be difficult or impossible to allocate funds in a way that meets the needs of all entities. Although we anticipate that the Company will be able to satisfy the cash requirements of its operations through at least the next twelve months with current cash resources, we may be unable to obtain long-term funding and our near-term expenses could be greater than projected.

***The current financial market conditions may exacerbate certain risks affecting our business.***

We do not yet generate substantial revenue, and our operations and research and development activities have been primarily funded to date through the sale of Company securities and securities of our Subsidiaries. The global financial markets are volatile and those market conditions, as well as possible concerns over the value of the U.S. dollar denominated investments, may impair our ability to raise the capital we require. If we are unable to secure additional cash resources from the sale of securities or other sources, it could become necessary to slow or suspend development efforts. In addition, we may have to reduce expenses, which could impair our ability to manage our business. Even if investment capital is available to us, the terms may be onerous. If outside capital is invested directly into a subsidiary and Arrowhead does not have the funds to make a pro rata investment, our ownership interest could be diluted. The sale of additional Arrowhead stock could result in significant dilution to stockholders.

The potential monetization of our Subsidiaries through an ownership position might not occur in an orderly manner. Exit opportunities could include an initial public offering ("IPO") for the subsidiary or acquisition of the subsidiary by another company. During the recent economic recession, companies have been adopting conservative acquisition strategies and, even if there is interest, we may not be able to sell our Subsidiaries on terms that are attractive to us. These factors could reduce the realizable return on our investment if we are able to sell a subsidiary. Additionally, the market for IPOs continues to be unpredictable, which limits public exit opportunities for our Subsidiaries.

***Because we have not generated significant revenues to cover our operating expenses, we are dependent on raising additional capital from investors or lenders.***

To date, we have only generated a small amount of revenue. Given our strategy of financing new and unproven technology research, there can be no assurance we will ever generate significant revenue. Our revenue-producing opportunities depend on liquidity events within our Subsidiaries, such as a sale of the Subsidiary, licensing transaction or initial public offering. We cannot be certain that we will be able to create a liquidity event for any of our Subsidiaries and, even if we are able to, we cannot be certain of the timing or the potential proceeds to Arrowhead as a stockholder. Accordingly, our revenue prospects are uncertain and we must plan to finance our operations through the sales of equity securities or debt financing. If we are unable to continue raising operating capital from these sources, we may be forced to curtail or cease our operations.

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### ***We will need to achieve commercial acceptance of our applications to generate revenues and achieve profitability.***

Even if our research and development efforts yield technologically feasible applications, we may not successfully develop commercial products which would take years to study in human clinical trials prior to regulatory approval, and, even if successfully developed, we may not do so on a timely basis. During this development period, superior competitive technologies may be introduced which could diminish or extinguish the potential commercial uses for our drug candidates. Additionally, the degree to which patients and consumers will adopt any product we develop is uncertain. We cannot predict whether significant commercial market acceptance for our products, if approved, will ever develop, and we cannot reliably estimate the projected size of any such potential market. Our revenue growth and achievement of profitability will depend substantially on our ability to introduce new technological applications to manufacturers for products accepted by customers. If we are unable to cost-effectively achieve acceptance of our technology among the medical establishment and patients, or if the associated products do not achieve wide market acceptance, our business will be materially and adversely affected.

### ***We have debt on our consolidated balance sheet through our subsidiary, Calando, which could have negative consequences if we were unable to repay the principal or interest due.***

Calando has a \$500,000 unsecured convertible promissory note outstanding. The note bears 10% interest accrued annually, and matures in November 2013. The note is payable at two times face value at maturity and upon the occurrence of certain events, including, the license of Calando's siRNA delivery system. If Calando is unable to meet its obligations to the bearer of the note, Arrowhead may not be in a position to lend Calando sufficient cash to pay such demand note. Unless other sources of financing become available, this could result in Calando's insolvency.

### ***Our Subsidiaries are party into technology license agreements with third parties that require us to satisfy obligations to keep them effective and, if these agreements are terminated, our technology and our business would be seriously and adversely affected.***

Through our Subsidiaries, we are party into exclusive, long-term license agreements with California Institute of Technology, Alnylam Pharmaceuticals, Inc. and other entities to incorporate their proprietary technologies into our proposed products. These license agreements require us to pay royalties and satisfy other conditions, including conditions in some cases related to the commercialization of the licensed technology. We may not be able to successfully incorporate these technologies into marketable products or, if we do, whether sales will be sufficient to recover the amounts that we are obligated to pay to the licensors. Failure by us to satisfy our obligations under these agreements may result in the modification of the terms of the licenses, such as by rendering them non-exclusive, or may give our licensors the right to terminate their respective agreement with us, which would limit our ability to implement our current business plan and harm our business and financial condition.

## **Risks Related to Our Company**

### ***Drug development is time consuming, expensive and risky.***

We are focused on technology related to new and improved pharmaceutical candidates. Product candidates that appear promising in the early phases of development, such as in early animal and human clinical trials, often fail to reach the market for a number of reasons, such as:

- Clinical trial results may be unacceptable, even though preclinical trial results were promising;
- Inefficacy and/or harmful side effects in humans or animals;
- The necessary regulatory bodies, such as the U.S. Food and Drug Administration, may not approve our potential product for the intended use; and
- Manufacturing and distribution may be uneconomical.

For example, the positive pre-clinical results studying Adipotide in animals may not be replicated in human clinical studies or that this drug candidate may be found to be unsafe in humans. Additionally, clinical trial results are frequently susceptible to varying interpretations by scientists, medical personnel, regulatory personnel, statisticians and others, which often delays, limits, or prevents further clinical development or regulatory approvals of potential products. Clinical trials can take years to complete, including the process of study design, clinical site selection and the enrollment of patients. As a result, we can experience significant delays in completing clinical studies, which can increase the cost of developing a drug candidate. If our drug candidates are not successful in human clinical trials, we may be forced to curtail or abandon certain development programs and if we experience significant delays in commencing or completing our clinical studies, we could suffer from significant cost overruns, which could negatively affect our capital resources and our ability to complete these studies.

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***We may be unable to attract revenue-generating collaborations with other pharmaceutical and biotech companies to advance our drug candidates.***

Our business strategy includes collaborations with other pharmaceutical and biotech companies to provide funding and therapeutic siRNA candidates to which we can apply our various siRNA delivery technologies. We may not be able to attract such partners, and even if we are able to enter into such partnerships, the terms may be less favorable than anticipated. Further, entering into partnership agreements may limit our commercialization options and/or require us to share revenues and profits with our partners.

***We may lose a considerable amount of control over our intellectual property and may not receive anticipated revenues in strategic transactions involving our Subsidiaries, particularly where the consideration is contingent on the achievement of development or sales milestones.***

Our business model has been to develop new technologies and to exploit the intellectual property created through the research and development process to develop commercially successful products. Calando has licensed a portion of its technology to Cerulean Pharma, Inc. and we intend to pursue licensing arrangements with other companies. A significant portion of the potential value from these licenses is tied to the achievement of the development and sales milestones, which we cannot control. Similarly, the majority of the consideration, up to \$140 million, potentially payable by Wisepower in connection with our sale of Unidym is tied to the achievement of commercialization milestones, over which we cannot exercise control. Although Wisepower and Cerulean are required to use certain minimum efforts to achieve the post-closing milestones, we cannot control whether they actually achieve these milestones. If the acquirers fail to achieve performance milestones, we may not receive a significant portion of the total value of any sale, license or other strategic transaction.

***There are substantial risks inherent in attempting to commercialize new technological applications, and, as a result, we may not be able to successfully develop nanotechnology for commercial use.***

Much of the Company research and development efforts involve nanotechnology and RNAi, which are largely unproven technologies. Our scientists and engineers are working on developing technology in various stages. However, such technology's commercial feasibility and acceptance are unknown. Scientific research and development requires significant amounts of capital and takes a long time to reach commercial viability, if at all. To date, our research and development projects have not produced commercially viable applications, and may never do so. During the research and development process, we may experience technological barriers that we may be unable to overcome. Because of these uncertainties, it is possible that none of our potential applications will be successfully developed. If we are unable to successfully develop nanotechnology applications for commercial use, we will be unable to generate revenue or build a sustainable or profitable business.

***We will need to establish additional relationships with strategic and development partners to fully develop and market our products.***

We do not possess all of the resources necessary to develop and commercialize products that may result from our technologies on a mass scale. Unless we expand our product development capacity and enhance our internal marketing capability, we will need to make appropriate arrangements with strategic partners to develop and commercialize current and future products. If we do not find appropriate partners, or if our existing arrangements or future agreements are not successful, our ability to develop and commercialize products could be adversely affected. Even if we are able to find collaborative partners, the overall success of the development and commercialization of product candidates in those programs will depend largely on the efforts of other parties and is beyond our control. In addition, in the event we pursue our commercialization strategy through collaboration, there are a variety of technical, business and legal risks, including:

- A development partner would likely gain access to our proprietary information, potentially enabling the partner to develop products without us or design around our intellectual property;
- We may not be able to control the amount and timing of resources that our collaborators may be willing or able to devote to the development or commercialization of our product candidates or to their marketing and distribution; and
- Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts our management's resources.

The occurrence of any of the above events or other related events not foreseen by us could impair our ability to generate revenues and harm our business and financial condition.

***We may not be able to effectively secure first-tier technologies when competing against other investors.***

Our success may require that we acquire new or complimentary technologies. However, we compete with a substantial number of other companies that may also compete for technologies we desire. In addition, many venture capital firms and other institutional investors, as well as other pharmaceutical and biotech companies, invest in companies seeking to commercialize various types of emerging technologies. Many of these companies have greater financial, scientific and commercial resources than us. Therefore, we may not be able to secure the technologies we desire. Furthermore, should any commercial undertaking by us prove to be successful, there can be no assurance competitors with greater financial resources will not offer competitive products and/or technologies.

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### ***We rely on outside sources for various components and processes for our products.***

We rely on third parties for various components and processes for our products. While we try to have at least two sources for each component and process, we may not be able to achieve multiple sourcing because there may be no acceptable second source, other companies may choose not to work with us, or the component or process sought may be so new that a second source does not exist, or does not exist on acceptable terms. In addition, due to the continued tightening of global credit markets, there may be a disruption or delay in the performance of our third-party contractors, suppliers or collaborators. If such third parties are unable to satisfy their commitments to us, our business would be adversely affected. Therefore, it is possible that our business plans will have to be slowed down or stopped completely at times due to our inability to obtain required raw materials, components and outsourced processes at an acceptable cost, if at all, or to get a timely response from vendors.

### ***We must overcome the many obstacles associated with integrating and operating varying business ventures to succeed.***

Our model to integrate and oversee the strategic direction of various Subsidiaries and research and development projects presents many risks, including:

- The difficulty of integrating operations and personnel; and
- The diversion of our management's attention as a result of evaluating, negotiating and integrating acquisitions or new business ventures.

If we are unable to timely and efficiently design and integrate administrative and operational support for our Subsidiaries, we may be unable to manage projects effectively, which could adversely affect our ability to meet our business objectives and the value of an investment in the Company could decline.

In addition, consummating acquisitions and taking advantage of strategic relationships could adversely impact our cash position, and dilute stockholder interests, for many reasons, including:

- Changes to our income to reflect the amortization of acquired intangible assets, including goodwill;
- Interest costs and debt service requirements for any debt incurred to fund our growth strategy; and
- Any issuance of securities to fund our operations or growth, which dilutes or lessens the rights of current stockholders.

### ***Our success depends on the attraction and retention of senior management and scientists with relevant expertise.***

Our future success will depend to a significant extent on the continued services of our key employees, including Dr. Anzalone, our President and Chief Executive Officer, Kenneth Myszkowski, our Chief Financial Officer and Bruce Given, our Chief Operating Officer. We do not maintain key man life insurance for any of our executives. Our ability to execute our strategy also will depend on our ability to continue to attract and retain qualified scientists and additional managerial personnel. If we are unable to find, hire and retain qualified individuals, we could have difficulty implementing our business plan in a timely manner, or at all. We may need to terminate additional employees, including senior management and technical employees, or such employees may seek other employment which may result in the loss of valuable know-how and development efforts could be negatively affected.

### ***Members of our senior management team and Board may have a conflict of interest in also serving as officers and/or directors of our Subsidiaries.***

While we expect that our officers and directors who also serve as officers and/or directors of our Subsidiaries will comply with their fiduciary duties owed to our stockholders, they may have conflicting fiduciary obligations to our stockholders and the minority stockholders of our Subsidiaries. Specifically, Dr. Anzalone, our President and CEO, is the founder, CEO and a board member of Nanotope, a regenerative medicine company in which the Company owns a 23% interest. Further, Dr. Anzalone as well as Dr. Mauro Ferrari, an Arrowhead board member, are board members of Leonardo, a drug delivery company in which Arrowhead owns a 5% interest. Dr. Anzalone owns a noncontrolling interest in the stock of Nanotope. Drs. Anzalone and Ferrari own a noncontrolling interest in Leonardo. Douglass Given, a member of our board of directors, is the brother of Bruce Given. To the extent that any of our directors choose to recuse themselves from particular Board actions to avoid a conflict of interest, the other members of our Board of Directors will have a greater influence on such decisions.

### ***We face uncertainty related to healthcare reform, pricing and reimbursement, which could reduce our revenue.***

In the United States, President Obama signed in March 2010 the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, "PPACA"), which is expected to substantially change the way health care is financed by both governmental and private payers. PPACA provides for changes to extend medical benefits to those

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who currently lack insurance coverage, encourages improvements in the quality of health care items and services, and significantly impacts the U.S. pharmaceutical industry in a number of ways, further listed below. By extending coverage to a larger population, PPACA may substantially change the structure of the health insurance system and the methodology for reimbursing medical services, drugs and devices. These structural changes, as well as other changes that may be made as part of deficit and debt reduction efforts in Congress, could entail modifications to the existing system of private payers and government programs, such as Medicare, Medicaid and State Children's Health Insurance Program, as well as the creation of a government-sponsored healthcare insurance source, or some combination of both. Such restructuring of the coverage of medical care in the United States could impact the extent of reimbursement for prescribed drugs, including our product candidates, biopharmaceuticals, and medical devices. Some of the specific PPACA provisions, among other things:

- Establish annual, non-deductible fees on any entity that manufactures or imports certain branded prescription drugs and biologics, beginning in 2011;
- Increase minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program;
- Extend manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- Establish a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research;
- Require manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D, beginning in 2011; and
- Increase the number of entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective January 2010.

If future reimbursement for approved product candidates, if any, is substantially less than we project, or rebate obligations associated with them are substantially increased, our business could be materially and adversely impacted.

Sales of any approved drug candidate will depend in part on the availability of coverage and reimbursement from third-party payers such as government insurance programs, including Medicare and Medicaid, private health insurers, health maintenance organizations and other health care related organizations. Accordingly, coverage and reimbursement may be uncertain. Adoption of any drug candidate by the medical community may be limited if third-party payers will not offer coverage. Cost control initiatives may decrease coverage and payment levels for any new drug and, in turn, the price that we will be able to charge. We are unable to predict all changes to the coverage or reimbursement methodologies that will be applied by private or government payers. Any denial of private or government payer coverage or inadequate reimbursement could harm our business and reduce our revenue.

In addition, both the federal and state governments in the United States and foreign governments continue to propose and pass new legislation affecting coverage and reimbursement policies, which are designed to contain or reduce the cost of health care, as well as hold public hearings on these matters, which has resulted in certain private companies dropping the prices of their drugs. Further federal and state proposals and healthcare reforms are likely, which could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunity. There may be future changes that result in reductions in current coverage and reimbursement levels for our product candidates, if approved and commercialized, and we cannot predict the scope of any future changes or the impact that those changes would have on our operations.

***There may be a difference in the investment valuations that we used when making initial and subsequent investments in our Subsidiaries and minority investments and actual market values.***

Our investments in our Subsidiaries and noncontrolling interests were the result of negotiation with subsidiary management and equity holders, and the investment valuations may not always have been independently verified. Traditional methods used by independent valuation analysts include a discounted cash flow analysis and a comparable company analysis. We have not generated a positive cash flow to date and do not expect to generate significant cash flow in the near future. Additionally, we believe that few comparable public companies exist to provide meaningful valuation comparisons. Accordingly, we have not always sought independent valuation analysis in connection with our investments and may have invested in our various holdings at higher or lower valuations than an independent source would have recommended. There may be no correlation between the investment valuations that we used over the years for our investments and the actual market values. If we should eventually sell all or a part of any of our consolidated business or that of a subsidiary, the ultimate sale price may be for a value substantially different than previously determined by us, which could materially and adversely impair the value of our Common Stock.

## **Risks Related to Our Intellectual Property**

***Our ability to protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage.***

Our Subsidiaries have licensed rights to pending patents and have filed and will continue to file patent applications. The researchers sponsored by us may also file patent applications that we choose to license. If a particular patent is not granted, the value of the invention described in the patent would be diminished. Further, even if these patents are granted, they may be difficult to enforce. Even if successful, efforts to enforce our patent rights could be expensive, distracting for management, cause our patents to be invalidated, and frustrate commercialization of products. Additionally, even if patents are issued and are enforceable, others may independently develop similar, superior or parallel technologies to any technology developed by us, or our technology may prove to infringe upon patents or rights owned by others. Thus, the patents held by or licensed to us may not afford us any meaningful competitive advantage. If we are unable to derive value from our licensed or owned intellectual property, the value of your investment may decline.

***Our ability to develop and commercialize products will depend on our ability to enforce our intellectual property rights and operate without infringing the proprietary rights of third parties.***

Our ability to develop and commercialize products based on our patent portfolios will depend, in part, on our ability to enforce those patents and operate without infringing the proprietary rights of third parties. We cannot be certain that any patents that may issue from patent applications owned or licensed by us will provide sufficient protection to conduct our respective businesses as presently conducted or as proposed to be conducted, or that we will remain free from infringement claims by third parties. In particular, there can be no assurance that we will be successful enforcing our rights in the intellectual property that we acquired in the Roche RNAi acquisition.

***We may be subject to patent infringement claims, which could result in substantial costs and liability and prevent us from commercializing our potential products.***

Because the nanotechnology intellectual property landscape is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate without infringing on third party rights. However, we are currently aware of certain patent rights held by third parties that, if found to be valid and enforceable, could be alleged to render one or more of our business lines infringing. If a claim should be brought and is successful, we may be required to pay substantial damages, be forced to abandon any affected business lines and/or seek a license from the patent holder. In addition, any patent infringement claims brought against us, whether or not successful, may cause us to incur significant expenses and divert the attention of our management and key personnel from other business concerns. These could negatively affect our results of operations and prospects. We cannot be certain that patents owned or licensed by us or our Subsidiaries will not be challenged by others.

In addition, if our potential products infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our customers, and we may be required to indemnify our customers for any damages they suffer as a result of these claims. The claims may require us to initiate or defend protracted and costly litigation on behalf of customers, regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of our customers or may be required to obtain licenses for the products they use. If we cannot obtain all necessary licenses on commercially reasonable terms, we may be unable to continue selling such products.

***Our technology licensed from various third parties may be subject to government rights and retained rights of the originating research institutions.***

We license technology from Caltech, and other universities and companies. Our licensors may have obligations to government agencies or universities. Under their agreements, a government agency or university may obtain certain rights over the technology that we have developed and licensed, including the right to require that a compulsory license be granted to one or more third parties selected by the government agency.

In addition, our collaborators often retain certain rights under their agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our collaborators limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

## **Risks Related to Regulation of Our Products**

***Our corporate compliance program cannot guarantee that we are in compliance with all applicable federal and state regulations.***

Our operations, including our research and development and our commercialization efforts, such as clinical trials, manufacturing and distribution, are subject to extensive federal and state regulation. While we have developed and instituted a corporate compliance program, we cannot be assured that the Company or our employees are, or will be in compliance with all potentially applicable federal and state regulations or laws. If we fail to comply with any of these regulations or laws, a range of actions could result, including, but not limited to, the termination of clinical trials, the failure to approve a commercialized product, significant fines, sanctions, or litigation, any of which could harm our business and financial condition.

## **Risks Related to our Stock**

***Stockholder equity interest may be substantially diluted in any additional financing.***

Our certificate of incorporation authorizes the issuance of 145,000,000 shares of Common Stock and 5,000,000 shares of Preferred Stock, on such terms and at such prices as our Board of Directors may determine. Adjusted for the 1 for 10 stock split that was implemented on November 17, 2011, as of September 30, 2011, we had 8,642,286 shares of Common Stock issued and outstanding. The issuance of additional securities in financing transactions by us or through the exercise of options or warrants will dilute the equity interests of our existing stockholders, perhaps substantially, and might result in dilution in the tangible net book value of a share of our Common Stock, depending upon the price and other terms on which the additional shares are issued.

***Our Common Stock price has fluctuated significantly over the last several years and may continue to do so in the future, without regard to our results of operations and prospects.***

Because we are a development stage company, there are few objective metrics by which our progress may be measured. Consequently, we expect that the market price of our Common Stock will likely continue to fluctuate significantly. We may not generate substantial revenue from the license or sale of our technology for several years, if at all. In the absence of product revenue as a measure of our operating performance, we anticipate that investors and market analysts will assess our performance by considering factors such as:

- Announcements of developments related to our business;
- Our ability to enter into or extend investigation phase, development phase, commercialization phase and other agreements with new and/or existing partners;
- Announcements regarding the status of any or all of our collaborations or products;
- Market perception and/or investor sentiment regarding our technology;
- Announcements regarding developments in the nanotechnology field in general;
- Market perception and/or announcements regarding the field of siRNA (small interfering, RNAs);
- The issuance of competitive patents or disallowance or loss of our patent rights; and
- Variations in our operating results.

We will not have control over many of these factors but expect that they may influence our stock price. As a result, our stock price may be volatile and could result in the loss of all or part of your investment. Additionally, in the past, when the market price of a stock has been volatile, holders of that stock have often initiated securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

***The market for purchases and sales of our Common Stock may be very limited, and the sale of a limited number of shares could cause the price to fall sharply.***

Although our Common Stock is listed for trading on the NASDAQ Capital Market, historically our securities have been relatively thinly traded. Investor trading patterns could serve to exacerbate the volatility of the price of the stock. For example, mandatory sales of our Common Stock by institutional holders could be triggered if an investment in our Common Stock no longer satisfies their investment standards and guidelines. Accordingly, it may be difficult to sell shares of our Common Stock quickly without significantly depressing the value of the stock. Unless we are successful in developing continued investor interest in our stock, sales of our stock could continue to result in major fluctuations in the price of the stock.

***If securities or industry analysts do not publish research reports about our business or if they make adverse recommendations regarding an investment in our stock, our stock price and trading volume may decline.***

The trading market for our Common Stock can be influenced by the research and reports that industry or securities analysts publish about our business. We do not currently have and may never obtain research coverage by industry or securities analysts. Investors have many investment opportunities and may limit their investments to companies that receive coverage from analysts. If no industry or securities analysts commence coverage of the Company, the trading price of our stock could be negatively impacted. In

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the event we obtain industry or security analyst coverage, if one or more of the analysts downgrade our stock or comment negatively on our prospects, our stock price may decline. If one or more of these analysts cease to cover our industry or us or fails to publish reports about the Company regularly, our Common Stock could lose visibility in the financial markets, which could also cause our stock price or trading volume to decline.

***The market price of our Common Stock may be adversely affected by the sale of shares by our management or founding stockholders.***

Sales of our Common Stock by our officers, directors and founding stockholders could adversely and unpredictably affect the price of those securities. Additionally, the price of our Common Stock could be affected even by the potential for sales by these persons. We cannot predict the effect that any future sales of our Common Stock, or the potential for those sales, will have on our share price. Furthermore, due to relatively low trading volume of our stock, should one or more large stockholders seek to sell a significant portion of their stock in a short period of time, the price of our stock may decline.

***We do not intend to declare cash dividends on our Common Stock.***

We will not distribute cash to our stockholders unless and until we can develop sufficient funds from operations to meet our ongoing needs and implement our business plan. The time frame for that is unpredictable and investors should not expect dividends in the near future, if at all.

***Our Board of Directors has the authority to issue shares of “blank check” preferred stock, which may make an acquisition of the Company by another company more difficult.***

We have adopted and may in the future adopt certain measures that may have the effect of delaying, deferring or preventing a takeover or other change in control of the Company that a holder of our Common Stock might consider in its best interest. Specifically, our Board of Directors, without further action by our stockholders, currently has the authority to issue up to 5,000,000 shares of preferred stock and to fix the rights (including voting rights), preferences and privileges of these shares (“blank check” preferred). Such preferred stock may have rights, including economic rights, senior to our Common Stock.

### **ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

### **ITEM 2. PROPERTIES**

At September 30, 2011, we had one outstanding lease for our corporate headquarters, which is located in Pasadena, California. The Company does not own any real property. The following table summarizes the company’s leased facilities:

	<u>Office Space</u>	<u>Monthly Rent</u>	<u>Lease Commencement</u>	<u>Lease Term</u>
Pasadena, CA	3,000 sq ft	\$8,000	May 1, 2011	Month to Month

On October 21, 2011, Arrowhead acquired the RNAi operations from Roche, including its research facility in Madison, Wisconsin. The following table summarizes the information on that leased facility:

	<u>Lab/Office Space</u>	<u>Monthly Rent</u>	<u>Lease Commencement</u>	<u>Lease Term</u>
Madison, WI	24,000 sq ft	\$56,500	February 16, 2009	10 Years

### **ITEM 3. LEGAL PROCEEDINGS**

None.

### **ITEM 4. [REMOVED AND RESERVED]**

**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES***Price Range of Common Stock*

Our Common Stock is traded on the NASDAQ Stock Market under the symbol "ARWR". The following table sets forth the high and low sales prices for a share of the Company's Common Stock during each period indicated. On November 17, 2011, the Company effected a 1 for 10 reverse stock split. The share prices in the table below are shown on a post-split basis.

	Fiscal Year Ended September 30,			
	2011		2010	
	High	Low	High	Low
1st Quarter	\$ 11.00	\$8.30	\$ 7.00	\$ 5.10
2nd Quarter	10.00	6.00	11.70	5.10
3rd Quarter	7.00	4.30	18.50	10.30
4th Quarter	5.90	3.70	11.70	8.50

*Shares Outstanding*

At December 15, 2011, an aggregate of 10,525,941 shares of the Company's Common Stock were issued and outstanding, and were owned by 280 stockholders of record, based on information provided by the Company's transfer agent.

*Dividends*

The Company has never paid dividends on its Common Stock and does not anticipate that it will do so in the foreseeable future.

*Securities Authorized for Issuance Under the Equity Compensation Plans*

The disclosure required under this item related to equity compensation plans is incorporated by reference from Item 12, under the caption "Equity Compensation Plan Information" in this Annual Report on Form 10-K.

*Sales of Unregistered Securities*

All information under this Item has been previously reported on our Current Reports on Form 8-K.

*Repurchases of Equity Securities*

We did not repurchase any shares of our Common Stock during fiscal 2011 or fiscal 2010.

**ITEM 6. SELECTED FINANCIAL DATA**

As a "Smaller Reporting Company," we are not required to provide this information.

**ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS***Description of Business*

Unless otherwise noted, (1) the term "Arrowhead" refers to Arrowhead Research Corporation, a Delaware corporation, (2) the terms the "Company," "we," "us," and "our," refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term "Subsidiaries" refers collectively to Arrowhead Madison Inc. ("Madison"), Calando Pharmaceuticals, Inc. ("Calando"), Ablaris Therapeutics, Inc. ("Ablaris"), Agonn Systems, Inc. ("Agonn"), and Tego Biosciences Corporation ("Tego") as well as our former subsidiary, Unidym, Inc. ("Unidym"), which was divested in January 2011, (4) the term "Minority Investments" refers collectively to Nanotope, Inc. ("Nanotope") and Leonardo Biosystems, Inc. ("Leonardo") in which the company holds a less than majority ownership position, and (5) the term "Common Stock" refers to Arrowhead's Common Stock and the term "stockholder(s)" refers to the holders of Arrowhead Common Stock.

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### **Overview**

Arrowhead Research Corporation is a nanomedicine company developing innovative therapies at the interface of biology and nanoengineering to cure disease and improve human health. Arrowhead has one of the most advanced and broadest technology platforms for therapeutics based on RNA interference (RNAi), including access to five different RNAi delivery systems and the three primary small interfering RNA (siRNA) structures in commercial development for RNAi therapeutics. This broad technology platform enables optimization of siRNA therapeutic candidates for delivery based on siRNA chemistry, tissue type, disease state, and target [gene] and siRNA type and chemistry on a target-by-target basis. Arrowhead is leveraging its in house R&D expertise and capabilities, as well as a broad intellectual property portfolio for RNAi therapeutics, to attract development partnerships with other pharmaceutical and biotech companies committed to bringing RNAi therapeutics to market, as well as continuing the preclinical and clinical development its own clinical candidates. Arrowhead's non-RNAi development programs include a unique therapeutic candidate that shows promise for the treatment of obesity and advanced bioactive materials for the regeneration of injured tissues.

### **Critical Accounting Policies and Estimates**

Management makes certain judgments and uses certain estimates and assumptions when applying accounting principles generally accepted in the United States in the preparation of our Consolidated Financial Statements. We evaluate our estimates and judgments on an ongoing basis and base our estimates on historical experience and on assumptions that we believe to be reasonable under the circumstances. Our experience and assumptions form the basis for our judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may vary from what we anticipate and different assumptions or estimates about the future could change our reported results. We believe the following accounting policies are the most critical to us, in that they are important to the portrayal of our consolidated financial statements and require our most difficult, subjective or complex judgments in the preparation of our consolidated financial statements. For further information, see *Note 1, Organization and Significant Accounting Policies*, to our Consolidated Financial Statements which outlines our application of significant accounting policies and new accounting standards.

#### *Revenue Recognition*

Revenue from product sales are recorded when persuasive evidence of an arrangement exists, title has passed and delivery has occurred, a price is fixed and determinable, and collection is reasonably assured.

We may generate revenue from technology licenses, collaborative research and development arrangements, research grants and product sales. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable and/or guaranteed technology license fees, collaborative research funding, and various milestone and future product royalty or profit-sharing payments.

Revenue associated with research and development funding payments under collaborative agreements is recognized ratably over the relevant periods specified in the agreement, generally the research and development period. Revenue from up-front license fees, milestones and product royalties are recognized as earned based on the completion of the milestones and product sales, as defined in the respective agreements. Payments received in advance of recognition as revenue are recorded as deferred revenue.

#### *Impairment of Long-lived Assets*

We review long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of assets may not be fully recoverable or that our assumptions about the useful lives of these assets are no longer appropriate. If impairment is indicated, recoverability is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset exceeds the fair value of the asset.

#### *Stock-Based Compensation*

We recognize stock-based compensation expense based on the grant date fair value using the Black-Scholes options pricing model, which requires us to make assumptions regarding certain variables including the risk-free interest rate, expected stock price volatility, and the expected life of the award. The assumptions used in calculating stock-based compensation expense represent management's best estimates, but these estimates involve inherent uncertainties, and if factors change or the Company used different assumptions, its stock-based compensation expense could be materially different in the future.

#### *Derivative Assets and Liabilities*

We account for warrants and other derivative financial instruments as either equity or assets/liabilities based upon the characteristics and provisions of each instrument. Warrants classified as equity are recorded as additional paid-in capital on our consolidated balance sheet and no further adjustments to their valuation are made. Some of our warrants were determined to be ineligible for equity classification because of provisions that may result in an adjustment to their exercise price. Warrants classified as derivative liabilities and other derivative financial instruments that require separate accounting as assets or liabilities are recorded on our consolidated balance sheet at their fair value on the date of issuance and are revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. We estimate the fair value of these assets/liabilities using option pricing models that are based on the individual characteristics of the warrants or instruments on the valuation date, as well as assumptions for expected volatility, expected life and risk-free interest rate. Changes in the assumptions used could have a material impact on the resulting fair value. The primary input affecting the value of our derivatives liabilities is the Company's stock price. For example, a 50% change in the value of the Company's stock price would affect the value of the derivative liability by approximately \$0.5 million to \$0.6 million, depending on other inputs.

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### *Intellectual Property*

Intellectual property consists of patents and patent applications internally developed, licensed from universities or other third parties or obtained through acquisition. Patents and patent applications are reviewed for impairment whenever events or circumstances indicate that the carrying amount may not be recoverable, and any impairment is recorded. Licensed or internally developed patents are amortized over the life of the patent. Purchased patents are amortized over three years.

### *Reverse Stock Split*

As of November 17, 2011, the Company effected a 1 for 10 reverse stock split (the "Reverse Stock Split"). As a result of the reverse stock split, each ten shares of the Company's Common Stock issued and outstanding immediately prior to the reverse split was combined into one share of Common Stock. Also, as a result of the Reverse Stock Split, the per share exercise price of, and the number of shares of Common Stock underlying outstanding Company stock options, warrants, Series A Preferred and any Common Stock based equity grants outstanding immediately prior to the reverse stock split was proportionally adjusted, based on the one-for-ten split ratio, in accordance with the terms of such options, warrants or other Common Stock based equity grants as the case may be. No fractional shares of Common Stock were issued in connection with the reverse split. Stockholders will instead receive cash payment in lieu of any fractional shares. Unless otherwise noted, all share and per share amounts in these have been retrospectively adjusted to reflect the reverse stock split.

### **Results of Operations**

The Company had a net loss of \$3.5 million for the year ended September 30, 2011, compared to a net loss of \$7.0 million for the year ended September 30, 2010, a decrease of \$3.5 million.

The change in the net loss was the result of a number of factors. Arrowhead divested Unidym in January 2011, accordingly, losses incurred at Unidym decreased from fiscal 2010 to fiscal 2011. During fiscal 2010, losses from Unidym were \$3 million, compared to income in fiscal 2011 of \$1.4 million, resulting in a change of \$4.4 million. The income from discontinued operations in fiscal 2011 was driven by revenue of \$4.7 million primarily from a license agreement with Samsung prior to the disposal of Unidym. Additionally, during fiscal 2011, Arrowhead recognized a gain from the disposal of Unidym of \$3.9 million. These variances were somewhat offset by the inclusion of Ablaris, which was acquired in December 2010, including a one-time license fee of \$2 million and other Ablaris operating expenses of approximately \$0.6 million. Other variances included higher general and administrative expenses of \$1.4 million, primarily due to costs related to the acquisition of Roche Madison which was completed in October 2011. Other income/expense was unfavorable by \$0.5 million primarily due to the change in the value of derivative liabilities as compared to the prior year.

### **Revenues**

The Company generated revenue of \$296,000 during the year ended September 30, 2011. Revenues were not recognized in the year ended September 30, 2010, as revenues previously recognized by Unidym are classified as a part of discontinued operations. The revenue in 2011 was primarily related to a qualifying therapeutic discovery grant received by Calando.

### **Operating Expenses**

The analysis below details the operating expenses and discusses the expenditures of the Company within the major expense categories. For purposes of comparison, the amounts for the years ended September 30, 2011 and 2010 are shown in the table below.

#### ***Salary & Wage Expenses - Fiscal 2011 compared to Fiscal 2010***

Arrowhead employs management, administrative and technical staff. Salary and wage expense consists of salary, benefits, and non-cash charges related to equity-based compensation from the issuance of stock options. Salary and benefits are allocated to two major categories: general and administrative compensation expense and research and development compensation expense depending on the primary activities of each employee. The following table provides details of salary and related expenses for fiscal 2011 and fiscal 2010.

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(in thousands)

	Twelve Months Ended	% of Expense	Twelve Months Ended	% of Expense	Increase (Decrease)	
	September 30, 2011	Category	September 30, 2010	Category	\$	%
G&A—compensation-related	\$ 1,143	81%	\$ 910	79%	\$ 233	26%
R&D—compensation-related	265	19%	236	21%	29	12%
Total	<u>\$ 1,408</u>	<u>100%</u>	<u>\$ 1,146</u>	<u>100%</u>	<u>\$ 262</u>	<u>23%</u>

During the year ended September 30, 2011, G&A compensation expense increased \$233,000. The prior year included a nonrecurring charge of certain general and administrative expenses to the Company's minority investment companies, Nanotope and Leonardo, for which the Company provides management services. This charge served to decrease the Company's consolidated salary costs during the year ended September 30, 2010. Arrowhead's management headcount has remained relatively constant over the past year. R&D compensation related costs remained relatively constant during the year and on a year-to-date basis, as compared to the prior periods. With the addition of personnel in Arrowhead's newly acquired Madison facility, salary and wage expenses are expected to increase sharply in fiscal 2012.

### General & Administrative Expenses – Fiscal 2011 compared to Fiscal 2010

The following table provides details of our general and administrative expenses for the fiscal years 2011 and 2010.

(in thousands)

	Twelve Months Ended	% of Expense	Twelve Months Ended	% of Expense	Increase (Decrease)	
	September 30, 2011	Category	September 30, 2010	Category	\$	%
Professional/outside services	\$ 2,384	63%	\$ 1,199	49%	\$ 1,185	99%
Patent expense	604	16%	352	14%	252	72%
Facilities and related	168	4%	278	11%	(110)	-40%
Travel	201	5%	161	6%	40	25%
Business insurance	194	5%	182	7%	12	7%
Depreciation	26	1%	35	1%	(9)	-26%
Communication and technology	96	3%	105	4%	(9)	-9%
Office expenses	54	1%	65	3%	(11)	-17%
Other	95	2%	114	5%	(19)	-17%
Total	<u>\$ 3,822</u>	<u>100%</u>	<u>\$ 2,491</u>	<u>100%</u>	<u>\$ 1,331</u>	<u>53%</u>

Professional/outside services include legal, accounting and other outside services retained by Arrowhead and its subsidiaries. All periods include normally occurring legal and accounting expenses related to SEC compliance and other corporate matters. Professional/outside services expense was \$2,384,000 during the year ended September 30, 2011, compared to \$1,199,000 in the comparable prior period. The increase in professional fees primarily relates to the legal costs, consulting services and other outside costs associated to the acquisition of Roche's RNAi assets and facility in Madison, Wisconsin.

Patent expense was \$604,000 during the year ended September 30, 2011, compared to \$352,000 in the comparable prior period. During the year ended September 30, 2011, patent expense was primarily related to fees paid to patent counsel for the maintenance of Calando's intellectual properties portfolio. The increase is primarily due to increased costs related to foreign patent filings. The Company expects to continue to invest in patent protection as the Company extends and maintains protection for its current portfolios and files new patent applications as its product applications are improved.

Facilities and related expense within general and administrative expenses primarily relate to rental costs associated with the Company's headquarters in Pasadena, California. Facilities expense decreased due to reduction in the company's rental expense because its lease for its corporate headquarters expired. Temporarily, the Company is occupying a smaller and less expensive office space, and is in negotiations for a new corporate office facility.

Travel expense was \$201,000 during the year ended September 30, 2011, compared to \$161,000 in the comparable prior period. Travel expense includes expenses related to travel by Company personnel for operational business meetings at other company locations, and for other business initiatives and collaborations throughout the world with other companies, and for marketing, investor relations, fund raising and public relations purposes. The increase in travel relates primarily to the travel costs associated with due diligence related to the acquisition of Roche's RNAi assets and facility in Madison, Wisconsin.

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Business insurance expense was \$194,000 during the year ended September 30, 2011, compared to \$182,000 in the comparable prior period. During the prior year, the company received a refund of \$55,000 for its insurance carrier related to clinical trial program premium coverage after an insurance audit. The company also experienced rate decreases in its Directors and Officers insurance coverage.

Depreciation expense was \$26,000 during the year ended September 30, 2011, compared to \$35,000 in the comparable prior period. The decrease in depreciation expense is related primarily to the assets that were fully depreciated during the year.

Communication and technology expense was \$96,000 during the year ended September 30, 2011, compared to \$105,000 in the comparable prior period. The decrease in communication and technology cost is due to lower technology consulting expense and lower telephone and software maintenance cost at Arrowhead and Calando.

Office expense was \$54,000 during the year ended September 30, 2011, compared to \$65,000 in the comparable prior period. The decrease in office expense primarily relates to the reduction of office costs after the company moved to a smaller temporary facility that provides certain amenities as part of the lease.

### **Research and Development Expenses – Fiscal 2011 compared to Fiscal 2010**

Most of Arrowhead's R&D expenses for fiscal 2011 and fiscal 2010 were related to research and development activities by Arrowhead's Subsidiaries. The following table provides details of R&D expenses for fiscal 2011 and 2010:

(in thousands)

	Twelve Months Ended	% of	Twelve Months Ended	% of	Increase (Decrease)	
	September 30, 2011	Expense Category	September 30, 2010	Expense Category	\$	%
Outside labs & contract services	\$ 776	24%	\$ 199	38%	\$ 577	290%
Consulting	440	13%	326	61%	114	35%
License, royalty & milestones	2,045	62%	(2)	0%	2,047	NM
Other research expenses	17	1%	7	1%	10	143%
Total	<u>\$ 3,278</u>	<u>100%</u>	<u>\$ 530</u>	<u>100%</u>	<u>\$ 2,748</u>	<u>518%</u>

Outside lab and services expense was \$776,000 during the year ended September 30, 2011, compared to \$199,000 in the comparable prior period. The majority of the increase was related to Calando. Outside lab services and contract services were higher in fiscal 2011 to support the clinical trial taking place. In the previous year, the clinical trial had lower enrollment and thus incurred lower cost. In addition, the company experienced outside costs related to its new subsidiary, Ablaris, which was not operating in the prior year.

Consulting expense was \$440,000 during the year ended September 30, 2011, compared to \$326,000 in the comparable prior period. The primary reason for the increase in consulting expense is due to technical consulting costs related to the company's new subsidiary, Ablaris Therapeutics, Inc. and the costs associated with new scientific advisory board members.

License, royalty & milestone expense was \$2,045,000 during the year ended September 30, 2011, compared to (\$2,000) in the comparable prior period. The licensing fees, royalty and milestones expenses during the year reflect to \$2 million in licensing fees paid to University of Texas M.D. Anderson Cancer Center related to a Patent and Technology License Agreement entered into in December 2010, and related to Ablaris.

### **Other Income / Expense**

Other income decreased from \$1,521,000 in fiscal 2010 to \$1,045,000 in fiscal 2011. The main reason for the decrease in other income was due to the change in the value of derivative liabilities, which contributed \$1.8 million to other income in fiscal 2010, compared to \$1.1 million in fiscal 2011. The change in the value of the derivative is related to warrants issued in June 2010, that contain antidilution protection (see Note 11 – Fair Value Measurements & Derivative Instruments), somewhat offset by the change in the value of the derivative asset related to a convertible bond, the value of which is affected by the price of the underlying equity security. Also contributing to other income/expense was the change in value of marketable securities, which decreased in value by \$261,000 during the year. The Company also recorded other income of \$250,000 in 2011 related to an insurance claim paid during the year.

## Liquidity and Cash Resources

As a development stage company, Arrowhead has historically financed its operations through the sale of securities of Arrowhead and its Subsidiaries. Research and development activities have required significant capital investment since the Company's inception, and are expected to continue to require significant cash investment in fiscal 2012.

At September 30, 2011, the Company had cash on hand of approximately \$7.5 million. Cash and cash equivalents increased during fiscal 2011 by \$660,000 to \$7.5 million at September 30, 2011 from \$6.8 million at September 30, 2010.

Cash used in operating activities was \$7.7 million, which represents the on-going expenses of Arrowhead and its Subsidiaries. Cash outlays were primarily composed of the following: salary and payroll-related costs were \$1.9 million, general and administrative costs were \$3.2 million, research and development costs were \$2.8 million. \$0.7 million was used to fund operating expenses at Arrowhead's two minority interest companies, Nanotope and Leonardo. It is expected that these funds will be repaid, or converted to equity in the future. Cash expenses were partially offset by cash received from revenues of \$0.3 million, proceeds from an insurance claim of \$0.3 million, and other cash flow of \$0.3 million.

Cash used in investing activities was \$0.2 million, primarily related to cash received from the sale of investment of \$1.5 million, offset by \$1.7 million of cash which was divested with the sale of Unidym.

Cash provided by financing activities of \$6.2 million includes \$1.7 million received from outside investors for an investment in Ablaris, \$4.6 million equity investment from the sale of Common Stock, and \$0.1 million from the exercise of stock options.

Cash provided from discontinued operations was \$2.3 million, representing the cash flow from Unidym, which was sold in January 2011.

On October 21, 2011, Arrowhead completed the acquisition of certain RNAi assets from Hoffmann-La Roche Inc. and F Hoffmann-La Roche Ltd., including intellectual property and a research and development facility based in Madison, Wisconsin. At the time of the acquisition, the facility had 41 employees. Due to the costs associated with the facility, including personnel costs, rent, research and development expenses, and other costs, it is expected that cash expenses will increase significantly in 2012 and beyond as the Company accelerates its preclinical and clinical development efforts.

### *Recent Financing Activity:*

On September 30, 2011, the Company entered into Subscription Agreements with certain accredited investors pursuant to which the Company agreed to issue and sell an aggregate of 1,458,917 shares of Common Stock, \$0.001 par value per share, at a purchase price of \$3.80 per share. The aggregate purchase price paid by the Purchasers for the shares of Common Stock was \$5,543,885, which includes \$193,885 of fees paid in stock. The closing of the sale of the shares occurred on September 30, 2011. Additionally, on October 5, 2011, a second closing under the same terms occurred resulting in the issuance of 138,157 additional shares of Common Stock for proceeds of \$525,000.

On October 20, 2011, the Company and Lincoln Park Capital Fund, LLC, an Illinois limited liability company ("LPC") entered into a \$15 million purchase agreement (the "Purchase Agreement"), together with a registration rights agreement, whereby LPC agreed to purchase up to \$15 million of Common Stock, subject to certain limitations, from time to time during the three-year term of the Purchase Agreement. Additionally, the Company agreed to file a registration statement with the U.S. Securities & Exchange Commission ("SEC") covering the resale of the shares that have been or may be issued to LPC under the Purchase Agreement. Upon the occurrence of certain events, including the SEC declaring effective the registration statement related to the resale of such shares, the Company will have the right, in its sole discretion, over a 36-month period to sell up to \$15 million of Common Stock (subject to certain limitations) to LPC, depending on certain conditions as set forth in the Purchase Agreement.

On October 21, 2011 and October 24, 2011, the Company entered into Subscription Agreements with certain accredited investors, pursuant to which the Company agreed to issue and sell an aggregate of 1,015 shares of Series A Preferred Convertible Stock, \$0.001 par value per share, at a purchase price of \$1,000 per share. The aggregate purchase price paid by the Series A Purchasers for the shares of Series A Preferred is \$1,015,000. Upon receipt of stockholder approval, each share of Series A Preferred will automatically convert into 263.158 shares of Common Stock, subject to a 19.99% beneficial ownership conversion limit. The Company intends to seek stockholder approval for the conversion of the Series A Preferred Stock at the 2012 Annual Meeting.

On October 21, 2011, the Company entered into a Subscription Agreement with a single accredited investor, pursuant to which the Company agreed to issue and sell an aggregate of 675,000 shares of Common Stock, \$0.001 par value per share, at a purchase price of \$3.70 per share. The aggregate purchase price for the shares of Common Stock was \$2,497,500.

Based upon the Company's cash on hand and operating plan at September 30, 2011, additional sources of financing since September 30, 2011 and other sources of liquidity, as described above, the Company's management anticipates that the Company will be able to satisfy the cash requirements of its operations through at least the next twelve months. However, the Company anticipates that further equity financings, and/or asset sales and license agreements will be necessary to continue to fund operations in the future.

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### **Off-Balance Sheet Arrangements**

As of September 30, 2011, we did not have any off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of SEC Regulation S-K.

### **ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

As a “Smaller Reporting Company,” we are not required to provide this information.

### **ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

The information required by this item is included in Item 15 of this Annual Report Form 10-K.

### **ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.**

None.

### **ITEM 9A. CONTROLS AND PROCEDURES.**

Our Chief Executive Officer and our Chief Financial Officer, after evaluating our “disclosure controls and procedures” (as defined in Securities Exchange Act of 1934 (the “Exchange Act”) Rules 13a-15(e) and 15d-15(e)) as of the end of the period covered by this Annual Report on Form 10-K (the “Evaluation Date”) have concluded that as of the Evaluation Date, our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms, and to ensure that information required to be disclosed by us in such reports is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer where appropriate, to allow timely decisions regarding required disclosure.

### **Management’s Annual Report on Internal Control over Financial Reporting**

#### ***Internal Control over Financial Reporting***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the United States. This process includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the internal control over financial reporting to future periods are subject to risk that the internal control may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

#### ***Management’s Assessment of the Effectiveness of our Internal Control over Financial Reporting***

Management has evaluated the effectiveness of our internal control over financial reporting as of September 30, 2011. In conducting its evaluation, management used the framework set forth in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on our evaluation under such framework, management has concluded that our internal control over financial reporting was effective as of September 30, 2011.

### **Changes in Internal Control Over Financial Reporting**

There was no change in our internal control over financial reporting that occurred during the fourth quarter of the year ended September 30, 2011, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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### ITEM 9B. OTHER INFORMATION

None

## PART III

### ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

#### Board of Directors:

The names and ages of our directors serving as of December 15, 2011 are provided below. Directors are elected annually for a one year term. Biographical information regarding these officers is set forth under the following table.

<u>Name</u>	<u>Age</u>	<u>Position with Arrowhead</u>
Christopher Anzalone	42	Chief Executive Officer & President and Director
R. Bruce Stewart	73	Executive Chairman of the Board
Mauro Ferrari	52	Director
Edward W. Frykman	75	Director
Douglass Given	59	Director
Charles P. McKenney	73	Director
Michael S. Perry	52	Director

**Dr. Christopher Anzalone** has been President, Chief Executive Officer and Director of the Company since December 1, 2007. In 2005, Dr. Anzalone formed and served as CEO of the Benet Group LLC, private equity firm focused on creating and building new nano-biotechnology companies from university-generated science. While at The Benet Group, Dr. Anzalone was founding CEO in two portfolio companies, Nanotope Inc., a tissue regeneration company, and Leonardo Biosystems Inc., a cancer drug delivery company. Dr. Anzalone remains CEO and director of Nanotope. Dr. Anzalone is a director of Arrowhead's wholly-owned subsidiary, Arrowhead Madison Inc., majority-owned subsidiaries, Calando Pharmaceuticals, Inc., Ablaris Therapeutics, Inc., and Tego Biosciences Corporation and minority investment, Leonardo Biosystems, Inc. Prior to his tenure at Benet Group, from 1999 until 2003, he was a partner at the Washington, DC-based private equity firm Galway Partners, LLC, where he was in charge of sourcing, structuring, and building new business ventures and was founding CEO of NanoInk, Inc., a leading nanolithography company. Dr. Anzalone holds a Ph.D. in Biology from UCLA and a B.A. in Government from Lawrence University. We believe Dr. Anzalone's qualifications to serve on the Board include his deep understanding of the business through his role as Chief Executive Officer; in addition Dr. Anzalone has extensive experience in nanotechnology, biotechnology, company-building and venture capital.

**R. Bruce Stewart** has been Executive Chairman of the Board of the Company since December 1, 2007. Mr. Stewart was Arrowhead's Chief Executive Officer and Chairman of the Board of the Company from January 2004 to November 30, 2007. Mr. Stewart was the Chairman of the Board of Arrowhead's predecessor company since its inception in May 2003 and devoted much of his time from early in 2003 to development of its plan of operations. Mr. Stewart is a director of Arrowhead's majority-owned subsidiaries Calando Pharmaceuticals, Inc., Ablaris Therapeutics, Inc., and Tego Biosciences Corporation. Mr. Stewart founded Acacia Research Corporation in March 1991, and was employed by Acacia Research Corporation in various capacities until January 2003, serving as its President from inception through January 1997, Chairman until April 2000, and as a senior advisor until January 2003. We believe Mr. Stewart's qualifications to serve on the Board includes his long tenure as Chief Executive Officer and as a member of the Board during which time he gained an extensive understanding of the Company's operations, strategy and finances, as well as his extensive experience in the field of finance.

**Dr. Mauro Ferrari** was appointed to the Arrowhead Board of Directors in 2010. Dr. Ferrari is the President and CEO of The Methodist Hospital Research Institute (TMHRI). He is also the President of The Alliance for NanoHealth. Dr. Ferrari is a director of Arrowhead's minority investment, Leonardo Biosystems, Inc. Dr. Ferrari is an internationally recognized expert in nanomedicine and biomedical nanotechnology. Prior to assuming leadership of TMHRI, Dr. Ferrari was Professor and Chairman of The Department of NanoMedicine and Biomedical Engineering at The University of Texas Health Science Center at Houston, Professor of Experimental Therapeutics at the MD Anderson Cancer Center, Adjunct Professor of Bioengineering at Rice University, and Adjoint Professor of Biomedical Engineering at the University of Texas in Austin. His previous academic appointments include professorships at UC Berkeley and Ohio State University.

From 2003 to 2005, he served as Special Expert on Nanotechnology and Eminent Scholar at The National Cancer Institute, where he led in the development of the NCI's program in Nanotechnology, which remains the largest program in NanoMedicine in the world. Dr. Ferrari has been serving as the Editor-in-Chief for "Biomedical Microdevices: BioMEMS and Biomedical Nanotechnology" since 1997. We believe Dr. Ferrari's qualifications to serve on the Board include his extensive training and experience in the fields of nanotechnology, biotechnology and biomedical applications. Dr. Ferrari has significant technical training, several academic appointments and numerous published articles and patents. Additionally, Dr. Ferrari has extensive experience in developmental stage organizations having founded several startup companies.

**Edward W. Frykman** has been a director of the Company since January 2004. Mr. Frykman was an Account Executive with Crowell, Weedon & Co., a position he held from 1992 until 2008 when he retired. Before his service at Crowell, Weedon & Co., Mr. Frykman served as Senior Vice President of L.H. Friend & Co. Both Crowell Weedon & Co. and L.H. Friend & Co. are

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investment brokerage firms located in Southern California. In addition, Mr. Frykman was a Senior Account Executive with Shearson Lehman Hutton, where he served as the Manager of the Los Angeles Regional Retail Office of E. F. Hutton & Co. Mr. Frykman was a director in Arrowhead's predecessor company since its inception in May 2003 until January 2004, when he became a director of the Company. Mr. Frykman is also a director of Acacia Research Corporation, a publicly-held corporation based in Newport Beach, California. Mr. Frykman is a director of Arrowhead's majority-owned subsidiaries Calando Pharmaceuticals, Inc., Ablaris Therapeutics, Inc., and Tego Biosciences Corporation. We believe Mr. Frykman's qualifications to serve on the Board include his long tenure as a member of the Board which enabled Mr. Frykman to gain a deep understanding of the company's operations, strategy and finances. Mr. Frykman also has extensive experience in the fields of finance and public company oversight.

**Dr. Douglass Given** has been a director of the company since November 2010. He is an Investment Partner at Bay City Capital and has been with the firm since October 2000. He was formerly Chief Executive Officer and a director of NeoRx, Corporate Sr. Vice President and Chief Technical Officer of Mallinckrodt, and Chief Executive Officer and a director of Progenitor and Mercator Genetics. He held positions as Vice President at Schering Plough Research Institute, Vice President at Monsanto/G.D. Searle Research Laboratories, and Medical Advisor at Lilly Research Laboratories. Dr. Given is the Chairman of VIA Pharmaceuticals, and Chairman of Vivaldi Biosciences. He is Chairman of the Visiting Committee to the Division of Biological Sciences and the Pritzker School of Medicine at the University of Chicago, a member of the Johns Hopkins Bloomberg School of Public Health Advisory Board, and a member of the Harvard School of Public Health AIDS Initiative International Advisory Council.

Dr. Given holds an MD with honors and a PhD from the University of Chicago, and an MBA from the Wharton School, University of Pennsylvania. He was a fellow in Internal Medicine and Infectious Diseases at Harvard Medical School and Massachusetts General Hospital. We believe Dr. Given's qualifications to serve on the Board include his extensive experience in finance and business transactions, particularly investments in the life sciences industry as well as directorship roles in start-up biotechnology companies. Dr. Given also has significant leadership roles, including CEO and Senior Vice President, at several large pharmaceutical companies. Dr. Douglass Given is a brother of Dr. Bruce Given, our chief operating officer.

**Charles P. McKenney** has been a director of the Company since April 2004. Mr. McKenney has maintained a government affairs law practice in Pasadena, California since 1989, representing businesses and organizations in their relations with state and local government regarding their obligations under state and local land use and trade practices laws. From 1973 through 1989, he served as Attorney for Corporate Government Affairs for Sears, Roebuck and Co., helping organize and carry out Sears's western state and local government relations programs. Mr. McKenney has served two terms on the Pasadena, California, City Council as well as on several city boards and committees, including three city Charter Reform Task Forces. Mr. McKenney is a director of Arrowhead's majority-owned subsidiaries Calando Pharmaceuticals, Inc., Ablaris Therapeutics, Inc., and Tego Biosciences Corporation. We believe Mr. McKenney's qualifications to serve on the Board include his long tenure as a member of the Board resulting in a deep understanding of the Company's operations, strategy and finances. Mr. McKenney also has extensive experience providing strategic legal and advisory services to developmental stage organizations.

**Dr. Michael S. Perry** was appointed to the Company's Board of Directors on December 19, 2011. Dr. Perry has been a Venture Partner with Bay City Capital LLP since 2005. Dr. Perry was appointed President and Chief Medical Officer of Poniard Pharmaceuticals, a Bay City Capital portfolio company (NASDAQ: PARD) in 2010. He also currently serves as a member of the board of directors of AmpliPhi Biosciences Corporation (APHB.PK). He was Chief Development Officer at VIA Pharmaceuticals, Inc., a publicly held drug development company, from April 2005 until May 2009. Prior thereto, he served as Chairman and Chief Executive Officer of Extropy Pharmaceuticals, Inc., a privately held pediatric specialty pharmaceutical company, from June 2003 to April 2005. From 2002 to 2003, Dr. Perry served as President and Chief Executive Officer of Pharsight Corporation, a publicly held software and consulting services firm. From 2000 to 2002, Dr. Perry served as Global Head of Research and Development for Baxter BioScience. From 1997 to 2000, Dr. Perry was President and Chief Executive Officer of both SyStemix Inc. and Genetic Therapy Inc., two wholly owned subsidiaries of Novartis Corp., and from 1994 to 1997, he was Vice President of Regulatory Affairs for Novartis Pharma (previously Sandoz Pharmaceuticals). Prior to 1994, Dr. Perry held various management positions with Syntex Corporation, Schering-Plough Corporation and BioResearch Laboratories, Inc. Dr. Perry holds a Doctor of Veterinary Medicine, a Ph.D. in Biomedical Pharmacology and a B.Sc. in Physics from the University of Guelph, Ontario, Canada. He is a graduate of the International Management Program at Harvard Business School. We believe Dr. Perry's qualifications to serve on the board include his medical expertise and his extensive experience in preclinical and clinical drug development, including executive level leadership roles in several publicly held biotech companies.

### **Executive Officers:**

The names and ages of our executive officers and the positions held by each as of December 15, 2011 are as follows:

<u>Name</u>	<u>Age</u>	<u>Position with Arrowhead</u>
Christopher Anzalone	42	Chief Executive Officer & President and Director
R. Bruce Stewart	73	Executive Chairman of the Board
Kenneth A. Myszkowski	45	Chief Financial Officer
Bruce Given	57	Chief Operating Officer

**Dr. Christopher Anzalone** (see Board of Directors)

**R. Bruce Stewart** (see Board of Directors)

**Kenneth A. Myszkowski**, Chief Financial Officer, joined Arrowhead in 2009. Prior to joining Arrowhead, Mr. Myszkowski served as the corporate controller for Broadwind Energy, a public energy company which provides products and services to the wind energy industry. Previous to his position at Broadwind, Mr. Myszkowski was controller for Epcor USA, the U.S. headquarters for Epcor Utilities, Inc., a public energy company. Prior to Epcor, Mr. Myszkowski was controller for two start-up ventures: NanoInk, specializing in Dip Pen Nanolithography, a nanofabrication technology, and Delphion, which provided on-line tools for intellectual property research. Mr. Myszkowski also held several corporate roles at FMC Corporation, and Premark International, both Fortune 500 conglomerates. He began his career in the audit practice of Arthur Andersen & Co. in Chicago, Illinois. Mr. Myszkowski received his undergraduate degree from the University of Illinois, and his MBA from the University of Chicago Booth School of Business. He is a certified public accountant.

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**Dr. Bruce Given**, Chief Operating Officer, joined Arrowhead in 2011. Since October 1, 2009, Dr. Given has been a director of the Company's subsidiary, Calando Pharmaceuticals, Inc., and since February 1, 2010, Dr. Given has been Chief Executive Officer of Leonardo Biosystems, Inc., a company in which Arrowhead holds a minority equity interest. Dr. Given has been a member of the Board of Directors for ICON, plc. since 2007, and Chairman of the Board of Directors since 2010. Dr. Given served as the President and Chief Executive Officer, and as a member of the Board of Directors of Encysive Pharmaceuticals, an R&D-based commercial pharmaceutical company, roles he held from 2002 through 2007. Subsequent to his tenure at Encysive until present, Dr. Given has been President of Bruce Given Consulting, a firm that provides consulting services to biotech companies. Prior to his tenure at Encysive, Dr. Given held several senior executive roles at Johnson and Johnson, Sandoz Pharmaceuticals, and Schering-Plough. Dr. Given obtained his bachelor of sciences degree from Colorado State University, graduating Phi Beta Kappa. He received his M.D. degree with honors from the University of Chicago, Pritzker School of Medicine and completed his medical training at the University of Chicago and at Brigham and Women's Hospital in Boston, where he was a Clinical Fellow at Harvard Medical School. He is board certified in internal medicine and endocrinology and metabolism and has authored 33 scientific publications. Dr. Bruce Given is a brother of Dr. Douglass Given, a director of the company.

### Section 16(a) Beneficial Ownership Reporting Compliance

Under Section 16(a) of the Securities Exchange Act of 1934, the Company's directors and officers and its significant stockholders (defined by statute as stockholders beneficially owning more than ten percent (10%) of the Common Stock) are required to file with the SEC and the Company reports of ownership, and changes in ownership, of common stock. Based solely on a review of the reports received by it, the Company believes that, during the fiscal year ended September 30, 2011, all of its officers, directors and significant stockholders complied with all applicable filing requirements under Section 16(a).

### Code of Ethics

We have adopted a code of conduct that applies to our Chief Executive Officer, Chief Financial Officer, and to all of our other officers, directors and employees. The code of conduct is available at the Corporate Governance section of the Investor Relations page on our website at [www.arrowheadresearch.com](http://www.arrowheadresearch.com). Any waivers from or amendments to the code of conduct, if any, will be posted on our website.

### Corporate Governance

The Audit Committee of the Board is currently comprised of three directors and operates under a written charter adopted by the Board. The members of the Audit Committee are Edward W. Frykman, Charles P. McKenney and Mauro Ferrari. All members of the Audit Committee are "independent," as defined in Rule 10A-3 under the Exchange Act and Rule 4200(a)(14) of the NASDAQ Marketplace Rules, and financially literate. The Board has determined that Mr. Frykman is an "audit committee financial expert" in accordance with the applicable regulations.

## ITEM 11. EXECUTIVE COMPENSATION.

### Executive Officers

#### Summary Compensation Table

The following table summarizes compensation paid, awarded or earned for services rendered during fiscal 2011 and fiscal 2010 by our Chief Executive Officer, and Kenneth Myszkowski, our other executive officer serving the Company as of September 30, 2011. We refer to those persons collectively as our "Named Executive Officers".

<u>Name and Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Bonus (\$)</u>	<u>Stock Awards (\$)</u>	<u>Option Awards (\$)(1)</u>	<u>All Other Compensation (\$)(2)</u>	<u>Total (\$)</u>
Christopher Anzalone President & Chief Executive Officer	2011	400,000	25,000	—	—	—	425,000
	2010	400,000	—	—	1,134,094	—	1,534,094
Ken Myszkowski Chief Financial Officer	2011	225,000	7,500	—	—	9,000	241,500
	2010	185,096	27,419	—	249,172	1,731	463,418

(1) This column represents the total grant date fair value, computed in accordance with ASC 718, of stock options granted during fiscal year 2011. The assumptions used to calculate the value of the stock underlying the option awards are set forth in Note 7 of the Notes to the Consolidated Financial Statements attached hereto.

(2) Amounts consist of 401(k) matching contributions.

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Additional disclosure related to executive compensation required by Item 11 is hereby incorporated by reference from the information under the caption “Executive Compensation” contained our definitive Proxy Statement for the 2011 Annual Meeting of Stockholders.

### Outstanding Equity Awards at Fiscal Year-End

The following table provides information, with respect to the Named Executive Officers, concerning the Outstanding Equity Awards of the Company’s stock as of September 30, 2011. Note that the information in Item 11 reflect the adjustment related to the 1 for 10 reverse stock split which occurred on November 17, 2011.

	Option Awards (1)			
	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date
Christopher Anzalone	2,500	—	21.30	6/11/2018
	100,117	12,532	5.10	10/8/2019
	42,243	14,081	5.20	3/4/2020
	10,416	36,458	9.90	8/16/2020
Ken Myszkowski	10,676	14,323	7.00	11/16/19
	6,000	2,000	5.20	3/4/2020
	3,250	8,750	9.90	8/16/2020

- (1) All option awards were granted under the 2000 Stock Option Plan or the 2004 Equity Incentive Plan of the Company. Options are priced at the market closing price on the day of the award. Options have various vesting parameters, but generally vest within 48 months or less after the award is granted.

### Director Compensation

Directors who are also employees of the Company receive no separate compensation from the Company for their service as members of the Board. Non-employee directors currently receive a cash retainer of \$20,000 per year. Additionally, non-employee directors who have served on the Board for at least six months receive an automatic grant of non-qualified stock options to purchase 4,000 shares of Common Stock upon re-election each year. Based on the policies of their current employers, Dr. Perry and Dr. Given have waived their right to cash compensation and have waived their right to received stock option grants. The following table sets forth the total compensation paid to our directors in fiscal 2011.

Name	Fee Earned or Paid in Cash (\$)(1)	Option Awards (\$)(2)(3)	Total (\$)
Bruce Stewart (4)	\$ —	\$ —	\$ —
Edward Frykman	\$ 20,000	\$ 15,020	\$ 35,020
Charles McKenney	\$ 20,000	\$ 15,020	\$ 35,020
Mauro Ferrari	\$ —	\$ —	\$ —
Douglass Given	\$ —	\$ —	\$ —

- (1) Each non-employee director received \$5,000 per quarter for his service as a director. There are no additional payments for being a member of a committee. Mr. Ferrari and Mr. Given have declined to receive cash compensation.
- (2) This column represents the total grant date fair value, computed in accordance with ASC 718, of stock options granted during fiscal year 2011. The assumptions used to calculate the value of option awards are set forth under Note 7 to the Consolidated Financial Statements attached hereto.
- (3) Annual option grant to non-employee directors vest one year from date of grant. At September 30, 2011, Mr. Frykman had outstanding option grants to purchase 30,500 shares at prices ranging from \$4.90 to \$20.20; Mr. McKenney had outstanding option grants to purchase 28,000 shares at prices ranging from \$4.90 to \$20.20; and Mr. Ferrari had outstanding option grants to purchase 24,843 shares at prices ranging from \$9.60 to \$28.70.
- (4) Excludes \$50,000 paid to Mr. Stewart in his role as Executive Chairman of the Company.

**ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.**

The following table sets forth the beneficial ownership of the Company's Common Stock as of November 30, 2011, by (i) each of the named executive officers named in the table under "Executive Compensation and Related Information," (ii) each director, (iii) all current directors and executive officers as a group, and (iv) the holders of greater than 5% of our total shares outstanding known to us. Unless otherwise specified in the footnotes to the table below, the persons and entities named in the table have sole voting and investment power with respect to all shares beneficially owned, subject to community property laws, where applicable and the address of each stockholder is c/o Arrowhead Research Corporation, 225 South Lake Avenue, Suite 300, Pasadena, California 91101. All information in Item 12 has been adjusted to reflect the 1 for 10 reverse stock split which was effected on November 17, 2011.

	Number and Percentage of Shares Beneficially Owned (1)	
	Shares	Percentage
<b>5% Beneficial Owners</b>		
M. Robert Ching (2)	1,042,068	9.9%
Roche Finance Ltd. (3)	901,702	8.6%
Galloway Ltd. (4)	727,233	6.9%
Vermögensverwaltungs - Gesellschaft Zurich (5)	675,000	6.4%
<b>Executive Officers and Directors</b>		
R. Bruce Stewart (6)	137,608	1.3%
Chris Anzalone (7)	250,836	2.4%
Kenneth Myszkowski (8)	25,843	*
Edward Frykman (9)	33,042	*
Charles McKenney (10)	24,353	*
Mauro Ferrari (11)	26,797	*
Douglass Given	—	—
All executive officers and directors as a group (7 persons) (12)	498,479	4.7%

\* Less than 1%

- (1) Based on 10,525,941 common shares issued and outstanding as of November 30, 2011. Shares not outstanding but deemed beneficially owned by virtue of the right of a person to acquire them as of November 30, 2011, or within sixty days of such date, are treated as outstanding only when determining the percentage owned by such individual and when determining the percentage owned by a group.
- (2) Includes 793,611 shares of common stock and 111,039 shares of common stock issuable upon the exercise of common stock purchase warrants, of which 45,600 shares of common stock, and 18,240 shares of common stock issuable upon the exercise of common stock purchase warrants are held by BBB Assets for which M. Robert Ching holds investment and voting control. Also includes 137,418 shares of common stock issuable upon conversion of Series A Preferred Stock, including additional shares of Series A Preferred Stock issuable in in-kind distribution as payment of dividends through March 31, 2012, conversion of which is subject to stockholder approval. Certain of the warrants and the conversion of the preferred stock are subject to a contractual blocker whereby the right to exercise or convert such warrant or preferred stock is limited such that Dr. and Mrs. Ching will not have greater than 9.99% beneficial ownership of the outstanding common stock. Warrants to purchase 746,628 shares are currently not exercisable due to this limitation.
- (3) Carole Nuechterlein, Head of Roche Venture Fund, holds voting and investment control with respect to the shares owned by Roche Finance, Ltd. The address for Roche Finance Ltd. is Grenzacherstrasse 124, 4058 Basel Switzerland.
- (4) Denham Eke holds voting and investment control with respect to the shares owned by Galloway, Ltd. The address for Galloway, Ltd. is Viking House, Nelson Street, Douglas, Isle of Man, IM1 2AH
- (5) Markus Winkler holds voting and investment control with respect to the shares owned by Vermögensverwaltungs - Gesellschaft Zurich (VGZ), the address for VGZ is Mainaustrasse 30, CH - 8034 Zurich Switzerland
- (6) Includes 86,458 shares issuable upon the exercise of stock options that are exercisable within 60 days of November 30, 2011.
- (7) Includes 184,489 shares issuable upon the exercise of stock options, and 32,172 shares issuable upon the exercise of common stock purchase warrants that are exercisable within 60 days of November 30, 2011.
- (8) Includes 24,342 shares issuable upon the exercise of stock options that are exercisable within 60 days of November 30, 2011.
- (9) Includes 26,041 shares issuable upon the exercise of stock options that are exercisable within 60 days of November 30, 2011.
- (10) Includes 23,333 shares issuable upon the exercise of stock options that are exercisable within 60 days of November 30, 2011.
- (11) Includes 24,845 shares issuable upon the exercise of stock options that are exercisable within 60 days of November 30, 2011.
- (12) Includes 369,511 shares issuable upon the exercise of stock options, and 32,112 shares issuable upon the exercise of common stock purchase warrants that are exercisable within 60 days of November 30, 2011.

**EQUITY COMPENSATION PLAN INFORMATION**

The following table provides information as of September 30, 2011 with respect to shares of our Common Stock that may be issued under our equity compensation plans. On November 17, 2011, the Company effected a 1 for 10 reverse stock split. The share data in the table below are listed on a post-split basis.

<u>Plan Category</u>	<u>Equity Compensation Plan Information</u>		
	<u>Number of securities to be issued upon exercise of outstanding options, warrants and rights</u>	<u>Weighted average exercise price of outstanding options, warrants and rights</u>	<u>Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))</u>
Equity compensation plans approved by security holders <sup>(1)</sup>	729,096	\$ 9.03	394,548
Equity compensation plans not approved by security holders	N/A	N/A	—
<b>Total</b>	<b>729,096</b>		<b>394,548</b>

(1) Includes options outstanding representing 575,896 shares subject to the 2004 Equity Incentive Plan and 153,200 shares subject to the 2000 Option Plan. No shares are available for issuance under the 2000 option plan.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.**

As of September 30, 2011, a majority of the members of the Board are independent directors, as defined by the NASDAQ Marketplace Rules. The Board has determined that all of the Company's directors are independent, except Mr. Stewart, the Company's Executive Chairman and former Chief Executive Officer, and Dr. Anzalone, the Company's Chief Executive Officer. Effective upon the hiring of Dr. Bruce Given as the Company's Chief Operating Officer on October 26, 2011, Dr. Doug Given is no longer considered an independent director under Nasdaq Marketplace Rules. With the appointment of Michael Perry as a member of the Company's Board of Directors and Audit Committee on December 19, 2011, a majority of independent directors was restored and compliance with Nasdaq's Marketplace Rules was regained. Dr. Perry was also appointed to each of the Compensation and Nominating Committees concurrent with his appointment. Independent directors do not receive consulting, legal or other fees from the Company, other than Board compensation.

Nanotope and Leonardo were co-founded by the Company's President and Chief Executive Officer, Dr. Christopher Anzalone, who beneficially owns approximately 14.2% and 15.9% of the outstanding voting securities of Nanotope and Leonardo, respectively. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Nanotope or Leonardo. Dr. Anzalone has the right to appoint a representative to the Board of Directors of each Nanotope and Leonardo. Dr. Anzalone is serving as the President and Chief Executive Officer of Nanotope. Dr. Anzalone has not received any compensation for his work on behalf of Nanotope or Leonardo since joining the Company on December 1, 2007.

During fiscal 2011, a portion of Arrowhead employee salary costs, including Dr. Anzalone's salary and administrative overhead, was charged to Nanotope and Leonardo for management and administrative services provided by Arrowhead to Nanotope and Leonardo. During fiscal 2011, the charge for services provided to Nanotope and Leonardo were \$313,282 and \$168,403, respectively. In addition, Arrowhead made cash advances to Nanotope of \$432,502 and to Leonardo of \$100,000 during fiscal 2011. The majority of the balance due Arrowhead is expected to be repaid in cash or converted to equity in fiscal 2012. In addition, the Bruce Given, Chief Operating Officer and CEO of Leonardo, Bruce Given, is the brother of Doug Given, a member of Arrowhead's Board of Directors. Doug Given has no financial interest in Leonardo.

In August 2010, the Company retained Mr. Vincent Anzalone, the brother of Arrowhead's Chief Executive Officer, as a consultant for the Company, focusing on business development and market analysis. Mr. Vincent Anzalone was paid \$20,000 during the fiscal year ended September 30, 2010, and \$120,000 during the fiscal year ended September 30, 2011. Since October 1, 2011 through the date of this filing, December 20, 2011, Mr. Vincent Anzalone was paid \$30,000.

**ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

The Audit Committee regularly reviews and determines whether specific projects or expenditures with our independent auditors, Rose, Snyder & Jacobs (RS&J), may potentially affect their independence. The Audit Committee's policy is to pre-approve all audit and permissible non-audit services provided by RS&J. Pre-approval is generally provided by the Audit Committee for up to one year, detailed to the particular service or category of services to be rendered and is generally subject to a specific budget. The Audit Committee may also pre-approve additional services of specific engagements on a case-by-case basis. All engagements of our independent registered public accounting firm in 2011 and 2010 were pre-approved by the audit committee.

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The following table sets forth the aggregate fees invoiced by RS&J for the fiscal years ended September 30, 2011, and September 30, 2010:

	<u>Year Ended September 30,</u>	
	<u>2011</u>	<u>2010</u>
Audit fees (1)	\$ 116,200	\$ 126,200
Audit-related fees (2)	16,150	76,300
Tax fees (3)	20,085	47,050
Total	<u>\$ 152,435</u>	<u>\$ 249,550</u>

(1) Fees invoiced by RS&J include year-end audit and quarterly reviews of Form 10-Q.

(2) Fees invoiced by RS&J related to Arrowhead Comfort Letter and Consents, and other agreed-upon procedures.

(3) This category consists of professional services rendered by RS&J for tax return preparation.

## **PART IV**

### **ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

The following documents are filed as part of this Annual Report on Form 10-K:

#### **(1) Financial Statements.**

See Index to Financial Statements and Schedule on page F-1.

#### **(2) Financial Statement Schedules.**

See Index to Financial Statements and Schedule on page F-1. All other schedules are omitted as the required information is not present or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements or notes thereto.

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### (3) Exhibits.

The following exhibits are filed (or incorporated by reference herein) as part of this Annual Report on Form 10-K:

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
2.1	Stock and Asset Purchase Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011*†		
3.1	Certificate of Incorporation of InterActive Group, Inc., a Delaware corporation, dated February 13, 2001	Schedule 14C, as Exhibit A	December 22, 2000
3.2	Certificate of Amendment to Certificate of Incorporation of InterActive Group, Inc. (effecting, among other things a change in the corporation's name to "Arrowhead Research Corporation"), filed with the Secretary of State of the State of Delaware on January 12, 2004	Schedule 14C, as Exhibit 1	December 22, 2003
3.3	Certificate of Amendment to Certificate of Incorporation of Arrowhead Research Corporation, dated January 25, 2005	Form 10-QSB for the quarter ended December 31, 2004, as Exhibit 3.4	February 11, 2005
3.4	Certificate of Amendment to Certificate of Incorporation of Arrowhead Research Corporation, dated October 13, 2009	Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 3.4	December 22, 2009
3.5	Series A Certificate of Designations, dated October 25, 2011	Current Report on Form 8-K, as Exhibit 3.1	October 26, 2011
3.6	Certificate of Amendment to Certificate of Incorporation of Arrowhead Research Corporation, dated November 17, 2011	Current Report on Form 8-K, as Exhibit 3.1	November 17, 2011
3.7	Bylaws	Schedule 14C, as Exhibit B	December 22, 2000
3.8	Amendment No. 1 to the Bylaws of Arrowhead Research Corporation	Current Report on Form 8-K, as Exhibit 3.1	April 27, 2010
4.1	Form of Registration Rights Agreement, July and August 2009	Current Report on Form 8-K, as Exhibit 10.2	July 17, 2009
4.2	Form of Registration Rights Agreement, dated December 11, 2009	Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 4.2	December 22, 2009
4.3	Form of Warrant to Purchase Shares of Common Stock expiring in July and August 2013	Current Report on Form 8-K, as Exhibit 10.2	August 26, 2008
4.4	Form of Common Stock Warrant expiring in September 2013	Current Report on Form 8-K, as Exhibit 10.2	September 11, 2008
4.5	Form of Warrant to Purchase Capital Stock expiring June 2014	Current Report on Form 8-K, as Exhibit 4.1	July 17, 2009
4.6	Form of Warrant to Purchase Capital Stock expiring December 2014	Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 4.7	December 22, 2009
4.7	Form of Warrant to Purchase Common Stock expiring May 2017	Current Report on Form 8-K, as Exhibit 4.1	May 30, 2007

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<u>Exhibit Number</u>	<u>Description</u>	<u>Incorporated by Reference Herein</u>	
		<u>Form</u>	<u>Date</u>
4.8	Form of Warrant to Purchase Common Stock, dated June 2010	Current Report on Form 8-K, as Exhibit 4.1	June 18, 2010
4.9	Form of Registration Rights Agreement between Arrowhead Research Corporation and Lincoln Park Capital Fund, LLC, dated October 20, 2011	Current Report on Form 8-K, as Exhibit 10.2	October 26, 2011
4.10	Form of Registration Rights Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011*		
4.11	Form of Warrant to Purchase Shares of Capital Stock of Arrowhead Research Corporation expiring September 16, 2015	Current Report on Form 8-K, as Exhibit 4.1	September 22, 2010
4.12	Form of Common Stock Certificate	Amendment No. 2 to Registration Statement on Form S-1, as Exhibit 4.7	September 11, 2009
4.13	Form of Series A Preferred Stock Certificate*		
10.1**	Arrowhead Research Corporation (fka InterActive, Inc.) 2000 Stock Option Plan	Schedule 14C, as Exhibit D	December 22, 2000
10.2**	Arrowhead Research Corporation 2004 Equity Incentive Plan, as amended	Schedule 14C, as Annex A	April 30, 2010
10.3**	Executive Incentive Plan, adopted December 12, 2006	Annual Report on Form 10-K for the fiscal year ended September 30, 2006, as Exhibit 10.11	December 14, 2006
10.4**	Compensation Policy for Non-Employee Directors, as amended	Annual Report on Form 10-K for the fiscal year ended September 30, 2006, as Exhibit 10.12	December 14, 2006
10.5**	Severance Agreement by and between Arrowhead and R. Bruce Stewart, dated May 24, 2007	Current Report on Form 8-K, as Exhibit 10.1	May 30, 2007
10.6**	Amendment to Severance Agreement between Arrowhead and R. Bruce Stewart, effective May 12, 2009	Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 10.6	December 22, 2009
10.7**	Employment Agreement between Arrowhead and Dr. Christopher Anzalone, dated June 11, 2008	Current Report on Form 8-K, as Exhibit 10.1	June 13, 2008
10.8**	Amendment to Employment Agreement between Arrowhead and Dr. Christopher Anzalone, effective May 12, 2009	Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 10.8	December 22, 2009
10.9	Insert Therapeutics, Inc. Amended and Restated Investors' Rights Agreement, dated April 17, 2008	Current Report on Form 8-K, as Exhibit 10.3	April 23, 2008
10.10	Second Amended and Restated Investors' Rights Agreement, by and between Nanotope, Inc and the Investors and Stockholders listed therein, dated July 23, 2008	Current Report on Form 8-K, as Exhibit 10.2	July 25, 2008
10.11	Form of Unsecured Convertible Promissory Note Agreement, dated November 26, 2008	Current Report on Form 8-K, as Exhibit 10.1	December 3, 2008

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Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
10.12	Platform Agreement by and between Calando Pharmaceuticals, Inc and Cerulean Pharma Inc., dated as of June 23, 2009 †	Form 10-Q for the quarter ended June 30, 2009, as Exhibit 10.1	August 10, 2009
10.13	IT-101 Agreement by and between Calando Pharmaceuticals, Inc and Cerulean Pharma, Inc., dated as of June 23, 2009†	Form 10-Q for the quarter ended June 30, 2009, as Exhibit 10.2	August 10, 2009
10.14	Asset Purchase Agreement between Tego BioSciences, Inc. and Luna Innovations, Inc., dated November 13, 2009	Form 10-Q for the quarter ended December 31, 2009 as Exhibit 10.1	February 11, 2010
10.15	Form of Exchange Agreement between Arrowhead Research Corporation and several investors, dated September 28, 2009	Form 10-Q for the quarter ended December 31, 2009, as Exhibit 10.2	February 11, 2010
10.16	Form of Subscription Agreement between Arrowhead Research Corporation and certain investors, dated December 11, 2009	Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 10.24	December 22, 2009
10.17**	Amendment to Employment Agreement between Arrowhead and R. Bruce Stewart, effective May 27, 2010	Current Report on Form 8-K, as Exhibit 10.1	May 28, 2010
10.18	Form of Subscription Agreement between Arrowhead and certain investors, dated June 17, 2010	Current Report on Form 8-K, as Exhibit 10.2	June 18, 2010
10.19	Form of Exchange Agreement between Arrowhead and certain stockholders, dated September 16, 2010	Current Report on Form 8-K, as Exhibit 10.1	September 22, 2010
10.20	License and Enforcement Agreement between Unidym, Inc. and Samsung Electronics Co., Ltd., dated December 2010	Form 10-Q for the quarter ended December 31, 2010, as Exhibit 10.1	February 10, 2011
10.21	CNT Production Patent License Agreement between Unidym, Inc. and Samsung Electronics Co., Ltd., dated December 2010	Form 10-Q for the quarter ended December 31, 2010, as Exhibit 10.2	February 10, 2011
10.22	Intellectual Property Purchase and Business Cooperation Agreement between Unidym, Inc. and Samsung Electronics Co., Ltd., dated December 2010	Form 10-Q for the quarter ended December 31, 2010, as Exhibit 10.3	February 10, 2011
10.23	Patent and Technology License Agreement between Arrowhead Research Corporation and the Board of Regents of The University of Texas System, dated December 14, 2010	Form 10-Q for the quarter ended December 31, 2010, as Exhibit 10.4	February 10, 2011
10.24	Form of Series A Preferred Stock Purchase Agreement among Ablaris Therapeutics Inc. and certain investors, dated January 2011	Form 10-Q for the quarter ended March 31, 2011, as Exhibit 10.2	May 12, 2011
10.25	Stock Purchase Agreement between Arrowhead Research Corporation and Calando Pharmaceuticals, Inc., dated January 10, 2011	Form 10-Q for the quarter ended March 31, 2011, as Exhibit 10.1	May 12, 2011

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<u>Exhibit Number</u>	<u>Description</u>	<u>Incorporated by Reference Herein</u>	
		<u>Form</u>	<u>Date</u>
10.26	Agreement and Plan of Merger among Wisepower Co., Ltd., Unicycle Acquisition Corp, Unidym, Inc. and Arrowhead Research Corporation, dated January 17, 2011	Current Report on Form 8-K, as Exhibit 10.1	January 21, 2011
10.27	Stock Purchase Agreement between Wisepower Co., Ltd. and Arrowhead Research Corporation, dated January 17, 2011	Current Report on Form 8-K, as Exhibit 10.2	January 21, 2011
10.28	Bond Purchase Agreement between Wisepower Co., Ltd. and Arrowhead Research Corporation, dated January 17, 2011	Current Report on Form 8-K, as Exhibit 10.3	January 21, 2011
10.29	Form of Subscription Agreement between Arrowhead Research Corporation and certain Investors, dated September 2011	Current Report on Form 8-K, as Exhibit 10.1	October 6, 2011
10.30	Form of Series A Subscription Agreement between Arrowhead Research Corporation and certain investors	Current Report on Form 8-K, as Exhibit 10.3	October 26, 2011
10.31	Form of Purchase Agreement between Arrowhead Research Corporation and Lincoln Park Capital Fund, LLC, dated October 20, 2011	Current Report on Form 8-K, as Exhibit 10.1	October 26, 2011
10.32	Form of Common Stock Subscription Agreement between Arrowhead Research Corporation certain Investors, dated October 21, 2011	Current Report on Form 8-K, as Exhibit 10.4	October 26, 2011
10.33	Non-Exclusive License Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011*†		
10.34	Form of Investor Subscription Agreement between Arrowhead Research Corporation and Lincoln Park Capital Fund, LLC, dated October 24, 2011	Current Report on Form 8-K, as Exhibit 10.1	October 27, 2011
10.35	License and Collaboration Agreement, dated July 8, 2007* †		
10.36	Collaboration Agreement by and among Alnylam Pharmaceuticals, Inc. and F. Hofmann-La Roche Ltd and Hoffman-La Roche Inc., dated October 29, 2009* †		
21.1	List of Subsidiaries*		
23.1	Consent of Independent Public Registered Accounting Firm*		
24.1	Power of Attorney (contained on signature page)		
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002*		

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<b>Exhibit Number</b>	<b>Description</b>	<b>Incorporated by Reference Herein</b>	
		<b>Form</b>	<b>Date</b>
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002*		
32.1	Certification by Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*		
32.2	Certification by Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*		
101.INS	XBRL Instance Document*		
101.SCH	XBRL Schema Document*		
101.CAL	XBRL Calculation Linkbase Document*		
101.LAB	XBRL Label Linkbase Document*		
101.PRE	XBRL Presentation Linkbase Document*		
101.DEF	XBRL Definition Linkbase Document*		

Pursuant to Rule 406T of Regulation S-T, the Interactive Data Files included in Exhibit 101 hereto are deemed not filed or a part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act of 1933, as amended, are deemed not filed for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, and otherwise are not subject to liability under those sections.

\* Filed herewith

\*\* Indicates compensation plan, contract or arrangement.

† Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.



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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Stockholders of Arrowhead Research Corporation

We have audited the accompanying consolidated balance sheets of Arrowhead Research Corporation (a Delaware corporation) and Subsidiaries (the "Company") as of September 30, 2011 and 2010 and the related consolidated statements of operations, stockholders' equity and cash flows for the years ended September 30, 2011, and 2010 and for the period from May 7, 2003 (inception) through September 30, 2011. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Arrowhead Research Corporation and Subsidiaries as of September 30, 2011 and 2010, and the consolidated results of their operations and their cash flows for the years ended September 30, 2011 and 2010, and for the period from May 7, 2003 (inception) through September 30, 2011 in conformity with accounting principles generally accepted in the United States of America.

Rose, Snyder & Jacobs  
A Corporation of Certified Public Accountants

Encino, California

December 20, 2011

**Arrowhead Research Corporation and Subsidiaries**  
**(A Development Stage Company)**  
**Consolidated Balance Sheets**

	September 30, 2011	September 30, 2010
<b>ASSETS</b>		
<b>CURRENT ASSETS</b>		
Cash and cash equivalents	\$ 7,507,389	\$ 6,847,162
Trade receivable, net of allowance for doubtful accounts of \$90,789 at September 30, 2010	—	58,864
Other receivables	1,608,382	871,819
Prepaid expenses and other current assets	110,818	353,930
Marketable securities	634,585	—
<b>TOTAL CURRENT ASSETS</b>	<b>9,861,174</b>	<b>8,131,775</b>
<b>PROPERTY AND EQUIPMENT</b>		
Computers, office equipment and furniture	285,266	335,784
Research equipment	3,515	752,850
Software	77,020	150,445
Leasehold improvements	—	78,594
	365,801	1,317,673
Less: Accumulated depreciation and amortization	(340,364)	(1,176,404)
<b>PROPERTY AND EQUIPMENT, NET</b>	<b>25,437</b>	<b>141,269</b>
<b>OTHER ASSETS</b>		
Rent deposit	—	34,735
Patents	1,731,211	2,046,836
Note Receivable, net	2,272,868	—
Derivative asset	161,125	—
Investment in Nanotope Inc., equity basis	1,649,748	1,812,927
Investment in Leonardo Biosystems Inc., at cost	187,000	187,000
<b>TOTAL OTHER ASSETS</b>	<b>6,001,952</b>	<b>4,081,498</b>
<b>TOTAL ASSETS</b>	<b>\$ 15,888,563</b>	<b>\$ 12,354,542</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
<b>CURRENT LIABILITIES</b>		
Accounts payable	\$ 576,809	\$ 681,563
Accrued expenses	864,511	494,736
Accrued payroll and benefits	195,649	191,425
Derivative liabilities	944,980	2,408,522
Note payable	—	500,000
<b>TOTAL CURRENT LIABILITIES</b>	<b>2,581,949</b>	<b>4,276,246</b>
<b>LONG-TERM LIABILITIES</b>		
Other non-current liabilities	135,660	—
Note payable	606,786	—
<b>TOTAL LONG-TERM LIABILITIES</b>	<b>742,446</b>	<b>—</b>
Commitments and contingencies		
<b>STOCKHOLDERS' EQUITY</b>		
Arrowhead Research Corporation stockholders' equity:		
Preferred stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, \$0.001 par value; 145,000,000 shares authorized; 8,642,286 and 7,172,014 shares issued and outstanding as of September 30, 2011 and September 30, 2010, respectively	86,423	71,735
Additional paid-in capital	127,476,435	119,716,834
Subscription receivable	(900,000)	—
Accumulated deficit during the development stage	(113,871,752)	(110,742,867)
Total Arrowhead Research Corporation stockholders' equity	12,791,106	9,045,702
Noncontrolling interest	(226,938)	(967,406)
<b>TOTAL STOCKHOLDERS' EQUITY</b>	<b>12,564,168</b>	<b>8,078,296</b>
<b>TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY</b>	<b>\$ 15,888,563</b>	<b>\$ 12,354,542</b>

*The accompanying notes are an integral part of these consolidated financial statements.*

**Arrowhead Research Corporation and Subsidiaries**  
**(A Development Stage Company)**  
**Consolidated Statements of Operations**

	Year Ended September 30,		May 7, 2003 (Inception) to September 30, 2011
	2011	2010	
<b>REVENUE</b>	<b>\$ 296,139</b>	<b>\$ —</b>	<b>\$ 3,991,959</b>
<b>OPERATING EXPENSES</b>			
Salaries	1,408,366	1,146,394	19,977,209
General and administrative expenses	3,821,550	2,490,725	25,590,815
Research and development	3,277,760	529,601	40,428,729
Stock-based compensation	1,376,921	1,424,293	12,340,064
Patent amortization	241,808	241,808	1,781,944
<b>TOTAL OPERATING EXPENSES</b>	<b>10,126,405</b>	<b>5,832,821</b>	<b>100,118,761</b>
<b>OPERATING LOSS</b>	<b>(9,830,266)</b>	<b>(5,832,821)</b>	<b>(96,126,802)</b>
<b>OTHER INCOME (EXPENSE)</b>			
Loss on equity of investments - Nanotope	(163,180)	(219,540)	(723,253)
Gain on sale of stock in subsidiary	—	—	2,292,800
Gain/(loss) on sale of fixed assets, net	—	1,772	(127,088)
Realized and unrealized gain (loss) on marketable securities	(261,219)	—	121,045
Interest income (expense), net	86,530	(22,783)	2,714,478
Change in value of derivatives	1,133,127	1,761,385	2,894,512
Other income	250,000	—	250,000
<b>TOTAL OTHER INCOME (EXPENSE)</b>	<b>1,045,258</b>	<b>1,520,834</b>	<b>7,422,494</b>
<b>LOSS FROM CONTINUING OPERATIONS BEFORE INCOME TAXES</b>	<b>(8,785,008)</b>	<b>(4,311,987)</b>	<b>(88,704,308)</b>
Provision for income taxes	—	—	—
<b>LOSS FROM CONTINUING OPERATIONS</b>	<b>(8,785,008)</b>	<b>(4,311,987)</b>	<b>(88,704,308)</b>
Income (loss) from discontinued operations	1,373,396	(2,645,051)	(47,546,562)
Gain on disposal of discontinued operations	3,919,213	—	4,708,588
<b>NET INCOME (LOSS) FROM DISCONTINUED OPERATIONS</b>	<b>5,292,609</b>	<b>(2,645,051)</b>	<b>(42,837,974)</b>
<b>NET LOSS</b>	<b>(3,492,399)</b>	<b>(6,957,038)</b>	<b>(131,542,282)</b>
Net (income) loss attributable to noncontrolling interests	363,514	1,182,990	17,834,490
<b>NET LOSS ATTRIBUTABLE TO ARROWHEAD</b>	<b>\$ (3,128,885)</b>	<b>\$ (5,774,048)</b>	<b>\$ (113,707,792)</b>
<b>Earnings per share - basic:</b>			
Income (loss) from continuing operations attributable to Arrowhead common shareholders	\$ (1.18)	\$ (0.49)	
Income (loss) from discontinued operations attributable to Arrowhead common shareholders	0.74	(0.41)	
<b>Net loss attributable to Arrowhead shareholders</b>	<b>\$ (0.44)</b>	<b>\$ (0.90)</b>	
Weighted average shares outstanding	7,181,121	6,434,245	
<b>Earnings per share - diluted:</b>			
Income (loss) from continuing operations attributable to Arrowhead common shareholders	\$ (1.08)	\$ (0.49)	
Income (loss) from discontinued operations attributable to Arrowhead common shareholders	0.68	(0.41)	
<b>Net loss attributable to Arrowhead shareholders</b>	<b>\$ (0.40)</b>	<b>\$ (0.90)</b>	
Weighted average shares outstanding	7,830,407	6,434,245	

*The accompanying notes are an integral part of these consolidated financial statements.*

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**Arrowhead Research Corporation and Subsidiaries**  
**(A Development Stage Company)**  
**Consolidated Statement of Stockholders' Equity**  
**From inception to September 30, 2011**

	Common Stock		Additional Paid-in Capital	Subscription Receivable	Accumulated Deficit during the Development Stage	Noncontrolling interest	Totals
	Shares	Amount					
<b>Initial Issuance of Stock:</b>							
Common stock & warrants issued for cash @ \$0.01 per unit	300,000	\$ 3,000	\$ —	\$ —	\$ —	\$ —	\$ 3,000
Common stock & warrants issued for cash @ \$10.00 per unit	168,000	1,680	1,678,320	—	—	—	1,680,000
Stock issuance cost charged to additional paid-in capital	—	—	(168,000)	—	—	—	(168,000)
Net loss for period from inception to September 30, 2003	—	—	—	—	(95,238)	—	(95,238)
<b>Balance at September 30, 2003</b>	<b>468,000</b>	<b>4,680</b>	<b>1,510,320</b>	<b>—</b>	<b>(95,238)</b>	<b>—</b>	<b>1,419,762</b>
Exercise of stock options	7,500	75	14,925	—	—	—	15,000
Common stock & warrants issued for cash @ \$10.00 per unit	47,500	475	474,525	—	—	—	475,000
Common stock & warrants issued for marketable securities @ \$10.00 per unit	50,000	500	499,500	—	—	—	500,000
Stock issuance cost charged to additional paid-in capital	—	—	(96,500)	—	—	—	(96,500)
Common stock and warrants issued for cash @ \$15.00 per unit	660,879	6,609	9,906,573	—	—	—	9,913,182
Common stock issued in reverse acquisition	70,553	706	(151,175)	—	—	—	(150,469)
Common stock issued as a gift for \$10.90 per share	15,000	163	162,587	—	—	—	162,750
Common stock and warrants issued as stock issuance cost @ \$15.00 per unit	35,623	356	533,988	—	—	—	534,344
Stock issuance cost charged to additional paid-in capital	—	—	(991,318)	—	—	—	(991,318)
Exercise of stock option @ \$2.00 per share	7,500	75	14,925	—	—	—	15,000
Exercise of stock options @ \$10.00 per share	600	6	5,994	—	—	—	6,000
Stock-based compensation	—	—	175,653	—	—	—	175,653
Net loss for the year ended September 30, 2004	—	—	—	—	(2,528,954)	1,777,699	(751,255)
<b>Balance at September 30, 2004</b>	<b>1,363,155</b>	<b>13,645</b>	<b>12,059,997</b>	<b>—</b>	<b>(2,624,192)</b>	<b>1,777,699</b>	<b>11,227,149</b>
Exercise of warrants @ \$15.00 per share	1,381,289	13,813	20,705,522	—	—	—	20,719,335
Exercise of stock options @ \$10.00 per share	2,500	25	24,975	—	—	—	25,000
Common stock issued to purchase Insert Therapeutics share @ \$39.80 per share	50,226	502	1,999,498	—	—	—	2,000,000
Common stock issued for services	1,250	12	49,988	—	—	—	50,000
Stock-based compensation	—	—	508,513	—	—	—	508,513
Change in percentage of ownership in subsidiary	—	—	230,087	—	—	—	230,087
Net loss for the year ended September 30, 2005	—	—	—	—	(6,854,918)	121,491	(6,733,427)
<b>Balance at September 30, 2005</b>	<b>2,798,419</b>	<b>27,997</b>	<b>35,578,580</b>	<b>—</b>	<b>(9,479,110)</b>	<b>1,899,190</b>	<b>28,026,657</b>
Exercise of stock options	11,579	116	341,421	—	—	—	341,537
Common stock issued @ \$48.80 per share	20,485	205	999,795	—	—	—	1,000,000
Common stock issued @ \$38.40 per share	1,500	15	57,585	—	—	—	57,600
Common stock issued @ \$35.00 per share	559,000	5,590	19,539,410	—	—	—	19,545,000
Common stock issued @ \$59.10 per share	2,536	25	149,975	—	—	—	150,000
Common stock issued to purchase Calando Pharmaceuticals, Inc. @ \$51.70 per share	20,838	208	1,077,125	—	—	—	1,077,333
Stock-based compensation	—	—	1,369,478	—	—	—	1,369,478
Net loss for the year ended September 30, 2006	—	—	—	—	(18,997,209)	(964,752)	(19,961,961)

<b>Balance at September 30, 2006</b>	<b>3,414,359</b>	<b>34,156</b>	<b>59,113,369</b>	<b>—</b>	<b>(28,476,319)</b>	<b>934,438</b>	<b>31,605,644</b>
Exercise of stock options	18,616	186	434,541	—	—	—	434,727
Common stock issued @ \$57.80 per share, net	284,945	2,849	15,149,366	—	—	—	15,152,215
Arrowhead's increase in proportionate share of Insert Therapeutics' equity	—	—	2,401,394	—	—	—	2,401,394
Common stock issued for purchase of Carbon Nanotechnologies, Inc. @ \$37.70 per share	143,122	1,431	5,398,569	—	—	—	5,400,000
Stock-based compensation	—	—	2,175,544	—	—	—	2,175,544
Net loss for the year ended September 30, 2007	—	—	—	—	(29,931,118)	(781,829)	(30,712,947)
<b>Balance at September 30, 2007</b>	<b>3,861,042</b>	<b>38,622</b>	<b>84,672,783</b>	<b>—</b>	<b>(58,407,437)</b>	<b>152,609</b>	<b>26,456,577</b>
Exercise of stock options	10,536	106	289,921	—	—	—	290,027
Common stock issued at approximately \$18.00 per share, net	386,399	3,867	6,956,718	—	—	—	6,960,585
Arrowhead's increase in proportionate share of Unidym's equity	—	—	1,720,962	—	—	—	1,720,962
Common stock issued @ \$27.20 per share to Rice University	5,000	50	135,950	—	—	—	136,000
Common stock issued @ \$28.30 per share to purchase shares of Unidym, Inc.	7,055	71	199,929	—	—	—	200,000
Common stock issued @ \$29.50 per share to purchase MASA Energy, LLC	10,505	105	309,895	—	—	—	310,000
Common stock issued @ \$21.90 per share to Unidym for the acquisition of Nanoconduction	11,416	114	249,886	—	—	—	250,000
Common stock issued @ \$21.80 per share	1,500	15	32,685	—	—	—	32,700
Stock-based compensation	—	—	3,187,397	—	—	—	3,187,397
Net loss for the year ended September 30, 2008	—	—	—	—	(27,089,030)	(152,609)	(27,241,639)
<b>Balance at September 30, 2008</b>	<b>4,293,452</b>	<b>42,950</b>	<b>97,756,126</b>	<b>—</b>	<b>(85,496,467)</b>	<b>—</b>	<b>12,302,609</b>
Common Stock issued @ \$5.50 per share to Unidym stockholder in exchange for Unidym's shares	205,839	2,059	1,131,617	—	—	—	1,133,676
Common Stock issued @ \$5.20 per share to TEL Ventures in exchange for Unidym's shares	222,222	2,222	1,156,111	—	—	—	1,158,333
Reclassification of former Unidym mezzanine debt to equity	—	—	2,000,000	—	—	—	2,000,000
Arrowhead's increase in proportionate share of Calando's equity	—	—	2,120,250	—	—	—	2,120,250
Common stock issued @ \$3.00 per share	919,664	9,197	2,749,796	—	—	—	2,758,993
Change in percentage ownership in subsidiary	—	—	16,297	—	—	—	16,297
Stock-based compensation	—	—	2,676,170	—	—	—	2,676,170
Issuance of Preferred Stock for Subscription in Unidym	—	—	300,000	(300,000)	—	—	—
Amortization of discount on Unidym Series D Preferred Stock	—	—	163,960	—	(163,960)	—	—
Net loss for the year ended September 30, 2009	—	—	—	—	(19,308,392)	—	(19,308,392)
<b>Balance at September 30, 2009</b>	<b>5,641,177</b>	<b>56,428</b>	<b>110,070,327</b>	<b>(300,000)</b>	<b>(104,968,819)</b>	<b>—</b>	<b>4,857,936</b>
Exercise of stock options	688	7	7,624	—	—	—	7,631
Issuance of Preferred Stock for Subscription in Unidym	—	—	—	300,000	—	—	300,000
Issuance of Unidym's common stock to minority shareholders	—	—	245,345	—	—	54,655	300,000
Common stock issued @ \$6.30 per share	508,343	5,083	3,217,813	—	—	—	3,222,896
Common stock issued @ \$13.12 per share	659,299	6,593	3,692,078	—	—	—	3,698,671
Common Stock issued to Calando stockholders in exchange for Calando's shares	122,000	1,220	(160,667)	—	—	159,447	—
Common Stock issued to Unidym stockholders in exchange for Unidym's shares	15,318	153	(1,435)	—	—	1,282	—
Stock-based compensation	—	—	1,582,149	—	—	—	1,582,149
Exercise of warrants	225,189	2,251	1,063,600	—	—	200	1,066,051
Net loss for the year ended September 30, 2010	—	—	—	—	(5,774,048)	(1,182,990)	(6,957,038)
<b>Balance at September 30, 2010</b>	<b>7,172,014</b>	<b>71,735</b>	<b>119,716,834</b>	<b>—</b>	<b>(110,742,867)</b>	<b>(967,406)</b>	<b>8,078,296</b>
Exercise of warrants	8,656	87	43,192	—	—	—	43,279
Exercise of stock options	2,700	27	13,857	—	—	—	13,884

Divestiture of Unidym	—	—	—	—	—	254,275	254,275
Issuance of preferred stock in subsidiary	—	—	1,618,509	—	—	—	1,618,509
Change in percentage of ownership in subsidiary	—	—	(849,707)	—	—	849,707	—
Stock-based compensation	—	—	1,404,640	—	—	—	1,404,640
Common stock issued @ \$3.80 per share	1,458,917	14,574	4,629,110	—	—	—	4,643,684
Issuance of Common Stock for Subscription			900,000	(900,000)			—
Net loss for the year ended September 30, 2011	—	—	—	—	(3,128,885)	(363,514)	(3,492,399)
<b>Balance at September 30, 2011</b>	<b>8,642,286</b>	<b>\$86,423</b>	<b>\$127,476,435</b>	<b>\$ (900,000)</b>	<b>\$ (113,871,752)</b>	<b>\$ (226,938)</b>	<b>12,564,168</b>

*The accompanying notes are an integral part of these consolidated financial statements.*

**Arrowhead Research Corporation and Subsidiaries**  
**( A Development Stage Company )**  
**Consolidated Statements of Cash Flows**

	<u>Year ended September 30,</u>		<u>May 7, 2003</u> <u>(Date of inception) to</u> <u>September 30, 2011</u>
	<u>2011</u>	<u>2010</u>	
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>			
Net income (loss)	\$(3,492,399)	\$ (6,957,038)	\$ (131,542,282)
Net (income) loss attributable to noncontrolling interests	363,514	1,182,990	17,834,490
Net loss attributable to Arrowhead	(3,128,885)	(5,774,048)	(113,707,792)
(Income) loss from discontinued operations	(5,292,609)	2,645,051	42,837,974
Realized and unrealized (gain) loss on investments	261,218	—	(821,045)
(Gain) loss from sale of subsidiary	—	—	(306,344)
Loss on sale/donation of fixed assets	—	—	127,088
Stock issued as gift	—	—	298,750
Stock issued for professional services	193,885	—	442,882
Stock issued for in-process research and development	—	—	13,166,347
Change in value of derivatives	(1,133,127)	(1,761,385)	(2,894,512)
Purchased in-process research and development - Nanoconduction	—	—	2,685,208
Stock-based compensation	1,376,921	1,424,293	12,340,064
Depreciation and amortization	267,977	277,650	5,660,311
Amortization (accretion) of note discounts, net	(7,938)	—	(7,938)
Gain on sale of stock in subsidiary	—	—	(2,292,800)
Non-cash (gain) loss from equity investment	163,180	219,540	723,253
Noncontrolling interest	(363,514)	(1,182,990)	(17,834,490)
Gain on renegotiation of accrued severance	—	—	(726,500)
Changes in operating assets and liabilities:			
Receivables	—	—	(62,815)
Other receivables	(736,253)	(872,128)	(1,604,963)
Prepaid expenses	99,006	110,152	(142,568)
Other current assets	18,473	(114,833)	(96,360)
Deposits	—	60,105	(36,795)
Accounts payable	157,079	(203,253)	206,434
Accrued expenses	452,843	110,873	534,540
Accrued severance and other liabilities	15,751	7,556	974,365
NET CASH USED IN OPERATING ACTIVITIES OF CONTINUING OPERATIONS	(7,655,993)	(5,053,417)	(60,537,706)
<b>CASH FLOWS FROM INVESTING ACTIVITIES OF CONTINUING OPERATIONS:</b>			
Purchase of marketable securities - US Treasury Bills	—	—	(18,575,915)
Purchase of property and equipment	(9,674)	—	(3,565,599)
Purchase of MASA Energy, LLC	—	—	(250,000)
Minority equity investment	—	—	(2,000,000)
Cash paid for interest in Insert	—	—	(10,150,000)
Cash obtained from interest in Insert	—	—	10,529,594
Proceeds from sale of marketable securities - US Treasury Bills	—	—	18,888,265
Proceeds from sale of investments	1,534,687	—	2,804,600
Proceeds from sale of subsidiaries	—	—	359,375
Proceeds from sale of fixed assets	—	—	142,375
Payment for patents	—	—	(303,440)
Restricted cash	—	—	50,773
Cash transferred in sale of subsidiary	(1,700,398)	—	(1,700,398)
NET CASH USED IN INVESTING ACTIVITIES OF CONTINUING OPERATIONS	(175,385)	—	(3,770,370)
<b>CASH FLOWS FROM FINANCING ACTIVITIES OF CONTINUING OPERATIONS:</b>			
Proceeds from issuance of Calando debt	—	—	2,516,467
Proceeds from sale of stock in subsidiary	1,718,932	—	20,894,100
Proceeds from issuance of common stock and warrants, net	4,507,389	12,165,156	95,294,780
NET CASH PROVIDED BY FINANCING ACTIVITIES OF CONTINUING OPERATIONS	6,226,321	12,165,156	118,705,347
<b>Cash flows from discontinued operations:</b>			
Operating cash flows	2,265,284	(2,645,860)	(46,003,507)
Investing cash flows	—	487,593	790,625
Financing cash flows	—	(126,534)	(1,677,000)
<b>Net cash provided by (used in) discontinued operations:</b>	<b>2,265,284</b>	<b>(2,284,801)</b>	<b>(46,889,882)</b>
NET INCREASE IN CASH	660,227	4,826,938	7,507,389
<b>CASH AT BEGINNING OF PERIOD</b>	<b>6,847,162</b>	<b>2,020,224</b>	<b>—</b>
<b>CASH AT END OF PERIOD</b>	<b>\$ 7,507,389</b>	<b>\$ 6,847,162</b>	<b>\$ 7,507,389</b>
<b>Supplementary disclosures:</b>			
Interest paid	\$ 105,000	\$ —	\$ 230,419
Taxes paid	\$ 742,500	\$ —	\$ 742,500

*The accompanying notes are an integral part of these consolidated financial statements.*



**Arrowhead Research Corporation and Subsidiaries  
(A Development Stage Company)**

**Consolidated Statements of Cash Flows—(Continued)**

**SUPPLEMENT NON CASH TRANSACTIONS**

All Arrowhead share amounts have been adjusted to reflect the 1 for 10 reverse stock split effected on November 17, 2011.

On March 23, 2005, Arrowhead purchased 7,375,000 shares of Insert Therapeutics, Inc. common stock from two minority stockholders of Insert for 50,226 newly issued shares of Arrowhead Common Stock valued at \$2,000,000 based on the closing market price of Arrowhead Common Stock on NASDAQ on the date of the closing.

On March 31, 2006, Arrowhead purchased 964,000 shares of Calando Pharmaceuticals, Inc. common stock from minority stockholders of Calando for \$1,928,000 consisting of 20,838 newly issued shares of Arrowhead Common Stock valued at \$1,077,333 plus \$850,667 in cash. The 20,838 shares of Arrowhead Common Stock were valued based on the average closing price of Arrowhead's Common Stock on NASDAQ the ten trading days immediately prior to the date of the closing.

On April 20, 2007, Arrowhead purchased the Series E Preferred Stock of Carbon Nanotechnologies, Inc. in exchange for 143,122 shares of Arrowhead Common Stock with an estimated fair market value of \$5,400,000 based on the average closing price of Arrowhead's Common Stock on NASDAQ the ten trading days immediately prior to March 24, 2007, as set forth in the Agreement and Plan of Merger among Unidym, Carbon Nanotechnologies, Inc., Arrowhead, and others.

On April 23, 2008, Arrowhead purchased 200,000 shares of the Common Stock of Unidym Inc., in exchange for 7,054 shares of Arrowhead Common Stock with an estimated fair market value of \$200,000 based on the average closing price of Arrowhead's Common Stock on NASDAQ the ten trading days immediately prior to the date of the closing.

On April 29, 2008, Arrowhead purchased all of the membership units of MASA Energy, LLC for \$560,000. The purchase price consisted of 10,504 shares of Arrowhead Common Stock with an estimated fair market value of \$310,000 based on the average closing price of Arrowhead's Common Stock on NASDAQ the ten trading days immediately prior to the date of the closing, plus \$250,000 in cash.

On August 8, 2008, Unidym acquired all of the outstanding stock of Nanoconduction, Inc. in exchange for 11,411 shares of Arrowhead stock with an estimated fair market value of \$250,000.

On June 11, 2009, Arrowhead issued 132,462 shares of Common Stock with an estimated fair market value of \$688,802 in exchange for an equal number of Series A Preferred Stock of Unidym, with minority stockholders of Unidym.

On June 25, 2009, Arrowhead issued 194,444 shares of Common Stock with an estimated fair market value of \$972,222 in exchange for an equal number of Series C Preferred Stock of Unidym, with a minority stockholder of Unidym.

On September 22, 2009, Arrowhead issued 9,149 shares of Common Stock with an estimated fair market value of \$46,662 in exchange for an equal number of Series A Preferred Stock of Unidym with a minority stockholder of Unidym.

On September 28, 2009, Arrowhead issued 64,227 shares of Common Stock with an estimated fair market value of \$398,209 in exchange for 5,574 shares of Series A Preferred Stock and 636,699 shares of Series C Preferred Stock of Unidym, with several minority stockholders of Unidym.

On September 30, 2009, Arrowhead issued 27,777 shares of Common Stock with an estimated fair market value of \$186,111 in exchange for an equal number of Series C-1 Preferred Stock of Unidym, with a minority stockholder of Unidym.

In October and November 2009, Arrowhead issued 15,317 shares of Common Stock with an estimated fair market value of \$47,485 in exchange for an equal number of shares of Series C Preferred Stock of Unidym, with several minority stockholders of Unidym.

In October and November 2009, Arrowhead issued 114,000 shares of Common Stock with an estimated fair market value of \$706,800 in exchange for 2,850,000 shares of Calando's common stock, with several minority stockholders of Calando. In conjunction with the exchange, Arrowhead also issued 24,000 Warrants to purchase Arrowhead Common Stock in exchange for 600,000 Warrants to purchase Calando common stock.

In February 2010, Arrowhead issued 8,000 shares of Common Stock and 2,400 warrants to purchase Arrowhead Common Stock, at an exercise price of \$5.00, to several Calando shareholders, in exchange for 200,000 shares of Calando common stock and 60,000 warrants to purchase Calando common stock.

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In March 2010, a warrant holder exercised 24,788 warrants to purchase Arrowhead Common Stock, in a cashless exercise, whereby Arrowhead issued to the warrant holder 12,870 shares of Arrowhead Common Stock.

In September 2010, Arrowhead issued warrants to purchase 390,625 shares of Arrowhead Common Stock, at an exercise price of \$5.00, to two Calando shareholders, in exchange for 1,562.5 shares of Series A Preferred Stock of Calando Pharmaceuticals, Inc.

**Arrowhead Research Corporation  
(A Development Stage Company)**

**Notes to Consolidated Financial Statements  
September 30, 2011**

Unless otherwise noted, (1) the term “Arrowhead” refers to Arrowhead Research Corporation, a Delaware corporation, (2) the terms the “Company,” “we,” “us,” and “our,” refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term “Subsidiaries” refers collectively to Arrowhead Madison Inc. (“Madison”), Calando Pharmaceuticals, Inc. (“Calando”), Ablaris Therapeutics, Inc. (“Ablaris”), Agonn Systems, Inc. (“Agonn”), and Tego Biosciences Corporation (“Tego”) as well as our former subsidiary, Unidym, Inc. (“Unidym”), which was divested in January 2011, (4) the term “Minority Investments” refers collectively to Nanotope, Inc. (“Nanotope”) and Leonardo Biosystems, Inc. (“Leonardo”) in which the company holds a less than majority ownership position, and (5) the term “Common Stock” refers to Arrowhead’s Common Stock and the term “stockholder(s)” refers to the holders of Arrowhead Common Stock.

**NOTE 1. ORGANIZATION AND SIGNIFICANT ACCOUNTING POLICIES**

*Nature of Business and Going Concern*

Arrowhead Research Corporation is a nanomedicine company developing innovative therapies at the interface of biology and nanoengineering to cure disease and improve human health. Arrowhead has one of the most advanced and broadest technology platforms for therapeutics based on RNA interference (RNAi), including access to five different RNAi delivery systems and the three primary small interfering RNA (siRNA) structures in commercial development for RNAi therapeutics. This broad technology platform enables optimization of siRNA therapeutic candidates for delivery based on siRNA chemistry, tissue type, disease state, and target [gene] and siRNA type and chemistry on a target-by-target basis. Arrowhead is leveraging its in house R&D expertise and capabilities, as well as a broad intellectual property portfolio for RNAi therapeutics, to attract development partnerships with other pharmaceutical and biotech companies committed to bringing RNAi therapeutics to market, as well as continuing the preclinical and clinical development its own clinical candidates. Arrowhead’s non-RNAi development programs include a unique therapeutic candidate that shows promise for the treatment of obesity and advanced bioactive materials for the regeneration of injured tissues.

Arrowhead operates a wholly-owned subsidiary, Arrowhead Madison, which is focused on the development of RNAi therapeutics, two majority owned subsidiaries, Calando, a leader in delivering small interfering RNAs for gene silencing, and Ablaris, an anti-obesity therapeutics company, and has minority investments in Nanotope, a regenerative medicine company and Leonardo, a multistage drug delivery company.

*Liquidity*

Arrowhead has historically financed its operations through the sale of securities of Arrowhead and its Subsidiaries. Development activities at our Subsidiaries has required significant capital investment since the Company’s inception and we expect our current portfolio companies to continue to require cash investment in fiscal 2012 and beyond to continue development.

At September 30, 2011, the Company had \$7.5 million in cash to fund operations. During the year ended September 30, 2011, the Company’s cash position increased by \$0.7 million, primarily due to the issuance of Common Stock on September 30, 2011. This financing generated \$6.0 million of which \$4.4 million was received in fiscal 2011, while the balance is to be received in fiscal 2012. This inflow was mostly offset by operational spending at Arrowhead, Calando and Ablaris during fiscal 2011. In January 2011, Arrowhead sold its ownership interest in Unidym; therefore the cash burn associated with Unidym ceased in January 2011. As a result of the sale of Unidym, the Company received \$2.5 million in stock of the acquirer, Wisepower Co. Ltd. (“Wisepower”) and a \$2.5 million convertible bond from Wisepower, of which approximately \$200,000 is owed to a third party, who was a minority investor in Unidym. As of September 30, 2011, the Company sold approximately 60% of the stock for approximately \$1.5 million. The remaining shares were sold in October 2011, generating proceeds of \$0.5 million. The convertible bond with a face value of \$2.5 million, is convertible into Wisepower common stock beginning on January 17, 2012 at a price of \$2.00 per share, and can be redeemed on January 17, 2013, and at which time would represent an additional source of liquidity for the company. In October 2011, the Company raised an additional \$3.9 million through the issuance of preferred stock and Common Stock. The Company also entered into a facility whereby it has the ability to draw capital up to \$15 million, and may do so depending on cash needs and market conditions.

On October 21, 2011, Arrowhead completed the acquisition of certain RNAi assets from Hoffmann-La Roche Inc. and F Hoffmann-La Roche Ltd., including intellectual property and a research and development facility based in Madison, Wisconsin. At the time of the acquisition, the facility had 41 employees. Due to the costs associated with the facility, including personnel costs, rent, research and development expenses, and other costs, it is expected that cash expenses will increase significantly in 2012 and beyond as the Company accelerates its preclinical and clinical development efforts.

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Based upon the Company's cash on hand, other sources of liquidity, as described above, and based upon the Company's operating plan, the Company's management anticipates that the Company will be able to satisfy the cash requirements of its operations through at least the next twelve months. The Company anticipates that further equity financings, and/or asset sales and license agreements will be necessary to continue to fund operations in the future.

### *Summary of Significant Accounting Policies*

**Principles of Consolidation**—The consolidated financial statements include the accounts of Arrowhead and its Subsidiaries, Calando, Ablaris, Tego, Agonn, and until its disposition in January 2011, Unidym. Prior to April 2008, Arrowhead's Subsidiaries included Insert Therapeutics, Inc. ("Insert"), which was merged with Calando in April 2008. The merged entity is majority-owned by Arrowhead and continues to operate under the name of Calando. On January 17, 2011, Arrowhead sold its interests in Unidym to Wisepower, and on December 23, 2009, Tego completed a sale of its assets to Luna Innovations, Inc. Unidym and Tego results are included in the Income (Loss) from Discontinued Operations. Income (Loss) from Discontinued Operations also includes Aonex Technologies, Inc. ("Aonex"), sold in May 2008 and Nanotechnica, Inc. ("Nanotechnica"), dissolved in June 2005. All significant intercompany accounts and transactions are eliminated in consolidation, and noncontrolling interests are accounted for in the Company's financial statements.

**Basis of Presentation and Use of Estimates**—The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the accompanying financial statements. Significant estimates made in preparing these financial statements include valuing the stock of the Subsidiaries, assumptions to calculate stock-based compensation expense, allowance for doubtful accounts, deferred tax asset valuation allowance, derivative assets and liabilities, noncontrolling interest and useful lives for depreciable and amortizable assets. Actual results could differ from those estimates. Additionally, certain reclassifications have been made to prior period financial statements to conform to the current period presentation. In the opinion of management, all adjustments, including normal recurring accruals considered necessary for a fair presentation, have been included.

**Cash and Cash Equivalents**—The Company considers all liquid debt instruments purchased with a maturity of three months or less to be cash equivalents.

**Concentration of Credit Risk**—The Company maintains checking accounts for Arrowhead and separate accounts for each Subsidiary at any of three financial institutions. These accounts are insured by the Federal Deposit Insurance Corporation (FDIC) for up to \$250,000 per account. The Company has two wealth management accounts at the same financial institutions that invest in higher yield money market accounts and in government securities. Management believes the Company is not exposed to significant credit risk due to the financial position of the depository institution in which these deposits are held.

**Property and Equipment**—Property and equipment are recorded at cost. Depreciation of property and equipment is recorded using the straight-line method over the respective useful lives of the assets ranging from three to seven years. Leasehold improvements are amortized over the lesser of the expected useful life or the remaining lease term.

**Intellectual Property**—At September 30, 2011, intellectual property consisted of patents and patent applications licensed or purchased in the gross amount of \$3,349,563. The accumulated amortization of patents totaled \$1,618,352 at September 30, 2011. Patents are amortized over three years to twenty years. The weighted average original amortization period is twelve years. The weighted average remaining amortization period is seven years. Amortization is expected to be \$241,808 for fiscal years 2012, 2013, 2014, 2015 and 2016, and \$522,174 thereafter. Long-lived assets, such as property, equipment and intangible assets subject to amortization are reviewed for impairment whenever events or circumstances indicate that the carrying amount of these assets may not be recoverable. In reviewing for impairment, we compare the carrying value of such assets to the estimated undiscounted future cash flows expected from the use of the assets and their eventual disposition. When the estimated undiscounted future cash flows are less than their carrying amount, an impairment loss is recognized equal to the difference between the assets' fair value and their carrying value.

**Equity Investments**—Arrowhead has a non-controlling equity investment in Nanotope, a privately held biotechnology company, which is recorded in Other Assets. This investment is carried at cost less Arrowhead's proportionate share of Nanotope's operating loss for the period since investment. Arrowhead utilizes the equity method of accounting as it owns more than 20% of the voting equity and has the ability to exercise significant influence over this company. This investment is risky as the technologies and markets for Nanotope's products are still in the development stage, commercially viable products may never be developed, and markets for such products may never be significant. Arrowhead could lose its entire investment in Nanotope. Arrowhead monitors this investment for impairment and makes appropriate reductions in carrying value when necessary.

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**Minority Equity Investments**—The Company’s minority equity investment in Leonardo, a privately held biotechnology company, is recorded in Other Assets. This investment is accounted for under the cost method of accounting as Arrowhead owns less than 20% of the voting equity and only has the ability to exercise nominal, not significant, influence over this company. This investment is risky as the technologies and markets for Leonardo’s products are still in the development stage, commercially viable products may never be developed, and markets for such products may never be significant. Arrowhead could lose its entire investment in Leonardo. Arrowhead monitors this investment for impairment and makes appropriate reductions in carrying value when necessary.

**Noncontrolling Interests in Majority-Owned Subsidiaries**—Operating losses applicable to majority-owned Calando, Ablaris and Unidym have periodically exceeded the noncontrolling interests in the equity capital of either Subsidiary. Such excess losses applicable to the noncontrolling interests have been and are borne by the Company as there is no obligation of the noncontrolling interests to fund any losses in excess of their original investment. There is also no obligation or commitment on the part of the Company to fund operating losses of any Subsidiary whether wholly-owned or majority-owned. The Company allocates the noncontrolling interest’s share of net loss in excess of the noncontrolling interest’s initial investment in accordance with FASB ASC 810-10, which was effective for the Company on October 1, 2009.

When there is a change in the Company’s proportionate share of a development-stage Subsidiary resulting from additional equity transactions in a Subsidiary, the change is accounted for as an equity transaction in consolidation. To the extent that the increase in the calculated value of the Company’s interest in the equity of the Subsidiary exceeds the Company’s investment in the offering, that increase in value is referred to as the Company’s “increase in its proportionate share of the Subsidiary’s equity” and the amount is recorded as an increase in the Company’s Additional Paid-in Capital.

**Revenue Recognition**—Revenue from product sales are recorded when persuasive evidence of an arrangement exists, title has passed and delivery has occurred, a price is fixed and determinable, and collection is reasonably assured. We may generate revenue from product sales, technology licenses, collaborative research and development arrangements, and research grants. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable and/or guaranteed technology license fees, collaborative research funding and various milestone and future product royalty or profit-sharing payments.

Revenue associated with research and development funding payments, under collaborative agreements, is recognized ratably over the relevant periods specified in the agreement, generally the research and development period. Revenue from up-front license fees and milestones and product royalties are recognized as earned based on the completion of the milestones and product sales, as defined in the respective agreements. Payments received in advance of recognition as revenue are recorded as deferred revenue.

**Allowance for Doubtful Accounts**—The Company accrues an allowance for doubtful accounts based on estimates of uncollectible revenues by analyzing historical collections, accounts receivable aging and other factors. Accounts receivable are written off when all collection attempts have failed.

**Research and Development**—Costs and expenses that can be clearly identified as research and development are charged to expense as incurred in accordance with FASB ASC 730-10.

**Earnings (Loss) per Share**—Basic earnings (loss) per share is computed using the weighted-average number of common shares outstanding during the period. Diluted earnings (loss) per share are computed using the weighted-average number of common shares and dilutive potential common shares outstanding during the period. Dilutive potential common shares primarily consist of stock options issued to employees and consultants and warrants to purchase Common Stock of the Company.

**Stock-Based Compensation**—The Company accounts for share-based compensation arrangements in accordance with FASB ASC 718, which requires the measurement and recognition of compensation expense for all share-based payment awards to be based on estimated fair values. We use the Black-Scholes option valuation model to estimate the fair value of our stock options at the date of grant. The Black-Scholes option valuation model requires the input of subjective assumptions to calculate the value of stock options. We use historical data among other information to estimate the expected price volatility and the expected forfeiture rate.

**Income Taxes**—The Company accounts for income taxes under the liability method, which requires the recognition of deferred income tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred income taxes are recognized for the tax consequences in future years of differences between the tax bases of assets and liabilities and their financial reporting amounts at each period end based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect taxable income. Valuation allowances are established, when necessary, to reduce deferred income tax assets to the amount expected to be realized. The provision for income taxes, if any, represents the tax payable for the period and the change in deferred income tax assets and liabilities during the period.

### Recently Issued Accounting Standards

In June 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition—Milestone Method (Topic 605): Milestone Method of Revenue Recognition*. This ASU codifies the consensus reached in EITF Issue No. 08-9, “Milestone Method of Revenue Recognition.” The amendments to the Codification provide guidance on defining a milestone and determining when it may be appropriate to apply the milestone method of revenue recognition for research or development transactions. Consideration that is contingent on achievement of a milestone in its entirety may be recognized as revenue in the period in which the milestone is achieved only if the milestone is judged to meet certain criteria to be considered substantive. Milestones should be considered substantive in their entirety and may not be bifurcated. An arrangement may contain both substantive and nonsubstantive milestones, and each milestone should be evaluated individually to determine if it is substantive. This guidance was adopted effective October 1, 2010. The adoption of this guidance did not have a material impact on our consolidated financial statements.

In January 2010, the FASB issued Accounting Standards Update ASU No. 2010-06, “Fair Value Measurements and Disclosures (Topic 820) – Improving Disclosures about Fair Value Measurements”. This guidance requires new disclosures related to recurring and nonrecurring fair value measurements. The guidance requires disclosure of transfers of assets and liabilities between Level 1 and Level 2 of the fair value measurement hierarchy, including the reasons and the timing of the transfers and information on purchases, sales, issuance, and settlements on a gross basis in the reconciliation of the assets and liabilities measured under Level 3 of the fair value measurement hierarchy. The adoption of this guidance is effective for interim and annual reporting periods beginning after December 15, 2009. We have adopted this guidance in the financial statements presented herein, which did not have a material impact on our consolidated financial position or results of operations.

In October 2009, the FASB issued ASU 2009-13, which amends ASC Topic 605, *Revenue Recognition*. This new accounting guidance relates to the revenue recognition of multiple element arrangements. The new guidance states that, if vendor specific objective evidence or third party evidence for deliverables in an arrangement cannot be determined, companies will be required to develop a best estimate of the selling price for separate deliverables and allocate arrangement consideration using the relative selling price method. We adopted this guidance as of January 1, 2010 on a prospective basis. The adoption of this guidance did not have a material impact on our consolidated financial statements.

In October 2009, the FASB issued authoritative guidance on multiple-deliverable revenue arrangements, ASC 605-25. This guidance amends the existing criteria for separating consideration received in multiple-deliverable arrangements and requires that arrangement consideration be allocated at the inception of the arrangement to all deliverables based on their relative selling price. The guidance establishes a hierarchy for determining the selling price of a deliverable which is based on vendor-specific objective evidence, third-party evidence, or management estimates. Expanded disclosures related to multiple-deliverable revenue arrangements are also required. This guidance is effective for the Company beginning fiscal year 2011. We have adopted this guidance in the financial statements presented herein, which did not impact our consolidated financial position or results of operations.

### NOTE 2. INVESTMENT IN SUBSIDIARIES

*Calando Pharmaceuticals, Inc. (formerly known as Insert Therapeutics, Inc.)*

On April 17, 2008, Calando merged with and into Insert, with Insert as the surviving company. Prior to the merger, Arrowhead invested an aggregate of \$23.2 million in Calando through equity and debt financings. As a condition of the merger, the Preferred Stock of each of Calando and Insert was converted into common stock and the loans were converted to equity. As a result of the merger, shares of Insert common stock were issued to the stockholders of the former Calando, and Insert changed its name to Calando Pharmaceuticals, Inc.

On November 26, 2008, Calando entered into Unsecured Convertible Promissory Note Agreements (“Notes”) for \$2.5 million with accredited investors and Arrowhead, which invested \$200,000 in the Notes offering. Arrowhead subsequently invested an additional \$600,000 in the same offering. Subsequently, most of the Notes were converted to equity as described below. At September 30, 2011 and 2010, one Note for \$500,000 remained outstanding. The Notes had a 10% interest rate and matured on November 26, 2010. The \$500,000 remaining Note is convertible into Calando common stock and can be redeemed for two times their face value plus interest in the event of a sale of Calando or at maturity. To facilitate this investment in Calando, Arrowhead subordinated a series of 6% simple interest loans and advances totaling approximately \$5.3 million of principal plus interest.

Effective June 23, 2009, to facilitate licensing transactions with a third party, holders (including Arrowhead) of an aggregate of \$2.9 million of the Notes, including accrued but unpaid interest, converted the principal and accrued interest into newly authorized Calando Series A Preferred Stock. The non-voting Series A Preferred Stock has a liquidation preference of 2.5 times the Series A Original Issue Price of \$1,000 per share and is convertible into common stock at a conversion price of \$0.576647 per share. Arrowhead converted all of its Notes representing a principal balance of \$800,000, plus accrued but unpaid interest, into 829 shares of Series A Preferred Stock. One third-party Note for \$500,000 plus interest remains outstanding.

As of September 30, 2011, Arrowhead had a 10% simple-interest working promissory note and advances outstanding to Calando totaling \$907,501, which are payable upon demand.

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In fiscal 2010, Arrowhead issued 122,000 shares of its Common Stock in exchange for 3,050,000 shares of Calando common stock, with several minority stockholders of Calando. In conjunction with this exchange, Arrowhead also issued 26,400 warrants to purchase Arrowhead Common Stock in exchange for 660,000 warrants to purchase Calando common stock.

In January 2011, Arrowhead invested \$9.1 million, through a cash investment of \$1.0 million and the conversion of \$8.1 million intercompany debt, acquiring newly issued Calando Series B and Series C preferred stock.

As of September 30, 2011, Arrowhead owned 79% of the outstanding shares of Calando and 74% on a fully diluted basis.

### *Ablaris Therapeutics, Inc.*

Ablaris was formed and began operations in the first quarter of fiscal 2011 through the licensing of certain anti-obesity technology developed at the MD Anderson Cancer Center at the University of Texas. During the year ended September 30, 2011, Ablaris raised \$2.9 million in cash, of which \$1.3 million was invested by Arrowhead and \$1.6 million was invested by outside investors, through the issuance of Series A Preferred stock.

As of September 30, 2011, Arrowhead owned 64% of the outstanding shares of Ablaris and 64% on a fully diluted basis.

### *Nanotope, Inc.*

Nanotope is developing advanced nanomaterials for the treatment of spinal cord injuries, cartilage regeneration and wound healing. In April 2008, Arrowhead acquired a 5.8% ownership interest in Nanotope. In July and September 2008, Arrowhead acquired 1,801,802 shares of Series B Preferred Stock of Nanotope for two payments of \$1 million each, increasing Arrowhead's ownership interest in Nanotope to approximately 23%. Since inception, Nanotope's revenue has been negligible. Operating expenses for the twelve months ended September 30, 2011 were approximately \$1,161,000. Nanotope's net loss for the twelve months ended September 30, 2011 was \$709,000. Arrowhead accounts for its investment in Nanotope using the equity method of accounting. As of September 30, 2011, Nanotope had indebtedness to Arrowhead in the amount of \$1,213,000, included in other receivables, which is expected to be repaid or converted to equity.

Summarized financial information for Nanotope, Inc. is as follows:

	<u>September 30, 2011</u>	<u>September 30, 2010</u>
Current assets	\$ 21,000	\$ 16,000
Non-current assets	85,000	130,000
Liabilities	1,255,000	585,000
Equity	(1,149,000)	(439,000)
	<u>For the year ended</u> <u>September 30, 2011</u>	<u>For the year ended</u> <u>September 30, 2010</u>
Revenue	\$ 515,000	\$ 9,000
Operating expenses	1,161,000	975,000
Net Loss	\$ (709,000)	\$ (955,000)
	<u>For the year ended</u> <u>September 30, 2011</u>	<u>For the year ended</u> <u>September 30, 2010</u>
Cash flows used in operating activities	\$ (705,000)	\$ (329,000)
Cash flows used in investing activities	(31,000)	(7,000)
Cash flows provided by financing activities	746,000	—

### *Leonardo Biosystems, Inc.*

Leonardo is developing a drug-delivery platform technology based on novel methods of designing spheroid porous silicon microparticles that selectively accumulate in tumor vasculature. In April 2008, Arrowhead acquired a 6.13% ownership interest in Leonardo. Arrowhead accounts for its investment in Leonardo using the cost method of accounting. As of September 30, 2011, Leonardo had indebtedness to Arrowhead in the amount of \$396,000, included in other receivables, which is expected to be repaid or converted to equity. As of September 30, 2011, Arrowhead's ownership interest in Leonardo was 5%.

**NOTE 3. DISCONTINUED OPERATIONS**

*Unidym, Inc.*

Founded by Arrowhead in 2005, Unidym is developing electronic applications of carbon nanotubes. In line with the Company's strategy to focus on nanomedicine, Arrowhead sold its ownership interest in Unidym to Wisepower in January 2011. The consideration included \$5.0 million in Wisepower stock and bonds, a percentage of certain revenue streams, as well as contingent payments up to \$140 million based on revenue milestones over a ten-year period.

In conjunction with the disposition of Unidym, the gain on the sale and the results of historical operations are recorded as discontinued operations in the Company's Statements of Operations. Additionally, the cash flows from Unidym are reflected separately as cash flows from discontinued operations. Potential future cash flows as discussed above will be reflected as a part of cash flows from discontinued operations in the Company's Consolidated Statements of Cash Flows.

*Tego Biosciences, Inc.*

On April 20, 2007, Tego, a wholly-owned subsidiary of Arrowhead, acquired the assets of C Sixty, Inc., a Texas-based company developing protective products based on the anti-oxidant properties of fullerenes.

On December 23, 2009, Tego completed the sale of all of its non-cash intellectual property assets to Luna Innovations, Inc. The consideration included an upfront purchase price of \$350,000 and reimbursements of patent and license expenses of \$80,000, as well as contingent payments based on milestones and royalties for each fullerene product developed by Luna and covered by Tego intellectual property.

Due to the sale of substantially all of Tego's assets, the operations of Tego ceased and the gain on the sale and the results of historical operations are recorded as discontinued operation in the Company's Statements of Operations. Additionally, the cash flows from Tego are reflected separately as cash flows from discontinued operations. Potential future cash flows associated with the Luna APA, as discussed above, will be reflected as a part of cash flows from discontinued operations in the Company's Consolidated Statements of Cash Flows.

**NOTE 4. NOTES PAYABLE**

On November 26, 2008, Calando entered into Unsecured Convertible Promissory Note Agreements ("Notes") for \$2.5 million with accredited investors and Arrowhead, which invested \$200,000 in the Notes offering. Arrowhead subsequently invested an additional \$600,000 in the same offering. Except for one Note in the principal amount of \$500,000, all Notes and accrued interest were converted into a total of 2,950 shares of Calando Series A Preferred Stock on June 23, 2009. The remaining Note had a 10% interest rate, matured on November 26, 2010, and was renegotiated and extended until November 26, 2013. The terms of the new note include a 10% interest rate and require two times principal payment upon certain events as defined in the note and at maturity.

**NOTE 5. STOCKHOLDERS' EQUITY**

At September 30, 2011, the Company had a total of 150,000,000 shares of capital stock authorized for issuance, consisting of 145,000,000 shares of Common Stock, par value \$0.001, and 5,000,000 shares of Preferred Stock, par value \$0.001. On November 17, 2011, the Company effected a reverse stock split in the ratio of 1 for 10, all share and per share data below reflects an adjustment for the reverse stock split.

At September 30, 2011, 8,642,286 shares of Common Stock were outstanding. At September 30, 2011, 153,200 shares and 575,896 shares were reserved for issuance upon exercise of options granted under Arrowhead's 2000 Stock Option Plan and 2004 Equity Incentive Plan, respectively.

On December 11, 2009, the Company sold an aggregate of 508,343 units in a private placement transaction with accredited investors. Each unit consisted of one share of Arrowhead Common Stock and a warrant to purchase an additional share of Common Stock exercisable at \$5.09 per share. The unit price was \$6.34, based upon the closing bid price on the Company's Common Stock on December 11, 2009, which was \$5.09, plus \$1.25 for the purchase of the warrant. The warrants became exercisable on June 12, 2010 and remain exercisable until December 11, 2014. The market conditions required for redemption provided for in the warrants has been met and the warrants are eligible for redemption by the Company. Gross proceeds of the offering were approximately \$3.2 million.

On June 17, 2010, the Company sold an aggregate of 659,298 units at a price of \$13.12 per unit in a registered offering to institutional and accredited investors. Each unit consisted of one share of Arrowhead Common Stock and a warrant to purchase 0.5 share of Common Stock exercisable at \$16.50 per share. The warrants contain an antidilution provision which can result in an adjustment to the exercise price under certain circumstances, and the current exercise price is \$3.70. Gross proceeds from the offering were \$8.65 million before deducting placement agent commission and other offering expenses of approximately \$800,000.

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On September 30, 2011, the Company sold 1,458,917 shares of Common Stock at a price of \$3.80 per share. Cash proceeds received in fiscal 2011 were \$4.6 million, \$0.9 million are expected to be received in fiscal 2012, and \$0.2 million related to a reduction in professional fees.

The following table summarizes information about warrants outstanding at September 30, 2011:

<u>Exercise prices</u>	<u>Number of Warrants</u>	<u>Remaining Life in Years</u>
\$70.60	94,896	5.6
\$20.00	386,399	1.9
\$5.00	1,163,033	3.2
\$5.10	461,024	3.2
\$3.80	329,649	4.2
Total warrants outstanding	<u>2,435,001</u>	

### NOTE 6. LEASES

In April 2011, the Company's corporate headquarters lease expired, and the Company did not exercise its renewal option. The company is currently leasing temporary offices. The temporary offices are expected to be utilized for several months at a rental rate of approximately \$8,000 per month. The current rental agreement is on a month-to-month basis and there were no long-term commitments at September 30, 2011. On October 21, 2011, Arrowhead acquired the RNAi operations from Roche, including its research facility in Madison, Wisconsin. Its lease expires on February 28, 2019; monthly rental expense is approximately \$56,500.

Facility and equipment rent expense for the year ended September 30, 2011 and 2010 was \$161,759 and \$268,330, respectively. From inception to date, rent expense was \$3,645,381. Rent expense related to Unidym, until its disposal in January 2011, is included as a part of income/loss from discontinued operations.

### NOTE 7. STOCK-BASED COMPENSATION

Arrowhead has two plans that provide for equity-based compensation. Under the 2000 Stock Option Plan, 153,200 shares of Arrowhead's Common Stock are reserved for issuance upon exercise of non-qualified stock options. No further grants can be made under the 2000 Stock Option Plan. The 2004 Equity Incentive Plan reserves 970,443 shares for the grant of stock options, stock appreciation rights, restricted stock awards and performance unit/share awards by the Board of Directors to employees, consultants and others. As of September 30, 2011, there were options granted and outstanding to purchase 153,200 and 575,896 shares of Common Stock under the 2000 Stock Option Plan and the 2004 Equity Incentive Plan, respectively. During the year ended September 30, 2011, 20,000 options were granted under the 2004 Equity Incentive Plan. All share and per share data in this footnote has been adjusted to reflect the 1 for 10 reverse stock split effected on November 17, 2011.

The following tables summarize information about stock options:

	<u>Number of Options Outstanding</u>	<u>Weighted-Average Exercise Price Per Share</u>	<u>Weighted-Average Remaining Contractual Term</u>	<u>Aggregate Intrinsic Value</u>
Balance At September 30, 2009	290,158	\$ 17.35		
Granted	525,175	6.88		
Cancelled	(2,312)	11.10		
Exercised	(687)	11.10		
Balance At September 30, 2010	812,334	10.62		
Granted	20,000	5.86		
Cancelled	(100,539)	21.32		
Exercised	(2,699)	5.10		
Balance At September 30, 2011	<u>729,096</u>	<u>\$ 9.03</u>	<u>7.0 years</u>	<u>\$ —</u>
Exercisable At September, 30, 2011	<u>570,307</u>	<u>\$ 9.39</u>	<u>6.6 years</u>	<u>\$ —</u>

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Stock-based compensation expense for the years ended September 30, 2011 and 2010 was \$1,404,430 and \$1,582,149, respectively. For the year ended September 30, 2011 and 2010, \$27,519 and \$157,856, respectively, of this expense is included in discontinued operations, and the balance is included in Salary expense in the Company's consolidated statements of operations. There is no income tax benefit as the company is currently operating at a loss and an actual income tax benefit may not be realized. The result of the loss creates a timing difference, resulting in a deferred tax asset, which is fully reserved by a valuation allowance.

The fair value of the options granted by Arrowhead for the years ended September 30, 2011 and 2010 is estimated at \$93,004 and \$2,939,928, respectively. The aggregate fair value of options granted by Calando for the years ended September 30, 2011 is estimated at \$33,870. No Calando options were issued during the year ended September 30, 2010. The intrinsic value of the options exercised during fiscal 2011 and 2010 was \$3,666 and \$6,875, respectively.

As of September 30, 2011, the pre-tax compensation expense for all unvested stock options at Arrowhead in the amount of approximately \$1,091,513 will be recognized in our results of operations over a weighted average period of 2.4 years. As of September 30, 2011, the pre-tax compensation expense for all unvested stock options at Calando in the amount of approximately \$69,183 will be recognized in our results of operations over a weighted average period of 2.8 years.

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option pricing model. The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options, which do not have vesting restrictions and are fully transferable. The determination of the fair value of each stock option is affected by our stock price on the date of grant, as well as assumptions regarding a number of highly complex and subjective variables. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options. The assumptions used to value stock options are as follows:

	Year Ended September 30,	
	2011	2010
Dividend yield	—	—
Risk-free interest rate	1.11% to 2.90%	2.00% to 3.42%
Volatility	100%	100%
Expected life (in years)	5.5 to 6.25	5 to 6.25
Weighted average grant date fair value per share of options granted	\$4.70	\$5.60

The dividend yield is zero as the Company currently does not pay a dividend.

The risk-free interest rate is based on the U.S. Treasury bond.

Volatility is estimated based on volatility average of the Company's Common Stock price.

### **NOTE 8. FAIR VALUE MEASUREMENTS & DERIVATIVE INSTRUMENTS**

The Company measures its financial assets and liabilities at fair value. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (i.e., exit price) in an orderly transaction between market participants at the measurement date. Additionally, the Company is required to provide disclosure and categorize assets and liabilities measured at fair value into one of three different levels depending on the assumptions (i.e., inputs) used in the valuation. Level 1 provides the most reliable measure of fair value while Level 3 generally requires significant management judgment. Financial assets and liabilities are classified in their entirety based on the lowest level of input significant to the fair value measurement. The fair value hierarchy is defined as follows:

Level 1—Valuations are based on unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2—Valuations are based on quoted prices for similar assets or liabilities in active markets, or quoted prices in markets that are not active for which significant inputs are observable, either directly or indirectly.

Level 3—Valuations are based on prices or valuation techniques that require inputs that are both unobservable and significant to the overall fair value measurement. Inputs reflect management's best estimate of what market participants would use in valuing the asset or liability at the measurement date.

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The following table summarizes fair value measurements at September 30, 2010 and September 30, 2011 for assets and liabilities measured at fair value on a recurring basis:

September 30, 2010:

	<u>Level I</u>	<u>Level II</u>	<u>Level III</u>	<u>Total</u>
Cash and cash equivalents	\$6,847,162	\$ —	\$ —	\$6,847,162
Derivative liabilities	\$ —	\$ —	\$2,408,522	\$2,408,522

September 30, 2011:

	<u>Level I</u>	<u>Level II</u>	<u>Level III</u>	<u>Total</u>
Cash and cash equivalents	\$7,507,389	\$ —	\$ —	\$7,507,389
Marketable securities	\$ 634,585	\$ —	\$ —	\$ 634,585
Derivative assets	\$ —	\$ —	\$ 161,125	\$ 161,125
Derivative liabilities	\$ —	\$ —	\$ 944,980	\$ 944,980

As part of the sale of Unidym in January 2011, Arrowhead received common stock in Wisepower, originally valued at \$2.5 million, \$100,000 of which is due to a third party. Arrowhead has the ability to sell the shares of stock in Wisepower, subject to certain limits on volume of sales over a nine-month period ending in October 2011. During the year ended September 30, 2011, Arrowhead sold approximately 60% of the original holdings; the remaining shares had a market value of \$0.6 million at September 30, 2011, and were sold for \$0.5 million in October 2011. The recorded value of the stock is adjusted to fair market value based on quotations from the KOSDAQ, a Korean stock exchange, and published foreign exchange rates. Marketable securities are included as part of other current assets in the Company's consolidated balance sheet.

As part of the sale of Unidym in January 2011, Arrowhead received a bond from Wisepower in the face amount of \$2.5 million. The bond is convertible to Wisepower common stock beginning on January 17, 2012 at a price of \$2.00 per share. The conversion feature is subject to derivative accounting as prescribed under ASC 815. Accordingly, the fair value of the conversion feature on the date of issuance was estimated using an option pricing model and recorded on the Company's consolidated balance sheet as a derivative asset. The fair value of the conversion feature is estimated at the end of each reporting period and the change in the fair value of the conversion feature is recorded as a nonoperating gain/loss as change in value of derivatives in Company's consolidated statement of operations. A portion of the bond is owed to a third party, as such the company records a derivative asset for the entire conversion feature and records a derivative liability for the portion related to the third party. The original fair value of the derivative relating to the third party was \$26,310; the fair value at September 30, 2011 was \$6,854. The loss from the change in value of the derivative asset, net of the derivative liability of \$437,919 is reflected in the change in value of derivatives in the Company's consolidated statement of operations.

During the year ended September 30, 2011, the Company recorded a loss from the change in fair value of the derivative asset, net of \$437,919. The assumptions used in valuing the derivative asset as of September 30, 2011 were as follows:

Risk free interest rate	0.4%
Expected life	2.3 Years
Dividend yield	none
Volatility	72%

The following is a reconciliation of the derivative asset for the year ended September 30, 2011:

Value at October 1, 2010	\$ —
Receipt of instruments	618,500
Decrease in value	(457,375)
Net settlements	—
Value at September 30, 2011	<u>\$ 161,125</u>

As part of the equity financing on June 17, 2010, as described in Note 5, Arrowhead issued warrants to acquire up to 329,649 shares of Common Stock (the "Warrants") which contain anti-dilution protection. Under the certain provisions of the Warrants, if, during the term of the Warrants, the Company issues Common Stock at a price lower than the exercise price of the Warrants, the exercise price of the Warrants would be reduced to the amount equal to the issuance price of the Common Stock. Because the Warrants have this feature, the Warrants are subject to derivative accounting as prescribed under ASC 815. Accordingly, the fair value of the Warrants on the date of issuance was estimated using an option pricing model and recorded on the Company's

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consolidated balance sheet as a derivative liability. The fair value of the Warrants is estimated at the end of each reporting period and the change in the fair value of the Warrants is recorded as a nonoperating gain or loss in the Company's consolidated statement of operations. During the year ended September 30, 2011, the Company recorded a gain from the change in fair value of the derivative liability of \$1,501,289. The assumptions used in valuing the derivative liability as of September 30, 2011 were as follows:

Risk free interest rate	0.9%
Expected life	4.2 Years
Dividend yield	none
Volatility	100%

The following is a reconciliation of the derivative liability related to these warrants for through September 30, 2011:

Value at October 1, 2009	\$ —
Receipt of instruments	4,169,907
Decrease in value	(1,761,385)
Net settlements	—
Value at October 1, 2010	\$ 2,408,522
Receipt of instruments	—
Decrease in value	(1,501,289)
Net settlements	—
Value at September 30, 2011	<u>\$ 907,233</u>

In conjunction with the financing of Ablaris during the year ended September 30, 2011, Arrowhead sold exchange rights to certain investors whereby the investors have the right to exchange their shares of Ablaris for a prescribed number of Arrowhead shares based upon a predefined ratio. The exchange rights have a seven-year term. During the first year, the exchange right allows the holder to exchange one Ablaris share for 0.6 Arrowhead shares. This ratio declines to 0.4 in the second year, 0.3 in the third year and 0.2 in the fourth year. In the fifth year and beyond the exchange ratio is 0.1. Exchange rights for 675,000 Ablaris shares were sold during the year ended September 30, 2011, and remain outstanding at September 30, 2011. The exchange rights are subject to derivative accounting as prescribed under ASC 815. Accordingly, the fair value of the exchange rights on the date of issuance was estimated using an option pricing model and recorded on the Company's consolidated balance sheet as a derivative liability. The fair value of the exchange rights is estimated at the end of each reporting period and the change in the fair value of the exchange rights is recorded as a nonoperating gain or loss in the Company's consolidated statement of operations. During the year ended September 30, 2011, the Company recorded a gain from the change in fair value of the derivative liability of \$69,758. The assumptions used in valuing the derivative liability as of September 30, 2011 were as follows:

Risk free interest rate	1.3%
Expected life	6.3 Years
Dividend yield	none
Volatility	100%

The following is a reconciliation of the derivative liability related to these exchange rights for the year ended September 30, 2011:

Value at October 1, 2010	\$ —
Issuance of instruments	100,650
Change in value	(69,758)
Net settlements	—
Value at September 30, 2011	<u>\$ 30,892</u>

The carrying amounts of the Company's other financial instruments, which include accounts receivable, accounts payable, and accrued expenses approximate their respective fair values due to the relatively short-term nature of these instruments.

### **NOTE 9. INCOME TAXES**

The Company utilizes the guidance issued by the FASB for accounting for income taxes which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns.

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Under this method, deferred income taxes are recognized for the tax consequences in future years of differences between the tax bases of assets and liabilities and their financial reporting amounts at each year-end based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect taxable income. Valuation allowances are established, when necessary, to reduce deferred tax assets to the amount expected to be realized. The provision for income taxes represents the tax payable for the period and the change during the period in deferred tax assets and liabilities.

For the years ended September 30, 2011 and 2010, the Company had consolidated net book losses of \$3.5 million and \$7.0 million, respectively. The losses result in a deferred income tax benefit which is offset by a deferred tax provision for the valuation allowance for a net deferred provision of zero. Since the Company is a development stage company, management has provided a 100% valuation allowance against its deferred tax assets until such time as management believes that its projections of future profits as well as expected future tax rates make the realization of these deferred tax assets more-likely-than-not. Significant judgment is required in the evaluation of deferred tax benefits and differences in future results from our estimates could result in material differences in the realization of these assets.

As of September 30, 2011, the Company has available gross federal net operating loss (NOL) carry forwards of \$65.3 million and gross state NOL carry forwards of \$52.1 million which expire at various dates through 2029.

As of September 30, 2011, the deferred tax assets were \$25.2 million. The Company has recorded a full valuation allowance of \$25.2 million related to federal and state net operating loss carry forwards. The Company has performed an assessment of positive and negative evidence regarding the realization of the net deferred tax asset in accordance with ASC 740-10, "Accounting for Income Taxes." This assessment included the evaluation of scheduled reversals of deferred tax liabilities, the availability of carry forwards and estimates of projected future taxable income.

The Company has adopted guidance issued by the FASB that clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements and prescribes a recognition threshold of more likely than not and a measurement process for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. In making this assessment, a company must determine whether it is more likely than not that a tax position will be sustained upon examination, based solely on the technical merits of the position and must assume that the tax position will be examined by taxing authorities. Our policy is to include interest and penalties related to unrecognized tax benefits in income tax expense. Interest and penalties totaled \$0 for the years ended September 30, 2011 and 2010, respectively, and \$0 for the period from May 7, 2003 (date of inception) through September 30, 2011. The Company files income tax returns with the Internal Revenue Service ("IRS"), the state of California and certain other taxing jurisdictions. For jurisdictions in which tax filings are prepared, the Company is no longer subject to income tax examinations by state tax authorities for years through fiscal 2006, and by the IRS

### **NOTE 10. RELATED PARTY TRANSACTIONS**

Dr. Anzalone owns 1,395,900 shares of Nanotope, Inc. common stock or approximately 14.2% of Nanotope's outstanding voting securities. Dr. Anzalone does not hold options, warrants or any other rights to acquire securities of Nanotope. Dr. Anzalone has the right to appoint a representative to the board of directors of Nanotope. Dr. Anzalone currently serves on the Nanotope board in a seat reserved for Nanotope's CEO, and another individual holds the seat designated by Dr. Anzalone. Dr. Anzalone has served as President and Chief Executive Officer of Nanotope since its formation and continues to serve in these capacities. Dr. Anzalone has not received any compensation for his work on behalf of Nanotope since joining the Company on December 1, 2007. Dr. Anzalone has also waived his right to any unpaid compensation accrued for work done on behalf of Nanotope before he joined the Company.

Dr. Anzalone did not participate on behalf of the Company in the negotiations of the terms of the Nanotope Series B Preferred Stock issued to the Company and did not negotiate on behalf of Nanotope after becoming the Chief Executive Officer and President of the Company. Dr. Anzalone did respond to questions asked of him by the Company's Board of Directors and management regarding Nanotope's business plan, operations and the terms of the Series B Stock Purchase Agreement and ancillary agreements.

During fiscal 2009, Calando raised \$2.5 million through the sale of senior unsecured convertible promissory notes ("New Notes"), to accredited investors, plus \$800,000 from Arrowhead. Dr. Anzalone, Arrowhead's President and CEO, personally participated in the offering by buying \$100,000 of the New Notes.

As part of the private placement on December 11, 2009 (see Note 6. Stockholder's Equity), Dr. Anzalone, Arrowhead's President and CEO, personally invested \$100,000.

In August 2010, the Company retained Mr. Vincent Anzalone, the brother of Arrowhead's Chief Executive Officer, as a consultant for the Company, focusing on business development and market analysis, with a monthly remuneration of \$10,000 per month. Mr. Vincent Anzalone was paid \$20,000 during the fiscal year ended September 30, 2010, and \$120,000 during the fiscal year ended September 30, 2011.

### **NOTE 11. EMPLOYEE BENEFIT PLANS**

In January 2005, the Company began sponsoring a defined contribution 401(k) retirement savings plan covering substantially all of its employees. The Plan was administered under the "safe harbor" provision of ERISA. Under the terms of the plan, an eligible employee may elect to contribute a portion of their salary on a pre-tax basis, subject to federal statutory limitations. The plan allowed for a discretionary match in an amount up to 100% of each participant's first 3% of compensation contributed plus 50% of each participant's next 2% of compensation contributed.

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For the years ended September 30, 2011 and 2010, we recorded expenses under these plans of approximately \$43,000 and \$9,000, respectively and \$448,000 since inception of the Company.

In addition to the employee benefit plans described above, the Company participates in certain customary employee benefits plans, including those which provide health and life insurance benefits to employees.

### **NOTE 12. SUBSEQUENT EVENTS**

On October 21, 2011, the Company entered into a Stock and Asset Purchase Agreement (the "RNAi Purchase Agreement") with Hoffmann-La Roche Inc. and F Hoffmann-La Roche Ltd (collectively, "Roche"), pursuant to which the Company purchased from Roche (i) all of the outstanding common stock of Roche Madison Inc. ("Roche Madison") and (ii) the intellectual property rights currently held by Roche related to its RNAi business and identified in the RNAi Purchase Agreement (the "Transaction"). In consideration for the purchase of Roche Madison and the Roche RNAi assets, the Company issued to Roche a promissory note with a principal value of \$50,000 and 901,702 shares of Common Stock (as adjusted for a subsequent reverse split). Additionally, the Company agreed that, subject to stockholder approval under the NASDAQ Marketplace Rules, the Company would issue an additional 146,562 (as adjusted for a subsequent reverse split) shares of Common Stock, plus a number of additional shares equal to 9.9% of the shares of Common Stock (or common stock equivalents) sold by the Company in capital raising transactions within one year from the closing, but only with respect to the first \$3,118,615 of gross offering proceeds (the "Top-up Shares"). If the Company is prohibited from issuing the Top-up Shares due to NASDAQ Marketplace Rules, then the Company must instead pay the cash value of the Top-up Shares, based on the then-current fair value of such shares.

Pursuant to the RNAi Purchase Agreement, Roche has a right of first negotiation on certain product candidates developed by the Company and its affiliates relating to the purchased assets. If the Company proposes to out-license, or enters into substantive negotiations to out-license, any Clinical Candidate or Existing Candidate (as such terms are defined in the RNAi Purchase Agreement), the Company must give detailed notice of the Candidate it proposes to out-license and negotiate exclusively and in good faith with Roche for a period of time regarding the applicable out-license. This right of first negotiation applies to all Existing Candidates and the first five Clinical Candidates for which the Company delivers notice to Roche and subsequently enters into an out-license.

In addition to the consideration paid by the Company at the closing of the Transaction, the Company is obligated to make certain royalty and milestone payments to Roche upon the occurrence of certain events. For certain product candidates that are developed by the Company or its affiliates and that are covered by a valid claim by the patent rights transferred in the Transaction for which the Company and Roche do not enter into a licensing arrangement, the Company will be obligated to pay a 3% royalty on Net Sales (as defined in the RNAi Purchase Agreement), provided that the royalty rate may be reduced or offset in certain circumstances. The obligation to pay royalties on such candidates will last until the later of (i) the expiration of the last to expire patent right related to such product candidate that was transferred in the Transaction and (ii) ten years after the first commercial sale of such product candidate.

The Company will also be obligated to make cash payments to Roche upon the achievement of various milestones, including the first regulatory approval of an Existing Candidate in certain jurisdictions and upon certain annual sales milestones for Existing Candidates that may receive regulatory approval. The potential payments range from \$2,500,000 to \$6,000,000 per milestone.

On October 4, 2011, the Company completed a second closing to the private placement stock issuance of September 30, 2011. On October 4, 2011, the Company sold 138,157 shares of Common Stock at a price of \$3.80 per share. Cash proceeds were \$525,000.

On October 20, 2011, the Company and Lincoln Park Capital Fund, LLC, an Illinois limited liability company ("LPC") entered into a \$15 million purchase agreement (the "Purchase Agreement"), together with a registration rights agreement, whereby LPC agreed to purchase up to \$15 million of Common Stock, subject to certain limitations, from time to time during the three-year term of the Purchase Agreement. Additionally, the Company agreed to file a registration statement with the U.S. Securities & Exchange Commission covering the resale of the shares that may be issued to LPC under the Purchase Agreement. After the SEC declares effective the registration statement related to the resale of such shares, the Company will have the right, in its sole discretion, over a 36-month period to sell up to \$15 million of Common Stock (subject to certain limitations) to LPC, depending on certain conditions as set forth in the Purchase Agreement.

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On October 21, 2011 and October 24, 2011, the Company entered into Subscription Agreements with certain accredited investors (the “Series A Purchasers”), pursuant to which the Company agreed to issue and sell an aggregate of 1,015 shares of Series A Preferred Convertible Stock, \$0.001 par value per share, at a purchase price of \$1,000 per share. The aggregate purchase price to be paid by the Series A Purchasers for the shares of Series A Preferred is \$1,015,000. The closing of the sale of the shares occurred on October 26, 2011.

On October 21, 2011, the Company entered into a Subscription Agreement with a single accredited investor, pursuant to which the Company agreed to issue and sell an aggregate of 675,000 shares of Common Stock, \$0.001 par value per share, at a purchase price of \$3.70 per share. The aggregate purchase price to be paid by the purchaser for the shares of Common Stock was \$2,497,500. The closing of the sale of the Common Shares is expected to occur in fiscal 2012.

As of November 17, 2011, the Company effected a 1 for 10 reverse stock split. As a result of the reverse stock split, each ten shares of the Company’s Common Stock issued and outstanding immediately prior to the reverse split was combined into one share of Common Stock. Also, as a result of the Reverse Stock Split, the per share exercise price of, and the number of shares of Common Stock underlying Company stock options, warrants, Series A Preferred and any Common Stock based equity grants outstanding immediately prior to the reverse stock split was proportionally adjusted, based on the one-for-ten split ratio, in accordance with the terms of such options, warrants or other Common Stock based equity grants as the case may be. No fractional shares of Common Stock were issued in connection with the reverse split. Stockholders received a cash payment in lieu of any fractional shares. Unless otherwise noted, all share and per share amounts in these financial statements have been retrospectively adjusted to reflect the reverse stock split.

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT WERE OMITTED AND REPLACED WITH “[\*\*]”. A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECRETARY OF THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO AN APPLICATION REQUESTING CONFIDENTIAL TREATMENT UNDER RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934.

**STOCK AND ASSET PURCHASE AGREEMENT**

dated as of

October 21, 2011

among

**ARROWHEAD RESEARCH CORPORATION,**

**HOFFMANN-LA ROCHE INC.**

and

**F. HOFFMANN-LA ROCHE LTD**

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

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## STOCK AND ASSET PURCHASE AGREEMENT

AGREEMENT (this “**Agreement**”) dated as of October 21, 2011 by and among Arrowhead Research Corporation, a Delaware corporation (“**Buyer**”), Hoffmann-La Roche Inc., a New Jersey corporation (“**Roche Nutley**”), and F. Hoffmann-La Roche Ltd, a Swiss corporation (“**Roche Basel**” and, together with Roche Nutley, “**Sellers**”).

### WITNESSETH:

WHEREAS, Roche Nutley is the record and beneficial owner of the Shares (as defined herein) and desires to sell the Shares to Buyer, and Buyer desires to purchase the Shares from Roche Nutley, upon the terms and subject to the conditions hereinafter set forth;

WHEREAS, Sellers wish to transfer to Buyer their respective right, title and interest in, to and under the Transferred Assets, and Buyer desires to purchase from Sellers their respective right, title and interest in, to and under, and to assume the obligations of Sellers under, the Transferred Assets (as defined herein), upon the terms and subject to the conditions hereinafter set forth; and

WHEREAS, Sellers and Buyer intend (i) Roche Nutley’s sale of the Shares, (ii) Sellers’ transfer of their respective right, title and interest in, to and under the Transferred Assets and (iii) Buyer’s purchase of the Shares and of Sellers’ respective right, title and interest in, to and under the Transferred Assets and assumption of the obligations of Sellers under the Transferred Assets, in each case to be treated as a taxable disposition of the Shares and the Transferred Assets for United States federal income tax purposes;

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NOW THEREFORE, in consideration of the terms and conditions and the respective representations, warranties, covenants and agreements set forth herein, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree as follows:

ARTICLE 1  
DEFINITIONS

Section 1.01. *Definitions.* (a) As used herein, the following terms have the following meanings:

“**Affiliate**” means, with respect to any Person, any other Person directly or indirectly controlling, controlled by, or under common control with such Person; *provided* that (i) the Company shall not be considered an Affiliate of any Seller; (ii) neither Chugai Pharmaceutical Co., Ltd (at 1-1 Nihonbashi-Muromachi 2-chome, Chuo-ku, Tokyo, 103-8324, Japan) nor any of its subsidiaries shall be considered an Affiliate of any Seller, unless Sellers elect, in a written notice delivered to Buyer, to have any such Person considered an Affiliate of Sellers; and (iii) none of Roche Holding Ltd or any of its subsidiaries shall be considered an Affiliate of Buyer. For purposes of this definition, “**control**” when used with respect to any Person means the power to direct the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise, and the terms “**controlling**” and “**controlled**” have correlative meanings.

“**Alnylam Agreements**” means collectively the License and Collaboration Agreement dated July 8, 2007 among F. Hoffmann-La Roche Ltd, Hoffmann-La Roche Inc., Alnylam Pharmaceuticals, Inc., and Alnylam Europe AG; and the Collaboration Agreement dated October 29, 2009 among Alnylam Pharmaceuticals, Inc., F. Hoffmann-La Roche Ltd, and Hoffmann-La Roche Inc.

“**Applicable Law**” means, with respect to any Person, any transnational, domestic or foreign federal, state or local law (statutory, common or otherwise), constitution, treaty, convention, ordinance, code, rule, regulation, order, injunction, judgment, decree, ruling or other similar requirement enacted, adopted, promulgated or applied by a Governmental Authority that is binding upon or applicable to such Person, as amended unless expressly specified otherwise.

“**Business Day**” means a day, other than Saturday, Sunday or other day on which commercial banks in New York, New York are authorized or required by Applicable Law to close.

“**Buyer Disclosure Schedule**” means the disclosure schedule delivered concurrently herewith by Buyer to Sellers and dated as of the date hereof.

“**Buyer Employee Plan**” means any Employee Plan that is or has been entered into, sponsored, maintained, administered or contributed to, as the case may be, by Buyer or any of its Affiliates.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

**“Buyer Material Adverse Effect”** means a material adverse effect on the financial condition, business, assets or results of operations of Buyer and the Buyer Subsidiaries, taken as a whole, excluding any effect resulting from (A) changes in GAAP or the interpretation thereof, (B) changes in the general economic or political conditions or financial markets in the United States or elsewhere in the world, (C) changes (including changes of Applicable Law) or conditions generally affecting the industry in which Buyer and the Buyer Subsidiaries operate or (D) acts of war, sabotage or terrorism or natural disasters.

**“Buyer Note”** means the \$50,000 principal amount promissory note dated as of the date hereof delivered by Buyer to Roche Nutley substantially in the form of Exhibit A hereto.

**“Buyer Savings Plan”** means any tax-qualified defined contribution plan that is maintained by Buyer or any of its Affiliates.

**“Buyer Stock”** means the common stock, par value \$0.001 per share, of Buyer.

**“Buyer Subsidiary”** means any entity of which securities or other ownership interests having ordinary voting power to elect a majority of the board of directors or other persons performing similar functions are at the time directly or indirectly owned by Buyer.

**“Candidate”** means a Clinical Candidate or an Existing Candidate, as the case may be.

**“Change of Control”** means, with respect to any Person, (a) a sale of all or substantially all of the assets, voting stock or securities of such Person, (b) a merger, reorganization, spin-off or consolidation involving such Person, in which the holders of common stock or similar equity interests of such Person immediately prior to such transaction cease to own collectively a majority of the voting equity securities of its successor entity or (c) the acquisition by any other Person, or group of other Persons acting in concert, of 50% or more of the voting equity securities of such Person.

**“Clinical Candidate”** means any product owned, licensed or developed by Buyer or any of its Affiliates (including, after the Closing, the Company) Covered by a Valid Claim and with respect to which Buyer or any of its Affiliates has completed all requirements to initiate (under Buyer’s policies and procedures as in effect from time to time and in accordance with customary industry practices), or has previously initiated, [\*\*]; *provided* that no Existing Candidate shall be a Clinical Candidate. Notwithstanding the foregoing, the term Clinical

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Candidate shall not include any product candidate or composition of matter discovered, or first tested by Buyer or any of its Affiliates for activity against the applicable biological target based upon a compound supplied by a Third Party, in the course of a sponsored research, joint development or other collaborative research and development arrangement between Buyer (or any of its Affiliates, including, after the Closing, the Company) and any Third Party. Notwithstanding the foregoing, in no event shall the term Clinical Candidate include any product that targets either the [\*\*] or the [\*\*] genes, or any product that relies on a linear cyclodextrin or silicon microparticle delivery system, except where the applicable active compound originated from the Intellectual Property Rights transferred by Sellers or the Company under this Agreement. For the avoidance of doubt, Buyer Affiliate's candidate drugs known as CALAA-01 and CALAA-02 are not Clinical Candidates.

“**Closing Date**” means the date of the Closing.

“**Code**” means the United States Internal Revenue Code of 1986.

“**Combination Product**” means any product that contains, in addition to a Royalty Product (or pharmaceutically active ingredient thereof), one or more other pharmaceutically active ingredients that are not Royalty Products.

“**Common Stock**” means the common stock, par value \$0.01 per share, of the Company.

“**Company**” means Roche Madison Inc., a Delaware corporation.

“**Company Employee**” means each individual who is a current employee or independent contractor of the Company.

“**Company Intellectual Property Rights**” means all Intellectual Property Rights owned by the Company.

“**Company Material Adverse Effect**” means a material adverse effect on the financial condition, business, assets or results of operations of the Company, excluding any effect resulting from (A) changes in GAAP or IFRS or the interpretation thereof, (B) changes in the general economic or political conditions or financial markets in the United States or elsewhere in the world, (C) changes (including changes of Applicable Law) or conditions generally affecting the industry in which the Company operates or (D) acts of war, sabotage or terrorism or natural disasters.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

“**Company Return**” means any Tax Return of, with respect to or that includes the Company.

“**Contingent Consideration**” means the payments, if any, required to be made by Buyer pursuant to Section 6.02 and Section 6.03.

“**Cover,**” “**Covered**” or “**Covering**” means that an issued or applied for patent claim encompasses a particular process, method, machine, article of manufacture, or composition of matter, such that any making, using, offering to sell, selling, supplying, importing or exporting of the process, method, machine, article of manufacture, or composition of matter, without a license, would (i) in the case of any such issued patent claim, constitute infringement of such patent claim or (ii) in the case of any such applied for patent claim, constitute infringement of such patent claim were such patent claim to issue.

“**Covered Tax**” means (i) any Tax with respect to which the Company has filed or will file a Company Return with a member of any Seller Group on a consolidated basis pursuant to Section 1501 of the Code, (ii) any income or franchise Tax relating to any Pre-Closing Tax Period payable to any state, local or foreign taxing jurisdiction in which the Company has filed or will file a Company Return with a member of any Seller Group on an affiliated, consolidated, combined or unitary basis with respect to such Tax, (iii) any Tax imposed on the Company solely by reason of having been prior to the Closing Date a member of an affiliated, consolidated, combined or unitary group, (iv) any other Tax imposed on or in relation to the Company or the Transferred Assets for any Pre-Closing Tax Period; and (v) Sellers’ share of any of the Transfer Taxes under Section 7.02(f). For the avoidance of doubt, “Covered Tax” shall include any Tax imposed on or in relation to Roche Kulmbach GmbH.

“**DPC Patents**” means the patents and patent applications listed in Section 1.01 of the Sellers Disclosure Schedule.

“**DPC Product**” means any RNAi Product that is Covered by a Valid Claim of the DPC Patents.

“**Employee Plan**” means each “employee benefit plan,” as such term is defined in Section 3(3) of ERISA, whether or not such plan is subject to ERISA, and each employment, consulting, compensation, severance, continuation pay, termination pay, layoff or other similar written contract, plan, arrangement or policy and each written contract, plan, policy or arrangement providing for health, medical, life or other welfare benefit insurance coverage, workers’ compensation, disability benefits, supplemental unemployment benefits, holiday, dependent care assistance, education or vacation benefits, retirement benefits, deferred compensation, equity-based or other forms of incentive compensation, post-retirement or other similar benefits.

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“**Environmental Laws**” means any Applicable Law that has as its principal purpose the protection of the environment.

“**Environmental Permits**” means all permits, licenses, registrations, and other authorizations of any Governmental Authority required under applicable Environmental Laws.

“**ERISA**” means the Employee Retirement Income Security Act of 1974.

“**ERISA Affiliate**” of any entity means any other entity that, together with such entity, would be, or at the relevant time would have been, treated as a single employer under Section 414 of the Code.

“**Existing Candidate**” means any product owned, licensed or developed by Buyer or any of its Affiliates (including, after the Closing, the Company) (i) with respect to which Buyer or any of its Affiliates has completed all requirements to initiate (under Buyer’s policies and procedures as in effect from time to time and in accordance with customary industry practices), or has previously initiated, a GLP Toxicology Study; [\*\*]; and (iii) that is Covered by a Valid Claim.

“**First Commercial Sale**” means, with respect to any Royalty Product in any given country, (i) the date following the receipt of any applicable Regulatory Approval on which such Royalty Product is first sold in such country by Buyer or any of its Affiliates, or its or their respective licensee or sublicensee, to or for the benefit of end-users of such Royalty Product or (ii) if no such Regulatory Approval is required, the date on which such Royalty Product is first commercially launched in such country for sale to or for the benefit of end-users of such product.

“**GAAP**” means generally accepted accounting principles in the United States.

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“**GLP Toxicology Study**” means a toxicology study in accordance with then current “Good Laboratory Practices” (as such term is defined from time to time by the U.S. Food and Drug Administration), or comparable standards or requirements of Regulatory Authorities outside of the United States, which study is required to meet the requirements for filing an application with applicable Regulatory Authorities to initiate human clinical trials involving such product, including an Investigational New Drug application filed with the U.S. Food and Drug Administration or any foreign equivalent thereof.

“**Governmental Authority**” means any transnational, domestic or foreign federal, state or local governmental, regulatory or administrative authority, department, court, agency or official, including any political subdivision thereof.

“**IFRS**” means international financial reporting standards.

“**Intellectual Property Right**” means any and all: (a) Patent Rights; (b) know-how; (c) trademarks, service marks, trade names, mask works, logos, trade dress, goodwill and the applications for registration and registrations thereof; (d) rights to protect and limit the use or disclosure of trade secrets and confidential information; (e) copyrights, copyright applications, and copyright registrations; and (f) other similar types of proprietary intellectual property rights.

“**knowledge of Buyer**”, “**Buyer’s knowledge**” or any other similar knowledge qualification in this Agreement means to the actual knowledge of [\*\*].

“**knowledge of Sellers**”, “**Sellers’ knowledge**” or any other similar knowledge qualification or reference in this Agreement means to the actual knowledge of [\*\*].

“**License Agreement**” means the license agreement dated as of the date hereof between Sellers and Buyer substantially in the form of Exhibit B hereto.

“**Lien**” means, with respect to any property or asset, any mortgage, lien, pledge, charge, security interest or encumbrance in respect of such property or asset.

“**Materials of Environmental Concern**” means any pollutants or contaminants or any hazardous, acutely hazardous, radioactive or toxic substance, material or waste defined and regulated as such under Environmental Laws.

“**1934 Act**” means the Securities Exchange Act of 1934.

“**1933 Act**” means the Securities Act of 1933.

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**“Out-License”** means, with respect to any Candidate, (i) when used as a verb, to license and/or sell to a non-affiliated Person the right to test, make, market, promote, detail, distribute, offer for sale and/or sell such Candidate in any country and (ii) when used as a noun, the license or sale to a non-affiliated Person of the right to test, make, market, promote, detail, distribute, offer for sale and/or sell such Candidate in any country; *provided* that an Out-License shall not include any transaction that does not include the grant to such non-affiliated Person of the right (or an option to obtain the right) to promote, detail, distribute, offer for sale and/or sell such Candidate in such country. For the avoidance of doubt, an Out-License of a Candidate shall be deemed to include a sale of all or substantially all of the equity interests in one or more Affiliates of Buyer that hold all or substantially all of Buyer’s and its Affiliates’ right to test, make, market, promote, detail, distribute, offer for sale and/or sell such Candidate in any country; *provided* that a Change of Control with respect to Buyer shall not constitute an Out-License of a Candidate.

**“Patent Assignment Agreements”** means the patent assignment agreements substantially in the form of Exhibit C.

**“Patent Rights”** means all patents (including all reissues, reexamined patents, extensions, substitutions, confirmations, re-registrations, invalidations, supplementary protection certificates and patents of addition), patent applications (including all provisional applications, continuations, continuations-in-part and divisionals), as well as design patents, utility models or applications therefor.

**“Post-Closing Tax Period”** means any Tax period beginning after the Closing Date; and, with respect to a Straddle Tax Period, the portion of such Tax period beginning after the Closing Date.

**“Person”** means an individual, corporation, partnership, limited liability company, association, trust or other entity or organization, including a Governmental Authority.

**“Pre-Closing Tax Period”** means any Tax period ending on or before the Closing Date; and, with respect to a Straddle Tax Period, the portion of such Tax period ending on the Closing Date.

**“Registration Rights Agreement”** means the registration rights agreement dated as of the date hereof among Sellers and Buyer substantially in the form of Exhibit D.

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**“Regulatory Approval”** means, with respect to a Royalty Product in a given country, the approval of the applicable Regulatory Authority necessary for the marketing and sale of such Royalty Product in such country.

**“Regulatory Authority”** means the U.S. Food and Drug Administration or other Governmental Authorities (within or outside the United States) charged with the authority to regulate the pricing, marketing, promotion, manufacture, testing, distribution or sale of pharmaceutical products in a country or countries.

**“Required Third Party Payments”** shall mean royalty or milestone payments due to a Third Party from Buyer or the Company to license the Third Party’s Intellectual Property Rights which are reasonably necessary for Buyer to research, develop, make, have made, sell, offer to sell or import RNAi Products.

**“RNAi Business”** means any and all activities directed to RNAi Product drug discovery and development, including test method development and stability testing, toxicology, animal efficacy studies, formulation, clinical studies, clinical trials and testing, chemical development and manufacturing development and development documentation efforts in support of development activities anywhere in the world.

**“RNAi Products”** means products which include double-stranded oligonucleotide molecules that engage the RNA interference mechanisms in a cell.

**“Royalty Product”** means any Existing Candidate or DPC Product, as the case may be.

**“Sellers Disclosure Schedule”** means the disclosure schedule delivered concurrently herewith by Sellers to Buyer and dated as of the date hereof.

**“Seller Employee Plan”** means any Employee Plan that (i) is or has been entered into, sponsored, maintained, administered or contributed to, as the case may be, by any Seller, the Company or any of their respective Affiliates and (ii) covers any Company Employee or former employee of the Company.

**“Seller Group”** means any affiliated, consolidated, combined or unitary group (including any affiliated group of corporations as defined in Section 1504(a) of the Code) of which any of Sellers or any of their Affiliates is a member.

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“**Seller Savings Plan**” means any tax-qualified defined contribution plan that (i) is or has been entered into, maintained, administered or contributed to, as the case may be, by any Seller, the Company or any of their respective Affiliates and (ii) covers any Company Employee.

“**Shares**” means 100 shares of Common Stock, representing all of the outstanding shares of Common Stock.

“**Straddle Tax Period**” means a Tax period that begins on or before the Closing Date and ends thereafter.

“**Tax**” means (i) any tax, governmental fee or other like assessment or charge of any kind whatsoever (including, but not limited to, all federal, state, local, foreign, income, gross receipts, license, payroll, employment, excise, escheat, severance, stamp, occupation, premium, windfall, profits, environmental, customs, duties, capital stock, franchise, profits, withholding, social security (or similar, including FICA), unemployment, disability, real property, personal property, sales, use, transfer, registration, value added, alternative or add-on minimum, or estimated tax), together with any interest, penalty, addition to tax or additional amount, and any liability for any of the foregoing as transferee or successor, by contract or otherwise, (ii) in the case of the Company, liability for the payment of any amount of the type described in clause (i) as a result of being or having been before the Closing a member of an affiliated, consolidated, combined or unitary group, or a party to any agreement or arrangement, as a result of which liability of the Company to a Taxing Authority is determined or taken into account with reference to the activities of any other Person, and (iii) liability of the Company for the payment of any amount as a result of being party to any Tax Sharing Agreement.

“**Tax Asset**” means any net operating loss, net capital loss, investment tax credit, foreign tax credit, charitable deduction or any other credit or tax attribute that could be carried forward or back to reduce Taxes (including without limitation deductions and credits related to alternative minimum Taxes).

“**Tax Return**” means any Tax return, statement, report, election, declaration, disclosure, schedule, claim for refund, form, statement or document (including any estimated tax or information return or report) related to Taxes, including any schedule or attachment thereto, and including any amendment thereof.

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“**Tax Sharing Agreement**” means any agreement or arrangement (whether or not written) entered into prior to the Closing binding the Company that provide for the allocation, apportionment, sharing or assignment of any Tax liability or benefit, or the transfer or assignment of income, revenues, receipts, or gains for the purpose of determining any Person’s Tax liability.

“**Taxing Authority**” means any Governmental Authority responsible for the imposition or collection of any Tax.

“**Third Party**” means any Person other than Buyer, any Seller, the Company or any of their respective Affiliates.

“**Trademarks**” means any and all trademarks, trade names, corporate names, company names, business names, service marks, logos, brand names, domain names and all other source or business identifiers, and the rights in any of the foregoing which arise under Applicable Law, including all goodwill symbolized thereby or associated therewith.

“**Transaction Documents**” means this Agreement, the License Agreement, the Registration Rights Agreement, the Buyer Note and the Transition Services Agreement.

“**Transfer Taxes**” means all transfer, documentary, sales, use, stamp, registration and other such Taxes and fees (including any penalties and interest) incurred in connection with transactions contemplated by this Agreement (including any real property transfer Tax and any similar Tax).

“**Transferred Assets**” means, collectively, the Assigned Nutley Patents, the Assigned Basel Patents, the Assigned Nutley Licenses and the Assigned Basel Licenses.

“**Transferred Patent Rights**” means the Patent Rights included in the Transferred Assets or the Company Intellectual Property Rights.

“**Transition Services Agreement**” means the transition services agreement dated as of the date hereof between Roche Nutley and the Company, substantially in the form of Exhibit E hereto.

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“Valid Claim” means, as applicable, an enumerated claim in:

(i) any unexpired and issued patent included within the Transferred Patent Rights, as well as any patent filed by or on behalf of Buyer or the Company after the Closing which claims priority to, or shares a common priority date with, any such patent within the Transferred Patent Rights, in each case to the extent that such patents have not been disclaimed, canceled, revoked or held invalid, unenforceable, or otherwise unpatentable, by a final non-appealable decision of a court of competent jurisdiction or other Governmental Authority; or

(ii) any pending patent application for any applicable country: (A) that is on file with the applicable patent office and has shown evidence of reasonably consistent activity to advance to issuance of a patent, (B) which application has been on file with the applicable patent office for no more than five years from the earliest date to which the patent application claims its earliest priority, *provided* that the period shall extend to seven years from the earliest date to which the patent application claims its earliest priority for any application with the patent office in Japan, and (C) which is either included within the Transferred Patent Rights or was filed by or on behalf of Buyer or any of its Affiliates (including the Company) after Closing, but claims priority to, or shares a common priority date with, any patent or patent application included within the Transferred Patent Rights;

*provided, however,* that a Valid Claim shall not include any claim from a patent or patent application owned or controlled by, or licensed to, Buyer or its Affiliates immediately prior to Closing, or a patent or patent application that claims priority from any such patent or patent application.

(b) Each of the following terms is defined in the Section set forth opposite such term:

<u>Term</u>	<u>Section</u>
Agreement	Preamble
Assigned Basel Licenses	2.01
Assigned Basel Patents	2.01
Assigned Nutley Licenses	2.01
Assigned Nutley Patents	2.01
Assignment Prohibition	2.03
Balance Sheet Date	3.08
Buyer	Preamble
Buyer Equity Securities	Section 2.08

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<u>Term</u>	<u>Section</u>
Buyer SEC Documents	4.09
Capital Raise	4.07
Closing	2.02
Company Balance Sheet	3.08
Current Representation	10.13
Damages	9.02
Data Package	6.01
Designated Person	10.13
e-mail	10.01
Exclusivity Period	6.01
Generic Version	6.02
Indemnified Party	9.03
Indemnifying Party	9.03
Independent Accounting Firm	2.07
Leave Recipient	8.01
Loss	7.02
Market Price	2.08
Net Liabilities	2.04
Net Sales	6.02
Patent Service Provider	5.09
Permitted Liens	3.14
Post-Closing Capital Raise	2.08
Post-Closing Payment Date	2.08
Post-Closing Representation	10.13
Potential Contributor	9.06
Purchase Price	2.01
[**]	8.07
Roche Basel	Preamble
Roche Nutley	Preamble
Royalty Period	6.02
Seller Marks	5.05
Sellers	Preamble
Tax Benefit	7.06
Term Sheet Period	6.01
Total Consideration	2.07
Third Party Claim	9.03
Transferred Employee	8.01
WARN	8.09
Warranty Breach	9.02

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Section 1.02. *Other Definitional and Interpretative Provisions.* The words “hereof”, “herein” and “hereunder” and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. The captions herein are included for convenience of reference only and shall be ignored in the construction or interpretation hereof. References to Articles, Sections, Exhibits and Schedules are to Articles, Sections, Exhibits and Schedules of this Agreement unless otherwise specified. All Exhibits and Schedules annexed hereto or referred to herein are hereby incorporated in and made a part of this Agreement as if set forth in full herein. Any capitalized terms used in any Exhibit or Schedule but not otherwise defined therein, shall have the meaning as defined in this Agreement. Any singular term in this Agreement shall be deemed to include the plural, and any plural term the singular. Whenever the words “include”, “includes” or “including” are used in this Agreement, they shall be deemed to be followed by the words “without limitation”, whether or not they are in fact followed by those words or words of like import. “Writing”, “written” and comparable terms refer to printing, typing and other means of reproducing words (including electronic media) in a visible form. References to any statute shall be deemed to refer to such statute as amended from time to time and to any rules or regulations promulgated thereunder. References to any agreement or contract are to that agreement or contract as amended, modified or supplemented from time to time in accordance with the terms hereof and thereof. References to any Person include the successors and permitted assigns of that Person. References from or through any date mean, unless otherwise specified, from and including or through and including, respectively. References to “law”, “laws” or to a particular statute or law shall be deemed also to include any and all Applicable Law.

ARTICLE 2  
CLOSING

Section 2.01. *Purchase, Sale and Transfer.* Upon the terms and subject to the conditions of this Agreement, at the Closing:

(a) Roche Nutley agrees to sell to Buyer, and Buyer agrees to purchase from Roche Nutley, the Shares;

(b) Roche Nutley agrees to sell, convey, transfer, assign and deliver to Buyer, and Buyer agrees to acquire and accept, all of Roche Nutley’s right, title and interest in, to and under the patents and patent applications set forth on Section 2.01(b) of the Sellers Disclosure Schedule (collectively, the “**Assigned Nutley Patents**”);

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(c) Roche Basel agrees to sell, convey, transfer, assign and deliver to Buyer, and Buyer agrees to acquire and accept, all of Roche Basel's right, title and interest in, to and under the patents and patent applications set forth on Section 2.01(c) of the Sellers Disclosure Schedule (collectively, the "**Assigned Basel Patents**");

(d) subject to Section 2.03, Roche Nutley agrees to sell, convey, transfer, assign and deliver to Buyer, and Buyer agrees to acquire and accept, all of Roche Nutley's right, title and interest in and to, and Buyer agrees to assume, perform and discharge all of the obligations and liabilities of Roche Nutley under, all contracts, licenses, agreements and commitments listed on Section 2.01(d) of the Sellers Disclosure Schedule (collectively, the "**Assigned Nutley Licenses**"); and

(e) subject to Section 2.03, Roche Basel agrees to sell, convey, transfer, assign and deliver to Buyer, and Buyer agrees to acquire and accept, all of Roche Basel's right, title and interest in and to, and Buyer agrees to assume, perform and discharge all of the obligations and liabilities of Roche Basel under, all contracts, licenses, agreements and commitments listed on Section 2.01(e) of the Sellers Disclosure Schedule (the "**Assigned Basel Licenses**").

The purchase price for the Shares and the Transferred Assets (the "**Purchase Price**") is the Buyer Note and 9,017,021 shares of Buyer Stock issuable at the Closing and that number of shares of Buyer Stock (if any) and cash (if any) issuable or payable pursuant to Section 2.08 on the Post-Closing Payment Date. The Purchase Price shall be paid as provided in Section 2.02 and Section 2.08 and shall be allocated, along with the Contingent Consideration, as between Sellers and the Shares and Transferred Assets as set forth in Section 2.07.

Section 2.02. *Closing*. The closing (the "**Closing**") of the purchase and sale of the Shares and the transfer of the Transferred Assets hereunder shall take place at the offices of Davis Polk & Wardwell LLP, 450 Lexington Avenue, New York, New York, on the date hereof. At the Closing:

(a) Buyer shall deliver:

(i) to Sellers the Buyer Note duly executed by Buyer;

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(ii) to Buyer's registered transfer agent, with a copy to Sellers, irrevocable instructions, executed by an officer of Buyer and in a form reasonably acceptable to Sellers, instructing the transfer agent (A) to issue certificates for 9,017,021 shares of Buyer Stock registered in the name of Sellers (or such other Person as Sellers may designate), with any required transfer stamps affixed thereto and bearing the legend required pursuant to Section 2.05, and (B) to deliver such certificates to such address as Sellers may designate (it being understood that (x) Buyer shall cause the issuance and delivery of such share certificates as contemplated herein within five Business Days after the Closing and (y) such issuance shall be effective as of the Closing and the transfer agent shall be instructed accordingly);

(iii) to Sellers the Patent Assignment Agreements with respect to the Assigned Nutley Patents and the Assigned Basel Patents, duly executed by Buyer; and

(iv) to Sellers counterparts to each of the other Transaction Documents, duly executed by Buyer and each of its Affiliates party thereto.

(b) Sellers shall deliver to Buyer:

(i) certificates in proper form evidencing the Shares duly endorsed or accompanied by stock powers duly endorsed in blank, with any required transfer stamps affixed thereto;

(ii) the Patent Assignment Agreements with respect to the Assigned Nutley Patents and the Assigned Basel Patents, duly executed by Roche Nutley or Roche Basel, as applicable, and such customary bills of sale and/or other agreements or instruments of transfer, in each case as are reasonably satisfactory to Buyer and Sellers, to the extent necessary to evidence the transfer of the Assigned Nutley Licenses and the Assigned Basel Licenses hereunder; and

(iii) counterparts to each of the other Transaction Documents, duly executed by each Seller party thereto.

Section 2.03. *Understanding Regarding Assignment of Licenses and Rights.* Notwithstanding anything to the contrary herein, this Agreement shall not constitute an agreement to assign any Assigned Nutley License or Assigned Basel License or any claim or right or any benefit arising thereunder if such assignment,

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without the consent of a third party thereto, would constitute a breach or other contravention of such contract (an “**Assignment Prohibition**”); *provided* that the foregoing shall not limit or affect Sellers’ representations and warranties in Article 3. If an Assignment Prohibition shall exist, each party shall, and shall cause its Affiliates to, use its commercially reasonable efforts to obtain the consent of the other parties to any such Assigned Nutley License or Assigned Basel License or any claim or right or any benefit arising thereunder for the assignment thereof to the applicable Person pursuant to Section 2.01(d) or Section 2.01(e), as applicable, as Buyer may reasonably request (*provided* that neither Seller nor any Affiliate of any Seller shall be required to expend money or grant any accommodation (financial or otherwise) to any third party in connection therewith). If such consent is not obtained, or if an attempted assignment thereof would be ineffective or would adversely affect the rights of any Seller thereunder so that Buyer would not in fact receive all such rights, Sellers and Buyer shall cooperate in a mutually agreeable arrangement under which Buyer would obtain the benefits and assume the obligations thereunder in accordance with this Agreement, including sub-contracting, sub-licensing, or sub-leasing to Buyer, or under which the applicable Seller would enforce (at the direction of Buyer) for the benefit of Buyer, with Buyer assuming such Seller’s obligations, any and all rights of such Seller against a third party thereto (including, if applicable, the right to elect to terminate such Assigned Nutley License or Assigned Basel License in accordance with the terms thereof upon Buyer’s request); *provided* that neither Seller nor any Affiliate of any Seller shall be required to expend money or grant any accommodation (financial or otherwise) to any third party in connection therewith, unless Buyer agrees to promptly reimburse Sellers or their Affiliates (as applicable) for any such expenses. Promptly after any required consents to assignment are obtained for any such Assigned Nutley License or Assigned Basel License after the Closing, such Assigned Nutley License or Assigned Basel License shall be transferred and assigned to the applicable assignee as contemplated under Section 2.01(d) or Section 2.01(e), as applicable.

Section 2.04. *Intercompany Accounts; Net Liabilities; Cash Distributions; Accounts Payable.* (a) All intercompany account balances as of the Closing between any Seller or any of its Affiliates, on the one hand, and the Company, on the other hand, shall be cancelled, paid or otherwise settled or terminated immediately prior to the Closing. Except for the Transaction Documents or as provided on Section 2.04(a) of the Sellers Disclosure Schedule, all intercompany agreements or arrangements between any Seller or any of its Affiliates, on the one hand, and the Company, on the other hand, shall be terminated immediately prior to the Closing without any further liability or obligation on the part of any party thereto.

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(b) Immediately prior to the Closing, Sellers shall cause the Company to have cash and cash equivalents in an amount at least equal to the aggregate net amount of the assets and liabilities set forth on Section 2.04(b) of the Sellers Disclosure Schedule (the “**Net Liabilities**”). At the Closing, Sellers and Buyer shall cause the Company to distribute to Sellers all cash and cash equivalents then held by the Company in excess of the aggregate amount of the Net Liabilities.

(c) If as of the Closing, the Company has received, or following the Closing receives, any invoice for goods delivered or services rendered to the Company prior to the Closing which was not taken into account in the calculation of Net Liabilities, then, in each case, Buyer may promptly submit such invoice to Roche Nutley and request that Roche Nutley reimburse the Company for that portion of the invoiced amount that relates to goods delivered or services provided prior to the Closing. Roche Nutley shall pay such amount to the Company unless Roche Nutley disputes such amount, in which case the parties will work in good faith to determine the amount, if any, to be paid by Roche Nutley. Unless otherwise required by law, any amounts paid by Roche Nutley pursuant to this Section 2.04(c) shall, for U.S. federal income tax purposes, be treated as a contribution by Roche Nutley to the Company at the time immediately prior to the Closing.

Section 2.05. *Legends*. Each certificate representing shares of Buyer Stock issued to Sellers or any Person designated by Sellers pursuant to Section 2.02(a) (ii) shall bear a legend in substantially the following form:

THE SECURITIES REPRESENTED BY THIS INSTRUMENT HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE “SECURITIES ACT”), OR ANY STATE SECURITIES LAWS, AND NO SALE, ASSIGNMENT, PLEDGE, HYPOTHECATION, GIFT, TRANSFER OR OTHER DISPOSITION OR OFFER TO DO ANY OF THE FOREGOING MAY BE MADE UNLESS A REGISTRATION STATEMENT UNDER THE SECURITIES ACT AND OTHER APPLICABLE SECURITIES LAWS WITH RESPECT TO SUCH SECURITIES IS THEN IN EFFECT, OR IN THE OPINION OF COUNSEL, ACCEPTABLE TO THE ISSUER, SUCH REGISTRATION UNDER THE SECURITIES ACT AND OTHER APPLICABLE SECURITIES LAWS IS NOT REQUIRED.

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Section 2.06. *Resignations*. At the Closing, Sellers shall deliver to Buyer the resignations of all directors of the Company who will be officers, directors or employees of any Seller or any of Sellers' respective Affiliates after the Closing from their position with the Company.

Section 2.07. *Allocation of Consideration*. (a) Buyer and Sellers agree (i) that for U.S. federal income tax purposes, the consideration for the Shares and the Transferred Assets (for purposes of this Section 2.07 only, the Transferred Assets shall be deemed to include the materials required to be delivered by Sellers to Buyer under Section 5.03 of the Agreement) shall include the Purchase Price and the Contingent Consideration (the "**Total Consideration**") and (ii) with respect to the allocation of the Total Consideration described in Section 2.07(b), to be bound by such allocation in the preparation, filing and audit of any Tax Return; provided that, while the parties shall be obligated to defend in good faith such allocation in connection with any audit of any Tax Return, the parties shall not be required to litigate in any court any challenge to such allocation by any Taxing Authority.

(b) Buyer and Sellers agree to negotiate in good faith to agree on an allocation of the Total Consideration among the Sellers and the Shares and the Transferred Assets; provided that, notwithstanding anything to the contrary in this Agreement, Buyer and Sellers agree that, in all events, (x) the [\*\*] shall be allocated solely to the [\*\*], (y) the [\*\*] and the shares of, [\*\*] in each case, shall be allocated *pro rata* among the [\*\*], the [\*\*], the [\*\*], the [\*\*] and the [\*\*] according to the relative fair market values of the [\*\*], the [\*\*], the [\*\*], the [\*\*] and the [\*\*] and (z) of the shares of [\*\*] allocated to the [\*\*] and the [\*\*], a number of shares with a fair market value as of the Closing Date of [\*\*] shall be allocated to the laboratory books required to be delivered by Roche Basel to Buyer under Section 5.03 of the Agreement.

(c) If, within 90 days after the Closing, the parties are unable to reach agreement on the allocation described in Section 2.07(b), Buyer and Sellers shall refer the matter to an independent accounting firm in the United States to be mutually agreed upon by the parties (the "**Independent Accounting Firm**"), and the Independent Accounting Firm shall resolve any such disputes in a manner consistent with the proviso to Section 2.07(b). Buyer and Sellers agree that the Independent Accounting Firm's resolution shall be conclusive for the purposes of determining the allocation as of the Closing Date. The costs of any such resolution by the Independent Accounting Firm shall be borne equally by the parties.

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(d) To the extent that any Seller receives any portion of the Purchase Price or Contingent Consideration that has been allocated to the other Seller, such Seller shall be deemed to have received such portion on behalf of the other Seller.

Section 2.08 *Post-Closing Payment*. (a) After the Closing Date, Buyer shall use its reasonable best efforts to raise at least \$3,118,615 in cash in exchange for the issuance of Buyer Stock pursuant to one or more capital-raising transactions within the first anniversary of the Closing Date (including any such issuance occurring after the Closing pursuant to an agreement entered into on or prior to the Closing Date) (the “**Post-Closing Capital Raises**”). As used herein, “**Buyer Equity Securities**” means shares of Buyer Stock or any debt, equity, option, warrant, right or other security that is “linked” to Buyer Stock (including any debt, equity, option, warrant, right or other security that is convertible into, exchangeable for, or exercisable for, as the case may be, Buyer Stock). For the avoidance of doubt, issuance of warrants by Buyer to its consultants or other service providers in the ordinary course of business consistent with past practices for services rendered will not constitute a Post-Closing Capital Raise.

(b) On the Post-Closing Payment Date, Buyer shall issue and deliver to Sellers (or any Person designated by Sellers) certificates for that number of shares of Buyer Stock equal to 1,465,626 Shares *plus* 9.9% of the shares of Buyer Stock issued by Buyer in exchange for up to \$3,118,615 of cash (or, if Buyer fails to raise such amount in the period between the Closing Date and the Post-Closing Payment Date, such lesser amount actually raised, but including, in any case, the amount of consideration required to be paid in connection with the conversion, exchange or exercise of Buyer Equity Securities into or for Buyer Stock) raised by Buyer in any Post-Closing Capital Raises (assuming for purposes of this Section 2.08(b) that all Buyer Equity Securities (other than shares of Buyer Stock) issued in such Post-Closing Capital Raises are converted into or exchanged or exercised for, as applicable, shares of Buyer Stock); *provided* that if the issuance of all or any portion of such shares of Buyer Stock to Sellers (or any Person designated by Sellers) would require the approval of Buyer’s stockholders pursuant to Rule 5635(A)(1) of the NASDAQ Listing Rules and such approval has not been obtained on or prior to the Post-Closing Payment Date, Buyer shall (i) issue to Sellers (or any Person designated by Sellers) the maximum number of shares of Buyer Stock issuable to Sellers in compliance with Rule 5635(A)(1) of the NASDAQ Listing Rules in the absence of such stockholder approval and (ii)

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pay to Sellers an amount in cash (by wire transfer of immediately available funds to an account designated by Sellers) equal to the Market Price *multiplied by* a number equal to (A) the number of shares of Buyer Stock issuable to Sellers pursuant to this Section 2.08(b) (disregarding this proviso for such purposes) *less* (B) the number of shares of Buyer Stock issued to Sellers pursuant to clause (i) of this proviso. As used herein, “**Market Price**” means the average closing price of Buyer Stock for the ten trading days ending two trading days prior to the Post-Closing Payment Date on the NASDAQ Capital Market (or, if Buyer Stock is not then listed on such market, on the principal other U.S. national or regional securities exchange on which Buyer Stock is then listed or principal other U.S. national or regional market on which Buyer Stock is then traded).

(c) Notwithstanding the foregoing, Buyer shall not issue shares of Buyer Stock to Sellers (or any Person designated by Sellers) pursuant to Section 2.08(b) to the extent that such issuance would result in Roche Holding Ltd being deemed a “beneficial owner” of more than 9.9% of Buyer Stock (as determined in accordance with Rule 16a-1 promulgated under the 1934 Act).

(d) If, during the period between the Closing Date and the Post-Closing Payment Date, the outstanding shares of Buyer Stock shall be changed into a different number of shares or a different class (including by reason of any subdivision, reclassification, recapitalization, reorganization, stock split, reverse stock split, combination or exchange or readjustment of shares, or stock dividend thereon with a record date during such period), the calculation of the shares of Buyer Stock issuable to Sellers pursuant to Section 2.08(b) shall be appropriately adjusted.

(e) From and after the Closing Date, Buyer shall use its reasonable best efforts to obtain any approval of its stockholders required for the issuance of any shares of Buyer Stock that may be issuable to Sellers pursuant to Section 2.08(b).

(f) As used herein, “**Post-Closing Payment Date**” means the earlier to occur of (i) the first anniversary of the Closing Date (or, if such date is not a Business Day, on the next succeeding Business Day) or (ii) the Business Day immediately preceding the date on which a Change in Control with respect to Buyer is consummated.

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ARTICLE 3  
REPRESENTATIONS AND WARRANTIES OF SELLERS

Except as set forth in the Sellers Disclosure Schedule, Sellers jointly and severally represent and warrant to Buyer as of the date hereof that:

Section 3.01. *Corporate Existence and Power.* Each of Roche Basel, Roche Nutley and the Company is a corporation duly incorporated, validly existing and (to the extent applicable) in good standing under the laws of its jurisdiction of incorporation and has all corporate powers and all governmental licenses, authorizations, permits, consents and approvals required to carry on its business as now conducted, except for those licenses, authorizations, permits, consents and approvals the absence of which would not have a Company Material Adverse Effect. The Company is duly qualified to do business as a foreign corporation and is in good standing in each jurisdiction where such qualification is necessary, except for those jurisdictions where failure to be so qualified would not, individually or in the aggregate, have a Company Material Adverse Effect.

Section 3.02. *Corporate Authorization.* The execution, delivery and performance by each Seller of the Transaction Documents to which it is a party and the consummation of the transactions contemplated hereby and thereby are within such Seller's corporate powers and have been duly authorized by all necessary corporate action on the part of such Seller. Each Transaction Document to which such Seller is a party constitutes a valid and binding agreement of such Seller.

Section 3.03. *Governmental Authorization.* The execution, delivery and performance by each Seller of the Transaction Documents to which it is a party and the consummation of the transactions contemplated hereby and thereby require no action by or in respect of, or filing with, any Governmental Authority other than (i) compliance with the applicable requirements of the 1933 Act, the 1934 Act and any other federal state securities laws and (ii) any such action or filing as to which the failure to make or obtain would not have a Company Material Adverse Effect.

Section 3.04. *Noncontravention.* The execution, delivery and performance by each Seller of the Transaction Documents to which it is a party and the consummation of the transactions contemplated hereby and thereby do not and will not (i) violate the organizational documents of such Seller or the Company, (ii) assuming compliance with the matters referred to in Section 3.03, violate any Applicable Law, (iii) require any consent or other action by any

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Person under, constitute a default under, or give rise to any Assignment Prohibition or right of termination, cancellation or acceleration of any right or obligation of such Seller or the Company or to a loss of any benefit to which such Seller or the Company is entitled under any provision of any agreement or other instrument binding upon such Seller or the Company or (iv) result in the creation or imposition of any Lien on any asset of the Company, except for any Permitted Liens and with such exceptions, in the case of each of clauses (ii) through (iv), as would not have, individually or in the aggregate, a Company Material Adverse Effect.

Section 3.05. *Capitalization.* (a) The authorized capital stock of the Company consists of 100 shares of Common Stock, all of which are issued and outstanding.

(b) All outstanding shares of capital stock of the Company have been duly authorized and validly issued and are fully paid and non-assessable. Except as set forth in this Section 3.05, there are no outstanding (i) shares of capital stock or voting securities of the Company, (ii) securities of the Company convertible into or exchangeable for shares of capital stock or voting securities of the Company, (iii) options or other rights to acquire from the Company, or other obligation of the Company to issue, any capital stock, voting securities or securities convertible into or exchangeable for capital stock or voting securities of the Company or (iv) restricted shares, stock appreciation rights, performance units, contingent value rights, "phantom" stock or similar securities or rights that are derivative of, or provide economic benefits based, directly or indirectly, on the value or price of, any capital stock or voting securities of, or other ownership interests in, the Company. There are no outstanding obligations of the Company to repurchase, redeem or otherwise acquire any securities or other equity interests of the type described in clauses (i) through (iv) of the preceding sentence.

Section 3.06. *Ownership of Assets.* (a) Roche Nutley is the record and beneficial owner of the Shares, free and clear of any Lien, and will transfer and deliver to Buyer at the Closing valid title to the Shares free and clear of any Lien.

(b) Roche Nutley and Roche Basel (i) are the sole and exclusive owners of all patents included in the Assigned Nutley Patents and the Assigned Basel Patents, respectively, (ii) subject to the rights licensed to the Company, hold all right, title and interest in and to such patents free and clear of all Liens or licenses and (iii) will convey to Buyer at the Closing good and marketable title to and ownership of the Assigned U.S. Patents and the Assigned Basel Patents, respectively, free and clear all Liens or licenses (other than any licenses to the Company), except, in each of clauses (i) through (iii), as would not reasonably be expected to be material.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

(c) The Company (i) is the sole and exclusive owner of all Patent Rights included in the Company Intellectual Property Rights and (ii) holds all right, title and interest in and to such Patent Rights free and clear of all Liens or licenses (other than Permitted Liens or non-exclusive licenses granted by the Company in the ordinary course of business), except, in the case of each of clauses (i) and (ii), as would not reasonably be expected to be material.

Section 3.07. *Subsidiary*. There is no Person of which the Company directly or indirectly owns voting securities or other equity interests.

Section 3.08. *Financial Statements*. Section 3.08 of the Sellers Disclosure Schedule sets forth the unaudited stand-alone balance sheet of the Company as of June 30, 2011 (the “**Company Balance Sheet**”), derived from the accounting books and records of Sellers, their respective Affiliates and the Company and prepared in accordance with Sellers’ internal financial reporting practices. As used herein, “**Balance Sheet Date**” means June 30, 2011.

Section 3.09. *Absence of Certain Changes*. Since the Balance Sheet Date, the business of the Company has been conducted in the ordinary course consistent with past practices and there has not been any event, occurrence, development or state of circumstances or facts that has had or would reasonably be expected to have, individually or in the aggregate, a Company Material Adverse Effect; *provided, however*, that any material event, occurrence, development or state of circumstances or facts with respect to compensation and benefits practices related to Company Employees that is materially inconsistent with past practices since the Balance Sheet Date is listed in Section 3.09 of the Sellers Disclosure Schedule.

Section 3.10. *No Undisclosed Material Liabilities*. There are no liabilities of the Company of any kind, other than:

- (a) liabilities provided for in the Company Balance Sheet;
- (b) liabilities incurred in the ordinary course of business consistent with past practice since the Balance Sheet Date;
- (c) liabilities disclosed on Section 2.04(b) or Section 3.10 of the Sellers Disclosure Schedule;

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(d) liabilities disclosed in, related to or arising under any agreements, instruments or other matters disclosed in this Agreement or the Sellers Disclosure Schedule; or

(e) other undisclosed liabilities which, whether considered individually or in the aggregate, are not material to the Company.

Section 3.11. *Material Contracts.* (a) The Company is neither a party to nor bound by:

(i) any lease (whether of real or personal property) providing for annual rentals of \$25,000 or more that cannot be terminated on not more than 60 days' notice without payment by the Company of any material penalty;

(ii) any material partnership, joint venture or other similar agreement or arrangement;

(iii) any agreement relating to indebtedness for borrowed money or the deferred purchase price of property (in either case, whether incurred, assumed, guaranteed or secured by any asset), except any such agreement with an aggregate outstanding principal amount not exceeding \$50,000;

(iv) any material agreement that limits the freedom of the Company to compete in any line of business or with any Person or in any area; or

(v) any other agreement, commitment, arrangement or plan not made in the ordinary course of business that is material to the Company.

(b) Each agreement, contract, plan, lease, arrangement or commitment required to be disclosed pursuant to Section 3.11(a) is a valid and binding agreement of the Company, and is in full force and effect, and none of the Company or, to the knowledge of Sellers, any other party thereto is in default or breach in any respect under the terms of any such agreement, contract, plan, lease, arrangement or commitment, except for any such defaults or breaches which would not have a Company Material Adverse Effect.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

(c) Each Assigned Nutley License and Assigned Basel License is a valid and binding agreement of Roche Nutley or Roche Basel, as the case may be, and is in full force and effect, and neither such Seller nor, to the knowledge of Sellers, any other party thereto is in default or breach in any respect under the terms of any such Assigned Nutley License or Assigned Basel License, except for any such defaults or breaches which would not have a Company Material Adverse Effect. Other than as listed on Section 3.11(c) of the Sellers Disclosure Schedule, to the knowledge of Sellers, none of Roche Nutley, Roche Basel or the Company has received any written notice under any of the Assigned Nutley Licenses and Assigned Basel Licenses asserting that there has been or that there is likely to occur a breach or default under such Assigned Nutley Licenses and Assigned Basel Licenses.

Section 3.12. *Litigation*. There is no action, suit, investigation, claim, arbitration or proceeding pending against, or to the knowledge of Sellers, threatened against or affecting, any Seller, the Company or any of their respective properties before any arbitrator or any Governmental Authority which is reasonably likely to be material to the Company. There is no action, suit, investigation, claim, arbitration or proceeding initiated by any Seller or the Company relating to RNAi Products which is reasonably likely to be material to the Company.

Section 3.13. *Compliance with Laws and Court Orders*. The Company is not in violation of any Applicable Law, except for violations that have not had and would not reasonably be expected to have, whether considered individually or in the aggregate, a Company Material Adverse Effect.

Section 3.14. *Properties*. The Company has good title to, or in the case of leased property and assets has valid leasehold interests in, all property and assets (whether real, personal, tangible or intangible) reflected on the Company Balance Sheet, except for properties and assets sold since the Balance Sheet Date in the ordinary course of business consistent with past practices or where the failure to have such good title or valid leasehold interests would not have a Company Material Adverse Effect. The Company does not own any real property. None of such property or assets is subject to any Lien, except:

(i) Liens disclosed on Schedule 3.14;

(ii) Liens for Taxes, assessments and similar charges that are not yet due or are being contested in good faith, in each case for which adequate reserves have been made in accordance with GAAP;

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(iii) mechanic's, materialman's, carrier's, repairer's and other similar Liens arising or incurred in the ordinary course of business or that are not yet due and payable or are being contested in good faith;

(iv) Liens incurred in the ordinary course of business that would not have a Company Material Adverse Effect; or

(v) other Liens which would not reasonably be expected to be material to the Company (paragraphs (i)-(v) of this Section 3.14 are, collectively, the "**Permitted Liens**").

Section 3.15. *Intellectual Property*. (a) Section 3.15(a) of the Sellers Disclosure Schedule contains a list of all patents, material registered trademarks, registered copyrights and applications for the foregoing that are included in the Company Intellectual Property Rights.

(b) Sellers have no knowledge that any material Company Intellectual Property Right is subject to any outstanding judgment, injunction, order, decree or agreement restricting the use thereof by the Company or restricting the licensing thereof by the Company to any Person.

(c) To the knowledge of Sellers, the Transferred Patent Rights constitute all of the material Patent Rights owned by Sellers or the Company that are exclusively used in the RNAi Business as currently conducted by the Company, to the extent that Sellers and the Company have such Patent Rights.

(d) Sellers have no knowledge of any infringement, misappropriation or other violation of any Intellectual Property Right of any Third Party in any respect by the Company.

(e) Sellers have no knowledge of any claims made or threatened in writing (including any demand, offer or request to license) by Third Parties asserting that the Sellers or the Company have infringed (or would infringe) or misappropriated the Intellectual Property Rights of any Third Party.

(f) Sellers have no knowledge of the invalidity or unenforceability, in whole or in part, of the Company Intellectual Property.

(g) Sellers have no knowledge of any Third Party claims in writing asserting the invalidity or unenforceability of any portion of the Company Intellectual Property Rights.

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(h) Sellers have no knowledge of (i) any Third Party claims in writing contesting the inventorship of any material portion of the Company Intellectual Property Rights or (ii) the failure to name any inventor required to be named in any of the Transferred Patent Rights.

(i) Neither the Company nor any Sellers has notified any Third Party in writing that such Third Party has or would infringe or misappropriate any portion of the material Company Intellectual Property.

(j) Sellers have no knowledge that any of the material Company Intellectual Property Rights set forth on the Sellers Disclosure Schedule have been abandoned, disclaimed, or allowed to expire due to the failure to pay applicable maintenance and renewal fees as of the Closing Date, except as otherwise indicated.

(k) As of the Closing, there are no Required Third Party Payments that are due and payable by the Company to Third Parties under the Alnylam Agreements.

Section 3.16. *Finders' Fees*. There is no investment banker, broker, finder or other intermediary that has been retained by or is authorized to act on behalf of any Seller or the Company who might be entitled to any fee or commission in connection with the transactions contemplated by this Agreement.

Section 3.17. *Employee Matters*. (a) Section 3.17(a) of the Sellers Disclosure Schedule sets forth each material Seller Employee Plan. With respect to each such Seller Employee Plan, Sellers have furnished or made available to Buyer a true and complete copy of the summary plan description or other written summary of all material plan terms. No Seller Employee Plan is sponsored or maintained by the Company. The Company will not have any liabilities with respect to any Seller Employee Plan or any Employee Plan covering any former employee of Roche Kulmbach GmbH following the Closing.

(b) With respect to each Seller Employee Plan, no event has occurred and no circumstance exists that has resulted or could reasonably be expected to result in a liability or Tax that would be a liability or Tax of the Company following the Closing pursuant to Sections 409 or 502(i) of ERISA or Section 4975 of the Code. There are no pending or, to the knowledge of Sellers or the Company, threatened or anticipated claims (other than routine claims for benefits) by, on behalf of, or against any Seller Employee Plan or any Employee Plan covering any former employee of Roche Kulmbach GmbH or any trusts related to any such Seller Employee Plan or Employee Plan that could reasonably be expected to result in any liability that would be a liability of the Company following the Closing.

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(c) Within the past seven years, (i) neither the Company nor any ERISA Affiliate has sponsored, contributed to, been required to contribute to, or had any obligations or liability with respect to a “multiemployer plan” within the meaning of Section 3(37) of ERISA and (ii) neither the Company nor Roche Kulmbach GmbH has sponsored, contributed to, been required to contribute to, or had any obligations or liability with respect to a “defined benefit plan” within the meaning of Section 3(35) of ERISA. No event has occurred, and no circumstance exists, that has resulted or could reasonably be expected to result in (A) a liability to the Company that would be a liability of the Company following the Closing with respect to the Company’s or any ERISA Affiliate’s sponsorship of, contribution (or obligation to contribute) to, or payment of (or any obligation to pay) benefits or premiums under any “defined benefit plan” or (B) a lien on the assets of the Company that would arise or continue following the Closing arising by reason of such liability.

(d) No Seller Employee Plan provides medical, life insurance or death benefits with respect to former employees of the Company or Roche Kulmbach GmbH, other than benefits that are required to be provided pursuant to Section 4980B of the Code or other Applicable Law, that would become the liability of Buyer or the Company as a result of the consummation of the transactions contemplated by this Agreement.

(e) The consummation of the transactions contemplated by this Agreement will not, separately or in conjunction with any other event, entitle any Company Employee to receive from the Company severance pay, unemployment compensation or any other payment or accelerate the time of payment, vesting, or funding of, or increase the amount of, compensation due to any Company Employee. Section 3.17(e) of the Sellers Disclosure Schedule sets forth the recipient and the amount of each lump sum cash retention payment to be made on or prior to Closing Date by Sellers or their Affiliates to the Company Employees.

(f) With respect to the Company Employees, (i) none of any Seller or the Company is a party to, or is otherwise subject to, a collective bargaining, works council or similar agreement, (ii) there are no unfair labor practice complaints pending against any Seller or the Company before any labor relations tribunal or authority, (iii) no petition has been filed or proceedings instituted with any labor relations board seeking recognition of a bargaining representative and to

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the knowledge of Sellers no demand for recognition has been made by, or on behalf of, any labor union or similar organization, (iv) Sellers and the Company are in material compliance with all Applicable Laws respecting employment and employment practices and terms and conditions of employment, including but not limited to wages and hours and the classification of employees and independent contractors, and are not engaged in any unfair labor practice as defined in the National Labor Relations Act, and (v) there is not, nor to the knowledge of Sellers, there is not now threatened, any walkout, strike, lockout, union activity, picketing, work stoppage, work slowdown, material effort to organize or represent the Company Employees, or any other similar occurrence, and there has been no such activity during the past three years. To the knowledge of Sellers, no Company Employee is represented by a labor union. All Company Employees are employees at-will.

(g) Section 3.17(g) of the Sellers Disclosure Schedule sets forth a true and complete list as of the date of this Agreement of the name, title and annual salary of each Company Employee. To the knowledge of Sellers, no current executive or key Company Employee has, nor have Company Employees that in the aggregate are equal to more than 20% of the total number of Company Employees, given notice of termination of employment, or otherwise disclosed to any Seller or the Company plans to terminate employment, with any Seller or the Company.

(h) The Company has not, during the three-year period prior to the date hereof, taken any action that would constitute a "Mass Layoff" or "Plant Closing" within the meaning of the WARN Act or would otherwise trigger notice requirements or liability under any state or local plant closing notice law. No court decision, governmental order, material contract or collective bargaining agreement to which any Seller or the Company is a party or is subject in any way limits or restricts the Company from relocating or closing any of the operations of the Company.

(i) Sellers, the Company and the relevant plan administrator if other than Sellers or the Company have at all relevant times properly classified each provider of services to the Company as an employee or independent contractor, as the case may be, for all purposes relating to each Seller Employee Plan for which such classification could be material, except for any failure to classify properly any such provider of services that has not resulted and could not reasonably be expected to result in any material liability to the Company.

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Section 3.18. *Environmental Matters.* (a) Except as to matters that would not reasonably be expected to have a Company Material Adverse Effect:

(i) (A) no written notice, order, request for information, complaint or penalty has been received by any Seller or the Company, and (B) there are no judicial, administrative or other actions, suits or proceedings pending or threatened, in the case of each of (A) and (B), which allege a violation of any Environmental Law and relate to the Company;

(ii) there has been no written environmental audit conducted within the past two years by any Seller or the Company in the possession of a Seller or the Company of any property currently owned or leased by the Company which has not been delivered to Buyer prior to the date hereof;

(iii) the Company has complied since October 1, 2008 with all applicable Environmental Laws, which compliance includes obtaining, maintaining and complying with all applicable Environmental Permits required under such Environmental Laws for the Company to operate;

(iv) to the knowledge of Sellers, there are no Materials of Environmental Concern at any of the properties which the Company owns, leases or operates or at properties formerly owned, leased or operated by the Company, under circumstances that are reasonably likely to result in liability of the Company under any applicable Environmental Law; and

(v) to the knowledge of Sellers, there are no current facts, circumstances or conditions relating to the operations of the Company or any currently or formerly owned, leased or operated properties of the Company that would reasonably be expected to result in the Company incurring liability under any applicable Environmental Law.

(b) Except as set forth in this Section 3.18, no representations or warranties are being made with respect to matters arising under or relating to Environmental Law or other environmental matters.

Section 3.19. *Accredited Investor; Purchase for Investment.* (a) Each Seller is an “accredited investor” as that term is defined in Rule 501(a) of Regulation D, promulgated under the 1933 Act.

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(b) Sellers are acquiring the shares of Buyer Stock hereunder for investment for their own account and not with a view to, or for sale in connection with, any distribution thereof. Sellers (either alone or together with their advisors) have sufficient knowledge and experience in financial and business matters so as to be capable of evaluating the merits and risks of such investment in the shares of Buyer Stock and are capable of bearing the economic risks of such investment.

Section 3.20. *No Other Representations.* Except as expressly set forth in this Agreement, Buyer disclaims any express or implied representations or warranties of any nature relating to Buyer or the Buyer Stock.

ARTICLE 4  
REPRESENTATIONS AND WARRANTIES OF BUYER

Except as set forth in the Buyer Disclosure Schedule or the Buyer SEC Documents filed after September 30, 2010 and before the date of this Agreement, Buyer represents and warrants to Sellers as of the date hereof that:

Section 4.01. *Corporate Existence and Power.* Buyer is a corporation duly incorporated, validly existing and in good standing under the laws of Delaware and has all corporate powers and all material governmental licenses, authorizations, permits, consents and approvals required to carry on its business as now conducted, except for those licenses, authorizations, permits, consents and approvals the absence of which would not have a Buyer Material Adverse Effect. Buyer is duly qualified to do business as a foreign corporation and is in good standing in each jurisdiction where such qualification is necessary, except for those jurisdictions where failure to be so qualified would not, individually or in the aggregate, have a Buyer Material Adverse Effect.

Section 4.02. *Corporate Authorization.* (a) The execution, delivery and performance by Buyer of the Transaction Documents and the consummation of the transactions contemplated hereby and thereby are within the corporate powers of Buyer and have been duly authorized by all necessary corporate action on the part of Buyer. Each Transaction Document constitutes a valid and binding agreement of Buyer. No vote by holders of any of Buyer's capital stock is necessary in connection with the consummation of the transactions contemplated by the Transaction Documents.

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(b) At meetings duly called and held, Buyer's board of directors has (i) unanimously determined that this Agreement and the other Transaction Documents and the transactions contemplated hereby and thereby, including the issuance of the shares of Buyer Stock at the Closing pursuant to Section 2.02(a)(ii) and on the Post-Closing Payment Date pursuant to Section 2.08, are fair to and in the best interests of Buyer's stockholders and (ii) unanimously approved, adopted and declared advisable this Agreement and the transactions contemplated hereby, including the issuance of the shares of Buyer Stock at the Closing pursuant to Section 2.02(a)(ii) and on the Post-Closing Payment Date pursuant to Section 2.08.

Section 4.03. *Governmental Authorization.* The execution, delivery and performance by Buyer of the Transaction Documents and the consummation of the transactions contemplated hereby and thereby require no material action by or in respect of, or material filing with, any Governmental Authority other than (i) compliance with the applicable requirements of the 1933 Act, the 1934 Act and any other federal state securities laws, (ii) compliance with the applicable requirements of the NASDAQ Capital Market and (iii) any such action or filing as to which the failure to make or obtain would not have a Buyer Material Adverse Effect.

Section 4.04. *Noncontravention.* The execution, delivery and performance by Buyer of the Transaction Documents and the consummation of the transactions contemplated hereby and thereby do not and will not (i) violate the certificate of incorporation or bylaws of Buyer, (ii) assuming compliance with the matters referred to in Section 4.03, violate any Applicable Law (iii) require any consent or other action by any Person under, constitute a default under, or give rise to any right of termination, cancellation or acceleration of any right or obligation of Buyer or to a loss of any benefit to which Buyer is entitled under any provision of any agreement or other instrument binding upon Buyer or (iv) result in the creation or imposition of any material Lien on any asset of Buyer, with such exceptions, in the case of each of clauses (ii) through (iv), as would not have, individually or in the aggregate, a Buyer Material Adverse Effect.

Section 4.05. *Financing.* Buyer has sufficient cash, available lines of credit or other sources of immediately available funds to enable it to pay the Purchase Price and any other amounts to be paid by it hereunder.

Section 4.06. *Buyer Stock.* The shares of Buyer Stock delivered pursuant to Section 2.02(a)(ii) have been, and the shares of Buyer Stock issued pursuant to Section 2.08 will be when issued, duly authorized and validly issued and are (or will be when issued) fully paid and non-assessable and the issuance thereof is not subject to any preemptive or other similar right.

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Section 4.07. *Capitalization.* (a) The authorized capital stock of Buyer consists of 145,000,000 shares of Buyer Stock and 5,000,000 shares of preferred stock, par value \$0.001 per share. As of October 19, 2011, (i) 87,804,443 shares of Buyer Stock were outstanding, (ii) 7,290,947 shares of Buyer Stock were subject to options to purchase shares of Buyer Stock under compensatory stock options or compensation plans or arrangements of Buyer at a weighted-average exercise price of \$0.90 per share (of which options to purchase an aggregate of 5,221,980 shares of Buyer Stock were exercisable), (iii) 0 shares of Buyer Stock were subject to awards made in the form of restricted common stock or rights to receive unrestricted common stock, (iv) 24,350,044 shares of Buyer Stock were issuable upon exercise of outstanding warrants to purchase shares of Buyer Stock at a weighted-average exercise price of \$0.98, and (v) 0 shares of Series A Preferred Stock, par value \$0 per share, of Buyer were issued or outstanding.

(b) All outstanding shares of capital stock of Buyer have been duly authorized and validly issued and are fully paid and non-assessable, and all shares of capital stock of Buyer that may be issued pursuant to any compensatory stock option or other compensation plan or arrangement will be, when issued, duly authorized and validly issued, fully paid and non-assessable and free of preemptive rights. Except as set forth in this Section 4.07 and for changes since October 5, 2011 resulting from the exercise of warrants or options to purchase shares of Buyer Stock under compensatory stock options or compensation plans or arrangements outstanding on such date and the vesting of awards made in the form of rights to receive unrestricted common stock outstanding on such date, there are no outstanding (i) shares of capital stock or voting securities of Buyer, (ii) securities of Buyer convertible into or exchangeable for shares of capital stock or voting securities of Buyer, (iii) options or other rights to acquire from Buyer, or other obligation of Buyer to issue, any capital stock, voting securities or securities convertible into or exchangeable for capital stock or voting securities of Buyer or (iv) restricted shares, stock appreciation rights, performance units, contingent value rights, "phantom" stock or similar securities or rights that are derivative of, or provide economic benefits based, directly or indirectly, on the value or price of, any capital stock or voting securities of, or other ownership interests in, the Company. There are no outstanding obligations of Buyer or any subsidiary of Buyer to repurchase, redeem or otherwise acquire any securities or other equity interests of the type referred to in clauses (i) through (iv) of the preceding sentence. As of the date hereof, there are no outstanding bonds, debentures, notes or other indebtedness of Buyer having the right to vote (or convertible into, or exchangeable for, securities having the right to vote) on any matters on which stockholders of Buyer may vote.

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(c) Concurrently with or prior to the consummation of the transactions contemplated hereby, Buyer is consummating or has consummated a capital raise (the “**Capital Raise**”) by (i) selling 23,720,750 shares of Buyer Stock and 915 shares of Buyer’s Series A Preferred Stock, par value \$0.001 per share, for aggregate proceeds of at least \$9,881,385 and (ii) entering into an equity line agreement by which Buyer may sell a number of shares of Buyer Stock for up to \$15,000,000 (the “**Equity Line**”). Section 4.07(c) of the Buyer Disclosure Schedule sets forth the name of each investor who is participating or has participated in the Capital Raise or Equity Line, the number of shares of Buyer Stock purchased or to be purchased by each such investor and the purchase price therefor and the agreement(s) pursuant to which such purchase has been or is being consummated.

(d) Each agreement that Buyer has entered into on or prior to the date hereof with respect to the Capital Raise or any contemplated Post-Closing Capital Raise (including that Purchase Agreement dated as of October 20, 2011 by and between Buyer and Lincoln Park Capital Fund, LLC) is a valid and binding agreement of Buyer and is in full force and effect, and neither Buyer nor, to the knowledge of Buyer, any other party thereto is, or has threatened or would reasonably be expected to be, in default or breach in any respect under the terms of any such agreement. Buyer has made available to Sellers a true and complete copy of each such agreement.

(e) After giving effect to the Capital Raise, immediately after the Closing, the shares of Buyer Stock issued to Sellers pursuant to Section 2.02(a)(ii) will represent approximately [\*\*]% of the issued and outstanding Buyer Stock and [\*\*]% of Buyer’s share capital on a fully diluted basis (*i.e.*, assuming the conversion, exchange or exercise, as applicable, of (i) all securities convertible into or exchangeable for shares of capital stock or voting securities of Buyer and (ii) all options or other rights to acquire from Buyer, or other obligation of Buyer to issue, any capital stock, voting securities or securities convertible into or exchangeable for capital stock or voting securities of Buyer).

Section 4.08. *Buyer Subsidiaries.* (a) Each Buyer Subsidiary is an entity duly organized, validly existing and (where applicable) in good standing under the laws of its jurisdiction of formation and has all company powers and all governmental licenses, authorizations, permits, consents and approvals required to

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carry on its business as now conducted, except for those licenses, authorizations, consents and approvals the absence of which would not have a Buyer Material Adverse Effect. Section 4.08 of the Buyer Disclosure Schedule identifies all material Buyer Subsidiaries and their respective jurisdictions of organization.

(b) All of the outstanding capital stock or other voting securities of each Buyer Subsidiary is owned by Buyer, directly or indirectly, free and clear of any Lien. There are no outstanding (i) securities of Buyer or any Buyer Subsidiary convertible into or exchangeable for shares of capital stock or voting securities of any Buyer Subsidiary, (ii) options or other rights to acquire from Buyer or any Buyer Subsidiary, or other obligation of Buyer or any Buyer Subsidiary to issue, any capital stock, voting securities or securities convertible into or exchangeable for capital stock or voting securities of any Buyer Subsidiary or (iii) restricted shares, stock appreciation rights, performance units, contingent value rights, “phantom” stock or similar securities or rights that are derivative of, or provide economic benefits based, directly or indirectly, on the value or price of, any capital stock or voting securities of, or other ownership interests in, the Company. There are no outstanding obligations of Buyer or any Buyer Subsidiary to repurchase, redeem or otherwise acquire any outstanding securities or other equity interests of the type described in clauses (i) through (iii) of the preceding sentence. Except for the capital stock or other voting securities of, or ownership interests in, the Buyer Subsidiaries, Buyer does not own, directly or indirectly, any capital stock or other voting securities of, or ownership interests in, any Person.

Section 4.09. *SEC Filings.* (a) Buyer has filed with or furnished to the Securities and Exchange Commission all reports, schedules, forms, statements, prospectuses, registration statements and other documents required to be filed or furnished by Buyer since September 30, 2009 (collectively, together with any exhibits and schedules thereto and other information incorporated therein, the “**Buyer SEC Documents**”).

(b) As of its filing date (and as of the date of any amendment), each Buyer SEC Document complied as to form in all material respects with the applicable requirements of the 1933 Act and the 1934 Act, as the case may be.

(c) As of its filing date (or, if amended or superseded by a filing prior to the date hereof, on the date of such filing), each Buyer SEC Document filed pursuant to the 1934 Act did not contain any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements made therein, in the light of the circumstances under which they were made, not misleading.

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(d) Each Buyer SEC Document that is a registration statement, as amended or supplemented, if applicable, filed pursuant to the 1933 Act, as of the date such registration statement or amendment became effective, did not contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading.

(e) Buyer has established and maintains disclosure controls and procedures (as defined in Rule 13a-15 under the 1934 Act). Such disclosure controls and procedures are designed to ensure that material information relating to Buyer, including the Buyer Subsidiaries, is made known to Buyer's principal executive officer and its principal financial officer by others within those entities, particularly during the periods in which the periodic reports required under the 1934 Act are being prepared. Such disclosure controls and procedures are effective in timely alerting Buyer's principal executive officer and principal financial officer to material information required to be included in Buyer's periodic and current reports required under the 1934 Act.

(f) Buyer and the Buyer Subsidiaries have established and maintained a system of internal controls over financial reporting (as defined in Rule 13a-15 under the 1934 Act) sufficient to provide reasonable assurance regarding the reliability of Buyer's financial reporting and the preparation of Buyer's financial statements for external purposes in accordance with GAAP. Since September 30, 2009, there have not been any (i) significant deficiencies or material weaknesses in the design or operation of internal controls which are or were reasonably likely to adversely affect Buyer's ability to record, process, summarize and report financial information or (ii) fraud, whether or not material, that involved management or other employees who have or had a significant role in Buyer's and the Buyer Subsidiaries' internal controls.

(g) Since September 30, 2009, Buyer has complied in all material respects with the applicable listing and corporate governance rules and regulations of the NASDAQ Capital Market.

(h) Each of the principal executive officer and principal financial officer of Buyer (or each former principal executive officer and principal financial officer of Buyer, as applicable) have made all certifications required by Rule 13a-14 and 15d-14 under the 1934 Act and Sections 302 and 906 of the Sarbanes-Oxley Act of 2002 and any related rules and regulations promulgated by the Securities and Exchange Commission and the NASDAQ Capital Market, and the statements contained in any such certifications are complete and correct.

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Section 4.10. *Buyer Financial Statements*. The audited consolidated financial statements and unaudited consolidated interim financial statements of Buyer included or incorporated by reference in the Buyer SEC Documents fairly present in all material respects, in conformity with GAAP applied on a consistent basis (except as may be indicated in the notes thereto), the consolidated financial position of Buyer and its consolidated Buyer Subsidiaries as of the dates thereof and their consolidated results of operations and cash flows for the periods then ended (subject to normal year-end audit adjustments in the case of unaudited financial statements).

Section 4.11. *Absence of Certain Changes*. Since June 30, 2011, the business of Buyer and the Buyer Subsidiaries has been conducted in the ordinary course consistent with past practices and there has not been any event, occurrence, development or state of circumstances or facts that has had or would reasonably be expected to have, individually or in the aggregate, a Buyer Material Adverse Effect.

Section 4.12. *No Undisclosed Material Liabilities*. There are no liabilities of Buyer or any Buyer Subsidiary of any kind, other than:

(a) liabilities provided for in Buyer's most recent audited consolidated balance sheet included in a Buyer SEC Document prior to the date hereof or in the notes thereto;

(b) liabilities incurred in the ordinary course of business of Buyer and the Buyer Subsidiaries consistent with past practices since the date of Buyer's most recent audited consolidated balance sheet included in a Buyer SEC Document prior to the date hereof;

(c) liabilities disclosed on Schedule 4.12;

(d) liabilities disclosed in, related to or arising under any agreements, instruments or other matters disclosed by Buyer in this Agreement or the Buyer Disclosure Schedule; or

(e) other undisclosed liabilities which, individually or in the aggregate, are not material to Buyer and the Buyer Subsidiaries, taken as a whole.

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Section 4.13. *Litigation*. There is no action, suit, investigation or proceeding pending against, or to the knowledge of Buyer threatened against or affecting, Buyer or any Buyer Subsidiary or any of their respective properties before any arbitrator or any Governmental Authority which is reasonably likely to have a Buyer Material Adverse Effect or which in any manner challenges or seeks to prevent, enjoin, alter or materially delay the transactions contemplated by this Agreement.

Section 4.14. *Compliance with Laws and Court Orders*. Neither Buyer nor any Buyer Subsidiary is in violation of any Applicable Law, except for violations that have not had and would not reasonably be expected to have, individually or in the aggregate, a Buyer Material Adverse Effect.

Section 4.15. *Taxes*. (a) All federal income Tax Returns and all other material Tax Returns required to be filed with any Taxing Authority on or before the Closing Date with respect to any Pre-Closing Tax Period by, or with respect to, Buyer have been duly and timely filed on or before the Closing Date, and such Tax Returns were accurate in all material respects;

(b) Buyer has timely paid all material Taxes (whether or not shown as due and payable on any Tax Return) owed by Buyer, including Taxes required to be withheld from amounts owing to any employee, creditor, shareholder or other third party;

(c) The charges, accruals and reserves for Taxes with respect to Buyer reflected on the books of Buyer (excluding any reserve for deferred Taxes established to reflect timing differences between book and Tax income) are adequate to cover material Tax liabilities accruing through the end of the last period for which Buyer ordinarily records items on its books; and

(d) To Buyer's knowledge, there is no action, suit, proceeding, investigation, audit or claim pending or proposed in writing, threatened or pending against or with respect to the Buyer in respect of any material Tax.

Section 4.16. *Antitakeover Statutes*. No antitakeover, "control share acquisition," "fair price," "moratorium" or other antitakeover laws enacted under Applicable Law apply to Sellers' acquisition of shares of Buyer Stock hereunder.

Section 4.17. *Finders' Fees*. There is no investment banker, broker, finder or other intermediary that has been retained by or is authorized to act on behalf of Buyer who might be entitled to any fee or commission in connection with the transactions contemplated by this Agreement.

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Section 4.18. *Accredited Investor; Purchase for Investment.* (a) Buyer is an “accredited investor” as that term is defined in Rule 501(a) of Regulation D, promulgated under the 1933 Act.

(b) Buyer is acquiring the Shares hereunder for investment for its own account and not with a view to, or for sale in connection with, any distribution thereof. Buyer (either alone or together with its advisors) has sufficient knowledge and experience in financial and business matters so as to be capable of evaluating the merits and risks of its investment in the Shares and is capable of bearing the economic risks of such investment.

Section 4.19. *Inspections; No Other Representations.* Except as expressly set forth in this Agreement, Sellers disclaim any express or implied representations or warranties of any nature relating to the Shares, the Transferred Assets and the Company, and Buyer agrees to accept the Shares, the Transferred Assets and the Company without reliance upon any express or implied representations or warranties of any nature made by or on behalf of or imputed to any Seller or any of its Affiliates, except as expressly set forth in this Agreement. Without limiting the generality of the foregoing, Buyer acknowledges that no Seller makes any representation or warranty with respect to (i) any projections, estimates or budgets delivered to or made available to Buyer of future revenues, future results of operations (or any component thereof), future cash flows or future financial condition (or any component thereof) of the Company or the future business and operations of the Company, (ii) any other information or documents made available to Buyer or its counsel, accountants or advisors with respect to the Transferred Assets or the Company or their respective businesses or operations or (iii) the condition of the tangible assets of the Company, except in each case as expressly set forth in this Agreement.

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ARTICLE 5  
CERTAIN COVENANTS OF BUYER AND SELLERS

Buyer and Sellers agree that:

Section 5.01. *Reasonable Best Efforts; Further Assurances.* Subject to the terms and conditions of this Agreement and each other Transaction Document, Buyer and Sellers will use their reasonable best efforts to take, or cause to be taken, all actions and to do, or cause to be done, all things necessary or desirable under Applicable Law to consummate the transactions contemplated by this Agreement and the other Transaction Documents. Sellers and Buyer agree, and Buyer, after the Closing, agrees to cause the Company, to execute and deliver such other documents, certificates, agreements and other writings and to take such other actions as may be necessary or desirable in order to consummate or implement expeditiously the transactions contemplated by this Agreement and the other Transaction Documents.

Section 5.02. *Public Announcements.* The parties agree to consult with each other before issuing any press release or making any public statement with respect to this Agreement or any other Transaction Document or the transactions contemplated hereby or thereby and, except for any press releases and public announcements the making of which may be required by Applicable Law or any listing agreement with any national securities exchange, will not issue any such press release or make any such public statement without the consent of the other party.

Section 5.03. *Buyer Access to Information.* Sellers will deliver to Buyer (i) at the Closing, any laboratory books of Sellers that relate exclusively to the Transferred Assets, (ii) within 45 days after the Closing, those portions of any other laboratory books of Sellers that relate primarily to the Transferred Assets, and (iii) within 10 days after the Closing, copies (in CD ROM or comparable format) of all documents in the electronic dataroom that the Sellers made available to Buyer; *provided* that Sellers shall be entitled to maintain copies of any materials referred to in each of clauses (i), (ii) and (iii) (and, in the event Sellers have not made any such copies before delivering such materials to Buyer, Buyer shall provide Sellers with “pdf” copies of such materials within 45 days of Buyer’s receipt thereof), which materials shall be subject to the confidentiality obligations set forth in Section 5.04. From and after the Closing Date, Sellers will afford promptly to Buyer and its agents reasonable access to its books of account, financial and other records (including accountant’s work papers), information, employees and auditors to the extent necessary or useful for Buyer in connection with any audit, investigation, dispute or litigation or any other reasonable business purpose relating to the Company; *provided* that any such access by Buyer shall not unreasonably interfere with the conduct of the business of any Seller. Notwithstanding anything to the contrary contained herein, nothing in this Section 5.03 shall require (i) a Seller or any of its Affiliates to violate any Applicable Law or a contract or obligation of confidentiality owing to a third party or waive the protection of an attorney-client privilege or (ii) the auditors and independent

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accountants of a Seller or any of its Affiliates to make any work papers available to any Person unless and until such Person has signed a customary confidentiality and hold harmless agreement relating to such access to work papers in form and substance reasonably acceptable to such auditors or independent accountants. Buyer shall bear all of the out-of-pocket costs and expenses (including attorneys' fees, but excluding reimbursement for general overhead, salaries and employee benefits) reasonably incurred in connection with the foregoing.

Section 5.04. *Seller Access to Information; Cooperation on Certain Matters.* (a) From and after the Closing Date, Buyer will cause the Company to afford promptly to Sellers and their agents reasonable access to their properties, books, records, employees and auditors to the extent necessary to permit Sellers to determine any matter relating to their respective rights and obligations hereunder or to any period ending on or before the Closing Date and shall permit Sellers to make and maintain, solely for archival purposes, copies of any laboratory books of the Company or the Sellers that directly relate to the Transferred Assets; *provided* that any such access by Sellers shall not unreasonably interfere with the conduct of the business of Buyer and shall not grant Sellers any proprietary rights to own or use the information contained therein. Notwithstanding anything to the contrary contained herein, nothing in this Section 5.04 shall require Buyer or any of its Affiliates to violate any Applicable Law or a contract or obligation of confidentiality owing to a third party or waive the protection of an attorney-client privilege. Sellers will hold, and will use their best efforts to cause their respective officers, directors, employees, accountants, counsel, consultants, advisors and agents to hold, in confidence, unless compelled to disclose by judicial or administrative process or by other requirements of Applicable Law, all confidential documents and information concerning the Company provided to them pursuant to this Section. Sellers shall bear all of the out-of-pocket costs and expenses (including attorneys' fees, but excluding reimbursement for general overhead, salaries and employee benefits) reasonably incurred in connection with the foregoing.

(b) From and after the Closing Date, except as otherwise required by Applicable Law or agreed to in writing, Buyer and its Affiliates shall, and shall cause the Company to, retain all information and records (including, without limitation, records relating to Taxes) relating to the businesses of the Company that were in the possession of the Company as of the Closing Date and, with respect to Taxes, all records related to Tax Returns for Pre-Closing Tax Periods. In addition, Buyer and its Affiliates shall retain all information and records relating to any matter as to which any party seeks or may seek indemnification

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from any other party hereunder, in each case until final resolution of the matter to which such information and records relate. Notwithstanding the prior two sentences of this Section 5.04(b), Buyer and its Affiliates may destroy or otherwise dispose of any such information and records at any time, provided that, prior to such destruction or disposal, (i) Buyer shall provide not less than 90 days' prior written notice to Sellers, specifying the information and records proposed to be destroyed or disposed of, and (ii) if Sellers shall request in writing prior to the scheduled date for such destruction or disposal that any of the information and records proposed to be destroyed or disposed of be delivered to any Seller, Buyer shall promptly arrange for the delivery of such information and records as was requested.

Section 5.05. *Seller Marks*. As soon as reasonably practicable after the Closing, but in any event within 40 days following the Closing, Buyer shall cause the Company to (i) cease all use of the Seller Marks, (ii) remove, destroy or strike over all Seller Marks from the Company's assets and other materials, including as part of its stationary, displays, signs, promotional materials, manuals, forms, websites, email and other materials and (iii) file amendments to their respective certificates of incorporation, articles of association or other organizational documents with the applicable Governmental Authorities changing the names of the Company to names that do not include any of the Seller Marks. Any use by the Company of the Seller Marks during the limited phase-out period provided in this Section 5.05 shall be (A) solely in connection with goods, products and services that are (x) the type of goods, products and services in connection with which the Company were using the Seller Marks immediately prior to the Closing and (y) of a quality at least as high as the quality of goods, products and services provided by the Company immediately prior to the Closing and (B) subject to all style and other usage guidelines in effect for the Seller Marks (as may be modified by Sellers from time to time). All goodwill associated with the use by the Company of the Seller Marks shall inure to the benefit of Sellers or their respective Affiliates, as applicable. Following the Closing, none of Buyer, its Affiliates nor the Company shall (1) contest the validity or ownership of any of the Seller Marks or (2) subject to the limited phase-out period provided in this Section 5.05, use, adopt or employ any Seller Mark or any variation or derivative of any Seller Mark, including any Trademark that is confusingly similar to any Seller Mark. For the purposes of this Section 5.05, "**Seller Marks**" shall mean any and all Trademarks owned or controlled by Sellers or any of their respective Affiliates, including the Trademark "Roche".

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Section 5.06. *NASDAQ Listing; Listing of Buyer Stock.* (a) Buyer will use its reasonable best efforts to maintain the listing of Buyer Stock on the NASDAQ Capital Market for at least one year after the Post-Closing Payment Date, including, if necessary, by effecting a reverse stock split with respect to the outstanding shares of Buyer Stock.

(b) Buyer shall take all necessary action to cause the shares of Buyer Stock to be issued to a Person designated by Sellers (i) pursuant to Section 2.02(a)(ii) to be listed on the NASDAQ Capital Market promptly following the Closing (but no later than 30 days thereafter) and (ii) pursuant to Section 2.08 to be listed on the NASDAQ Capital Market (or if Buyer Stock is not then listed on such market, on the principal other U.S. national or regional securities exchange on which Buyer Stock is then listed or principal other U.S. national or regional market on which Buyer Stock is then traded) promptly following the Post-Closing Payment Date (but no later than 30 days thereafter).

Section 5.07. *Legend Removal.* Buyer will use its best efforts to replace as soon as possible the certificates or book entries representing the shares of Buyer Stock conveyed by Buyer pursuant to Section 2.02(a)(ii) and Section 2.08 with certificates or book entries not bearing the legend required by Section 2.05 if Buyer receives such representations from Sellers as Buyer may reasonably request to enable Buyer to provide an opinion of counsel (which may be in-house counsel), in reliance on such representations, that such legends are no longer required for purposes of applicable securities law.

Section 5.08. *Notices of Certain Events.* Each party shall promptly notify the other of:

(a) any notice or other communication from any Person alleging that the consent of such Person is or may be required in connection with the transactions contemplated by this Agreement or any other Transaction Document; or

(b) any notice or other communication from any Governmental Authority in connection with the transactions contemplated by this Agreement or any other Transaction Document.

Section 5.09. *Patent Service Providers.* Within 45 days after the Closing, Sellers agree to deliver a notice, with copy to Buyer, to each non-Affiliated Person (each, a “**Patent Service Provider**”) engaged on the date hereof by or on behalf of any Seller or any of its Affiliates with respect to the registration or

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protection of, or prosecution or defense of claims related to, any patents included in the Transferred Patent Rights. Such notice shall inform the Patent Service Provider of the assignment of the applicable Transferred Patent Rights hereunder and shall instruct the Patent Service Provider to cease any work relating thereto on behalf of Sellers or any of their respective Affiliates. For the avoidance of doubt, none of Sellers or any of their respective Affiliates shall have any liability or obligation hereunder with respect to (i) the continued engagement of any Patent Service Provider from and after the Closing or (ii) any fees or other charges of any Patent Service Provider incurred after the earlier of the 45-day period following the Closing or the date of delivery of the notice contemplated in this Section to such Patent Service Provider.

Section 5.10. *Insurance.* Buyer agrees that all insurance policies covering the Company maintained by or on behalf of any Seller or any of its Affiliates shall not provide coverage to the Company following the Closing and that, after the Closing, each Seller and its Affiliates shall have no obligation of any kind to maintain any form of insurance covering the Company.

Section 5.11. *Mutual Release.* (a) Effective immediately prior to the Closing, each Seller hereby irrevocably waives, releases and discharges the Company from any and all liabilities and obligations to such Seller and its Affiliates of any kind or nature whatsoever (including, without limitation, in respect of rights of contribution or indemnification), in each case whether absolute or contingent, liquidated or unliquidated, and whether arising under any agreement or understanding, or the certificate of incorporation, bylaws, or other constitutive documents of the Company or otherwise at law or equity. The foregoing waiver, release and discharge shall not apply in respect of any liability or obligation arising under (i) any intercompany agreements or arrangements set forth in Section 2.04(a) of the Sellers Disclosure Schedule, (ii) any of the other terms of the Transaction Documents (including, without limitation, Section 2.04(b) and indemnification obligations arising under this Agreement), (iii) any other agreement or instrument delivered in connection with a Transaction Document or (iv) any agreement entered into on or after the Closing Date.

(b) At the Closing, Buyer shall cause the Company to irrevocably waive, release and discharge each Seller and its Affiliates from any and all liabilities and obligations to the Company of any kind or nature whatsoever (including, without limitation, in respect of rights of contribution or indemnification), in each case whether absolute or contingent, liquidated or unliquidated, and whether arising under any agreement or understanding, or the

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certificate of incorporation, bylaws, or other constitutive documents of the Company or otherwise at law or equity. The foregoing waiver, release and discharge shall not apply in respect of any liability or obligation arising under (i) any intercompany agreements or arrangements set forth in Section 2.04(a) of the Sellers Disclosure Schedule, (ii) any of the other terms of the Transaction Documents (including, without limitation, indemnification obligations arising under this Agreement), (iii) any other agreement or instrument delivered in connection with a Transaction Document or (iv) any agreement entered into on or after the Closing Date.

Section 5.12. *Covenant Not to Challenge Patent Rights.* From and after the Closing, Sellers shall not, and shall cause their Affiliates not to, challenge or knowingly assist any Third Party in challenging the validity or enforceability of the Patent Rights included within the Transferred Patent Rights.

ARTICLE 6  
CERTAIN COVENANTS RELATING TO BUYER PRODUCTS

Section 6.01. *Rights of First Negotiation.* (a) From and after the Closing Date, if Buyer or any of its Affiliates proposes to Out-License any Clinical Candidate, subject to the limitations set forth in Section 6.01(f), or Existing Candidate, or to enter into substantive discussions or negotiations with any non-Affiliated Person relating to the Out-License of any such Clinical Candidate or Existing Candidate, Buyer shall give Sellers written notice thereof. Such notice shall include (i) a description in reasonable detail of the Candidate, including the status of its development and the status of any discussions with Regulatory Authorities relating thereto and (ii) the territory to which such Out-License would apply.

(b) Sellers shall have [\*\*] after receipt of a notice delivered pursuant to Section 6.01(a) to notify Buyer in writing that Sellers are interested in negotiating the applicable Out-License on commercially reasonable terms. If Sellers so notify Buyer within this [\*\*] period (such notice being an “**Opt-in Notice**”), Buyer shall as promptly as reasonably practicable thereafter provide Sellers with detailed information (including confidential information) regarding the applicable Candidate, including a summary of all biological, chemical and other Candidate data and an identification of all patents, trademarks and/or other Intellectual Property Rights that are owned (wholly or partly), used or in-licensed by Buyer or its Affiliates and that are practiced by, arise from and/or otherwise relate to the Candidate and/or the manufacture or sale thereof (collectively, the “**Data**”).

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**Package**”). If Sellers do not timely provide an Opt-in Notice pursuant to this Section 6.01(b) with respect to a particular proposed Out-License, then, subject to Section 6.01(e), Buyer shall be free for a period of [\*\*] from the expiration of the [\*\*] notice period to pursue that proposed Out-License with any Third Party.

(c) During the Term Sheet Period with respect to any proposed Out-License, Buyer will negotiate exclusively and in good faith with Sellers regarding the applicable Out-License. During such Term Sheet Period, Buyer shall provide (or cause to be provided) such additional information regarding the applicable Candidate reasonably requested by Sellers that is in Buyer’s possession or control, *provided* that Buyer shall not be required to perform any studies or expend any material funds to generate such information. During such Term Sheet Period, Sellers may (but are not required to) submit a proposal in the form of a written term sheet with respect to the definitive terms of such Out-License, including the consideration proposed to be paid in connection with such Out-License, (including, to the extent applicable, the amount of the upfront and deferred cash consideration and, to the extent that any portion of such cash consideration is to be subject to earn out obligations, milestones or other contingencies, the nature of such contingencies, the amount and term of any royalties and the amount of any research and development funding) and other material terms and conditions of such Out-License. The “**Term Sheet Period**” with respect to any proposed Out-License means that number of days following Sellers’ receipt of the applicable Data Package equal to [\*\*] less the number of days that elapsed between Sellers’ receipt of Buyer’s applicable notice delivered pursuant to Section 6.01(a) and Sellers’ delivery of the applicable Opt-In Notice.

(d) Until the expiration of the Exclusivity Period with respect to a Candidate, Buyer shall not (and shall cause its Affiliates not to) negotiate, discuss or enter into any agreement with any Person other than Sellers or an Affiliate of Sellers with respect to any Out-License of such Candidate. The “**Exclusivity Period**” with respect to any Candidate means the period beginning on the date hereof and ending (i) if Sellers have not delivered a notice in accordance with Section 6.01(b), on the [\*\*] following Sellers’ receipt of Buyer’s notice delivered pursuant Section 6.01(a) or (ii) if Sellers have delivered a notice in accordance with Section 6.01(b), at the end of the applicable Term Sheet Period; *provided* that the Exclusivity Period may be extended by mutual written agreement of the parties.

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(e) Following the Exclusivity Period with respect to any Candidate, Buyer and its Affiliates shall be entitled to negotiate and enter into a definitive agreement with respect to an Out-License of such Candidate with any other Person; *provided* that (i) if Sellers have submitted a written term sheet to Buyer pursuant to Section 6.01(c) during the applicable Exclusivity Period, the terms of such Out-License with any other Person may not be less favorable, on the whole, to Buyer or its applicable Affiliates than the terms last proposed by Sellers in any such term sheet delivered to Buyer during the Exclusivity Period; (ii) such Out-License must apply to the same territory identified in the applicable notice delivered by Buyer to Sellers pursuant to Section 6.01(a) and not to any portion thereof or any other territory; and (iii) if Buyer does not consummate an arrangement with a non-affiliated Person with respect to such Out-License within [\*\*] after the end of the applicable Exclusivity Period, Buyer's right to negotiate with and enter into such Out-License with any Person other than Sellers shall terminate until Buyer has complied again with the procedures set forth in this Section 6.01.

(f) Notwithstanding anything to the contrary herein, Buyer's obligations under this Section 6.01 with respect to Out-Licenses of Candidates that are Clinical Candidates shall apply only to the first five Clinical Candidates with respect to which Buyer has (i) delivered Sellers a notice pursuant to Section 6.01(a), (ii) fully complied with the terms of this Section 6.01 and (iii) entered into an Out-License with Sellers, any Affiliate of Sellers or any other Person not affiliated with Buyer. For the avoidance of doubt, Buyer shall not at any time be entitled to Out-License Candidates that are Existing Candidates without first complying with the procedures set forth in Section 6.01(a)-(e).

(g) Sellers will hold, and will use their best efforts to cause their Affiliates, officers, directors, employees, accountants, counsel, consultants, advisors and agents to hold, in confidence (meaning that the applicable information will not be disclosed to any Third Party or used for any purpose other than as necessary to evaluate a potential Out-License), unless compelled to disclose by judicial or administrative process or by other requirements of Applicable Law, all confidential documents and information concerning a Candidate provided to Sellers pursuant to this Section 6.01. and Sellers shall be liable for any unauthorized disclosure or use of such confidential documents or information by their Affiliates, officers, directors, employees, accountants, counsel, consultants, advisors or agents.

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Section 6.02. *Royalty Payments*. (a) For sales of any Candidate for which Sellers or any of their Affiliates, on the one hand, and Buyer or any of its Affiliates, on the other hand, do not enter into an Out-License pursuant to Section 6.01, Buyer shall pay Sellers royalty payments in an amount equal to three percent (3%) of Net Sales with respect to each Royalty Product during the applicable Royalty Period; *provided* that if there is no Valid Claim Covering such Royalty Product in a given country, or if a Generic Version of the Royalty Product has been approved for commercialization in such country, then in either case the royalty payments on such Royalty Product with respect to Net Sales generated in such country shall be reduced to an amount [\*\*] of such Net Sales generated in such country during the applicable Royalty Period. Such royalty payments shall be paid in accordance with this Section 6.02(b). For purposes of this Section 6.02(b), a “**Generic Version**” of a Royalty Product shall mean (i) a generic or follow-on drug product marketed in the United States that has been approved by the U.S. Food and Drug Administration (FDA) under 21 USC § 505(j) or 21 USC § 505(b)(2); (ii) a biosimilar or interchangeable biological product marketed in the United States that has been approved by FDA under 42 USC § 262(k); and (iii) a drug or biological product marketed outside the United States for which the equivalent foreign application for approval of a generic drug or biosimilar product has been approved by the applicable Regulatory Authority in the relevant foreign jurisdiction.

(b) Until the termination of all applicable Royalty Periods, Buyer shall, within 90 days after the end of each fiscal quarter, (i) deliver to Sellers a statement setting forth in reasonable detail its calculation of Net Sales for the fiscal quarter then ended with respect to each Royalty Product that has had a First Commercial Sale, which statements will be held in confidence in accordance with Section 6.01(g), and (ii) pay Sellers any royalty amounts, as determined in accordance with this Section 6.02, that are accrued and unpaid as of the end of the fiscal quarter then ended.

(c) The “**Royalty Period**” with respect to any Royalty Product in a given country shall begin on the First Commercial Sale of such Royalty Product in such country and shall continue until the later of (i) the expiration of the last-to-expire Valid Claim Covering such Royalty Product in such country and (ii) [\*\*] after the First Commercial Sale of such Royalty Product in such country.

(d) As used herein, “**Net Sales**” with respect to any Royalty Product means the amount of gross sales of such Royalty Product worldwide that are invoiced by Buyer or any of its Affiliates, or any of its or their licensees or sublicensees, to any Person, as reduced by the following deductions to the extent actually allowed or incurred with respect to the sales of such Royalty Product and accounted for on a product by product basis, and in each case in accordance with GAAP or, if the Person that is commercializing the Royalty Product does not report Net Sales in accordance with GAAP, in accordance with IFRS:

(i) [\*\*]; [\*\*]; [\*\*]; [\*\*]; [\*\*];

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(e) Buyer shall be entitled to deduct from royalty payments payable hereunder for a given Royalty Product [\*\*] of Required Third Party Payments paid by Buyer with respect to such Royalty Product during the applicable reporting period; *provided* that in no event shall a deduction under this Section 6.02(e) reduce any royalty payment with respect to any such Royalty Product payable by Buyer hereunder by more than [\*\*].

(f) For purposes of determining Net Sales with respect to any Royalty Product that is to be sold as part of a Combination Product:

(i) If any Royalty Product is to be sold as part of a Combination Product, Buyer shall so notify Sellers approximately 180 days prior to the anticipated First Commercial Sale in any country of such Combination Product. The parties shall promptly thereafter meet to negotiate in good faith to agree on an appropriate adjustment to the Net Sales of such Combination Product in order to determine the Net Sales with respect to such Royalty Product for purposes of this Section 6.02. Any such adjustment shall be determined on a country-by-country basis and shall reflect the relative fair market value of the Royalty Product and any other pharmaceutically active ingredients contained in such Combination Product.

(ii) If the parties cannot reach agreement as contemplated in Section 6.02(f)(i), then the Net Sales of such Royalty Product, for purposes of this Section 6.02, shall be determined by multiplying the Net Sales of the Combination Product (which shall be computed as though such Combination Product were a Royalty Product for purposes of the definition of “Net Sales” in Section 6.02(d)) on a country-by-country basis, during the applicable royalty reporting period, by the fraction [\*\*], where A is the average sale price of the applicable Royalty Product when sold separately in finished form in the applicable country and B is the average sale price of the other active pharmaceutical product(s) included in the Combination Product when sold separately in finished form in the applicable country, in each case during the applicable royalty reporting period or, if sales of both the applicable Royalty Product and the other product(s) did not occur in such period, then in the most recent royalty reporting period in which such separate sales of both such Royalty Product and the other product(s) occurred.

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(iii) In the event that an average sale price cannot be determined for both the applicable Royalty Product and all other active pharmaceutical products(s) included in such Combination Product in accordance with Section 6.02(f)(ii), then Net Sales of the applicable Royalty Product for purposes of this Section 6.02 shall be calculated by multiplying the Net Sales of such Combination Product by the fraction  $\frac{C}{C+D}$ , where C is the fair market value of the Royalty Product and D is the fair market value of all other active pharmaceutical product(s) included in the Combination Product. If the parties cannot promptly agree on the respective fair market values of such Royalty Product and such other product(s), they shall engage a mutually acceptable expert to determine, as promptly as practicable, the respective fair market values of such Royalty Product and such other product(s). Such expert determination shall be final and binding on Buyer and Sellers for purposes of this Section 6.02. The cost of such expert's review shall be borne equally by Buyer and Sellers.

Section 6.03. *Milestone Payments.* (a) Subject to Section 6.03(c), with respect to each Existing Candidate as to which Buyer or any of its Affiliates, on the one hand, and Sellers or any of their Affiliates, on the other hand, have not entered into an Out-License pursuant to Section 6.01, Buyer shall pay Sellers the following amounts upon the achievement of each of the following milestones:

- (i) \$ [\*\*] upon the first Regulatory Approval of such Existing Candidate in the United States;
- (ii) \$ [\*\*] upon the first Regulatory Approval of such Existing Candidate in any member country of the European Union;
- (iii) \$ [\*\*] upon the first Regulatory Approval of such Existing Candidate in Japan;
- (iv) \$ [\*\*] upon the achievement of Net Sales of \$ [\*\*] in any calendar year with respect to such Existing Candidate;
- (v) \$ [\*\*] upon the achievement of Net Sales of \$ [\*\*] in any calendar year with respect to such Existing Candidate.

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(b) For purposes of this Section 6.03, Net Sales with respect to each Existing Candidate shall be calculated in accordance with Section 6.02(d). Within 30 days after the achievement of any of the milestones set forth in Section 6.03(a), Buyer shall notify Sellers thereof and shall pay the amounts due hereunder.

(c) Buyer shall be obligated to make each of the payments described in clauses (i) through (v) of Section 6.03(a) (x) once (but no more than once) with respect to all Existing Candidates derived directly from the Company's research program with respect to [\*\*], (y) once (but no more than once) with respect to all Existing Candidates derived directly from the Company's research program with respect to [\*\*] and (z) once (but no more than once) with respect to Existing Candidates derived directly from the Company's research program with respect to [\*\*]; *provided* in each case that the applicable Existing Candidate has achieved a corresponding milestone event set forth in clauses (i) through (v) of Section 6.03(a).

ARTICLE 7  
TAX MATTERS

Section 7.01. *Tax Representations.* (a) Sellers represent and warrant to Buyer as of the date hereof that except as set forth on Section 7.01(a) of the Sellers Disclosure Schedule, (i) all federal income Tax Returns and all other material Tax Returns required to be filed with any Taxing Authority on or before the Closing Date with respect to any Pre-Closing Tax Period by, or with respect to, the Company or any Transferred Assets have been duly and timely filed on or before the Closing Date; (ii) the Company has timely paid all material Taxes (whether or not shown as due and payable on any Tax Return) owed by the Company or with respect to the Transferred Assets, including Taxes required to be withheld from amounts owing to any employee, creditor, shareholders or other third party; (iii) the Tax Returns that have been filed are true, correct and complete in all material respects; (iv) the charges, accruals and reserves for Taxes with respect to the Company reflected on the face (rather than any notes thereto) of the most recent Balance Sheet (excluding any reserve for deferred Taxes established to reflect timing differences between book and Tax income) are adequate to cover Tax liabilities as of the most recent Balance Sheet Date; (v) to Sellers' knowledge, there is no action, suit, proceeding, investigation, audit or claim now proposed, threatened or pending against or with respect to the Company or any Transferred Assets in respect of any material Tax; (vi) the Company has not distributed stock of another corporation or has had its stock

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distributed in a transaction that was purported or intended to be governed, in whole or in part, by Section 355 or Section 361 of the Code within the preceding two (2) years; (vii) the Company has not participated, or is not currently participating, in a “reportable transaction” as defined in Treasury Regulations Section 1.6011-4(b); (viii) the Company is not a party to any agreement or arrangement relating to the apportionment, sharing, assignment or allocation of Taxes, or has any liability for Taxes of any Person (other than the Company) under Treasury Regulations Section 1.1502-6 or any similar provision of state, local or foreign Law, as a transferee or successor, by contract or otherwise; (ix) to Sellers’ knowledge, no claim has been made by an authority in a jurisdiction where the Company does not file Tax Returns that the Company or may be subject to Tax, or that the Transferred Assets are subject to Tax, in such jurisdiction; and (x) the Company has not waived any statute of limitations in respect of any material Taxes or agreed to any extension of time with respect to Taxes, and no such waiver or agreement has been made with respect to the Transferred Assets.

(b) Buyer represents and warrants to Sellers as of the date hereof that (i) Buyer Stock is the only class of equity securities of Buyer currently outstanding; (ii) the Buyer has not issued any shares of Buyer Stock, other than in connection with this Agreement and to purchasers participating in the Capital Raise, since April 29, 2011; (iii) after giving effect to the Capital Raise, immediately after the Closing, the sum of (A) the number of shares of Buyer Stock issued to Sellers hereunder and (B) the aggregate number of shares of Buyer Stock held by all purchasers participating in the Capital Raise (including, for the avoidance of doubt, all shares of Buyer Stock that such persons held immediately before the consummation of the Capital Raise) will be less than 80% of the total number of shares of Buyer Stock then outstanding; and (iv) Buyer has no present intention or obligation to issue, to any person or group of persons (including pursuant to the Post-Closing Capital Raises), additional shares of any class of stock of Buyer that, when aggregated with (A) the shares of any class of stock of Buyer held by all such persons or groups immediately prior to the issuance of such additional shares and (B) the shares of Buyer Stock described in clauses (iii)(A) and (iii)(B) above, in each case properly adjusted to reflect any subdivision, reclassification, recapitalization, reorganization, stock split, reverse stock split, combination or exchange or readjustment of shares, or stock dividend thereon with a record date during the period between Closing Date and the date of the issuance of such additional shares, would constitute 80% or more of the total voting power of all classes of stock of Buyer entitled to vote.

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Section 7.02. *Tax Covenants.* (a) Buyer covenants that it will not, and will not cause or permit the Company or any Affiliate of Buyer to, (i) take any action on the Closing Date other than in the ordinary course of business, including but not limited to the distribution of any dividend or the effectuation of any redemption that could give rise to any Tax liability or reduce any Tax Asset of the Seller Group or give rise to any loss of any Seller or the Seller Group under this Agreement, or (ii) amend any Tax Return for a Pre-Closing Tax Period.

(b) Buyer (or any Affiliate of Buyer) or Sellers (or any of their respective Affiliates), as the case may be, shall (i) be entitled to deduct and withhold any Taxes required under the Code or any Applicable Law to be deducted and withheld from any and all payments by or on account of any obligation of Buyer (or any Affiliate of Buyer) or Sellers (or any of their respective Affiliates) under this Agreement, (ii) pay the full amount deducted to the relevant Taxing Authority in accordance with Applicable Law and (iii) provide the recipient of such payment with the original or a certified copy of a receipt issued by such Taxing Authority evidencing the payment of such Taxes, a copy of the Tax Return reporting the payment of such Taxes or other evidence of the payment of such Taxes reasonably satisfactory to the recipient. To the extent that any amounts are deducted or withheld, such amounts will be treated for all purposes of this Agreement as having been paid to the person in respect of which such deduction and withholding was made. Buyer and Sellers agree to reasonably cooperate to minimize any Taxes otherwise required to be withheld or deducted from any and all payments made under this Agreement.

(c) All Tax Returns required to be filed after the Closing Date with respect to the Company with respect to any Tax period that ends on or before the Closing Date and all Tax Returns relating to Roche Kulmbach GmbH will be filed by Sellers or their applicable Affiliate(s) when due (taking into account any extension of a required filing date).

(d) Buyer shall prepare, or cause to be prepared, all Tax Returns required to be filed by the Company after the Closing Date with respect to any Straddle Tax Period (other than any Tax Returns related to Roche Kulmbach GmbH, which shall be prepared by Sellers or their applicable Affiliate(s)). Each such Tax Return shall be prepared in a manner consistent with the prior practice of the Company, unless otherwise required by law. Buyer shall submit each such Tax Return to Sellers (together with schedules, statements and, to the extent reasonably requested by Sellers, supporting documentation) at least 30 days prior to the due date (including extensions) of such Tax Return. Sellers shall provide

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Buyer with comments, if any, within 15 days of receipt of any such draft Tax Return. To the extent that Sellers have commented on any Tax Return in accordance with this Section 7.02(d), Buyer shall consider such comments in good faith, and shall not file any such Tax Return without the prior written consent of Sellers, not to be unreasonably withheld or delayed. Sellers shall pay promptly to Buyer, or at Buyer's request, to the applicable Taxing Authority, any Covered Taxes attributable (as defined in the manner described in Section 7.06(b)) to the Pre-Closing Tax Period included in the Straddle Tax Period with respect to which such Tax Return is filed.

(e) Buyer shall promptly pay or cause to be paid to Sellers all refunds of Taxes and interest thereon received by Buyer, any Affiliate of Buyer or the Company attributable to Taxes paid by any Seller, the Company (or any predecessor or Affiliate of any Seller) with respect to any Pre-Closing Tax Period, net of any resulting correlative adjustments imposed upon Buyer or the Company and not otherwise subject to Sellers' obligations under Section 7.06. If, in lieu of receiving any such refund, the Company (i) actually reduces a cash Tax liability with respect to a Post-Closing Tax Period or (ii) increases a Tax Asset that can be carried forward to a Post-Closing Tax Period and, with respect to such Tax Asset, Buyer actually realizes value in cash in the taxable year such increase is made or any of the five immediately succeeding taxable years, Buyer shall promptly pay or cause to be paid to Sellers the amount of such reduction in Tax liability or the amount of any benefit resulting from such increase in Tax Assets, as the case may be.

(f) All Transfer Taxes in respect of the transfer of the Shares pursuant to this Agreement (and all costs and expenses relating to the preparation and filing of Tax Returns with respect thereto) shall be borne equally by Buyer and Sellers. All Transfer Taxes in respect of the transfer of the Transferred Assets pursuant to this Agreement (and all costs and expenses relating to the preparation and filing of Tax Returns with respect thereto) shall be borne solely by the Sellers. Buyer will file all necessary Transfer Tax Returns and other documentation with respect to Transfer Taxes and fees, and Sellers shall promptly reimburse Buyer for Sellers' portion of the costs and expenses associated with the preparation and filing of such Transfer Tax Returns. For the avoidance of doubt, this Section 7.02(f) shall not apply to any withholding Taxes or value added Taxes. If required by Applicable Law, each Seller will, and will cause its Affiliates to, join in the execution of any such Transfer Tax Returns and other documentation.

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(g) Except as contemplated by this Agreement, Buyer agrees that no Seller nor any of its Affiliates shall have any liability for any Tax resulting from any action referred to in Section 7.02(a) taken by the Company, Buyer or any Affiliate of Buyer, and agrees to indemnify and hold harmless each Seller and each of its Affiliates against (i) any such Tax (together with any interest, penalty or addition to Tax), (ii) any Tax incurred or suffered by any Seller or any of its Affiliates, arising out of a breach of any other covenant or agreement contained in this Article 7, (iii) any Tax imposed on the Company relating to a Post-Closing Period and that is not subject to Sellers' indemnification obligation under Section 7.06(a), (iv) any Tax imposed on the Company, Sellers or any of their Affiliates as a result of an election made or deemed made by Buyer under Section 338 of the Code or any comparable provision of Applicable Law, (v) any Tax incurred or suffered by any Seller or any of its Affiliates, arising out of a breach of Buyer's representations in Section 7.01(b), (vi) any Covered Tax described in Section 7.02(d) to the extent that Sellers have previously paid such Covered Tax to Buyer or the applicable Taxing Authority in accordance with the terms of Section 7.02(d) and (vii) any liabilities, costs, expenses (including, without limitation, reasonable expenses of investigation and attorneys' fees and expenses), losses, damages, assessments, penalties, fines, fees, settlements, judgments or other charges ("Losses") as a result of, arising out of, or directly or indirectly relating to the imposition, assessment or assertion of any Tax described in clause (i), (ii), (iii), (iv), (v) or (vi) above, including those incurred in the contest in good faith in appropriate proceedings relating to the imposition, assessment or assertion of any such Tax. Sellers agree to give notice to Buyer within 10 business days of the commencement of any action or proceeding, in respect of which indemnity may be sought under this Section 7.02(g). Buyer may, at its own expense, participate in and, upon notice to Sellers, assume the defense of any such suit, action, litigation or proceeding (including any Tax Audit), but only to the extent any such suit, action, litigation or proceeding relates to a claim for Taxes in respect of which indemnification may be sought pursuant to this Section 7.02(g). If Buyer assumes such defense, Buyer shall have the sole discretion as to the conduct of such defense and Sellers shall have the right (but not the duty) to participate in the defense thereof and to employ counsel, at their own expense, separate from the counsel employed by Buyer. Whether or not Buyer chooses to defend or prosecute any such suit, action or proceeding, Buyer shall not, without the prior written consent of Sellers (not to be unreasonably withheld), settle any such suit, action, litigation or proceeding if such settlement would have a significant adverse effect on the Tax liability of the Company, any Seller or any of its Affiliates with respect to a Pre-Closing Tax Period. For the avoidance of doubt, any such claims for indemnification shall not be subject to any limitations on survival, cap and/or minimum claim amounts provided in Article 9.

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Section 7.03. *Tax Sharing*. Any and all existing Tax Sharing Agreements between the Company and any member of the Seller Group shall be terminated as of the Closing Date. After such date none of the Company, any Seller or any Affiliate of any Seller shall have any further rights or liabilities thereunder. This Agreement shall be the sole Tax sharing agreement relating to the Company for all Pre-Closing Tax Periods.

Section 7.04. *Cooperation on Tax Matters*. Buyer and Sellers agree to reasonably cooperate to furnish or cause to be furnished to each other, upon request, as promptly as practicable, such information (including access to books and records) and assistance relating to the Company as is reasonably necessary for the filing of any return (including any report required pursuant to Section 6043A of the Code and all Treasury Regulations promulgated thereunder), for the preparation for any audit, and for the prosecution or defense of any claim, suit or proceeding relating to any proposed adjustment. Buyer and Sellers agree to retain or cause to be retained all books and records pertinent to the Company until the applicable period for assessment under Applicable Law (giving effect to any and all extensions or waivers) has expired, and to abide by or cause the abidance with all record retention agreements entered into with any Taxing Authority. The Company agrees to give Sellers reasonable notice prior to transferring, discarding or destroying any such books and records relating to Tax matters for a Pre-Closing Tax Period and, if any Seller so requests, the Company shall allow such Seller to take possession of such books and records. Buyer and Sellers shall reasonably cooperate with each other in good faith in the conduct of any audit or other proceedings involving the Company for any Tax purposes and each shall execute and deliver such powers of attorney and other documents as are necessary to carry out the intent of this subsection.

Section 7.05. *FIRPTA Certificates*. Prior to the Closing, Roche Nutley will have delivered to Buyer a certificate (in a form reasonable acceptable to Buyer) that satisfies the requirements of Treasury Regulation Section 1.1445-2(b)(2) and confirms that Roche Nutley is not a “foreign person” as defined in Section 1445 of the Code.

Section 7.06. *Indemnification by Sellers*. (a) Sellers jointly and severally hereby indemnify Buyer against and agree to hold it harmless from any (i) Covered Tax, (ii) Tax incurred or suffered by Buyer or any of its Affiliates, arising out of a breach of any covenant or agreement contained in this Article 7

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and (iii) Losses incurred or suffered by Buyer and its Affiliates and, effective as of the Closing, the Company, as a result of, arising out of or directly or indirectly relating to the imposition, assessment or assertion of any such Covered Tax, including those incurred in the contest in good faith in appropriate proceedings related to the imposition, assessment or assertion of any Covered Tax; *provided, however*, that Sellers shall have no liability for the payment of any Loss attributable to or resulting from any action described in Section 7.02(a) hereof. For the avoidance of doubt, any such claims for indemnification shall not be subject to any limitations on survival, cap and/or minimum claim amounts provided in Article 9.

(b) For purposes of this Section, in the case of any Taxes (other than Transfer Taxes, which will be allocated under Section 7.02(f)) that are payable for a Straddle Tax Period, the portion of such Tax related to the portion of such Tax period ending on and including the Closing Date shall (x) in the case of any Taxes other than gross receipts, sales or use Taxes and income Taxes, be deemed to be the amount of such Tax for the entire Tax period multiplied by a fraction the numerator of which is the number of days in the Tax period ending on and including the Closing Date and the denominator of which is the number of days in the entire Tax period, and (y) in the case of any income Tax and any gross receipts, sales or use Tax, equal the portion of such Tax that would have been payable if the relevant Tax period ended on and included the Closing Date, determined in a manner consistent with prior practice of the Company.

(c) If Sellers' indemnification obligation under this Section 7.06 arises in respect of an adjustment which makes allowable to Buyer, any of its Affiliates or, effective upon the Closing, the Company any deduction, amortization, exclusion from income or other allowance (a "**Tax Benefit**") which would not, but for such adjustment, be allowable, then any payment by any Seller to Buyer shall be an amount equal to (x) the amount otherwise due but for this Section 7.06(c), minus (y) the value actually realized in cash with respect to the Tax Benefit in (i) the Tax year with respect to which such adjustment is made and (ii) any succeeding Tax year ending on or prior to the date of such payment by such Seller. Such value shall be considered equal to the excess of (I) the amount of Taxes that, in the absence of such Tax Benefit, would have been payable in cash by Buyer, any of its Affiliates or, effective upon the Closing, the Company over (II) the amount of Taxes actually paid in cash by Buyer, any of its Affiliates or, effective upon the Closing, the Company (taking into account any Tax refund, offset or other reduction in Tax liability resulting from the Tax Benefit). If, in any of the first five Tax years ending after the date of such payment by such

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Seller, Buyer actually realizes value in cash with respect to a Tax Benefit made allowable by such adjustment, Buyer shall pay such Seller an amount equal to the value so realized within 90 days of the filing of the applicable Tax Return or any adjustment for the Tax year in which the Tax Benefit is made allowable.

(d) Any payment by any Seller pursuant to this Section 7.06 shall be made not later than 30 days after receipt by Sellers of written notice from Buyer stating that any Loss has been paid by Buyer, any of its Affiliates or, effective upon the Closing, the Company and the amount thereof and of the indemnity payment requested.

(e) If any claim or demand for Taxes in respect of which indemnity may be sought pursuant to this Section 7.06 is asserted in writing against Buyer, any of its Affiliates or, effective upon the Closing, the Company, Buyer shall notify Sellers of such claim or demand within 10 business days of receipt thereof and shall give Sellers such information with respect thereto as Sellers may reasonably request and that is reasonably available to Buyer. Sellers may discharge, at any time, their indemnification obligation under this Section 7.06 by paying to Buyer the amount payable pursuant to this Section 7.06, calculated on the date of such payment. Any Seller may, at its own expense, participate in and, upon notice to Buyer, assume the defense of any such claim, suit, action, litigation or proceeding (including any Tax audit), but only to the extent that such claim, suit action, litigation or proceeding relates to a claim or demand for Taxes in respect of which indemnity may be sought pursuant to this Section 7.06. If any Seller assumes such defense, such Seller shall have the sole discretion as to the conduct of such defense and Buyer shall have the right (but not the duty) to participate in the defense thereof and to employ counsel, at its own expense, separate from the counsel employed by such Seller. Whether or not any Seller chooses to defend or prosecute any claim, (i) all of the parties hereto shall reasonably cooperate in the defense or prosecution thereof and (ii) Sellers shall not, without Buyer's prior written consent (not to be unreasonably withheld), settle any such claim, suit, action, litigation or proceeding if such settlement would have a significant adverse effect on the Tax liability of the Company, Buyer or any of its Affiliates with respect to a Post-Closing Tax Period.

(f) Neither Seller shall be liable under this Section 7.06 for any Tax (i) the payment of which was made without a Seller's prior written consent, unless such payment was made pursuant to the final determination of a claim, suit, action, litigation or proceeding with respect to which Sellers were notified pursuant to Section 7.06(e) or (ii) resulting from any claim, suit, action, litigation or proceeding with respect to which Sellers were not notified pursuant to Section 7.06(e) and such failure actually prejudiced the Sellers defense of claim, suit, action, litigation or proceeding.

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Section 7.07. *Purchase Price Adjustment and Interest.* Any amount paid by Sellers or Buyer under Article 7, Article 9 or Section 2.08(b) (including any shares of Buyer Stock issued and delivered pursuant to Section 2.08(b)) will be treated as an adjustment to the Total Consideration to the extent permitted by law (including extensions).

Section 7.08. *Survival.* Notwithstanding anything to the contrary in Section 9.01, the indemnities and covenants contained in this Article 7 shall survive until 60 days after the expiration of the applicable statute of limitations.

ARTICLE 8  
EMPLOYEE BENEFITS

Section 8.01. *Transferred Employees.* (a) As of the Closing Date, and subject to Section 8.11(b), Buyer shall cause the Company to continue to employ each Company Employee who is not a Leave Recipient.

(b) As of the Closing Date and subject to Section 8.01 of the Sellers Disclosure Schedule, Sellers shall caused to be transferred to a Seller or one of Sellers' Affiliates the employment of each Company Employee who is receiving short-term disability benefits from Sellers or one of their Affiliates (each, a "**Leave Recipient**"). Prior to a Leave Recipient's return to active work, Buyer shall, or shall cause one of its Affiliates to, make a written offer of employment to such Leave Recipient for the same position such Leave Recipient held prior to the Closing or a position that is substantially equivalent thereto effective as of such Leave Recipient's return to active work upon or prior to the expiration date of such Leave Recipient's eligibility for such short-term disability benefits. Each such Leave Recipient shall be deemed to have accepted such offer unless he or she affirmatively declines such offer. No later than five days following the Closing Date, Sellers will provide Buyer with a schedule setting forth the name, job title, annual salary, leave status and expected leave period for each Leave Recipient.

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(c) Each Company Employee (which, for the avoidance of doubt, includes Leave Recipients) who continues or commences active employment with Buyer or one of its Affiliates (including, after the Closing, the Company), whether by operation of law or by the acceptance of an offer of employment, shall be a **“Transferred Employee”** as of the effective date of such commencement of active employment.

Section 8.02. *Maintenance of Compensation and Benefits.* Notwithstanding anything herein to the contrary, for a period of [\*\*]following the Closing Date, Buyer shall, or shall cause the Company or one of Buyer’s Affiliates to, provide each Transferred Employee with terms and conditions of employment and benefits and compensation levels that are at least substantially comparable to those provided to similarly situated employees of Buyer. For the sake of clarity, Buyer may take into account the payments to be made in accordance with Section 8.06 hereof when determining any annual bonus amount that it may pay to Transferred Employees following the Closing Date that would have otherwise covered any period prior to the Closing Date.

Section 8.03. *Credit for Past Service; Deductibles; Preexisting Conditions.* With respect to any Buyer Employee Plan in which any Transferred Employee becomes a participant, Buyer shall, or shall cause the Company or one of Buyer’s Affiliates to, (i) recognize all service to any Seller, the Company, their respective Affiliates or, to the extent recognized by any Seller, the Company or the respective Affiliate, any of their respective predecessors prior to the Closing Date as service to Buyer and its Affiliates for the purposes of eligibility, vesting and the level of benefits under any vacation, paid time off or severance plan or policy; (ii) make its commercially reasonable efforts to cause its insurance carriers to fully credit each Transferred Employee for any deductibles and out-of-pocket expenses paid by such Transferred Employee prior to the date such Transferred Employee became a participant in such Buyer Employee Plan with respect to the calendar year in which such participation commences, provided that such efforts shall not require Buyer, the Company, or any of Buyer’s Affiliates to incur incremental costs in excess of \$5,000 and (iii) make its commercially reasonable best efforts to waive, or cause their insurance carriers to waive, all limitations as to preexisting or at-work conditions and exclusions with respect to participation and coverage requirements applicable to such Transferred Employees.

Section 8.04. *Employee Liabilities.* Effective as of the Closing Date, Buyer shall, or shall cause the Company or one of Buyer’s Affiliates to, assume all obligations and liabilities of each Seller or the Company and their respective Affiliates related to the Transferred Employees (i) that are incurred prior to the

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Closing Date with respect to accrued but unused paid time off and (ii) that are incurred following the Closing Date or, in the case of any Leave Recipient, the date such Leave Recipient becomes a Transferred Employee. At and following the Closing Date, Seller shall be solely responsible for all obligations and liabilities associated with the employment or termination of employment of any Person who is or was employed by or otherwise providing services to Roche Kulmbach GmbH.

Section 8.05. *Qualified Savings Plans.* On or as soon as practicable following the Closing Date, one or more Buyer Savings Plans shall, if elected by Transferred Employees, accept individual rollovers in cash of such Transferred Employees' distributions from any Seller Savings Plan, subject to the terms and conditions of such Buyer Savings Plans and Applicable Law.

Section 8.06. *Annual Incentive Compensation.* In respect of the performance year in which the Closing Date occurs, each Company Employee shall be entitled to receive a payment in cash under each annual incentive compensation plan, agreement, program or other arrangement in which such Company Employee participates as of immediately prior to the Closing Date, based on the deemed achievement of target performance and prorated to reflect the portion of such performance year starting on the first day of such performance year and ending on the day immediately prior to the Closing Date. Each such cash payment shall be made on or prior to the Closing Date by Sellers.

Section 8.07. [\*\*] (a) Each [\*\*] listed in Section 8.07 of the Sellers Disclosure Schedule shall be paid [\*\*] (each, a [\*\*]) on each date that is, [\*\*] and [\*\*] following the Closing Date, subject to such Company Employee being employed by Buyer or one of its Affiliates on the respective payment date, and so long as, prior to receiving such payment, [\*\*]. For the avoidance of doubt, if a Company Employee ceases to be employed by Buyer or any of its Affiliates for any reason prior to the scheduled payment date of a [\*\*], such Company Employee forfeits such [\*\*]. Each [\*\*] shall be equal to the amount set forth for such Company Employee in Section 8.07 of the Sellers Disclosure Schedule.

(b) All [\*\*] shall be paid to the Company Employees directly by the Company or by Buyer or one of its Affiliates on behalf of the Company. Upon the presentation to Sellers of a statement setting forth the dollar amount of [\*\*] paid by Buyer or one of its Affiliates to the Company Employees, Roche Nutley shall, within [\*\*], reimburse the Company for the [\*\*] incurred by or on behalf of the Company of the [\*\*], taking into account, without limitation, [\*\*] incurred by the Company or its Affiliates. Unless otherwise required by law; any amount paid

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by Roche Nutley pursuant to this Section 8.07(b) shall, for U.S. federal income tax purposes, be treated as a contribution by Roche Nutley to the Company at the time immediately prior to the Closing. To the extent that the Company or its Affiliates actually realize value in cash (such value to be calculated in accordance with the method described in Section 7.06(c)) with respect to the Tax Benefit resulting from any such [\*\*] in (A) the year such [\*\*] were made or (B) any of the immediately succeeding taxable years, the Company or its Affiliates shall pay or cause to be paid to Roche Nutley an amount equal to the value so realized within [\*\*] of the filing the applicable Tax Return. Unless otherwise required by law; any amount paid by or on behalf of the Company or its Affiliates pursuant to this Section 8.07(b) shall, for U.S. federal income tax purposes, be treated as a distribution by the Company to Roche Nutley at the time immediately prior to the Closing.

Section 8.08. *Participation in Seller Employee Plans.* Each Transferred Employee will cease, effective as of the date of such Transferred Employee's commencement of employment with Buyer or its Affiliates, any participation in and any benefit accrual under each of the Seller Employee Plans other than under any equity-based compensation plan solely to the extent that such Transferred Employee holds an outstanding award that by its terms has rights that extend past such Transferred Employee's termination of employment with Sellers and Sellers' Affiliates. Sellers shall, or shall cause their Affiliates to, take all necessary actions to effect such cessation.

Section 8.09. *WARN and/or Labor Department Notifications.* In the event that Buyer determines to terminate, or determines to cause the Company or one of Buyer's Affiliates to terminate, any Transferred Employee during the 90-day period following the Closing Date, Buyer and Sellers agree to, and Buyer agrees to cause the Company or Buyer's Affiliates to, cooperate and exchange such data and information as is reasonably necessary to determine whether such termination would reasonably be expected to result in liability to Buyer or any Seller under the U.S. Worker Adjustment and Retraining Notification Act ("**WARN**") or any displaced worker notification statutes.

Section 8.10. *Cooperation; Necessary Actions.* Sellers and Buyer agree to reasonably cooperate and to take all action, or cause such action to be taken, which may be necessary in order to effectuate the transactions contemplated by this Article 8, including without limitation adopting any necessary amendments to the Seller Employee Plans and the Buyer Employee Plans, making all necessary filings and submissions to the appropriate governmental agencies and providing Company Employees with any notification required by Applicable Law.

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Section 8.11. *No Third-Party Beneficiaries; No Amendment.* (a) Without limiting the generality of Section 10.08, nothing in this Article 8 shall create any third-party beneficiary rights in any Company Employee (including any beneficiary or dependent thereof).

(b) Nothing in this Article 8 shall (i) be treated as an amendment of any benefit plan or (ii) obligate Buyer, any Seller, the Company or any of their respective Affiliates to retain the employment of any particular employee or the continued employment of any particular employee for any period of time.

ARTICLE 9  
SURVIVAL; INDEMNIFICATION

Section 9.01. *Survival.* The representations and warranties of the parties hereto contained in this Agreement shall survive the Closing until the date that is eighteen months following the Closing Date, at which time they shall terminate (and no claims shall be made for indemnification under Section 9.02 for Warranty Breaches thereafter); *provided* that the representations and warranties contained in Sections 4.06 and 4.18 shall survive indefinitely or until the latest date permitted by law. The covenants and agreements of the parties hereto contained in this Agreement or in any certificate or other writing delivered pursuant hereto or in connection herewith shall survive the Closing indefinitely or for the shorter period explicitly specified therein, except that for such covenants and agreements that survive for such shorter period, breaches thereof shall survive indefinitely or until the latest date permitted by law. Notwithstanding the preceding sentences, any breach of representation, warranty, covenant or agreement in respect of which indemnity may be sought under this Agreement shall survive the time at which it would otherwise terminate pursuant to the preceding sentences if notice of the inaccuracy or breach thereof giving rise to such right of indemnity shall have been given to the party against whom such indemnity may be sought prior to such time.

Section 9.02. *Indemnification.* (a) Effective at and after the Closing, each Seller, jointly and severally, hereby indemnifies Buyer and its Affiliates against and agrees to hold each of them harmless from any and all damage, loss and expense (including reasonable expenses of investigation and reasonable attorneys' fees and expenses in connection with any action, suit or proceeding whether involving a third party claim or a claim solely between the parties hereto)

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("Damages") actually suffered by Buyer or any of its Affiliates arising out of any misrepresentation or breach of warranty (each such misrepresentation and breach of warranty a "Warranty Breach") or breach of covenant or agreement made or to be performed by Sellers pursuant to this Agreement (other than, in the case of Sellers, any representation or warranty or covenant or agreement set forth in Article 7); *provided* that with respect to indemnification by Sellers for Warranty Breaches pursuant to this Section 9.02(a), (i) Sellers shall not be liable for Damages with respect to any claim or series of related claims arising out of or related to similar facts or circumstances for an amount of less than [\*\*] and (ii) Sellers' maximum liability shall not exceed [\*\*].

(b) Effective at and after the Closing, Buyer hereby indemnifies each Seller and its Affiliates against and agrees to hold each of them harmless from any and all Damages actually suffered by such Seller or any of its Affiliates arising out of (i) any Warranty Breach or breach of covenant or agreement made or to be performed by Buyer pursuant to this Agreement, (ii) any matter relating to actions taken or omitted to be taken by the Company prior to the Closing Date, except to the extent any such matter is indemnifiable by Sellers pursuant to Section 9.02(a), (iii) any matter relating to actions taken or omitted to be taken by Buyer or any of its Affiliates (including, after the Closing, the Company) on or after the Closing Date or (iv) any liability or obligation relating to or arising out of a Transferred Asset (other than any matter relating to a Transferred Asset that is indemnifiable by Sellers pursuant to Section 9.02(a); *provided* that with respect to indemnification by Buyer for Warranty Breaches pursuant to Section 9.02(b)(i), (A) Buyer shall not be liable for Damages with respect to any claim or series of related claims arising out of or related to similar facts or circumstances for an amount of less than \$50,000 and (B) Buyer's maximum liability shall not exceed [\*\*].

(c) Notwithstanding any of the provisions of this Article 9, Section 7.06 shall provide the exclusive remedy for Buyer's and its Affiliates' recovery of any Loss with respect to any Covered Tax from Sellers and their Affiliates, and the procedures set forth in Section 7.06 shall govern any claim for indemnification under such provision. For the avoidance of doubt, the monetary limitations set forth in this Section 9.02 shall not apply with respect to any claim made pursuant to Section 7.02(g) or Section 7.06.

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Section 9.03. *Third Party Claim Procedures.* (a) The party seeking indemnification under Section 9.02 (the “**Indemnified Party**”) agrees to give prompt notice to the party against whom indemnity is sought (the “**Indemnifying Party**”) of the assertion of any claim or the commencement of any suit, action or proceeding by any third party (each, a “**Third Party Claim**”) in respect of which indemnity may be sought under Section 9.02. Such notice shall set forth in reasonable detail such Third Party Claim and the basis for indemnification (taking into account the information then available to the Indemnified Party). The failure to so notify the Indemnifying Party shall not relieve the Indemnifying Party of its obligations hereunder, except to the extent such failure shall have adversely prejudiced the Indemnifying Party. Thereafter, the Indemnified Party shall deliver to the Indemnifying Party, as promptly as reasonably practicable following the Indemnified Party’s receipt thereof, copies of all written notices and documents (including any court papers) received by the Indemnified Party relating to the Third Party Claim and the Indemnified Party shall provide the Indemnifying Party with such other information with respect to any such Third Party Claim reasonably requested by the Indemnifying Party.

(b) The Indemnifying Party shall be entitled to participate in the defense of any Third Party Claim and may, upon written notice to the Indemnified Party, assume control of the defense, appeal and settlement of such Third Party Claim and appoint lead counsel for such defense, in each case at its sole cost and expense; *provided, however*, that the Indemnifying Party shall not be entitled to (i) assume the defense, appeal or settlement of any Third Party Claim if (A) the Third Party Claim relates to or arises in connection with any criminal proceeding, action, indictment, allegation or investigation or (B) the Third Party Claim seeks any injunction or equitable relief against the Indemnified Party or (ii) maintain control of the defense, appeal or settlement of any Third Party Claim if the Indemnifying Party has failed or is failing to defend in good faith the Third Party Claim and the Indemnified Party has provided prior written notice and a reasonable opportunity for the Indemnifying Party to cure such failure.

(c) If the Indemnifying Party is entitled to do so and has assumed the defense, appeal or settlement proceedings of the Third Party Claim in accordance herewith, the Indemnified Party may retain separate counsel at its sole cost and expense and participate in the defense, appeal or settlement proceedings of the Third Party Claim; *provided* that if the Indemnified Party shall reasonably conclude that (i) there is a material conflict of interest between the Indemnifying Party and the Indemnified Party in the conduct of the defense of such claim or (ii) there are specific defenses or claims available to the Indemnified Party which are different from or additional to those available to the Indemnifying Party and which could be materially adverse to the Indemnifying Party, then the reasonable fees and disbursements of one counsel for the Indemnified Party shall be paid by

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the Indemnifying Party; *provided* that the Indemnifying Party shall not be required to pay for more than one counsel for all Indemnified Parties in connection with any Third Party Claim. The Indemnified Party may take any actions reasonably necessary to defend such Third Party Claim prior to the date the Indemnifying Party assumes control of the defense of the Third Party Claim and shall be entitled to all reasonable fees and expenses of counsel incurred in connection therewith prior to such date.

(d) If the Indemnifying Party is entitled to do so and has assumed the defense, appeal or settlement proceedings of the Third Party Claim in accordance herewith, the Indemnifying Party shall not enter into any settlement with respect to the Third Party Claim without the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld, conditioned or delayed); *provided* that consent of the Indemnified Party shall not be required for any such settlement if (i) the sole relief provided is monetary damages that are paid in full by the Indemnifying Party, (ii) such settlement does not permit any order, injunction or other equitable relief to be entered, directly or indirectly, against the Indemnified Party and (iii) such settlement includes an unconditional release of such Indemnified Person from all liability on claims that are the subject matter of such Third Party Claim and does not include any statement as to or any admission of fault, culpability or a failure to act by or on behalf of any Indemnified Person. Whether or not the Indemnifying Party has assumed the defense, appeal or settlement proceedings, the Indemnifying Party shall not be obligated to indemnify any Indemnified Party hereunder for any settlement entered into or any judgment that was consented to without the Indemnifying Party's prior written consent (which consent shall not be unreasonably withheld, conditioned or delayed).

(e) Each party shall cooperate, and cause its Affiliates to cooperate, in the defense or prosecution of any Third Party Claim and shall furnish or cause to be furnished such records, information and testimony, and attend such conferences, discovery proceedings, hearings, trials or appeals, as may be reasonably requested in connection therewith.

Section 9.04. *Direct Claim Procedures.* In the event an Indemnified Party has a claim for indemnity under Section 9.02 against an Indemnifying Party that does not involve a Third Party Claim, the Indemnified Party agrees to give prompt notice in writing of such claim to the Indemnifying Party. The notice shall set forth (i) that such Indemnified Party has paid, incurred or reasonably anticipates incurring Damages, for which such Indemnified Party is entitled to

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recovery under Section 9.02, (ii) a written statement describing the nature of the claim and the basis therefor, (iii) the amount of such Damages incurred or that such Indemnified Party reasonably estimates in good faith is likely to be incurred in connection with such claim and (iv) if applicable, the instructions for payment to such Indemnified Party (taking into account, for purposes of the foregoing clauses, the information then available to the Indemnified Party). The failure to so notify the Indemnifying Party shall not relieve the Indemnifying Party of its obligations hereunder, except to the extent such failure shall have actually prejudiced the Indemnifying Party. If the Indemnifying Party disputes its indemnity obligation for any Damages with respect to such claim, the parties shall proceed in good faith to negotiate a resolution of such dispute and, if not resolved through negotiations, such dispute shall be resolved by litigation in an appropriate court of jurisdiction determined pursuant to Section 10.06.

Section 9.05. *Calculation of Damages.* (a) The amount of any Damages payable under Section 9.02 by the Indemnifying Party shall be net of any (i) amounts recovered or recoverable by the Indemnified Party under applicable insurance policies or from any other Person alleged to be responsible therefor, and (ii) the value of any Tax Benefit actually realized in cash by the Indemnified Party (such value to be calculated in accordance with the method described in Section 7.06(c)) arising from the incurrence or payment of any such Damages in (x) the Tax year such Damages were incurred and (y) any succeeding Tax year ending on or prior to the date of payment of such Damages. If, in any of the first five Tax years ending after the date of such payment, the Indemnified Party actually realizes value in cash with respect to a Tax Benefit made allowable by such incurrence or payment of any such Damages, the Indemnified Party shall pay the Indemnifying Party an amount equal to the value so realized within 90 days of the filing of the applicable Tax Return or any adjustment for the Tax year in which the Tax Benefit is made allowable. If the Indemnified Party receives any amounts under applicable insurance policies, or from any other Person alleged to be responsible for any Damages, subsequent to an indemnification payment by the Indemnifying Party, then such Indemnified Party shall promptly reimburse the Indemnifying Party for any payment made or expense incurred by such Indemnifying Party in connection with providing such indemnification payment up to the amount received by the Indemnified Party, net of any expenses incurred by such Indemnified Party in collecting such amount.

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(b) For the avoidance of doubt, the Indemnifying Party shall not be liable under Section 9.02 for (i) special, punitive, indirect or consequential Damages, (iii) any Damages to the extent not the probable and reasonably foreseeable result of any breach by the Indemnifying Party of a representation and warranty or covenant contained in this Agreement or (iii) Damages for lost profits; *provided* that this Section 9.05(b) shall not apply to any Damages that are recovered by third parties in connection with a Third Party Claim. Notwithstanding anything in this Agreement to the contrary, no Damages shall be determined or increased based on any multiple of any financial measure (including earnings, sales or other benchmarks) that might have been used by Buyer in the valuation of the Company or their businesses and operations. No Indemnified Party shall be entitled to recover Damages or otherwise be indemnified hereunder (or receive other payment, reimbursement or restitution) more than once in respect of any one given liability, loss, cost or shortfall, regardless of whether more than one claim for Damages arises in respect of it.

(c) Each Indemnified Party must mitigate in accordance with Applicable Law any loss for which such Indemnified Party seeks indemnification under this Agreement. If such Indemnified Party mitigates its loss after the Indemnifying Party has paid the Indemnified Party under any indemnification provision of this Agreement in respect of that loss, the Indemnified Party must notify the Indemnifying Party and pay to the Indemnifying Party the extent of the value of the benefit to the Indemnified Party of that mitigation (less the Indemnified Party's reasonable costs of mitigation) within two Business Days after the benefit is received.

(d) Each Indemnified Party shall use reasonable efforts to collect any amounts available under insurance coverage, or from any other Person alleged to be responsible, for any Damages payable under Section 9.02.

Section 9.06. *Assignment of Claims.* If the Indemnified Party receives any payment from an Indemnifying Party in respect of any Damages pursuant to Section 9.02 and the Indemnified Party could have recovered all or a part of such Damages from a third party (a "**Potential Contributor**") based on the underlying Claim asserted against the Indemnifying Party, the Indemnified Party shall assign such of its rights to proceed against the Potential Contributor as are necessary to permit the Indemnifying Party to recover from the Potential Contributor the amount of such payment.

Section 9.07. *Exclusivity.* Except as specifically set forth in this Agreement, effective as of the Closing (i) Buyer waives, and shall cause the Company to waive, any rights and claims Buyer or any of its Affiliates (including the Company) may have against any Seller or any of its Affiliates, whether in law or in equity, relating to the Company, the Shares or the Transferred Assets or the

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transactions contemplated hereby and (ii) each Seller waives any such rights and claims such Seller and its Affiliates may have against Buyer or any of its Affiliates and the Company. The rights and claims waived by Buyer, the Company, Sellers and their respective Affiliates include claims for contribution or other rights of recovery arising out of or relating to any Environmental Law (whether now or hereinafter in effect), claims for breach of contract, breach of representation or warranty, negligent misrepresentation and all other claims for breach of duty. Subject to Section 10.12, after the Closing, Sections 7.02(g), 7.06, 8.09 and 9.02 will provide the exclusive remedy for any misrepresentation or breach of warranty, covenant or other agreement or other claim arising out of this Agreement or the transactions contemplated hereby.

ARTICLE 10  
MISCELLANEOUS

Section 10.01. *Notices.* All notices, requests and other communications to any party hereunder shall be in writing (including facsimile transmission and electronic mail (“**e-mail**”) transmission, so long as a receipt of such e-mail is requested and received) and shall be given,

if to Buyer, to:

Arrowhead Research Corporation  
225 South Lake Avenue, Suite 300  
Pasadena, California 91101  
Attention: Christopher Anzalone, Ph.D.  
Facsimile No.: (626) 304-3401  
E-mail: canzalone@arrowres.com

with a copy to:

Ropes & Gray LLP  
Three Embarcadero Center  
San Francisco, California 94111  
Attention: Ryan A. Murr  
Facsimile No.: (415) 315-6026  
E-mail: ryan.murr@ropesgray.com

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if to Sellers, to each of:

Hoffmann-La Roche Inc.  
340 Kingsland Street  
Nutley, NJ 07110  
Attention: General Counsel  
Facsimile No.: (973) 235-3500  
E-mail: kentz.frederick@gene.com

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4058 Basel  
Switzerland  
Attention: Group Legal Department  
Facsimile No.: +41 61 68 81396  
E-mail: beat.kraehenmann@roche.com  
peter.trybus@roche.com

with a copy to:

Davis Polk & Wardwell LLP  
450 Lexington Avenue  
New York, New York 10017  
Attention: Marc O. Williams  
Facsimile No.: (212) 701-5800  
E-mail: marc.williams@davispolk.com

or such other address or facsimile number as such party may hereafter specify for the purpose by notice to the other parties hereto. All such notices, requests and other communications shall be deemed received on the date of receipt by the recipient thereof if received prior to 5 p.m. in the place of receipt and such day is a Business Day in the place of receipt. Otherwise, any such notice, request or communication shall be deemed not to have been received until the next succeeding Business Day in the place of receipt.

Section 10.02. *Amendments and Waivers.* (a) Any provision of this Agreement may be amended or waived if, but only if, such amendment or waiver is in writing and is signed, in the case of an amendment, by each party to this Agreement, or in the case of a waiver, by the party against whom the waiver is to be effective.

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(b) No failure or delay by any party in exercising any right, power or privilege hereunder shall operate as a waiver thereof nor shall any single or partial exercise thereof preclude any other or further exercise thereof or the exercise of any other right, power or privilege. Except as set forth in Section 10.07, the rights and remedies herein provided shall be cumulative and not exclusive of any rights or remedies provided by law.

Section 10.03. *Expenses.* Except as otherwise provided herein, all costs and expenses incurred in connection with this Agreement shall be paid by the party incurring such cost or expense.

Section 10.04. *Successors and Assigns.* The provisions of this Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns; *provided* that no party may assign, delegate or otherwise transfer any of its rights or obligations under this Agreement without the consent of the other party hereto, except that (i) any Seller may transfer or assign its rights and obligations under this Agreement in whole or from time to time in part to one or more of its Affiliates and (ii) any party may transfer or assign its rights and obligations under this Agreement (including, without limitation, the rights of Buyer arising under Section 5.12), in whole or from time to time in part, to any successor in interest by way of a Change of Control; *provided* that (A) in the case of clause (ii), such successor shall have executed and delivered to the other party or parties, as applicable, an acknowledgement in writing that effective as of such transfer or assignment, such successor shall be bound by this Agreement to the identical extent applicable the assignor or transferor, as applicable, and (B) in the case of clauses (i) and (ii), no such transfer or assignment shall relieve the assigning or transferring party of its obligations hereunder or enlarge, alter or change any obligation of any other party hereto. If a Change of Control occurs with respect to Buyer, Buyer shall cause each successor in interest and acquiring Person (to the extent such Person would not, by the nature of the transaction, become so bound by operation law) to execute and deliver to Sellers an acknowledgement in writing that such Person shall be bound by the terms of Article 6 to the identical extent applicable to Buyer.

Section 10.05. *Governing Law.* This Agreement shall be governed by and construed in accordance with the law of the State of Delaware, without regard to the conflicts of law rules of such state.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

Section 10.06. *Jurisdiction*. The parties hereto agree that any suit, action or proceeding seeking to enforce any provision of, or based on any matter arising out of or in connection with, this Agreement or the transactions contemplated hereby shall be brought in the United States District Court for the District of Delaware or the Court of Chancery of the State of Delaware, so long as one of such courts shall have subject matter jurisdiction over such suit, action or proceeding, and that any cause of action arising out of this Agreement shall be deemed to have arisen from a transaction of business in the State of Delaware, and each of the parties hereby irrevocably consents to the jurisdiction of such courts (and of the appropriate appellate courts therefrom) in any such suit, action or proceeding and irrevocably waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of the venue of any such suit, action or proceeding in any such court or that any such suit, action or proceeding brought in any such court has been brought in an inconvenient forum. Process in any such suit, action or proceeding may be served on any party anywhere in the world, whether within or without the jurisdiction of any such court. Without limiting the foregoing, each party agrees that service of process on such party as provided in Section 10.01 shall be deemed effective service of process on such party.

Section 10.07. *WAIVER OF JURY TRIAL*. EACH OF THE PARTIES HERETO HEREBY IRREVOCABLY WAIVES ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.

Section 10.08. *Counterparts; Effectiveness; Third Party Beneficiaries*. This Agreement may be signed in any number of counterparts, each of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument. This Agreement shall become effective when each party hereto shall have received a counterpart hereof signed by the other party hereto. Until and unless each party has received a counterpart hereof signed by the other party hereto, this Agreement shall have no effect and no party shall have any right or obligation hereunder (whether by virtue of any other oral or written agreement or other communication). No provision of this Agreement is intended to confer any rights, benefits, remedies, obligations, or liabilities hereunder upon any Person other than the parties hereto and their respective successors and assigns.

Section 10.09. *Entire Agreement*. This Agreement and the other Transaction Documents constitute the entire agreement between the parties with respect to the subject matter of this Agreement and supersede all prior agreements and understandings, both oral and written, between the parties with respect to the subject matter of this Agreement and each other Transaction Document.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

Section 10.10. *Severability*. If any term, provision, covenant or restriction of this Agreement is held by a court of competent jurisdiction or other Governmental Authority to be invalid, void or unenforceable, the remainder of the terms, provisions, covenants and restrictions of this Agreement shall remain in full force and effect and shall in no way be affected, impaired or invalidated so long as the economic or legal substance of the transactions contemplated hereby is not affected in any manner materially adverse to any party. Upon such a determination, the parties shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner in order that the transactions contemplated hereby be consummated as originally contemplated to the fullest extent possible.

Section 10.11. *Disclosure Schedules; Buyer SEC Documents*. (a) Sellers and Buyer have set forth information on the Sellers Disclosure Schedule and the Buyer Disclosure Schedule, respectively, in a section thereof that corresponds to the section of this Agreement to which it relates. A matter set forth in one section of a Schedule need not be set forth in any other section so long as its relevance to such other section of the Schedule or section of the Agreement is reasonably apparent on the face of the information disclosed therein to the Person to which such disclosure is being made. The parties acknowledge and agree that (i) the Schedules to this Agreement may include certain items and information solely for informational purposes for the convenience of the other party and (ii) the disclosure by either party of any matter in the Schedules shall not be deemed to constitute an acknowledgment by such party that the matter is required to be disclosed by the terms of this Agreement or that the matter is material.

(b) The parties hereto agree that any information contained in any part of any Buyer SEC Document shall be deemed an exception to (or a disclosure for purposes of) a representation and warranty of Buyer only if the relevance of that information as an exception to (or a disclosure for purposes of) such representation and warranty is reasonably apparent on the face of the information disclosed therein to the Person to which such disclosure is being made; *provided* that in no event shall any information contained in any part of any Buyer SEC Document entitled "Risk Factors" (or words of similar import) or containing a description or explanation of "Forward-Looking Statements" be deemed to be an exception to (or a disclosure for purposes of) any representations and warranties of Buyer contained in this Agreement.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

Section 10.12. *Specific Performance*. The parties hereto agree that irreparable damage would occur if any provision of this Agreement were not performed in accordance with the terms hereof and that the parties shall be entitled to an injunction or injunctions to prevent breaches of this Agreement or to enforce specifically the performance of the terms and provisions hereof in the United States District Court for the District of Delaware or the Court of Chancery of the State of Delaware, in addition to any other remedy to which they are entitled at law or in equity.

Section 10.13. *Waiver of Conflicts Regarding Representation; Non-assertion of Attorney-Client Privilege*. (a) Buyer waives and will not assert, and agrees to cause the Company to waive and not to assert, any conflict of interest arising out of or relating to the representation, after the Closing (the “**Post-Closing Representation**”), of any Seller, any Affiliate of any Seller or any stockholder, officer, employee or director of Company (any such Person, a “**Designated Person**”) in any matter involving the Transaction Documents or any other agreements or transactions contemplated hereby or thereby, by any legal counsel currently representing any Seller, any Affiliate of any Seller or the Company in connection with the Transaction Documents or any other agreements or transactions contemplated hereby or thereby (the “**Current Representation**”).

(b) Buyer waives and will not assert, and agrees to cause the Company to waive and to not assert, any attorney-client privilege with respect to any communication between any legal counsel and any Designated Person occurring during the Current Representation in connection with any Post-Closing Representation, including in connection with a dispute with Buyer, and following the Closing, with the Company, it being the intention of the parties hereto that all such rights to such attorney-client privilege and to control such attorney-client privilege shall be retained by Sellers; *provided* that the foregoing waiver and acknowledgement of retention shall not extend to any communication not involving the Transaction Documents or any other agreements or transactions contemplated hereby or thereby, or to communications with any Person other than the Designated Persons.

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Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be duly executed by their respective authorized officers as of the day and year first above written.

ARROWHEAD RESEARCH CORPORATION

By: /s/ Christopher Anzalone  
Name: Christopher Anzalone  
Title: Chief Executive Officer

HOFFMANN-LA ROCHE INC.

By: /s/ Guido Kaiser  
Name: Guido Kaiser  
Title: Legal Representative

By: /s/ Peter Trybus  
Name: Peter Trybus  
Title: Legal Representative

F. HOFFMANN-LA ROCHE LTD

By: /s/ Guido Kaiser  
Name: Guido Kaiser  
Title: Legal Representative

By: /s/ Peter Trybus  
Name: Peter Trybus  
Title: Legal Representative

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Schedules (or similar attachments) referred to and listed herein shall have been omitted pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule (or similar attachment) will be furnished to the Commission upon request.

**REGISTRATION RIGHTS AGREEMENT**

dated as of

October 21, 2011

among

**ARROWHEAD RESEARCH CORPORATION**

and

**THE SHAREHOLDERS PARTY HERETO**

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## REGISTRATION RIGHTS AGREEMENT

AGREEMENT dated as of October 21, 2011 (this “**Agreement**”) between Arrowhead Research Corporation, a Delaware corporation (the “**Company**”) and Roche Finance Ltd, a Swiss corporation (including each of its Permitted Transferees, collectively, the “**Shareholders**” and each individually, a “**Shareholder**”).

In consideration of the mutual promises made herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

### ARTICLE 1 DEFINITIONS

Section 1.01. *Definitions.* (a) The following terms, as used herein, have the following meanings:

“**Affiliate**” means, with respect to any Person, any other Person directly or indirectly controlling, controlled by, or under common control with such Person; *provided* that for purposes of this definition, (i) none of the Company, Roche Madison Inc., a Delaware corporation, or Roche Kulmbach GmbH, a German limited liability company, shall be considered an Affiliate of any Shareholder; (ii) neither Chugai Pharmaceutical Co., Ltd (at 1-1 Nihonbashi-Muromachi 2-chome, Chuo-ku, Tokyo, 103-8324, Japan) nor any of its subsidiaries shall be considered an Affiliate of a Shareholder, unless a Shareholder elect, in a written notice delivered to Buyer, to have any such Person considered an Affiliate of such Shareholder; and (iii) none of Roche Holding Ltd or any of its subsidiaries shall be considered an Affiliate of the Company. For purposes of this definition, “control” when used with respect to any Person means the power to direct the management and policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise, and the terms “controlling” and “controlled” have correlative meanings.

“**Business Day**” means any day except a Saturday, Sunday or other day on which commercial banks in New York City are authorized by law to close.

“**Closing**” means the Closing as defined in the Stock and Asset Purchase Agreement.

“**Common Stock**” means the common stock, par value \$0.001 per share, of the Company and any class of securities into which such Common Stock may be converted or changed.

“**Effectiveness Date**” means the earlier of (i) the 90<sup>th</sup> day following the date of the Closing (or the 120<sup>th</sup> day if the SEC reviews and has written comments to the Shelf Registration Statement that would require the filing of a pre-effective amendment thereto with the SEC) and (ii) the fifth Trading Day following the date on which the Company is notified by the SEC that the Shelf Registration Statement will not be reviewed or is no longer subject to further review and comments.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended.

“**Filing Date**” means the 30<sup>th</sup> day following the date of the Closing.

“**FINRA**” means the Financial Industry Regulatory Authority (formerly, the National Association of Securities Dealers, Inc.) and any successor thereto.

“**Permitted Transferee**” means a Person to whom Registrable Securities are transferred by any Shareholder; *provided* that (i) such transfer is not made in a registered offering or pursuant to Rule 144 and (ii) such transferee shall only be a Permitted Transferee if and to the extent the transferor designates the transferee as a Permitted Transferee entitled to rights hereunder pursuant to Section 4.01(b).

“**Person**” means an individual, corporation, limited liability company, partnership, association, trust or other entity or organization, including a government or political subdivision or an agency or instrumentality thereof.

“**Post-Closing Payment Date**” means the Post-Closing Payment Date as defined in the Stock and Asset Purchase Agreement.

“**Public Offering**” means an underwritten public offering of Common Stock of the Company pursuant to an effective registration statement under the Securities Act, other than pursuant to a registration statement on Form S-4 or Form S-8 or any similar or successor form.

“**Registrable Securities**” means, at any time, any shares of Common Stock beneficially owned by any Shareholder and any other securities beneficially owned by any Shareholder issued or issuable by the Company or any of its successors or assigns in respect of any such shares of Common Stock by way of conversion, exchange, exercise, dividend, split, reverse split, combination, recapitalization, reclassification, merger, consolidation, sale of assets, other reorganization or otherwise until (i) a registration statement covering such shares of Common Stock or such other securities has been declared effective by the SEC and such shares of Common Stock or such other securities have been disposed of pursuant to such effective registration statement or (ii) such shares of Common Stock or such other securities are sold under circumstances in which all of the applicable conditions of Rule 144 are met.

“**Registration Expenses**” means any and all expenses incident to the performance of, or compliance with, any registration or marketing of securities, including all (i) registration and filing fees, and all other fees and expenses payable in connection with the listing of securities on any securities exchange or

automated interdealer quotation system, (ii) fees and expenses of compliance with any securities or “blue sky” laws (including reasonable fees and disbursements of counsel in connection with “blue sky” qualifications of the securities registered), (iii) expenses in connection with the preparation, printing, mailing and delivery of any registration statements, prospectuses and other documents in connection therewith and any amendments or supplements thereto, (iv) security engraving and printing expenses, (v) internal expenses of the Company (including all salaries and expenses of its officers and employees performing legal or accounting duties), (vi) fees and disbursements of counsel for the Company and fees and expenses for independent certified public accountants retained by the Company (including the expenses relating to any comfort letters or costs associated with the delivery by independent certified public accountants of any comfort letters requested pursuant to Section 2.02(g)), (vii) reasonable fees and expenses of any special experts retained by the Company in connection with such registration, (viii) reasonable fees, out-of-pocket costs and expenses of the Shareholders, including the reasonable fees and disbursements of one counsel for all of the Shareholders participating in the applicable offering or registration selected by the Shareholders holding the majority of the Registrable Securities of the Shareholders to be included in the offering or registration; provided that the aggregate fees paid by the Company under this clause (viii) shall not exceed \$15,000, (ix) fees and expenses in connection with any review by FINRA of the underwriting arrangements or other terms of the offering, and all fees and expenses of any “qualified independent underwriter,” including the fees and expenses of any counsel thereto, (x) fees and disbursements of underwriters customarily paid by issuers of securities, but excluding any underwriting fees, discounts and commissions attributable to the sale of Registrable Securities, (xi) costs of printing and producing any agreements among underwriters, underwriting agreements, any “blue sky” or legal investment memoranda and any selling agreements and other documents in connection with the offering, sale or delivery of the Registrable Securities, (xii) transfer agents’ and registrars’ fees and expenses and the fees and expenses of any other agent or trustee appointed in connection with such offering and (xiii) all out-of-pocket costs and expenses incurred by the Company or its appropriate officers in connection with their compliance with Section 2.02(j). Except as set forth in clause (viii) above, Registration Expenses shall not include any out-of-pocket expenses of the Shareholders (or the agents who manage their accounts).

“**Rule 144**” means Rule 144 (or any successor or similar provisions) under the Securities Act.

“**SEC**” means the Securities and Exchange Commission.

“**Securities Act**” means the Securities Act of 1933, as amended.

“**Stock and Asset Purchase Agreement**” means the stock and asset purchase agreement dated as of the date hereof among the Company, Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd.

“**Trading Day**” means a day on which trading in the Common Stock generally occurs on the NASDAQ Capital Market or, if the Common Stock is not then listed on the NASDAQ Capital Market, on the principal other U.S. national or regional securities exchange on which the Common Stock is then listed or principal other U.S. national or regional market on which the Common Stock is then traded. If the Common Stock is not so listed or traded, “Trading Day” means a Business Day.

“**Transfer**” means, with respect to any Registrable Securities, (i) when used as a verb, to sell, assign, dispose of, exchange, pledge, encumber, hypothecate or otherwise transfer such Registrable Securities or any participation or interest therein, whether directly or indirectly, or agree or commit to do any of the foregoing and (ii) when used as a noun, a direct or indirect sale, assignment, disposition, exchange, pledge, encumbrance, hypothecation, or other transfer of such Registrable Securities or any participation or interest therein or any agreement or commitment to do any of the foregoing.

(b) Each of the following terms is defined in the Section set forth opposite such term:

<u>Term</u>	<u>Section</u>
Agreement	Preamble
Company	Preamble
Damages	3.01
Effectiveness Period	2.01(a)
Event	2.01(e)
Event Date	2.01(e)
Indemnified Party	3.03
Indemnifying Party	3.03
Inspectors	2.02(f)
Joinder Agreement	4.01(b)
Notice	4.02(b)
Shareholder	Preamble
Shelf Offering Notice	2.01(c)
Shelf Underwritten Offering	2.01(c)
Shelf Registration Statement	2.01(a)
Shelf Resale	2.01(b)
Suspension Period	2.01(d)

Section 1.02. *Other Definitional and Interpretative Provisions.* The words “hereof”, “herein” and “hereunder” and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. The captions herein are included for convenience of reference only and shall be ignored in the construction or interpretation hereof. References to Articles, Sections or Exhibits are to Articles, Sections and Exhibits of this Agreement unless otherwise specified. All Exhibits annexed hereto or referred to herein are hereby incorporated in and made a part of this Agreement as if set forth in full herein. Any capitalized term used in any Exhibit but not otherwise defined therein shall have the meaning as defined in this Agreement. Any singular term in this Agreement shall be deemed to include the plural, and any plural term the singular. Whenever the words “include”, “includes” or “including” are used in this Agreement, they shall be deemed to be followed by the words “without limitation”, whether or not they are in fact followed by those words or words of like import. “Writing”, “written” and comparable terms refer to printing, typing and other means of reproducing words (including electronic media) in a visible form. References to any agreement or contract are to that agreement or contract as amended, modified or supplemented from time to time in accordance with the terms hereof and thereof. References to any Person include the successors and permitted assigns of that Person. References from or through any date mean, unless otherwise specified, from and including or through and including, respectively. References to “law”, “laws” or to a particular statute or law shall be deemed also to include any applicable transnational, domestic or foreign federal, state or local law (statutory, common or otherwise), constitution, treaty, convention, ordinance, code, rule, regulation, order, injunction, judgment, decree, ruling or other similar requirement enacted, adopted, promulgated or applied by a governmental entity, as amended unless expressly specified otherwise.

ARTICLE 2  
REGISTRATION RIGHTS

Section 2.01. *Shelf Registration.* (a) As soon as possible, but no later than the Filing Date, the Company shall prepare and file with the SEC a shelf registration statement covering the resale of all Registrable Securities held by each Shareholder immediately after the Closing for one or more offerings to be made pursuant to Rule 415 on Form S-3 (or on any successor or similar form appropriate for such purpose) (the “**Shelf Registration Statement**”). As soon as possible, but no later than the Effectiveness Date, the Company shall (i) cause the Shelf Registration Statement to be declared effective under the Securities Act and (ii) unless such Shareholders are required to be named earlier pursuant to SEC rules, file pursuant to Rule 424 (or any similar provision then in force) a prospectus relating to the Shelf Registration Statement, which prospectus shall contain the names and addresses of the Shareholders and all of the Registrable Securities owned by the Shareholders immediately after the Closing. The Company shall use its reasonable best efforts to keep the Shelf Registration Statement continuously effective under the Securities Act until the date which is the earlier of (i) such time as all such Registrable Securities have been publicly sold by the Shareholders or (ii) the later of (A) the eighteen-month anniversary of

the Effectiveness Date and (B) such time as all such Registrable Securities may be sold by the Shareholders pursuant to Rule 144 without any volume limitations as determined by counsel to the Company pursuant to a written opinion letter to such effect, addressed and acceptable to the Company's transfer agent and the Shareholders (the "**Effectiveness Period**").

(b) *Shelf Resales*. If at any time during the Effectiveness Period a Shareholder desires to sell all or any portion of its Registrable Securities under the Shelf Registration Statement in a non-underwritten sale (a "**Shelf Resale**"), such Shareholder shall notify the Company of such intent at least one Business Day prior to such proposed sale. The Shareholders shall be entitled to effectuate an unlimited number of Shelf Resales during the Effectiveness Period.

(c) *Shelf Underwritten Offering*.

(i) *Shelf Underwritten Notice*. If at any time during the Effectiveness Period a Shareholder desires to sell all or any portion of its Registrable Securities under the Shelf Registration Statement in an underwritten sale (a "**Shelf Underwritten Offering**"), such Shareholder shall notify the Company of such intent (such notice, the "**Shelf Offering Notice**"). The Company shall give notice to the other Shareholders of the requested Shelf Underwritten Offering as promptly as practicable, and in any event within two Business Days, following the Company's receipt of the Shelf Offering Notice and shall include in such Shelf Underwritten Offering all of the Registrable Securities requested to be included therein by any Shareholders that respond within five Business Days of the Company's notification delivered pursuant to this subsection. As soon as practicable after receipt of a Shelf Offering Notice, the Company shall prepare and file a supplement to the related prospectus, post-effective amendment to the Shelf Registration Statement and/or Exchange Act reports incorporated by reference into the Shelf Registration Statement and take such other actions as are reasonably necessary or appropriate to permit the consummation of such Shelf Underwritten Offering with respect to all Registrable Securities requested to be sold thereunder.

(ii) *Limitation on Shelf Underwritten Offerings*. Notwithstanding anything to the contrary herein, (i) the Company shall not be required to effectuate more than three Shelf Underwritten Offerings hereunder, (ii) a Shelf Offering Notice may be delivered to the Company only by a Shareholder or group of Shareholders holding at least 25% of the then-outstanding Registrable Securities and (iii) if the Registrable Securities proposed to be sold in any Shelf Underwritten Offering are less than all of the Registrable Securities, the Company shall not be required to effectuate such Shelf Underwritten Offering unless the aggregate proceeds expected to be received from the sale of Registrable Securities thereunder equal or exceed \$2,000,000. A Shelf Underwritten Offering shall be deemed not to have occurred if:

(A) the Shelf Registration Statement is interfered with by any stop order, injunction or other order or requirement of the SEC or other governmental agency or court and less than 75% of the Registrable Securities sought to be included in such Shelf Underwritten Offering have been sold therein; or

(B) the Shareholder(s) participating in a Shelf Underwritten Offering withdraw the applicable Shelf Offering Notice, by written notice to the Company, prior to consummation of the Shelf Underwritten Offering; *provided* that if such withdrawal is not attributable to any action or inaction of the Company that would reasonably have been expected to materially and adversely affect the proposed Shelf Underwritten Offering (including with respect to the proceeds expected to be received by the Shareholders), the participating Shareholder(s) shall reimburse the Company for its reasonable out-of-pocket expenses incurred in connection with the proposed Shelf Underwritten Offering.

(iii) In any Shelf Underwritten Offering, the Shareholders holding the majority of the Registrable Securities to be sold in such offering shall have the right to select an underwriter, which shall be reasonably acceptable to the Company. In connection with any Shelf Underwritten Offering, the Company shall enter into customary agreements (including an underwriting agreement in customary form) and take such all other actions as are reasonably required in order to expedite or facilitate the disposition of the Registrable Securities in such offering.

(d) *Suspension of Shelf Registration Statement.* Notwithstanding anything to the contrary herein, the Company shall be entitled to suspend the use of the Shelf Registration Statement for a period of time not to exceed 30 days in succession or 90 days in the aggregate in any 12-month period (a “**Suspension Period**”); *provided* that the Company shall deliver a written certificate to the Shareholders signed by either the Chief Executive Officer or the Chief Financial Officer of the Company, certifying that the board of directors of the Company has determined, in its good faith judgment, that usage of the Shelf Registration Statement during such proposed Suspension Period would materially and adversely affect or interfere with any proposal or plan by the Company to engage in any material financing or in any material acquisition, merger, consolidation, tender offer, business combination, securities offering or other material transaction. Immediately upon receipt of such notice, the Shareholders shall discontinue the disposition of Registrable Securities under the Shelf Registration Statement until the termination of such Suspension Period. The Company agrees that it will terminate any Suspension Period as promptly as reasonably practicable and will promptly notify the Shareholders of such termination. Upon the occurrence of any Suspension Period, the Effectiveness Period shall be extended by the number of days in such Suspension Period.

(e) *Additional Registration Statement.*

(i) If, after the date hereof, a Shareholder receives any Registrable Securities pursuant to Section 2.08 of the Stock and Asset Purchase Agreement, the Company shall prepare and file as promptly as practicable thereafter an additional registration statement to permit the resale of all such Registrable Securities on the same basis and subject to the same terms and conditions, as nearly as practicable, applicable to the sale of Registrable Securities pursuant to the Shelf Registration Statement hereunder, except that (A) references in this Agreement to the “Closing” and “the date of the Closing” shall be deemed to be references to “the Post-Closing Payment Date”, (B) clause (ii)(A) of the definition of Effectiveness Period shall be deemed to be replaced with “the six-month anniversary of the Effectiveness Date of the registration statement filed pursuant to Section 2.01(e)(i)” and (C) any other time periods in this Agreement shall be adjusted accordingly with respect to such Registrable Securities.

(ii) If for any reason any of the Registrable Securities held by or issued to a Shareholder immediately after the Closing or Post-Closing Payment Date are not covered by an effective registration statement at any time during the Effectiveness Period applicable to such Registrable Securities, the Company shall prepare and file as promptly as practicable an additional registration statement to permit the resale of all such Registrable Securities on the same basis and subject to the same terms and conditions, as nearly as practicable, applicable to the sale of Registrable Securities pursuant to the Shelf Registration Statement hereunder.

(iii) Any registration statement required to be filed pursuant to this Section 2.01(e) shall be deemed to be a “Shelf Registration Statement” for purposes of Section 2.02 and Section 4.02 of this Agreement.

Section 2.02. *Registration Procedures.* Whenever a registration or sale is to be effected in accordance with Section 2.01, subject to the provisions of such Section, the Company shall use all commercially reasonable efforts to effect the registration and sale of Registrable Securities covered thereby in accordance with the intended method of disposition thereof as quickly as practicable, and, in connection with any such request:

(a) (i) in the case of a Shelf Underwritten Offering, or in the case of any Shelf Resale if requested by any of the Shareholders or to the extent required by law, prepare and file with the SEC a supplement to the related prospectus to give effect to the sale of the Registrable Securities by the Shareholders and furnish to each selling Shareholder, its counsel and the managing underwriter(s), if any, copies of such prospectus supplement; *provided* that before filing such prospectus supplement, the Company will furnish to each selling Shareholder, its counsel and the managing underwriter(s), if any, copies of such prospectus supplement proposed to be filed, which will be subject to the reasonable review and comment of such counsel (such review to be conducted with reasonable promptness) and (ii) prior to filing any other registration statement or prospectus or any amendment or supplement thereto (other than any report filed pursuant to the Exchange Act that is incorporated by reference therein), the Company shall, if requested, furnish to each Shareholder, its counsel and the managing underwriter(s), if any, of the Registrable Securities covered by such registration statement copies of such registration statement as proposed to be filed, and thereafter the Company shall furnish to each Shareholder and underwriter, if any, such number of copies of such registration statement, each amendment and supplement thereto (in each case including all exhibits thereto and documents incorporated by reference therein), the prospectus included in such registration statement (including each preliminary prospectus and any summary prospectus) and any other prospectus filed under Rule 424, Rule 430A, Rule 430B or Rule 430C under the Securities Act and such other documents as such Shareholder or underwriter may reasonably request in order to facilitate the disposition of the Registrable Securities of such Shareholder.

(b) After the filing of the Shelf Registration Statement, the Company shall (i) cause the related prospectus to be supplemented by any required prospectus supplement and, as so supplemented, to be filed pursuant to Rule 424 under the Securities Act, (ii) comply with the provisions of the Securities Act with respect to the disposition of all Registrable Securities covered by the Shelf Registration Statement during the applicable period in accordance with the intended methods of disposition by the Shareholders thereof set forth in the Shelf Registration Statement or supplement to such prospectus and (iii) promptly notify each Shareholder holding Registrable Securities covered by the Shelf Registration Statement of (A) any stop order issued or threatened by the SEC or any state securities commission (or any other investigation or inquiry relating to the subject matter of this Agreement), and take all reasonable actions required to prevent the entry of such stop order or to remove it if entered; (B) any request by the SEC or any other governmental entity for amendments or supplements to such registration statement or related prospectus or issuer free writing prospectus or for additional information, including the receipt of comments from the SEC; or (C) when any supplement to any related prospectus and any amendments to any related prospectus shall have been filed.

(c) As promptly as practicable after the Company's receipt of an executed Joinder Agreement pursuant to Section 4.01(b) (or, if received during a Suspension Period, within five Business Days after expiration of the Suspension Period), the Company shall take all necessary action to cause the Person that

delivered the Joinder Agreement to be named as a selling securityholder in the Shelf Registration Statement and the related prospectus, as supplemented (or in such other registration statement filed, or to be filed, pursuant to Section 2.01(e)) in such a manner as to permit such Person to deliver the related prospectus and prospectus supplement in connection with sales of its Registrable Securities to purchasers thereof in accordance with applicable law.

(d) The Company shall use all commercially reasonable efforts to register or qualify the Registrable Securities under such other securities or “blue sky” laws of such jurisdictions in the United States as any Shareholder may reasonably request, *provided* that the Company shall not be required to (A) qualify generally to do business in any jurisdiction where it would not otherwise be required to qualify but for this Section 2.02(d) or (B) consent to general service of process in any such jurisdiction.

(e) The Company shall immediately notify each Shareholder holding Registrable Securities covered by the Shelf Registration Statement, at any time when a prospectus relating thereto is required to be delivered under the Securities Act, of the occurrence of an event requiring the preparation of a supplement or amendment to such prospectus so that, as thereafter delivered to the purchasers of such Registrable Securities, such prospectus (as amended or supplemented) will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading and, subject to Section 2.02(a), promptly prepare and make available to each Shareholder and file with the SEC any such supplement or amendment.

(f) The Company shall, in connection with any Public Offering, make available for inspection by any Shareholder and any underwriter participating in any disposition pursuant to the Shelf Registration Statement and any attorney, accountant or other professional retained by any such Shareholder or underwriter (collectively, the “**Inspectors**”), all financial and other records, pertinent corporate documents and properties of the Company as shall be reasonably necessary or desirable to enable any of the Inspectors to exercise its due diligence responsibility, and cause the Company’s officers, directors and employees to supply all information reasonably requested by any Inspectors in connection with such registration statement.

(g) In connection with any Shelf Underwritten Offering, the Company shall use all commercially reasonable efforts to furnish to each underwriter, if any, a signed counterpart, addressed to such underwriter, of (i) an opinion or opinions of counsel to the Company and (ii) a comfort letter or comfort letters from the Company’s independent public accountants, each in customary form and covering such matters of the kind customarily (with respect to issuers of securities in the biotechnology industry) covered by opinions or comfort letters, as the case may be, as the managing underwriter therefor reasonably requests.

(h) The Company shall otherwise use all commercially reasonable efforts to comply with all applicable rules and regulations of the SEC, and make available to its security holders, as soon as reasonably practicable, an earnings statement or such other document covering a period of 12 months, beginning within three months after the effective date of the registration statement, which earnings statement satisfies the requirements of Rule 158 under the Securities Act.

(i) The Company shall be liable for and shall pay all Registration Expenses in connection with any registration or sale effected pursuant to Section 2.01. For the avoidance of doubt, all underwriting fees, discounts, selling commissions and stock transfer taxes in connection with any offering hereunder shall be borne by the Persons selling securities in such offering, pro rata based on the number of securities of such Person sold in such offering.

(j) In any Public Offering, the Company shall have appropriate officers of the Company use their reasonable efforts to cooperate as reasonably requested by the underwriters in the offering, marketing or selling of the Registrable Securities.

(k) The Company shall deliver to each selling Shareholder, and the managing underwriter(s), if any, without charge, as many copies of each applicable prospectus and prospectus supplement (including each form of prospectus and any issuer free writing prospectus related to any such prospectuses) as such Person may reasonably request in connection with the distribution of the Registrable Securities, and the Company, subject to Section 2.02(n), hereby consents to the use of any such prospectus and prospectus supplement by each of the selling Shareholders and the managing underwriter(s), if any, in connection with the offering and sale of the Registrable Securities covered by such prospectus and prospectus supplement.

(l) The Company shall provide and cause to be maintained a transfer agent and registrar for all Registrable Securities from and after the Effectiveness Date. The Company shall cooperate with the Shareholders and the managing underwriter(s), if any, to enable such Registrable Securities to be registered in such names as the managing underwriter(s) or selling Shareholders may request.

(m) The Company may require each Shareholder promptly to furnish in writing to the Company such information regarding the distribution of the Registrable Securities as the Company may from time to time reasonably request and such other information as may be legally required in connection with such registration.

(n) Each Shareholder agrees that, upon receipt of any notice from the Company of the happening of any event of the kind described in Section 2.02(e), such Shareholder shall forthwith discontinue disposition of Registrable Securities pursuant to the Shelf Registration Statement until such Shareholder's receipt of the copies of the supplemented or amended prospectus contemplated by Section

2.02(e), and, if so directed by the Company, such Shareholder shall deliver to the Company all copies, other than any permanent file copies then in such Shareholder's possession, of the most recent prospectus covering such Registrable Securities at the time of receipt of such notice. If the Company shall give such notice, the Company shall extend the period during which such registration statement shall be maintained effective (including the Effectiveness Period) by the number of days in the period from and including the date of the giving of notice pursuant to Section 2.02(e) to the date when the Company shall make available to such Shareholder a prospectus supplemented or amended to conform with the requirements of Section 2.02(e).

(o) Each Shareholder agrees that, in connection with any offering pursuant to this Agreement, it will not distribute any written materials in connection with the offer or sale of the Registrable Securities pursuant to any registration statement hereunder other than the prospectus and any approved free writing prospectus.

Section 2.03. *Rule 144 Sales; Cooperation by the Company.* If any Shareholder shall transfer or propose to transfer any Registrable Securities pursuant to Rule 144, the Company shall cooperate with such Shareholder and shall provide to such Shareholder such information as such Shareholder may reasonably request. Without limiting the foregoing, the Company shall, until at least the eighteen-month anniversary of the Closing (or, upon the occurrence of the Post-Closing Payment Date as contemplated by the Stock and Asset Purchase Agreement, until at least the first anniversary of the Post-Closing Payment Date): (i) make and keep available public information, as those terms are contemplated by Rule 144; (ii) timely file with the SEC all reports and other documents required to be filed under the Securities Act and the Exchange Act; and (iii) furnish to each Shareholder upon request a written statement by the Company as to its compliance with the reporting requirements of the Securities Act and the Exchange Act, a copy of the most recent annual or quarterly report of the Company, and such other information as such Shareholder may reasonably request in order to avail itself of any rule or regulation of the SEC allowing such Shareholder to sell any Registrable Securities without registration.

ARTICLE 3  
INDEMNIFICATION AND CONTRIBUTION

Section 3.01. *Indemnification by the Company.* The Company agrees to indemnify and hold harmless each Shareholder beneficially owning any Registrable Securities covered by a registration statement, its officers, directors, employees, partners and agents, and each Person, if any, who controls such Shareholder within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act from and against any and all losses, claims, damages, liabilities and expenses (including reasonable expenses of investigation and reasonable attorneys' fees and expenses) (collectively, "**Damages**") caused by or

relating to any untrue statement or alleged untrue statement of a material fact contained in any registration statement or prospectus relating to the Registrable Securities (as amended or supplemented if the Company shall have furnished any amendments or supplements thereto) or any preliminary prospectus or free writing prospectus (as defined in Rule 405 under the Securities Act), or caused by or relating to any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, except insofar as such Damages are caused by any such untrue statement or omission or alleged untrue statement or omission so made based upon information furnished in writing to the Company by such Shareholder or on such Shareholder's behalf expressly for use therein. The Company also agrees to indemnify any underwriters of the Registrable Securities, their officers and directors and each Person who controls such underwriters within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act on substantially the same basis as that of the indemnification of the Shareholders provided in this Section 3.01.

Section 3.02. *Indemnification by Participating Shareholders.* Each Shareholder holding Registrable Securities included in any registration statement agrees, severally but not jointly, to indemnify and hold harmless the Company, its officers, directors and agents and each Person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act to the same extent as the indemnity from the Company to such Shareholder provided in Section 3.01, but only with respect to Damages caused by information furnished in writing by such Shareholder or on such Shareholder's behalf expressly for use in any registration statement or prospectus relating to the Registrable Securities, or any amendment or supplement thereto, or any preliminary prospectus or free writing prospectus. Each such Shareholder also agrees to indemnify and hold harmless underwriters of the Registrable Securities, their officers and directors and each Person who controls such underwriters within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act on substantially the same basis as that of the indemnification of the Company provided in this Section 3.02.

Section 3.03. *Conduct of Indemnification Proceedings.* If any proceeding (including any governmental investigation) shall be brought or asserted against any Person in respect of which indemnity may be sought pursuant to this Article 3, such Person (an "**Indemnified Party**") shall promptly notify the Person against whom such indemnity may be sought (the "**Indemnifying Party**") in writing and the Indemnifying Party shall assume the defense thereof, including the employment of counsel reasonably satisfactory to such Indemnified Party, and shall assume the payment of all fees and expenses, *provided* that the failure of any Indemnified Party so to notify the Indemnifying Party shall not relieve the Indemnifying Party of its obligations hereunder except to the extent that the Indemnifying Party is materially prejudiced by such failure to notify. In any such proceeding, any Indemnified Party shall have the right to retain its own counsel,

but the fees and expenses of such counsel shall be at the expense of such Indemnified Party unless (a) the Indemnifying Party and the Indemnified Party shall have mutually agreed to the retention of such counsel, (b) in the reasonable judgment of such Indemnified Party representation of both parties by the same counsel would be inappropriate due to actual or potential differing interests between them, including one or more defenses or counterclaims that are different from or in addition to those available to the Indemnifying Party, or (c) the Indemnifying Party shall have failed to assume the defense within a reasonable time of notice pursuant to this Section 3.03. It is understood that, in connection with any proceeding or related proceedings in the same jurisdiction, the Indemnifying Party shall not be liable for the reasonable fees and expenses of more than one separate firm (in addition to one local counsel per jurisdiction) at any time for all such Indemnified Parties, and that all such fees and expenses shall be reimbursed within 30 days of the date on which the Indemnifying Party receives an invoice for such fees and expenses. In the case of any such separate firm for the Indemnified Parties, such firm shall be designated in writing by the Indemnified Parties. If the Indemnifying Party shall have promptly assumed the defense of any such proceeding, the Indemnifying Party shall not be liable for any settlement thereof effected without its written consent. If any such proceeding is settled with the consent of the Indemnifying Party, or if there be a final judgment for the plaintiff, the Indemnifying Party shall indemnify and hold harmless such Indemnified Parties from and against any loss or liability (to the extent stated above) by reason of such settlement or judgment. Without the prior written consent of the Indemnified Party, no Indemnifying Party shall effect any settlement of any pending or threatened proceeding in respect of which any Indemnified Party is or could have been a party and indemnity could have been sought hereunder by such Indemnified Party, unless such settlement (A) includes an unconditional release of such Indemnified Party from all liability arising out of such proceeding, and (B) does not include any injunctive or other equitable or non-monetary relief applicable to or affecting such Indemnified Person.

Section 3.04. *Contribution.* If the indemnification provided for in this Article 3 is unavailable or unenforceable to the Indemnified Parties in respect of any Damages, then each Indemnifying Party, in lieu of indemnifying the Indemnified Parties, shall contribute to the amount paid or payable by such Indemnified Party, in such proportion as is appropriate to reflect the relative fault of the Indemnifying Party and Indemnified Party in connection with the actions, statements or omissions that resulted in such Damages as well as any other relevant equitable considerations. The relative fault of such Indemnifying Party and Indemnified Party shall be determined by reference to, among other things, whether any action in question, including any untrue or alleged untrue statement of a material fact or omission or alleged omission of a material fact, has been taken or made by, or relates to information supplied by, such Indemnifying Party or Indemnified Party, and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such action, statement or omission. The amount paid or payable by a party as a result of any Damages shall

be deemed to include, subject to the limitations set forth in this Agreement, any reasonable attorneys' or other reasonable fees or expenses incurred by such party in connection with any proceeding to the extent such party would have been indemnified for such fees or expenses if the indemnification provided for in this Article 3 was available to such party in accordance with its terms.

The parties hereto agree that it would not be just and equitable if contribution pursuant to this Section 3.04 were determined by pro rata allocation or by any other method of allocation that does not take into account the equitable considerations referred to in the immediately preceding paragraph. Notwithstanding the provisions of this Section 3.04, no Shareholder shall be required to contribute, in the aggregate, any amount in excess of the amount by which the proceeds actually received by such Shareholder from the sale of the Registrable Securities subject to the proceeding exceeds the amount of any damages that such Shareholder has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission, except in the case of fraud by such Shareholder. Each Shareholder's obligation to contribute pursuant to this Section 3.03 is several in the proportion that the proceeds of the offering received by such Shareholder bears to the total proceeds of the offering received by all such Shareholders and not joint.

No Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation. The remedies provided for in this Article 3 are not exclusive and shall not limit any rights or remedies that may otherwise be available to any Indemnified Party at law or in equity.

Section 3.05. *Other Indemnification.* Indemnification similar to that provided in this Article 3 (with appropriate modifications) shall be given by the Company and each Shareholder participating therein with respect to any required registration or other qualification of securities under any foreign, federal or state law or regulation or governmental authority other than the Securities Act.

#### ARTICLE 4 MISCELLANEOUS

Section 4.01. *Binding Effect; Assignability; Benefit.* (a) This Agreement shall inure to the benefit of and be binding upon the parties hereto and their respective heirs, successors, legal representatives and permitted assigns. Any Shareholder that ceases to own beneficially any Registrable Securities shall cease to be subject to the terms hereof (other than (i) the provisions of Article 3 applicable to such Shareholder with respect to any offering of Registrable Securities completed before the date such Shareholder ceased to own any Registrable Securities and (ii) this Article 4).

(b) Neither this Agreement nor any right, remedy, obligation or liability arising hereunder or by reason hereof shall be assignable by any party hereto pursuant to any transfer of Registrable Securities or otherwise, except that each Shareholder may assign all or any portion of its rights hereunder to any Permitted Transferee of such Shareholder. Any such Permitted Transferee shall (unless already bound hereby) execute and deliver to the Company an agreement to be bound by this Agreement in the form of Exhibit A hereto (a “**Joinder Agreement**”) and shall thenceforth be a “Shareholder.”

(c) Nothing in this Agreement, expressed or implied, is intended to confer on any Person other than the parties hereto, and their respective heirs, successors, legal representatives and permitted assigns, any rights, remedies, obligations or liabilities under or by reason of this Agreement.

Section 4.02. *No Inconsistent Agreements; Adjustments Affecting Registrable Securities.* (a) During the Effectiveness Period, the Company will not, and will not permit any of its Affiliates to, enter into any agreement with respect to its securities that is inconsistent or conflicts with the rights granted to the Shareholders in this Agreement.

(b) The Company will not take any action, or permit any change to occur, with respect to its securities which would materially and adversely affect the ability of a Shareholder to include its Registrable Securities in the Shelf Registration Statement or which would adversely affect the marketability of such Registrable Securities (including, without limitation, effecting a share split or a combination of shares that would have such an adverse effect).

Section 4.03. *Notices.* All notices, requests and other communications (each, a “**Notice**”) to any party shall be in writing and shall be delivered in person, mailed by certified or registered mail, return receipt requested, or sent by facsimile transmission or email transmission so long as receipt of such email is requested and received,

if to the Company, to:

Arrowhead Research Corporation  
225 South Lake Avenue, Suite 300  
Pasadena, California 91101  
Attention: Christopher Anzalone, Ph.D.  
Facsimile No.: (626) 304-3401  
E-mail: canzalone@arrowres.com

with a copy to:

Ropes & Gray LLP  
Three Embarcadero Center  
San Francisco, California 94111  
Attention: Ryan A. Murr  
Facsimile No.: (415) 315-6026  
E-mail: ryan.murr@ropesgray.com

if to Roche Finance Ltd, to:

Roche Finance Ltd  
Grenzacherstrasse 124  
4058 Basel  
Switzerland  
Attention: Simon Meier  
Roche Venture Fund  
Facsimile No.: +41 61 68 81396  
E-mail: simon.meier@roche.com  
beat.kraehenmann@roche.com  
peter.trybus@roche.com

with a copy to:

Davis Polk & Wardwell LLP  
450 Lexington Avenue  
New York, New York 10017  
Attention: Marc O. Williams  
Facsimile No.: (212) 701-5800  
E-mail: marc.williams@davispolk.com

Any Notice shall be deemed received on the date of receipt by the recipient thereof if received prior to 5:00 p.m. in the place of receipt and such day is a Business Day in the place of receipt. Otherwise, such Notice shall be deemed not to have been received until the next succeeding Business Day in the place of receipt. Any Notice sent by facsimile transmission also shall be confirmed by certified or registered mail, return receipt requested, posted within one Business Day after the date of the sending of such facsimile transmission, or by personal delivery, whether courier or otherwise, made within two Business Days after the date of such facsimile transmission.

Any Person that becomes a Shareholder after the date hereof shall provide its address, fax number and email address to the Company.

Section 4.04. *Waiver; Amendment; Termination.* No provision of this Agreement may be waived except by an instrument in writing executed by the party against whom the waiver is to be effective. No provision of this Agreement may be amended or otherwise modified except by an instrument in writing executed by the Company and the holders of at least a majority of the Registrable Securities held by the parties hereto at the time of such proposed amendment or modification, *provided* that no such amendment or modification shall adversely affect the economic interests of any holder of Registrable Securities hereunder disproportionately to other holders of Registrable Securities without the written consent of such holder.

Section 4.05. *Governing Law.* This Agreement shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to the conflicts of laws rules of such state.

Section 4.06. *Jurisdiction.* The parties hereby agree that any suit, action or proceeding seeking to enforce any provision of, or based on any matter arising out of or in connection with, this Agreement or the transactions contemplated hereby shall be brought in any state or federal court in The City of Wilmington, Delaware so long as one of such courts shall have subject matter jurisdiction over such suit, action or proceeding, and that any cause of action arising out of this Agreement shall be deemed to have arisen from a transaction of business in the State of Delaware, and each of the parties hereby irrevocably consents to the jurisdiction of such courts (and of the appropriate appellate courts therefrom) in any such suit, action or proceeding and irrevocably waives, to the fullest extent permitted by law, any objection that it may now or hereafter have to the laying of the venue of any such suit, action or proceeding in any such court or that any such suit, action or proceeding which is brought in any such court has been brought in an inconvenient form. Process in any such suit, action or proceeding may be served on any party anywhere in the world, whether within or without the jurisdiction of any such court. Without limiting the foregoing, each party agrees that service of process on such party as provided in Section 4.03 shall be deemed effective service of process on such party.

Section 4.07. *WAIVER OF JURY TRIAL.* EACH OF THE PARTIES HERETO HEREBY IRREVOCABLY WAIVES ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.

Section 4.08. *Specific Enforcement.* Each party hereto acknowledges that the remedies at law of the other parties for a breach or threatened breach of this Agreement would be inadequate and, in recognition of this fact, any party to this Agreement, without posting any bond or furnishing other security, and in addition to all other remedies that may be available, shall be entitled to obtain equitable relief in the form of specific performance, a temporary restraining order, a temporary or permanent injunction or any other equitable remedy that may then be available.

Section 4.09. *Counterparts; Effectiveness.* This Agreement may be executed (including by facsimile or other electronic image scan transmission) with counterpart signature pages or in any number of counterparts, each of which shall be deemed to be an original, and all of which shall, taken together, be considered one and the same agreement, it being understood that each party need not sign the same counterpart. This Agreement shall become effective when each party hereto shall have executed and delivered this Agreement. Until and unless each party has executed and delivered this Agreement, this Agreement shall have no effect and no party shall have any right or obligation hereunder (whether by virtue of any other oral or written agreement or other communication).

Section 4.10. *Entire Agreement.* Except as specifically provided in this Agreement, this Agreement constitutes the entire agreement and understanding among the parties hereto and supersedes all prior and contemporaneous agreements and understandings, both oral and written, among the parties hereto with respect to the subject matter hereof.

Section 4.11. *Severability.* If any term, provision, covenant or restriction of this Agreement is held by a court of competent jurisdiction or other authority to be invalid, void or unenforceable, the remainder of the terms, provisions, covenants and restrictions of this Agreement shall remain in full force and effect and shall in no way be affected, impaired or invalidated so long as the economic or legal substance of the transactions contemplated hereby is not affected in any manner materially adverse to any party. Upon such a determination, the parties shall negotiate in good faith to modify this Agreement so as to effect the original intent of the parties as closely as possible in an acceptable manner so that the transactions contemplated hereby be consummated as originally contemplated to the fullest extent possible.

Section 4.12. *Independent Nature of Shareholders' Obligations and Rights.* The obligations of each Shareholder hereunder are several and not joint with the obligations of any other Shareholder hereunder, and no Shareholder shall be responsible in any way for the performance of the obligations of any other Shareholder hereunder. Nothing contained herein or in any other agreement or document delivered at any closing, and no action taken by any Shareholder pursuant hereto or thereto, shall be deemed to constitute the Shareholders as a partnership, an association, a joint venture or any other kind of entity, or create a presumption that the Shareholders are in any way acting in concert with respect to such obligations or the transactions contemplated by this Agreement. Each Shareholder shall be entitled to protect and enforce its rights, including the rights arising out of this Agreement, and it shall not be necessary for any other Shareholder to be joined as an additional party in any proceeding for such purpose.

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*[Signature pages follow]*

IN WITNESS WHEREOF, the parties hereto have duly executed this Agreement or have caused this Agreement to be duly executed by their respective authorized officers as of the day and year first above written.

ARROWHEAD RESEARCH CORPORATION

By: /s/ Christopher Anzalone

Name: Christopher Anzalone

Title: Chief Executive Officer

ROCHE FINANCE LTD

By: /s/ Beat Kraehenmann

Name: Beat Kraehenmann

Title: Head Legal M&A Group Structure & Finance

By: /s/ Andreas Knierzinger

Name: Andreas Knierzinger

JOINDER TO REGISTRATION RIGHTS AGREEMENT

This Joinder Agreement (this "**Joinder Agreement**") is made as of the date written below by the undersigned (the "**Joining Party**") in accordance with the Registration Rights Agreement dated as of September 30, 2011 (as the same may be amended from time to time, the "**Registration Rights Agreement**"), among Arrowhead Research Corporation and Roche Finance Ltd. Capitalized terms used, but not defined, herein shall have the meaning ascribed to such terms in the Registration Rights Agreement.

The Joining Party hereby acknowledges, agrees and confirms that, by its execution of this Joinder Agreement, the Joining Party shall be deemed to be a party to the Registration Rights Agreement as of the date hereof as a "**Permitted Transferee**" of a Shareholder thereto, and shall have all of the rights and obligations of a "**Shareholder**" and a "**Permitted Transferee**" thereunder as if it had executed the Registration Rights Agreement. The Joining Party hereby ratifies, as of the date hereof, and agrees to be bound by, all of the terms, provisions and conditions contained in the Registration Rights Agreement (including, without limitation, Section 4.01 thereof).

IN WITNESS WHEREOF, the undersigned has executed this Joinder Agreement as of the date written below.

Date: \_\_\_\_\_.

[NAME OF JOINING PARTY]

By: \_\_\_\_\_

Name:

Title:

Address for Notices:

[Address]

[Fax number]

[Email address]

**ARROWHEAD RESEARCH CORPORATION**  
A Delaware Corporation

THIS CERTIFIES THAT **Share Owner Name** is the record holder of **Shares Written Out (XX)** shares of Series A Preferred Stock of Arrowhead Research Corporation (the "Corporation") transferable only on the books of the Corporation by the holder, in person, or by duly authorized attorney, upon surrender of this certificate properly endorsed or assigned.

This Certificate and the shares represented hereby are issued and shall be held subject to all the provisions of the Certificate of Incorporation and the Bylaws of the Corporation and any amendments thereto, to all of which the holder of this Certificate, by acceptance hereof, assents.

A statement of all the rights, preferences, privileges and restrictions granted to or imposed upon the respective classes and/or series of shares of stock of the corporation and upon the holders thereof as established by the Certificate of Incorporation may be obtained by any stockholder upon request and without charge, at the principal office of the Corporation.

The shares of Series A Preferred Stock are convertible into Common Stock at the times and on the terms set forth in the Certificate of Incorporation of the Corporation.

IN WITNESS WHEREOF, the Corporation has caused this Certificate to be signed by its duly authorized officers this \_\_ day of \_\_\_\_\_, 2011.

\_\_\_\_\_  
[Name]  
Secretary

\_\_\_\_\_  
[Name]  
President

FOR VALUE RECEIVED \_\_\_\_\_ HEREBY SELLS, ASSIGNS AND TRANSFERS UNTO \_\_\_\_\_  
\_\_\_\_\_  
SHARES REPRESENTED BY THE WITHIN CERTIFICATE AND DOES HEREBY IRREVOCABLY CONSTITUTE AND  
APPOINT \_\_\_\_\_ ATTORNEY TO TRANSFER THE SAID SHARES ON THE SHARE REGISTER OF THE WITHIN  
NAMED CORPORATION WITH FULL POWER OF SUBSTITUTION IN THE PREMISES.

DATED \_\_\_\_\_, \_\_\_\_\_

\_\_\_\_\_  
(signature)

NOTICE: THE SIGNATURE ON THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME AS WRITTEN UPON THE FACE OF THIS  
CERTIFICATE, IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT, OR ANY CHANGE WHATEVER.

**THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933 OR ANY APPLICABLE STATE SECURITIES  
LAWS. THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED OR HYPOTHECATED IN THE ABSENCE OF A REGISTRATION  
STATEMENT IN EFFECT WITH RESPECT TO THE SECURITIES UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS OR AN  
OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED OR UNLESS SOLD  
PURSUANT TO RULE 144 OR RULE 144A OF SUCH ACT.**

**THE SHARES EVIDENCED HEREBY ARE SUBJECT TO THE TERMS AND CONDITIONS OF A SERIES A PREFERRED SUBSCRIPTION  
AGREEMENT (A COPY OF WHICH MAY BE OBTAINED FROM THE COMPANY UPON WRITTEN REQUEST), AND BY ACCEPTING ANY  
INTEREST IN SUCH SHARES THE PERSON ACCEPTING SUCH INTEREST SHALL BE DEEMED TO AGREE TO AND SHALL BECOME  
BOUND BY ALL THE PROVISIONS AND RESTRICTIONS OF SAID SERIES A PREFERRED SUBSCRIPTION AGREEMENT, INCLUDING  
SUCH CONVERSION RESTRICTIONS CONTAINED THEREIN.**

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT WERE OMITTED AND REPLACED WITH “[\*\*]”. A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECRETARY OF THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO AN APPLICATION REQUESTING CONFIDENTIAL TREATMENT UNDER RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934.

### **NON-EXCLUSIVE LICENSE AGREEMENT**

This Non-Exclusive License Agreement (this “Agreement”), made and entered into as of October 21, 2011 (the “Effective Date”), is by and between, on the one hand, F. Hoffmann-La Roche Ltd, a corporation organized under the laws of Switzerland, with an office and place of business at Grenzacherstrasse 124, 4070 Basel, Switzerland (“Roche Basel”) and Hoffmann-La Roche Inc., a corporation organized under the laws of the State of New Jersey, with an office and place of business at 340 Kingsland Street, Nutley, New Jersey 07110, U.S.A. (“Roche Nutley”; Roche Basel and Roche Nutley together referred to as “Roche”), and, on the other hand, Arrowhead Research Corporation, a corporation organized under the laws of the State of Delaware, having a primary business address at 225 South Lake Avenue, 3<sup>rd</sup> Floor, Pasadena, California 91101 (“Arrowhead”) (collectively, the “Parties”, or each separately, a “Party”).

WHEREAS, Arrowhead and Roche are concurrently entering into a business transaction pursuant to a stock and asset purchase agreement dated as of the date hereof and in connection with such transaction each of Roche and Arrowhead desire to obtain a non-exclusive license under certain patent rights belonging to the other Party; and

WHEREAS, the Parties are willing to grant such licenses under the terms and conditions set forth herein.

NOW, THEREFORE, for and in consideration of the mutual covenants and agreements contained herein, the Parties hereto, intending to be legally bound, do hereby agree as follows:

### **ARTICLE 1 – DEFINITIONS**

As used in this Agreement, the following terms, when used with initial capital letters, shall have the following respective meanings, the singular shall include the plural and vice-versa:

1.1 “**Affiliate**” shall mean any individual or entity directly or indirectly controlling, controlled by or under common control with a Party to this Agreement. For the purposes of this Agreement, the direct or indirect ownership of fifty percent (50%) or more

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of the outstanding voting securities of an entity, or the right to receive fifty percent (50%) or more of the profits or earnings of an entity shall be deemed to constitute control. Such other relationship as in fact results in actual control over the management, business and affairs of an entity shall also be deemed to constitute control. Notwithstanding the above, Chugai Pharmaceutical Co. Ltd., 1-1 Nihonbashi-Muromachi 2-chome, Chuo-ku, Tokyo, 103-8324, Tokyo, 104-8301, Japan ("Chugai"), shall not be deemed an Affiliate of Roche, unless Roche opts for the inclusion of Chugai by giving written notice to Arrowhead.

1.2 "**Arrowhead Field**" shall mean researching, developing, and/or commercializing products related to RNA interference.

1.3 "**Arrowhead Patent Rights**" shall mean the patents and patent applications listed in attached Schedule A and any patents or patent applications in the Territory claiming priority thereto, including all substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protections certificates or any like filing thereof, and provisional applications of any such patents and patent applications and any international equivalent of the foregoing.

1.4 "**Arrowhead Licensed Product**" shall mean any invention claimed in the Roche Patent Rights that is within the Arrowhead Field.

1.5 "**Roche Field**" shall mean all fields excluding the Arrowhead Field.

1.6 "**Roche Patent Rights**" shall mean the patents and patent applications listed in attached Schedule B and any patents or patent applications in the Territory claiming priority thereto, including all substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protections certificates or any like filing thereof, and provisional applications of any such patents and patent applications and any international equivalent of the foregoing.

1.7 "**Roche Licensed Product**" shall mean any invention claimed in the Arrowhead Patent Rights that is within the Roche Field.

1.8 "**Territory**" means the entire world.

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## ARTICLE 2 – LICENSE GRANT

### 2.1 License Grant.

(a) Arrowhead hereby grants to Roche and its Affiliates an irrevocable, fully paid up, royalty-free, non-exclusive license, including the right to sublicense, under the Arrowhead Patent Rights to make or have made, use, sell, offer for sale and import and otherwise exploit, Roche Licensed Product in the Territory. Should this Agreement or the rights granted to Roche hereunder terminate for any reason, Arrowhead shall be obligated to acknowledge and assume any sublicense granted by Roche to a Roche sublicensee on the same terms and conditions as if Arrowhead were Roche.

(b) Roche hereby grants to Arrowhead and its Affiliates an irrevocable, fully paid up, royalty-free, non-exclusive license, including the right to sublicense, under the Roche Patent Rights to make or have made, use, sell, offer for sale and import and otherwise exploit, Arrowhead Licensed Product in the Territory. Should this Agreement or the rights granted to Arrowhead hereunder terminate for any reason, Roche shall be obligated to acknowledge and assume any sublicense granted by Arrowhead to an Arrowhead sublicensee on the same terms and conditions as if Roche were Arrowhead.

2.2 Limitations. Any rights not expressly granted to a Party in Section 2.1 shall be retained by the Party owning the patent rights.

### 2.3 Caveats.

(a) Arrowhead shall have no obligation to file, prosecute or maintain any patent or patent application within the Arrowhead Patent Rights. Subject to Section 7.1, if Arrowhead assigns any patent or patent application within the Arrowhead Patent Rights, then Arrowhead shall ensure that the assignee agrees in writing to be bound by the terms and conditions of this Agreement including Section 2.1(a).

(b) Roche shall have no obligation to file, prosecute or maintain any patent or patent application within the Roche Patent Rights. Subject to Section 7.1, if Roche assigns any patent or patent application within the Roche Patent Rights, then Roche shall ensure that the assignee agrees in writing to be bound by the terms and conditions of this Agreement including Section 2.1(b).

(c) If Arrowhead were to identify a patent or patent application that (i) was on file with a patent office as of the Effective Date, (ii) claims an invention within the Arrowhead Field, and (iii) reasonably could have been considered for inclusion as a Roche Patent Right as of the Effective Date, then, upon written notice from Arrowhead, Roche shall within thirty (30) days after Roche receives such notice either (x) make such patent or patent application part of the Roche Patent Rights as of the Effective Date, or (y) notify Arrowhead that it reasonably objects the inclusion of such patent or patent application in the Roche Patent Rights, specifying in reasonable detail (without the need to disclose Roche confidential information) the basis for Roche's conclusion, in which case such patent or patent application shall not be part of the Roche Patent Rights.

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2.4 Bankruptcy. All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for the purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of rights to “Intellectual property” as defined under Section 101 of the U.S. Bankruptcy Code.

### ARTICLE 3 – WARRANTIES AND REPRESENTATIONS

3.1 Warranties. Each Party hereby represents, warrants and covenants to the other Party as follows:

(a) it is a corporation or entity duly organized and validly existing under the laws of the state or other jurisdiction of its incorporation or formation;

(b) it has the corporate power and authority to execute and deliver this Agreement and to perform its obligations hereunder;

(c) it has the full right and authority to grant the rights as set forth in this Agreement;

(d) this Agreement has been duly authorized, executed and delivered and constitutes such Party’s legal, valid and binding obligations, enforceable against it in accordance with its terms, subject as to enforcement, to bankruptcy, insolvency, reorganization and other laws of general applicability relating to or affecting creditors’ rights and to the availability of particular remedies under general equity principles; and

(e) this Agreement does not conflict with such Party’s duties and obligations under any other agreement to which such Party is bound.

3.2 Covenants. Each Party hereby covenants that after the Effective Date it will not enter into any oral or written agreement or arrangement that would be inconsistent with its obligations and the rights granted under this Agreement and shall comply with all applicable laws and regulations relating to its activities under this Agreement.

3.3 DISCLAIMER. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING ANY EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO THE LICENSES GRANTED IN THIS AGREEMENT. FURTHERMORE, NOTHING IN THIS AGREEMENT SHALL BE CONSTRUED AS A WARRANTY THAT ANY PATENT IS VALID OR ENFORCEABLE OR A PARTY’S USE OF THE PATENTS LICENSED UNDER THIS AGREEMENT WILL NOT INFRINGE ANY PATENT RIGHTS OR OTHER INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.

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## ARTICLE 4 – PUBLICITY

Neither Party shall make any public statement with respect to this Agreement, beyond acknowledging its existence if asked, nor shall either of the Parties disclose to any third party the terms of this Agreement without the prior written consent of the other Party, except as required by law or regulation or where the content of such statement is already public knowledge as of the date of such statement due to no fault of the disclosing Party.

## ARTICLE 5 – INDEMNIFICATION

### 5.1 Indemnification.

(a) Roche shall indemnify, defend and hold harmless Arrowhead and its Affiliates, and each of its and their respective employees, officers, directors and agents from and against any and all liabilities, claims, demands, expenses (including, without limitation, reasonable fees and expenses for attorneys and other professionals), losses or causes of action asserted by a third party (each, a “Liability” and collectively “Liabilities”) arising out of or in connection with: (i) the breach by Roche or its Affiliates of any material representation, warranty, covenant or other provision of this Agreement, or (ii) the use of the Arrowhead Patent Rights by Roche or its Affiliates.

(b) Arrowhead shall indemnify, defend and hold harmless Roche and its Affiliates, and each of its and their respective employees, officers, directors and agents from and against any and all Liabilities arising out of or in connection with (i) the breach by Arrowhead or its Affiliates of any material representation, warranty, covenant or other provision of this Agreement, or (ii) the use of the Roche Patent Rights by Arrowhead or its Affiliates.

5.2 Procedure. The indemnified Party shall promptly notify the indemnifying Party in writing of any claim, complaint, suit, proceeding, cause of action or other potential Liability for which it intends to claim such indemnification (for purposes of this Section, each a “Claim”), and the indemnifying Party shall have sole control of the defense and/or settlement thereof; provided that the indemnified Party shall have the right to participate, at its own expense, with counsel of its own choosing in the defense and/or settlement of such Claim. The indemnification under this Article 5 shall not apply to amounts paid with respect to settlement of any Claim if such settlement is effected without the prior written consent of the indemnified Party, which consent will not be unreasonably withheld, delayed, or conditioned. The failure to deliver written notice to the indemnifying Party within a reasonable period of time after the commencement of any such Claim, if prejudicial to its ability to defend such action, shall relieve indemnifying Party of any liability to indemnified Party under this Article for that specific Claim, but the omission to

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so deliver written notice to indemnifying Party shall not relieve indemnifying Party of any other liability to indemnified Party. Without limiting the foregoing, indemnified Party shall keep indemnifying Party fully informed of the progress of any Claim for which it intends to claim indemnification under this Article 5. Indemnifying Party shall not be responsible for any costs or expenses incurred by indemnified Party without indemnifying Party's prior written consent, which consent will not be unreasonably withheld. Without indemnified Party's prior written consent (such consent not to be unreasonably withheld, delayed, or conditioned), indemnifying Party may not settle a Claim if such settlement would impose any monetary obligation on indemnified Party, require indemnified Party to submit to an injunction, limit indemnified Party's material rights under this Agreement, or affect any intellectual property rights of indemnified Party.

5.3 Insurance. Each Party shall maintain, through purchase or self-insurance, adequate insurance, including products liability coverage and comprehensive general liability insurance, adequate to cover its obligations under this Agreement and which are consistent with normal business practices of prudent companies similarly situated.

#### ARTICLE 6 – TERM AND TERMINATION

6.1 Term. This Agreement shall be effective as of the Effective Date and shall continue in effect until the expiration of the last to expire patent within the Arrowhead Licensed Patent Rights and the Roche Licensed Patent Rights, unless terminated earlier under this Article.

6.2 Termination for Breach or Bankruptcy. This Agreement may be terminated by written notice at any time:

(a) by either Party, if the other Party is in breach of its material obligations hereunder and has not cured such breach within ninety (90) days after written notice requesting cure of the breach with reasonable detail of the particulars of the alleged breach; or

(b) by either Party upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party, or in the event a receiver or custodian is appointed for such other Party's business, or if a substantial portion of such other Party's business is subject to attachment or similar process; provided, however, that in the case of any involuntary bankruptcy proceeding such right to terminate shall only become effective if the proceeding is not dismissed within sixty (60) days after the filing thereof.

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### 6.3 Termination for Patent Challenge.

(a) Arrowhead shall have the right to terminate this Agreement with respect to a given patent within the Arrowhead Licensed Patent Rights upon delivery of thirty (30) days written notice to Roche, if Roche, or its Affiliates or sublicensees, challenges or knowingly supports a challenge to the validity of such patent in any country of the Territory and does not withdraw such challenge or support to such challenge within such notice period.

(b) Roche shall have the right to terminate this Agreement with respect to a given patent within the Roche Licensed Patent Rights upon delivery of thirty (30) days written notice to Arrowhead, if Arrowhead, or its Affiliates or sublicensees, challenges or knowingly supports a challenge to the validity of such patent in any country of the Territory and does not withdraw such challenge or support to such challenge within such notice period.

6.4 Survival. Articles 1, 4, 5, and 7 and Sections 2(a)(i), 2(b)(i) shall survive the expiration and any termination of this Agreement. Except as provided for in this Article 6m all other provisions of the expiration or termination of this Agreement.

## ARTICLE 7 – MISCELLANEOUS

7.1 Assignment. This Agreement and the rights and obligations hereunder may not be assigned, delegated, sold, transferred, (except as expressly permitted hereunder) or otherwise disposed of, by operation of law or otherwise, to any third party without the prior written consent of the other Party, which consent shall not be unreasonably withheld. Any attempted assignment, delegation, sale, transfer, sublicense or other disposition, by operation of law or otherwise, of this Agreement or of any rights or obligations hereunder contrary to this Section 7.1 shall be a material breach of this Agreement by the attempting Party, and shall be void and without force or effect; provided, however, either Party may, without such consent, assign this Agreement and its rights and obligations hereunder, in whole or in part, to an Affiliate or in connection with the transfer or sale of all or substantially all of its assets related to the Field, or in the event of its merger or consolidation or change in control or similar transaction. This Agreement shall be binding upon, and inure to the benefit of each Party, its Affiliates, and its permitted successors and assigns. Each Party shall be responsible for the compliance by its Affiliates with the terms and conditions of this Agreement.

7.2 Governing Law. This Agreement shall be governed, interpreted and construed in accordance with the laws of the State of Delaware, U.S.A., without giving effect to conflict of law principles.

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7.3 Waiver. Any delay or failure in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights to the future enforcement of such rights under this Agreement, nor operate to bar the exercise or enforcement thereof at any time or times thereafter, excepting only as to an express written and signed waiver as to a particular matter for a particular period of time.

7.4 Independent Relationship. Nothing in this Agreement shall be deemed to create an employment, agency, joint venture or partnership relationship between the Parties hereto or any of their respective Affiliates, agents or employees, or any other legal arrangement that would impose liability upon one Party for the act or failure to act of the other Party. Neither Party shall have any power to enter into any contracts or commitments or to incur any liabilities in the name of, or on behalf of, the other Party, or to bind the other Party in any respect whatsoever.

7.5 Entire Agreement; Amendment. This Agreement sets forth the complete, final and exclusive agreement between the Parties with respect to the subject matter hereof and supersedes and terminates all prior and contemporaneous agreements and understandings between the Parties, whether oral or in writing. No subsequent alteration, amendment, change, waiver or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized representative of each Party. Each Party in deciding to execute this Agreement has not relied on any understanding, agreement, representation or promise by the other Party which is not explicitly set forth herein.

7.6 Notices. Any notice required or permitted to be given or sent under this Agreement shall be hand delivered or sent by express delivery service or certified or registered mail, postage prepaid, or by facsimile transmission (with written confirmation copy by registered first-class mail) to the Parties at the addresses and facsimile numbers indicated below.

If to Arrowhead to:                    Arrowhead Research Corporation  
225 South Lake Avenue, 3<sup>rd</sup> Floor  
Parsadena, California 91101  
Telephone No.: + 1 626 304-3400  
Attn: Christopher Anzalone, Ph.D.  
Facsimile No.: +1 626 204-3401

with copy to:                            Fanelli Haag PLLC  
1909 K Street, N.W., Suite 1120  
Washington, D.C. 20006  
Attn: Thomas Haag, Ph.D., Esq.  
Facsimile No.: +1 202 706-7920

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and

Ropes & Gray, LLP  
3 Embarcadero Center  
San Francisco, California 94111  
Attn: Ryan A. Murr, Esq.  
Facsimile No.: +1 415 315-6026

If to Roche to:

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4070 Basel  
Switzerland  
Attn: Legal Department  
Facsimile No.: +41 61 688 13 96

and

Hoffmann-La Roche Inc.  
340 Kingsland Street  
Nutley, New Jersey 07110 U.S.A.  
Attn. Corporate Secretary  
Facsimile No.: +1 973 235-3500

with copies to:

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4070 Basel  
Switzerland  
Attn: Guido Kaiser

and

Hoffmann-La Roche Inc.  
340 Kingsland Street  
Nutley, New Jersey 07110 U.S.A.  
Attn. Petra Sansom

Any such notice shall be deemed to have been received on the date actually received. Either Party may change its address or its facsimile number by giving the other Party written notice, delivered in accordance with this Section 7.6.

7.7 Force Majeure. Failure of any Party to perform its obligations under this Agreement (except the obligation to make payments when properly due) shall not subject such Party to any liability to the other Party if such failure is due to any cause beyond the reasonable control of such non-performing Party ("Force Majeure"). Causes of non-performance constituting Force Majeure shall include, without limitation, acts of God, fire, explosion, flood, drought, war, riot, sabotage, embargo, strikes or other labor trouble, failure in whole or in part of suppliers to deliver on schedule materials, equipment

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or machinery, interruption of or delay in to transportation, a national health emergency or compliance with any order or regulation of any government entity acting with color of right. The Party affected shall promptly notify the other Party of the condition constituting Force Majeure as defined herein and shall exert reasonable efforts to eliminate, cure and overcome any such causes and to resume performance of its obligation with all possible speed; provided, however, that nothing contained herein shall require any Party to settle on terms unsatisfactory to such Party any strike, lock-out or other labor difficulty, any investigation or proceeding by any public authority, or any litigation by any third party. If a condition constituting Force Majeure as defined herein exists for more than ninety (90) consecutive days, the Parties shall meet to negotiate a mutually satisfactory resolution to the problem, if practicable.

7.8 Severability. If any provision of this Agreement is declared illegal, invalid or unenforceable by a court having competent jurisdiction, it is mutually agreed that this Agreement shall endure except for the part declared illegal, invalid or unenforceable by order of such court; provided, however, that in the event that the terms and conditions of this Agreement are materially altered, the Parties will, in good faith, renegotiate the terms and conditions of this Agreement to reasonably substitute such illegal, invalid or unenforceable provisions in light of the intent of this Agreement.

7.9 Counterparts. This Agreement shall become binding when any one or more counterparts hereof, individually or taken together, shall bear the signatures of each of the Parties hereto. This Agreement may be executed in any number of counterparts, each of which shall be an original as against either Party whose signature appears thereon, but all of which taken together shall constitute but one and the same instrument.

7.10 Captions. The captions of this Agreement are solely for the convenience of reference and shall not affect its interpretation.

7.11 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement including, without limitation, any filings with any antitrust agency which may be required.

7.12 Third-Party Beneficiaries. This Agreement is not intended to confer any rights or remedies hereunder upon any person or entity that is not a Party to this Agreement.

[SIGNATURE PAGE FOLLOWS]

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IN WITNESS WHEREOF, the Parties intending to be legally bound have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

**ARROWHEAD**

By: /s/ Christopher Anzalone  
Name: Christopher Anzalone  
Title: Chief Executive Officer

**HOFFMANN-LA ROCHE INC.**

By: /s/ Guido Kaiser  
Name: Guido Kaiser  
Title: Legal Representative

By: /s/ Peter Trybus  
Name: Peter Trybus  
Title: Legal Representative

**F. HOFFMANN-LA ROCHE LTD**

By: /s/ Guido Kaiser  
Name: Guido Kaiser  
Title: Legal Representative

By: /s/ Peter Trybus  
Name: Peter Trybus  
Title: Legal Representative

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**SCHEDULE A**

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**SCHEDULE B**

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CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT WERE OMITTED AND REPLACED WITH “[\*\*]”. A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECRETARY OF THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO AN APPLICATION REQUESTING CONFIDENTIAL TREATMENT UNDER RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934.

## LICENSE AND COLLABORATION AGREEMENT

This LICENSE AND COLLABORATION AGREEMENT (this “Agreement”), is entered into as of July 8, 2007 (the “Execution Date”), by and among F. Hoffmann-La Roche Ltd, a Swiss corporation (“Roche Basel”), having a place of business at Grenzacherstrasse 124, CH-4070 Basel, Switzerland, and Hoffmann-La Roche Inc., a New Jersey corporation (“Roche Nutley”), having a place of business at 340 Kingsland Street, Nutley, New Jersey 07110, U.S.A. (Roche Basel and Roche Nutley, collectively, “Licensee”), and Alnylam Pharmaceuticals, Inc., a Delaware corporation, having a place of business at 300 Third Street, 3rd Floor, Cambridge, Massachusetts 02142, U.S.A. (“Alnylam”), and, solely for the purposes set forth in Section 9.15 of this Agreement, Alnylam Europe AG, a German stock corporation, with a registered office in Kulmbach, Germany (“Alnylam Europe AG”).

### INTRODUCTION

1. Licensee is engaged in the business of Discovering, Developing, Commercializing and Manufacturing therapeutic products (each as defined below).
2. Alnylam has developed, acquired and licensed technology useful for the Discovery, Development, Manufacture, characterization and use of therapeutic products that function through the mechanism of RNA interference (“RNAi”).
3. Alnylam desires to grant licenses to such technology to Licensee, and the Parties desire to collaborate on certain research and development activities, in each case upon the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the respective representations, warranties, covenants and agreements contained herein, and for other valuable consideration, the receipt and adequacy of which are hereby acknowledged, Alnylam and Licensee agree as follows:

### ARTICLE I

#### DEFINITIONS

**1.1 Definitions.** For the purpose of this Agreement, the following terms, whether used in singular or plural form, shall have the respective meanings set forth below:

“Accounting Period” shall have the meaning set forth in Section 5.8.

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“Additional Field” shall mean the treatment or prophylaxis of all Indications in any Supplemental Therapeutic Area, where such treatment or prophylaxis comprises an RNAi Compound complementary to, and functional in mediating the RNAi of, a Target known or believed to be primarily implicated in such Supplemental Therapeutic Area.

“Affiliate” shall mean any Person who directly or indirectly controls or is controlled by or is under common control with another Person. For purposes of this definition, “control” or “controlled” shall mean ownership directly or through one or more Affiliates, of fifty percent (50%) or more of the shares of stock entitled to vote for the election of directors, in the case of a corporation, or fifty percent (50%) or more of the equity interest in the case of any other type of legal entity, status as a general partner in any partnership, or any other arrangement whereby a Party controls or has the right to control the Board of Directors or equivalent governing body of a corporation or other entity, or the ability to direct the management or policies of a corporation or other entity. The Parties acknowledge that in the case of certain entities organized under the laws of certain countries outside of the United States, the maximum percentage ownership permitted by law for a foreign investor may be less than fifty percent (50%), and that in such case such lower percentage shall be substituted in the preceding sentence, provided that such foreign investor has the power to direct the management and policies of such entity. For purposes of this Agreement, [\*\*], each shall not be deemed an “Affiliate” of Licensee; provided, however, that if Licensee were to assume day-to-day control of either [\*\*], then Licensee shall have the right, at its sole option, to designate [\*\*], as applicable, to be an Affiliate. For purposes of Sections 6.1, 6.2, 9.8, 9.12 (the second sentence only), and 9.14, Alnylam’s Affiliates shall not include [\*\*], any Affiliates of [\*\*] (other than Alnylam and Persons “controlled” by Alnylam on the Execution Date) or any Person that becomes an Affiliate of Alnylam as a result of a [\*\*].

“Agreement” shall have the meaning set forth in the Preamble, and shall include, for the avoidance of doubt, all Exhibits and Schedules attached hereto.

“Alnylam Change of Control” shall be deemed to occur upon the closing of (a) a merger, reorganization or consolidation involving Alnylam in which its shareholders immediately prior to such transaction would hold less than fifty percent (50%) of the securities or other ownership or voting interests representing the equity of the surviving entity immediately after such merger, reorganization or consolidation, or (b) a sale to a Third Party of all or substantially all of Alnylam’s assets or business relating to this Agreement.

“Alnylam Third Party Obligations” shall mean (a) Alnylam’s obligations to, and the rights of, Pre-Existing Alliance Parties and Listed Counterparties with respect to the Licensed Intellectual Property under Pre-Existing Alliance Agreements and Listed Alnylam Third Party Agreements, respectively, and (b) Alnylam Europe AG’s obligations to, and the rights of, Max Planck with respect to certain Architecture and Chemistry Patent Rights under the Max Planck European License Agreement; including without limitation Listed Alnylam Third Party Payment obligations.

“Annual Net Sales” shall mean, with respect to a Licensed Product, the Net Sales of such Licensed Product during a calendar year.

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“Architecture and Chemistry Intellectual Property” shall mean Architecture and Chemistry Know-How and Architecture and Chemistry Patent Rights.

“Architecture and Chemistry Know-How” shall mean Know-How Controlled by Alnylam as of the Effective Date that relates to (a) the general structure, architecture, or design of double-stranded oligonucleotide molecules which engage RNAi mechanisms in a cell; (b) chemical modifications of double-stranded oligonucleotides (including any modification to the base, sugar or internucleoside linkage, nucleotide mimetics, and any end modifications) which do not abolish the RNAi activity of the double-stranded oligonucleotides in (a); (c) manufacturing techniques for the double-stranded oligonucleotide molecules or chemical modifications of (a) and (b); or (d) all uses or applications of double-stranded oligonucleotide molecules or chemical modifications in (a) or (b); but excluding (i) Know-How to the extent specifically related to Blocked Targets, and (ii) Delivery Know-How.

“Architecture and Chemistry Patent Rights” shall mean the Patent Rights listed on Schedule C Controlled by Alnylam or, solely in the case of Patent Rights licensed under the Max Planck European License Agreement, by Alnylam Europe AG, each as of the Effective Date, together with any future Patent Rights that claim priority to or common priority with any of the aforementioned Patent Rights, that Cover (a) the general structure, architecture, or design of double-stranded oligonucleotide molecules which engage RNAi mechanisms in a cell; (b) chemical modifications of double-stranded oligonucleotides (including any modification to the base, sugar or internucleoside linkage, nucleotide mimetics, and any end modifications) which do not abolish the RNAi activity of the double-stranded oligonucleotides in (a); (c) manufacturing techniques for the double-stranded oligonucleotide molecules or chemical modifications of (a) and (b); or (d) all uses or applications of double-stranded oligonucleotide molecules or chemical modifications in (a) or (b); but excluding (i) Patent Rights which specifically relate to Blocked Targets, and (ii) Delivery Patent Rights. Notwithstanding anything in this Agreement to the contrary, should it be reasonably determined after the Effective Date that (x) any omitted Patent Rights which Alnylam Controlled as of the Effective Date disclose any Valid Claims that Cover any of clause (a) through (d) above, but excluding any Patent Rights which specifically relate to Blocked Targets and Patent Rights licensed under the [\*\*] Agreement (except as set forth in Section 2.3(b)(ii)), or (y) in the course of prosecution of any Valid Claims under any of the Patent Rights listed on Schedule C, any such Valid Claim either no longer Covers any of clause (a) through (d) above or specifically relates to Blocked Targets, Schedule C shall be amended to reflect the inclusion or deletion, as the case may be, of such Patent Right, to the extent that it does not conflict with the terms of any Listed Alnylam Third Party Agreement or Pre-Existing Alliance Agreement to do so. For the avoidance of doubt, any Patent Rights which are subsequently included on Schedule C pursuant to clause (x) above shall be deemed “Architecture and Chemistry Patent Rights” for all purposes hereunder.

“Blocked Target” shall mean any Target that is subject to a contractual obligation of a Pre-Existing Alliance Agreement that would be breached by the inclusion of such Target as a Designated Target under this Agreement.

“Blocked Target List” shall mean a list of Blocked Targets maintained by the Gatekeeper, as such list may be updated from time to time.

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

“Business Day” shall mean a day on which banking institutions in Boston, Massachusetts are open for business.

“[\*\*] Agreement” shall have the meaning set forth in Section 2.3(b)(ii).

“Collaboration Target” shall have the meaning set forth in Section 4.1.

“Combination Product” shall mean a Licensed Product combined with any other clinically active therapeutic or prophylactic ingredient, mechanism or device.

“Commercialization” or “Commercialize” shall mean any and all activities directed to marketing, promoting, detailing, distributing, importing, having imported, exporting, having exported, selling or offering to sell, or seeking to obtain reimbursement for, a product, whether before or after Regulatory Approval for such product has been obtained.

“Common Stock Purchase Agreement” shall mean the Common Stock Purchase Agreement entered into by Licensee and Alnylam on the Execution Date.

“Confidential Information” shall mean the terms of this Agreement and all Know-How or other information, including proprietary information and materials (whether or not patentable) regarding a Party’s technology, products, business information or objectives, that is treated as confidential by the disclosing Party in the regular course of business or is otherwise designated as confidential by the disclosing Party. For the avoidance of doubt, the identity of any Designated Targets, Submitted Targets and Blocked Targets shall be deemed the Confidential Information of both Parties.

“Control” or “Controlled” shall mean, with respect to any intellectual property right or other intangible property, the possession by a Party (whether by ownership or license) (other than a license granted pursuant to this Agreement), or “control” (as defined in the definition of “Affiliate” above) over an Affiliate having possession (by ownership or license), of the ability to grant access to, or a license or sublicense of, such rights or property as contemplated under this Agreement.

“Cover”, “Covered” or “Covering” shall mean, with respect to a Patent Right, that, in the absence of a license granted to a Person under a Valid Claim included in such Patent Right, the practice by such Person of an invention claimed in such Patent Right would infringe such Valid Claim (or, in the case of a Patent Right that is a patent application, would infringe a Valid Claim in such patent application if it were to issue as a patent).

“Delivery Intellectual Property” shall mean Delivery Know-How and Delivery Patent Rights.

“Delivery Know-How” shall mean Know-How Controlled by Alnylam as of the Effective Date that relates to (a) delivery technologies which may be necessary or useful for delivery of double-stranded oligonucleotide molecules; or (b) manufacturing techniques for the delivery technologies of (a); but excluding Know-How to the extent specifically related to Blocked Targets.

“Delivery Patent Rights” shall mean Patent Rights listed on Schedule C Controlled by Alnylam as of the Effective Date (or, solely with respect to the Patent Rights covered by any option under Section 2.3(b)(ii) below, as of the effective date of Licensee’s exercise of such option), together with any future Patent Rights that claim priority to or common priority with any of the aforementioned Patent Rights, that Cover (a) delivery technologies necessary or useful for delivery of double-stranded oligonucleotide molecules; or (b) manufacturing techniques for the delivery technologies of (a); but excluding Patent Rights which relate specifically to Blocked Targets. Notwithstanding anything in this Agreement to the contrary, should it be reasonably determined after the Effective Date that (x) any omitted Patent Rights which Alnylam Controlled as of the Effective Date disclose any Valid Claims that Cover any of clause (a) through (b) above, but excluding any Patent Rights which specifically relate to Blocked Targets and Patent Rights licensed under the [\*\*] Agreement (except as set forth in Section 2.3(b)(ii)), or (y) in the course of prosecution of any Valid Claims under any of the Patent Rights listed on Schedule C, any such Valid Claim either no longer Covers any of clause (a) through (b) above or specifically relates to Blocked Targets, Schedule C shall be amended to reflect the inclusion or deletion, as the case may be, of such Patent Right, to the extent that it does not conflict with the terms of any Listed Alnylam Third Party Agreement or Pre-Existing Alliance Agreement to do so. For the avoidance of doubt, any Patent Rights which are subsequently included on Schedule C pursuant to clause (x) above shall be deemed “Delivery Patent Rights” for all purposes hereunder.

“Designated Target” shall mean (a) at any time during the Novartis Exclusivity Term, any Target which is (i) selected by Licensee pursuant to Section 2.4(a) of this Agreement which is not a Blocked Target, (ii) submitted to Novartis pursuant to Licensee’s exercise of the Designated Target Option pursuant to Section 2.6 of this Agreement, and (iii) rejected or waived by Novartis, as evidenced by Alnylam’s written notice to Licensee pursuant to Section 2.6 of this Agreement; and (b) at any time following the end of the Novartis Exclusivity Term, any Target selected by Licensee pursuant to Section 2.4(a) of this Agreement which is not a Blocked Target. For the avoidance of doubt, (x) if Licensee selects any Target prior to the end of the Novartis Exclusivity Term for submission to Novartis, but such Target is not submitted to Novartis until after the end of the Novartis Exclusivity Term, or (y) if Licensee selects any Target prior to the end of the Novartis Exclusivity Term for submission to Novartis and such Target is submitted to Novartis prior to the end of the Novartis Exclusivity Term, but the time period during which Novartis is obligated to reply does not end until after the end of the Novartis Exclusivity Term, then such Target shall not be deemed a “Designated Target” hereunder until such Target has been rejected or waived by Novartis pursuant to the terms of the Novartis Agreement.

“Designated Target Option” shall have the meaning set forth in Section 2.6.

“[\*\*]” shall have the meaning set forth in Section 5.5.

“Develop” or “Development” shall mean any and all preclinical and clinical drug development activities, including test method development and stability testing, toxicology, animal efficacy studies, formulation, quality assurance/quality control development, statistical analysis, clinical studies, clinical trials and testing, regulatory affairs, product approval and registration, chemical development and Manufacturing development, packaging development and Manufacturing and development documentation efforts in support of development activities anywhere in the world.

“Discover” or “Discovery” shall mean any and all research or discovery activities.

“Discovery Collaboration” shall mean collaboration between the Parties regarding the Discovery and/or Development of potential RNAi Compounds directed to a Designated Target [\*\*], pursuant to the terms of Article IV.

“Discovery Collaboration Opportunity” shall have the meaning set forth in Section 4.1.

“Effective Date” shall mean the latest of (a) HSR Clearance Date, (b) if no filing is to be made pursuant to the HSR Act, the Execution Date, and (c) the Closing Date as defined in the Share Purchase Agreement (such date being referred to as the “Scheduled Date”), it being understood that the Closing Date of the Share Purchase Agreement and the Effective Date of this Agreement shall occur simultaneously; provided, however, that if between the Execution Date and the Scheduled Date there occurs an event or series of events that result in a material adverse impact upon the Licensed Patent Rights, taken as a whole, (including, for example, the termination of any of the Listed Alnylam Third Party Agreements, or Alnylam’s receipt of written notice of termination from a party to a Listed Alnylam Third Party Agreement (i) that has not been cured prior to the Scheduled Date, or (ii) cannot be cured within the applicable cure period under the Listed Alnylam Third Party Agreement), then Licensee shall have the unilateral right to cause this Agreement not to become effective resulting in no Effective Date; provided, further, that, notwithstanding anything in the parenthetical above to the contrary, if between the Execution Date and the Scheduled Date, Alnylam receives a written notice of termination from a party to a Listed Alnylam Third Party Agreement that results in a material adverse impact upon the Licensed Patent Rights, taken as a whole, and such notice of termination can be cured within the applicable cure period under such Listed Alnylam Third Party Agreement, but such cure period ends after the Scheduled Date, then Licensee shall have the unilateral right (x) to delay the effectiveness of this Agreement until Alnylam has effected the cure, at which time the Effective Date shall be deemed to have occurred, or (y) if the applicable cure period has lapsed without a cure having been effected, to cause this Agreement not to become effective following the end of such cure period, resulting in no Effective Date.

“Execution Date” shall have the meaning set forth in the preamble to this Agreement.

“FDA” shall mean the United States Food and Drug Administration or any successor agency thereto.

“Field” shall mean the Primary Field and, subject to the exercise by Licensee of a Field Option with respect to any Additional Field(s) pursuant to Section 2.5, any such Additional Field(s).

“Field Definition Panel” shall have the meaning set forth in Section 2.5(a)(iv).

“Field Extension Opportunity” shall have the meaning set forth in Section 2.5(b)(i).

“Field Option” shall have the meaning set forth in Section 2.5(b)(ii).

“Field Option Fee” shall have the meaning set forth in Section 5.6.

“First Commercial Sale” shall mean the first sale of a Licensed Product by or on behalf of Licensee or any of its Affiliates or Licensee Partners to a Third Party in a country following Regulatory Approval of such Licensed Product in that country or, if no such Regulatory Approval or similar marketing approval is required, the date upon which such Licensed Product is first commercially launched in such country.

“Future Technology Patent Rights” shall mean Patent Rights Controlled by a Party after the Effective Date that Cover (a) delivery technologies which may be necessary or useful for delivery of double-stranded oligonucleotide molecules; or (b) manufacturing techniques for the delivery technologies of (a); but excluding (i) Patent Rights which specifically relate to Blocked Targets, and (ii) Licensed Patent Rights.

“Gatekeeper” shall have the meaning set forth in Section 2.4(b).

“GLP Toxicology Study” shall mean a toxicology study that is conducted in compliance with GLP and is required to meet the requirements for filing an IND.

“HSR Act” shall mean the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended (15 U.S.C. Sec. 18a), and the rules and regulations promulgated thereunder.

“HSR Clearance Date” shall mean the earlier of (a) the second Business Day after the date on which the United States Federal Trade Commission shall notify Licensee and Alnylam of early termination of the applicable waiting period under the HSR Act, or (b) the second Business Day after the date on which the applicable waiting period under the HSR Act expires.

“IND” shall mean an application submitted to a Regulatory Authority to initiate human clinical trials, including (a) an Investigational New Drug application or any successor application or procedure filed with the FDA, or any foreign equivalent thereof, and (b) all supplements and amendments that may be filed with respect to the foregoing.

“IND-Enabling Studies” shall mean pharmacokinetic and toxicology studies required to meet the requirements for filing an IND, including without limitation any GLP Toxicology Study.

“Indication” shall mean any disease or condition, or sign or symptom of a disease or condition.

“Initial Discovery Collaboration Opportunity Period” shall have the meaning set forth in Section 4.1.

“Joint Future Technology Committee” shall have the meaning set forth in Section 3.2.

“Know-How” shall mean any information, inventions, trade secrets or technology, whether or not proprietary or patentable and whether stored or transmitted in oral, documentary, electronic or other form. Know-How shall include ideas, concepts, formulas, methods, procedures, designs, compositions, plans, documents, data, discoveries, developments, techniques, protocols, specifications, works of authorship, biological materials, and any information relating to research and development plans, experiments, results, compounds,

therapeutic leads, candidates and products, clinical and preclinical data, clinical trial results, and Manufacturing information and plans (but excluding any scientific, regulatory, pre-clinical or clinical information or data regarding specific Indications and any marketing, financial, commercial, personnel and other business information and plans).

“Kulmbach Facility” shall have the meaning set forth in Section 3.1(a).

“Law” shall mean any law, statute, rule, regulation, ordinance or other pronouncement having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, domestic or foreign.

“Licensed Collaboration Product” shall mean any Licensed Product directed to a Designated Target for which the Parties have entered into a Discovery Collaboration pursuant to Article IV.

“Licensed Intellectual Property” shall mean the Licensed Know-How and Licensed Patent Rights.

“Licensed Know-How” shall mean (a) the Architecture and Chemistry Know-How, and (b) the Delivery Know-How.

“Licensed Patent Rights” shall mean (a) the Architecture and Chemistry Patent Rights, and (b) the Delivery Patent Rights.

“Licensed Product” shall mean any RNAi Product (a) whose manufacture, use or sale would, but for the licenses granted pursuant to this Agreement, infringe one or more Valid Claims of the Licensed Patent Rights, or (b) which embodies Licensed Know-How. All references to Licensed Product in this Agreement shall be deemed to include Combination Product, to the extent applicable.

“Licensee Partner” shall mean any Third Party to which a sublicense is granted by Licensee in accordance with Section 2.1(b), including without limitation Third Party distributor whose obligations to Licensee or its Affiliates include responsibility for sales, marketing and/or distribution efforts in a country on behalf of Licensee or its Affiliates, excluding wholesale distributors who purchase Licensed Products from Licensee or its Affiliates in an arm’s length transaction and who have no other obligation to Licensee or its Affiliates.

“Listed Alnylam Third Party Agreement” shall mean an agreement listed on Schedule D-1.

“Listed Alnylam Third Party Payment” shall have the meaning set forth in Section 5.4(d).

“Listed Counterparties” shall mean the Third Party counterparties to Listed Alnylam Third Party Agreements and their respective successors in interest.

“Major Market Countries” shall have the meaning set forth in Section 2.1(b).

“Manufacture” or “Manufacturing” shall mean any and all activities and operations involved in or relating to the manufacturing, quality control testing (including in-process, release and stability testing), releasing or packaging, for pre-clinical, clinical or commercial purposes.

“Max Planck” shall mean Max Planck Innovation GmbH (formerly Garching Innovation GmbH).

“Max Planck European License Agreement” shall mean Co-Exclusive License Agreement between Max Planck and Alnylam Europe AG (formerly Ribopharma AG), dated July 30, 2003, as amended by the Requirement Amendment effective June 15, 2005.

“NDA” shall mean an application submitted to a Regulatory Authority for marketing approval of a product, including (a) a New Drug Application, Product License Application or Biologics License Application filed with FDA or any successor applications or procedures, or any foreign equivalent thereof, and (b) all supplements and amendments that may be filed with respect to the foregoing.

“Net Sales” shall mean the amount calculated by subtracting from the amount of Adjusted Gross Sales (as defined below) the following:

(a) With respect to Net Sales in the United States, a lump sum deduction of [\*\*] percent ([\*\*]%) of Adjusted Gross Sales in lieu of those sales-related deductions which are not accounted for by Licensee, its Affiliates and Licensee Partners on a product-by-product basis (e.g. outward freights, postage charges, transportation insurance, packaging materials for dispatch of goods, custom duties, bad debt expense, discounts granted later than at the time of invoicing);

(b) With respect to Net Sales in the Major Market Countries (other than the U.S.) and Canada, a lump sum deduction of [\*\*] percent ([\*\*]%) of Adjusted Gross Sales in lieu of those sales-related deductions which are not accounted for by Licensee, its Affiliates and Licensee Partners on a product-by-product basis (e.g. outward freights, postage charges, transportation insurance, packaging materials for dispatch of goods, custom duties, bad debt expense, discounts granted later than at the time of invoicing); and

(c) With respect to Net Sales in all territories other than those set forth in subsections (a) and (b) above, a lump sum deduction of [\*\*] percent ([\*\*]%) of Adjusted Gross Sales in lieu of those sales-related deductions which are not accounted for by Licensee, its Affiliates and Licensee Partners on a product-by-product basis (e.g. outward freights, postage charges, transportation insurance, packaging materials for dispatch of goods, custom duties, bad debt expense, discounts granted later than at the time of invoicing).

For purposes of this definition of “Net Sales”, “Adjusted Gross Sales” shall mean the amount of gross sales of the Licensed Product invoiced by Licensee, its Affiliates and its Licensee Partners to Third Parties less deductions of returns and return reserves (including allowances actually given for spoiled, damaged, out-dated, rejected, returned Licensed Product sold, withdrawals and recalls), rebates and rebate reserves (to the extent consistently applied by Licensee to its products), price reductions, rebates to managed care organizations or social and

welfare systems, charge backs or reserves for chargebacks, cash sales incentives (but only to the extent it is a sales related deduction which is accounted for within Licensee on a product-by-product basis), cash discounts, government mandated rebates and similar types of rebates (e.g., Pharmaceutical Price Regulation Scheme, Medicaid, each as consistently applied by Licensee to its products), volume (quantity) discounts, taxes (value added or sales taxes, government mandated exceptional taxes and other taxes directly linked to the gross sales amount).

In the case where a Licensed Product is a Combination Product, the Parties shall meet approximately [\*\*] prior to commercial launch of such Combination Product to negotiate in good faith and agree to an appropriate adjustment to Net Sales to reflect the relative significance of the RNAi Compound and the other pharmaceutically active agent(s) contained in the Combination Product. If the Parties are unable to agree upon such adjustment to Net Sales, royalties with respect to a Combination Product in a country shall be equal to the rates set forth in Section 5.4(a), multiplied by a fraction whose numerator is Licensee's published sales price in such country for an equivalent dosage of RNAi Compound contained in a given Combination Product, and whose denominator is Licensee's published sale prices in such country for an equivalent dosage of all active pharmaceutical ingredients contained therein. If the numerator or denominator cannot be determined in the manner set forth above within ninety (90) days following the meeting between the Parties described in the first sentence of this paragraph, then such matter shall be determined by binding arbitration conducted by one (1) arbitrator in accordance with the rules of Judicial Arbitration and Mediation Services, Inc. (JAMS). The arbitration shall be held in the State of Delaware and shall not last for a period longer than six (6) months. In such arbitration, the arbitrator shall be an independent expert in worldwide marketing in the pharmaceutical industry mutually acceptable to the Parties or, if the Parties are unable to agree upon such arbitrator, shall be selected by the President of the JAMS office located in the State of Delaware.

"Novartis" shall mean Novartis Institutes for BioMedical Research, Inc.

"Novartis Agreement" shall mean the Research Collaboration and License Agreement, effective as of October 12, 2005, by and between Alnylam and Novartis, as amended by the Addendum Re: Influenza Program effective as of December 13, 2005, Amendment No. 1 to such Addendum effective as of March 14, 2006, and Amendment No. 2 to such Addendum effective as of May 5, 2006, and as the same may be amended from time to time after the Execution Date in accordance with Section 2.7(c).

"Novartis Exclusivity Term" shall mean the "Exclusivity Term" as defined in the Novartis Agreement.

"[\*\*]" shall have the meaning set forth in Section 2.7(b).

"[\*\*]" shall have the meaning set forth in Section 2.7(b)(ii).

"Option Term" shall mean the period commencing on the Effective Date and ending on the fifth (5th) anniversary thereof.

“Other Transaction Documents” shall mean (a) the Common Stock Purchase Agreement, and (b) the Share Purchase Agreement.

“Party” shall mean Alnylam or Licensee, as the case may be; “Parties” shall mean both Alnylam and Licensee.

“Patent Rights” shall mean all patents (including all reissues, extensions, substitutions, confirmations, re-registrations, re-examinations, invalidations, supplementary protection certificates and patents of addition) and patent applications (including all provisional applications, continuations, continuations-in-part and divisionals), and foreign equivalents of any of the foregoing.

“Person” shall mean any corporation, limited or general partnership, limited liability company, joint venture, trust, unincorporated association, governmental body, authority, bureau or agency, any other entity or body, or an individual.

“Phase I Study” shall mean a human clinical trial in any country that would satisfy the requirements of 21 C.F.R. § 312.21(a), as amended from time to time, and the foreign equivalent thereof.

“Phase II Study” shall mean a human clinical trial, for which the primary endpoints include a determination of dose ranges and/or a preliminary determination of efficacy in patients being studied as described in 21 C.F.R. § 312.21(b), or similar clinical study in a country other than the United States.

“Phase III Study” shall mean a human clinical trial that is prospectively designed to demonstrate statistically whether a product is safe and effective for use in humans in a manner sufficient to obtain regulatory approval to market such product in patients having the disease or condition being studied as described in 21 C.F.R. § 312.21(c), or a similar clinical study in a country other than the United States.

“Pre-Existing Alliance Agreements” shall mean the agreements set forth on Schedule E.

“Pre-Existing Alliance Parties” shall mean the Third Party counterparties to Pre-Existing Alliance Agreements and their respective successors in interest.

“Primary Field” shall mean the treatment or prophylaxis of all Indications in the Primary Therapeutic Areas, where such treatment or prophylaxis comprises an RNAi Compound complementary to, and functional in mediating the RNAi of, a Target known or believed to be primarily implicated in one or more Primary Therapeutic Areas.

“Primary Therapeutic Area” shall mean each of the disease area fields set forth on Schedule A to this Agreement.

“Product Liability Claim” shall mean, with respect to a product, any Third Party claim, suit, action, proceeding, liability or obligation involving any actual or alleged death or bodily injury arising out of or resulting from the use of such product.

“Regulatory Approval” shall mean, with respect to a product in a country, the approval of the applicable Regulatory Authority necessary for the marketing and sale of such product in such country.

“Regulatory Authority” shall mean any federal, national, multinational, state, provincial or local regulatory agency, department, bureau or other governmental entity with authority over the marketing, pricing or sale of a pharmaceutical product in a country, including the FDA.

“Required Third Party Payments” shall mean royalty payments to a Third Party made by Licensee under Third Party agreements (other than Listed Alnylam Third Party Agreements or Pre-Existing Alliance Agreements) to license Patent Rights Covering such Third Party’s technology if, in the absence of such license, the licensed use by Licensee of the Licensed Patent Rights licensed by Alnylam under Section 2.1(a) would infringe such Patent Rights; provided, however, that Required Third Party Payments shall not include any royalties or other amounts payable to obtain access to (a) a specific Target or Targets so that such Target or Targets can be the subject of research and development efforts, or (b) Third Party delivery technologies (other than Delivery Patent Rights) which may be necessary or useful for delivery of double-stranded oligonucleotide molecules, or manufacturing techniques for such delivery technologies.

“RNAi Compound” shall mean any compound that, in vitro or otherwise, functions through the mechanism of RNAi and consists of or encodes double-stranded oligonucleotides, and which double-stranded oligonucleotides optionally may be chemically modified to contain modified nucleotide bases or non-RNA nucleotides, and optionally may be administered in conjunction with a delivery vehicle or vector.

“RNAi Product” shall mean any product that contains one or more RNAi Compounds as an active ingredient.

“Royalty Term” shall mean, separately with respect to each Licensed Product in each country, the period commencing on the First Commercial Sale of such Licensed Product in such country (provided that either (x) such Licensed Product is Covered by a Valid Claim of a Licensed Patent Right in such country at the time of such First Commercial Sale in such country, or (y) the Manufacture of such Licensed Product is Covered by a Valid Claim of a Licensed Patent Right in the country or countries in which such Licensed Product is Manufactured) and concluding on the expiration of the later of (a) the last to expire Licensed Patent Right containing a Valid Claim Covering the Development, Commercialization or Manufacture of such Licensed Product in that country, (b) the last to expire Licensed Patent Right containing a Valid Claim Covering the Manufacture of such Licensed Product in the country or countries in which such Licensed Product was Manufactured, or (c) ten (10) years from the date of First Commercial Sale of such Licensed Product in such country. For the avoidance of doubt, if (x) a Licensed Product is not Covered by a Valid Claim of a Licensed Patent Right in a country at the time of such First Commercial Sale in such country, and (y) the Manufacture of such Licensed Product is not Covered by a Valid Claim of a Licensed Patent Right in the country or countries in which such Licensed Product is Manufactured at the time of First Commercial Sale, but at any time following First Commercial Sale, the Licensed Product, or the Manufacture thereof, is Covered by a Valid Claim of any patent under the Licensed Patent Rights that issues following the time of such First Commercial Sale, then the Royalty Term shall commence with respect to such Licensed Product at the time of such issuance.

“Share Purchase Agreement” shall mean the Share Purchase Agreement entered into by and among Licensee, Licensee’s Affiliate, Alnylam and Alnylam Europe AG on the Execution Date.

“Submitted Target” shall have the meaning set forth in Section 2.6.

“Supplemental Therapeutic Area” shall mean each of the disease area fields set forth on Schedule B to this Agreement.

“Target” shall mean (a) a polypeptide or entity comprising a combination of at least one polypeptide and other macromolecules, that is a site or potential site of therapeutic intervention by a therapeutic agent; or a nucleic acid which is required for expression of such polypeptide; (b) variants of a polypeptide (including any splice variant thereof), cellular entity or nucleic acid described in clause (a); or (c) a defined non-peptide entity, including a microorganism, virus, bacterium or single cell parasite; provided that the entire genome of a virus shall be regarded as a single Target.

“Technology Transfer Period” shall have the meaning set forth in Section 3.1(a).

“Technology Transfer Plan” shall have the meaning set forth in Section 3.1(a).

“Terminated Patent Rights” shall have the meaning set forth in Section 5.4(f).

“Third Party” shall mean any Person other than Alnylam or Licensee and their respective Affiliates.

“Third Party Infringement Claim” shall have the meaning set forth in Section 2.8(a)(i).

“UBC” shall mean the University of British Columbia.

“UBC Sublicense Agreement” shall mean the Sublicense Agreement between Tekmira Pharmaceuticals Corporation (formerly INEX Pharmaceuticals Corporation) and Alnylam Pharmaceuticals, Inc., dated January 8, 2007.

“Valid Claim” shall mean a claim (a) of any issued, unexpired patent that has not been revoked or held unenforceable or invalid by a decision of a court or governmental agency of competent jurisdiction from which no appeal can be taken, or with respect to which an appeal is not taken within the time allowed for appeal, and that has not been disclaimed or admitted to be invalid or unenforceable through reissue, disclaimer or otherwise, or (b) of any patent application that has not been cancelled, withdrawn or abandoned, or been pending for more than [\*\*] from the earliest priority date for such patent application.

ARTICLE II

GRANT OF RIGHTS

INTELLECTUAL PROPERTY MATTERS

2.1 License Grants.

(a) License Grants to Licensee.

(i) Alnylam hereby grants to Licensee and its Affiliates a non-exclusive, worldwide, perpetual, irrevocable, royalty-bearing right and license, subject to the terms and conditions of this Agreement and to Alnylam Third Party Obligations, under the Licensed Intellectual Property to engage in any and all Discovery, Development, Commercialization and Manufacturing activities in the Field (and, to the extent expressly permitted in Section 2.5(a), any Additional Field), including to make, have made, use, offer for sale, sell and import Licensed Products in the Field (and, to the extent expressly permitted in Section 2.5(a), any Additional Field).

(ii) Alnylam Europe AG hereby grants to Licensee and its Affiliates a non-exclusive, worldwide, perpetual, irrevocable, royalty-bearing right and license, subject to the terms and conditions of this Agreement and to Alnylam Third Party Obligations, under Alnylam Europe AG's rights to the Architecture and Chemistry Patent Rights licensed to Alnylam Europe AG pursuant to the terms of the Max Planck European License Agreement, to engage in any and all Discovery, Development, Commercialization and Manufacturing activities in the Field (and, to the extent expressly permitted in Section 2.5(a), any Additional Field), including to make, have made, use, offer for sale, sell and import Licensed Products in the Field (and, to the extent expressly permitted in Section 2.5(a), any Additional Field).

(b) Sublicense Rights. Subject to Alnylam Third Party Obligations, Licensee shall have the right to grant sublicenses within the scope of the licenses granted to it in Section 2.1(a), on a Licensed Product-by-Licensed Product basis, to a Third Party in the Field (and, to the extent expressly permitted in Section 2.5(a), any Additional Field) solely for purposes of Developing and/or Commercializing a Licensed Product which has achieved the appropriate stage of Development (as determined by Licensee using its reasonable business judgment in the management of such Licensed Product within its portfolio of products, but in no event [\*\*] other than to Third Party contractors, including contract research organizations, contract employees, consultants, contract manufacturers and the like in connection with the licensed activities); provided, however, that in no event shall Licensee grant any sublicense of any right granted to Licensee under Section 2.1(a) for the Development and/or Commercialization of any Third Party product unless such product is licensed by Licensee from such Third Party and Licensee and such Third Party are collaborating on the Development and/or Commercialization of such Third Party product. Each such sublicense agreement shall be consistent with the terms and conditions of this Agreement. Licensee shall remain liable to Alnylam and Alnylam Europe AG for each of its sublicensees' failure to comply with all applicable restrictions, limitations and obligations

under the sublicense agreement and this Agreement. No sublicense granted by Licensee hereunder may be assigned, transferred or further sublicensed to any Third Party without the prior written consent of Alnylam or Alnylam Europe AG, as the case may be. Licensee shall provide a redacted copy of such sublicense agreement to Alnylam (such redactions to exclude only the financial terms of such sublicense and other information normally redacted from a document filed with the U.S. Securities and Exchange Commission), (x) if such sublicense impacts upon one or more of the following countries: USA, Germany, France, United Kingdom, Italy, Spain, and Japan (“Major Market Countries”), and (y) upon request by Alnylam, in any country other than those listed under clause (x) above.

**2.2 No Other Rights.** Only the licenses granted to Licensee under Section 2.1(a) hereof shall be of legal force and effect and are limited to the scope expressly granted. Accordingly, except for the rights expressly granted under Section 2.1(a) hereof, no license, right, title or interest of any nature whatsoever is granted hereunder by implication, estoppel, reliance or otherwise, by Alnylam or Alnylam Europe AG to Licensee, and any of Alnylam’s or Alnylam Europe AG’s rights to Licensed Intellectual Property not specifically licensed to Licensee under Section 2.1(a) hereof shall be retained by Alnylam or Alnylam Europe AG, as the case may be. For purposes of clarity, nothing contained in this Agreement shall prevent or restrict Alnylam or Alnylam Europe AG from (a) granting to any Third Party any non-exclusive licenses under Alnylam’s or Alnylam Europe AG’s rights, as the case may be, in any Licensed Intellectual Property, or (b) subject to the provisions of Section 2.5(b)(i), granting to any Third Party any exclusive licenses under Alnylam’s or Alnylam Europe AG’s rights in any Licensed Intellectual Property outside of the then-current Field.

### **2.3 Certain License Limitations.**

#### **(a) Pre-Existing Alliance Agreements.**

(i) The grants by Alnylam and Alnylam Europe AG under Licensed Intellectual Property set forth in Section 2.1(a) are subject to, and are limited to the extent of, the rights that Alnylam has previously granted and is required to grant under Licensed Intellectual Property to Pre-Existing Alliance Parties under the terms of the Pre-Existing Alliance Agreements. As and to the extent that such rights previously granted to Pre-Existing Alliance Parties under Licensed Intellectual Property (whether such rights are previously or subsequently exercised) lapse, terminate or otherwise revert to Alnylam, they shall be automatically included in the non-exclusive rights under Licensed Intellectual Property granted to Licensee in the Field under Section 2.1(a).

(ii) Licensee acknowledges that a Pre-Existing Alliance Party may from time to time request rights under Licensed Intellectual Property with respect to a particular Target that Alnylam is required, pursuant to the terms of a Pre-Existing Alliance Agreement, to grant such rights to such Pre-Existing Alliance Party with respect to such Target.

(b) Contractual Obligations under Listed Alnylam Third Party Agreements.

(i) For the avoidance of doubt, the grants by Alnylam under Licensed Intellectual Property set forth in Section 2.1(a) include, subject to Section 2.3(b)(ii), the sublicense of Licensed Intellectual Property that is not owned by Alnylam or Alnylam Europe AG. Licensee's rights and licenses under such Licensed Intellectual Property are limited to the rights granted by Listed Counterparties to Alnylam under the Listed Alnylam Third Party Agreements and by Max Planck to Alnylam Europe AG under the Max Planck European License Agreement, and Licensee shall comply, and cause its Affiliates and Licensee Partners to comply, with those restrictions and other terms applicable to sublicensees under such agreements, certain of which restrictions and terms are summarized on Schedule D-2. Without limiting the generality of the foregoing, Licensee acknowledges that certain obligations are imposed on sublicensees of certain of the sublicensed Licensed Intellectual Property, and agrees to comply (to the extent access to obligations and requirements have been made available to Licensee in unredacted form), and to require its Affiliates and Licensee Partners to comply, with such obligations and requirements. Notwithstanding the above, at the request of Licensee, which request shall be made within the [\*\*] period prior to First Commercial Sale of the first Licensed Product, Alnylam shall use commercially reasonable efforts to seek to harmonize the accounting and royalty reporting provisions under the Listed Third Party Agreements with the accounting and royalty reporting provisions set forth in this Agreement.

(ii) Notwithstanding anything to the contrary herein, the licenses to Licensed Patent Rights hereunder initially shall not include licenses to Patent Rights licensed by Alnylam or its Affiliates under the Non-Exclusive License Agreement between [\*\*] and Alnylam, dated [\*\*] (the "[\*\*] Agreement"), which Patent Rights Licensee shall have the option, exercisable upon written notice to Alnylam hereunder, to license, on a Licensed Collaboration Product-by-Licensed Collaboration Product basis, upon commencement of a Discovery Collaboration hereunder. Upon such election, (x) the license granted to Licensee under Alnylam's rights to Delivery Patent Rights pursuant to Section 2.1(a) shall include such Patent Rights with respect to the designated Licensed Collaboration Product(s), (y) Schedule C shall be amended to include such Patent Rights, and (z) the [\*\*] Agreement shall be deemed a Listed Alnylam Third Party Agreement and Schedule D-1 and Schedule D-2 shall be amended accordingly.

**2.4 Blocked Targets; Gatekeeper.**

(a) Blocked Targets.

(i) From time to time during the term of this Agreement but no more frequently than [\*\*] (except as set forth in clause (ii) of this Section 2.4(a)), following an affirmative decision by Licensee to initiate a program directed to the Discovery, Development or Commercialization of RNAi Compounds directed to a particular Target, Licensee may inquire of the Gatekeeper in writing whether or not such Target is on the Blocked Target List by virtue of being subject to a then-current exclusive or co-exclusive grant, option, right of first refusal or similar right under a Pre-Existing Alliance Agreement. The Gatekeeper shall, within [\*\*] days following the Gatekeeper's receipt of such complete written request from Licensee, notify Licensee in writing whether or not such Target is on the Blocked Target List; provided, however, that in no event will the Gatekeeper directly or indirectly notify or communicate to any other Alnylam employee or consultant or any Alnylam Affiliate or Third Party the contents or the existence of Licensee's inquiry hereunder without Licensee's prior written consent, which may be withheld at Licensee's sole discretion.

(ii) If Alnylam becomes aware of the removal of any Target from the Blocked Target List, Alnylam shall notify Licensee of such removal (but not the identity of the Target which was removed) and Licensee shall have the right to inquire of the Gatekeeper pursuant to, and in compliance with, clause (i) above whether or not a Target is on the Blocked Target List; provided, however, that the [\*\*] limit set forth in clause (i) above on the frequency of inquiries which may be made of the Gatekeeper shall not apply with respect to an inquiry made under this Section 2.4(a)(ii), nor shall an inquiry made under this Section 2.4(a)(ii) be counted towards such [\*\*] limit.

(iii) Notwithstanding the foregoing, the Parties acknowledge that a Pre-Existing Alliance Party may subsequently request exclusive or co-exclusive rights from Alnylam with respect to a particular Target as described in Section 2.3(a)(ii) and the provisions of Section 2.3(a)(ii) shall control.

(b) Gatekeeper. Subject to the provisions of Section 2.7(b), the inquiries and responses made by one Party to the other in connection with Section 2.4(a) shall be made in writing to the attention of a designated employee of Alnylam mutually agreeable to both Parties (the “Gatekeeper”) who will be bound by confidentiality obligations to both Parties. Each Party agrees to provide the Gatekeeper with full and complete copies of all records and information (including un-redacted copies of the relevant Third Party agreements) that are necessary for the Gatekeeper to render his or her determination.

## 2.5 Additional Fields; Field Option.

### (a) Additional Fields.

(i) Licensee shall initially conduct Discovery, Development, Commercialization and Manufacturing activities directed to Targets only with respect to Indications in the Field. After Licensee’s completion of a Phase II Study with respect to any Licensed Product directed to a specific Target in the Field, Licensee may engage in Discovery, Development, and/or Manufacturing activities directed to such Target for any Indication (each, an “Additional Indication”) in any Additional Field (if such Additional Field has not been the subject of Licensee’s exercise of a Field Option) without having to pay a Field Option Fee; provided, however, that (A) Licensee shall notify Alnylam of its extension of Discovery, Development and/or Manufacturing activities directed to such Target for such Additional Indication in such Additional Field, and (B) Licensee shall pay Alnylam the following amounts (which shall be in addition to any event payments which may be owed under Section 5.3 below and except as provided in clause (ii) below) upon achievement of the following events by Licensee, its Affiliates or Licensee Partners with respect to each such Additional Indication:

<u>Development Event:</u>	Payment for Licensed Products (in [**]):
Initiation of Phase III for each Additional Indication	\$ [**]
Filing of an NDA for each Additional Indication	\$ [**]
Regulatory Approval for each Additional Indication	\$ [**]

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(ii) Notwithstanding the foregoing provisions of clause (i) above, Licensee shall pay Alnylam the following amounts (which shall be in addition to any event payments which may be owed under Section 5.3 below and in lieu of any amounts which may otherwise be owed under clause (i) above) upon achievement of the following events by Licensee, its Affiliates or Licensee Partners solely with respect to a Licensed Product with respect to which Licensee extends its activities for the first time to an Additional Indication in a given Additional Field:

<u>Development Event:</u>	Payment for Licensed Products (in [**]):
Initiation of Phase III for a Licensed Product for the first Additional Indication in a given Additional Field	\$ [**]
Filing of an NDA for a Licensed Product for the first Additional Indication in a given Additional Field	\$ [**]
Regulatory Approval for a Licensed Product for the first Additional Indication in a given Additional Field	\$ [**]

(iii) The amounts paid under subsections (i) and (ii) of this Section 2.5(a) for Additional Indications within a given Additional Field shall be fully creditable against Field Option Fees which may be paid by Licensee pursuant to Section 5.6 for such Additional Field. In no event shall the total event payments made under this provision exceed \$[\*\*] for a given Additional Field.

(iv) For the avoidance of doubt, in no event shall Licensee conduct Discovery, Development, Commercialization and Manufacturing activities directed to any Target in any Additional Field other than as permitted in this Section 2.5. In the event that the Parties are unable to agree on whether or not Licensee's activities fall within or outside the Primary Field or any Additional Field in a manner prohibited by this Agreement, the Parties shall submit such dispute to a panel (the "Field Definition Panel") consisting of three (3) independent experts in clinical development, with each Party having the right to select a single expert and the two (2) selected experts selecting the third expert by mutual agreement. Such third expert shall serve as the chairperson of the Field Definition Panel. The selection of the experts for the Field Definition Panel shall occur within thirty (30) days following the Parties' decision to submit such dispute to such a panel, and the Parties shall consult with such Field Definition Panel for a period not to exceed thirty (30) days from the selection of such experts. The Field Definition Panel shall render a decision with respect to such dispute, based on a majority vote, with each expert having one (1) vote, within ten (10) days following the end of such consultation period, which

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decision shall be binding on the Parties. In the event that the Field Definition Panel determines that Licensee's Discovery, Development, Commercialization or Manufacturing activities are being conducted in any Additional Field in a manner which is prohibited hereunder, Licensee shall, within ten (10) Business Days after such determination by the Field Definition Panel, cease such proscribed activity.

(b) Field Option.

(i) During the Option Term, if Alnylam intends to grant to any Third Party (other than Listed Counterparties or Pre-Existing Alliance Parties, subject to the terms of the applicable Listed Alnylam Third Party Agreements or Pre-Existing Alliance Agreements, as the case may be) an exclusive license to any Additional Field(s) which is not included in the then-current Field, Alnylam shall notify Licensee thereof ("Field Extension Opportunity"). Licensee shall have the right to extend the licenses granted under Section 2.1(a) to include the Additional Field(s) covered by such Field Extension Opportunity by notifying Alnylam in writing of such intent within sixty (60) days after Alnylam's notice and paying the Field Option Fee for each such Additional Field pursuant to Section 5.6. For the avoidance of doubt, Alnylam and Alnylam Europe AG shall have the right to grant to any Third Party any exclusive licenses under Alnylam's or Alnylam Europe AG's rights, as the case may be, in any Licensed Intellectual Property in any Additional Field to which Licensee has not extended its licenses granted under Section 2.1(a) pursuant to Licensee's exercise of the Field Option under this Section 2.5(b).

(ii) From time to time during the Option Term, Licensee shall have the right, upon written notice to Alnylam, to request the extension of the license granted under Section 2.1(a) to include one or more Additional Field(s) ("Field Option") in which Licensee has a good faith intention to seek to Discover, Develop, Commercialize and Manufacture RNAi Compounds or RNAi Products, which right shall be subject to any agreement which Alnylam may have entered into with a Third Party with respect to such Additional Field(s) following Licensee's rejection of, or failure to pay the Field Option Fee for, any Field Extension Opportunity pursuant to clause (i) above. Upon Licensee's payment of the Field Option Fee for each such Additional Field pursuant to Section 5.6, the licenses granted to Licensee under Section 2.1(a) shall include such Additional Field(s).

**2.6 Designated Target Option.** From time to time during the Novartis Exclusivity Term, Licensee shall have the right, upon written notice to Alnylam, to select any Target in the Field which is not a Blocked Target for submission by Alnylam to Novartis pursuant to the terms of the Novartis Agreement (a "Submitted Target"). Alnylam shall promptly provide notice to Novartis of the Submitted Target(s) in accordance with the provisions of the Novartis Agreement, and Licensee shall cooperate with Alnylam in providing any information reasonably requested by Novartis (but not the identity of Licensee or any of Licensee's RNAi Compounds) in order for Novartis to determine whether or not to pursue Discovery, Development and/or Commercialization activities directed to such Submitted Target. If Novartis notifies Alnylam that it wishes (as such term is used in the Novartis Agreement) to pursue Discovery, Development and/or Commercialization activities directed to such Submitted Target, then Alnylam shall so notify Licensee promptly upon Alnylam's receipt of such notification, and such Target shall be deemed a Blocked Target for purposes of this Agreement. If Alnylam receives notice from Novartis that Novartis has no interest in pursuing Discovery, Development and/or

Commercialization activities directed to such Submitted Target, or if Novartis otherwise waives its right to such Submitted Target under the terms of the Novartis Agreement, then Alnylam shall notify Licensee promptly upon Alnylam's receipt of such notification or waiver. In such event, such rejected or waived Submitted Target shall be deemed a "Designated Target" for all purposes under this Agreement, Licensee shall be deemed to have exercised its option with respect to such Submitted Target (each, a "Designated Target Option"), and Licensee shall be free, upon [\*\*] pursuant to Section 5.5, to Discover, Develop, Commercialize or Manufacture RNAi Compounds and RNAi Products directed to such Designated Target in accordance with the terms hereof without further risk of such Target becoming a Blocked Target.

## 2.7 Special Provisions Relating to Novartis.

(a) Compliance with Novartis Agreement. It is the intent of the Parties that this Agreement be construed in a manner which is consistent with and in compliance with the terms of the Novartis Agreement in all respects.

(b) Alnylam Change of Control. In the event that, at any time during the [\*\*], an Alnylam Change of Control occurs in which [\*\*] (other than [\*\*] or any controlled [\*\*]) is the acquiring entity (a "[\*\*]"), it shall be a condition precedent to such [\*\*] that:

(i) Section 2.4(b) of this Agreement shall be amended to provide that the "Gatekeeper" shall not be a designated employee of Alnylam but instead (A) shall be a Third Party who shall have no material relationship (other than as Gatekeeper) with Alnylam, [\*\*], (B) shall be mutually agreeable to both Parties and (C) shall be bound by confidentiality obligations to both Parties, and to the extent that the consent of [\*\*] shall be required for such amendment, such consent shall have been obtained; and

(ii) [\*\*], to the extent required, shall have agreed [\*\*] that the [\*\*] contained therein (i.e., [\*\*] thereof) shall terminate upon such [\*\*] and that [\*\*] as a result of any obligations under the [\*\*] or as a result of any other actions [\*\*] in connection with [\*\*] hereunder after the date of the agreement providing for such [\*\*] or, if there is no [\*\*], after the date of such [\*\*]. Alnylam agrees that the [\*\*] shall include the consent of [\*\*], as applicable, required by clause (i) above and the agreement of [\*\*], as applicable, to the amendment required by clause (ii) above. If, notwithstanding the foregoing, the [\*\*] shall occur without the amendment and consent contemplated by clause (i) above or without the agreement and amendment contemplated by clause (ii) above, then (A) [\*\*] and (B) Alnylam shall pay to Licensee an amount equal to [\*\*]. Each Party agrees that if the [\*\*] shall occur without the amendment and consent contemplated by clause (i) above or without the agreement and amendment contemplated by clause (ii) above, the damages that Licensee and its Affiliates would suffer would be irreparable and difficult to calculate with certainty but in such event the amounts payable by Alnylam pursuant to the immediately preceding sentence shall constitute fair and reasonable amounts and not penalties.

(c) No Adverse Amendments. Alnylam agrees not to enter into any amendment or modification to the [\*\*] which would have an adverse impact on Licensee's rights under this Agreement, without the prior written consent of Licensee. Without limiting the foregoing, the Parties acknowledge and agree that the following amendments/modifications would have an adverse impact on Licensee's rights under this Agreement: [\*\*]; (iv) any amendment that would require Alnylam to provide to [\*\*] any Confidential Information of Licensee; and (v) any provision that is inconsistent with the obligations of Alnylam to Licensee hereunder.

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(d) Specific Performance. The Parties hereto agree that irreparable damage would occur if any provision of this Section 2.7 were not performed in accordance with the terms hereof and that Licensee shall be entitled to an injunction or injunctions to prevent breaches of this Agreement or to enforce specifically the performance of the terms and provisions hereof in any federal court located in the State of Delaware or any Delaware state court, in addition to any other remedy to which they are entitled at law or in equity.

## 2.8 Certain Intellectual Property Matters

### (a) Claimed Infringement.

(i) In the event that a Third Party at any time asserts a claim, or brings an action, suit or proceeding against a Party or any of its Affiliates or, with respect to Licensee, Licensee Partners, claiming infringement of such Third Party's Patent Rights or unauthorized use or misappropriation of such Third Party's Know-How, based upon an assertion or claim arising out of any of the activities taken in respect of the Discovery, Development, Commercialization or Manufacture of Licensed Products, where such claim, action, suit or proceeding and/or the defense thereof involves, or is likely to involve, the validity, scope and/or enforceability of the Licensed Intellectual Property ("Third Party Infringement Claim"), such Party shall promptly notify the other Party in writing of the claim or the commencement of such action, suit or proceeding, enclosing a copy of the claim and all papers served.

(ii) Within thirty (30) days after delivery of the notification required to be delivered under clause (i) above, as between Alnylam and Licensee and subject to Alnylam Third Party Obligations, Alnylam shall, upon written notice thereof to Licensee, assume control of the defense of those aspects of any such Third Party Infringement Claim which involve the validity, scope and/or enforceability of Licensed Intellectual Property (either alone or in combination with any other Patent Rights or Know-How), and Licensee shall, upon written notice thereof to Alnylam, assume control of the defense of any other Third Party Infringement Claim or aspect thereof, as the case may be. Licensee and Alnylam, subject to Alnylam Third Party Obligations, shall keep the other Party advised of the status of such action, suit, proceeding or claim and the defense thereof and shall consider recommendations made by the other Party with respect thereto.

(iii) The Party controlling the action, suit, proceeding, claim or defense under Section 2.8(a) shall not agree to any settlement of such action, suit, proceeding, claim or defense without the prior written consent of the other Party, which shall not be unreasonably withheld, conditioned or delayed; provided, that Alnylam may settle or compromise any action, suit, proceeding, claim or defense relating to Licensed Intellectual Property without the prior written consent of Licensee.

(b) Trademarks. Each Party and its Affiliates shall retain all right, title and interest in and to its and their respective corporate names and logos. Licensee shall not acquire any rights under this Agreement in any trademark, service mark or Internet domain name including the word “Alnylam” or any other trademarks or trade dress of Alnylam or its Affiliates, and Alnylam shall not acquire any rights under this Agreement in any trademark, service mark or Internet domain name including the word “Roche” or any other trademarks or trade dress of Licensee or its Affiliates.

(c) Enforcement of Licensed Intellectual Property. Alnylam shall take reasonable measures to protect and, to the extent Alnylam has such a right, to enforce the Licensed Intellectual Property in the Field, consistent with prudent commercial practices in the biotechnology industry.

(d) Notice of Changes. Within sixty (60) days after each anniversary of the Effective Date, Alnylam shall provide to Licensee an updated Schedule C that reflects any changes to the list of Licensed Patent Rights set forth on Schedule C which have occurred during the prior year.

**2.9 Obligation to Maintain Listed Alnylam Third Party Agreements.** Alnylam shall use commercially reasonable efforts to maintain the Listed Alnylam Third Party Agreements in full force and effect as they relate to the Licensed Patent Rights. If a Listed Alnylam Third Party Agreement provides Alnylam with the opportunity to assume prosecution of any Licensed Patent Right or risk that such right will be abandoned, then Alnylam shall take reasonable measures to prosecute such Licensed Patent Right in the Field, consistent with prudent commercial practices in the biotechnology industry.

### ARTICLE III

#### TECHNOLOGY TRANSFER;

#### JOINT FUTURE TECHNOLOGY COMMITTEE

##### 3.1 Technology Transfer.

###### (a) Initial Technology Transfer.

(i) Within a period of [\*\*] months following the Effective Date (“Technology Transfer Period”), Alnylam shall complete the activities assigned to Alnylam as set forth on the technology transfer plan attached hereto as Schedule F (as it may be amended from time to time by mutual agreement of the Parties, the “Technology Transfer Plan”), at no additional cost to Licensee (subject to subsection 3.1(d) below), to effect the transfer to Licensee (or its designated Affiliate(s)) of Licensed Intellectual Property that is reasonably necessary for the exercise of Licensee’s rights under the licenses granted pursuant to Section 2.1(a) and for the operation of the facility in Kulmbach, Germany which is being transferred to Licensee pursuant to the terms of the Share Purchase Agreement (“Kulmbach Facility”). Alnylam shall make available to Licensee such number of technical personnel as may be set forth in the Technology Transfer Plan to answer any questions or provide instruction as reasonably requested by Licensee concerning the items delivered pursuant to this Section 3.1(a), in connection with Licensee’s Discovery, Development, Commercialization and Manufacture of Licensed Products hereunder and the operation of the Kulmbach Facility.

(ii) During the Technology Transfer Period, Licensee shall conduct, and shall cause Licensee's applicable Affiliate(s) to conduct, the activities assigned to Licensee (and/or its Affiliates) as set forth on the Technology Transfer Plan, at no additional cost to Alnylam, to effect the transfer to Alnylam (or its designated Affiliate(s)) of Know-How which is reasonably necessary to enable Alnylam (or its Affiliate(s)) to transfer the performance of the activities conducted at the Kulmbach Facility prior to the Effective Date to an alternate facility in Cambridge, MA, U.S.A, designated by Alnylam.

(b) Technology Transfer to Alnylam After Technology Transfer Period. Without limiting Licensee's obligations under Section 3.1(a), following the end of the Technology Transfer Period, Licensee shall conduct, and shall cause Licensee's applicable Affiliates to conduct, the activities assigned to Licensee and/or its Affiliates as set forth in the Technology Transfer Plan, at no additional cost to Alnylam, to effect the transfer to Alnylam (or its designated Affiliate(s)) of Know-How associated with, or arising from, the Discovery, Development, Commercialization and/or Manufacturing activities performed by Licensee (and/or its Affiliate(s)) and its or its Affiliates' employees and subcontractors at the Kulmbach Facility on behalf of Alnylam and/or its Affiliates before and/or during the Transition Period (as defined in the Share Purchase Agreement). Licensee shall make available to Alnylam such number of technical personnel as may be set forth in the Technology Transfer Plan to answer any questions or provide instruction as reasonably requested by Alnylam concerning the items delivered pursuant to this Section 3.1(b).

(c) Management of Transition Activities. Each Party shall designate personnel to the Joint Transition Team (as defined in the Share Purchase Agreement) who shall be responsible for coordinating the technology transfer activities under the Technology Transfer Plan. Each Party shall cooperate with the other Party in such other Party's conduct of technology transfer activities under the Technology Transfer Plan.

(d) Additional Services. If Licensee desires that Alnylam continue to provide technology transfer services with respect to Licensed Intellectual Property (i) beyond the scope of the Technology Transfer Plan, or (ii) following the end of the Technology Transfer Period, Alnylam shall, at its discretion and upon mutual agreement of the Parties on the terms of such services (including, as necessary, an amended Technology Transfer Plan), continue to provide such services on terms to be agreed upon by the Parties.

**3.2 Joint Future Technology Committee.** Within thirty (30) days after the Effective Date, the Parties shall establish a "Joint Future Technology Committee", comprised of at least one (1) representative from each of Licensee and Alnylam, to exchange information and facilitate discussions concerning any Future Technology Patent Rights which may arise during the Option Term. Unless otherwise agreed by the Parties, the Joint Future Technology Committee shall remain in effect during the Option Term and shall meet on a bi-annual basis, in a manner and at a location mutually agreed by the Parties (including via telephone). During the Option Term, either Party may notify the other Party of its interest in obtaining a license under such other Party's rights to any Future Technology Patent Rights. Upon such notification and subject to any rights of Third Parties to such Future Technology Patent Rights, the Parties shall negotiate in good faith for a period not to exceed one hundred twenty (120) days the terms of any license to such Future Technology Patent Rights, provided that neither Party shall be obligated to grant any licenses to the other Party. For the avoidance of doubt, the Joint Future Technology Committee shall have no decision-making authority with respect to the acquisition or grant of any licenses under any Future Technology Patent Rights.

## ARTICLE IV

### DISCOVERY COLLABORATION

**4.1 Discovery Collaboration.** Within [\*\*] months following the Effective Date during the Option Term (“Initial Discovery Collaboration Opportunity Period”), Licensee shall propose to Alnylam at least [\*\*] Targets which are not Blocked Targets with respect to which Licensee has an interest in entering into a Discovery Collaboration with Alnylam (“Discovery Collaboration Opportunity”), and shall provide to Alnylam any available information concerning such Targets which Licensee reasonably believes may be material to Alnylam in its evaluation of such Discovery Collaboration Opportunity and the rationale for pursuing an RNAi Compound directed to such Target. If Alnylam has an interest in pursuing any such Discovery Collaboration Opportunity with Licensee with respect to one or more of the proposed Targets (each, a “Collaboration Target”), then Alnylam shall so respond within thirty (30) days of Licensee’s notice. If any such Collaboration Target is not already a Designated Target at the time of Licensee’s proposal of the Discovery Collaboration Opportunity directed to such Collaboration Target, then Licensee shall submit such Collaboration Target(s) to Novartis during the Novartis Exclusivity Term in accordance with Section 2.6 hereof. In the event that Novartis rejects or waives such Collaboration Target and such Collaboration Target becomes a Designated Target hereunder, [\*\*], and the Parties shall negotiate in good faith, for a period not to exceed six (6) months, the terms of a Discovery Collaboration Opportunity directed to such Designated Target in accordance with Section 4.2. If the Parties are unable to negotiate the terms of a Discovery Collaboration Opportunity within such six (6) month period, the Parties shall refer the matter(s) under negotiation to the Chief Executive Officer of Alnylam and the Global Head of Pharma Research of Licensee, for discussion and resolution within a thirty (30) day period. Licensee shall have no obligation to pursue more than [\*\*]; provided, that, the Parties shall enter into at least [\*\*] directed to at least [\*\*] within the Option Term.

**4.2 Minimum Terms.** The terms of any Discovery Collaboration negotiated between the Parties pursuant to Section 4.1 shall include, at a minimum, the following: (a) each Party shall be responsible for the costs of its own employees who perform work under the Discovery Collaboration, (b) Licensee shall pay to Alnylam event payments and royalties with respect to Licensed Collaboration Product(s) which shall be in addition to those which would have been payable by Licensee with respect to such Licensed Collaboration Product(s) had Licensee independently Discovered, Developed, Commercialized and/or Manufactured such Licensed Collaboration Product(s) as Licensed Product(s) outside of any Discovery Collaboration, which shall be commensurate with Alnylam’s contributions to the Discovery Collaboration (taking into account, at a minimum, the Patent Rights referred to in subsection (c) below which shall be licensed to Licensee in connection with such Discovery Collaboration in addition to the Licensed Patent Rights); (c) the grant of licenses under each Party’s rights to Patent Rights and Know-How developed by such Party, its Affiliates and/sublicensees, either individually or jointly with each other, during and in the performance of the Discovery

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Collaboration; (d) the rights and obligations of each Party with respect to prosecution, maintenance and enforcement of the intellectual property rights set forth in the immediately preceding clause (c); and (e) termination rights. Upon finalization of the terms of any Discovery Collaboration pursuant to this Section 4.2, the Parties shall (x) develop a research plan in accordance with which each Party shall perform activities specified under such Discovery Collaboration, and (y) establish a joint steering committee made up of an equal number of representatives from each Party to oversee, review and coordinate the activities of the Parties under such Discovery Collaboration. Notwithstanding the foregoing, if there is an Alnylam Change of Control, then Licensee shall have the right not to (i) begin, or continue, to propose Discovery Collaboration Opportunities pursuant to Section 4.1, (ii) begin, or continue to engage in, any negotiations with Alnylam with respect to any such Discovery Collaboration Opportunity, or (iii) continue with any ongoing Discovery Collaboration.

**ARTICLE V**

**FINANCIAL PROVISIONS**

**5.1 Equity Investment.** As of the Execution Date, the Parties have entered into the Common Stock Purchase Agreement pursuant to which Licensee has agreed to purchase shares of Alnylam’s Common Stock (as defined in the Common Stock Purchase Agreement) for a total consideration of Forty-Two Million Four Hundred Sixty-Two Thousand Five Hundred dollars (\$42,462,500).

**5.2 License Grant Consideration.** In consideration of the rights granted to Licensee under this Agreement as of the Effective Date, Licensee shall pay, or cause to be paid, to Alnylam Two Hundred Seventy-Three Million Five Hundred Five Thousand Five Hundred dollars (\$273,505,500) within ten (10) Business Days following the Effective Date.

**5.3 Event Payments.**

(a) Development Events. In connection with the Discovery and Development of Licensed Products that are Covered by a Valid Claim of Licensed Patent Rights, or the Manufacture of which Licensed Products is Covered by a Valid Claim of a Licensed Patent Right, and directed against a given Target hereunder, Licensee shall pay, or cause to be paid, to Alnylam the following payments upon the achievement of the events set forth below:

<u>Development Event:</u>	Payment for Licensed Products (in [**]):
Initiation of GLP Toxicology Studies	\$ [**]
Initiation of the first Phase I Study	\$ [**]
Initiation of the first Phase II Study	\$ [**]

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

- Initiation of the first Phase III Study for the first Indication
- Initiation of first Phase III Study for a second Indication
- First filing of an NDA in the U.S. for the first Indication
- First filing of an NDA in the EU for the first Indication
- First filing of an NDA in Japan for the first Indication
- First filing of an NDA in the U.S. or EU for a second Indication
- Regulatory Approval in the U.S. for the first Indication
- Regulatory Approval in the EU for the first Indication
- Regulatory Approval in Japan for the first Indication
- Regulatory Approval in the U.S. or EU for a second Indication

(b) Sales Events. With respect to each Target, Licensee shall pay, or cause to be paid, to Alnylam the following payments based on Net Sales of Licensed Products that are Covered by a Valid Claim of Licensed Patent Rights, or the Manufacture of which Licensed Products is Covered by a Valid Claim of a Licensed Patent Right, upon the achievement of the events set forth below:

<u>Development Event:</u>	Payment for Licensed Products (in [**]):
Aggregate worldwide Annual Net Sales of all Licensed Product(s) directed to such Target reach or exceed \$[**] (≥\$[**])	\$ [**]
Aggregate worldwide Annual Net Sales of all Licensed Product(s) directed to such Target reach or exceed \$[**] (≥\$[**])	\$ [**]

(c) Achievement of Events. Licensee shall notify Alnylam within thirty (30) days following achievement or occurrence of an event under Section 2.5(a) and this Section 5.3, and Alnylam shall deliver to Licensee an invoice for such event. Each event payment under Section 2.5(a) and this Section 5.3 shall be deemed earned as of the achievement or occurrence of the related event and shall be paid by Licensee within sixty (60) days following such achievement or occurrence.

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(d) **Event Payments Payable Only Once.** Each event payment under this Section 5.3 shall be payable only once in relation to each Target. By way of example, in the event that Licensee elects not to proceed with the Development or Commercialization of a Licensed Product directed to a Target for which one or more of the foregoing event payments have been paid, Licensee shall not be required to make any event payments previously paid under this Section 5.3 with respect to any back-up Licensed Product(s) directed at such Target. In addition, if, with respect to the Development of a Licensed Product, Licensee satisfies an event under this Section 5.3, Licensee shall pay to Alnylam all earlier event payments under this Section 5.3 that have not otherwise been paid with respect to such Target (regardless of whether such earlier events have been satisfied).

**5.4 Royalties.**

(a) **Royalty Rate.** Subject to subsections (b)-(g) of this Section 5.4, during each relevant Royalty Term, Licensee shall pay, or cause to be paid, to Alnylam the following royalties on Annual Net Sales of each Licensed Product:

Annual Net Sales of a Licensed Product (on a Target-by-Target basis) during the applicable calendar year:	Royalty Rate Applicable to Such Annual Net Sales of Such Licensed Product:
Less than or equal to \$[**]:	[**]%
Greater than \$[**], but less than or equal to \$[**]:	[**]%
Greater than \$[**], but less than or equal to \$[**]:	[**]%
Greater than \$[**], but less than or equal to \$[**]:	[**]%
Greater than \$[**], but less than or equal to \$[**]:	[**]%
Greater than \$[**], but less than or equal to \$[**]:	[**]%
Greater than \$[**]:	[**]%

By way of example, if Annual Net Sales of a Licensed Product are [\*\*] dollars and no deductions were to apply under Sections 5.4(b)-(g), then the royalty payable by Licensee to Alnylam would be as follows:

\$[**] million at [**]%	= \$[**] million
\$[**] million at [**]%	= \$[**] million
\$[**] million at [**]%	= \$[**] million
\$[**] million at [**]%	= \$[**] million
\$[**] million at [**]%	= \$[**] million
\$[**] million at [**]%	= \$[**] million
<b>Total Royalty Due</b>	<b>= \$[**] million</b>

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

For the avoidance of doubt, Licensee's obligation to pay royalties under this Section 5.4 is imposed only once with respect to the same unit of Licensed Product, including by reason of such Licensed Product being Covered by more than one Valid Claim of Licensed Patent Rights.

(b) Expiration of Patent Coverage. If no Valid Claim of Licensed Patent Rights Covers a Licensed Product in a given country, and the Manufacture of such Licensed Product is not Covered by a Valid Claim of Licensed Patent Rights in the country of manufacture, then the royalty rate applicable to such Licensed Product in such country shall be reduced to [\*\*] percent ([\*\*]%) of the rate set forth in Section 5.4(a) above for any remaining portion of the Royalty Term which applies to such Licensed Product in such country.

(c) Royalty Stacking. Licensee shall be entitled to deduct, from the royalty payments payable by Licensee under Section 5.4(a) for a reporting period, [\*\*] percent ([\*\*]%) of Required Third Party Payments paid by Licensee with respect to Licensed Products during the applicable reporting period; provided that in no event shall a deduction under this subsection (c) reduce any royalty payment payable by Licensee under Section 5.4(a) by more than [\*\*] percent ([\*\*]%).

(d) Payments in Respect of Alnylam In-Licenses. In addition to any royalty set forth in Section 5.4(a) during the Royalty Term, Licensee shall reimburse Alnylam for [\*\*] percent ([\*\*]%) of all royalty payments payable (each such payment, a "Listed Alnylam Third Party Payment," collectively, the "Listed Alnylam Third Party Payments") to Third Parties pursuant to Listed Alnylam Third Party Agreements in respect of Net Sales of Licensed Products; provided that in no event shall the royalty payments payable by Licensee hereunder in respect of such Listed Alnylam Third Party Payments in any reporting period exceed in the aggregate [\*\*] percent ([\*\*]%) of Net Sales of Licensed Products for such reporting period. The Parties shall cooperate to coordinate such reimbursements by Licensee in a manner that ensures all amounts payable by Licensee hereunder pursuant to Listed Alnylam Third Party Agreements are paid in a timely manner and otherwise in compliance with such Listed Alnylam Third Party Agreements. Licensee shall have the right to have an independent public accountant reasonably acceptable to Alnylam audit Alnylam's books and records solely for purposes of verifying such Listed Alnylam Third Party Payments, which right shall be exercisable [\*\*] per year solely with respect to records covering up to the [\*\*] calendar years prior to audit notification, upon reasonable advance notice and during Alnylam's business hours, subject to the confidentiality provisions of Article VI hereof. Audit results and findings shall be shared by Licensee and Alnylam. If the audit reveals an overpayment by Licensee under this Section 5.4(d), the amount of such overpayment shall be credited towards any future reimbursement amounts payable by Licensee under this Section 5.4(d), subject to Section 5.4(e). If the audit reveals an underpayment by Licensee, Licensee shall make up such underpayment within thirty (30) days. The failure of Licensee to request verification of any Listed Alnylam Third Party Payments hereunder within the [\*\*] calendar year period set forth above shall be deemed acceptance of the calculation of such Listed Alnylam Third Party Payments.

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

(e) Deductions. Notwithstanding anything in this Agreement to the contrary, in no event shall total deductions under Sections 5.4(b) and 5.4(c) reduce any quarterly royalty payment by Licensee in respect of Net Sales of a given Licensed Product to less than [\*\*]. Alnylam shall have the burden of demonstrating the amount of royalty payments payable to Third Parties pursuant to Listed Alnylam Third Party Agreements. Any deductions allowable under Sections 5.4(b) and 5.4(c) which cannot be used against any quarterly royalty payment due to the foregoing limitation may be carried forward and used against future quarterly royalty payments, subject to the limitation set forth above.

(f) Loss of Listed Alnylam Third Party Agreements. If Alnylam ceases to be a licensee of Licensed Patent Rights (as such, "Terminated Patent Rights") under any Listed Alnylam Third Party Agreement (other than as a result of any action or omission by Licensee) and Licensee directly licenses such Terminated Patent Rights from that Third Party, then Licensee may deduct the full amount of any [\*\*] paid to such Third Party for such license(s) that is attributable to Licensed Products Covered by such Terminated Patent Rights from any royalties otherwise payable to Alnylam hereunder; provided, that prior to Licensee entering into any such license of such Terminated Patent Rights from such Third Party, Licensee shall notify Alnylam of its intent to do so and shall provide to Alnylam an opportunity to explain its rationale for ceasing to license such Terminated Patent Rights and Licensee shall consider in good faith such rationale. If Licensee does not agree with Alnylam's rationale, then, at Licensee's request, Alnylam shall use commercially reasonable efforts to reinstate the license for such Terminated Patent Rights within a sixty (60) day period; provided, however, that Alnylam shall not be required to continue to undertake such efforts if the Third Party requires payments which are incremental to what would otherwise be owed to such Third Party had such Terminated Patent Rights not been terminated, or the imposition of additional terms and conditions. If Alnylam is unable to reinstate the license, then Licensee may obtain a direct license for such Terminated Patent Rights from such Third Party; provided, that in no event shall total deductions under this Section 5.4(f) reduce any quarterly royalty payment by Licensee in respect of Net Sales of a given Licensed Product to less than [\*\*].

(g) Duration of Royalty Payments; First Commercial Sale. The royalties payable under Section 5.4(a) shall be paid on a country-by-country basis on each Licensed Product commencing upon the occurrence of the First Commercial Sale of such Licensed Product until the expiration of the applicable Royalty Term for such Licensed Product. Licensee shall notify Alnylam of the occurrence of First Commercial Sale of each Licensed Product within fifteen (15) days of its occurrence.

**5.5 [\*\*]**. If Licensee exercises the [\*\*] with respect to a Target pursuant to Section 2.6, and such Target is deemed a [\*\*] hereunder, then Licensee shall pay Alnylam a fee (the [\*\*]) of (a) [\*\*] Dollars (\$[\*\*]) for each of the first [\*\*] Targets to be [\*\*] pursuant to Licensee's exercise of the [\*\*] in any calendar year, (b) following the [\*\*] of the [\*\*] Target as a [\*\*] hereunder in any calendar year, [\*\*] Dollars (\$[\*\*]) for each of the next [\*\*] Targets [\*\*] pursuant to Licensee's exercise of the [\*\*] hereunder; (c) following the [\*\*] of the [\*\*] Target as a [\*\*] hereunder in any calendar year, [\*\*] Dollars (\$[\*\*]) for each of the next [\*\*] Targets [\*\*]

pursuant to Licensee's exercise of the [\*\*] hereunder; and (d) following the [\*\*] of the [\*\*] Target as a [\*\*] hereunder in any calendar year, [\*\*] Dollars (\$[\*\*]) for each Target [\*\*] pursuant to Licensee's exercise of the [\*\*] hereunder. Licensee shall pay such [\*\*] within thirty (30) days following receipt of Alnylam's invoice with respect to the [\*\*] hereunder.

**5.6 Field Option Fee.** If Licensee exercises the Field Option with respect to any Additional Field pursuant to Section 2.5, Licensee shall pay Alnylam a fee (the "Field Option Fee") of [\*\*] Dollars (\$[\*\*]) for each such Additional Field. Licensee shall pay such Field Option Fee within thirty (30) days following receipt of Alnylam's invoice therefor.

**5.7 Most Favored Licensee.** During the Option Term, in the event that Alnylam grants to a Third Party (other than Listed Counterparties or Pre-Existing Alliance Parties) rights including a non-exclusive, worldwide license under the Licensed Intellectual Property to Discover, Develop, Manufacture and Commercialize Licensed Products, at a royalty rate (taking into account any obligations to make payments to Third Parties) that is more favorable to such Third Party than the royalty rate (taking into account any obligations to make payments to Third Parties) set forth in Section 5.4 of this Agreement with respect to such license grant, then the royalty rate (taking into account any obligations to make payments to Third Parties) under this Agreement shall be reduced or adjusted to such more favorable Third Party royalty rate on a prospective basis from the effective date of Alnylam's agreement with such Third Party with respect to such rights. Notwithstanding the foregoing, if (a) the Third Party has paid cash or other consideration, or there are other elements of the overall transaction with such Third Party, that justifies a royalty rate below the rate set forth in Section 5.4 of this Agreement, or (b) the license has been granted as part of a joint venture or similar collaborative agreement, then such royalty rate reduction shall not apply. For the avoidance of doubt, such more favorable royalty rate shall have no retroactive effect and shall not apply to any royalties which have been paid by Licensee or which have otherwise accrued under this Agreement prior to the date of such reduction or adjustment.

**5.8 Payment of Royalty.** Licensee shall calculate royalties on Net Sales quarterly as of March 31, June 30, September 30 and December 31 (each being the last day of an "Accounting Period") and shall pay royalties on Net Sales within the sixty (60) days after the end of each Accounting Period in which such Net Sales occur. Royalties on Net Sales shall be paid by Licensee in U.S. Dollars.

**5.9 Currency Computation.** Whenever calculating royalties requires conversion from any currency, Licensee shall make such conversion as follows: When calculating the Adjusted Gross Sales for countries other than the United States of America, Licensee shall convert the amount of such sales in currencies other than Swiss Francs into Swiss Francs using for internal foreign currency translation Licensee's then current standard practices actually used on a consistent basis in preparing its audited financial statements. Upon converting the amount of Adjusted Gross Sales into Swiss Francs, Licensee shall convert into US Dollars (or other currency), using the daily rate (Reuters) at the last working day for the applicable period.

**5.10 Reporting.** With each payment Licensee shall provide in writing for the relevant Accounting Period the following information split by U.S., each of the Major Market Countries, and rest of world (a) Adjusted Gross Sales; (b) Net Sales; (c) the total royalties payable for the applicable period; and (d) any other information necessary for Alnylam to comply with its reporting and payment obligations to Third Parties under Alnylam Third Party Obligations, subject to Alnylam's obligations under Section 2.3(b)(i).

**5.11 Withholding Taxes.** Any tax required to be withheld by Licensee under the laws of any country for the account of Alnylam shall be promptly paid by Licensee for and on behalf of Alnylam to the appropriate governmental authority, and Licensee shall furnish Alnylam with proof of payment of such tax. Any such tax actually paid on Alnylam's behalf shall be deducted from royalty payments due to Alnylam hereunder. Licensee shall assist Alnylam in minimizing the withholding taxes applicable to any payment made by Licensee and in claiming tax refunds at Alnylam's request.

**5.12 Financial Records.** Licensee shall keep, and shall require its Affiliates and Licensee Partners to keep, for [\*\*] years, full, true and accurate books of account containing all particulars that may be necessary for the purpose of calculating all amounts payable under this Agreement or to verify compliance with this Agreement. Such books of accounts shall be kept at their principal place of business.

**5.13 Audits by Alnylam.** At the expense of Alnylam, Alnylam has the right to engage an independent public accountant reasonably acceptable to Licensee to perform, on behalf of Alnylam, an audit of such books and records of Licensee and its Affiliates and Licensee Partners, that are deemed necessary by Alnylam's independent public accountant to verify amounts paid or payable under this Agreement for the period or periods requested by Alnylam and the correctness of any report or payments made under this Agreement. Upon timely request and at least thirty (30) Business Days' prior written notice from Alnylam, such audit shall be conducted in the countries specifically requested by Alnylam, during regular business hours in such a manner as to not unnecessarily interfere with Licensee's (or its Affiliates' or Licensee Partners', as the case may be) normal business activities, and shall be limited to results in the [\*\*] calendar years prior to audit notification. Such audit shall not be performed more frequently than [\*\*] per calendar year nor more frequently than [\*\*] with respect to records covering any specific period of time. All information, data documents and abstracts herein referred to shall be used only for the purpose of verifying royalty statements and other amounts payable under this Agreement, or compliance with this Agreement, shall be treated as Confidential Information of Licensee subject to the obligations of this Agreement and need neither be retained more than [\*\*] year after completion of an audit hereof, if an audit has been requested; nor more than [\*\*] years from the end of the calendar year to which each shall pertain; nor more than [\*\*] year after the date of termination of this Agreement. Audit results and findings shall be shared by Licensee and Alnylam. If the audit reveals an overpayment, Alnylam shall reimburse Licensee for the amount of the overpayment within thirty (30) days. If the audit reveals an underpayment, Licensee shall make up such underpayment within thirty (30) days with interest as set forth in Section 5.14 below. In addition, if the underpayment is equal to or greater than five percent (5%) of the amount that was otherwise due, Licensee shall pay all of the costs of such audit. The failure of Alnylam to request verification of any royalty calculation within the period during which corresponding records must be maintained shall be deemed acceptance of the royalty reporting.

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**5.14 Late Payments.** Licensee shall pay interest to Alnylam on the aggregate amount of any payments that are not paid on or before the date such payments are due under this Agreement at a rate per annum equal to the lesser of the one month London Interbank Offering Rate of interest plus one percent (1%), as reported by The Wall Street Journal for the applicable period, or the highest rate permitted by applicable law, calculated on the number of days such payment is delinquent.

## ARTICLE VI

### CONFIDENTIAL INFORMATION

**6.1 Confidential Information.** All Confidential Information disclosed by a Party to the other Party in connection with the activities contemplated by this Agreement shall not be used by the receiving Party except in connection with the activities and licenses contemplated by this Agreement, shall be maintained in confidence by the receiving Party, and shall not otherwise be disclosed by the receiving Party to any other Person, without the prior written consent of the disclosing Party, except to the extent that the Confidential Information (as determined by competent documentation):

(a) was known or used by the receiving Party or its Affiliates prior to its date of disclosure to the receiving Party; or

(b) either before or after the date of the disclosure to the receiving Party or its Affiliates, is lawfully disclosed to the receiving Party or its Affiliates by sources other than the disclosing Party who are rightfully in possession of the Confidential Information and not subject to an obligation of confidentiality or non-use owed to the disclosing Party; or

(c) either before or after the date of the disclosure to the receiving Party or its Affiliates, becomes published or generally known to the public other than through the wrongful act or default of the receiving Party or its Affiliates or its or its Affiliates' representatives; or

(d) is independently developed by the receiving Party or its Affiliates without reference to or reliance upon the Confidential Information.

Notwithstanding anything set forth herein to the contrary, this Article VI shall not prohibit the receiving Party from disclosing Confidential Information of the disclosing Party to defend or prosecute litigation; provided that, to the extent practicable, the receiving Party provides prior written notice of such disclosure to the disclosing Party and assists the disclosing Party in its reasonable and lawful efforts to avoid or minimize the degree of such disclosure. Notwithstanding the foregoing provisions of this Section 6.1, either Party may only disclose the terms of this Agreement if such Party reasonably determines, based on advice from its counsel, that it is required to make such disclosure by applicable Law, regulation or legal process, including without limitation by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or NASDAQ, or pursuant to relevant accounting standards, such as IFRS or GAAP, in which event such Party shall provide prior notice of such intended disclosure to the other Party sufficiently in advance to enable the other Party to seek confidential treatment or other protection for such information unless the disclosing Party is prevented by Law from providing such advance notice and shall disclose only such terms of this Agreement as such

disclosing Party reasonably determines, based on advice from its counsel, are required by applicable Law or legal process to be disclosed. Alnylam shall be permitted to disclose in confidence (pursuant to a written agreement with confidentiality obligations no less restrictive than set forth herein) the terms of this Agreement to the extent Alnylam is contractually obligated to do so pursuant to Alnylam Third Party Obligations and to potential and existing investors, lenders and acquirors; provided, that Alnylam shall redact such portions as Licensee reasonably requests.

**6.2 Employee and Advisor Obligations.** Each Party agrees that it may provide Confidential Information received from the other Party (including the terms of this Agreement) only to its and its Affiliates' (a) employees, consultants, advisors and contractors who have a need to know such information in order for the receiving Party to exercise its rights or perform its obligations under this Agreement, and (b) potential and existing investors, lenders and acquirors, in each case who have an obligation to treat such information and materials as confidential under terms no less restrictive than those set forth herein.

**6.3 Publicity.** Upon execution of this Agreement, the Parties shall jointly issue a press release announcing the execution of this Agreement in form and substance substantially as set forth on Schedule G hereto. Thereafter, neither Party shall issue any press release or public announcement relating to this Agreement or any Discovery Collaboration without the prior written approval of the other Party, which approval shall not be unreasonably withheld, conditioned or delayed, except that a Party may issue a press release or public announcement if required by Law, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or NASDAQ or pursuant to relevant accounting standards, such as IFRS or GAAP; provided that the other Party has received prior notice of such intended press release or public announcement if practicable under the circumstances and the Party subject to the requirement includes in such press release or public announcement only such information relating to this Agreement as is necessary to comply with applicable Law. Alnylam shall not issue any press release or public announcement relating to Licensed Products without the prior written approval of Licensee. The rights of approval and notice granted to a Party in accordance with the preceding sentence shall only apply for the first time that specific information is to be disclosed, and shall not apply to the subsequent disclosure of substantially similar information that has previously been made public other than through a breach of this Agreement by the issuing Party or its Affiliates.

## ARTICLE VII

### REPRESENTATIONS AND WARRANTIES

#### 7.1 Mutual Representations and Warranties.

(a) Representations of Authority. Each Party represents and warrants to the other Party that, as of the Effective Date, it has full corporate right, power and authority to enter into this Agreement and to perform its obligations under this Agreement.

(b) Consents. Each Party represents and warrants to the other Party that all necessary consents, approvals and authorizations of all government authorities and other Persons required to be obtained by it as of the Effective Date in connection with the execution, delivery and performance of this Agreement have been obtained.

(c) No Conflict. Each Party represents and warrants to the other Party that the execution and delivery of this Agreement and the performance of its obligations hereunder (i) does not violate or conflict with the provisions of its certificate of incorporation or by-laws, (ii) does not conflict with or violate any requirement of applicable Laws effective as of the Effective Date, and (iii) does not and will not conflict with, violate, breach or constitute a default under any contractual obligations of it or any of its Affiliates existing as of the Effective Date.

(d) Authorization and Binding Nature. Each Party represents and warrants to the other Party that the execution, delivery and performance of this Agreement and the performance of all obligations hereunder have been duly authorized by all requisite corporate action on the part of such Party and this Agreement constitutes valid and legally binding obligations of such Party, limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting the enforcement of creditors' rights generally and (ii) as may be limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies.

(e) Employee Obligations. Each Party represents and warrants that all of its employees, officers and consultants have executed agreements or have existing obligations under Law requiring assignment to such Party of all intellectual property and proprietary rights made during the course of and as the result of their association with such Party, and obligating such individuals to maintain as confidential the Confidential Information of such Party and of a Third Party which such Party may receive.

**7.2 Representations and Warranties of Alnylam.** Alnylam represents and warrants to Licensee that, as of the Effective Date:

(a) Organization and Good Standing. Alnylam is a corporation duly organized, validly existing and in good standing under the Laws of the State of Delaware.

(b) Non-Infringement. To Alnylam's knowledge, (i) no Third Party is currently infringing or misappropriating any Licensed Intellectual Property, it being understood that there may be Third Parties that are conducting research or clinical development under the "safe harbor" exemption from patent infringement under 35 USC 271(e)(1) or similar exemptions in other jurisdictions, and (ii) the practice of the Licensed Intellectual Property as contemplated under this Agreement does not violate the intellectual property rights of any Third Party.

(c) Validity. All Licensed Intellectual Property that is owned by Alnylam, and, to the best of Alnylam's knowledge, all Licensed Intellectual Property that is licensed by Alnylam pursuant to Listed Alnylam Third Party Agreements, is in full force and effect and all necessary registration, maintenance, and renewal fees for such Licensed Intellectual Property have been paid on time. Except for those oppositions or challenges which are publicly disclosed in Alnylam's filings with the U.S. Securities and Exchange Commission, no Third Party has initiated a suit or other proceedings to challenge the validity of the Licensed Patent Rights. Alnylam has no reason to believe that the Licensed Patent Rights are other than valid and enforceable.

(d) Litigation. Alnylam and its Affiliates are not aware of any pending or threatened claim or litigation (nor has Alnylam received notice of a potential claim or litigation) (i) which alleges that any issued patents of a Third Party would be infringed by the Development and Commercialization of any Licensed Product hereunder or (ii) that questions the validity of this Agreement or the right of Alnylam to enter into this Agreement, or to consummate the transactions contemplated hereby. To Alnylam's knowledge, there are no legal actions or investigations pending or threatened involving the employment by or with Alnylam of any of Alnylam's current or former officers, their use in connection with Alnylam's business or any information or techniques allegedly proprietary to any of their former employers, or their obligations under any agreements with prior employers or alleging a violation of Law. Alnylam is not a party to any order, writ, injunction, judgment or decree of any court. There is no action, suit, proceeding or investigation by Alnylam currently pending or that Alnylam intends to initiate.

(e) Authority. Alnylam and its Affiliates have the right and authority to grant the licenses to Licensee set forth in Section 2.1(a) of this Agreement as contemplated under this Agreement.

(f) Certain Exclusive Rights. Alnylam has granted exclusive licenses under Licensed Intellectual Property to Third Parties, or options to acquire exclusive licenses under Licensed Intellectual Property, for an aggregate of no more than [\*\*] Targets.

(g) Listed Alnylam Third Party Agreements. Schedule D-1 identifies all Listed Alnylam Third Party Agreements existing as of the Effective Date, and Schedule D-2 summarizes certain relevant Alnylam Third Party Obligations under such Listed Alnylam Third Party Agreements, including without limitation Listed Alnylam Third Party Payment obligations. All Listed Alnylam Third Party Agreements are in full force and effect, and no dispute presently exists between Alnylam and such Listed Counterparties and Pre-Existing Alliance Parties that would place in jeopardy any of the licenses granted by Alnylam under this Agreement.

(h) Pre-Existing Alliance Agreements. Schedule E identifies all Pre-Existing Alliance Agreements existing as of the Effective Date.

(i) Isis. Alnylam, through its Affiliate or a Third Party collaborator, has commenced an IND-Enabling Study for [\*\*] product candidate as set forth in Section 5.2(b) of the Listed Alnylam Third Party Agreement with Isis Pharmaceuticals, Inc. Alnylam presently has the exclusive right under the "Isis Patents" (as defined on Schedule C) and the right to grant sublicenses under the Listed Alnylam Third Party Agreement with Isis Pharmaceuticals, Inc.

(j) Protecting IP Rights. Alnylam and its Affiliates have taken reasonable measures to protect the Licensed Intellectual Property, consistent with prudent commercial practices in the biotechnology industry.

(k) **Completeness.** Schedule C provides a complete listing of the Licensed Patent Rights as of the Effective Date. Alnylam does not Control as of the Effective Date any Patent Rights other than the Licensed Patent Rights that Cover (a) the general structure, architecture, or design of double-stranded oligonucleotide molecules which engage RNAi mechanisms in a cell; (b) chemical modifications of double-stranded oligonucleotides (including any modification to the base, sugar or internucleoside linkage, nucleotide mimetics, and any end modifications) which do not abolish the RNAi activity of the double-stranded oligonucleotides in (a); (c) manufacturing techniques for the double-stranded oligonucleotide molecules or chemical modifications of (a) and (b); or (d) all uses or applications of double-stranded oligonucleotide molecules or chemical modifications in (a) or (b); (e) delivery technologies necessary or useful for delivery of double-stranded oligonucleotide molecules; or (f) manufacturing techniques for the delivery technologies in clause (e); but excluding Patent Rights which specifically relate to Blocked Targets.

(l) **Forthrightness.** Alnylam has not intentionally withheld or omitted any information from Licensee which Alnylam believes would be material in Licensee's decision to enter into this Agreement.

**7.3 Representations and Warranties of Licensee.** Licensee represents and warrants to Alnylam that, as of the Effective Date, Licensee is not engaged in a dispute with UBC.

**7.4 No Warranties.** EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN SECTIONS 7.1, 7.2 or 7.3, OR IN THE COMMON STOCK PURCHASE AGREEMENT, OR IN THE SHARE PURCHASE AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, TO THE OTHER PARTY, INCLUDING ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

## ARTICLE VIII

### TERM AND TERMINATION

**8.1 Term.** This Agreement shall be effective as of the Effective Date and shall continue, subject to Sections 8.2, 8.3 and 8.4, in accordance with its terms until, with respect to a Licensed Product in a particular country, the expiration of such Licensed Product's Royalty Term in such country. Without prejudice to any other rights or remedies available at law or in equity, neither Party shall have the right to terminate any right or obligation under this Agreement except pursuant to Section 8.2, 8.3 or 8.4. Notwithstanding the foregoing, in the event that the Effective Date does not occur on or before December 15, 2007, this Agreement shall terminate automatically on December 15, 2007 and be of no further force or effect, unless otherwise agreed upon by the Parties.

## 8.2 Termination for Cause.

(a) Licensee may terminate this Agreement upon sixty (60) calendar days' prior written notice to Alnylam upon the material breach by Alnylam of any of its representations, warranties or obligations under this Agreement; provided that such termination shall become effective only if (i) Alnylam fails to remedy or cure the breach within such sixty (60) day period, or (ii) if such breach cannot be remedied or cured through the application of commercially reasonable efforts within such sixty (60) day period, and Alnylam has (within such time period) submitted a plan for cure as promptly as is reasonably practicable (but in no event beyond an additional sixty (60) day period) through the application of commercially reasonable efforts with a remedy or cure period reasonably acceptable to Licensee, then after the earlier of the remedy or cure date accepted by Licensee or the date Alnylam ceases to use commercially reasonable efforts to remedy or cure such breach.

(b) Alnylam may terminate this Agreement upon sixty (60) calendar days' prior written notice to Licensee upon the material breach by Licensee of any of its representations, warranties or obligations under this Agreement; provided that such termination shall become effective only if (i) Licensee fails to remedy or cure the breach within such sixty (60) day period, or (ii) if such breach cannot be remedied or cured through the application of commercially reasonable efforts within such sixty (60) day period, and Licensee has (within such time period) submitted a plan for cure as promptly as is reasonably practicable (but in no event beyond an additional sixty (60) day period) through the application of commercially reasonable efforts with a remedy or cure period reasonably acceptable to Alnylam, then after the earlier of the remedy or cure date accepted by Alnylam or the date Licensee ceases to use commercially reasonable efforts to remedy or cure such breach.

**8.3 Termination for Patent Challenge.** If Licensee or any of its Affiliates or Licensee Partners initiates, maintains or supports any action to (a) oppose the grant of a patent, or (b) challenge the validity, patentability, enforceability and/or scope of an issued patent, in each case under the Licensed Patent Rights, then Alnylam shall have the right, upon thirty (30) days' prior written notice to Licensee, to terminate this Agreement; provided, however, that if Licensee or any of its Affiliates or Licensee Partners, as relevant, cease such opposition or challenge within such thirty (30) day period, then Alnylam shall not have the right to terminate this Agreement.

**8.4 Termination At Will.** Licensee shall have the right to terminate this Agreement on a Licensed Product-by-Licensed Product, Licensed Patent Right-by-Licensed Patent Right, and country-by-country basis after the first (1st) anniversary of the Effective Date for any reason upon one hundred and eighty (180) days prior written notice to Alnylam; provided, however, that if royalties were payable for any of the prior four (4) Accounting Periods or are currently payable hereunder with respect to such Licensed Product in such country, Licensee shall continue to comply with the terms of this Agreement with respect to such Licensed Product in such country as if the Agreement had not terminated hereunder, as such terms relate to the payment of royalties and event payments with respect to such Licensed Product in such country, and the related accounting provisions of this Agreement.

**8.5 Effect of Expiration or Termination.** Unless otherwise expressly set forth herein, all rights and obligations of the Parties hereunder shall terminate as of the effective date of such expiration or termination.

(a) Termination by Licensee For Alnylam Breach. If Licensee terminates this Agreement pursuant to Section 8.2(a), then the licenses granted to Licensee under Section 2.1(a) shall continue subject only to the restrictions set forth in Sections 2.1, 2.2, 2.3, 2.4, 2.5, 2.6 and 2.7, and Licensee's obligation to pay to Alnylam the royalties and event payment amounts due under Sections 2.5(a), 5.3 and 5.4 and under any applicable terms of the Discovery Collaboration as they become due; provided, however, that Licensee may withhold [\*\*] percent ([\*\*]%) of each event and royalty payment due hereunder until the actual amount of damages owed by Alnylam to Licensee with respect to the breach of this Agreement resulting in such termination is determined, whereupon such withheld amount shall be credited against such damages and any amount remaining shall be paid to Alnylam within thirty (30) days after such determination.

(b) Termination by Alnylam For Licensee Breach or Patent Challenge; Termination by Licensee For Convenience. If (i) Alnylam terminates this Agreement pursuant to Section 8.2(b) or 8.3, or (ii) Licensee terminates this Agreement, in its entirety or with respect to certain Licensed Products or Licensed Patent Rights, pursuant to Section 8.4, then all provisions of this Agreement, including the licenses granted under Section 2.1(a) by Alnylam to Licensee hereunder, shall terminate with respect to the Agreement in its entirety or, solely with respect to a termination of a Licensed Product or Licensed Patent Right by Licensee under the immediately preceding clause (ii), with respect to such terminated Licensed Product or Licensed Patent Right.

(c) Paid-Up License. Upon the expiration of the Royalty Term applicable to any Licensed Product in a country, subject to Alnylam Third Party Obligations, Licensee's and its Affiliates' licenses under Section 2.1(a) with respect to such Licensed Product in such country shall become a fully paid-up, royalty-free license, with the right to sublicense, to Discover, Develop, Commercialize or Manufacture such Licensed Product in such country.

(d) Survival. The expiration or termination of any right or obligation under this Agreement for any reason will not affect obligations, including the payment of any royalties and event payments, that have accrued as of the date of such expiration or termination, as the case may be, and the provisions set forth in Sections 2.5(a), 5.3-5.6 and 5.8-5.14 (with respect to each of the foregoing Sections, solely to the extent that any amounts are due but unpaid thereunder), Section 8.4, this Section 8.5, and Articles VI and IX hereof, shall survive such expiration or termination.

## ARTICLE IX

### MISCELLANEOUS

#### 9.1 Indemnification.

(a) By Alnylam. Alnylam shall defend, indemnify and hold harmless Licensee, its Affiliates and their respective directors, officers, employees and agents, at Alnylam's cost and expense, from and against any liabilities, losses, costs, damages, fees or expenses (including reasonable fees and expenses of legal counsel) arising out of any Third Party claim based on (i) any breach by Alnylam of any of its representations, warranties or obligations pursuant to this Agreement, or (ii) the negligence or willful misconduct of Alnylam or its Affiliates or sublicensees, or any of their respective directors, officers, employees and agents, in the performance of obligations or exercise of rights under this Agreement; except to the extent that such claims arise out of any negligence or willful misconduct of Licensee or its Affiliates, Licensee Partners or sublicensees, or any of their respective directors, officers, employees and agents.

(b) By Licensee. Licensee shall defend, indemnify and hold harmless Alnylam, its Affiliates and their respective directors, officers, employees and agents at Licensee's cost and expense, from and against any liabilities, losses, costs, damages, fees or expenses (including reasonable fees and expenses of legal counsel) arising out of any Third Party claim based on (i) any breach by Licensee of any of its representations, warranties or obligations pursuant to this Agreement, or (ii) the negligence or willful misconduct of Licensee or its Affiliates, Licensee Partners or sublicensees, or any of their respective directors, officers, employees and agents, in the performance of obligations or exercise of rights under this Agreement, or (iii) any Product Liability Claim relating to a Licensed Product; except to the extent that such claims arise out of any negligence or willful misconduct of Alnylam or its Affiliates or sublicensees, or any of their respective directors, officers, employees and agents.

(c) Claims for Indemnification with respect to Third Parties.

(i) With regard to any Third Party claim for which indemnification may be sought under this Section 9.1 against a person entitled to indemnification under this Section 9.1 (an "Indemnified Party"), the Indemnified Party shall give prompt written notification to the person from whom indemnification is sought (the "Indemnifying Party") of the commencement of any action, suit or proceeding relating to such Third Party claim or, if earlier, upon the assertion of any such claim by a Third Party (it being understood and agreed, however, that the failure by an Indemnified Party to give notice of a Third Party claim as provided in this Section 9.1(c) shall not relieve the Indemnifying Party of its indemnification obligation under this Agreement except and only to the extent that such Indemnifying Party is actually prejudiced as a result of such failure to give notice).

(ii) Within thirty (30) days after delivery of such notification, the Indemnifying Party may, upon written notice thereof to the Indemnified Party, assume control of the defense of such action, suit, proceeding or claim with counsel reasonably satisfactory to the Indemnified Party. If the Indemnifying Party does not assume control of such defense, the Indemnified Party shall control such defense.

(iii) The Party not controlling such defense may participate therein at its own expense; provided that if the Indemnifying Party assumes control of such defense and the Indemnified Party reasonably concludes, based on advice from counsel, that the Indemnifying Party and the Indemnified Party have conflicting interests with respect to such action, suit, proceeding or claim, the Indemnifying Party shall be responsible for the reasonable fees and expenses of counsel to the Indemnified Party solely in connection therewith; provided further, however, that in no event shall the Indemnifying Party be responsible for the fees and expenses of more than one counsel in any one jurisdiction for all Indemnified Parties.

(iv) The Party controlling such defense shall keep the other Party advised of the status of such action, suit, proceeding or claim and the defense thereof and shall consider recommendations made by the other Party with respect thereto.

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

(v) The Indemnified Party shall not agree to any settlement of such action, suit, proceeding or claim without the prior written consent of the Indemnifying Party, which shall not be unreasonably withheld. The Indemnifying Party shall not, without the prior written consent of the Indemnified Party, agree to any settlement of such claim or consent to any judgment in respect thereof that does not include a complete and unconditional release of the Indemnified Party from all liability with respect thereto or that imposes any liability or obligation on the Indemnified Party.

**9.2 Choice of Law.** This Agreement shall be governed by and interpreted under the laws in effect in the State of Delaware, excluding its conflicts of laws principles.

**9.3 Notices.** Any notice or report required or permitted to be given or made under this Agreement by one of the Parties to the other shall be in writing and shall be deemed to have been delivered upon personal delivery or (a) in the case of notices provided between Parties in the continental United States, four (4) days after deposit in the mail or the next Business Day following deposit with a reputable overnight courier and (b) in the case of notices provided by telecopy (which notice shall be followed immediately by an additional notice pursuant to clause (a) above if the notice is of a default hereunder), upon completion of transmissions to the addressee's telecopier, as follows (or at such other addresses or facsimile numbers as may have been furnished in writing by one of the Parties to the other as provided in this Section 9.3):

If to Alnylam:

Alnylam Pharmaceuticals, Inc.  
300 Third Street, 3rd Floor  
Cambridge, Massachusetts 02142  
Attention: Vice President — Legal  
Fax: (617) 551-8101

With a copy (which shall not constitute notice) to:

WilmerHale LLP  
60 State Street  
Boston, MA 02109  
Attention: Steven D. Singer, Esq.  
Fax: (617) 526-5000

If to Licensee:

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4070 Basel  
Switzerland  
Attention: Legal Department  
Fax: 41 61 688 1396

And: Hoffmann-La Roche Inc.  
340 Kingsland Street  
Nutley, New Jersey 07110  
USA  
Attention: Corporate Secretary  
Fax: (973) 235-3500

With a copy (which shall not constitute notice) to:

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4070 Basel  
Switzerland  
Attention: Pharma Partnering  
Fax: 41 61 688 7990

**9.4 Severability.** If, under applicable Law any provision hereof is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision(s) of this Agreement (“Severed Clause”), then, it is mutually agreed that this Agreement shall endure except for the Severed Clause. The Parties shall consult and use their best efforts to agree upon a valid and enforceable provision which shall be a reasonable substitute for such Severed Clause in light of the intent of this Agreement.

**9.5 Interpretation.** Whenever the context may require, any pronoun shall include the corresponding masculine, feminine and neuter forms. The words “include”, “includes” and “including” shall be deemed to be followed by the phrase “without limitation.” The word “will” shall be construed to have the same meaning and effect as the word “shall.” The word “or” shall be construed to have the same meaning and effect as “and/or.” Unless the context requires otherwise, (a) any definition of or reference to any agreement, instrument or other document herein shall be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein or therein), (b) any reference to any Laws herein shall be construed as referring to such Laws as from time to time enacted, repealed or amended, (c) any reference herein to any Person shall be construed to include the Person’s successors and assigns, (d) the words “herein”, “hereof” and “hereunder”, and words of similar import, shall be construed to refer to this Agreement in its entirety and not to any particular provision hereof, and (e) all references herein to Articles, Sections, Exhibits or Schedules shall be construed to refer to Articles, Sections, Exhibits and Schedules of this Agreement. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

**9.6 Integration.** This Agreement constitutes the entire agreement between the Parties with respect to the within subject matter and supersedes all previous agreements, whether written or oral; provided, that the Parties acknowledge the contemporaneous execution and delivery of the Other Transaction Documents, which shall not be superseded by this Agreement. This Agreement may be amended only in writing signed by properly authorized representatives of each of the Parties.

**9.7 Independent Contractors; No Agency.** Neither Party shall have any responsibility for the hiring, firing or compensation of the other Party's employees or for any employee benefits. No employee or representative of a Party shall have any authority to bind or obligate the other Party to this Agreement for any sum or in any manner whatsoever, or to create or impose any contractual or other liability on the other Party without said Party's written approval. For all purposes, and notwithstanding any other provision of this Agreement to the contrary, each Party's legal relationship under this Agreement to the other Party shall be that of independent contractor. The Parties agree and acknowledge that neither owes any fiduciary duties to the other.

**9.8 Assignment; Successors.** Neither Alnylam nor Licensee may assign this Agreement in whole or in part without the prior written consent of the other Party and such attempted assignment shall be deemed null and void; provided, however, that either Party may assign this Agreement without the prior written consent of the other Party (a) to an Affiliate of such Party, provided that the assigning Party shall remain primarily liable hereunder for the performance of all obligations by the assignee, or (b) to a Third Party in connection with a merger, sale or transfer of all or substantially all of the assigning Party's business (in the case of Licensee, its pharmaceutical business related to RNAi technology and in the case of an assignment from Alnylam to [\*\*] to which this Agreement relates, provided that such assignee shall agree in writing to be bound by the terms and conditions of this Agreement. This Agreement shall be binding upon, and shall inure to the benefit of, all permitted successors and assigns.

**9.9 Execution in Counterparts; Facsimile Signatures.** This Agreement may be executed in counterparts, each of which counterparts, when so executed and delivered, shall be deemed to be an original, and all of which counterparts, taken together, shall constitute one and the same instrument even if both Parties have not executed the same counterpart. Signatures provided by facsimile transmission shall be deemed to be original signatures.

**9.10 Waivers.** No failure on the part of Licensee or Alnylam to exercise and no delay in exercising any right, power, remedy or privilege under this Agreement, or provided by statute or at law or in equity or otherwise, shall impair, prejudice or constitute a waiver of any such right, power, remedy or privilege or be construed as a waiver of any breach of this Agreement or as an acquiescence therein, nor shall any single or partial exercise of any such right, power, remedy or privilege preclude any other or further exercise thereof or the exercise of any other right, power, remedy or privilege.

**9.11 No Consequential or Punitive Damages.** NEITHER PARTY HERETO WILL BE LIABLE FOR INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, EXEMPLARY OR MULTIPLE DAMAGES ARISING OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, OR FOR LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF, OR OTHERWISE UNDER, THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES. NOTHING IN THIS SECTION 9.11 IS INTENDED TO LIMIT OR RESTRICT (A) THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY WITH RESPECT TO THIRD PARTY CLAIMS UNDER SECTION 9.1 OR (B) REMEDIES AVAILABLE TO EITHER PARTY WITH RESPECT TO A BREACH OF ARTICLE VI.

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**9.12 Actions of Affiliates.** Except as set forth in Section 9.15 below, each Party shall be liable for any failure by its Affiliates to comply with the restrictions, limitations and obligations set forth in this Agreement. Each Party may perform its obligations hereunder personally or through one or more Affiliates, although each Party shall nonetheless be solely responsible for the performance of its Affiliates. Neither Party shall permit any of its Affiliates to commit any act (including any act of omission) that such Party is prohibited hereunder from committing directly. To the extent that the rights granted to a Party hereunder may be and are exercised by an Affiliate of such Party, such Affiliate shall be bound by the corresponding obligations of such Party.

**9.13 Expenses.** Except as otherwise expressly set forth in this Agreement, each Party shall be solely responsible for the expenses it incurs in connection with its performance of the activities contemplated by this Agreement.

**9.14 No Third Party Beneficiaries.** Except as expressly set forth in this Agreement, no Person other than the Parties and their respective Affiliates and permitted assignees hereunder shall be deemed an intended third party beneficiary hereunder or have any right to enforce any obligation of this Agreement. Notwithstanding the foregoing, the Parties agree that UBC shall be deemed a third party beneficiary of, and shall have the right to enforce directly against Licensee, its Affiliates and/or Licensee Partners, certain terms of this Agreement as set forth in the UBC Sublicense Agreement.

**9.15 Alnylam Europe AG.** Solely for the limited purposes of Sections 2.1, 2.2 and 2.3 hereof, Alnylam Europe AG shall be a party to this Agreement. Alnylam Europe AG shall have no other right or obligation other than as set forth under the aforementioned provisions of this Agreement.

**9.16 Bankruptcy.** All licenses (and to the extent applicable rights) granted under or pursuant to this Agreement by Alnylam and its Affiliates to Licensee are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11, US Code (the "Bankruptcy Code") licenses of rights to "intellectual property" as defined under Section 101(60) of the Bankruptcy Code. Unless Licensee elects to terminate this Agreement, the Parties agree that Licensee shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code, subject to the continued performance of its obligations under this Agreement.

*[Remainder of This Page Intentionally Left Blank]*

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

IN WITNESS WHEREOF, Alnylam, Alnylam Europe AG and Licensee have caused this License and Collaboration Agreement to be duly executed by their authorized representatives, as of the date first written above.

F. HOFFMANN-LA ROCHE LTD

By: /s/ Nigel Sheeil

Name: Nigel Sheeil

Title: Vice President

Global Head Licensing  
HOFFMANN-LA ROCHE INC.

By: /s/ Warwick S. Bedwell

Name: Warwick S. Bedwell

Title: Vice President

Global Head of Business Development  
ALNYLAM PHARMACEUTICALS, INC.

By: /s/ John Maraganore

Name: John Maraganore

Title: President & CEO

*Solely for purposes of Sections 2.1, 2.2 and 2.3 hereof:*

ALNYLAM EUROPE AG

By: /s/ Kreutzer Bossko

Name: Kreutzer Bossko

Title:

**Schedule A**

**Primary Therapeutic Areas**

**Cancer:** Targets principally involved in [\*\*], excluding Targets involved in [\*\*], including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Hepatic:** Targets principally involved in [\*\*], including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Metabolic Disease:** Targets principally involved in diseases of metabolism, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Pulmonary Disease:** Targets principally involved in diseases of the pulmonary system, including, without limitation, [\*\*], but excluding Targets of [\*\*].

Page 1, Schedule A

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Schedule B**

**Supplemental Therapeutic Areas**

**Autoimmune Disease:** Targets principally involved in [\*\*]. Such disorders include, without limitation [\*\*], but excluding Targets of [\*\*].

**Bacterial Infection:** Targets principally involved in bacterial infection [\*\*], including, without limitation, Targets [\*\*].

**Cardiovascular:** Targets principally involved in diseases of the heart or of the vascular system, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Oral:** Targets principally involved in diseases of the oral cavity, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Dermatology:** Targets principally involved in diseases of the skin, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Endocrine:** Targets principally involved in diseases of the endocrine system, including, without limitation, [\*\*], but excluding [\*\*] and excluding Targets of [\*\*].

**Ex Vivo Therapy:** Genes that are targeted as part of ex vivo therapy, including, without limitation, [\*\*] including, without limitation, [\*\*].

**Gastrointestinal:** Targets principally involved in diseases of the gastrointestinal system, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Genitourinary:** Targets principally involved in diseases of the genitourinary system, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Hematology:** Targets principally involved in [\*\*], including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Inflammatory Disease:** Targets principally involved in [\*\*]. Such disorders include, without limitation, those [\*\*], including [\*\*], but excluding Targets of [\*\*].

**Musculoskeletal Disease:** Targets principally involved in diseases of the muscles, ligaments or bone, including, without limitation, [\*\*], but excluding targets of [\*\*].

**Neurological Disease:** Targets principally involved in [\*\*], including, without limitation, [\*\*], but excluding those [\*\*].

**Ophthalmic Disease:** Targets principally involved in diseases of the eye, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Parasitic Disease:** Targets principally involved in parasitic [\*\*], including, without limitation, Targets [\*\*].

Page 1, Schedule B

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**Renal Disease:** Targets principally involved in diseases of the kidney, including, without limitation, [\*\*], but excluding Targets of [\*\*].

**Transplantation Medicine:** Targets principally involved in [\*\*], but excluding Targets of [\*\*].

**Viral Disease:** Targets principally involved in viral [\*\*], including, without limitation, Targets [\*\*].

Page 2, Schedule B

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**Schedule C**

**Licensed Patent Rights**

[\*\*]

Page 1, Schedule C

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Schedule C(1)**

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Page 1, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Anylam Pharmaceutical, Inc.**  
**Core Patents**

<u>CaseNumber</u>	<u>InvTitle</u>	<u>Country</u>	<u>CaseType</u>	<u>AppNumber</u>	<u>FilDate</u>	<u>PubNumber</u>	<u>PubDate</u>	<u>PatNumber</u>	<u>IssDate</u>	<u>ApplicationStatus</u>
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Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 5 pages have been omitted pursuant to a request for confidential treatment.

Page 2, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**PATENT RIGHTS CONTROLLED BY TEKIRA (INEX) THROUGH AN  
OWNERSHIP INTEREST**

Page 3, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 9 pages have been omitted pursuant to a request for confidential treatment.

Page 4, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**PATENT RIGHTS CONTROLLED BY TEKIRA (INEX) UNDER A LICENSE FROM  
A THIRD PARTY**

Page 5, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 16 pages have been omitted pursuant to a request for confidential treatment.

Page 6, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**M.I.T. Patent Rights**

**M.I.T. Case No. [\*\*]**

I. United States Patents and Applications

[\*\*]

II. International (non-U.S.) Patents and Applications

[\*\*]

**M.I.T. Case No. [\*\*]**

I. United States Patents and Applications

[\*\*]

Page 7, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**CANCER RESEARCH/STANFORD  
PATENT RIGHTS**

<u>CaseNumberInvTitle</u>	<u>Country</u>	<u>CaseType</u>	<u>AppNumber</u>	<u>FileDate</u>	<u>ApplicationStatus</u>	<u>PubNumber</u>	<u>PubDate</u>	<u>PatNumber</u>	<u>IssDate</u>
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Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 2 pages have been omitted pursuant to a request for confidential treatment.

Page 8, Schedule C(1)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**PATENTS AND PATENT APPLICATIONS LICENSED FROM ISIS PHARMACEUTICALS INC.**

**Schedule C(2)(a): Isis Chemistry Patents**

Page 1, Schedule C(2)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Isis Current Chemistry Patents**

<i>Isis Docket Number</i>	<i>Country Name</i>	<i>Status</i>	<i>Patent Number</i>	<i>Grant Date</i>	<i>Title</i>	<i>3rd Party</i>	<i>3rd Party</i>
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Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 51 pages have been omitted pursuant to a request for confidential treatment.

Page 2, Schedule C(2)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Isis Current Chemistry Patents (June 2007 Updates)**

Isis Docket  
Number

Country

Status

Serial  
Number

Filing  
Date

Title

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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Page 3, Schedule C(2)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Isis Current Chemistry Patents (as at June 27, 2007)

<u>Isis Docket Number</u>	<u>Country</u>	<u>Status</u>	<u>Serial Number</u>	<u>Filing Date</u>	<u>Title</u>
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Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 3 pages have been omitted pursuant to a request for confidential treatment.

Page 4, Schedule C(2)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

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**Isis Current Motif and Mechanism Patents (June 2007 Updates)**

<i>Isis Docket Number</i>	<i>Country Name</i>	<i>Status</i>	<i>Patent Number</i>	<i>Grant Date</i>	<i>Title</i>	<i>3rd Party</i>	<i>3rd Party</i>
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Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 10 pages have been omitted pursuant to a request for confidential treatment.

Page 2, Schedule C(2)(b)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Isis Current Mechanism and Motif Patents (June 2007 Updates)**

Isis Docket  
Number

Country

Status

Serial  
Number

Filing  
Date

Title

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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Page 3, Schedule C(2)(b)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Isis Future Motif and Mechanism Patents (as at June 2007)

<u>Isis Docket Number</u>	<u>Country</u>	<u>Status</u>	<u>Serial Number</u>	<u>Filing Date</u>	<u>Title</u>
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Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Asterisks denote omissions.

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A total of 3 pages have been omitted pursuant to a request for confidential treatment.

Page 4, Schedule C(2)(b)

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

**Schedule D-1**

**Listed Alnylam Third Party Agreements**

Copies of the following agreements, some in redacted form, have been, or shall be, made available to Licensee as of the Effective Date:

1. Co-Exclusive License Agreement between Max Planck Innovation GmbH (formerly Garching Innovation GmbH) and Alnylam Pharmaceuticals, Inc., dated December 20, 2002, as amended by Amendment dated July 2, 2003, and the Requirements Amendment effective June 15, 2005
2. Co-Exclusive License Agreement between Max Planck Innovation GmbH (formerly Garching Innovation GmbH) and Alnylam Europe AG (formerly Ribopharma AG), dated July 30, 2003, as amended by the Requirements Amendment effective June 15, 2005
3. Licence Agreement between Cancer Research Technology Ltd. and Alnylam Pharmaceuticals, Inc., dated July 18, 2003
4. Agreement between the Board of Trustees of the Leland Stanford Junior University and Alnylam Pharmaceuticals, Inc., dated September 17, 2003
5. Strategic Collaboration & License Agreement between Isis Pharmaceuticals, Inc., and Alnylam Pharmaceuticals, Inc., dated March 11, 2004, as supplemented or amended by letter agreements dated March 9, 2004 (as amended by letter agreement dated October 28, 2005), March 11, 2004, and June 10, 2005
6. Amended and Restated Exclusive Patent License Agreement between Alnylam Pharmaceuticals, Inc. and Massachusetts Institute of Technology, dated May 9, 2007
7. License and Collaboration Agreement between Tekmira Pharmaceuticals Corporation (formerly INEX Pharmaceuticals Corporation) and Alnylam Pharmaceuticals, Inc., dated January 8, 2007
8. The Sublicense Agreement between Tekmira Pharmaceuticals Corporation (formerly INEX Pharmaceuticals Corporation) and Alnylam Pharmaceuticals, Inc., dated January 8, 2007

Page 1, Schedule D-1

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## Schedule D-2

### Certain Alnylam Third Party Obligations

This Schedule D-2 highlights certain obligations of, or restrictions on, Alnylam and/or its sublicensees of Licensed Intellectual Property under Listed Alnylam Third Party Agreements, including without limitation Listed Third Party Payment obligations, which are applicable to Licensee under this Agreement, in each case subject to the terms and conditions of such Listed Alnylam Third Party Agreements. The summaries set forth in this Schedule D-2 are not intended to be comprehensive or inclusive of all obligations or restrictions which may be applicable to sublicensees of Licensed Intellectual Property under such Listed Alnylam Third Party Agreements.

Unless otherwise expressly stated, capitalized terms not otherwise defined in this Schedule D-2 shall have the meanings ascribed to them in the applicable Listed Alnylam Third Party Agreement, and references to sections, articles, schedules or exhibits made in this Schedule D-2 shall be to sections, articles, schedules or exhibits, as the case may be, in or to such applicable Listed Alnylam Third Party Agreement.

### MAX PLANCK (US)

- 1. Co-Exclusive License Agreement between Max Planck Innovation (formerly Garching Innovation GmbH) ("Max Planck") and Alnylam Pharmaceuticals, Inc. ("Alnylam"), dated December 20, 2002, as amended by Amendment dated July 2, 2003 and the Requirement Amendment ("Requirement Amendment") effective June 15, 2005 (as amended, "Max Planck US License Agreement")**

#### Limitations on License Grant (Section 2.1)

- Alnylam's co-exclusive license is limited to a license to develop, make, have made, use, sell and import Licensed Products in the Field.
- Owners retain the right to practice under the Patent Rights for research, teaching, education, non-commercial collaboration and publication purposes. The German and the U.S. federal government retain a royalty-free, non-exclusive, non-transferable license to practice any government-funded invention claimed in any Patent Rights for government purposes.

#### Certain Sublicense Terms (Sections 2.4 and 11.8)

- Immediately after the signature of each sublicense granted under the Max Planck US License Agreement, Alnylam is required to provide Max Planck with a copy of the signed sublicense agreement.
- Sublicensees are required to perform their sublicense agreement in accordance with the Max Planck US License Agreement. If Max Planck determines that Alnylam or any of its Sublicensees has failed to fulfill any of its obligations under Section 4 (including without limitation diligence and reporting obligations), then Max Planck may treat such failure as a material breach in accordance with Section 11.7.

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

- In the event that any license granted to Alnylam under the Max Planck US License Agreement is terminated, any sublicense under such license granted prior to termination of said license shall remain in full force and effect, provided that (i) the Sublicensee is not then in breach of its sublicense agreement; and (ii) the Sublicensee agrees to be bound to Max Planck as licensor under the terms and conditions of the sublicense agreement, provided that Max Planck shall have no other obligation than to leave the sublicense granted by Alnylam in place.

Diligence and Reporting (Sections 4.1 and 4.2; Sections 1 and 3 of Requirement Amendment)

- Sublicensees are required to use commercially reasonable efforts to develop and to introduce into the commercial market Licensed Products at the earliest practical date.
- Sublicensees are required to furnish information to Alnylam for inclusion in its reports to Max Planck, which reports are due within 30 days after the end of each calendar quarter with Alnylam's standard R&D report, on the progress of its efforts during the immediately preceding calendar quarter to develop and commercialize Licensed Products for each indication and sub-indication within the Field. The report shall also contain a discussion of intended R&D efforts for the calendar quarter in which the report is submitted.
- Under the Requirement Amendment, Alnylam is required to comply with certain operational and reporting obligations relating to Alnylam Europe AG.

Royalty Payment Obligation (Sections 5.2 and 5.3)

- The following running royalties are payable to Max Planck on Net Sales of therapeutic and prophylactic Licensed Products by Alnylam and its Sublicensees:
  - (i) [\*\*]% ([\*\*] percent) of the first US\$[\*\*] US Dollars) of annual accumulated Net Sales of all Licensed Products;
  - (ii) [\*\*]% ([\*\*] percent) of annual accumulated Net Sales of all Licensed Products between US\$[\*\*] US Dollars) and US\$[\*\*] US Dollars);
  - (iii) [\*\*]% ([\*\*] percent) of annual accumulated Net Sales of all Licensed Products between US\$[\*\*] US Dollars) and US\$[\*\*] US Dollars);
  - (iv) [\*\*]% ([\*\*] percent) of annual accumulated Net Sales of all Licensed Products between US\$[\*\*] US Dollars) and US\$[\*\*] US Dollars);
  - (v) [\*\*]% ([\*\*] percent) of annual accumulated Net Sales of all Licensed Products between US\$[\*\*] US Dollars) and US\$[\*\*] US Dollars); and

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(vi) [\*\*]% ([\*\*] percent) of annual accumulated Net Sales of all Licensed Products above US\$[\*\*] US Dollars).

- If the sale of any Licensed Product is covered by more than one of the Patent Rights, multiple royalties shall not be due.
- Non-cash consideration shall not be accepted by any Sublicensee for Licensed Products without the prior written consent of Max Planck.
- In the event any Sublicensee takes, for objective commercial and/or legal reasons, a license from any third party under any patent applications or patents that dominate the Patent Rights or is dominated by the Patent Rights in order to develop, make, use, sell or import any Licensed Product (explicitly excluding, without limitation, any third party patents and patent applications for formulation, stabilization and delivery), then up to [\*\*]% of any additional running royalties to be paid to such third party may be deducted, up to [\*\*]% ([\*\*] percent) of the running royalties stated in Section 5.2, from the date such running royalties must be paid to such third party. However, the running royalties stated in Section 5.2 shall not be reduced to less than a minimum of [\*\*]% ([\*\*] percent) of Net Sales in any case. For avoidance of doubt, if a Sublicensee takes a license to a third party target, in no event is a deduction allowed on any license fees for such target from running royalties due to Max Planck under the Max Planck US License Agreement.
- If (i) Sublicensees sell a Licensed Product in a country where no Patent Rights are issued and no patent applications that are part of the Patent Rights are pending that have not been pending for less than [\*\*] years after filing national patent applications in the country in question, and (ii) such Licensed Product is manufactured in a country where Patent Rights are issued or patent applications that are part of the Patent Rights are pending that have not been pending for more than [\*\*] years after filing national patent applications in the country in question, the royalties stated in Section 5.2 will be reduced by [\*\*]% ([\*\*] percent) for such Licensed Product, until the expiration or abandonment of all issued patents and filed patent applications within the Patent Rights in the country in which the Licensed Product is manufactured.

#### Royalty Payment and Reports (Sections 5.4 and 5.5)

- Within 30 days after the end of each calendar half year, Alnylam is required to deliver a detailed report to Max Planck for the immediately preceding calendar half year showing at least (i) the number of Licensed Products sold by Alnylam and its Sublicensees in each country, (ii) the gross price charged by Alnylam and its Sublicensees for each Licensed Products in each country, (iii) the calculation of Net Sales, and (iv) the resulting running royalties due to Max Planck according to those figures. If no running royalties are due to Max Planck, the report shall so state.
- Running royalties shall be payable for each calendar half year, and shall be due to Max Planck within 60 days after the end of each calendar half year.

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Bookkeeping and Auditing (Sections 5.6 and 5.7)

- Sublicensees are obliged to keep complete and accurate books on any reports and payments due to Max Planck under the Max Planck US License Agreement, which books shall contain sufficient information to permit Max Planck to confirm the accuracy of any reports and payments made to Max Planck. Upon Max Planck's request, Alnylam, or agents appointed by Max Planck for Alnylam, shall check the books of its Sublicensees for Max Planck, once a year. This right of auditing by Max Planck shall expire five years after each report or payment has been made. Alnylam shall have the right to check the books of its Sublicensees according to Section 5.6. All payments made by Sublicensees under the Max Planck US License Agreement are nonrefundable and noncreditable against each other.

Compliance with Laws (Section 10.1)

- Alnylam is required to use commercially reasonable efforts to comply with all local, state, federal, and international laws and regulations relating to the development, manufacture, use and sale of Licensed Products.

Non-Use of Owners Names (Section 10.2)

- Sublicensees are prohibited from using the name of "Massachusetts Institute of Technology", "University of Massachusetts", "Whitehead Institute", "Max Planck Institute", "Max Planck Society", "Garching Innovation" or any variation, adaptation, or abbreviation thereof, or of any of its trustees, officers, faculty, students, employees, or agents, or any trademark owned by any of the Owners, in any promotional material or other public announcement or disclosure without the prior written consent of the Owners or in the case of an individual, the consent of that individual.

Termination for Patent Challenge (Section 11.5)

- To the extent legally enforceable, if any Sublicensee attacks, or has attacked or supports an attack through a third party, the validity of any of the Patent Rights, Alnylam shall have the right to terminate the sublicense agreement immediately; upon request of Max Planck, Alnylam shall have the obligation to terminate such sublicense agreement.

**MAX PLANCK (EUROPEAN)**

2. **Co-Exclusive License Agreement between Max Planck and Alnylam Europe AG (formerly Ribopharma AG), dated July 30, 2003, as amended by the Requirement Amendment effective June 15, 2005 (as amended, "Max Planck European License Agreement")**

Limitations on License Grant (Sections 2.1 and 11.9)

- Alnylam Europe AG's co-exclusive license is limited to a license to develop, make, have made, use, sell and import Licensed Products in the Field.

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- The Approving Owners retain the right to practice under the Patent Rights for research, teaching, education, non-commercial collaboration and publication purposes. The \*German and the U.S. federal government retain a royalty-free, non-exclusive, non-transferable license to practice any government-funded invention claimed in any Patent Rights for government purposes.
- In countries where it is legally impossible to grant license to jointly owned patent rights without the approval of all joint owners, Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V. (“Max Planck Gesellschaft”) has agreed to partially assign its ownership position in the Joint Patent Rights in such countries to Alnylam Europe AG, restricted to develop, make, have made, use, sell and import Licensed Products in the Field, whereby Alnylam Europe AG is allowed to further assign such ownership position, restricted to develop, make, have made, use, sell and import Licensed Products in the Field in such countries to Third Parties and Sublicensees only with the prior written approval of Max Planck (formerly Garching Innovation GmbH), which shall not unreasonably be withheld. In any event, the ownership position assigned to Alnylam Europe AG and, as the case may be, sub-assigned by Alnylam Europe AG to its assignees, shall entitle neither Alnylam Europe AG nor its assignees to any actions, claims or anything which exceed the rights granted to them under the Patent Rights by the Max Planck European License Agreement.
- If Max Planck Gesellschaft has partially assigned its ownership position in the Joint Patent Rights in certain countries to Alnylam Europe AG according to Section 2.1, Alnylam Europe AG is obligated to cost-free re-assign such ownership position in such countries to Max Planck Gesellschaft on or before the effective date of termination of the Max Planck European License Agreement. In the event that Alnylam Europe AG has further assigned its ownership position in certain countries in accordance with Section 2.1, such further assignment shall remain in full force and effect, provided that (a) the sub-assignee is not then in breach of its sub-assignment agreement; and (b) the sub-assignee agrees to be bound to Max Planck as assignor under the terms and conditions of the sub-assignment agreement, provided that Max Planck shall have no other obligation than to leave the sub-assignment granted by Alnylam Europe AG in place.

Royalty Payment Obligation (Section 5.2 and 5.3)

- The same royalty rates and substantially similar deductions apply with respect to Net Sales of Licensed Products as those set forth under the Max Planck US License Agreement. Alnylam or Alnylam Europe AG shall only pay royalties on sales of such Licensed Products to a Third Party.
- Notwithstanding the foregoing, in no event shall royalties be due under both the Max Planck European License Agreement and the Max Planck US License Agreement on the Net Sale of a particular Licensed Product.

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#### Other Obligations and Restrictions

- Other obligations and restrictions under the Max Planck European License Agreement are substantially similar to those set forth in the summary above with respect to the Max Planck US License Agreement.
- Section 12.7 states that in the event of any discrepancies between the Max Planck European License Agreement and Max Planck US License Agreement due to the fact that the Max Planck US License Agreement does not reflect, among other things, that UMASS' ownership position in the Joint Patent Rights is excluded from the Joint Patent Rights with respect to the Max Planck US License Agreement and the Max Planck European License Agreement, the Max Planck European License Agreement shall prevail.

### **CANCER RESEARCH TECHNOLOGY**

#### **3. Licence Agreement between Cancer Research Technology Ltd. ("CRT") and Alnylam, dated July 18, 2003 ("CRT Agreement")**

##### Limitations on License Grants (Sections 2.1 and 2.3)

- Alnylam's license is limited to the Field under the CRT Patent Rights to research, develop, have developed, use, keep, make, have made, import, have imported, sell, have sold and otherwise dispose of Licensed Products. Except as necessary for the development and/or sale of Licensed Products in the Field, Alnylam does not have rights to make use of the CRT Patent Rights for any diagnostic application, as research tools or reagents, for target validation, or for small molecule drug discovery.
- CRT and Cancer Research UK shall have the right to use, and CRT shall have the right to consent to the use by academic research institutions (including for the sake of clarity those in receipt of Cancer Research UK funding) of, the CRT Patent Rights in the Field for internal, or in collaboration with another academic research institution, non-commercial, non-commercially sponsored research. For the sake of clarity, Cancer Research UK-funded Researchers shall be permitted under the CRT Patent Rights to conduct clinical trials of potential dsRNA therapeutic agents as part of their Cancer Research UK-funded academic research.

##### Certain Sublicense Terms (Section 2.4)

- Any Sub-license entered into by Alnylam must be limited to the Field and contain restrictions in equivalent terms to those set out in Clause 2.1.
- Any Sub-license shall terminate automatically on the expiry or termination for whatever reason of the CRT Agreement. If the CRT Agreement is terminated pursuant to Clause 10, CRT has agreed to enter into a direct licensing arrangement with any Sub-licensee on terms substantially similar to those contained in the CRT Agreement save that any license granted by CRT to any Sub-licensee shall be consistent with the terms of the Sub-license

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granted by Alnylam (or its Affiliate) in relation to field, territory, exclusivity, rights to sub-license and payment provisions. However, if the CRT Agreement is terminated by Alnylam pursuant to Clause 10.2, the foregoing shall apply save that the granting of such license by CRT shall be subject to CRT's consent. Nothing in Clause 2.4 shall confer upon CRT any obligation to enter into a direct licensing arrangement with the Sub-licensee where the Sub-licensee is in default of its obligations under the Sub-license. CRT shall not be expected to take any responsibility for any disputes between Alnylam (or its Affiliate) and its Sub-licensees relating to the terms of the Sub-license(s) and notwithstanding the foregoing, CRT shall not be obliged to enter into a direct license with a Sub-licensee in circumstances in which the Sub-licensee reserves any right to maintain a claim against CRT where such claim was previously maintained against Alnylam (or its Affiliate).

Sublicensees are required to undertake to CRT directly to allow the same access to the books and records as CRT has to Alnylam's books and records under the CRT Agreement.

- Sublicensees are restricted with respect to rights to assign in equivalent terms to those set out in Clause 15 and any further sublicensing must be subject to the terms of Clause 2.4.

#### Royalty Payment Obligation (Sections 3.2.1 and 3.3)

- Royalties of [\*\*]% of Net Sales of Royalty Licensed Products in the Field are payable to CRT.
- If at any time prior to or during the period for the payment of royalties under the CRT Agreement in relation to any particular territory, a Sub-licensee elects in its reasonable opinion to take a license from a Third Party to any Blocking IP to develop, make, sell, or otherwise dispose of Licensed Products, the royalties set forth in Clause 3.2.1 shall be reduced by [\*\*]% of the amount paid to such Third Party to access said Blocking IP. In no event shall the royalty payable to CRT be reduced below [\*\*]%.

#### Royalty Reports and Payment (Sections 4.2.1 and 5.1)

- Royalty payments are required to be made to CRT within 30 days of the end of the Quarter in which sales of the relevant Licensed Products took place.
- Following the earlier of first commercial sale of a Licensed Product in the Field by Alnylam or its Affiliate or the grant of a Sub-license, Alnylam is required to prepare an annual statement showing all monies due to CRT under the CRT Agreement for the previous calendar year, on a country by country basis. The statement shall include the number of units of each Royalty Licensed Product sold in each country in which sales occurred, and shall be submitted to CRT within 60 Business Days of March 31st of each year. If CRT gives notice pursuant to the CRT Agreement that it does not accept the statement, Alnylam shall make available to an independent accountant all books and records required for the purpose of certifying such statement.

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#### Books and Records (Section 5.2)

- Sub-licensees are required to keep true and accurate records and books of account containing all data necessary for calculating amounts payable to CRT. Such records and books of account shall be kept for 5 years following the end of the calendar year to which they relate, and shall, upon reasonable notice having been given by CRT, be open at all reasonable times on Business Days for inspection by an independent firm of accountants.

#### Diligence and Reporting (Article 6)

- Alnylam shall use reasonable efforts to develop, make, market, sell, and otherwise dispose of Licensed Products in all therapeutic areas within the Field and market each Licensed Product in the Field throughout the United States, Europe and Japan.
- If CRT believes that Alnylam has failed to meet the diligence requirements set forth in Clause 6, but Alnylam fails to reestablish diligence within [\*\*] of receipt of notice from CRT, CRT's remedy is limited to, at CRT's discretion, termination of Alnylam's license under the CRT Patent Rights in the particular territory or therapeutic area or, with respect to Clause 6.2, indication within the cancer therapeutic area for which Alnylam has failed to meet the diligence requirements. For the sake of clarity, should Alnylam's license be terminated in respect of a therapeutic area or territory pursuant to Clause 6.3, CRT shall be free to offer such therapeutic area or territory to a potential licensee.
- Within 30 days of the end of each Year, Alnylam shall provide CRT with a written report of the steps taken by Alnylam, its Affiliates and Sub-licensees to comply with the performance obligations of Clause 6.1 and Clause 6.2. Alnylam's annual statement shall also include a detailed description of therapeutic areas and territories under development and an overview of Alnylam's development plans for the forthcoming year (itself or through Affiliates or Sub-licensees).
- If Alnylam intends to undertake a Phase I Clinical Trial of any Licensed Product in the UK, Alnylam shall, at its option, notify CRT with the particulars of the proposed investigation, and allow Cancer Research UK the opportunity of conducting or procuring the conduct of the investigation on behalf of Alnylam or participate in such an investigation, subject to the agreement of terms acceptable to Alnylam, CRT and Cancer Research UK.

#### Claimed Infringement (Sections 7.4 and 7.5)

- Alnylam shall, at its option and at its own cost, defend and enforce or shall procure the defence or enforcement of the rights under the CRT Patent Rights. If Alnylam opts not to defend or enforce the relevant CRT Patent Rights, Alnylam shall grant to CRT (if CRT so requests) any and all rights that would be necessary for CRT to undertake the enforcement or defence. If Alnylam is unable to grant such rights, then it shall, at CRT's request, grant to CRT the right to conduct such an action in its name. Alnylam shall provide, at CRT's request and CRT's reasonable expense, such reasonable assistance as CRT may reasonably request in any such proceedings.

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Limitation of Liability (Section 8.6)

- It is agreed that CRT shall not be liable to Alnylam's Sub-licensees in contract, tort, negligence, breach of statutory duty or otherwise for any loss, damage, cost or expense of an indirect or consequential nature (including any economic loss or other loss of turnover, profits, business or goodwill) arising out of or in connection with the CRT Agreement or the subject matter thereof.

Termination for Patent Challenge (Section 10.5)

- CRT may terminate the CRT Agreement upon 30 days' written notice to Alnylam if Alnylam or its Affiliate commences legal proceedings, with the exception of interference proceedings declared by the USPTO or any other patent office, contesting the validity of the CRT Patent Rights; or commences itself, or provides any material assistance to a Third Party in relation to, legal proceedings contesting the ownership of the CRT Patent Rights. Any actions taken concerning determination of priority of invention under US patent law between a CRT Patent Right and claims in a patent or patent application which is owned by or licensed by Alnylam or its Affiliate shall not be considered a contest of validity or ownership under Clause 10.5.

**STANFORD**

**4. Agreement between the Board of Trustees of the Leland Stanford Junior University ("Stanford") and Alnylam, dated September 17, 2003 ("Stanford Agreement")**

Limitations on License Grant (Articles 3 and 4)

- Alnylam's license is limited to a license in the Licensed Field of Use to make, have made, use, have used, sell, have sold, import, and have imported Licensed Product in the Licensed Territory.
- Stanford may practice the Invention and use the Technology for its own bona fide research, including sponsored research and collaborations. Stanford has the right to publish any information included in Technology and Licensed Patents.
- The Stanford Agreement is subject to all of the terms and conditions of Title 25 USC 200-204, including an obligation that Licensed Product sold or produced in the U.S. be "manufactured substantially in the U.S." Alnylam shall take all reasonable action necessary on its part as licensee to enable Stanford to satisfy its obligations to the U.S. Government under Title 35.

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#### Diligence and Reporting (Article 5)

- Alnylam is required to use all commercially reasonable efforts and diligence to develop, manufacture, and sell or lease Licensed Product and to diligently develop markets for the Licensed Product. In particular, Alnylam is required to meet the milestones shown in Appendix A to the Stanford Agreement, which shall satisfy Alnylam's diligence obligations. If Alnylam in good faith fails to meet a milestone set forth on Appendix A, and Alnylam fails to reestablish diligence within [\*\*], Stanford may terminate the Stanford Agreement.
- Stanford may terminate the Stanford Agreement if Alnylam or a sublicensee has not sold licensed Product for any [\*\*] period after Alnylam's or a sublicensee's first commercial sale of Licensed Product.
- On or before September 30 of each year until Alnylam markets a Licensed Product, Alnylam is required to make a written annual report covering the preceding year ending June 30, regarding progress toward commercialization of Licensed Product. The report must include, as a minimum, information (e.g., summary of work completed, key scientific discoveries, summary of work in progress, current schedule of anticipated events or milestones and market plans for introduction of Licensed Product) sufficient to enable Stanford to satisfy reporting requirements of the U.S. Government, and for Stanford to ascertain progress by Alnylam toward meeting the diligence requirements of Article 5.

#### Royalty Payment Obligation (Article 6)

- On each anniversary of the Effective Date, a minimum yearly royalty of \$[\*\*] must be paid to Stanford, which payments are non-refundable but creditable against earned royalties to the extent provided in Section 6.4.
- Earned royalties of [\*\*]% of Net Sales for Licensed Product are payable to Stanford, subject to the following:
  - (i) Royalty Payments are reduced up to [\*\*]% (from [\*\*]% of Net Sales down to [\*\*]% of Net Sales) by the amount of royalty paid to access additional intellectual property necessary in order to sell Licensed Products ("Additional Earned Royalties").
  - (ii) Such royalty payments shall be reduced as follows:
    - (1) [\*\*]% if Additional Earned Royalties are [\*\*]% or less.
    - (2) [\*\*]% if Additional Earned Royalties are greater than [\*\*]% but less than [\*\*]%.
    - (3) [\*\*]% if Additional Earned Royalties are equal to or greater than [\*\*]% but less than [\*\*]%.
    - (4) [\*\*]% if Additional Earned Royalties are equal to or greater than [\*\*]% but less than [\*\*]%.
    - (5) [\*\*]% if Additional Earned Royalties are equal to or higher than [\*\*]%.

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- (iii) Only one royalty is due on each Licensed Product, regardless of whether its manufacture, use, importation, or sale is covered by more than one patent or patent application included in Licensed Patents, and no further royalties will be due for use of such Licensed Product by Alnylam or its sublicensee's customers.
- Creditable payments under the Stanford Agreement will be an offset against each earned royalty payment which is required to be paid under Section 6.3 until the entire credit is exhausted.
- If the Stanford Agreement is not terminated in accordance with other provisions, royalties must continue to be paid on all Licensed Products that are either sold or produced under the license granted in Article 3, whether or not such Licensed Products are produced before the Effective Date or sold after the Licensed Patents have expired.

Certain Sublicense Terms (Sections 13.3-13.5)

- Any sublicense granted by Alnylam under the Stanford Agreement must be subject and subordinate to the terms and conditions of the Stanford Agreement.
- Sublicensees may not further sublicense, except that Sublicensees may further sublicense rights under Licensed Patents only as needed or implied in the course of distribution or performance of service as required for the sale to an end user of Licensed Products.
- Any sublicense will expressly include the provisions of Articles 7, 8 and 9 for the benefit of Stanford.
- If a sublicensee desires that its sublicense survive the termination of the Stanford Agreement, Stanford has agreed that the sublicense will revert to Stanford subject to the transfer of all obligations, including the payment of royalties specified in the sublicense, to Stanford or its designee, if the Stanford Agreement is terminated.
- Alnylam will provide Stanford in confidence a copy of all relevant portions of any sublicenses granted pursuant to Article 13.

Royalty Reports, Payments, and Accounting (Article 7)

- Beginning with the first sale of a Licensed Product, Alnylam is required to make written reports (even if there are no sales) and earned royalty payments within 30 days after the end of each calendar quarter. The report must be in the form of Appendix B to the Stanford Agreement and state the number, description, and aggregate Net Sales of Licensed Product during the completed calendar quarter, and calculation of earned royalty payment due. With each report, royalty payments due for the completed calendar quarter must be paid.
- A written report is due within 90 days after the license expires under Section 3.2. Alnylam is required to continue to make reports after the license has expired, until all Licensed Product produced have been sold or destroyed. Royalty payments must also continue to be made, concurrent with the submittal of each post-termination report.

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- Records must be kept and maintained for 3 years showing the manufacture, sale, use, and other disposition of products sold or otherwise disposed of under the license, including general-ledger records of cash receipts and expenses, as well as other information sufficient to determine royalties due, including production records, customers, and serial numbers, and related information in sufficient detail to enable Alnylam to determine the royalties payable under the Stanford Agreement.
- An independent certified public accountant selected by Stanford and acceptable to Alnylam is permitted to examine such books and records from time to time (but no more than once a year) to the extent necessary to verify the royalty and termination reports as detailed in the Stanford Agreement.

#### Negation of Warranties (Article 8)

- Stanford has represented and warranted to Alnylam that, to the best of Stanford's OTL knowledge, Stanford is the sole owner of Stanford Licensed Patents and has the right to enter into the Stanford Agreement and to grant the rights and licenses set forth therein.
- Notwithstanding the foregoing, nothing in the Stanford Agreement or any sublicense agreement shall be construed as:
  - (i) Stanford's warranty or representation as to the validity or scope of any Licensed Patent;
  - (ii) A warranty or representation that anything made, used, sold, or otherwise disposed of under any license granted under the Stanford Agreement or any sublicense agreement is or will be free from infringement of patents, copyrights, and other rights of third parties;
  - (iii) An obligation to bring suit against third parties for infringement, except as described in Article 12 of the Stanford Agreement;
  - (iv) Granting by implication, estoppel, or otherwise any licenses or rights under patents or other rights of Stanford or other persons other than Licensed Patents, regardless of whether the patents or other rights are dominant or subordinate to any Licensed Patents; or
  - (v) An obligation to furnish any technology or technological information.

Except as expressly set forth in the Stanford Agreement, it is acknowledged and agreed that Stanford makes no representations and extends no warranties of any kind, either express or implied. There are no express or implied warranties of merchantability or fitness for a particular purpose, or that Licensed Products will not infringe any patent, copyright, trademark, or other rights, or any other express or implied warranties.

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- Nothing in the Stanford Agreement or any sublicense agreement grants any sublicensee any express or implied license or right under or to U.S. Patent 4,656,134 entitled "Amplification of Eucaryotic Genes" or any patent application corresponding thereto.

#### Indemnification and Insurance (Article 9)

- Alnylam is required to indemnify, hold harmless, and defend Stanford and Stanford Hospitals and Clinics, and their respective trustees, officers, employees, students, and agents against all claims for death, illness, personal injury, property damage, and improper business practices arising out of the manufacture, use, sale, or other disposition of Invention, Licensed Patents, Licensed Products, by Alnylam or any sublicensee, or their customers except to the extent such claims are due to the gross negligence or willful misconduct of Stanford. Upon notification to Alnylam in writing of any such claim, Alnylam shall manage and control, at its own expense, the defense of such claim and its settlement. Alnylam agrees not to settle any such claim against Stanford without Stanford's written consent where such settlement would include any admission of liability on the part of Stanford, where the settlement would impose any restriction on the conduct by Stanford of any of its activities, or where the settlement would not include an unconditional release of Stanford from all liability for claims that are the subject matter of such claim.
- Subject to Section 9.1, neither Stanford nor Alnylam shall be liable to each other for any loss profit, expectation, punitive or other indirect, special, consequential, or other damages whatsoever, in connection with any claim arising out of or related to the Stanford Agreement whether grounded in tort (including negligence), strict liability, contract, or otherwise.
- Alnylam shall at all times comply, through insurance or self-insurance, with all statutory workers' compensation and employers' liability requirements covering all employees with respect to activities performed under the Stanford Agreement.
- Alnylam shall maintain, during the term of the Stanford Agreement, Comprehensive General Liability Insurance, including Product Liability Insurance prior to commercialization, with a reputable and financially secure insurance carrier to cover the activities of Alnylam and its sublicensees. Upon initiation of human clinical trials of any Licensed Product, such insurance will provide minimum limits of liability of Five Million Dollars and will include Stanford and Stanford Hospitals and Clinics, and their respective trustees, directors, officers, employees, students, and agents as additional insureds. Insurance will be written to cover claims incurred, discovered, manifested, or made during or after the expiration of the Stanford Agreement and must be placed with carriers with ratings of at least A- as rated by A.M. Best. Alnylam will furnish a Certificate of Insurance evidencing primary coverage and additional insured requirements and requiring thirty (30) days prior written notice of cancellation or material change to Stanford. Alnylam will advise Stanford, in writing, that it maintains excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All insurance of Alnylam will be primary coverage; insurance of Stanford and Stanford Hospitals and Clinics will be excess and noncontributory.

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Marking (Article 10)

- Before the issuance of Licensed Patents, Licensed Products made, sold, or otherwise disposed of under the license grant must be marked with the words “Patent Pending,” and following the issuance of one or more patents, with the numbers of the Licensed Patents.

Use of Stanford Names and Marks (Article 11)

- Stanford’s prior written consent is required for the use of its name or the names of faculty, students, employees or, or any trademark, service mark, trade name, or symbol of Stanford or Stanford Hospitals and Clinics, or any that is associated with any of them. Any use of Stanford’s name will be limited to statements of fact and will not imply endorsement of Alnylam’s products or services.

ISIS

**5. Strategic Collaboration & License Agreement between Isis Pharmaceuticals, Inc. (“Isis”), and Alnylam, dated March 11, 2004, as supplemented or amended by letter agreements dated March 9, 2004 (as amended by letter agreement dated October 28, 2005), March 11, 2004, and June 10, 2005 (as amended, “Isis Agreement”)**

**Limitations on License Grant (Section 5.1)**

- Alnylam’s licenses are limited to a license to research, develop, make, have made, use, import, offer to sell and sell Double Stranded RNA and Double Stranded RNA Products.
- The license excludes any right to practice the Isis Excluded Technology.
- Isis retains its rights in the Isis Patent Rights and in the Joint Patents (x) exclusively for the Isis Exclusive Targets and (y) exclusively for the Isis Encumbered Targets.
- Licenses to Isis Patent Rights that are joint patents with Third Parties (i.e., invented by one or more Isis inventors and one or more non-Isis inventors) are licensed subject to the retained rights of any non-Isis inventors and their assignees and licensees. Any such retained rights of non-Isis inventors and their assignees and licensees existing as of the Effective Date are set forth in Exhibit 5.3(c) attached to the Addendum Transmittal to the Isis Agreement.
- Licenses to Isis Patent Rights that are subject to contractual obligations between Isis and Third Parties in effect as of the Effective Date are licensed subject to the restrictions and other terms described in Exhibit 5.3(d) attached to the Addendum Transmittal to the Isis Agreement.

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- The license to Licensed Know-How under the Isis Agreement is subject to the non-disclosure obligations set forth in Article 12 of the Isis Agreement.

#### Certain Sublicense Terms (Sections 5.2, 5.3 and 14.4)

- Alnylam cannot sublicense its right to grant Naked Sublicenses under the Isis Agreement except that Alnylam may permit its sublicensees to grant further sublicenses in connection with an Alnylam Product.
- The rights of any sublicensee under any permitted sublicense granted in accordance with Section 5.2 will survive the termination of the Isis Agreement.

#### Royalty Payment Obligations (Section 7.2)

- Royalties are payable to Isis on sales of Alnylam Products, equal to [\*\*]% of Net Sales.
- The royalty may be reduced by [\*\*]% of any additional royalties that Alnylam owes to Third Parties on such Alnylam Product that arise from Alnylam acquiring access to new technologies after the Effective Date (as defined in the Isis Agreement); provided, however that (a) the royalty due under this section can never be less than a floor of [\*\*]% and (b) additional royalties arising as the result of the addition, pursuant to Section 11.8, of Isis Future Chemistry Patents or Isis Future Motif and Mechanism Patents to the Isis Patent Rights licensed to Alnylam cannot be used to reduce the royalty.

#### Payment Terms (Section 9.1)

- Royalties payable under the Isis Agreement are payable on a quarterly basis within 45 days after the end of each calendar quarter. Alnylam is required to provide Isis with a report setting forth (i) gross sales of Alnylam Products by Alnylam, its Affiliates and sublicensees, (ii) all deductions from such gross sales taken in calculating Net Sales, (iii) Net Sales of Alnylam Products by Alnylam, its Affiliates and sublicensees, (iv) royalties payable based on such Net Sales and (v) all other information relevant to the calculation of such royalties, on a product-by-product and country-by-country basis, for each calendar quarter within [\*\*] after the end of such calendar quarter.

### MIT

#### **6. Amended and Restated Exclusive Patent License Agreement between Massachusetts Institute of Technology (“MIT”) and Alnylam, dated May 9, 2007 (“MIT Agreement”)**

##### Limitations on License Grant (Sections 2.1 and 2.5)

- Alnylam’s license is limited to a license to develop, make, have made, use and import Library Products and Licensed Processes to develop, make, have made, use, sell, offer to sell, lease, and import Licensed Products in the Field in the Territory and to develop and perform Licensed Processes in the Field in the Territory.

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- Alnylam may permit third parties (i) to use Library Products and Licensed Processes for the purpose of research with academic or nonprofit institutions and contract research, including for the conduct of clinical trials of a Licensed Product, and (ii) to sell Licensed Products under an agency, consignment or equivalent arrangement, wherein such rights are not sublicense rights.
- Alnylam does not have the right to sell or offer for sale the Library Products separately from a sale or offer for sale of a Licensed Product.
- MIT retains the right to practice under the Patent Rights for research, teaching, and educational purposes.
- The U.S. federal government retains a royalty-free, non-exclusive, non-transferable license to practice any government-funded invention claimed in any Patent Rights as set forth in 35 USC 201-211, and the regulations promulgated thereunder, as amended, or any successor statutes or regulations.
- The Patent Rights shall not be asserted against non-for-profit research institutions that practice the Patent Rights for research funded by (i) the institutions themselves, (ii) not-for profit foundations, or (iii) any federal, state or municipal government. If Alnylam wants to assert the Patent Rights against not-for-profit research institutions it may only do so if the infringement activity of the not-for-profit research institution was performed in the fulfillment of research sponsored by a for-profit entity and the assertion of infringement must be limited to those specific activities.

#### Certain Sublicense Terms (Section 2.3)

- Alnylam may grant sublicenses under commercially reasonable terms and conditions during the Exclusive Period.
- The sublicense must incorporate terms and conditions sufficient to enable Alnylam and its Affiliates to comply with the MIT Agreement. Such sublicenses shall also include provisions to provide that if Sublicensee brings a Patent Challenge against MIT (except as required under a court order or subpoena), Alnylam may terminate the sublicense.
- Alnylam shall promptly furnish MIT with a fully signed photocopy of any sublicense agreement, which copy may be redacted except with respect to terms directly relevant to Alnylam's obligations under the MIT Agreement.
- Upon termination of the MIT Agreement, any Sublicensee not then in default shall have the right to seek a license from MIT, and MIT agrees to negotiate such licenses in good faith under reasonable terms and conditions.

#### U.S. Manufacturing Requirement (Section 2.4)

- Library Products, whether or not part of Licensed Products, used or sold in the U.S. shall be manufactured substantially in the U.S.

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### Diligence and Reporting (Sections 3.1 and 3.2)

- Sublicensees are required to use diligent efforts to develop Library Products and Licensed Products and to introduce Licensed Products into the commercial market; thereafter Sublicensees are required to make Licensed Products reasonably available to the public. Specifically, the following obligations must be fulfilled:
  - (i) Written reports are due within [\*\*] days after the end of each calendar year on the progress of efforts during the immediately preceding calendar year to develop and commercialize Licensed Products. Such reports shall include the number of [\*\*], a description of [\*\*], and the [\*\*] that have been tested. The report shall also contain a discussion of intended efforts and sales projections for the year in which the report is submitted.
  - (ii) Within [\*\*] after the Effective Date, [\*\*] shall be evaluated for use in [\*\*] of RNAi Products.
  - (iii) Prior to [\*\*], at least [\*\*] shall be advanced to [\*\*] studies in support of [\*\*] for [\*\*] studies.
  - (iv) Filing of [\*\*] for Licensed Product [\*\*] by [\*\*].
  - (v) Commencement of [\*\*] for a Licensed Product within [\*\*] for such Licensed Product.
  - (vi) First Commercial Sale of a Licensed Product within [\*\*] for each such Licensed Product.
- If any Sublicensee is determined to have failed to fulfill any obligation under Sections 3.1(a) and 3.1(c) — (g), MIT may treat such failure as a material breach in accordance with Section 12.3(b), subject to any mutually-agreed upon changes to such diligence requirements pursuant to Section 3.2.

### Royalty Payment Obligations (Section 4.1)

- Royalties of [\*\*]% of Net Sales of Licensed Products and Licensed Processes are due within [\*\*] days of the end of each calendar quarter.
- If Alnylam or an Affiliate is legally required to pay royalties to one or more third parties in order to obtain a license or similar right necessary to practice the Patent Rights, Alnylam shall be entitled to a credit up to [\*\*] percent ([\*\*]%) of the amounts payable to such third parties against the royalties due to MIT for the same Reporting Period; provided, however, that (i) in no event will royalties due to MIT under Section 4.1(c), when aggregated with any other offsets and credits allowed under the MIT Agreement, be less than [\*\*]% of Net Sales in any Reporting Period, and (ii) royalties due to third parties with respect to [\*\*] patents (see Appendix B to MIT Agreement) shall not qualify for purposes of the offset against royalties under Section 4.1(d).

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- Multiple royalties are not due if the manufacture, use, lease, or sale of any Licensed Product or the performance of any Licensed Process is covered by more than one of the Patent Rights.

#### Royalty Payment and Reports (Sections 5.1 and 5.2)

- Royalties are payable for each Reporting Period and are due to MIT within [\*\*] days of the end of each Reporting Period.
- Prior to the First Commercial Sale of a Licensed Product or first commercial performance of a Licensed Process, Alnylam is required to deliver annual reports within [\*\*] days of the end of each calendar year, containing information concerning the immediately preceding year, as further described in Section 5.2.
- The date of First Commercial Sale of a Licensed Product or commercial performance of a Licensed Process must be reported to MIT within [\*\*] days of its occurrence.
- After First Commercial Sale of a Licensed Product or commercial performance of a Licensed Process, reports are required to be delivered to MIT within [\*\*] days of the end of each Reporting Period containing information concerning the immediately preceding Reporting Period, as further described in Section 5.2.
- Section 5.2 states that reports must include, among other things, information concerning the number of Licensed Products sold, leased, or distributed, the number of [\*\*], a description of Licensed Processes performed in each country as may be pertinent to a royalty accounting, gross price charged in each country, calculation of Net Sales in each country (including a listing of applicable deductions), total royalty payable on Net Sales, the exchange rate used for conversion, [\*\*] categorized by rights relating to [\*\*], and the [\*\*]. If no amounts are due to MIT for any Reporting Period, the report shall so state.

#### Recordkeeping and Audit Rights (Section 5.4)

- Sublicensees are required to maintain complete and accurate records reasonably relating to (i) the rights and obligations under the MIT Agreement, and (ii) any amounts payable to MIT in relation to the MIT Agreement, which records shall contain sufficient information to permit MIT to confirm the accuracy of any reports and payments delivered to MIT and compliance in other respects with the MIT Agreement. Such records shall be retained for at least [\*\*] years following the end of the calendar year to which they pertain, during which time a certified public accountant selected by MIT may inspect such records upon advance notice and during normal business hours solely for the purpose of verifying any reports and payments or compliance in other respects with the MIT Agreement.

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#### Claimed Infringement (Section 7.3)

- If a Patent Challenge is brought against Alnylam by a third party, MIT, at its option, shall have the right within 20 days after commencement of such action to take over the sole defense of the action. If MIT does not exercise this right, Alnylam may take over the sole defense of such action, subject to Sections 7.4 and 7.5.

#### Compliance with Laws (Sections 11.1 and 11.2)

- Alnylam is required to use reasonable commercial efforts to comply with all commercially material laws and regulations relating to development, manufacture, use, and sale of Library Products, Licensed Products, and Licensed Processes.
- Sublicensees are required to comply with all United States laws and regulations controlling the export of certain commodities and technical data.

#### Non-Use of MIT Name (Section 11.3)

- Sublicensees are prohibited from using the name of “Massachusetts Institute of Technology”, “Lincoln Laboratory” or any variation, adaption or abbreviation thereof, or of any of MIT’s trustees, officers, faculty, students, employees or agents, or any trademark owned by MIT, or any terms of the MIT Agreement in any promotional material or other public announcement or disclosure without MIT’s prior written consent, which may be withheld in MIT’s sole discretion.

#### Marking of Library and Licensed Products (Section 11.4)

- To the extent commercially feasible and consistent with prevailing business practices, Sublicensees are required to mark all Library Products (whether or not sold as part of Licensed Products) that are manufactured or sold under the MIT Agreement with the number of each issued patent under the Patent Rights that applies to such Library Product.

#### Termination for Patent Challenge (Section 12.5)

- If a Sublicensee brings a Patent Challenge (except as required under a court order or subpoena), MIT may send a written demand to Alnylam to terminate the sublicense. If Alnylam fails to so terminate such sublicense within 30 days of MIT’s demand, MIT may immediately terminate the MIT Agreement and/or the license granted thereunder.

#### Effect of Early Termination (Section 12.6)

- Upon any early termination of the MIT Agreement, Sublicensees may complete and sell any work-in-progress and inventory of Licensed Products that exist as of the date of termination, provided that such Sublicensees shall continue to pay applicable royalties, and shall complete and sell all work-in-progress and inventory of Licensed Products within six months of the date of termination.

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**7. License and Collaboration Agreement between Tekmira Pharmaceuticals Corporation (formerly INEX Pharmaceuticals Corporation) (“Tekmira”) and Alnylam, dated January 8, 2007 (“Tekmira Agreement”)**

Limitations on License Grant (Sections 6.1 and 6.4)

- Alnylam’s licenses are limited to a license to Develop, Manufacture and Commercialize Alnylam Royalty Products in the Alnylam Field and in and for the Territory.
- Section 6.4 states that all licenses and other rights granted to Alnylam with respect to INEX Technology under Article 6 are subject to (i) the rights granted to Tekmira, and to Tekmira’s ability to grant rights to Alnylam under the INEX In-Licenses, and (ii) the provisions of the UBC Sublicense Documents governing or relating to the rights sublicensed to Alnylam.

Certain Sublicense Terms (Sections 6.2 and 14.4(b))

- Alnylam may grant sublicenses to Third Parties to Develop, Manufacture and Commercialize Alnylam Royalty Products; provided, that (i) with respect to any sublicense of Alnylam’s rights under Section 6.1.1(a) in respect of any Alnylam Royalty Product for which Tekmira has not initiated Manufacturing of batches of finished dosage form for GLP toxicology studies, Alnylam is required to use Commercially Reasonable Efforts to facilitate a business discussion between Tekmira and Alnylam’s Sublicensee (other than Tekmira or its Affiliates) with respect to the provision of manufacturing services by Tekmira to such Sublicensee; and (ii) with respect to any sublicense of Alnylam’s rights under Section 6.1.1(a) in respect of any Alnylam Royalty Product for which Tekmira has initiated Manufacturing of batches of finished dosage form for GLP toxicology studies, Alnylam’s Sublicensee (other than Tekmira or its Affiliates) shall be required to obtain its requirements of the bulk finished dosage form of such Alnylam Royalty Product from Tekmira on the terms set forth in Article 5, however, Tekmira agrees to negotiate in good faith with Alnylam and/or Alnylam’s Sublicensee either an alternate or modified supply arrangement or the release of such Sublicensee from such exclusive supply obligation in return for reasonable compensation to Tekmira.
- Each license and/or sublicense granted by Alnylam pursuant to Section 6.2.2 must be subject and subordinate to the terms and conditions of the Tekmira Agreement and must contain terms and conditions consistent with those in the Tekmira Agreement, including, without limitation, the requirements of Section 6.4. Commercializing Sublicensees are required to: (i) submit applicable sales or other reports consistent with those required under the Tekmira Agreement; (ii) comply with an audit requirement similar to the requirement set forth in Section 7.6; and (iii) comply with the confidentiality and non-use provisions of Article 8 with respect to both Parties’ Confidential Information. If Alnylam becomes aware of a material breach of any sublicense by a Third Party Sublicensee, Alnylam is required to promptly notify Tekmira of the particulars of same and take all Commercially Reasonable Efforts to enforce the terms of such sublicense.

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- Any sublicense granted by Alnylam shall survive termination of the licenses or other rights granted to Alnylam under the Tekmira agreement in accordance with Article 6, and be assumed by Tekmira as long as (i) the Sublicensee is not then in breach of its license and/or sublicense agreement, (ii) the Sublicensee agrees in writing to be bound to Tekmira as a licensor under the terms and conditions of the license and/or sublicense agreement, and (iii) the Sublicensee agrees in writing that in no event shall Tekmira assume any obligations or liabilities, or be under any obligation or requirement of performance, under any such license and/or sublicense extending beyond Tekmira's obligations and liabilities under the Tekmira Agreement.

Diligence and Annual Reports (Section 6.7)

- Alnylam is required to use Commercially Reasonable Efforts to Develop and Commercialize an Alnylam Royalty Product in the Territory.
- Alnylam is required to deliver to Tekmira an annual report, due no later than December 31 of each Contract Year during the Agreement Term, which summarizes the major activities undertaken by Alnylam during the preceding twelve (12) months to Develop and Commercialize its Royalty Products in the Territory in the applicable field. The report will include an outline of the status of any such Royalty Products in clinical trials and the existence of any sublicenses with respect to such Royalty Products which have not been previously disclosed.

Compliance with Laws (Section 6.8)

- Alnylam is required to conduct its obligations under the Tekmira Agreement in accordance with all applicable laws, rules and regulations, including without limitation current governmental regulations concerning good laboratory practices, good clinical practices and cGMP, as applicable.

Royalty Payment Obligations (Sections 7.3 and 7.4; Section 6.1.3)

- Royalties are payable to Tekmira on Net Sales of Alnylam Royalty Products in the Territory as follows:

<u>Aggregate Calendar Year Net Sales of the Alnylam Royalty Product in the Territory</u>	<u>Royalty (as a percentage of Net Sales)</u>
on the first \$[**] — \$[**]	[**]%
On the subsequent \$[**] — \$[**]	[**]%
Greater than \$[**]	[**]%

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- Notwithstanding the foregoing, in the event that an Alnylam Royalty Product is comprised of a formulation Covered by or employing any Third Party Liposome Patent Rights then subject to the terms and conditions of the Tekmira Agreement, royalties on Net Sales of Alnylam Royalty Products in the Territory shall be calculated as follows:

<u>Aggregate Calendar Year Net Sales of the Alnylam Royalty Product in the Territory</u>	<u>Royalty (as a percentage of Net Sales)</u>
on the first \$[**] — \$[**]	[**]%
On the subsequent \$[**] — \$[**]	[**]%
Greater than \$[**]	[**]%

- Royalties on Alnylam Royalty Products at the rates set forth above are payable on a country-by-country and product-by-product basis commencing on the date of First Commercial Sale of such Alnylam Royalty Product in a country and continuing until the later of the expiration of the last Valid Claim Covering the Manufacture or Commercialization of such Alnylam Royalty Product in the country of sale, subject to the following conditions:
  - (i) only one royalty shall be due with respect to the same unit of Alnylam Royalty Product;
  - (ii) no royalties shall be due upon the sale or other transfer among a Party and its Related Parties, but in such cases the royalty shall be due and calculated upon such Party's or its Related Party's Net Sales to the first independent Third Party;
  - (iii) no royalties shall accrue on the sale or other disposition of the Alnylam Royalty Product by a Party or its Related Parties for use in a clinical study sponsored by such Party or under an IND prior to Regulatory Approval of such Alnylam Royalty Product in the applicable jurisdiction; and
  - (iv) no royalties shall accrue on the disposition of an Alnylam Royalty Product in reasonable quantities by a Party or its Related Parties as samples (promotion or otherwise) or as donations (for example, to non-profit institutions for a non-commercial purpose).
- If the Development, Manufacture or Commercialization of an Alnylam Royalty Product in accordance with the Tekmira Agreement infringes Necessary Third Party IP, the applicable royalties in each country in the Territory payable to Tekmira will be reduced by [\*\*] percent ([\*\*]%) of the amount paid by Alnylam of any royalties under all licenses of such Necessary Third Party IP that are reasonably allocable to the Development, Manufacture and Commercialization of the Alnylam Royalty Product in or for such country in the Alnylam Field; provided, however, that, on a country-by-country basis, in no event shall the royalties payable to Tekmira with respect to Net Sales in a country for any Calendar Quarter be reduced below the greater of: (i) [\*\*] percent ([\*\*]%) of the royalties otherwise payable to Tekmira for such Calendar Quarter as calculated pursuant to Section 7.3, and (ii) the amount of any royalties payable under the In-licenses of

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Alnylam that are reasonably allocable to the Commercialization or Manufacture of the Alnylam Royalty Product in or for such country in the Field (where the royalties are calculated by adding one percentage point to the applicable royalty rate(s) in the applicable In-License(s)).

- In the event that Alnylam is required to make any payments to UBC in respect of the INEX Technology or INEX Collaboration IP licensed to Alnylam pursuant to the UBC Sublicense Agreement, then Alnylam shall be entitled to offset any amounts payable by Alnylam to Tekmira under the Tekmira Agreement by the amount of Alnylam's payments to UBC until such amounts have been credited in full.

#### Royalty Reports; Payment (Section 7.3.4)

- During the Agreement Term, commencing upon the First Commercial Sale of an Alnylam Royalty Product, Alnylam is required to provide to Tekmira a quarterly written report showing the quantity of Alnylam Royalty Products sold in each country (as measured in saleable units of product), the gross sales of such Alnylam Royalty Product in each country, total deductions for such Alnylam Royalty Product for each country included in the calculation of Net Sales, the Net Sales in each country of such Alnylam Royalty Product subject to royalty payments sold by Alnylam and its Related Parties during the reporting period and the royalties payable with respect to such Alnylam Royalty Product under the Tekmira Agreement. Quarterly reports are due no later than the twenty-fifth (25th) day following the close of each Calendar Quarter. Royalties shown to have accrued by each royalty report are due and payable on the date such royalty report is due.
- Complete and accurate records must be kept in sufficient detail to enable the royalties and other payments payable under the Tekmira Agreement to be determined.

#### Audit Rights (Section 7.6)

- Upon the written request of Tekmira and not more than once in each Calendar Year, a Sublicensee must permit an independent certified public accounting firm of nationally recognized standing selected by Tekmira and reasonably acceptable to such Sublicensee to have access during normal business hours to such of the records of Sublicensee as may be reasonably necessary to verify the accuracy of the royalty and other financial reports required to be delivered under the Tekmira Agreement for any Calendar Year ending not more than [\*\*] months prior to the date of such request, for the sole purpose of verifying the basis and accuracy of payments made under Article 7.

#### Claimed Infringement (Section 10.4)

- Alnylam may, if it so desires, defend any Infringement Claim brought against either Alnylam or Tekmira or its Affiliates or Sublicensees arising out of the Development, Manufacture or Commercialization of any Alnylam Royalty Product in the Alnylam Field in the Territory. Alnylam must keep Tekmira informed, and from time to time consult with Tekmira regarding the status of any such claims and provide Tekmira with copies of

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all documents filed in, and all written communications relating to, any suit brought in connection with such claims. Tekmira also has the right to participate and to be presented in any such claim or related suit. If Alnylam fails to exercise its right to assume such defense within thirty (30) days following written notice of such Infringement Claim, Tekmira has the sole and exclusive right to control the defense of such Infringement Claim.

Patent Certification (Section 10.8)

- To the extent required or permitted by law, Alnylam is required to use Commercially Reasonable Efforts to maintain with the applicable Regulatory Authorities during the Agreement Term correct and complete listings of applicable Patent Rights for Alnylam Royalty Products being commercialized, including all so called "Orange Book" listings required under the Hatch-Waxman Act.

Termination for Patent Challenge (Section 11.5)

- If any Sublicensee asserts in any court or other governmental agency of competent jurisdiction that an INEX Patent Right or a Patent Right Controlled by Tekmira by virtue of the INEX-UBC License Agreement and sublicensed to Alnylam pursuant to the UBC Sublicense (in either case, an "INEX Patent") is invalid, unenforceable, or that no issued Valid Claim embodied in such INEX Patent excludes a Third Party from making, having made, using, selling, offering for sale, importing or having imported an Alnylam Royalty Product in such jurisdiction, then Tekmira shall be entitled, upon written notice to Alnylam, to terminate all licenses granted to Alnylam for such Alnylam Royalty Product(s) covered by such INEX Patent that is under challenge in the applicable jurisdiction; provided however, that Tekmira shall not terminate such license if within thirty (30) days of Alnylam's receipt of Tekmira's notification under the Tekmira Agreement:
  - (i) it is confirmed by written notice to Tekmira that Sublicensee no longer intends to challenge the validity or enforceability of such INEX Patent; or
  - (ii) documentation is provided to Tekmira to confirm Sublicensee's withdrawal of its filing, submission, or other process commenced in any court or other governmental agency of competent jurisdiction to challenge the validity or enforceability of any such INEX Patent.

**TEKMIRA/UBC**

**8. The Sublicense Agreement between Tekmira and Alnylam, dated January 8, 2007 ("UBC Sublicense Agreement")**

Limitations on License Grant (Sections 3.1 and 16.1)

- Alnylam's sublicense is limited to a license to research, develop, manufacture, have made, distribute, import, use, sell and have sold Products in and for the Alnylam Field.

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- University retains the right to use the Technology without charge in any manner whatsoever for non-commercial research, scholarly publication, educational or other non-commercial use.
- The UBC Sublicense Agreement and the license granted thereunder terminates on the expiration of a term of 20 years from the Date of Commencement or the expiration of the last Patent, whichever event shall last occur, unless earlier terminated as a result of the termination of Alnylam's rights to INEX Technology (as that term is defined in the Tekmira Agreement) under the Tekmira Agreement. Upon expiry of the UBC Sublicense Agreement, the licenses become perpetual, fully-paid up, worldwide licenses to use and sublicense the Technology and to manufacture, have made, distribute, import, use and sell Products in the Alnylam Field, without further payment of Royalties to Tekmira.

#### Certain Sublicense Terms (Section 4.2)

- Alnylam may grant sublicenses to third parties with respect to the Technology upon written notice to Tekmira and the University, provided that the Sublicensee agree (i) to perform the terms of the UBC Sublicense Agreement as if such Sublicensee were Alnylam under the UBC Sublicense Agreement; (ii) to represent that Sublicensee is not, as of the effective date of the relevant sublicense agreement, engaged in a dispute with the University; and (iii) to be subject to a written sublicense agreement that contains terms consistent with "the terms of this Agreement" described in Section 4.2(c) and that provides that the University is a third party beneficiary of, and has the right to enforce directly against the sublicensee, the terms in such sublicense agreement that are consistent with the terms listed in Section 4.2(c)(ii).
- Section 4.2(c)(ii) states that the "terms of this Agreement" means (i) the terms set forth in the UBC Sublicense Agreement; (ii) terms in such sublicense agreement consistent with Sections 1.3, 1.7, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8 and 2.13 of the Consent Agreement among Alnylam, Tekmira and the University of even date with the UBC Sublicense Agreement ("Consent Agreement"); and (iii) other customary and reasonable terms, including but not limited to terms relating to breach and termination, that are consistent with Alnylam's obligations to Tekmira under the UBC Sublicense Agreement and the Tekmira Agreement.

The terms of the Consent Agreement referenced in clause (ii) above are set forth below:

- 1.3 Alnylam Consent to Certain Disclosures to the University.** Alnylam consents to Tekmira disclosing to the University: (i) Alnylam's report to Tekmira made pursuant to Article 10.8 of the UBC Sublicense Agreement; and (ii) copies of Alnylam's sublicenses provided to Tekmira pursuant to Article 4.3 of the UBC Sublicense Agreement; solely for the purposes of calculation of royalties under the UBC License, determining compliance with Section 10.8 of the License Agreement between Tekmira and University dated July 1, 1998, as amended by an Amendment Agreement dated July 11, 2006, and a Second Amendment Agreement dated January 8, 2007 (as amended, the "UBC License") and determining compliance with Article 5 of the UBC Sublicense Agreement, and the University shall use reasonable efforts to ensure that all information provided to the University or its representatives pursuant to this Section 1.3 remains confidential and is treated as such by the University.

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**1.7 Rights of the University.** In consideration of the University providing its consent in the Consent Agreement, Tekmira and Alnylam agree that the University shall be entitled to rely upon any rights provided to the University pursuant to the terms of the UBC Sublicense Agreement, notwithstanding that the University is not a party to the UBC Sublicense Agreement.

**2.1 Limited Warranties.** Alnylam and its Affiliates expressly acknowledge and agree that:

- (a) Except as expressly set out in Section 2.1(c) of the Consent Agreement, the University makes no representations, conditions, or warranties, either express or implied, with respect to the Technology, Improvements, Patents or any Products. Without limiting the generality of the foregoing, the University specifically disclaims any implied warranty, condition, or representation that the Technology, Improvements, Patents or Products: (i) shall correspond with a particular description; (ii) are of merchantable quality; (iii) are fit for a particular purpose; or (iv) are durable for a reasonable period of time.
- (b) Except as expressly set out in Section 2.1(c) of the Consent Agreement, nothing in the UBC License, the Consent Agreement, or the UBC Sublicense Agreement shall be construed as: (i) a warranty or representation by the University as to title to the Technology, the Patents or any improvement or that anything made, used, sold or otherwise disposed of under the license granted in the Consent Agreement is or will be free from infringement of patents, copyrights, trademarks, industrial design or other intellectual property rights, (ii) an obligation by the University to bring or prosecute or defend actions or suits against third parties for infringement of patents, copyrights, trademarks, industrial designs or other intellectual property or contractual rights, or (iii) the conferring by the University of the right to use in advertising or publicity the name of the University or UBC Trademarks.
- (c) The University agrees that the warranty set forth in Section 7.4 of the UBC License will inure to the benefit of Alnylam and its sublicensees. For avoidance of doubt, such warranty is exactly as stated in the UBC License and its inclusion in the Consent Agreement will not change its terms in any way including, but not limited to, changing the date of such warranty from June 30, 2001.

**2.2 Disclaimer of Product Liability.** Alnylam and its Affiliates expressly acknowledge and agree that the University shall not be liable for any damages, or any other loss, whether direct, indirect consequential, incidental, or special which Alnylam or its Affiliates, or any further sublicense under any sublicense agreements between Alnylam and such further sublicensee, suffer, arising from any defect, error, fault, or failure to perform with respect to the Technology, Patents, Improvements or any Products, even if the University has been advised of the possibility of such defect, error, fault, or failure. Alnylam and its Affiliates acknowledge that they have been advised by the University to undertake their own due diligence with respect to the Technology, Patents, Improvements and Products.

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- 2.3 Indemnification of the University.** Alnylam and its Affiliates indemnify, hold harmless and defend the University, its Board of Governors, officers, employees, faculty, students, invitees and agents (the “**UBC Indemnitees**”) against any and all claims (including all legal fees and disbursements incurred in association therewith) arising out of the exercise of any rights under the Consent Agreement, the UBC License or the UBC Sublicense Agreement, including, without limiting the generality of the foregoing, against any damages or losses, consequential or otherwise, arising from or out of the use of the Technology, Patents, Improvements or Product(s) sublicensed under the UBC Sublicense Agreement by Alnylam or its Related Parties, or their respective customers or end-users howsoever the same may arise. For greater clarity, it is confirmed that, without limiting the generality of the foregoing, the indemnification by Alnylam and its Affiliates of the UBC Indemnitees set out in the Consent Agreement shall include an obligation to indemnify the UBC Indemnitees against any and all subrogated claims which may be brought against the UBC Indemnitees by any person(s) or entities (including without limitation Alnylam, its Related Parties, their respective customers or end-users, or their respective insurers) which may not have waived their rights of subrogation against the UBC Indemnitees, and shall also include, without limiting any of the foregoing, an obligation to indemnify the UBC Indemnitees against any and all claims relating to any injury or death to any person or damage to any property caused by any Product, whether claimed by reason of breach of warranty, negligence, product defect or otherwise, and regardless of the form in which any such claim is made.
- 2.4 Monetary Cap Respecting UBC License.** The University’s liability, whether under the express or implied terms of the Consent Agreement, the UBC License or the UBC Sublicense Agreement, in tort (including negligence), or at common law, for any loss or damage suffered by Alnylam or its Related Parties, whether direct, indirect, special, or any other similar or like damage, to the extent that such losses or damage may arise or does arise from any breaches of the UBC License, the Consent Agreement or the UBC Sublicense Agreement by UBC Indemnitees, shall be limited to the sum of \$[\*\*].
- 2.5 Disclaimer of Consequential Losses by the University.** In no event shall the University be liable for consequential or incidental damages arising from any breach or breaches of the UBC License, the UBC Sublicense Agreement or the Consent Agreement.
- 2.6 Litigation.** Provided that Tekmira has obtained the University’s consent required by Article 7 of the UBC License, Tekmira’s right to prosecute litigation in Article 7 of the UBC License may be exercised by Alnylam pursuant to Sections 7.5 and 7.6 of the UBC Sublicense Agreement.
- 2.7 UBC Trademarks.** Alnylam shall not use any of the University’s trademarks or make reference to the University or its name in any advertising or publicity whatsoever, without the prior written consent of the University, except as required by law. Nothing in the Consent Agreement shall prevent Alnylam from making or issuing factual statements to the public regarding its business or use of the Patent. If Alnylam is required by law to act in contravention of this provision, Alnylam shall provide the University with sufficient advance notice in writing to permit the University to bring an application or other proceeding to contest the requirement.

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**2.8 Confidentiality of Terms.** Alnylam requires of the University, and the University agrees insofar as it may be permitted to do so at law, that the Consent Agreement, the UBC Sublicense Agreement and each part of each of them, is confidential and shall not be disclosed to third parties, as Alnylam claims that such disclosure would or could reveal commercial, scientific or technical information and would significantly harm Alnylam's competitive position and/or interfere with Alnylam's negotiations with prospective sublicensees. Notwithstanding anything contained in this Section 2.8, the parties to the Consent Agreement acknowledge and agree that the University may identify the title of the Consent Agreement and/or the UBC Sublicense Agreement, the parties to the Consent Agreement and/or the UBC Sublicense Agreement, the inventors of the Technology, the term of the Consent Agreement and/or the UBC Sublicense Agreement, and the consideration actually paid to the University pursuant to the Consent Agreement and/or the UBC Sublicense Agreement.

**2.13 Alnylam Warranties.** Alnylam warrants and represents to the University that:

- (a) Alnylam is a corporation duly organized, existing, and in good standing under the laws of Delaware and has the power, authority, and capacity to enter into the Consent Agreement and to carry out the transactions contemplated by the Consent Agreement, all of which have been duly and validly authorized by all requisite corporate proceedings;
  - (b) the execution, delivery and performance by Alnylam of the Consent Agreement and the UBC Sublicense Agreement do not contravene or constitute a default under any provision of applicable law or its articles or by-laws (or equivalent documents) or of any judgment, injunction, order, decree or other instrument binding upon Alnylam; and
  - (c) the Consent Agreement constitutes a valid and binding agreement of Alnylam, enforceable against Alnylam in accordance with its terms.
- Alnylam is required to furnish Tekmira with a copy of each sublicense granted within 30 days after execution. Any such copy may contain reasonable redactions as Alnylam may make, provided that such redactions do not include provisions necessary to demonstrate compliance with the requirements of the UBC Sublicense Agreement. If University requests of Tekmira that a less redacted version of any sublicense be provided to University, Alnylam agrees to discuss in good faith with Tekmira and the University the University's concerns.
  - Sublicensee is required to observe and perform similar terms and conditions to those in the UBC Sublicense Agreement and those terms set forth in Section 4.2(c), including, without limitation, a restriction on the grant of further sublicenses without notice to Tekmira and the University.

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- Any sublicense granted by Alnylam under the UBC Sublicense Agreement shall survive termination of the licenses or other rights granted to Alnylam under the UBC Sublicense Agreement, and be assumed by Tekmira, as long as (i) the sublicensee is not then in breach of its sublicense agreement, (ii) the sublicensee agrees in writing to be bound to Tekmira as a sublicensor and to the University under the terms and conditions of the UBC Sublicense Agreement, and (iii) the sublicensee agrees in writing that in no event shall Tekmira assume any obligations or liabilities, or be under any obligation or requirement of performance, under any such sublicense extending beyond Tekmira's obligations and liabilities under the UBC Sublicense Agreement.

#### Royalty Obligations (Section 5.0)

- The consideration for the rights granted to Alnylam to the Technology under the UBC Sublicense Agreement, and the consideration for the rights granted by Tekmira to Alnylam to other technologies under the Tekmira Agreement, is the payment by Alnylam of milestones and royalties in accordance with the terms of Article 7 of the Tekmira Agreement.

#### Claimed Infringement (Section 7.7)

- If any complaint alleging infringement or violation of any patent or other proprietary rights is made against Alnylam (or a sublicensee of Alnylam) with respect to the manufacture, use or sale of Product, the following procedure shall be adopted:
  - (i) Alnylam shall promptly notify Tekmira upon receipt of any such complaint and shall keep Tekmira fully informed of the actions and positions taken by the complainant and taken or proposed to be taken by Tekmira (on behalf of itself or a sublicensee);
  - (ii) all costs and expenses incurred by Alnylam (or any sublicensee of Alnylam) in investigating, resisting, litigating and settling such a complaint, including the payment of any award or damages and/or costs to any third party, shall be paid by Alnylam (or any sublicensee of Alnylam, as the case may be); and
  - (iii) if as a result of such suit it is decided that a Product infringes any valid claim on a patent owned by another, Tekmira shall consider fair distribution of Royalty Income.

#### Use of Trademarks (Section 10.1)

- No use of or reference to the UBC Trade-marks or the University or its name is allowed in any advertising or publicity whatsoever, without the prior written consent of the University, except as required by law.

#### Diligence and Reporting (Section 10.2)

- Alnylam is required to use its reasonable commercial efforts to promote, market and sell the Products and utilize the Technology and to meet or cause to be met the market demand for the Products and the utilization of the Technology.

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- Alnylam is required to deliver to Tekmira an annual report, due on December 31 of each year during the term of the UBC Sublicense Agreement, which summarizes the major activities Alnylam has undertaken in the course of the preceding 12 months to develop and commercialize and/or market the Technology. The report must include an outline of the status of any Products in clinical trials and the existence of any sublicenses of the Technology.

Compliance with Laws (Section 18.0)

- Alnylam is required to comply with all laws, regulations and ordinances, whether Federal, Provincial, Municipal or otherwise with respect to the Technology and/or the UBC Sublicense Agreement.

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**Schedule E**

**Pre-Existing Alliance Agreements**

Copies of the following agreements, some in redacted form, have been, or shall be, made available to Licensee as of the Effective Date:

1. Strategic Collaboration & License Agreement between Isis Pharmaceuticals, Inc., and Alnylam Pharmaceuticals, Inc., dated March 11, 2004, as supplemented or amended by letter agreements dated March 9, 2004 (as amended by letter agreement dated October 28, 2005), March 11, 2004, and June 10, 2005
2. License and Collaboration Agreement between Tekmira Pharmaceuticals Corporation (formerly INEX Pharmaceuticals Corporation) and Alnylam Pharmaceuticals, Inc., dated January 8, 2007
3. The Research Collaboration and License Agreement, effective as of October 12, 2005, by and between Alnylam and Novartis, as amended by the Addendum Re: Influenza Program effective as of December 13, 2005, Amendment No. 1 to such Addendum effective as of March 14, 2006, and Amendment No. 2 to such Addendum effective as of May 5, 2006
4. Amended and Restated Research Collaboration and License Agreement between Merck & Co., Inc, Alnylam Pharmaceuticals, Inc. and Alnylam Holding Co., dated July 3, 2006
5. Amended and Restated Collaboration Agreement by and between Alnylam Pharmaceuticals, Inc. and Medtronic, Inc., dated July 27, 2007
6. Collaboration and License Agreement by and between Alnylam Pharmaceuticals, Inc. and Biogen Idec MA Inc., dated September 20, 2006

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## Schedule F

### Technology Transfer Plan

The Technology Transfer Plan outlined below between Licensee and Alnylam is designed to ensure that all capabilities and know-how related to the discovery and development of RNAi Therapeutics are efficiently and rapidly exchanged between both sites. The list of information and technologies to be transferred is divided into RNAi Pharmaceuticals [\*\*] and RNAi Platform [\*\*]. This will ensure that both Licensee and Alnylam will have acquired the knowledge and skills required in the development of RNAi Therapeutics from both a theoretical and practical standpoint.

The Technology Transfer Plan, as well as the Transition Services Plan (see Schedule A of Share Purchase Agreement) will be overseen and managed by the Joint Transitional Team (JTT), as outlined in the Share Purchase Agreement.

It is envisioned that the Technology transfer will take place in three stages:

- 1) **Plan roll-out (from Execution Date to Effective Date).** This stage would involve establishing contact with technology transfer counterparts in Licensee, Kulmbach Facility and Alnylam and begin writing SOPs. A preliminary list of Licensee, Kulmbach Facility and Alnylam contacts is shown in Table 1; this will be finalized during the plan roll-out period.
- 2) **Technology Transfer Period (as defined in Section 3.1).** This stage would involve finalization and transfer of SOPs between Licensee and Alnylam. This would involve frequent email and videoconference interactions. Face to face meetings will be utilized as required to ensure efficient transfer of technologies and capabilities. Ideally all technology transfer would be completed by this end of this phase.
- 3) **Additional technology transfer phase (up to [\*\*] after end of Technology Transfer Period).** Any additional technology transfer will be performed as required.

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**Table 1: Initial Proposed list of Contacts  
Involved in Licensee/Kulmbach Facility/Alnylam Technology Transfer**

<u>Technology</u>	<u>Licensee Contact</u>	<u>Kulmbach Facility Contact</u>	<u>Alnylam Contact</u>
<b>Alnylam to Licensee/Kulmbach Facility (RNAi Therapeutics)</b>			
1. Drug Substance Information	[**]	[**]	[**]
2.1. Drug Product Information: Overall	[**]	[**]	[**]
2.2. Drug Product Information: Safety/tox	[**]	[**]	[**]
3. Drug Substance Manufacturing	[**]	[**]	[**]
<b>Alnylam to Licensee/Kulmbach Facility (RNAi Platform)</b>			
4. Mid Scale Synthesis	[**]	[**]	[**]
5. Large Scale Synthesis	[**]	[**]	[**]
6. Conjugation Chemistry	[**]	[**]	[**]
7. Liposomal Formulations	[**]	[**]	[**]
8. Pulmonary Formulations	[**]	[**]	[**]
9. Analytic Methods	[**]	[**]	[**]
10. 5'RACE Assay	[**]	[**]	[**]
11. <i>In vivo</i> Models	[**]	[**]	[**]
<b>Licensee/Kulmbach Facility to Alnylam (RNAi Platform)</b>			
12. Bioinformatics and Database Systems	[**]	[**]	[**]
13. Small-scale Synthesis	[**]	[**]	[**]
14. Conjugation Chemistry	[**]	[**]	[**]
15. Peptide Formulations	[**]	[**]	[**]
16. Bioanalytics and Analytics	[**]	[**]	[**]
17. IFN and TNF Assays	[**]	[**]	[**]
18. <i>In vitro</i> Models	[**]	[**]	[**]
19. <i>In vivo</i> Models	[**]	[**]	[**]

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**RNAi Therapeutics Transfer from Alnylam to Licensee**

1. **Drug Substance Information:** Alnylam shall provide to Licensee the following test information for typical siRNA drug substance used in [\*\*] studies and those used in [\*\*] studies. Alnylam shall also provide to Licensee analogous information for typical reference standards.

<u>General Test</u>	<u>Typical Method (alternate if available)</u>
Appearance, solubility, pH of solution, molecular weight	[**]
Identity (individual strands and duplex)	[**]
Purity	[**]
Assay (%w/v)	[**]
Moisture content (if powder)	[**]
Organic volatiles	[**]
Heavy metals (if any)	
Sterility/bioburden	[**]
Bacterial endotoxins	[**]
Stability indicating test method	[**]
Other tests as relevant for the molecule depending on the chemical modifications involved	

2. **Drug Product Information (2.1 Overall, and 2.2 Safety/Tox):** Alnylam shall provide to Licensee the following information about siRNA drug products that have been subjected to more detailed characterization [\*\*]. The information that will be provided for the drug product is:
- a. Formulation composition
  - b. Formulation manufacturing procedure with in-process control specifications. Terminal sterilization procedure (if applicable) or in-process controls that are typically relevant of the dosage form [\*\*]
  - c. If new/novel formulation excipient(s) ([\*\*]) involved then Alnylam shall provide to Licensee the following additional information about that excipient(s):
    - i. Analytical profile

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- ii. Physico-chemical characterization
  - iii. Synthesis procedure
  - iv. Analytical release specification
  - v. Storage condition
  - vi. Safety/toxicity data supporting its human use on a chronic basis and any associated genotoxicity and immunostimulation.
  - vii. Justification for the use of the desired excipient
- d. Experience with different batch sizes and batch record information if available
- e. Equipment train (and specific parts if applicable)
- f. In addition to the above information, subject to availability, Alnylam will supply the following test information for drug product batches, their release specifications, and their stability (ICH protocol)

<u>General Test</u>	<u>Typical Method (alternate if available)</u>
Appearance	
Assay for siRNA (%w/v)	[**]
Moisture content (if powder)	
Particle size of the dosage form (if applicable)	[**]
Osmolarity (if applicable)	
Sterility/bioburden	[**]
Bacterial endotoxins	[**]
Stability indicating test method	[**]

Other test methods and experience with other dosage forms [\*\*]

For dispersed systems [\*\*], Alnylam shall provide to Licensee additional information about [\*\*] for the stability batches and their physico-chemical stability.

Alnylam shall provide to Licensee information on the impact of [\*\*] on the product's *in vivo* performance, [\*\*]

Alnylam shall provide to Licensee other applicable dosage form experience that would enable Licensee to transition/integrate the technology within Licensee and/or to third party contract manufacturer.

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**3. Drug Substance Manufacturing:**

- a.** Synthesis/manufacturing technology
  - i.** Overview on technology landscape: existing technologies, IP, CMO's
  - ii.** Technology used at Alnylam for small and large scale production
  - iii.** License terms for any IP covering synthesis and manufacturing technology
  - iv.** Preferred partners
  - v.** Knowledge of commercial suppliers and capacity of main players
- b.** Raw materials incl. solid support, HPLC columns
  - i.** Specifications
  - ii.** Suppliers
  - iii.** Costs
  - iv.** Solid supports: screened/tested? Advantages/disadvantages, regeneration/recycling?
  - v.** HPLC columns: technologies available, handling, containment, life times, costs, suppliers
  - vi.** Any animal-derived raw materials?
- c.** Process
  - i.** Description of chemistry involved
  - ii.** Detailed process flow and step description
  - iii.** Equipment/capacities/equipment suppliers
  - iv.** Overall and step yields, processing time
  - v.** Reproducibility
  - vi.** Critical steps, intermediates
  - vii.** Scale-up issues

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- viii. Process validation
- ix. Safety, health and environmental issues
- d. Analytics
  - i. Description of analytical methods for API characterization [\*\*], single strand and duplex
  - ii. Specifications and release methods
  - iii. IPC methods
  - iv. API stability, storage conditions, issues
  - v. Impurity profiles: what is acceptable, characterization of product-related compounds
  - vi. Endotoxin, adventitious agents control
  - vii. Comparability strategy
  - viii. History of difficulties with analytical methodologies
- e. Costs
  - i. Experience to date with typical manufacturing costs per development phase, at pre-commercial scale
- f. API CMC development
  - i. Typical development times, costs
  - ii. Typical API supply requirements per phase
  - iii. Supply outsourcing: typical lead times, technical transfer issues

**RNAi Platform Transfer from Alnylam to Licensee**

**4. Mid-scale Synthesis**

- a. Sourcing of raw materials and reagents
- b. SOP for synthesis and purification
- c. SOP for analytic characterization
- d. List of equipment required

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**5. Large-scale synthesis**

- a. Sourcing of raw materials and reagents
- b. SOP for synthesis and purification
- c. SOP for analytic characterization
- d. List of equipment required

**6. Conjugation chemistry**

- a. Overview of [\*\*] conjugates synthesized
  - i. Sourcing of raw materials and reagents
  - ii. Detailed synthesis schemes
  - iii. Analytic characterization
  - iv. Summary of Issues/Difficulties
  - v. Summary of in vitro and in vivo results to date with [\*\*] conjugates
- b. Overview of [\*\*] conjugates synthesized
  - i. Sourcing of raw materials and reagents
  - ii. Detailed synthesis schemes
  - iii. Analytic characterization
  - iv. Summary of Issues/Difficulties
  - v. Summary of in vitro and in vivo results to date with [\*\*] conjugates
- c. Overview of [\*\*] conjugates synthesized
  - i. Sourcing of raw materials and reagents
  - ii. Detailed synthesis schemes
  - iii. Analytic characterization
  - iv. Summary of Issues/Difficulties
  - v. Summary of in vitro and in vivo results to date with [\*\*] conjugates

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**7. Liposomal formulations**

- a. Overview of [\*\*] formulations tested
  - i. Sourcing of raw materials and reagents
  - ii. Detailed synthesis schemes
  - iii. Analytic characterization
  - iv. Summary of Issues/Difficulties
- b. Summary of in vitro and in vivo results to date with [\*\*]
- c. SOP for synthesis of [\*\*]
- d. SOP for preparing [\*\*] formulations
- e. SOP for analytic characterization methods for [\*\*] formulations
- f. List of formulation and analytic equipment required

**8. [\*\*] formulations**

- a. List of equipment required
- b. SOP for preparing [\*\*] formulations
- c. Analytic characterization methods

**9. Analytic methods**

- a. Summary of analytic methods tried and results

**10. 5' RACE assay for evaluation of RNAi-mediated silencing**

- a. Primer design
- b. Sourcing of reagents and kits
- c. Experimental SOP

**11. In vivo models for evaluation of RNAi delivery and activity**

- a. Animal models for delivery of siRNA to liver [\*\*]
  - i. Typical experimental design
  - ii. Experimental SOP for *in vivo* [\*\*] studies in rodent and non-human primate (where performed)

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- iii. Experimental SOP for *in vitro* [\*\*] activity assays in rodent and non-human primate (where performed).

**RNAi Platform Transfer From Kulmbach Facility to Alnylam**

**12. Bioinformatics and database systems**

- a. Transfer of bioinformatic search capability at Alnylam
  - i. Detailed information around the IT programs and sequence databases required to perform bioinformatic searches
  - ii. Detailed SOP for carrying out and analyzing bioinformatic searches
- b. [\*\*] siRNA chemical compound information storage database at Alnylam

**13. Small-scale synthesis**

- a. Overview of equipment requirements and small-scale process procedures
- b. Detailed SOP for synthesis, annealing, and QC

**14. Conjugation chemistry**

- a. Overview of [\*\*] conjugates synthesized
  - i. Sourcing of raw materials and reagents
  - ii. Detailed synthesis schemes
  - iii. Analytic characterization
  - iv. Summary of Issues/Difficulties
  - v. Summary of *in vitro* and *in vivo* results to date
- b. Experimental design and SOP for *in vitro* and *in vivo* screening
  - i. [\*\*] conjugates
  - ii. [\*\*] conjugates

**15. [\*\*] formulations**

- a. Overview of [\*\*] investigated
- b. Synthesis and/or sourcing of [\*\*]
- c. Formulation studies (including physico-chemical characterization and SOP)

- d. Summary of *in vitro* and *in vivo* results to date
- e. Experimental design and SOP for *in vitro* and *in vivo* screening

**16. Bioanalytics and analytics**

- a. Summary of analytic methods tried and results
- b. Summary of bioanalytic methods tried and results

**17. IFN/[\*\*] Assays**

- a. SOP for [\*\*] interferon [\*\*] induction assay
- b. Knowledge of specific siRNA sequence motifs that are known immunostimulators
- c. Summary on the role of chemical modifications in abrogating immunostimulation

**18. *In vitro* models for evaluation of RNAi delivery and activity**

- a. *In vitro* [\*\*] screening model
  - i. [\*\*] design
  - ii. [\*\*] construction
  - iii. Design of typical siRNA screen
  - iv. Experimental SOP
- b. *In vitro* cell line-based screen of [\*\*] target
  - i. Cell transfection optimization procedure
  - ii. mRNA assay readout [\*\*] – design and optimization
  - iii. Design of typical siRNA screen
  - iv. Experimental SOP

**19. *In vivo* models for evaluation of RNAi delivery and activity**

- a. [\*\*] model to analyse silencing in multiple tissues
  - i. Typical experimental design
  - ii. Experimental SOP

- 
- b.** [\*\*] lung model [\*\*]
    - i.** Typical experimental design
    - ii.** Experimental SOP

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Basel, 9 July 2007

**Roche and Alnylam form major alliance on RNAi therapeutics**

- **Roche accesses Nobel Prize winning technology for drug discovery and development**
- **Alnylam's site in Germany to become Roche's Center of Excellence for RNAi therapeutics**
- **Alnylam to receive 331 million US dollars in upfront payments and equity investment**

Roche and the US-based biopharmaceutical company Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY) announced today that they have entered into a major alliance in which Roche obtains a non-exclusive license to Alnylam's technology platform for developing RNAi (RNA interference) therapeutics. The alliance will initially cover four therapeutic areas: oncology, respiratory diseases, metabolic diseases, and certain liver diseases. Alnylam and Roche also will collaborate on RNAi drug discovery for one or more disease targets in these therapeutic areas. In addition, Roche will acquire Alnylam's European research site located in Kulmbach, Germany (Bavaria), subject to regulatory approval. This site will become Roche's Center of Excellence for RNAi therapeutics discovery.

RNAi is a potential foundation for a whole new class of human therapeutic products. RNAi is a natural mechanism that the body uses to inhibit expression of certain genes.

Harnessing the activity of RNAi creates a direct opportunity to develop specific and potent drugs against diseases that are difficult to treat.

"Alnylam has made significant advances in RNAi therapeutics, one of the most promising approaches to tomorrow's healthcare technology. Working together with Alnylam provides us with new capabilities to target complex diseases within our focus areas," said Lee E. Babiss, Head of Roche Global Pharma Research. "Our mission is to find novel solutions for patients who suffer from difficult to treat diseases and we will be fully committed to this goal, together with our new colleagues located at the acquired site in Kulmbach."

"We are pleased to form this new alliance with Roche, which is widely recognised for its commitment to innovation in biotechnology. We look forward to working together to advance our transformative technology into a whole new class of drugs," said John Maraganore, Ph.D.,

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President and Chief Executive Officer of Alnylam. “Such significant support from Roche will also strengthen Alnylam’s efforts to build a leading innovation-based biopharmaceutical company. Indeed, together with our demonstrated commitment to scientific excellence, advancement of our pipeline and unparalleled intellectual property estate, we believe that this new alliance greatly extends our leadership position in the discovery and development of RNAi therapeutics.”

### **Alnylam-Roche Collaboration**

Alnylam has granted to Roche a non-exclusive license providing Roche access to broad Alnylam intellectual property (IP) and know-how, including fundamental, chemistry and delivery IP. Indications will initially include oncology, respiratory disease, metabolic disease and certain liver diseases. Alnylam maintains the right to non-exclusively license its IP to additional partners in potential future agreements. In addition, Alnylam and Roche will collaborate on one or more disease targets to be identified in the future in exchange for milestone and royalty payments.

The transaction includes Roche’s acquisition of Alnylam’s European research site in Kulmbach, Germany (Bavaria), with about 40 employees. The team in Kulmbach will remain dedicated to RNAi therapeutics discovery as a new Center of Excellence for RNAi therapeutics within Roche’s global research organisation.

The alliance could be valued at over 1 billion US dollars in consideration of upfront payments, potential product milestone payments for multiple products and field expansion payments, excluding potential royalties on future sales of commercial products. Under the terms of the agreement, Roche will pay Alnylam 331 million US dollars in upfront cash payments and equity investment, including 1.975 million shares of Alnylam common stock the Roche Venture Fund agreed to purchase at 21.50 US dollars per share, representing just less than five percent of Alnylam’s outstanding common stock. Roche will also pay Alnylam milestones on products as they advance in development and commercialisation as well as royalties on future sales of commercial products. Further, Roche may pay Alnylam field expansion payments to increase the number of therapeutic areas.

The close of the agreements, including Roche’s purchase of Alnylam shares and purchase of Alnylam’s site in Germany, is subject to certain regulatory approvals and is expected to occur within approximately 30 days.

### **About RNAi**

RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as “a major scientific breakthrough that happens once every decade or so,” and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the Nobel Prize in October 2006. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of a major new class of medicines, known as RNAi therapeutics, is on the

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horizon. RNAi therapeutics target the cause of diseases by potently silencing specific messenger RNAs (mRNAs), thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

#### **About Alnylam Pharmaceuticals**

Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is applying its therapeutic expertise in RNAi to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Alnylam is leading the translation of RNAi as a new class of innovative medicines with peer-reviewed research efforts published in the world's top scientific journals including *Nature*, *Nature Medicine*, and *Cell*. The company is leveraging these capabilities to build a broad pipeline of RNAi therapeutics; its most advanced program is in Phase II human clinical trials for the treatment of respiratory syncytial virus (RSV) infection. In addition, the company is developing RNAi therapeutics for the treatment of influenza, hypercholesterolemia, and liver cancers, amongst other diseases. The company's leadership position in fundamental patents, technology, and know-how relating to RNAi has enabled it to form major alliances with leading companies including Merck, Medtronic, Novartis, Biogen Idec, and Roche. The company, founded in 2002, maintains global headquarters in Cambridge, Massachusetts. For more information, visit [www.alnylam.com](http://www.alnylam.com).

#### **About the Roche Venture Fund**

The Roche Venture Fund makes investments in early stage biotech and diagnostics companies to support innovative technologies and medicines. Based in Basel, Switzerland, the Roche Venture Fund manages a portfolio of over 25 companies in 10 countries.

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As one of the world's biggest biotech companies and an innovator of products and services for the early detection, prevention, diagnosis and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is one of the world leaders in in-vitro diagnostics and drugs for cancer and transplantation, a market leader in virology and active in other major therapeutic areas such as autoimmune diseases, inflammation, metabolism and central nervous system. In 2006 sales by the Pharmaceuticals Division totalled 33.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.7 billion Swiss francs. Roche employs roughly 75,000 people worldwide and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet at [www.roche.com](http://www.roche.com).

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**Roche Group Media Office**

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- Daniel Piller (Head of Roche Group Media Office)
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- Baschi Dürr
- Claudia Schmitt

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CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT WERE OMITTED AND REPLACED WITH “[\*\*]”. A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECRETARY OF THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO AN APPLICATION REQUESTING CONFIDENTIAL TREATMENT UNDER RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934.

**COLLABORATION AGREEMENT**

**BY AND AMONG**

**ALNYLAM PHARMACEUTICALS, INC.**

**AND**

**F. HOFFMANN-LA ROCHE LTD**

**AND**

**HOFFMANN-LA ROCHE INC.**

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Exhibits

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EXHIBIT B-2	Certain Listed Alnylam Third Party Agreements

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EXHIBIT G	Baseball Arbitration Provisions

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## COLLABORATION AGREEMENT

This Collaboration Agreement (this "Agreement") is entered into as of the 29th day of October 2009 (the "Effective Date"), by and among F. Hoffmann-La Roche Ltd, a Swiss corporation ("Roche Basel"), having a place of business at Grenzacherstrasse 124, CH-4070 Basel, Switzerland, and Hoffmann-La Roche Inc., a New Jersey corporation ("Roche Nutley"), having a place of business at 340 Kingsland Street, Nutley, New Jersey 07110, U.S.A. (Roche Basel and Roche Nutley, collectively, "Roche"), and Alnylam Pharmaceuticals, Inc., a Delaware corporation, having a place of business at 300 Third Street, 3rd Floor, Cambridge, Massachusetts 02142, U.S.A. ("Alnylam").

### INTRODUCTION

WHEREAS, Alnylam and Roche are parties to a License and Collaboration Agreement dated as of July 8, 2007, as supplemented by the letter agreement dated May 29, 2009 between the Parties (the "LCA"), pursuant to which Alnylam granted to Roche certain non-exclusive licenses to Alnylam's proprietary RNAi platform technology;

WHEREAS, pursuant to the LCA, Alnylam and Roche have agreed to pursue a collaboration regarding the Discovery and Development of potential RNAi Compounds directed to certain Targets through at least initiation of IND-Enabling Studies; and

WHEREAS, Alnylam and Roche desire to undertake a collaboration regarding an RNAi Product initially directed to the [\*\*], and to apply Alnylam's proprietary lipid nanoparticle (LNP) technology, Roche's proprietary dynamic polyconjugate (DPC) technology and other relevant technologies to such collaboration, on the terms and conditions of this Agreement.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants herein contained, the Parties hereby agree as follows:

### ARTICLE I

#### DEFINITIONS

The definitions are set forth on Exhibit A.

### ARTICLE II

#### MANAGEMENT OF COLLABORATIVE ACTIVITIES

Section 2.1. Joint Steering Committee. The Parties hereby establish a joint committee to facilitate the Collaboration as follows:

(a) Composition of the Joint Steering Committee. The Discovery and Development elements of the Collaboration shall be conducted under the direction of a joint steering committee (the "JSC") comprised of three (3) named representatives of Roche and three (3) named representatives of Alnylam or such other number of representatives as the Parties may from time to time mutually agree. Each Party shall appoint its respective representatives to the

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JSC from time to time, and may substitute one or more of its representatives, in its sole discretion, effective upon notice to the other Party of such change. Each Party shall have at least one JSC representative who is a senior employee (vice president level or above), and all JSC representatives shall have appropriate expertise and ongoing familiarity with the Collaboration. Each Party's respective representatives to the Joint Future Technology Committee may initially serve as such Party's representatives to the JSC hereunder. Additional representatives or consultants may from time to time, by mutual consent of the Parties, be invited to attend JSC meetings, provided such representatives' and consultants are subject to written obligations that are no less stringent than the confidentiality obligations and restrictions on use set forth in Article IX. All proceedings for the JSC shall take place in English. Each Party shall bear its own expenses relating to attendance at such meetings by its representatives.

(b) JSC Chairperson. The chairperson of the JSC (the "JSC Chairperson") shall rotate every twelve (12) months between Alnylam and Roche. The chairman of the Joint Future Technology Committee may serve as the initial JSC Chairperson. The JSC Chairperson's responsibilities shall include (i) scheduling meetings at least [\*\*] per Calendar Quarter, but more frequently if the JSC determines it necessary; (ii) setting agendas for meetings with solicited input from other members; and (iii) confirming and delivering minutes to the JSC for review and final approval.

(c) Meetings; Minutes. The first JSC meeting shall be held within [\*\*] days after the Effective Date, and the JSC shall meet in accordance with a schedule established by mutual agreement of the Parties, but no less frequently than [\*\*] each Calendar Quarter, with the location for such meetings alternating between Alnylam facilities in Massachusetts and Roche facilities in the U.S. (or such other locations as are determined by the JSC). Alternatively, the JSC may meet by means of teleconference, videoconference or other similar communications equipment, but at least [\*\*] meetings per Calendar Year shall be conducted in person. A secretary shall be appointed for each meeting and shall prepare minutes of the meeting, it being understood that the secretary and the JSC Chairperson shall not be representatives of the same Party (that is, if the JSC Chairperson is a representative of Roche, the secretary shall be a representative of Alnylam, and vice versa).

(d) JSC Responsibilities. The JSC shall have the following responsibilities with respect to the Collaboration, unless and until either Party exercises its Opt-Out Right or the JSC otherwise dissolves:

(i) reviewing, proposing to the Parties, and deciding, as necessary, (A) each annual update to the Joint Research Plan or the Development Plan, as applicable (with the goal of finalizing such annual update by [\*\*] of each Calendar Year), and (B) any modifications to the Joint Research Plan or the Development Plan, as applicable, in each case excluding any budgets;

(ii) regularly assessing, and updating the Parties as necessary on, the progress of the Parties in their conduct of the Joint Research Plan or the Development Plan, as applicable, against the timelines contained therein;

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- (iii) reviewing relevant data generated during the course of the Program and advising the Parties on general Development strategy and issues of priority;
- (iv) coordinating the Parties' efforts in the Discovery or Development of the Licensed Product(s) in the Field in the Territory, including regulatory matters;
- (v) establishing procedures for the calculation and maintenance of Development Costs incurred by each Party consistent with the guidelines set forth on Exhibit E;
- (vi) review, discuss and coordinate the scientific presentation and publication strategy relating to Licensed Products in the Field in the Territory prior to First Commercial Sale; and
- (vii) performing such other activities as the Parties agree in writing shall be the responsibility of the JSC.

For purposes of clarity, (I) it is expected that with respect to the sharing of information regarding the Licensed Product(s), each Party will, through the JSC and through regular communication between each Party's designated Alliance Manager (if the JSC remains in place), keep the other Party promptly informed at a reasonably detailed level about all activities related to the Discovery, Development, Manufacture and Commercialization of the Licensed Product(s) in the Field in each of the Major Market Countries and the rest of the Territory, and will promptly provide information reasonably requested of such Party by the other Party related thereto, and (II) the JSC shall have the authority to update or modify the Joint Research Plan or the Development Plan (in each case, excluding the budget), and to determine the allocation of resources among the various items set forth in the Joint Research Plan or Development Plan budget, provided that the JSC does not alter the overall budget or either Party's overall financial obligations under the Joint Research Plan or Development Plan, as applicable.

(e) Dissolution of JSC. The JSC shall be dissolved (i) if at the time of the First Commercial Sale of Licensed Product in the Territory there is no further Development contemplated for any Licensed Products for any indication beyond the indication approved on First Commercial Sale, or (ii) at such time as any exercise by either Party of its Opt-Out Right becomes effective under Section 4.9, in which case the JSC shall be dissolved solely with respect to the Opt-Out Product(s); provided that, after August 9, 2012, Alnylam shall have the right, but shall not be obligated, to participate on the JSC. If Alnylam elects not to participate in the JSC, then Roche shall have the right to make all decisions related to the Discovery and Development of Licensed Products under the Collaboration, subject to Section 2.5(d), Roche's diligence obligations under Article VIII, and other applicable terms and conditions of this Agreement.

#### Section 2.2. Joint Commercialization Team.

(a) Establishment of JCT. Commencing with the earlier of (x) initiation of the first Phase III Study of Licensed Product, and (y) the date [\*\*] prior to the anticipated launch of the first Licensed Product in the Territory, unless and until either Party exercises its Opt-Out Right, the Parties will establish a joint commercialization team ("JCT") to coordinate the Commercialization of the Licensed Product(s) in the United States. The provisions of Sections 2.1(a) (with each Party's respective representatives to the JSC initially serving as such Party's representatives to the JCT hereunder), 2.1(b) (with the chairman of the JSC serving as the initial JCT chairperson), 2.1(c) and 2.4 relating to the operation of the JSC shall also apply to the JCT.

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(b) Dissolution of the JCT. The JCT shall be dissolved solely with respect to the applicable Opt-Out Products upon the effective date of either Party's exercise of its Opt-Out Right; provided, however, that after August 9, 2012, Alnylam shall have the right, but not the obligation, to participate on the JCT. If Alnylam elects not to participate in the JCT, then Roche shall have the right to make all decisions related to the Commercialization of Licensed Products in the U.S. under the Collaboration, subject to Section 2.5(d), Roche's diligence obligations under Article VIII, and other applicable terms and conditions of this Agreement.

(c) JCT Responsibilities. The responsibilities of the JCT shall include:

- (i) reviewing, commenting on and advising the Parties on the initial Commercialization Plan;
- (ii) reviewing, proposing to the Parties, and deciding, as necessary, (A) each annual update to the Commercialization Plan (with the goal of finalizing such annual update by [\*\*] of each Calendar Year), and (B) any modifications to the Commercialization Plan, in each case excluding any budgets;
- (iii) regularly assessing, and updating the Parties as necessary on, the progress of the Parties in their conduct of the Commercialization Plan against the timelines contained therein;
- (iv) advising the Parties on general Commercialization strategy and issues of priority;
- (v) coordinating the Parties' efforts in the Commercialization of the Licensed Product(s) in the Field in the Territory, including regulatory matters;
- (vi) coordinating with the JSC regarding Development matters as necessary or appropriate to Commercialization of the Licensed Product(s) in the United States;
- (vii) performing such other activities as the Parties agree in writing shall be the responsibility of the JCT;
- (viii) coordinate the Parties' efforts with respect to the initiation and conduct of any Post-Approval Studies proposed to be conducted for Licensed Product(s) in the United States;
- (ix) review, discuss and coordinate the scientific presentation and publication strategy relating to Licensed Product(s) in the Field in the Territory following First Commercial Sale; and

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(x) attempting to resolve any and all disputes within the JCT's purview relating to the Commercialization of the Licensed Product(s) by consensus pursuant to Section 2.5.

(d) Limitations on JCT Authority. For purposes of clarity, the JCT shall have the authority to update or modify the Commercialization Plan (in each case, excluding the budget), and to determine the allocation of resources among the various items set forth in the Commercialization Plan budget, provided that the JCT does not alter the overall budget for the United States or either Party's overall financial obligations under the Commercialization Plan.

Section 2.3. Appointment of Subcommittees, Project Teams and Alliance Managers. The JSC shall be empowered to create such subcommittees of itself and project teams as it may deem appropriate or necessary. Each such subcommittee and project team shall report to the JSC, which shall have authority to approve or reject recommendations or actions proposed thereby subject to the terms of this Agreement. Each Party shall also designate an alliance manager (each, an "Alliance Manager"), who shall be responsible for the day-to-day coordination of the Collaboration and will serve to facilitate communication between the Parties. Each Party may change its designated Alliance Manager from time to time upon written notice to the other Party. Among the subcommittees contemplated, it is expected that the JSC will establish a joint project development team ("JPDT") to share information through regular communications regarding the Development of Licensed Product(s) in the Territory, a joint finance team ("JFT") regarding cost sharing and budgeting, and other joint teams as necessary regarding Manufacturing, patent and other matters. After August 9, 2012, Alnylam shall have the right, but not the obligation, to participate on any of the subcommittees contemplated in this Section 2.3.

Section 2.4. JSC and JCT Decisions by Consensus. Decisions within the purview of the JSC or, if applicable, the JCT shall be made by consensus, with the representatives of each Party collectively having one vote on behalf of such Party. For each meeting of the JSC or, if applicable, the JCT at least two (2) representatives of each Party shall constitute a quorum. Action on any matter may be taken at a meeting, by teleconference, videoconference or by written agreement, as may be mutually agreed by the Parties.

Section 2.5. JSC or JCT Deadlocks; Dispute Resolution; Decision-Making Authority.

(a) The JSC (or, if applicable, the JCT) shall attempt to resolve any and all disputes over any matter that is within such committee's purview relating to the Collaboration by consensus.

(b) If the JSC (or, if applicable, the JCT) is unable to reach a consensus with respect to a dispute within such committee's purview, then the dispute shall be submitted to escalating levels of Alnylam and Roche senior management for review. If such dispute cannot be resolved despite escalation, then the Executive Officers of Alnylam and Roche shall attempt to resolve such dispute.

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(c) If, despite the Executive Officers' efforts to resolve a dispute pursuant to clause (b), the Executive Officers cannot reach an agreement regarding such dispute within [\*\*] days after submission to them for resolution, then:

(i) unless either Party has exercised its Opt-Out Right hereunder, if the dispute relates to the Development of the Licensed Product(s) prior to First Phase II Completion, then [\*\*] shall have the final decision-making authority over operational matters related to any Clinical Study conducted by [\*\*];

(ii) unless either Party has exercised its Opt-Out Right hereunder, [\*\*] shall have final decision-making authority over Development and Commercialization activities that are specific to the ROW Territory so long as such decision does not materially negatively affect Development and Commercialization activities that are specific to the U.S.;

(iii) the Party that is responsible for booking sales in the U.S. shall have final decision-making authority over (A) the price and commercial terms of Licensed Product(s) in the U.S., (B) a policy governing the handling of all returns, recalls, order processing, invoicing and collection, distribution, and inventory and receivables for Licensed Product(s) in the U.S., (C) (1) any label or other written, printed or graphic matter upon (aa) any container or wrapper utilized with Licensed Product(s) in the U.S. or (bb) any written material accompanying any container or wrapper utilized with Licensed Product(s) in the U.S. including package inserts, and (2) any communication or program associated with the promotion of Licensed Product(s) in the U.S., including such communications and programs that (aa) specifically identify or describe Licensed Product(s) or (bb) otherwise support Licensed Product(s) or raise awareness of the Field, and (D) whether or not to recall or withdraw Licensed Product(s) in the U.S.; provided, however, that, such Party shall have the obligation to give due consideration to any recommendations or opinions offered by the other Party, consistent with the principle of setting the wholesale price of Licensed Product(s) to its maximum potential without regard to its effect on other products, to the extent permitted by applicable Laws; and

(iv) if the dispute does not fall within clause (i), (ii) or (iii) above, then neither Party may implement any activities that would result from resolution of the matter until consent of the other Party is achieved; it being understood that, in the event that either Party exercises its Opt-Out Right, the Continuing Party shall have final decision-making authority with respect the Discovery, Development, Commercialization and Manufacture of the Opt-Out Product(s), subject to Section 2.5(d), the Continuing Party's diligence obligations under Article VIII, and other applicable terms and conditions of this Agreement.

(d) Notwithstanding anything in this Agreement to the contrary, in no event may the JSC, the JCT or either Party have the unilateral right to amend any term of this Agreement. In addition, in no event shall either Party have the unilateral right to:

(i) increase the other Party's obligations or reduce the other Party's rights under this Agreement in connection with the Program Target(s) or Licensed Product(s), including any obligation to devote additional personnel or financial resources to a specific activity or project to be conducted by the other Party under the Joint Research Plan, Development Plan, or Commercialization Plan as applicable;

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- (ii) determine whether the events required for the payment of any event payments hereunder have occurred;
- (iii) determine whether a Party has fulfilled or breached any of its obligations under this Agreement;
- (iv) make a decision that is expressly stated in this Agreement to require the other Party's approval or consent, or the mutual agreement of the Parties; or
- (v) otherwise expand such Party's rights or reduce such Party's obligations under this Agreement in connection with the Program Target(s) or Licensed Product(s).

### ARTICLE III

#### LICENSE GRANTS; EXCLUSIVITY

Section 3.1. License Grants to Roche. Subject to the terms and conditions of this Agreement and to Alnylam Third Party Obligations:

(a) License During the Research Term. Alnylam hereby grants to Roche an exclusive, non-royalty-bearing right and license, with the right to grant sublicenses as set forth in Section 3.1(d), under Alnylam's rights to the Alnylam Technology, to perform the activities assigned to Roche under the Joint Research Plan in the Field in the Territory during the Research Term.

(b) License if Alnylam has not Opted-Out. Unless Alnylam exercises its Opt-Out Right (in which case Section 3.1(c) shall apply), subject to Alnylam's retained rights under Section 3.5, Alnylam hereby grants to Roche an exclusive right and license, with the right to grant sublicenses as set forth in Section 3.1(d), under Alnylam's rights to the Alnylam Technology, to Develop, Manufacture and Commercialize the Licensed Product(s) in the Field in the Territory. Such license shall be (i) subject to event payments pursuant to Section 9.1 and shall be royalty-bearing for the Royalty Term of each Licensed Product in each country of the ROW Territory as set forth in Section 9.3(a), and (ii) subject to the Parties' rights and obligations with respect to sharing of Profits and costs in the United States as set forth in Section 4.8 and Section 9.2.

(c) License if Alnylam Opts-Out. If Alnylam exercises its Opt-Out Right, Alnylam hereby grants to Roche an exclusive right and license, with the right to grant sublicenses as set forth in Section 3.1(d), under Alnylam's rights to the Alnylam Technology as has been incorporated into, or has been used in or (as documented in the Joint Research Plan, the Development Plan or the Commercialization Plan, or any approved JSC or JCT minutes, as applicable) has been intended for use in, the Development, Manufacture or Commercialization of the Licensed Product(s) under this Agreement as of the effective date of Alnylam's exercise of such Opt-Out Right, to Develop, Manufacture and Commercialize such Licensed Product(s) in the Field in the Territory. Such license shall be subject to event payments pursuant to Section 9.1 and shall be royalty-bearing for the Royalty Term of each Licensed Product in each country of the Territory as set forth in Section 9.3(b).

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(d) Roche Sublicense Rights.

(i) Roche shall have the right to grant sublicenses under the licenses granted to it pursuant to Sections 3.1(a), 3.1(b) and 3.1(c), and the right to grant licenses of its rights under any Joint Collaboration IP, to (x) an entity that is its Affiliate for so long as such entity remains an Affiliate of Roche and complies in all material respects with the obligations of Roche under this Agreement, or (y) to Third Party Contractors retained by Roche in accordance with Section 3.4. Roche hereby guarantees the full payment and performance of its Affiliates under this Agreement. In addition, Roche shall have the right to grant sublicenses under the licenses granted to it pursuant to Sections 3.1(a), 3.1(b) and 3.1(c), and the right to grant licenses of its rights under any Joint Collaboration IP, to Third Parties subject to the limitations of Section 3.1(d)(ii), Section 3.1(d)(iii) and Section 3.3.

(ii) Unless and until Alnylam has exercised its Opt-Out Right, and subject to Section 3.1(d)(iii), Roche shall not have any right to grant to any Third Party any sublicenses of its rights and the licenses granted to it under this Agreement, or any licenses under Roche's interest in any Joint Collaboration IP, in each case to Discover, Develop, Manufacture and Commercialize the Licensed Product(s) in the Field:

(A) for the United States, without the prior written consent of Alnylam; and

(B) for any of the Major EU Countries, without first notifying Alnylam of such proposed sublicense or license, on a sublicense-by-sublicense or license-by-license basis, including the Major EU Country(ies) proposed to be covered by the sublicense or license and any other terms as may be reasonably requested by Alnylam to allow Alnylam to decide whether or not to pursue the negotiation of such sublicense or license. If Alnylam notifies Roche within [\*\*] days after receipt of such notice from Roche that Alnylam does not want to pursue the negotiation of such sublicense (or Alnylam is silent during such 30-day period), Roche shall be free to negotiate and enter into a sublicense agreement with a Third Party for a period of [\*\*] months, after the expiration of which the terms of this Section 3.1(d)(ii)(B) shall once again apply. If Alnylam notifies Roche within such [\*\*]-day period that Alnylam desires to pursue such negotiations, the Parties shall negotiate in good faith and seek to finalize commercially reasonable terms of such sublicense or license within an additional [\*\*] days. If the Parties are able to finalize the terms of such sublicense within such [\*\*]-day period, the Parties shall enter into such agreement, either in the form of an amendment to this Agreement or a side letter, and the Development Plan or Commercialization Plan, as the case may be, shall be updated as necessary by mutual agreement of the Parties. If the Parties are unable to finalize the terms of such sublicense or license within such additional [\*\*]-day period, Roche may enter into negotiations with a Third Party with respect to such proposed sublicense or license; provided, however, that if the terms offered to such Third Party are more favorable in the aggregate to such Third Party than the terms last offered to Alnylam during the [\*\*]-day negotiation period set forth above, and Alnylam has at least comparable relevant capabilities as the respective sublicensee(s), then Roche shall first offer such more favorable terms to Alnylam.

(iii) Without limiting Section 3.1(d)(ii) above, any sublicenses granted by Roche hereunder shall be consistent with the sublicense terms and requirements under the LCA, and Roche shall provide Alnylam with reasonable notice of any such sublicense granted hereunder.

(e) Certain Limitations to Licenses Granted to Roche.

(i) The grants by Alnylam under Alnylam Technology set forth in Section 3.1 are subject to, and are limited to the extent of, the rights that Alnylam has previously granted and is required to grant under Alnylam Technology to Alnylam Pre-Existing Alliance Parties under the terms of the Alnylam Pre-Existing Alliance Agreements. As and to the extent that such rights previously granted to Alnylam Pre-Existing Alliance Parties under Alnylam Technology (whether such rights are previously or subsequently exercised) lapse, terminate or otherwise revert to Alnylam, they shall be automatically included in the rights under Alnylam Technology granted to Roche with respect to the Licensed Product(s) under Sections 3.1(a), 3.1(b) and 3.1(c) without any further consideration from Roche. For purposes of clarity, this Section 3.1(e)(i) is not intended to expand the rights or licenses granted to Roche if Alnylam exercises its Opt-Out Right prior to August 9, 2012, nor to expand the rights or licenses granted to Roche beyond those described in Section 3.1(c) or Section 14.5(b)(ix) (as applicable).

(ii) Roche acknowledges that an Alnylam Pre-Existing Alliance Party may from time to time request rights under Alnylam Technology with respect to a particular Target that Alnylam is required, pursuant to the terms of an Alnylam Pre-Existing Alliance Agreement, to grant such rights to such Alnylam Pre-Existing Alliance Party with respect to such Target.

(iii) For the avoidance of doubt, the grants by Alnylam under Alnylam Technology set forth in Sections 3.1(a), 3.1(b) and 3.1(c) include, subject to Section 3.1(f), the sublicense of Alnylam Technology that is not owned by Alnylam. Roche's rights and licenses under such Alnylam Technology are limited to the rights granted by Listed Alnylam Counterparties to Alnylam under the Listed Alnylam Third Party Agreements, and Roche shall comply, and cause its Affiliates and Licensee Partners to comply, with those restrictions and other terms applicable to sublicensees under such agreements, copies of which have been or will be made available to Roche, as applicable. Without limiting the generality of the foregoing, Roche acknowledges that certain obligations are imposed on sublicensees of certain of the sublicensed Alnylam Technology, and agrees to comply (to the extent access to obligations and requirements have been made available to Roche in unredacted form), and to require its Affiliates and Licensee Partners to comply, with such obligations and requirements. Notwithstanding the foregoing, at the request of Roche, which request shall be made within the [\*\*] period prior to First Commercial Sale of the first Licensed Product, Alnylam shall use commercially reasonable efforts to seek to harmonize the accounting and royalty reporting provisions under the Listed Alnylam Third Party Agreements with the accounting and royalty reporting provisions set forth in this Agreement.

(f) [\*\*] Patent Rights. Notwithstanding anything to the contrary herein, the licenses to Alnylam Patent Rights hereunder initially shall not include licenses to Patent Rights licensed by Alnylam or its Affiliates under the Non-Exclusive License Agreement between [\*\*] and Alnylam, dated [\*\*] (the "[\*\*] Agreement"), which Patent Rights Roche shall have the option, exercisable upon written notice to Alnylam at any time during the Term prior to August 9, 2012, to license solely with respect to Licensed Product(s) under this Collaboration. Upon such

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election, for no additional consideration from Roche (i) the license granted to Roche under Alnylam's rights to Alnylam Patent Rights pursuant to Sections 3.1(a), 3.1(b) and 3.1(c) of this Agreement shall include such Patent Rights with respect to the designated Licensed Product(s), and (ii) the [\*\*] Agreement shall be deemed a Listed Alnylam Third Party Agreement and Exhibit B-2 hereof shall be amended accordingly.

Section 3.2. License Grants to Alnylam. Subject to the terms and conditions of this Agreement:

(a) License During the Research Term. Roche hereby grants to Alnylam an exclusive, non-royalty-bearing right and license, with the right to grant sublicenses as set forth in Section 3.2(d), under Roche's rights to the Roche Technology, to perform the activities assigned to Alnylam under the Joint Research Plan in the Field in the Territory during the Research Term.

(b) License if Roche has not Opted-Out. Unless Roche exercises its Opt-Out Right (in which case Section 3.2(c) shall apply), Roche hereby grants to Alnylam an exclusive right and license, with the right to grant sublicenses as set forth in Section 3.2(d), under Roche's rights to the Roche Technology, to carry out Development, Commercialization and Manufacturing activities to the extent contemplated in the Development Plan, the Commercialization Plan, the Supply Agreement (as applicable) or as otherwise agreed by the Parties hereunder. Such license shall be subject to the Parties' rights and obligations with respect to sharing of Profits and costs in the United States as set forth in Section 4.8 and Section 9.2.

(c) License if Roche Opts-Out. If Roche exercises its Opt-Out Right, Roche hereby grants to Alnylam an exclusive right and license, with the right to grant sublicenses as set forth in Section 3.2(d), under Roche's rights to the Roche Technology as has been incorporated into, or has been used in or (as documented in the Joint Research Plan, the Development Plan or the Commercialization Plan, or any approved JSC or JCT minutes, as applicable) has been intended for use in, the Development, Manufacture or Commercialization of the Licensed Product(s) under this Agreement as of the effective date of Roche's exercise of such Opt-Out Right, to Develop, Manufacture and Commercialize such Licensed Product(s) in the Field in the Territory. Such license shall be subject to event payments pursuant to Section 9.1 and shall be royalty-bearing for the Royalty Term of each Licensed Product in each country of the Territory as set forth in Section 9.3(c).

(d) Alnylam Sublicense Rights.

(i) Alnylam shall have the right to grant sublicenses under the licenses granted to it pursuant to Sections 3.2(a), 3.2(b) and 3.2(c), and the right to grant licenses of its rights under any Joint Collaboration IP, to (x) an entity that is its Affiliate for so long as such entity remains an Affiliate of Alnylam and complies in all material respects with the obligations of Alnylam under this Agreement, and (y) to Alnylam's Third Party Contractors in accordance with Section 3.4. Alnylam hereby guarantees the full payment and performance of its Affiliates under this Agreement.

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(ii) Unless and until Roche has exercised its Opt-Out Right, Alnylam shall not have any right to grant to any Third Party any sublicenses of its rights and the licenses granted to it under this Agreement, or any licenses under Alnylam's interest in any Joint Collaboration IP, in each case to Discover, Develop, Manufacture and Commercialize the Licensed Product(s) in the Field in the Territory, without the prior written consent of Roche.

Section 3.3. Sublicensing Terms.

(a) Each sublicense agreement shall be consistent with the terms and conditions of this Agreement. Each Party shall remain liable to the other Party for each of such Party's (or its Affiliate's) sublicensees' failure to comply with all applicable restrictions, limitations and obligations under the sublicense agreement and this Agreement. No sublicense granted by a Party hereunder may be assigned, transferred or further sublicensed to any Third Party without the prior written consent of such Party.

(b) Each Party shall provide a redacted copy of any sublicense agreement entered into by such Party to the other Party (such redactions to exclude only the financial terms of such sublicense and other information normally redacted from a document filed with the U.S. Securities and Exchange Commission), (i) if such sublicense impacts upon one or more of the Major Market Countries, and (ii) upon request by such other Party, in any country other than a Major Market Country.

Section 3.4. Third Party Contractors. Either Party may perform its Collaboration responsibilities hereunder through the use of Third Party Contractors; provided that such Party shall remain primarily liable for such Party's obligations under this Agreement; and provided further that such Party shall ensure that any such Third Party Contractor is under an obligation to assign, or grant an exclusive, sublicensable license, to such Party under all Know-How, Patent Rights, and other intellectual property rights discovered, conceived, invented or reduced to practice by such Third Party Contractor pursuant to the conduct of such Party's Collaboration responsibilities hereunder and related to any Program Target, RNAi Product or Licensed Product hereunder.

Section 3.5. Retained Rights. Notwithstanding anything in this Agreement to the contrary, Alnylam retains all rights necessary under Alnylam Technology, and Roche retains all rights necessary under Roche Technology, to perform such Party's obligations and exercise such Party's rights under this Agreement, including conducting the activities assigned to such Party under the Joint Research Plan, Development Plan or Commercialization Plan, as the case may be.

Section 3.6. No Implied Licenses. Except as explicitly set forth in this Agreement, neither Party grants to the other Party any license, express or implied, under its intellectual property rights.

Section 3.7. Exclusivity Covenant. Subject to Alnylam Third Party Obligations and Section 15.15:

(a) During the Research Term and for a period of [\*\*] thereafter, neither Party nor such Party's Affiliates shall, except pursuant to this Agreement, directly or indirectly, conduct Development of, Manufacture or Commercialize, anywhere in the Territory, any Competitive Product, or grant any rights to a Third Party to do any of the foregoing.

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(b) After the Research Term, during the period of Development prior to the first Regulatory Approval in the Territory of a Licensed Product under the Program for the given Program Target(s) to which such Licensed Product is directed, neither Party nor such Party's Affiliates shall, except pursuant to this Agreement, directly or indirectly, conduct Development of, Manufacture or Commercialize, anywhere in the Territory, any Competitive Product directed to such given Program Target(s), or grant any rights to a Third Party to do any of the foregoing. Without limiting the foregoing exclusivity with respect to any Program Target(s) that remain in the Program, if either Party exercises its Opt-Out Right during such period of Development prior to the first Regulatory Approval for any Opt-Out Product(s) in the Territory and the other Party assumes the unilateral Development and Commercialization of such Opt-Out Product(s), the opting-out Party and its Affiliates shall not, except pursuant to this Agreement, directly or indirectly, conduct Development in a Phase II Study of, or Commercialize, anywhere in the Territory, any Competitive Product directed against the same Program Target(s) as the Opt-Out Product(s), or grant any rights to a Third Party to do any of the foregoing, for a period of [\*\*] from and after the effective date of such opt-out.

(c) For a period of [\*\*] after the first Regulatory Approval in the Territory for a Licensed Product under the Program for the given Program Target(s) to which such Licensed Product is directed, neither Party nor such Party's Affiliates shall, except pursuant to this Agreement, directly or indirectly, conduct Development in a Phase III Study of, or Commercialize, anywhere in the Territory, any Competitive Product directed to such given Program Target(s), or grant any rights to a Third Party to do any of the foregoing. Without limiting the foregoing exclusivity with respect to any Program Target(s) that remain in the Program, if either Party exercises its Opt-Out Right during such period of [\*\*] after the first Regulatory Approval for any Opt-Out Product(s) in the Territory and the other Party assumes the unilateral Development and Commercialization of such Opt-Out Product(s), the opting-out Party and its Affiliates shall not, except pursuant to this Agreement, directly or indirectly, conduct Development in a Phase III Study of, or Commercialize, anywhere in the Territory, any Competitive Product directed against the same Program Target(s) as the Opt-Out Product(s), or grant any rights to a Third Party to do any of the foregoing, for a period of [\*\*] from and after the effective date of such opt-out.

(d) For purposes of clarity, nothing in clause (a), (b) or (c) above is intended to prohibit the Party exercising the Opt-Out Right with respect to any Opt-Out Product(s) from continuing to Develop, Manufacture and Commercialize any Licensed Product(s) other than the Opt-Out Product(s), or from performing its Manufacturing obligations hereunder with respect to any Opt-Out Product(s), pursuant to, and in accordance with the terms of, this Agreement.

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COLLABORATION OVERVIEW; DEVELOPMENT OF LICENSED  
PRODUCT(S); OPT-OUT RIGHTS

Section 4.1. Collaboration Overview. During the Research Term, the Parties will collaborate in the initial Discovery and Development of an RNAi Product directed to [\*\*] or, subject to mutual agreement of the Parties pursuant to Section 4.3 with respect to an additional Program Target, another RNAi Product directed to both [\*\*] and such additional Program Target, in the Field in the Territory. Following the Research Term, subject to either Party's exercise of its Opt-Out Rights, the Parties will collaborate in the continued Development and Commercialization of the Licensed Product(s); provided that the Parties will Develop the Licensed Product(s) in the Field for the United States in accordance with the allocations of Development responsibilities set forth in the Development Plan as amended from time-to-time in accordance with Section 4.5; it being understood that Alnylam shall have operational responsibility for all Licensed Product Development activities prior to and through First Phase II Completion. For purposes of clarity, this Agreement does not contemplate the Development of multiple RNAi Products each directed to a different Program Target under the Collaboration, unless the Parties otherwise mutually agree to do so and mutually agree on the terms pursuant to which such Development of such RNAi Products may be undertaken. In addition the Agreement contemplates that the Parties will Develop the Licensed Product(s) for the U.S. and the Major EU Countries under a single global Development Plan governing Development of the Licensed Product(s) from IND-Enabling Studies onward; provided that none of Alnylam's participation rights or decision-making authority with respect to any activities under the Development Plan that are relevant for the U.S. shall be diminished by virtue of the Development Plan covering activities for both the U.S. and ROW Territory.

Section 4.2. Joint Research Plan; Amendments. The initial Discovery and pre-IND Enabling Development of the Licensed Product(s) shall be governed by the Joint Research Plan during the Research Term. In addition to annual updates or modifications to the Joint Research Plan decided by the JSC pursuant to Section 2.1(d), either Party may develop and submit to the JSC from time to time proposed amendments to the Joint Research Plan (excluding any amendment to the budget, which amendment shall require the approval of both Parties outside the JSC). Upon approval of such proposed amendments by the JSC (subject to the limitations set forth in Section 2.1(d)), the Joint Research Plan shall be amended accordingly.

Section 4.3. Selection of Program Targets.

(a) As of the Effective Date, the Parties have selected [\*\*] as the subject of the Program to be progressed by the Parties during the Research Term.

(b) Prior to [\*\*], Roche shall have the right to propose, in accordance with the remainder of this Section 4.3, additional Targets directed to [\*\*] until up to one (1) additional Target is accepted by Alnylam as a Program Target pursuant to Section 4.3(d) below. Notwithstanding anything in this Agreement to the contrary, Roche shall not have the right to propose any Blocked Target, VEGF or KSP for inclusion as a Program Target hereunder.

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(c) Alnylam shall submit any additional Target proposed by Roche in accordance with clause (b) above to Novartis in accordance with Section 2.6 of the LCA. Alnylam hereby waives, and Roche shall not be required to [\*\*] with respect to the Target proposed by Roche pursuant to this Section 4.3 which would otherwise have been payable to Alnylam pursuant to Section 2.6 of the LCA. If Roche submits multiple Targets simultaneously, then the Parties shall agree to present [\*\*] to Novartis, unless the Parties otherwise mutually agree that such [\*\*].

(d) Subject to Novartis' rejection or waiver of each proposed additional Target pursuant to clause (c) above, if Alnylam provides, in its sole discretion, written approval of such proposed additional Target (such approval not to be unreasonably withheld by Alnylam), such Target shall be deemed a Program Target for all purposes hereunder.

(e) If Novartis or Alnylam (approval not to be unreasonably withheld by Alnylam) rejects any proposed Target, Roche shall have the right to propose that an additional Target meeting the requirements set forth in Section 4.3(b) be included in the Program. If Roche does not propose any additional Target for inclusion as a Program Target by [\*\*], then Roche's right to propose an additional Program Target pursuant to this Section 4.3 shall have no further force or effect, and the sole subject of the Program and the Collaboration shall remain [\*\*]. Once the first such additional proposed Target is included in the Program, Alnylam shall have no obligation to waive, and Roche shall thereafter be obligated to [\*\*], unless the Parties otherwise mutually agree that such [\*\*] shall be waived.

(f) For purposes of clarity, while the Parties contemplate that Roche may use Alnylam Platform Patent Rights or Alnylam Platform Know-How under the LCA to perform activities with respect to the Program Target during the Term, any activities conducted with respect to a Program Target shall be conducted pursuant to this Agreement (and not pursuant to the LCA), and the terms of this Agreement (and not the LCA) shall govern the Parties' respective rights and obligations with respect to such Program Target and corresponding RNAi Products and Licensed Products, including financial obligations.

Section 4.4. Selection of Development Candidate. During the Research Term, using the candidate selection criteria set forth in the Joint Research Plan as a guide, each Party shall use Diligent Efforts to conduct studies under the Program with the goal of identifying at least one (1) RNAi Product directed to a Program Target (or, subject to Section 4.3, both Program Targets) that are suitable for advancement as a development candidate into IND-Enabling Studies under this Agreement. Within [\*\*] days following the completion of activities under the Joint Research Plan,

(a) the Parties may mutually agree on the selection of at least one (1) RNAi Product directed to a Program Target (or both Program Targets, if applicable) as a development candidate hereunder and on a Development Plan pursuant to which the Parties shall pursue the Development of such development candidate under the Program, in which event the Program, and each Party's rights and obligations under this Agreement, shall continue as to such RNAi Product(s) and such Program Target(s), subject to either Party's exercise of its Opt-Out Right(s); or

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(b) if the Parties are unable to mutually agree on the selection of at least one (1) development candidate hereunder, or are able to mutually agree on the selection of at least one (1) development candidate but are unable to mutually agree on a Development Plan for such development candidate, then (i) the Parties may agree to discontinue the Program, and all Discovery and Development activities hereunder, in which event this Agreement shall be terminated, subject to the Parties' mutual agreement on the terms of any necessary wind-down, or (ii) a Party may exercise its Opt-Out Right at Candidate Selection Stage with respect to a particular RNAi Product Developed under the Program during the Research Term pursuant to Section 4.9; provided, that, if a Party has no bona fide interest in pursuing the Program or any RNAi Product Developed under the Program, such Party shall have a good faith obligation to exercise its Opt-Out Right hereunder. Notwithstanding the above, in no event shall each Party progress the same development candidate separately because of being unable to mutually agree on a Development Plan for such development candidate.

Section 4.5. Development Plan; Amendments.

(a) Within [\*\*] days following the completion of activities under the Joint Research Plan, the Parties shall prepare an initial Development plan (as such plan may be updated or amended from time to time in accordance with this Agreement, the "Development Plan") that will cover Development activities commencing with IND-Enabling Studies through Phase I Completion with respect to the proposed development candidate(s) under the Program, including a [\*\*] budget for Development Costs. Each annual update to the Development Plan shall cover Development activities through completion of the next phase of Development and a [\*\*] budget (or longer, if the Development activities covered by the Development Plan extend for longer than [\*\*]).

(b) Unless and until either Party exercises its Opt-Out Right, in addition to annual updates or modifications to the Development Plan decided by the JSC pursuant to Section 2.1(d), either Party may develop and submit to the JSC from time to time proposed amendments to the Development Plan (excluding any amendment to the budget, which amendment shall require the approval of both Parties outside the JSC). Upon approval of such proposed amendments by the JSC (subject to the limitations set forth in Section 2.1(d)), the Development Plan shall be amended accordingly.

Section 4.6. Exchange of Know-How. During the Research Term, each Party shall make available to the other Party, at no cost or expense to such other Party, such Alnylam Know-How or Roche Know-How, as the case may be, as is requested by such other Party in connection with such other Party's performance of its obligations under the Joint Research Plan or in connection with the identification, evaluation or selection of development candidates. Upon selection of the first development candidate under this Agreement and thereafter during the Term, each Party shall make available to the other Party, at no cost or expense to such other Party, such Alnylam Know-How or Roche Know-How, as the case may be, as is requested by such other Party in connection with the Discovery, Development or Commercialization of Licensed Products hereunder, including all data from any and all clinical trials and preclinical studies and non-clinical development work for Licensed Products that are in existence as of the completion of all activities under the Joint Research Plan. Upon selection of the first development candidate under this Agreement and thereafter during the Term, each Party shall

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promptly update the other Party as to Alnylam Know-How or Roche Know-How, as the case may be, that has not previously been provided to such other Party under this Agreement, and shall promptly provide to such other Party any such additional Alnylam Know-How or Roche Know-How, as the case may be, as may be reasonably requested by such other Party.

Section 4.7. Records and Reports.

(a) Each Party will maintain scientific records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, which will fully and properly reflect all work done and results achieved in the performance of the Discovery, Development and Manufacturing activities with respect to the Licensed Product(s) by such Party and its permitted Third Party Contractors and permitted Licensee Partners. Each Party will [\*\*] under this Agreement. All such records, and the information disclosed therein, as well as all disclosures made pursuant to Sections 2.1(d), 4.6 and 4.7(b), will be maintained in confidence by the recipient in accordance with Article IX and will only be used for purposes of Discovery, Development, Manufacture and Commercialization of Licensed Product(s) under this Agreement.

(b) In addition to the other disclosure obligations set forth in this Section 4.7, at times and in a manner to be reasonably agreed by the Parties, each Party shall [\*\*] such disclosure. Upon the request of either Party, the other Party shall [\*\*] such Party; provided that in any such case the [\*\*]. If requested by either Party or the JSC, the Parties shall [\*\*] other Party. In addition to the foregoing, if required by a Regulatory Authority(ies) or if it is reasonably necessary for a Party or its Related Party(ies) to [\*\*] such Party. Section 4.7(b) shall apply [\*\*].

(c) For purposes of clarity, nothing in Section 4.6 or this Section 4.7 shall obligate a Party to disclose any Know-How or grant any rights to the other Party that are beyond the scope of the licenses granted to such other Party under Section 3.1, 3.2 or 14.5 (as applicable).

Section 4.8. Development Costs. During the Research Term, each Party shall be responsible for its own internal and out-of-pocket costs of performing activities assigned to such Party under the Joint Research Plan. Following the Research Term, unless and until either Party exercises its Opt-Out Right, the Parties shall each share fifty percent (50%) of Development Costs, as calculated in accordance with the Financial Appendix (Exhibit E).

Section 4.9. Opt-Out Right.

(a) Exercise of Opt-Out Right.

(i) Within [\*\*] days after any of the following stages of Development or Commercialization of a Licensed Product under the Program (each such stage, an "Opt-Out Point"), each Party shall have the right, in its sole discretion, to opt-out of further Development and Commercialization of the Licensed Product(s) under the Program, in its entirety or on a Licensed Product-by-Licensed Product basis (each such Licensed Product, an "Opt-Out Product"), by providing written notice to the other Party citing this Section 4.9(a):

(A) [\*\*];

[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

- (B) [\*\*];
- (C) [\*\*];
- (D) [\*\*]; and

(E) Thereafter on [\*\*] months prior written notice [\*\*] annually during the [\*\*] quarter of the other Party's fiscal year.

(ii) If a Party exercise its Opt-Out Right, then the other Party may (A) assume the unilateral Development and Commercialization of the Opt-Out Product(s), in which case such Party shall become the Continuing Party with respect to such Opt-Out Product(s); or (B) decide not to elect to assume such Development and Commercialization of the Opt-Out Product(s), in which case such Party shall be deemed to have terminated this Agreement at will pursuant to Section 14.4 solely with respect to such Opt-Out Product(s) (it being understood that the Parties shall have the right to continue to Collaborate on the Development and Commercialization of the remaining Licensed Product(s) under the Program subject to the terms and conditions of this Agreement).

(iii) Notwithstanding anything in this Agreement to the contrary, in no event shall either Party have the right to unilaterally Develop and Commercialize a Licensed Product beyond Phase I Completion at the same time that the Parties are also Collaborating on the Development and Commercialization of a Licensed Product in a Phase II Study or beyond hereunder.

(iv) For purposes of clarity, (A) no exercise by a Party of its Opt-Out Right shall constitute a breach of such Party's obligations under this Agreement, and (B) if a Party exercises its Opt-Out Right under this Section 4.9, then such Party shall be deemed to have opted-out of the Program, in its entirety or with respect to the Opt-Out Product(s), as applicable, for the entire Territory, regardless of whether any Licensed Product was being Developed under the Program for sale, or was being sold, in a particular part of the Territory.

(b) Effect of Opt-Out by a Party. If a Party exercises its Opt-Out Right, subject to the Continuing Party's right to terminate its licenses under Section 14.4 or 14.5(e), upon the effective date of such Party's exercise of its Opt-Out Right, the following shall occur:

(i) The Party that exercises its Opt-Out Right hereunder shall discontinue its participation, and shall have no further operational rights or obligations (except Manufacturing obligations hereunder, if any), with respect to the particular Opt-Out Product(s);

(ii) If applicable, the Parties shall perform a final reconciliation of applicable Profits, Development Costs and Commercialization Costs (as applicable) for the Opt-Out Product(s) under the Program pursuant to Exhibit E and neither Party shall have any further right to share in Profits, or any further obligation to share in Development Costs or Commercialization Costs (as applicable), with respect to such Opt-Out Product(s) pursuant to Sections 4.8 and 9.2; provided, however, that the Party that exercises its Opt-Out Right at or after First Phase II Completion shall remain responsible for its share of the costs of any Clinical Study(ies) conducted, or committed to be conducted, by the other Party with respect to such Opt-Out Product(s) at the time of the notice of the opt-out, through completion or earlier termination of such Clinical Study(ies);

(iii) If Roche is the Party opting out, the licenses granted to Roche under Section 3.1 for the given Opt-Out Product(s) shall terminate and, if Alnylam decides to continue to unilaterally pursue the Development and Commercialization of such Opt-Out Product(s) as the Continuing Party hereunder, (A) the license granted to Alnylam under Section 3.2(c) for the given Opt-Out Product(s) shall apply (subject to compliance with the financial obligations set forth therein) and (B) the terms of Sections 14.5(a)(iv), 14.5(a)(v), 14.5(a)(vi) and 14.5(a)(x) shall apply;

(iv) If Alnylam is the Party opting out, the licenses granted to Alnylam under Section 3.2 (or Section 14.5(a)(ix), as the case may be) for the given Opt-Out Product(s) shall terminate, and, if Roche decides to continue to unilaterally pursue the Development and Commercialization of such Opt-Out Product(s) as the Continuing Party hereunder, (A) the license granted to Roche under Section 3.1(c) (or Section 14.5(b)(ix), as the case may be) for the given Opt-Out Product(s) shall apply (subject to compliance with the financial obligations set forth therein), and (B) the terms of Sections 14.5(b)(iv), 14.5(b)(v), 14.5(b)(vi) and 14.5(b)(x) shall apply;

(v) Article VI (or the Supply Agreement) and Section 3.7 shall apply in accordance with its terms; and

(vi) As between the Parties, the Continuing Party (if any) shall have sole right and responsibility for the Development, Commercialization and (except to the extent that the opting-out Party remains responsible under Article VI or the Supply Agreement) Manufacture of the Opt-Out Product(s) in accordance with the terms of this Agreement, subject to diligence obligations pursuant to Section 8.2, provided, that such Continuing Party no longer be bound by the Development Plan or Commercialization Plan (as applicable).

## ARTICLE V

### COMMERCIALIZATION

Section 5.1. Commercialization Activities. Subject to the terms and conditions of this Agreement, the Commercializing Party or Commercializing Parties (as the case may be) shall be responsible for Commercializing the Licensed Product(s) in the Field in the Territory. Where Alnylam and Roche are both Commercializing Parties in the United States, unless otherwise mutually agreed by the Parties, Roche shall be responsible for booking sales in the U.S., which shall encompass setting the price and commercial terms of Licensed Product, as well as setting a policy governing the handling of all returns, recalls, order processing, invoicing and collection, distribution, and inventory and receivables for, Licensed Product(s) in the U.S.

Section 5.2. Commercialization Costs. If neither Party exercises its Opt-Out Right, then the Parties shall share in Profits and Commercialization Costs as set forth in Section 9.2; provided, however, that each Party shall be responsible for conducting the activities assigned to such Party under the Commercialization Plan, including all costs thereof.

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Section 5.3. Commercialization Plan.

(a) Unless and until either Party has exercised its Opt-Out Right, commencing no later than [\*\*] prior to the anticipated launch of the first Licensed Product, the Parties shall prepare and deliver to the JCT an initial written plan and budget that describes in detail the Commercialization activities (including pre-launch and launch activities, if applicable, but excluding Manufacturing activities which shall be addressed as set forth in Article VI) to be undertaken with respect to Licensed Product(s) in the United States in the next Calendar Year and the dates by which such activities are targeted to be accomplished (as such plan may be updated or amended from time to time in accordance with this Agreement, the “Commercialization Plan”). The Commercialization Plan (including the budget) shall allocate activities between the Parties, and shall contain sufficient detail with respect to Commercialization tactics and other matters to enable the JCT to conduct a meaningful review of the Commercialization Plan. The Parties shall seek to finalize the initial Commercialization Plan for the United States no later than [\*\*] prior to launch of the first Licensed Product in the United States. It is intended that the Commercialization Plan will contemplate that the Parties will co-promote Licensed Product in the United States in a manner that reflects each Parties’ capabilities and that is consistent with each Parties’ promotional efforts for its own products of similar market potential. The Parties shall negotiate in good faith a co-promotion agreement that is consistent with the terms of this Agreement, taking into account the Parties’ respective capabilities, including terms related to term of co-promotion activities, auditing of sales details, mechanisms to address underperformance and failure to perform details at agreed upon levels, sales force training, and other customary terms, with a view to finalizing and entering into such co-promotion agreement as soon as reasonably practicable.

(b) In addition to annual updates or modifications to the Commercialization Plan decided by the JCT pursuant to Section 2.2(c), either Party may develop and submit to the JCT from time to time proposed amendments to the Commercialization Plan (excluding any amendment to the budget, which amendment shall require the approval of both Parties outside the JCT). Upon approval of such proposed amendments by the JCT (subject to the limitations set forth in Section 2.2(d)), the Commercialization Plan shall be amended accordingly.

ARTICLE VI

MANUFACTURE AND SUPPLY

Section 6.1. Pre-Candidate Selection Supply. From and after the Effective Date and before Candidate Selection Stage, each Party will be responsible for supplying its own demands for API Bulk Drug Substance, Delivery Compound, and Formulated Bulk (as applicable) in quantities that are sufficient for the conduct of Discovery activities as defined in the Joint Research Plan.

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[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

Section 6.2. Supply for IND-Enabling Studies and Clinical Studies.

(a) Subject to Section 6.3 and Section 6.4, from and after Candidate Selection Stage, the Parties will agree on a single-source supply strategy and on which Party will be responsible for Manufacturing supplies for IND-Enabling Studies and Clinical Studies. The responsible Party will use Diligent Efforts, either itself or through Third Parties, to Manufacture, in accordance with applicable cGMP, pre-clinical and clinical supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable), in quantities that are reasonably sufficient for the conduct of Development of the Licensed Product(s) by the Parties under the Development Plan. If either Party exercises its Opt-Out Right and such Party has been the supplying Party for pre-clinical or clinical supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable), prior to the effective date of such opt-out, unless otherwise mutually agreed by the Parties, such Party shall be obligated to continue to undertake such Manufacturing until completion of the transfer of Manufacturing to the Continuing Party according to Section 6.4, but no longer than [\*\*\*], if Development is earlier than Phase I Completion, and no longer than [\*\*\*], if Development is after Phase I Completion. For purposes of clarity, upon either Party's exercise of its Opt-Out Right hereunder, the Continuing Party shall have the right to Manufacture API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, by itself (or any Related Party) or using a Third Party manufacturer.

(b) Each Party shall pay the supplying Party the following amounts (or the Parties shall share as Development Costs, as the case may be) for pre-clinical and clinical supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, as applicable: (i) if neither Party has exercised its Opt-Out Right, the supplying Party's FBMC in the United States and the supplying Party's FBMC in the ROW Territory, or (ii) if either Party has exercised its Opt-Out Right, subject to the principles set forth in Paragraph 6 of Exhibit D, the supplying Party's FBMC plus [\*\*\*] percent ([\*\*\*]%) for the entire Territory. A Party's FBMC for API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) supplied by such Party to the other Party pursuant to this Section 6.2 for Development in the United States shall be included as Development Costs.

(c) The terms of Exhibit D hereof (the "Supply Agreement Term Sheet") shall govern the Manufacture and supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) for pre-clinical and clinical Development purposes until such time as the Parties enter into a Supply Agreement hereunder.

Section 6.3. Supply Agreement. Subject to Section 6.4, the Parties contemplate that upon the earlier of (a) the effective date of either Party's exercise of its Opt-Out Right, or (b) initiation of the first Phase II Study under the Program, the Parties shall agree to commence discussions to finalize the terms of a supply agreement for clinical and commercial supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable) based on the Supply Agreement Term Sheet (the "Supply Agreement"). The Parties shall use Diligent Efforts to complete such discussions and execute the Supply Agreement within [\*\*\*] after either the exercise of a Party's Opt-Out Right or the initiation of the first Phase II Study, as the case may be. The transfer price for commercial supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable) shall be (i) if neither Party has exercised its Opt-Out Right, the supplying Party's FBMC in the United States

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and the supplying Party's FBMC plus [\*\*] percent ([\*\*]%) in the ROW Territory, or (ii) if either Party has exercised its Opt-Out Right, subject to the principles set forth in Paragraph 6 of Exhibit D, the supplying Party's FBMC plus [\*\*] percent ([\*\*]%) for the entire Territory. In no event shall any sale or transfer by the supplying Party of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product to the other Party under this Agreement be included in the calculation of Net Sales hereunder.

Section 6.4. Transition of Manufacturing Responsibilities to Continuing Party.

(a) The Parties contemplate that, at any time following the selection of a development candidate pursuant to Section 4.4 (but in no event later than First Phase II Completion), in lieu of Section 6.3 or 6.5, the Parties may agree to transfer responsibility for Manufacturing API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) to (i) one of the Commercializing Parties as may be mutually agreed by the Parties, (ii) if either Party has exercised its Opt-Out Right, the Continuing Party, or (iii) a Third Party manufacturer designated by such Commercializing Party or Continuing Party, as the case may be. The undertaking of such transfer shall not exceed a time period to be mutually agreed by the Parties.

(b) Promptly after a decision of the Parties pursuant to Section 6.4(a) to transfer Manufacturing of the API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable) to the Commercializing Party or to a Third Party supplier designated by the Commercializing Party, the other Party will transfer to the Commercializing Party or to such Third Party supplier all documents and Manufacturing information and other Know-How Controlled by such Party and used in the Manufacture of the API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product as of the date of such decision to transfer Manufacturing (as applicable) ("Manufacturing Technology").

(c) Unless and until either Party exercises its Opt-Out Right, the costs and expenses incurred in connection with any such transfer of Manufacturing Technology under this Section 6.4 shall be included as Development Costs or included in the calculation of Profit, as applicable. After such transition, unless and until either Party exercises its Opt-Out Right, the Commercializing Party's FBMC for API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) supplied for Development in the United States shall be included as Development Costs, and the Commercializing Party's FBMC for API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) supplied for Commercialization in the United States shall be included in the calculation of Profit as set forth on Exhibit E.

(d) From and after such time, if any, as responsibility for Manufacturing API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product is transitioned to the Commercializing Party, the Commercializing Party shall use Diligent Efforts to Manufacture or have Manufactured and supply sufficient quantities of the API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable) to enable such Party (or both Parties, if applicable) to respond on a timely basis to customer demand for the Licensed Product(s) in the Territory.

(e) Notwithstanding anything in this Agreement to the contrary, if, at any time prior to any transfer of Manufacturing responsibility for a particular API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable) to one Party hereunder, the Parties determine by mutual agreement that the Manufacture and supply of such API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable) by a Party to the other Party hereunder is no longer necessary in light of the Development or Commercialization activities and objectives under the Joint Research Plan, Development Plan or Commercialization Plan, as the case may be, and each Party's requirements and resources, such Party shall no longer be obligated to Manufacture and supply such API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable), or to undertake the transfer of Manufacturing technology or any other Manufacturing-related obligations related to such API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable), pursuant to this Article VI; provided, however, that this shall not relieve either Party of any of its other Manufacturing obligations hereunder.

Section 6.5. Backup Manufacturing Rights. Notwithstanding any of the foregoing in this Article VI, upon request by the purchasing Party at any time following the selection of a development candidate pursuant to Section 4.4 hereof, and at such purchasing Party's cost, the supplying Party shall enable the purchasing Party to purchase API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) directly from the supplying Party's existing Third Party suppliers in such a manner that such purchasing Party shall be assured of a secondary source of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) unless and until Manufacturing responsibility is transitioned to one Party under Section 6.3 or the supplying Party is relieved of its Manufacturing obligations pursuant to Section 6.3(e). If a Third Party supplier for the API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) does not exist or has not yet been established at the time of such request, or the purchasing Party reasonably determines that the supplying Party is otherwise unable to procure direct supply from such secondary source (e.g., due to the Third Party supplier's refusal to enter into a direct supply arrangement with the purchasing Party or due to the supplying Party's failure to promptly undertake necessary action), the supplying Party shall, upon the purchasing Party's request and at the supplying Party's cost, transfer all relevant Manufacturing Technology Controlled by such supplying Party and used in the Manufacture of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) as of the date of such request by the purchasing Party to a Third Party designated by the purchasing Party and reasonably acceptable to the supplying Party (such acceptance not to be unreasonably withheld, conditioned or delayed) to enable such Third Party designated manufacturer to supply to such purchasing Party the API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) as a secondary source and solely for purposes of this Agreement.

Section 6.6. Technical Regulatory Documentation. If the supplying Party is not the Lead Regulatory Party, then the supplying Party will be responsible for delivering all technical documentation necessary for regulatory submissions to the Lead Regulatory Party.

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Section 6.7. Auditing Rights. In addition to the provisions of financial audits regarding cost of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (FBMC) detailed in Section 9.6, both Parties grant to each other the right at any time and from time to time, upon reasonable advance notice and during business hours, as applicable, to inspect the manufacturing facilities of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product, including those of all possible sub-contractors (to the extent agreed to by such sub-contractors), which are engaged in the manufacture, preparation, shipping, processing or warehousing for the sole purpose of reviewing the other Party's compliance with applicable cGMP, reasonable quality assurance/control standards and applicable EH&S regulations agreed by the Parties in the quality agreement (cGMP agreement). Each Party shall bear its own out-of-pocket expenses and costs related to such audit.

## ARTICLE VII

### REGULATORY MATTERS

#### Section 7.1. Regulatory Filings.

(a) Except as may be otherwise specified by the JSC or JCT (as applicable), or as otherwise required for a Party to perform its obligations under this Agreement, unless and until either Party exercises its Opt-Out Right, Roche (or its Related Parties) shall be the holder of all Regulatory Approvals (including NDA submissions) for the Licensed Product(s) in the Territory; provided that Alnylam shall be the holder of all INDs and IND submissions for Licensed Product(s) in the Territory. The Party taking the lead with respect to a particular regulatory filing hereunder (each, the "Lead Regulatory Party") shall be Alnylam through First Phase II Completion and Roche thereafter, unless and until either Party exercises its Opt-Out Right, in which case the Continuing Party shall be the Lead Regulatory Party. Promptly following First Phase II Completion (or earlier in countries for which Roche is Lead Regulatory Party), Alnylam shall transfer to Roche all INDs and IND submissions for Licensed Product(s) in the Territory, to the extent permitted by applicable Laws and subject to Section 7.1(c).

(b) The Lead Regulatory Party shall have the right, with respect to regulatory activities within its purview, to (i) oversee, monitor and coordinate all regulatory actions, communications and filings with, and submissions to, each Regulatory Authority, (ii) be responsible for interfacing, corresponding and meeting with each Regulatory Authority, and (iii) be responsible for maintaining all applicable regulatory filings. The Lead Regulatory Party shall allow the other Party's representative(s) to attend Health Authority ("HA") meetings with respect to a Licensed Product, through Phase II Completion for such Licensed Product throughout the Territory and, solely with respect to the U.S., following Phase II Completion. The Lead Regulatory Party shall notify the other Party reasonably in advance of any such HA meeting(s) to permit the other Party a reasonable opportunity to prepare for and attend such meeting, and shall provide the other Party with copies of all material HA correspondence and relevant documents that the Lead Regulatory Party either receives from, or submits to, the HA throughout the Territory with respect to a Licensed Product.

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(c) Except as may be otherwise specified by the JSC or JCT (as applicable), or as otherwise required for a Party to perform its obligations under this Agreement, each Party and its Related Parties shall have the right to cross-reference all INDs, Regulatory Approvals and all other regulatory filings filed by the other Party or such other Party's respective Related Parties in the Territory with respect to the Development, Manufacture or Commercialization of the Licensed Product(s) by such Party hereunder. For purposes of clarity, following First Phase II Completion (or earlier in countries in which Roche is the Lead Regulatory Party), it is contemplated that Roche shall file all INDs and IND submissions directly with the appropriate Regulatory Authorities.

Section 7.2. Product Complaints; Pharmacovigilance.

(a) Each Party will maintain a record of any and all complaints it receives with respect to the Licensed Product(s), and will use Diligent Efforts to ensure that its Related Parties maintain such records. Each Party will notify the other Party in reasonable detail of any complaint it receives with respect to the Licensed Product(s) within sufficient time to allow the other Party and its Related Parties to comply with any and all regulatory and other requirements imposed upon them in any jurisdiction in which the Licensed Product(s) is being marketed or tested in Clinical Studies or Post-Approval Studies.

(b) In addition, each Party shall promptly notify the other Party if such Party becomes aware of any information or circumstance that is likely to have a material adverse effect on the Development, Manufacture or Commercialization of the Licensed Product(s) in the Territory. The Parties agree that they will execute a separate pharmacovigilance agreement ("Pharmacovigilance Agreement"), if legally required, specifying the procedure for the information exchange of adverse events which may occur during the Development of the first Licensed Product in the Territory.

Section 7.3. Product Withdrawals and Recalls. If any Regulatory Authority (a) threatens, initiates or advises any action against a Party or such Party's Affiliates or Licensee Partners to remove any Licensed Product(s) from the market in the Territory, or (b) requires or advises a Party or such Party's Affiliates or Licensee Partners to distribute a "Dear Doctor" letter or its equivalent regarding use of such Licensed Product(s) in the Territory, then such Party shall notify the other Party of such event within [\*\*] Business Days (or sooner if required by applicable Law) after such Party becomes aware of the action, threat, advice or requirement (as applicable). The Party that is responsible for booking sales in the U.S. shall decide whether to recall or withdraw such Licensed Product(s) in the U.S., and the Commercializing Party shall decide whether to recall or withdraw such Licensed Product(s) in any other territory, at such Party's own cost and expense; provided, however, that the Parties will discuss in good faith whether to recall or withdraw such Licensed Product(s), or to place a recalled or withdrawn Licensed Product(s) back on the market, in the relevant Territory. The deciding Party shall keep the other Party reasonably apprised of the efforts undertaken by such Party to recall or withdraw such Licensed Product(s), or to place such Licensed Product(s) back on the market, in the relevant Territory, and the other Party shall reasonably cooperate in such efforts.

Section 7.4. Regulatory Compliance. Each Party agrees that in performing its obligations under this Agreement, it shall comply in all material respects with all applicable FDA and other current international regulatory requirements and standards, including FDA's cGMP and Good Clinical Practices, and comparable foreign regulatory standards, and other applicable Laws.

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Section 7.5. Debarment.

(a) Each Party hereby certifies that it has not been debarred under the provisions of the Generic Drug Enforcement Act of 1992, 21 U.S.C. Sec. 335a(a) and (b). If during the term of this Agreement a Party or any of its employees engaged in the performance of activities under this Agreement (i) becomes debarred; or (ii) receives notice of an action or threat of an action with respect to its debarment ("Debarred Party"), at a time period when the Debarred Party is performing activities under this Agreement (and not if such Debarred Party only has a financial interest in the Agreement), then the Debarred Party (i) shall immediately notify the other Party, and (ii) shall immediately cease all activities relating to this Agreement, except to the extent permitted by applicable Laws and necessary to preserve the safety and welfare of any human subjects in any ongoing Clinical Studies.

(b) If a Party becomes debarred, or if a Party receives notice or otherwise becomes aware that (i) a debarment action has been brought against such Party or any of its employees engaged in the performance of activities under this Agreement; or (ii) such Party has been threatened with a debarment action, in each case other than if such Party only has a financial interest in the Agreement and is performing no activities under this Agreement, then the other Party shall have the right to terminate this Agreement immediately upon written notice to the Debarred Party.

(c) Each Party hereby certifies that it has not and will not use in any capacity the services of any individual, corporation, partnership or association which has been debarred under 21 U.S.C. Sec. 335(a) or (b) in the performance of any activities in connection with this Agreement. If a Party becomes aware of the debarment or threatened debarment of any individual, corporation, partnership or association providing services to such Party which directly or indirectly relate to the activities under this Agreement (but not if such Party only has a financial interest in the Agreement), then such Party shall notify the other Party immediately. Upon the receipt of such notice or if the other Party otherwise becomes aware of such debarment or threatened debarment (other than if such Party only has a financial interest in the Agreement), the other Party shall have the right to terminate this Agreement immediately upon written notice to such Party.

(d) Termination by a Party under this Section shall be deemed termination under Section 14.5(a) if the Debarred Party is Roche or Section 14.5(b) if the Debarred Party is Alnylam.

ARTICLE VIII

DILIGENCE

Section 8.1. General. Each of Alnylam and Roche shall use Diligent Efforts (a) to execute and to perform, or cause to be performed, the activities assigned to such Party under the Joint Research Plan and, unless and until either Party exercises its Opt-Out Right, under the

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Development Plan (as applicable), (b) with respect to technology Controlled by such Party, to apply, in the conduct of Discovery and Development activities under the Joint Research Plan or the Development Plan (as applicable), the technology that such Party believes to be the optimal technology to yield the desired results and data under the Program, and (c) to cooperate with the other in carrying out the Joint Research Plan and the Development Plan (as applicable), in each case in good scientific manner and in compliance with applicable Law, Good Clinical Practice and Good Laboratory Practice.

Section 8.2. Development and Commercialization. Subject to the obligation to update the JSC and JCT, and without limiting the generality of Section 8.1, unless and until either Party exercises its Opt-Out Right with respect to a particular Licensed Product(s), Roche will be solely responsible for, and with respect to the Major EU Countries shall use Diligent Efforts with respect to, the Development and Commercialization of such Licensed Product(s) in the Field in the ROW Territory. Without limiting the generality of the immediately foregoing sentence, the Commercializing Party(-ies) shall use Diligent Efforts to seek and obtain Regulatory Approval for the Licensed Product(s) in each Major Market Country, and to Commercialize the Licensed Product(s) in those countries in the Territory in which such Commercializing Party has obtained Regulatory Approval.

## ARTICLE IX

### FINANCIAL PROVISIONS

#### Section 9.1. Event Payments.

##### (a) Development Events.

(i) Until such time as either Party exercises its Opt-Out Right, Roche shall pay Alnylam [\*\*] percent ([\*\*]%) of the payments set forth in Column A below upon achievement of the corresponding event set forth below by or on behalf of Roche or any of its Related Parties.

(ii) If Alnylam unilaterally exercises its Opt-Out Right, Roche shall pay Alnylam an amount equal to [\*\*] percent ([\*\*]%) of the amount set forth in Column B, Column C, Column D or Column E in the chart below (as applicable) corresponding to the Opt-Out Point at which Alnylam exercised its Opt-Out Right, upon achievement of the corresponding event set forth below by or on behalf of Roche or any of its Related Parties from and after the effective date of Alnylam's exercise of such Opt-Out Right.

(iii) If Roche unilaterally exercises its Opt-Out Right, Alnylam shall pay Roche the following percentages of the amount set forth in Column B, Column C, Column D or Column E in the chart below (as applicable) corresponding to the Opt-Out Point at which Roche exercised its Opt-Out Right, upon achievement of the corresponding event set forth below by or on behalf of Alnylam or any of its Related Parties from and after the effective date of Roche's exercise of such Opt-Out Right:

(A) [\*\*] percent ([\*\*]%) if opt-out occurs at or before First Phase II Completion; and

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(B) [\*\*] percent ([\*\*]%) if opt-out occurs after First Phase II Completion.

Development Event	Payments (In US\$[**])				
	Column A	Column B	Column C	Column D	Column E
(1) Initiation of the first Phase I Study for Licensed Product	[**]	[**]	[**]	[**]	[**]
(2) Initiation of the first Phase II Study for Licensed Product	[**]	[**]	[**]	[**]	[**]
(3) Initiation of the first Phase III Study for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(4) Initiation of the first Phase III Study for Licensed Product for a second (2nd) Indication	[**]	[**]	[**]	[**]	[**]
(5) First filing of an NDA in the United States for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(6) First filing of an NDA in the EU or with the EMEA for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(7) First filing of an NDA in Japan for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(8) First filing of an NDA in the United States for Licensed Product for a second (2nd) Indication	[**]	[**]	[**]	[**]	[**]
(9) Regulatory Approval in the U.S. for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(10) Regulatory Approval in the EU or from the EMEA for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(11) Regulatory Approval in Japan for Licensed Product for the first (1st) Indication	[**]	[**]	[**]	[**]	[**]
(12) Regulatory Approval in the U.S. for Licensed Product for a second (2nd) Indication	[**]	[**]	[**]	[**]	[**]
<b>Total Development Event Payments</b>	[**]	[**]	[**]	[**]	[**]

The event payments set forth in this Section 9.1(a) are payable once for each Licensed Product to achieve the applicable event. If, upon achievement of a particular event for a Licensed Product, any previous (i.e., higher in the above table) event payment has not been paid for such Licensed Product, then each event payment payable upon achievement of any such previous event shall become payable with the payment of the event payment for the subsequent event then achieved. For purposes of clarity, if a Party opts-out, in no event shall the Continuing Party be responsible for payment of any previous event payment that was payable, but not paid, by the Party opting-out.

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[\*\*] = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

(b) Sales Events.

(i) Until such time as either Party exercises its Opt-Out Right, Roche shall pay Alnylam [\*\*] percent ([\*\*]%) of the amount set forth in Column A upon achievement of the corresponding event set forth below by or on behalf of Roche or any of its Related Parties.

(ii) If Alnylam unilaterally exercises its Opt-Out Right, Roche shall pay Alnylam [\*\*] percent ([\*\*]%) of the amount set forth in Column B, Column C, Column D or Column E below (as applicable) corresponding to the Opt-Out Point at which Alnylam exercised its Opt-Out Right, upon achievement of the corresponding event set forth below by or on behalf of Roche or any of its Related Parties from and after the effective date of Alnylam's exercise of such Opt-Out Right.

(iii) If Roche unilaterally exercises its Opt-Out Right, Alnylam shall pay Roche [\*\*] percent ([\*\*]%) of the amount set forth in Column B, Column C, Column D or Column E below (as applicable) corresponding to the Opt-Out Point at which Alnylam exercised its Opt-Out Right, upon achievement of the corresponding event set forth below by or on behalf of Alnylam or any of its Related Parties from and after the effective date of Roche's exercise of such Opt-Out Right.

<u>Sales Event</u>	Payments (In US\$[**])				
	Column A [**]	Column B [**]	Column C [**]	Column D [**]	Column E [**]
Aggregate Worldwide Annual Net Sales of all Licensed Products in the Territory equal to or greater than \$[**]	[**]	[**]	[**]	[**]	[**]
Aggregate Worldwide Annual Net Sales of all Licensed Products in the Territory equal to or greater than \$[**]	[**]	[**]	[**]	[**]	[**]
Total Sales Event Payments	[**]	[**]	[**]	[**]	[**]

(c) Achievement of Events. Where Roche is obligated to make a payment to Alnylam under Sections 9.1(a) or 9.1(b), Roche shall notify Alnylam within [\*\*] Business Days after achievement or occurrence of an event under Section 9.1(a) or 9.1(b), and Alnylam shall deliver an invoice reflecting such event and the payment amount to Roche. Where Alnylam is obligated to make a payment to Roche under Sections 9.1(a) or 9.1(b), Alnylam shall notify Roche within [\*\*] Business Days after achievement or occurrence of an event under Section 9.1(a) or 9.1(b), and Roche shall deliver to invoice reflecting such event and the payment amount to Alnylam. Each event payment under Section 9.1(a) and 9.1(b) shall be deemed earned as of the achievement or occurrence of the related event and, except as expressly provided otherwise pursuant to Section 9.1(a), shall be paid within [\*\*] days after such achievement or occurrence.

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(d) Event Payments Payable Only Once. Each event payment under this Section 9.1 shall be payable only once, upon the first achievement of the applicable event or, in the case of Section 9.1(b), upon the first achievement of the applicable Net Sales threshold in a given Calendar Year. If more than one of the sales events set forth in Section 9.1(b) first occurs based on sales of Licensed Product in the same Calendar Year, all of such event payments shall be paid for such Calendar Year.

Section 9.2. Profit-sharing and sharing of Commercialization Costs.

(a) Allocation of Profit and Commercialization Costs in the United States. If neither Party has exercised its Opt-Out Right, the Parties shall [\*\*] in Profit for as long as Licensed Product(s) are sold in the United States during the Term, as well as [\*\*] of the Commercialization Costs for as long as Licensed Product(s) are sold in the United States during the Term. Profit and Commercialization Costs shall be calculated in accordance with the Financial Appendix (Exhibit E).

(b) Effect of Opt-Out. For purposes of clarity, notwithstanding any of the foregoing in this Section 9.2, if either Party exercises its Opt-Out Right, and the other Party elects to continue Developing and Commercializing the Licensed Product(s), then (i) neither Party shall have any further rights or obligations to share in Profit and Commercialization Costs as set forth in clause (a) above, and (ii) the Party that is deemed the Commercializing Party with respect to such Licensed Product(s) under this Agreement shall be obligated to pay the other Party (A) event payments pursuant to Section 9.1 upon achievement by the Commercializing Party or its Related Parties of the relevant events with respect to such Licensed Product(s), and (B) royalties pursuant to Section 9.3 with respect to Net Sales of such Licensed Product(s) by such Commercializing Party or its Related Parties.

Section 9.3. Royalties.

(a) Ex-US Royalties Payable by Roche if Neither Party Opt-Out. Subject to the remainder of this Section 9.3, if neither Party has exercised its Opt-Out Right, Roche shall pay, or cause to be paid, to Alnylam the following royalties on Annual Net Sales of each Licensed Product in the ROW Territory during the Royalty Term:

Annual Net Sales of a Licensed Product in the ROW Territory during the applicable Calendar Year:	Incremental Royalty Rate Applicable to such Annual Net Sales
Less than or equal to \$[**]	[**]%
Greater than \$[**], but less than or equal to \$[**]	[**]%
Greater than \$[**], but less than or equal to \$[**]	[**]%
Greater than \$[**], but less than or equal to \$[**]	[**]%
Greater than \$[**], but less than or equal to \$[**]	[**]%
Greater than \$[**], but less than or equal to \$[**]	[**]%
Greater than \$[**]	[**]%

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By way of example, if Annual Net Sales of a Licensed Product are [\*\*] dollars and no deductions were to apply under the remainder of this Section 9.3, then the royalty payable by Roche to Alnylam under this Section 9.3(a) would be as follows:

[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
Total Royalty Due	=		[**]

(b) Worldwide Royalties Payable by Roche if Alnylam Opt-Out. Subject to the remainder of this Section 9.3, if Alnylam exercises its Opt-Out Right and Roche elects to continue Developing and Commercializing the Licensed Product(s), Roche shall pay, or cause to be paid, to Alnylam royalties on Annual Net Sales of each Licensed Product in the Territory during the Royalty Term, at the royalty rates set forth below corresponding to the Opt-Out Point at which Alnylam exercised its Opt-Out Right:

Annual Net Sales of a Licensed Product in the territory during the applicable Calendar Year	Column A [**]	Column B [**]	Column C [**]	Column D [**]
Less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**]	[**]	[**]	[**]	[**]

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By way of example, if Alnylam opted-out at First Phase II Completion and Annual Net Sales of a Licensed Product are [\*\*] dollars and no deductions were to apply under the remainder of this Section 9.3, then the royalty payable by Roche to Alnylam under this Section 9.3(b) would be as follows:

[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
Total Royalty Due	=		[**]

(c) Worldwide Royalties Payable by Alnylam if Roche Opts-Out. Subject to the remainder of this Section 9.3, if Roche exercises its Opt-Out Right and Alnylam elects to continue Developing and Commercializing the Licensed Product(s), then Alnylam shall pay, or cause to be paid, to Roche royalties on Annual Net Sales of each such Licensed Product in the Territory during the Royalty Term, at the following percentages of the royalty rates set forth below corresponding to the Opt-Out Point at which Roche exercised its Opt-Out Right:

- (i) [\*\*] percent ([\*\*]%) if opt-out occurs at or before First Phase II Completion; and
- (ii) [\*\*] percent ([\*\*]%) if opt-out occurs after First Phase II Completion.

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Annual Net Sales of a Licensed Product in the Territory during the applicable Calendar Year

	Column A	Column B	Column C	Column D
Less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**], but less than or equal to \$[**]	[**]	[**]	[**]	[**]
Greater than \$[**]	[**]	[**]	[**]	[**]

By way of example, if Roche opted-out at First Phase II Completion and Annual Net Sales of a Licensed Product are [\*\*] dollars and no deductions were to apply under the remainder of this Section 9.3, then [\*\*]% would be applied to the royalty rates set forth in Column B above and the royalty payable by Alnylam to Roche under this Section 9.3(c) would be as follows:

[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
Total Royalty Due	=	[**]	[**]

(d) Royalties Payable Only Once. For the avoidance of doubt, the Commercializing Party's obligation to pay royalties under this Section 9.3 is imposed only once with respect to the same unit of Licensed Product, including by reason of such Licensed Product being Covered by more than one Valid Claim of Alnylam Platform Patent Rights, Alnylam Patent Rights, Roche Patent Rights, Alnylam Collaboration Patent Rights, Roche Collaboration Patent Rights or Joint Collaboration Patent Rights.

(e) Expiration of Patent Coverage. If no Valid Claim of the Alnylam Platform Patent Rights, Alnylam Patent Rights, Roche Patent Rights, Alnylam Collaboration Patent Rights, Roche Collaboration Patent Rights or Joint Collaboration Patent Rights Covers a Licensed Product in a given country, and the Manufacture of such Licensed Product is not Covered by a Valid Claim of any such Patent Rights in the country of Manufacture, then the royalty rate applicable to such Licensed Product in such country shall be reduced to [\*\*] percent ([\*\*]%) of the applicable royalty rate set forth in Section 9.3(a), 9.3(b) or 9.3(c) (as applicable) for any remaining portion of the Royalty Term which applies to such Licensed Product in such country.

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(f) Royalty Stacking. The Commercializing Party shall be entitled to deduct, from the royalty payments payable by such Commercializing Party under Section 9.3(a), 9.3(b) or 9.3(c), as applicable, for a reporting period, [\*\*] percent ([\*\*]%) of Required Third Party Payments paid by such Commercializing Party with respect to Licensed Products during the applicable reporting period; provided that in no event shall a deduction under this Section 9.3(f) reduce any royalty payment payable by the Commercializing Party under Section 9.3(a), 9.3(b) or 9.3(c), as applicable, by more than [\*\*] percent ([\*\*]%).

(g) Payments in Respect of Third Party In-Licenses.

(i) In addition to any royalty set forth in Section 9.3(a), 9.3(b) or 9.3(c) which may be payable by Roche as the Commercializing Party during the Royalty Term, Roche shall reimburse Alnylam for [\*\*] percent ([\*\*]%) of all royalty payments payable (each such payment, a "Listed Third Party Payment," collectively, the "Listed Third Party Payments") to Third Parties pursuant to Listed Alnylam Third Party Agreements in respect of Net Sales of Licensed Products; provided that in no event shall the royalty payments payable by Roche as the Commercializing Party hereunder in respect of such Listed Third Party Payments in any reporting period exceed in the aggregate [\*\*] percent ([\*\*]%) of Net Sales of Licensed Products for such reporting period. The Parties shall cooperate to coordinate such reimbursements by Roche as the Commercializing Party in a manner that ensures all amounts payable by Roche hereunder pursuant to Listed Alnylam Third Party Agreements are paid in a timely manner and otherwise in compliance with such Third Party agreements.

(ii) Roche, if the Commercializing Party, shall have the right to have an independent public accountant reasonably acceptable to Alnylam audit Alnylam's books and records solely for purposes of verifying such Listed Third Party Payments, which right shall be exercisable [\*\*] per year solely with respect to records covering up to the [\*\*] Calendar Years prior to audit notification, upon reasonable advance notice and during Alnylam's business hours, subject to the confidentiality provisions of Article IX hereof. Audit results and findings shall be shared by the Parties. If the audit reveals an overpayment by Roche, as the Commercializing Party, under this Section 9.3(g), the amount of such overpayment shall be credited towards any future reimbursement amounts payable by Roche, as the Commercializing Party, under this Section 9.3(g), subject to Section 9.3(h). If the audit reveals an underpayment by Roche, Roche shall make up such underpayment within [\*\*] days. The failure of Roche to request verification of any Listed Third Party Payments hereunder within the [\*\*] Calendar Year period set forth above shall be deemed acceptance of the calculation of such Listed Third Party Payments.

(h) Deductions. Notwithstanding anything in this Agreement to the contrary, in no event shall total deductions under Sections 9.3(e) and 9.3(f) reduce any quarterly royalty payment by Roche as the Commercializing Party in respect of Net Sales of a given Licensed Product to less than [\*\*] percent ([\*\*]%) more than Alnylam owes with respect to royalty payments payable to Third Parties pursuant to Listed Alnylam Third Party Agreements based solely on Net Sales of such given Licensed Product. Alnylam (if Roche is the Commercializing Party) shall have the burden of demonstrating the amount of royalty payments payable to Third Parties pursuant to Listed Alnylam Third Party Agreements. Any deductions allowable under Sections 9.3(e) and 9.3(f) which cannot be used against any quarterly royalty payment payable by Roche as the Commercializing Party hereunder due to the foregoing limitation may be carried forward and used against future quarterly royalty payments that are payable by Roche as the Commercializing Party hereunder, subject to the limitation set forth above.

(i) Loss of Listed Third Party Agreements. If Roche is the Commercializing Party and Alnylam ceases to be a licensee of Alnylam Patent Rights under any Listed Alnylam Third Party Agreement other than as a result of any action or omission by Roche, and Roche directly licenses such terminated Patent Rights ("Terminated Patent Rights") from that Third Party, then Roche may deduct the full amount of any consideration paid to such Third Party for such license(s) that is attributable to Licensed Products Covered by such Terminated Patent Rights from any royalties otherwise payable to Alnylam hereunder; provided, that prior to Roche, as the Commercializing Party, entering into any such license of such Terminated Patent Rights from such Third Party, Roche shall notify Alnylam of its intent to do so and shall provide to Alnylam an opportunity to explain its rationale for ceasing to license such Terminated Patent Rights and Roche shall consider in good faith such rationale. If Roche does not agree with Alnylam's rationale, then, at Roche's request, Alnylam shall use commercially reasonable efforts to reinstate the license for such Terminated Patent Rights within a [\*\*] day period; provided, however, that Alnylam shall not be required to continue to undertake such efforts if the Third Party requires payments which are incremental to what would otherwise be owed to such Third Party had such Terminated Patent Rights not been terminated, or the imposition of additional terms and conditions. If Alnylam is unable to reinstate the license, then Roche, as the Commercializing Party, may obtain a direct license for such Terminated Patent Rights from such Third Party; provided, that in no event shall total deductions under this Section 9.3(i) reduce any quarterly royalty payment by Roche in respect of Net Sales of a given Licensed Product to less than the amount that Alnylam owes with respect to royalty payments payable to Third Parties pursuant to then-current Listed Alnylam Third Party Agreements based solely on Net Sales of such given Licensed Product.

(j) Duration of Royalty Payments; First Commercial Sale. The royalties payable under Section 9.3(a), 9.3(b) or 9.3(c), as applicable, shall be paid on a country-by-country basis on each Licensed Product commencing upon the occurrence of the First Commercial Sale of such Licensed Product until the expiration of the applicable Royalty Term for such Licensed Product. The Commercializing Party shall notify the other Party of the occurrence of First Commercial Sale of each Licensed Product within [\*\*] days after its occurrence.

(k) Payment of Royalty. The Commercializing Party shall calculate royalties on Net Sales quarterly as of March 31, June 30, September 30 and December 31 (each being the last day of an "Accounting Period") and shall pay royalties on Net Sales within the [\*\*] days after the end of each Accounting Period in which such Net Sales occur. Royalties on Net Sales shall be paid in U.S. Dollars.

(l) Reporting. With each payment the Commercializing Party shall provide in writing for the relevant Accounting Period the following information on a Licensed Product-by-Licensed Product and country-by-country basis, including without limitation the United States, each of the Major Market Countries, and each territory in the rest of world in which Licensed Product(s) are sold: (a) Adjusted Gross Sales; (b) Net Sales; (c) the total royalties payable for the applicable period; and (d) any other reasonable information necessary for Alnylam to comply with its reporting and payment obligations to Third Parties under Alnylam Third Party Obligations (if the Commercializing Party is Roche), subject to Alnylam's obligations under Section 3.1(e).

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(m) Currency Computation. Whenever calculating royalties requires conversion from any currency, the Commercializing Party shall make such conversion as follows:

(i) If Roche is the Commercializing Party, when calculating the Adjusted Gross Sales for countries other than the United States, Roche shall convert the amount of such sales in currencies other than Swiss Francs into Swiss Francs using for internal foreign currency translation Roche's then current standard practices actually used on a consistent basis in preparing its audited financial statements. Upon converting the amount of Adjusted Gross Sales into Swiss Francs, Roche shall convert into US Dollars (or other currency), using the daily rate (Reuters) at the last working day for the applicable period.

(ii) If Alnylam is the Commercializing Party, when calculating the Adjusted Gross Sales for countries other than the United States, Alnylam shall convert the amount of such sales directly into US Dollars (or other currency), using the daily rate (Reuters) at the last working day for the applicable period.

Section 9.4. Withholding Taxes. Any tax required to be withheld by the Commercializing Party under the laws of any country for the account of the other Party shall be promptly paid by such Commercializing Party for and on behalf of the other Party to the appropriate governmental authority, and such Commercializing Party shall furnish to the other Party with proof of payment of such tax. Any such tax actually paid on a Party's behalf shall be deducted from royalty payments due to such Party hereunder. The Commercializing Party shall assist the other Party in minimizing the withholding taxes applicable to any payment made by such Commercializing Party and in claiming tax refunds at the other Party's request.

Section 9.5. Financial Records. Each Party shall keep, and shall require its Affiliates and Licensee Partners to keep, for [\*\*] years, full, true and accurate books of account containing all particulars that may be necessary for the purpose of calculating all amounts payable under this Agreement or to verify compliance with this Agreement, including Development Costs, Commercialization Costs, Net Sales, FBMC, royalties, event payments, and other payments and the elements required to calculate Profit share, Development Cost share, Commercialization Cost share or royalty payments hereunder. Such books of accounts shall be kept at their principal places of business.

Section 9.6. Audits.

(a) At the expense of Alnylam, Alnylam has the right to engage an independent public accountant reasonably acceptable to Roche to perform, on behalf of Alnylam, an audit of such books and records of Roche and its Affiliates and Licensee Partners, that are deemed necessary by Alnylam's independent public accountant to verify amounts paid or payable under this Agreement for the period or periods requested by Alnylam and the correctness of any report or payments made under this Agreement. Upon timely request and at least [\*\*] Business Days' prior written notice from Alnylam, such audit shall be conducted in the countries specifically requested by Alnylam, during regular business hours in such a manner as to not unnecessarily

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interfere with Roche's (or its Affiliates' or Licensee Partners', as the case may be) normal business activities, and shall be limited to results in the [\*\*] Calendar Years prior to audit notification. Such audit shall not be performed more frequently than [\*\*] per Calendar Year nor more frequently than [\*\*] with respect to records covering any specific period of time. All information, data documents and abstracts herein referred to shall be used only for the purpose of verifying royalty statements and other amounts payable under this Agreement, or compliance with this Agreement, shall be treated as Confidential Information of Roche subject to the obligations of this Agreement and need neither be retained more than [\*\*] after completion of an audit hereof, if an audit has been requested; nor more than [\*\*] years from the end of the Calendar Year to which each shall pertain; nor more than [\*\*] after the date of termination of this Agreement. Audit results and findings shall be shared by the Parties. If the audit reveals an overpayment, Alnylam shall reimburse Roche for the amount of the overpayment within [\*\*] days. If the audit reveals an underpayment, Roche shall make up such underpayment within [\*\*] days with interest as set forth in Section 9.7. In addition, if the underpayment is equal to or greater than five percent (5%) of the amount that was otherwise due, Roche shall pay all of the costs of such audit. The failure of Alnylam to request verification of any royalty calculation within the period during which corresponding records must be maintained shall be deemed acceptance of the royalty reporting.

(b) At the expense of Roche, Roche has the right to engage an independent public accountant reasonably acceptable to Alnylam to perform, on behalf of Roche, an audit of such books and records of Alnylam and its Affiliates and Licensee Partners, that are deemed necessary by Roche's independent public accountant to verify amounts paid or payable under this Agreement for the period or periods requested by Roche and the correctness of any report or payments made under this Agreement. Upon timely request and at least [\*\*] Business Days' prior written notice from Roche, such audit shall be conducted in the countries specifically requested by Roche, during regular business hours in such a manner as to not unnecessarily interfere with Alnylam's (or its Affiliates' or Licensee Partners', as the case may be) normal business activities, and shall be limited to results in the [\*\*] Calendar Years prior to audit notification. Such audit shall not be performed more frequently than once per Calendar Year nor more frequently than [\*\*] with respect to records covering any specific period of time. All information, data documents and abstracts herein referred to shall be used only for the purpose of verifying royalty statements and other amounts payable under this Agreement, or compliance with this Agreement, shall be treated as Confidential Information of the audited Party subject to the obligations of this Agreement and need neither be retained more than [\*\*] after completion of an audit hereof, if an audit has been requested; nor more than [\*\*] years from the end of the Calendar Year to which each shall pertain; nor more than [\*\*] after the date of termination of this Agreement. Audit results and findings shall be shared by the Parties. If the audit reveals an overpayment, Roche shall reimburse Alnylam for the amount of the overpayment within [\*\*] days. If the audit reveals an underpayment, Alnylam shall make up such underpayment within [\*\*] days with interest as set forth in Section 9.7. In addition, if the underpayment is equal to or greater than five percent (5%) of the amount that was otherwise due, Alnylam shall pay all of the costs of such audit. The failure of Roche to request verification of any royalty calculation within the period during which corresponding records must be maintained shall be deemed acceptance of the royalty reporting.

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Section 9.7. Late Payments. A Party shall pay the other Party interest on the aggregate amount of any payments payable by such Party that are not paid on or before the date such payments are due under this Agreement at a rate per annum equal to the lesser of the one month London Interbank Offering Rate of interest plus one percent (1%), as reported by The Wall Street Journal for the applicable period, or the highest rate permitted by applicable Law, calculated on the number of days such payment is delinquent.

## ARTICLE X

### INTELLECTUAL PROPERTY OWNERSHIP, PROTECTION AND RELATED MATTERS

Section 10.1. Inventorship. Inventorship for patentable inventions conceived or reduced to practice during the course of the performance of activities pursuant to this Agreement shall be determined in accordance with United States patent laws for determining inventorship.

#### Section 10.2. Ownership of Collaboration IP.

(a) Subject to the licenses and rights granted to Roche under this Agreement, Alnylam shall own the entire right, title and interest in and to Alnylam Collaboration IP. Subject to the licenses and rights granted to Alnylam under this Agreement, Roche shall own the entire right, title and interest in and to Roche Collaboration IP.

(b) The Parties shall jointly own any Joint Collaboration IP. Subject to (a) the rights granted to each Party under this Agreement, including the licenses granted to a Party under Section 3.1(c) or Section 3.2(c) and patent prosecution, maintenance and enforcement rights and obligations of each Party hereunder, (b) the restrictions on licensing set forth in Sections 3.1(d) and 3.2(d), (c) the exclusivity obligations of the Parties set forth in Section 3.7, and (d) the payment obligations set forth in Section 4.8 and Article VII, each Party shall have the right to use, sell, keep, license, sublicense or assign its interest in Joint Collaboration IP (except for Product Specific Know-How or Product Specific Patent Rights) and otherwise undertake all activities a sole owner might undertake with respect to such Joint Collaboration IP (except for Product Specific Know-How or Product Specific Patent Rights) without the consent of and without accounting to the other Party.

#### Section 10.3. Prosecution and Maintenance of Patent Rights.

(a) Roche Technology (Other than Product Specific Patent Rights). Roche shall have the sole right to, at Roche's discretion, file, prosecute, and maintain (including the defense of any interference or opposition proceedings) all Patent Rights comprising Roche Technology (other than Roche Collaboration Patent Rights that constitute Product Specific Patent Rights) in Roche's name.

(b) Alnylam Technology (Other than Product Specific Patent Rights). Alnylam shall have the sole right to, at Alnylam's discretion, file, prosecute, and maintain (including the defense of any interference or opposition proceedings) all Patent Rights comprising Alnylam Technology (other than Alnylam Collaboration Patent Rights that constitute Product Specific Patent Rights) in Alnylam's name.

(c) Product Specific Patent Rights.

(i) Roche shall have the first right, but not the obligation, to, at Roche's discretion, file, prosecute, and maintain (including the defense of any interference or opposition proceedings) Roche Collaboration Patent Rights that constitute Product Specific Patent Rights. Roche shall provide to Alnylam copies of all prosecution filings related to such Product Specific Patent Rights sent to or received from patent offices in the Territory, unless otherwise directed by Alnylam, and, with respect to patent applications containing such Product Specific Patent Rights having information not previously filed that is intended to be submitted to patent offices in the Territory, shall use reasonable efforts to provide Alnylam with a draft of each such filing reasonably in advance of submission and shall consider in good faith any comments regarding such draft application that Alnylam may timely provide. If Roche decides (A) not to file a patent application on Roche Collaboration Know-How that would contain Product Specific Know-How, (B) to abandon prosecution of any Roche Collaboration Patent Right that would constitute a Product Specific Patent Right, or (C) not to otherwise maintain or extend any such Product Specific Patent Right, Roche shall give Alnylam written notice sufficiently in advance of any loss of rights to allow Alnylam to file, prosecute, maintain or extend, as the case may be, such Product Specific Patent Rights, in Roche's name.

(ii) Alnylam shall have the first right, but not the obligation, to, at Alnylam's discretion, file, prosecute, and maintain (including the defense of any interference or opposition proceedings) Alnylam Collaboration Patent Rights that constitute Product Specific Patent Rights. Alnylam shall provide to Roche copies of all prosecution filings related to such Product Specific Patent Rights sent to or received from patent offices in the Territory, unless otherwise directed by Roche, and, with respect to patent applications containing such Product Specific Patent Rights having information not previously filed that is intended to be submitted to patent offices in the Territory, shall use reasonable efforts to provide Roche with a draft of each such filing reasonably in advance of submission and shall consider in good faith any comments regarding such draft application that Roche may timely provide. If Alnylam decides (A) not to file a patent application on Alnylam Collaboration Know-How that would contain Product Specific Know-How, (B) to abandon prosecution of any Alnylam Collaboration Patent Right that would constitute a Product Specific Patent Right, or (C) not to otherwise maintain or extend any such Product Specific Patent Right, Alnylam shall give Roche written notice sufficiently in advance of any loss of rights to allow Roche to file, prosecute, maintain or extend, as the case may be, such Product Specific Patent Rights, in Alnylam's name.

(d) Joint Collaboration Patent Rights.

(i) Alnylam shall have the first right, but not the obligation, to, at Alnylam's discretion, file, conduct prosecution, and maintain (including the defense of any interference or opposition proceedings), all Joint Collaboration Patent Rights, in the names of both Alnylam and Roche. Roche shall use Diligent Efforts to make available to Alnylam or its authorized attorneys, agents or representatives, such of its employees as Alnylam in its reasonable judgment deems necessary in order to assist it in obtaining patent protection for such Joint Collaboration Patent Rights. Each Party shall sign, or use Diligent Efforts to have signed, all legal documents reasonably necessary to file and prosecute patent applications or to obtain or maintain patents in respect of such Joint Collaboration Patent Rights, at its own cost.

(ii) If Alnylam elects not to seek or continue to seek or maintain patent protection on any Joint Collaboration IP in the Territory, Roche shall have the right to, at Roche's discretion, to seek, prosecute and maintain in any country in the Territory patent protection on such Joint Collaboration IP in the names of both Alnylam and Roche. Alnylam shall use Diligent Efforts to make available to Roche its authorized attorneys, agents or representatives, such of Alnylam's employees as are reasonably necessary to assist Roche in obtaining and maintaining the patent protection described under this Section 10.3(d) (ii). Alnylam shall sign or use Diligent Efforts to have signed all legal documents reasonably necessary to file and prosecute such patent applications or to obtain or maintain such patents.

(iii) With respect to Joint Collaboration Patent Rights, the Party filing, prosecuting and maintaining such Patent Rights shall provide the other Party, within [\*\*] Business Days after submitting or receiving such filings or correspondence, with copies of all filings and correspondence submitted to and received from patent offices in the Territory and, with respect to substantive filings and correspondence to be submitted to patent offices in the Territory, shall use reasonable efforts to provide the other Party with drafts of such filings and correspondence reasonably in advance of submission and shall consider in good faith any comments regarding such filings and correspondence that the other Party may timely provide.

(e) Effects of Opt-Out. Notwithstanding any of the foregoing in this Section 10.3, if either Party exercises its Opt-Out Right, then the Continuing Party shall have the first right, but not the obligation, to, at such Continuing Party's discretion, file, prosecute, and maintain (including the defense of any interference or opposition proceedings) all Alnylam Collaboration Patent Rights, Roche Collaboration Patent Rights and Joint Collaboration Patent Rights, in each case solely to the extent that such Patent Rights constitute Product Specific Patent Rights. The Party that is not the Continuing Party shall have the step-in rights described in Section 10.3(c) or Section 10.3(d), as applicable.

(f) Patent Term Extensions. The Parties shall cooperate, if necessary and appropriate, with each other in gaining patent term extensions (including those extensions available under U.S. Drug Price Competition and Patent Term Restoration Act of 1984, the Supplementary Certificate of Protection of Member States of the EU and other similar measures in any other country) wherever applicable to Patent Rights Controlled by either Party that Cover the Licensed Product(s) in the Territory. The Parties shall, if necessary and appropriate, use reasonable efforts to agree upon a joint strategy relating to patent term extensions, but, in the absence of mutual agreement with respect to any extension issue, the patent or the claims of the patent shall be selected on the basis of the scope, enforceability and remaining term of the patent in the relevant country or region. All filings for such extensions shall be made by the Party responsible for filing, prosecuting and maintaining such Patent Rights in accordance with this Section 10.3.

(g) Patent Expenses. The patent filing, prosecution and maintenance expenses incurred after the Effective Date with respect to Patent Rights ("Patent Expenses") relating to Alnylam Technology and Roche Technology shall be borne by the Party responsible for filing, prosecuting and maintaining such Patent Rights under this Section 10.3, and any Patent Expenses related to Joint Collaboration Patent Rights shall be shared equally by the Parties.

Section 10.4. Third Party Infringement.

(a) Notices. Each Party shall promptly report in writing to the other Party any (i) known or suspected infringement of any Alynlam Technology or Roche Technology being used in the Collaboration, including any Joint Collaboration IP, or (ii) unauthorized use or misappropriation of any Confidential Information or Know-How of a Party by a Third Party of which it becomes aware, in each case only to the extent relevant to the Development, Manufacture or Commercialization of the Licensed Product(s) and involving a Competitive Product (“Competitive Infringement”) in the Territory, and shall provide the other Party with all available evidence supporting such infringement, or unauthorized use or misappropriation.

(b) Rights to Enforce.

(i) First Right to Enforce. Subject to Sections 10.4(b)(ii) and 10.4(iii), the Commercializing Party shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-How, comprising the Commercializing Party’s Patent Rights, Know-How, or Collaboration IP. Notwithstanding anything contained herein to the contrary, and subject to Sections 10.4(b)(ii) and 10.4(iii), outside the U.S., the Commercializing Party shall have the first right to initiate an infringement or other appropriate suit against any Third Party with respect to a Competitive Infringement in the Territory of any Product Specific Patent Rights or Product Specific Know-How regardless of which Party Controls such Product Specific Patent Rights or Product Specific Know-How. If both Parties are Commercializing Parties in the U.S., then Roche shall have the sole and exclusive right to initiate an infringement or other appropriate suit.

(ii) Requests to Initiate Enforcement Action. If the Commercializing Party, or Roche in the case of co-Commercialization in the U.S., elects not to initiate such suit with respect to any such Product Specific Patent Rights or Product Specific Know-How Controlled by Alynlam, or otherwise does not commence suit with respect to such Product Specific Patent Rights or Product Specific Know-How within [\*\*] days, reduced to [\*\*] days in the case of a certification filed pursuant to 21 U.S.C. §355(b)(2)(A)(iv) or 355(j)(2)(A)(vii)(IV), then the non-Commercializing Party shall have the right to initiate such suit with respect to such Product Specific Patent Rights or Product Specific Know-How and to join the Commercializing Party as a party if required.

(iii) Effect of Opt-Out. Notwithstanding any of the foregoing in this Section 10.4, if either Party exercises its Opt-Out Right, then the Continuing Party shall have the first right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-How, comprising Alynlam Collaboration IP, Roche Collaboration IP or Joint Collaboration IP, as the case may be, that constitute Product Specific Patent Rights or Product Specific Know-How. The Party that is not the Continuing Party shall have the right to request that the Continuing Party initiate action as described above in clause (ii).

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(c) Procedures; Expenses and Recoveries.

(i) The Party having the right to initiate any infringement suit under Section 10.4(b) shall have the sole and exclusive right to select counsel for any such suit and shall pay all expenses of the suit, including attorneys' fees and court costs and reimbursement of the other Party's reasonable out-of-pocket expense in rendering assistance requested by the initiating Party; provided that with respect to any such suit, the Parties may mutually agree to jointly bear such costs and expenses, in which case the allocation of recoveries described below may be adjusted as mutually agreed by the Parties. If required under applicable Law in order for the initiating Party to initiate or maintain such suit, or if either Party is unable to initiate or prosecute such suit solely in its own name or it is otherwise advisable to obtain an effective legal remedy, in each case, the other Party shall join as a party to the suit and will execute and cause its Affiliates to execute all documents necessary for the initiating Party to initiate litigation to prosecute and maintain such action. In addition, at the initiating Party's request, the other Party shall provide reasonable assistance to the initiating Party in connection with an infringement suit at no charge to the initiating Party except for reimbursement by the initiating Party of reasonable out-of-pocket expenses incurred in rendering such assistance. The non-initiating Party shall have the right to participate and be represented in any such suit by its own counsel at its own expense.

(ii) If the Parties obtain from a Third Party, in connection with such suit, any damages, license fees, royalties or other compensation (including any amount received in settlement of such litigation) in respect of a Competitive Infringement in the ROW Territory (if neither Party has exercised its Opt-Out Right) or the entire Territory, such amounts shall be allocated, subject to any adjustment to such allocation agreed by the Parties in connection with an agreement to jointly bear the costs and expenses of the infringement action as described above, as follows:

(A) first, to reimburse each Party for all expenses of the suit incurred by such Party, including attorneys' fees and disbursements, court costs and other litigation expenses; and

(B) then, [\*\*] percent ([\*\*]%) of the remainder to be paid to the Party initiating the suit and [\*\*] percent ([\*\*]%) of the remainder to be paid to the other Party.

(iii) With respect to any such suit in the United States (if neither Party has exercised its Opt-Out Right), any damages, license fees, royalties or other compensation (including any amount received in settlement of such litigation) in respect of a Competitive Infringement in the United States, shall be included in the calculation of Development Cost or Commercialization Cost, as applicable.

Section 10.5. Claimed Infringement; Third Party Challenges to Patent Rights.

(a) If a Party (i) becomes aware of any claim that the Development, Manufacture or Commercialization of the Licensed Product(s) in the Territory infringes the Patent Rights of any Third Party or (ii) receives any notices regarding or becomes party to any action in which a Third Party challenges or denies the validity or enforceability of any Patent Rights licensed to the other Party hereunder, or any claim thereof (A) Controlled by such Party in the United States, (B) Covering Licensed Product, (C) specific to Licensed Product and (D) not broadly applicable to RNAi Products, such Party shall promptly notify the other Party.

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(b) With respect to any matter described in the foregoing clause (a)(i), in any such instance, the Parties shall cooperate and shall mutually agree upon an appropriate course of action, which may include settlement of such claim. Each Party shall have an equal right to participate in any settlement discussions that are held with such Third Parties.

(c) If there is a dispute between the Parties as to whether or not Third Party Patent Rights at issue in such matter described in the foregoing clause (a)(i) Cover Licensed Product, the Parties agree to select an independent patent counsel to decide whether or not the subject Third Party Patent Rights Cover Licensed Product. The Parties agree that if such patent counsel determines that such Third Party Patent Rights Cover Licensed Product, they will accept such determination for purposes of calculating Commercialization Costs under Section 9.2 or royalties under Section 9.3, as the case may be. If the decision is that such Third Party Patent Rights do not Cover Licensed Product, either Party may still obtain a license, but shall be solely responsible for any payment obligations to the Third Party.

(d) With respect to any matter described in the foregoing clause (a)(ii), the Parties shall cooperate and shall mutually agree upon an appropriate course of action, and the Party responsible for filing, prosecuting and maintaining such Patent Rights pursuant to Section 10.3 shall have responsibility for defending the patentability, validity or enforceability of such Patent Rights in such action. If neither Party has exercised its Opt-Out Right, the reasonable out-of-pocket costs incurred by the defending Party or any of its Related Parties with respect to such action described in the foregoing clause (a)(ii) shall be included in Commercialization Costs as set forth in Section 5.2. For the avoidance of doubt, the costs incurred by a defending Party or any of its Related Parties with respect to an action of the kind described in the foregoing clause (a)(ii), but with respect to Patent Rights outside the United States, shall be borne solely by the Party defending such action; provided that, if such matter arises in the context of an action brought by a Party pursuant to Section 10.4, the costs of such action shall be borne as provided in Section 10.4.

(e) Each Party shall also provide to the other Party copies of any other notices it receives or has received from Third Parties regarding any patent nullity actions, any declaratory judgment actions and any alleged infringement or misappropriation of Third Party intellectual property relating to the Development, Manufacture or Commercialization of Licensed Product in the Territory. Such notices shall be provided promptly, but in no event after more than [\*\*] days after receipt thereof.

#### Section 10.6. Third Party Technology.

(a) If after the Effective Date, (i) Alnylam or any of its Affiliates acquires from a Third Party Know-How or Patent Rights that would fall within the definition of Alnylam Patent Rights but for payment obligations to such Third Party, or (ii) Roche or any of its Affiliates acquires from a Third Party Know-How or Patent Rights that would fall within the definition of Roche Patent Rights but for payment obligations to such Third Party (the foregoing clauses (i) and (ii), collectively, "Third Party Technology"), then the Party acquiring the Third Party Technology shall promptly so notify the other Party and provide such other Party with a copy of the agreement and a written description of the payment obligations that would be allocated to the other Party hereunder.

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(b) Roche may elect to include Third Party Technology acquired by Alnylam or any of its Affiliates in the rights and licenses granted to Roche under Section 3.1 with respect to the Discovery, Development, Manufacture or Commercialization of the Licensed Product(s) in the Field in the Territory by providing written notice to Alnylam of such election, and, in such event, (i) Roche shall be obligated to pay Alnylam the applicable amounts payable to such Third Party for such Third Party Technology, if Roche is the Commercializing Party, in accordance with Section 9.3(g) and subject to deduction from royalties payable to Alnylam pursuant to Section 9.3(f), (ii) such Third Party Technology shall be deemed included within the definition of Alnylam Patent Rights and Alnylam Know-How, as applicable, and (iii) the agreement with the Third Party under which such Third Party Technology was acquired shall be included in the definition of Listed Alnylam Third Party Agreements. Notwithstanding anything in this Agreement to the contrary, neither Alnylam nor any of its Affiliates shall enter into any agreement with any Third Party or take any other action that would prevent such Third Party Technology acquired by Alnylam or any of its Affiliates from becoming Alnylam Technology upon Roche's election in accordance with this Section 10.6(b).

(c) Alnylam may elect to include Third Party Technology acquired by Roche or any of its Affiliates in the rights and licenses granted to Alnylam pursuant to Section 3.2 with respect to the Discovery, Development, Manufacture or Commercialization of the Licensed Product(s) in the Field in the Territory by providing written notice to Roche of such election, and, in such event, (i) Alnylam shall be obligated to pay Roche the applicable amounts payable to such Third Party for such Third Party Technology, if Alnylam is the Commercializing Party, in accordance with Section 9.3(g) and subject to deduction from royalties payable to Roche pursuant to Section 9.3(f), and (ii) such Third Party Technology shall be deemed included within the definition of Roche Patent Rights and Roche Know-How, as applicable. Notwithstanding anything in this Agreement to the contrary, neither Roche nor any of its Affiliates shall enter into any agreement with any Third Party or take any other action that would prevent such Third Party Technology acquired by Roche or any of its Affiliates from becoming Roche Technology upon Alnylam's election in accordance with this Section 10.6(c).

Section 10.7. Patent Marking. Each Party agrees to comply with the patent marking statutes in each country in which a Licensed Product is sold by such Party or its Related Parties.

Section 10.8. Product Labeling.

(a) Each Party and its Affiliates shall retain all right, title and interest in and to its and their respective corporate names and logos.

(b) To the extent permitted under applicable Laws:

(i) the Licensed Product(s) offered for sale in the United States shall carry the Commercializing Party's name and logo; and

(ii) provided neither Party exercises its Opt-Out Right all written promotional materials associated with the Licensed Product(s) in the United States shall indicate that the Licensed Product(s) was co-developed by the Parties.

(c) Each Party shall have the right to monitor the quality of the Licensed Products on which such Party's name and logo appear in accordance with reasonable quality control procedures to be agreed upon by the Parties.

## ARTICLE XI

### CONFIDENTIALITY

Section 11.1. Confidential Information. All Confidential Information disclosed by a Party to the other Party in connection with the activities contemplated by this Agreement shall not be used by the receiving Party except in connection with the activities and licenses contemplated by this Agreement, shall be maintained in confidence by the receiving Party, and shall not be disclosed without the written consent of the disclosing Party, except to the extent that the Confidential Information (as determined by competent documentation):

(a) was known or used by the receiving Party or its Affiliates prior to its date of disclosure to the receiving Party; or

(b) either before or after the date of the disclosure to the receiving Party or its Affiliates, is lawfully disclosed to the receiving Party or its Affiliates by sources other than the disclosing Party who are rightfully in possession of the Confidential Information and not subject to an obligation of confidentiality or non-use owed to the disclosing Party; or

(c) either before or after the date of the disclosure to the receiving Party or its Affiliates, becomes published or generally known to the public other than through the wrongful act or default of the receiving Party or its Affiliates or its or its Affiliates' representatives; or

(d) is independently developed by the receiving Party or its Affiliates without reference to or reliance upon the Confidential Information.

Notwithstanding anything set forth herein to the contrary, this Article IX shall not prohibit the receiving Party from disclosing Confidential Information of the disclosing Party to defend or prosecute litigation; provided that, to the extent practicable, the receiving Party provides prior written notice of such disclosure to the disclosing Party and assists the disclosing Party in its reasonable and lawful efforts to avoid or minimize the degree of such disclosure. Notwithstanding the foregoing provisions of this Section 9.1, either Party may only disclose the terms of this Agreement if such Party reasonably determines, based on advice from its counsel, that it is required to make such disclosure by applicable Law, regulation or legal process, including without limitation by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or NASDAQ, or pursuant to relevant accounting standards, such as IFRS or GAAP, in which event such Party shall provide prior notice of such intended disclosure to the other Party sufficiently in advance to enable the other Party to seek confidential treatment or other protection for such information unless the disclosing Party is prevented by Law from providing such advance notice and shall disclose only such terms of this Agreement as such disclosing Party reasonably determines, based on advice from its counsel, are required by applicable Law or legal process to be disclosed. Alnylam shall be permitted to disclose in

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confidence (pursuant to a written agreement with confidentiality obligations no less restrictive than set forth herein) the terms of this Agreement to the extent Alnylam is contractually obligated to do so pursuant to Alnylam Third Party Obligations; provided, that Alnylam shall redact such portions as Roche reasonably requests.

Section 11.2. Employee and Advisor Obligations. Each Party agrees that it may provide Confidential Information received from the other Party (including the terms of this Agreement) only to its and its Affiliates' (a) employees, consultants, advisors and contractors who have a need to know such information in order for the receiving Party to exercise its rights or perform its obligations under this Agreement, and (b) potential and existing investors, lenders and acquirors, in each case who have an obligation to treat such information and materials as confidential under terms no less restrictive than those set forth herein; provided, that such Party shall redact such portions as the other Party reasonably requests.

Section 11.3. Publicity. Upon execution of this Agreement, the Parties shall jointly issue a press release announcing the execution of this Agreement in form and substance substantially as set forth on Exhibit F hereto. Thereafter, neither Party shall issue any press release or public announcement relating to this Agreement or the Collaboration or Licensed Products without the prior written approval of the other Party, which approval shall not be unreasonably withheld, conditioned or delayed, except that a Party may issue a press release or public announcement if required by Law, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or NASDAQ or pursuant to relevant accounting standards, such as IFRS or GAAP; provided that the other Party has received prior notice of such intended press release or public announcement if practicable under the circumstances and the Party subject to the requirement includes in such press release or public announcement only such information relating to this Agreement as is necessary to comply with applicable Law. The rights of approval and notice granted to a Party in accordance with the preceding sentence shall only apply for the first time that specific information is to be disclosed, and shall not apply to the subsequent disclosure of substantially similar information that has previously been made public other than through a breach of this Agreement by the issuing Party or its Affiliates.

Section 11.4. Publications. A Party (the "Publishing Party") shall provide the other Party with a copy of any proposed publication or presentation at least [\*\*] days (or at least [\*\*] days in the case of abstracts or oral presentations) prior to submission for publication by the Publishing Party or its Affiliates so as to provide such other Party with an opportunity to recommend any changes it reasonably believes are necessary to continue to maintain the Confidential Information disclosed by the other Party to the Publishing Party in accordance with the requirements of this Agreement. The incorporation of such recommended changes shall not be unreasonably refused; and if such other Party notifies the Publishing Party in writing, within [\*\*] days after receipt of the copy of the proposed publication or presentation (or at least [\*\*] days in the case of oral presentations), that such publication or presentation in its reasonable judgment (a) contains an invention, solely or jointly conceived or reduced to practice by the other Party, for which the other Party reasonably desires to obtain patent protection or (b) could be expected to have a material adverse effect on the commercial value of any Confidential Information disclosed by the other Party to the Publishing Party, the Publishing Party shall

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prevent such publication or delay such publication for a mutually agreeable period of time. In the case of inventions, a delay shall be for a period reasonably sufficient to permit the timely preparation and filing of a patent application(s) on such invention, and in no event less than [\*\*] days from the date of notice from the non-Publishing Party. In the case of Confidential Information, any of the non-Publishing Party's Confidential Information shall be deleted as requested.

Section 11.5. Clinical Trial Registry. Unless and until Roche exercises its Opt-Out Right hereunder, (a) Roche, in accordance with its internal policies and procedures, shall have the right to publish all Clinical Studies with respect to the Licensed Product(s) and results thereof on the clinical trial registries which are maintained by or on behalf of Roche, and (b) Alnylam shall have the right to access Roche's clinical trial registry via a link from Alnylam's clinical trial registry, and, in accordance with applicable Law, to post Clinical Study information with respect to the Licensed Product(s) on clinicaltrials.gov or any other mandated registry.

## ARTICLE XII

### REPRESENTATIONS AND WARRANTIES

#### Section 12.1. Mutual Representations and Warranties.

(a) Representations of Authority. Each Party represents and warrants to the other Party that, as of the Effective Date, it has full corporate right, power and authority to enter into this Agreement and to perform its obligations under this Agreement.

(b) Consents. Each Party represents and warrants to the other Party that all necessary consents, approvals and authorizations of all government authorities and other Persons required to be obtained by it as of the Effective Date in connection with the execution, delivery and performance of this Agreement have been obtained.

(c) No Conflict. Each Party represents and warrants to the other Party that the execution and delivery of this Agreement and the performance of its obligations hereunder (i) does not violate or conflict with the provisions of its certificate of incorporation or by-laws, (ii) does not conflict with or violate any requirement of applicable Laws effective as of the Effective Date, and (iii) does not and will not conflict with, violate, breach or constitute a default under any contractual obligations of it or any of its Affiliates existing as of the Effective Date.

(d) Authorization and Binding Nature. Each Party represents and warrants to the other Party that the execution, delivery and performance of this Agreement and the performance of all obligations hereunder have been duly authorized by all requisite corporate action on the part of such Party and this Agreement constitutes valid and legally binding obligations of such Party, limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting the enforcement of creditors' rights generally and (ii) as may be limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies.

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(e) Employee Obligations. Each Party represents and warrants that all of its employees, officers and consultants have executed agreements or have existing obligations under Law requiring assignment to such Party of all intellectual property and proprietary rights made during the course of and as the result of their association with such Party, and obligating such individuals to maintain as confidential the Confidential Information of such Party and of a Third Party which such Party may receive.

Section 12.2. Representations and Warranties of Alnylam. Alnylam represents and warrants to Roche that, as of the Effective Date:

(a) Organization and Good Standing. Alnylam is a corporation duly organized, validly existing and in good standing under the Laws of the State of Delaware.

(b) Authority. Alnylam and its Affiliates have the right and authority to grant the licenses to Roche set forth in Sections 3.1(a), 3.1(b) and 3.1(c) of this Agreement as contemplated under this Agreement.

(c) Listed Alnylam Third Party Agreements. Exhibit B-2 identifies all Listed Alnylam Third Party Agreements existing as of the Effective Date, excluding Listed Third Party Agreements (as defined in the LCA). All such Listed Alnylam Third Party Agreements are in full force and effect, and no dispute presently exists between Alnylam and Listed Alnylam Counterparties under the agreements listed on Exhibit B-2 or Alnylam Pre-Existing Alliance Parties under the agreements listed on Exhibit B-1 that would place in jeopardy any of the licenses granted by Alnylam under this Agreement.

(d) Alnylam Pre-Existing Alliance Agreements. Exhibit B-1 identifies all Alnylam Pre-Existing Alliance Agreements existing as of the Effective Date, excluding the Pre-Existing Alliance Agreements (as defined in the LCA).

(e) Protecting IP Rights. Alnylam and its Affiliates have taken reasonable measures to protect the Alnylam Technology, consistent with prudent commercial practices in the biotechnology industry.

Section 12.3. Representations and Warranties of Roche. Roche represents and warrants to Alnylam that, as of the Effective Date:

(a) No Dispute With UBC. Roche is not engaged in a dispute with UBC.

(b) Organization and Good Standing. Roche Basel is a corporation duly organized, validly existing and in good standing under the Laws of Switzerland; Roche Nutley is a corporation duly organized, validly existing and in good standing under the Laws of the State of New Jersey.

(c) Authority. Roche and its Affiliates have the right and authority to grant the licenses to Alnylam set forth in Sections 3.2(a), 3.2(b) and 3.2(c) of this Agreement as contemplated under this Agreement.

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(d) Protecting IP Rights. Roche and its Affiliates have taken reasonable measures to protect the Roche Technology, consistent with prudent commercial practices in the pharmaceutical industry.

Section 12.4. No Warranties. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS ARTICLE X, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, TO THE OTHER PARTY, INCLUDING ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

### ARTICLE XIII

#### INDEMNIFICATION; INSURANCE

Section 13.1. Indemnification by Roche. Roche shall defend, indemnify and hold harmless Alnylam, its Affiliates, and their respective directors, officers, employees and agents (the "Alnylam Indemnitees"), at Roche's cost and expense, from and against any liabilities, losses, costs, damages, fees or expenses (including reasonable attorneys' fees) (collectively, "Losses") arising out of any Third Party claim based on or resulting from: (a) any breach by Roche of any of its representations, warranties, covenants or obligations pursuant to this Agreement; (b) the negligence or willful misconduct of Roche or its Related Parties, or any of their respective directors, officers, employees and agents, in the performance of obligations or exercise of rights under this Agreement; (c) the Development, Manufacture, Commercialization, or use of the Licensed Product(s) by Roche as the Commercializing Party hereunder, or by any of its Related Parties, including any Product Liability Claim relating to such Licensed Product(s) (except as provided in Section 13.3); (c) any Advertising Claims; or (d) the pricing and commercial terms of Licensed Product(s) in the U.S., or any policy governing the handling of returns, recalls, order processing, invoicing and collection, distribution, and inventory and receivables for, Licensed Product(s) in the U.S., if Roche is responsible hereunder for booking sales of such Licensed Product(s) in the U.S. Roche shall have no obligation to indemnify the Alnylam Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, any breach of, or inaccuracy in, any representation or warranty made by Alnylam in this Agreement, or any breach or violation of any covenant or obligation of Alnylam or its Related Parties in or pursuant to this Agreement, or the negligence or willful misconduct by or of any of the Alnylam Indemnitees.

Section 13.2. Indemnification by Alnylam. Alnylam shall defend, indemnify and hold harmless Roche, its Affiliates and their respective directors, officers, employees and agents (the "Roche Indemnitees"), at Alnylam's cost and expense, from and against any Losses arising out of any Third Party claim based on or resulting from: (a) any breach by Alnylam of any of its representations, warranties, covenants or obligations pursuant to this Agreement; (b) the negligence or willful misconduct of Alnylam or its Related Parties, or any of their respective directors, officers, employees and agents, in the performance of obligations or exercise of rights under this Agreement; (c) the Development, Manufacture, Commercialization, or use of the Licensed Product(s) by Alnylam as the Commercializing Party hereunder, or by any of its Related Parties, including any Product Liability Claim relating to such Licensed Product(s) (except as provided in Section 13.3) and excluding Advertising Claims (except if and to the

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extent that Alnylam is the Party responsible hereunder for booking sales of such Licensed Product(s) in the U.S.); or (d) the pricing and commercial terms of Licensed Product(s) in the U.S., or any policy governing the handling of returns, recalls, order processing, invoicing and collection, distribution, and inventory and receivables for, Licensed Product(s) in the U.S., if Alnylam is responsible hereunder for booking sales of such Licensed Product(s) in the U.S. Alnylam shall have no obligation to indemnify the Roche Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, any breach of, or inaccuracy in, any representation or warranty made by Roche in this Agreement, or any breach or violation of any covenant or obligation of Roche or its Related Parties in or pursuant to this Agreement, or the negligence or willful misconduct by or of any of the Roche Indemnitees.

Section 13.3. Product Liability Claims. If neither Party has exercised its Opt-Out Right, any Losses arising out of Product Liability Claims shall be treated as Commercialization Costs, to the extent such Losses were incurred with respect to the Development, Manufacture or Commercialization of the Licensed Product(s) in the United States, except to the extent such Losses arise out of any Third Party claim based on (a) a Party's breach of any of its representations, warranties, covenants or obligations pursuant to this Agreement, or (b) the negligence or willful misconduct of a Party or its Related Parties, or any of their respective directors, officers, employees and agents, in the performance of obligations (including Manufacture and supply obligations) or exercise of rights under this Agreement.

Section 13.4. Claims for Indemnification with respect to Third Parties.

(a) With regard to any Third Party claim for which indemnification may be sought under this Article XI against a person entitled to indemnification under this Article XI (an "Indemnified Party"), the Indemnified Party shall give prompt written notification to the person from whom indemnification is sought (the "Indemnifying Party") of the commencement of any action, suit or proceeding relating to such Third Party claim or, if earlier, upon the assertion of any such claim by a Third Party (it being understood and agreed, however, that the failure by an Indemnified Party to give notice of a Third Party claim as provided in this Section 13.4(a) shall not relieve the Indemnifying Party of its indemnification obligation under this Agreement except and only to the extent that such Indemnifying Party is actually prejudiced as a result of such failure to give notice).

(b) Within [\*\*] days after delivery of such notification, the Indemnifying Party may, upon written notice thereof to the Indemnified Party, assume control of the defense of such action, suit, proceeding or claim with counsel reasonably satisfactory to the Indemnified Party. If the Indemnifying Party does not assume control of such defense, the Indemnified Party shall control such defense.

(c) The Party not controlling such defense may participate therein at its own expense; provided that if the Indemnifying Party assumes control of such defense and the Indemnified Party reasonably concludes, based on advice from counsel, that the Indemnifying Party and the Indemnified Party have conflicting interests with respect to such action, suit, proceeding or claim, the Indemnifying Party shall be responsible for the reasonable fees and expenses of counsel to the Indemnified Party solely in connection therewith; provided further, however, that in no event shall the Indemnifying Party be responsible for the fees and expenses of more than one counsel in any one jurisdiction for all Indemnified Parties.

(d) The Party controlling such defense shall keep the other Party advised of the status of such action, suit, proceeding or claim and the defense thereof and shall consider recommendations made by the other Party with respect thereto.

(e) The Indemnified Party shall not agree to any settlement of such action, suit, proceeding or claim without the prior written consent of the Indemnifying Party, which shall not be unreasonably withheld. The Indemnifying Party shall not, without the prior written consent of the Indemnified Party, agree to any settlement of such claim or consent to any judgment in respect thereof that does not include a complete and unconditional release of the Indemnified Party from all liability with respect thereto or that imposes any liability or obligation on the Indemnified Party.

Section 13.5. Insurance. Each Party shall maintain appropriate product liability insurance (or self-insurance) with respect to its Discovery, Development, Manufacture and Commercialization activities hereunder in such amount as such Party customarily maintains with respect to its other products for similar patient populations and commercial markets. Each Party shall maintain such insurance for so long as it continues to conduct such activities hereunder, and for so long as such Party customarily maintains insurance with respect to sales of its other products for similar patient populations and commercial markets.

#### ARTICLE XIV

##### TERM AND TERMINATION

Section 14.1. Term. Unless terminated earlier, this Agreement shall remain in force for the period commencing on the Effective Date and shall expire, on a Licensed Product-by-Licensed Product and country-by-country basis, upon the later of: (a) expiration of the applicable Royalty Term for such Licensed Product in such country, or (b) with respect to the United States, if neither Party has exercised its Opt-Out Right, until no Licensed Products have been Commercialized for a continuous period of six (6) months (the "Term"). Upon expiration of the Term, the licenses granted to the Commercializing Party(-ies) under Article III shall convert to perpetual, non-exclusive, fully paid-up, non-royalty-bearing licenses. Expiration or termination of this Agreement shall have no impact on the LCA.

##### Section 14.2. Termination for Cause.

(a) Roche may terminate this Agreement upon sixty (60) calendar days' prior written notice to Alnylam upon the material breach by Alnylam of any of its representations, warranties or obligations under this Agreement (except for any Diligence Breach by Alnylam); provided that such termination shall become effective only if (i) Alnylam fails to remedy or cure the breach within such sixty (60) day period, or (ii) if such breach cannot be remedied or cured through the application of Diligent Efforts within such sixty (60) day period, and Alnylam has (within such time period) submitted a plan for cure as promptly as is reasonably practicable (but in no event beyond an additional sixty (60) day period) through the application of Diligent Efforts with a remedy or cure period reasonably acceptable to Roche, then after the earlier of the remedy or cure date accepted by Roche or the date Alnylam ceases to use Diligent Efforts to remedy or cure such breach.

(b) Alnylam may terminate this Agreement upon sixty (60) calendar days' prior written notice to Roche upon the material breach by Roche of any of its representations, warranties or obligations under this Agreement (except for any Diligence Breach by Roche); provided that such termination shall become effective only if (i) Roche fails to remedy or cure the breach within such sixty (60) day period, or (ii) if such breach cannot be remedied or cured through the application of Diligent Efforts within such sixty (60) day period, and Roche has (within such time period) submitted a plan for cure as promptly as is reasonably practicable (but in no event beyond an additional sixty (60) day period) through the application of Diligent Efforts with a remedy or cure period reasonably acceptable to Alnylam, then after the earlier of the remedy or cure date accepted by Alnylam or the date Roche ceases to use Diligent Efforts to remedy or cure such breach.

(c) If one Party in good faith believes the other Party has committed a Diligence Breach, then the non breaching Party may terminate this Agreement upon ninety (90) calendar days' prior written notice to the breaching Party, specifying the Diligence Breach and, if applicable, the Major Territory(ies) as to which the Diligence Breach allegedly occurred. Such termination shall become effective only if the allegedly breaching Party fails to remedy or cure such Diligence Breach within such ninety (90) day period ("Diligence Breach Cure Period"); provided, that, the allegedly breaching Party shall have the option, in its sole discretion, of electing to terminate this Agreement without cause as set forth in Section 14.4 during the Diligence Breach Cure Period in lieu of undertaking efforts to remedy or cure such Diligence Breach. If the allegedly breaching Party fails to cure such Diligence Breach within the Diligence Breach Cure Period (either through actual cure or through electing to terminate at will pursuant to Section 14.4), but provides written notice to the non-breaching Party during the Diligence Breach Cure Period that such Party disputes in good faith the existence of such Diligence Breach, then either Party may submit such dispute to the Executive Officers of Alnylam and Roche for resolution. If, despite the Executive Officers' efforts to resolve such dispute, the Executive Officers cannot reach an agreement regarding such dispute within **[\*\*]** days after submission to them for resolution, then such dispute may be submitted to a court of competent jurisdiction for resolution, in which event this Agreement shall terminate only upon the rendering of a final decision by such court upholding the basis for termination (or once the breaching Party is no longer disputing such basis in good faith, if earlier).

#### Section 14.3. Termination for Patent Challenge.

(a) If Roche or any of its Related Parties initiates, maintains or supports any action to (i) oppose the grant of a patent, or (ii) challenge the validity, patentability, enforceability or scope of an issued patent, in each case under the Alnylam Patent Rights or Alnylam Collaboration Patent Rights, then Alnylam shall have the right, upon thirty (30) days' prior written notice to Roche, to terminate this Agreement; provided, however, that if Roche or any of its Related Parties, as relevant, cease such opposition or challenge within such thirty (30) day period, then Alnylam shall not have the right to terminate this Agreement.

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**[\*\*]** = Portions of this exhibit have been omitted pursuant to a confidential treatment request. An unredacted version of this exhibit has been filed separately with the Commission.

(b) If Alnylam or any of its Related Parties initiates, maintains or supports any action to (i) oppose the grant of a patent, or (ii) challenge the validity, patentability, enforceability or scope of an issued patent, in each case under the Roche Patent Rights or Roche Collaboration Patent Rights, then Roche shall have the right, upon thirty (30) days' prior written notice to Alnylam, to terminate this Agreement; provided, however, that if Alnylam or any of its Related Parties, as relevant, cease such opposition or challenge within such thirty (30) day period, then Roche shall not have the right to terminate this Agreement.

Section 14.4. Termination At Will.

(a) If neither Party has exercised its Opt-Out Right, Roche shall have the right to terminate, without cause, the licenses granted to Roche under this Agreement and all related terms and conditions, solely with respect to any Major Territory(ies) outside of the United States, by providing ninety (90) calendar days' prior written notice to Alnylam.

(b) The Continuing Party shall have the right to terminate, without cause, the licenses granted to such Continuing Party under this Agreement and all related terms and conditions, with respect to any Major Territory(ies) by providing ninety (90) calendar days' prior written notice to the other Party.

(c) In the event of an alleged Diligence Breach under Section 14.2(c), the breaching Party shall have the right to terminate, without cause, the licenses granted to such breaching Party under this Agreement and all related terms and conditions, solely with respect to the Major Territory(ies) as to which the Diligence Breach allegedly occurred by providing ninety (90) days' prior written notice to the non-breaching Party during the Diligence Breach Cure Period.

(d) The Party receiving the termination notice under Section 14.4(a), 14.4(b) or 14.4(c) above shall have the right to notify the terminating Party thereunder during such ninety (90) day period if such Party is interested in pursuing the Development and Commercialization of Licensed Product(s) in any of the Major Territory(ies) being terminated.

(i) If such Party notifies the terminating Party that such Party is interested in pursuing the Development and Commercialization of Licensed Product(s) in such terminated Major Territory(ies) during such 90-day period, the Parties shall negotiate in good faith the terms of (A) a transition agreement to cover the reasonable wind-down and transition of the Licensed Product(s) to such Party in such terminated Major Territory(ies), which wind-down and transition activities shall be performed for a period not to exceed [\*\*], with the pursuing Party bearing reasonable costs incurred by the terminating Party (at the terminating Party's FBMC plus the applicable percentage set forth in Article VI) in performing such wind-down and transition activities; and (B) the development, regulatory and sales events, the achievement of which shall trigger payment of event payment amounts, the event payment amounts themselves, and royalty rates payable by the pursuing Party with respect to Licensed Product(s) in such terminated Major Territory(ies); it being understood that the Parties intend that all other terms and conditions of this Agreement that otherwise apply to Licensed Product(s) shall remain in effect, subject to any minor adjustments, if necessary, to reflect the Major Territory(ies) being terminated (e.g., exclusive license grant as if the terminating Party had opted-out, general payment terms, royalty deductions). If, despite such good faith negotiations, the Parties are unable to finalize the

events/event payment amounts and royalty rates payable with respect to Licensed Product(s) in the terminated Major Territory(ies) within an additional ninety (90) calendar days, then the Parties shall submit such dispute for resolution by Baseball Arbitration pursuant to the terms of Exhibit G.

(ii) For purposes of clarity, if the Party receiving the termination notice under Section 14.4(a), 14.4(b) or 14.4(c) does not notify the terminating Party during such ninety (90) day period that such Party is interested in pursuing the Development and Commercialization of Licensed Product(s) in any of the Major Territory(ies) being terminated, the termination of this Agreement shall become effective at the end of such ninety (90) day period.

#### Section 14.5. Effects of Termination.

(a) Termination by Alnylam for Roche Material Breach (Other Than a Diligence Breach) or Roche Patent Challenge if Neither Party has Opted-Out. Without limiting any other legal or equitable remedies that Alnylam may have, if Alnylam terminates this Agreement as a result of Roche's uncured material breach pursuant to Section 14.2(a), or as a result of Roche (or its Related Parties) taking any of the prohibited actions pursuant to Section 14.3(a), and the Parties, at the time of such termination, were in a Profit and cost-sharing arrangement pursuant to Section 4.8 and 9.2, then:

(i) Roche's exclusivity obligations under Section 3.7 shall remain in effect for a period of [\*\*] after the effective date of termination;

(ii) if such termination occurs after the Research Term, Roche shall (A) continue to pay for any Clinical Study(ies) conducted, or committed to be conducted, by Alnylam at the time of such termination notice, through completion or earlier termination of such Clinical Study(ies), and (B) for a period of six (6) months following the date of notice of termination (if neither Party had exercised its Opt-Out Right prior to such date), continue to pay [\*\*] percent ([\*\*]%) of all other Development Costs actually incurred by Alnylam in connection with the Development of Licensed Products and in Field for the United States during such six (6) month period, in each case provided that such costs are shown on and consistent with the Development Plan in place as of the date of notice of termination;

(iii) the licenses granted to Roche in Section 3.1 shall terminate and have no further force or effect, and Roche shall be deemed to have exercised its Opt-Out Right (with the consequences set forth in this Section 14.5(a));

(iv) if requested by Alnylam, Roche shall as promptly as practicable transfer to Alnylam or Alnylam's designee (A) possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of the Licensed Product(s) and all Roche trademarks then being used in connection with the Licensed Product(s) (other than Roche's corporate trademarks); (B) copies of all data, reports, records and materials, Commercialization Plans, marketing plans, promotional materials, and other sales and marketing related information in Roche's possession or Control to the extent that such data, reports, records, materials or other information relate to

the Development, Manufacture or Commercialization of the Licensed Product(s), including all non-clinical and clinical data relating to the Licensed Product(s), and customer lists and customer contact information and all Safety Data and other adverse event data in Roche's possession or Control; provided that (I) Roche shall not be required by this provision to provide any Confidential Information to Alnylam and (II) Roche shall use Diligent Efforts to obtain for Alnylam the right to access all such data, reports, records, materials, and other sales and marketing related information; and (C) all records and materials in Roche's possession or Control containing Confidential Information of Alnylam;

(v) if requested by Alnylam, appoint Alnylam as Roche's or Roche's Related Parties' agent for all Licensed Product-related matters involving Regulatory Authorities in the Territory until all Regulatory Approvals and other regulatory filings have been transferred to Alnylam or its designee;

(vi) if the effective date of termination (or opt-out, solely for purposes of Section 4.9(b)(iii)) occurs after the First Commercial Sale of a Licensed Product in any country in the Territory and Roche was the Commercializing Party immediately prior to such termination (or opt-out, solely for purposes of Section 4.9(b)(iii)), then, if requested by Alnylam, Roche shall appoint Alnylam as its exclusive distributor of Licensed Product in the Territory and grant Alnylam the right to appoint sub-distributors, until such time as all Regulatory Approvals in the Territory have been transferred to Alnylam or its designee;

(vii) if Roche or its Related Parties are Manufacturing API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, at Alnylam's option, supply the API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, as applicable, to Alnylam in the Territory on terms no less favorable than those on which Roche supplied the API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, as applicable, prior to such termination to its most favored distributor in the Territory, until such time as all Regulatory Approvals in the Territory have been transferred to Alnylam or its designee, Alnylam has obtained all necessary manufacturing approvals and Alnylam has procured or developed its own source of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product supply, as applicable, provided, that such period of time shall not exceed [\*\*] (unless otherwise agreed by Roche);

(viii) if Alnylam so requests, Roche shall transfer to Alnylam any Third Party agreements solely relating to the Development, Manufacture or Commercialization of the Licensed Product(s) to which Roche is a party, subject to any required consents of such Third Party, which Roche shall use Diligent Efforts to obtain promptly;

(ix) subject to then-existing Third Party obligations, Roche hereby grants to Alnylam an exclusive right and license, with the right to grant sublicenses subject to Section 3.2(d)(i) and Section 3.3, under such Roche Technology as has been incorporated into, or has been used in or (as documented in the Joint Research Plan, the Development Plan or the Commercialization Plan, or any approved JSC or JCT minutes, as applicable) has been intended for use in, the Development, Manufacture or Commercialization of the Licensed Product(s) under this Agreement as of the effective date of such termination, solely to Develop, Manufacture and Commercialize the Licensed Product(s) in the Field in the Territory; provided,

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that, (A) Alnylam shall not be bound by the diligence obligations set forth in Article VIII, and (B) such license shall be subject to Alnylam's compliance with its obligation to pay to Roche (1) (if Alnylam had been the Commercializing Party immediately prior to such termination) royalties at the royalty rates and event payment amounts within the same Column as would have been payable to Roche had Alnylam remained the Commercializing Party, or (2) (if Roche had been the Commercializing Party immediately prior to such termination) royalties at the royalty rates and event payment amounts within the Column that would have applied had Roche exercised its Opt-Out Right; provided, however, that Alnylam may withhold [\*\*] percent ([\*\*]%) of each royalty payment due hereunder until the actual amount of damages owed by Roche to Alnylam with respect to the breach of this Agreement resulting in such termination is determined, whereupon such withheld amount shall be credited against such damages and any amount remaining shall be paid to Roche within [\*\*] days after such determination; and

(x) Roche shall execute all documents and take all such further actions, including, where applicable, the prompt assignment of Regulatory Approvals and Third Party agreements, as may be reasonably requested by Alnylam in order to give effect to the foregoing clauses (i) through (ix) as soon as practicable and in order to enable Alnylam to continue to Develop, Manufacture and Commercialize the Licensed Product(s) in the Territory in the same manner as was being conducted by the Commercializing Party prior to any such termination.

(b) Termination by Roche for Alnylam Material Breach (Other Than a Diligence Breach) or Alnylam Patent Challenge if Neither Party has Opted-Out. Without limiting any other legal or equitable remedies that Roche may have, if Roche terminates this Agreement as a result of Alnylam's material uncured breach pursuant to Section 14.2(a), or as a result of Alnylam (or its Related Parties) taking any of the prohibited actions pursuant to Section 14.3(b), and the Parties, at the time of such termination, were in a Profit and cost-sharing arrangement pursuant to Section 4.8 and 7.2, then:

(i) Alnylam's exclusivity obligations under Section 3.7 shall remain in effect for a period of [\*\*] after the effective date of termination;

(ii) if such termination occurs after the Research Term, Alnylam shall (A) continue to pay for any Clinical Study(ies) conducted, or committed to be conducted, by Roche at the time of such termination notice, through completion or earlier termination of such Clinical Study(ies), and (B) for a period of six (6) months following the date of notice of termination (if neither Party had exercised its Opt-Out Right prior to such date), continue to pay [\*\*] percent ([\*\*]%) of all other Development Costs actually incurred by Roche in connection with the Development of Licensed Products in the Field in the United States during such six (6) month period, in each case provided that such costs are shown on and consistent with the Development Plan in place as of the date of notice of termination;

(iii) the licenses granted to Alnylam in Section 3.2 shall terminate and have no further force or effect, and Alnylam shall be deemed to have exercised its Opt-Out Right (with the consequences set forth in this Section 14.5(b));

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(iv) if requested by Roche, Alnylam shall as promptly as practicable transfer to Roche or Roche's designee (A) possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of the Licensed Product(s) and all Alnylam trademarks then being used in connection with the Licensed Product(s) (other than Alnylam's corporate trademarks); (B) copies of all data, reports, records and materials, Commercialization Plans, marketing plans, promotional materials, and other sales and marketing related information in Alnylam's possession or Control to the extent that such data, reports, records, materials or other information relate to the Development, Manufacture or Commercialization of the Licensed Product(s), including all non-clinical and clinical data relating to the Licensed Product(s), and customer lists and customer contact information and all Safety Data and other adverse event data in Alnylam's possession or Control; provided that (I) Alnylam shall not be required by this provision to provide any Confidential Information to Roche and (II) Alnylam shall use Diligent Efforts to obtain for Roche the right to access all such data, reports, records, materials, and other sales and marketing related information; and (C) all records and materials in Alnylam's possession or Control containing Confidential Information of Roche;

(v) if requested by Roche, appoint Roche as Alnylam's or Alnylam's Related Parties' agent for all Licensed Product-related matters involving Regulatory Authorities in the Territory until all Regulatory Approvals and other regulatory filings have been transferred to Roche or its designee;

(vi) if the effective date of termination (or opt-out, solely for purposes of Section 4.9(b)(iv)) is after First Commercial Sale in any country in the Territory and Alnylam was the Commercializing Party immediately prior to such termination (or opt-out, solely for purposes of Section 4.9(b)(iv)), then, if requested by Roche, Alnylam shall appoint Roche as its exclusive distributor of Licensed Product in the Territory and grant Roche the right to appoint sub-distributors, until such time as all Regulatory Approvals in the Territory have been transferred to Roche or its designee;

(vii) if Alnylam or its Related Parties are Manufacturing API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, at Roche's option, supply the API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, as applicable, to Roche in the Territory on terms no less favorable than those on which Alnylam supplied the API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product, as applicable, prior to such termination to its most favored distributor in the Territory, until such time as all Regulatory Approvals in the Territory have been transferred to Roche or its designee, Roche has obtained all necessary manufacturing approvals and Roche has procured or developed its own source of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product supply, as applicable, provided, that such period of time shall not exceed [\*\*] (unless otherwise agreed by Alnylam);

(viii) if Roche so requests, Alnylam shall transfer to Roche any Third Party agreements relating to the Development, Manufacture or Commercialization of the Licensed Product(s) to which Alnylam is a party, subject to any required consents of such Third Party, which Alnylam shall use Diligent Efforts to obtain promptly;

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(ix) subject to Alnylam Third Party Obligations, Alnylam hereby grants to Roche an exclusive right and license, with the right to grant sublicenses subject to Section 3.1(d)(i) and Section 3.3, under such Alnylam Technology as has been incorporated into, or has been used in or (as documented in the Joint Research Plan, the Development Plan or the Commercialization Plan, or any approved JSC or JCT minutes, as applicable) has been intended for use in, the Development, Manufacture or Commercialization of the Licensed Product(s) under this Agreement as of the effective date of such termination, solely to Develop, Manufacture and Commercialize the Licensed Product(s) in the Field in the Territory; provided, that, (A) Roche shall not be bound by the diligence obligations set forth in Article VIII, and (B) such license shall be subject to Roche's compliance with its obligation to pay to Alnylam (1) (if Roche had been the Commercializing Party immediately prior to such termination) royalties at the royalty rates and event payment amounts within the same Column as would have been payable to Alnylam had Roche remained the Commercializing Party, or (2) (if Alnylam had been the Commercializing Party immediately prior to such termination) royalties at the royalty rates and event payment amounts within the Column that would have applied had Alnylam exercised its Opt-Out Right; provided, however, that Roche may withhold [\*\*] percent ([\*\*]%) of each event and royalty payment due hereunder until the actual amount of damages owed by Alnylam to Roche with respect to the breach of this Agreement resulting in such termination is determined, whereupon such withheld amount shall be credited against such damages and any amount remaining shall be paid to Alnylam within [\*\*] days after such determination; and

(x) Alnylam shall execute all documents and take all such further actions, including, where applicable, the prompt assignment of Regulatory Approvals and Third Party agreements, as may be reasonably requested by Roche in order to give effect to the foregoing clauses (i) through (ix) as soon as practicable and in order to enable Roche to continue to Develop, Manufacture and Commercialize the Licensed Product(s) in the Territory in the same manner as was being conducted by the Commercializing Party prior to any such termination.

(c) Termination for Material Breach (Other Than a Diligence Breach) or Patent Challenge if a Party has Opted-Out. Without limiting any other legal or equitable remedies that such Party may have, if a Party terminates this Agreement as a result of the other Party's material uncured breach pursuant to Section 14.2(a) or Section 14.2(b), as applicable, or as a result of the other Party (or such other Party's Related Parties) taking any of the prohibited actions pursuant to Section 14.3(a) or 14.3(b), as applicable, and either Party had exercised its Opt-Out Right at the time of such termination notice, then:

(i) if the Party that had exercised its Opt-Out Right is the Party being terminated above, then all rights and obligations of the Parties in effect immediately prior to such termination shall remain in effect immediately following such termination; provided, however, that, the Continuing Party shall not be bound by any diligence obligations hereunder; and

(ii) if the Continuing Party is the Party being terminated above, then Section 14.4 shall apply as if the Continuing Party had elected to terminate this Agreement at will.

(d) Termination for Diligence Breach. Without limiting any other legal or equitable remedies that such Party may have with respect to a Diligence Breach, if a court of competent jurisdiction renders a final decision upholding the basis of termination by the non-breaching

Party under Section 14.2(c) with respect to such Diligence Breach (or unless and until the breaching Party is no longer disputing such basis, if earlier), then, unless otherwise agreed by the Parties, at the non-breaching Party's request, the termination shall have the same effect as if the breaching Party terminated at will in accordance with Section 14.4.

(e) Subsequent Termination of Licenses by the Continuing Party following a Termination Under Section 14.2 or Section 14.3. For purposes of clarity, if, following a termination of this Agreement under Section 14.2 or 14.3, the Continuing Party (if any) decides to terminate the licenses granted to such Party under Section 14.5(a)(ix) or Section 14.5(b)(ix), as the case may be, Section 14.4 shall apply as if the Continuing Party had elected to terminate this Agreement at will.

Section 14.6. Effect of Expiration or Termination; Survival.

(a) Upon expiration or termination of this Agreement, each Party will within [\*\*] days return, or have returned by its Related Parties, to the other Party all tangible Confidential Information of the other Party, except that each Party may retain (i) one copy which may be retained in a secure location solely for evidentiary purposes in the event of a dispute and (ii) any of the other Party's Confidential Information to the extent necessary to exercise any rights of such Party which survive termination.

(b) Except as set forth in Section 14.5 above or this Section 14.6, upon expiration or termination of this Agreement, each Party's rights, obligations and licenses under this Agreement shall terminate, either in its entirety or with respect to particular Major Territory(ies), as the case may be; provided, however, that expiration or termination of this Agreement shall not relieve the Parties of any obligation, including payment obligations, accruing prior to such expiration or termination.

(c) The provisions of Sections 3.7 (solely as set forth in Section 14.5), 4.3(f), 9.1-9.3 (solely as set forth in Section 14.5), 9.4-9.7, 10.1-10.2, 10.7-10.8 (solely to the extent that a Party's rights to the Licensed Product(s) survive termination hereunder), 12.4, 14.1 (last sentence only), 14.5, 14.6, Articles XI, XIII and XV (except Section 15.15), and (if applicable) Section 14.4(d)(i) and Paragraph 4 of Exhibit G shall survive any expiration or termination of this Agreement in accordance with their terms.

ARTICLE XV

MISCELLANEOUS

Section 15.1. Choice of Law. This Agreement shall be governed by and interpreted under the laws in effect in the State of Delaware, excluding its conflicts of laws principles.

Section 15.2. Notices. Any notice or report required or permitted to be given or made under this Agreement by one of the Parties to the other shall be in writing and shall be deemed to have been delivered upon personal delivery or (a) in the case of notices provided between Parties in the continental United States, four (4) days after deposit in the mail or the next Business Day following deposit with a reputable overnight courier and (b) in the case of notices provided by

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teletype (which notice shall be followed immediately by an additional notice pursuant to clause (a) above if the notice is of a default hereunder), upon completion of transmissions to the addressee's telecopier, as follows (or at such other addresses or facsimile numbers as may have been furnished in writing by one of the Parties to the other as provided in this Section 15.2):

If to Alnylam:

Alnylam Pharmaceuticals, Inc  
300 Third Street, 3rd Floor  
Cambridge, Massachusetts 02142  
Attention: Vice President — Legal  
Fax: (617) 551-8101

With a copy (which shall not constitute notice) to:

WilmerHale LLP  
60 State Street  
Boston, MA 02109  
Attention: Steven D. Singer, Esq.  
Fax: (617) 526-5000

If to Roche:

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4070 Basel  
Switzerland  
Attention: Legal Department  
Fax: 41 61 688 1396

And: Hoffmann-La Roche Inc.  
340 Kingsland Street  
Nutley, New Jersey 07110  
USA  
Attention: Corporate Secretary  
Fax: (973) 235-3500

With a copy (which shall not constitute notice) to:

F. Hoffmann-La Roche Ltd  
Grenzacherstrasse 124  
4070 Basel  
Switzerland  
Attention: Pharma Partnering  
Fax: 41 61 688 7990

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Section 15.3. Severability. If, under applicable Law any provision hereof is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision(s) of this Agreement (“Severed Clause”), then, it is mutually agreed that this Agreement shall endure except for the Severed Clause. The Parties shall consult and use their best efforts to agree upon a valid and enforceable provision which shall be a reasonable substitute for such Severed Clause in light of the intent of this Agreement.

Section 15.4. Interpretation. Whenever the context may require, any pronoun shall include the corresponding masculine, feminine and neuter forms. The words “include”, “includes” and “including” shall be deemed to be followed by the phrase “without limitation.” The word “will” shall be construed to have the same meaning and effect as the word “shall.” The word “or” shall be construed to have the same meaning and effect as “and/or.” Unless the context requires otherwise, (a) any definition of or reference to any agreement, instrument or other document herein shall be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein or therein), (b) any reference to any Laws herein shall be construed as referring to such Laws as from time to time enacted, repealed or amended, (c) any reference herein to any Person shall be construed to include the Person’s successors and assigns, (d) the words “herein”, “hereof” and “hereunder”, and words of similar import, shall be construed to refer to this Agreement in its entirety and not to any particular provision hereof, and (e) all references herein to Articles, Sections, Exhibits or Schedules shall be construed to refer to Articles, Sections, Exhibits and Schedules of this Agreement. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

Section 15.5. Integration. This Agreement is being entered into in accordance with Article IV of the LCA and supplements the LCA, and the execution of this Agreement fulfills the Parties’ obligations under Article IV of the LCA. From and after the Effective Date of this Agreement, this Agreement constitutes the entire agreement between the Parties with respect to the within subject matter and supersedes all previous agreements, whether written or oral, including Article IV of the LCA which shall have no further force or effect. The Parties acknowledge that the LCA shall not be superseded by this Agreement except as expressly stated in this Agreement. This Agreement may be amended only in writing signed by properly authorized representatives of each of the Parties.

Section 15.6. Independent Contractors; No Agency. Neither Party shall have any responsibility for the hiring, firing or compensation of the other Party’s employees or for any employee benefits. No employee or representative of a Party shall have any authority to bind or obligate the other Party to this Agreement for any sum or in any manner whatsoever, or to create or impose any contractual or other liability on the other Party without said Party’s written approval. For all purposes, and notwithstanding any other provision of this Agreement to the contrary, each Party’s legal relationship under this Agreement to the other Party shall be that of independent contractor. The Parties agree and acknowledge that neither owes any fiduciary duties to the other.

Section 15.7. Assignment; Successors. Neither Alnylam nor Roche may assign this Agreement in whole or in part without the prior written consent of the other Party and such attempted assignment shall be deemed null and void; provided, however, that either Party may assign this Agreement without the prior written consent of the other Party (a) to an Affiliate of

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such Party, provided that the assigning Party shall remain primarily liable hereunder for the performance of all obligations by the assignee, or (b) subject to Section 15.15 to a Third Party in connection with a merger, sale or transfer of all or substantially all of the assigning Party's business (in the case of Roche, its pharmaceutical business related to RNAi technology and in the case of an assignment from Alnylam to [\*\*], treated as a [\*\*] under Section 2.7 of the LCA) to which this Agreement relates, provided that such assignee shall agree in writing to be bound by the terms and conditions of this Agreement. This Agreement shall be binding upon, and shall inure to the benefit of, all permitted successors and assigns.

Section 15.8. Execution in Counterparts; Facsimile Signatures. This Agreement may be executed in counterparts, each of which counterparts, when so executed and delivered, shall be deemed to be an original, and all of which counterparts, taken together, shall constitute one and the same instrument even if both Parties have not executed the same counterpart. Signatures provided by facsimile transmission shall be deemed to be original signatures.

Section 15.9. Waivers. No failure on the part of Roche or Alnylam to exercise and no delay in exercising any right, power, remedy or privilege under this Agreement, or provided by statute or at law or in equity or otherwise, shall impair, prejudice or constitute a waiver of any such right, power, remedy or privilege or be construed as a waiver of any breach of this Agreement or as an acquiescence therein, nor shall any single or partial exercise of any such right, power, remedy or privilege preclude any other or further exercise thereof or the exercise of any other right, power, remedy or privilege.

Section 15.10. No Consequential or Punitive Damages. NEITHER PARTY HERETO WILL BE LIABLE FOR INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, EXEMPLARY OR MULTIPLE DAMAGES ARISING OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, OR FOR LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF, OR OTHERWISE UNDER, THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES. NOTHING IN THIS SECTION 15.10 IS INTENDED TO LIMIT OR RESTRICT (A) THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY WITH RESPECT TO THIRD PARTY CLAIMS UNDER ARTICLE XI, OR (B) REMEDIES AVAILABLE TO EITHER PARTY WITH RESPECT TO A BREACH OF ARTICLE IX (CONFIDENTIALITY) OR SECTION 3.7 (EXCLUSIVITY).

Section 15.11. Actions of Affiliates. Each Party shall be liable for any failure by its Affiliates to comply with the restrictions, limitations and obligations set forth in this Agreement. Each Party may perform its obligations hereunder personally or through one or more Affiliates, although each Party shall nonetheless be solely responsible for the performance of its Affiliates. Neither Party shall permit any of its Affiliates to commit any act (including any act of omission) that such Party is prohibited hereunder from committing directly. To the extent that the rights granted to a Party hereunder may be and are exercised by an Affiliate of such Party, such Affiliate shall be bound by the corresponding obligations of such Party.

Section 15.12. Expenses. Except as otherwise expressly set forth in this Agreement, each Party shall be solely responsible for the expenses it incurs in connection with its performance of the activities contemplated by this Agreement.

Section 15.13. No Third Party Beneficiaries. Except as expressly set forth in this Agreement, no Person other than the Parties and their respective Affiliates and permitted assignees hereunder shall be deemed an intended third party beneficiary hereunder or have any right to enforce any obligation of this Agreement. Notwithstanding the foregoing, the Parties agree that UBC shall be deemed a third party beneficiary of, and shall have the right to enforce directly against Roche, its Affiliates or Licensee Partners, certain terms of this Agreement as set forth in the UBC Sublicense Agreement.

Section 15.14. Bankruptcy. All licenses (and to the extent applicable rights) granted under or pursuant to this Agreement by a Party to the other Party are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11, US Code (the "Bankruptcy Code") licenses of rights to "intellectual property" as defined under Section 101(60) of the Bankruptcy Code. Unless a Party elects to terminate this Agreement, the Parties agree that such Party shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code, subject to the continued performance of its obligations under this Agreement.

Section 15.15. Change of Control.

(a) If a Party undergoes a Change of Control (the "Acquired Party"), such Acquired Party shall provide the other Party with prompt written notice describing such Change of Control in reasonable detail (but in no event later than [\*\*] following the earlier of the public announcement or the consummation of such Change of Control). Notwithstanding anything in this Agreement to the contrary, the other Party may, by written notice to the Acquired Party within [\*\*] days following the consummation of such Change of Control, elect to do any or all of the following:

(i) If the Parties were in a Profit and cost-sharing arrangement under Sections 4.8 and 9.2 immediately prior to the consummation of such Change of Control, the non-Acquired Party may elect to have the Acquired Party transition to such Party all of the Development, Manufacturing and Commercialization operational responsibilities of the Acquired Party within [\*\*] following such notice pursuant to a transition plan to be mutually agreed by the Parties; provided, however, that following the transition of such responsibilities to the non-Acquired Party, (i) each Party's Opt-Out Right shall remain in effect, and (ii) the Profit and cost-sharing arrangement under Sections 4.8 and 9.2 shall remain in effect (unless and until either Party exercises its Opt-Out Right), provided, that, for as long as the Parties remain in a Profit and cost-sharing arrangement under this Agreement, the non-Acquired Party shall not incur Development Costs or Commercialization Costs exceeding the then-approved budget under the Development Plan or Commercialization Plan, respectively, for the remainder of the term of such Development Plan or Commercialization Plan, and that budgets for any period beyond such term be reasonable and appropriate; and

(ii) The non-Acquired Party may elect to terminate the Acquired Party's voting, participation and decision-making rights on any or all of the committees or subcommittees in existence at such time, provided, that the Acquired Party shall continue to have the right to receive and have access to information from the other Party, and the other Party shall continue to provide such information and access to the Acquired Party, including pursuant to Sections 2.1(d) (last paragraph), 3.1(e), 4.10(a), 9.1(c), 9.3(l), 9.5, 9.6 and 14.5, to the extent

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necessary for the Acquired Party (i) to comply with its obligations to any of its Third Party licensors, (ii) to determine whether or not to exercise its Opt-Out Right or, if the other Party exercises its Opt-Out Right, to determine whether or not to continue the unilateral Development and Commercialization of Licensed Product(s), as applicable, and (iii) to determine and verify amounts payable by the other Party (and its Related Parties) to the Acquired Party.

(b) Notwithstanding anything in Section 3.7 to the contrary, if a Third Party becomes an Affiliate of the Acquired Party as a result of the Change of Control and such Third Party conducts, or plans to conduct, any activities with respect to a Competitive Product(s) which would otherwise become subject to the exclusivity provisions pursuant to Section 3.7 following such Change of Control, the Acquired Party shall, in its sole discretion and within [\*\*] days following the consummation of such Change of Control, provide written notice to the other Party of its decision to either:

(i) discontinue such prohibited activities, with any necessary wind-down to occur within a reasonable period of time thereafter; or

(ii) exercise any Opt-Out Right with respect to the applicable Licensed Product(s), in which event the lower development and sales event payment and royalty payment obligations associated with an opt-out at the Opt-Out Point immediately preceding the actual Opt-Out Point shall apply to the Continuing Party from the effective date of the opt-out.

*[Remainder of This Page Intentionally Left Blank]*

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IN WITNESS WHEREOF, Alnylam and Roche have caused this Collaboration Agreement to be duly executed by their authorized representatives, as of the Effective Date.

F. HOFFMANN-LA ROCHE LTD

By: /s/ Nigel Sheail  
Name: Nigel Sheail  
Title: Head of Corporate Business Development

By: /s/ Stefan Arnold  
Name: Stefan Arnold  
Title: Head Corporate Law Pharma

HOFFMANN-LA ROCHE INC.

By: /s/ Ivor Macleod  
Name: Ivor Macleod  
Title: Vice President & CFO

ALNYLAM PHARMACEUTICALS, INC.

By: /s/ John Maraganore  
Name: John Maraganore  
Title: Chief Executive Officer

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## EXHIBIT A

### Definitions

As used in this Agreement, the following terms shall have the meanings set forth below:

1. “Accounting Period” has the meaning set forth in Section 9.3(k).
2. “Advertising Claim” means, with respect to a Licensed Product(s), any Third Party claim, suit, action, proceeding, liability or obligation involving any actual or alleged death or bodily injury arising out of or resulting from the use of such Licensed Product(s) based upon (i) any label or other written, printed or graphic mater upon (a) any container or wrapper utilized with such Licensed Product(s) in the U.S. or (b) any written material accompanying any container or wrapper utilized with such Licensed Product(s) in the U.S. including package inserts, and (ii) any communication or program associated with the promotion of such Licensed Product(s) in the U.S., including such communications and programs that (a) specifically identify or describe such Licensed Product(s) or (b) otherwise support such Licensed Product(s) or raise awareness of the Field.
3. “Affiliate” means any Person who directly or indirectly controls or is controlled by or is under common control with another Person. For purposes of this definition, “control” or “controlled” shall mean ownership, directly or through one or more Affiliates, of fifty percent (50%) or more of the shares of stock entitled to vote for the election of directors, in the case of a corporation, or fifty percent (50%) or more of the equity interest in the case of any other type of legal entity, status as a general partner in any partnership, or any other arrangement whereby a Party controls or has the right to control the Board of Directors or equivalent governing body of a corporation or other entity, or the ability to direct the management or policies of a corporation or other entity. The Parties acknowledge that in the case of certain entities organized under the laws of certain countries outside of the United States, the maximum percentage ownership permitted by law for a foreign investor may be less than fifty percent (50%), and that in such case such lower percentage shall be substituted in the preceding sentence, provided that such foreign investor has the power to direct the management and policies of such entity. For purposes of this Agreement, [\*\*], shall not be deemed an “Affiliate” of Roche; provided, however, that if Roche were to assume day-to-day control of [\*\*], then Roche shall have the right, at its sole option, to designate [\*\*] to be an Affiliate upon written notice to Alnylam. For purposes of Sections 11.1, 11.2, 15.7, 15.11 (the second sentence only), and 15.13, Alnylam’s Affiliates shall not include [\*\*], any Affiliates of [\*\*] (other than Alnylam and Persons “controlled” by Alnylam on the Effective Date) or any Person that becomes an Affiliate of Alnylam as a result of a [\*\*].
4. “Agreement” shall have the meaning set forth in the Preamble, and shall include, for the avoidance of doubt, all Exhibits attached hereto.
5. “Alliance Manager” shall have the meaning set forth in Section 2.3.
6. “Alnylam” shall have the meaning set forth in the Preamble.

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7. “Alnylam Collaboration IP” means Alnylam Collaboration Know-How and Alnylam Collaboration Patent Rights.
8. “Alnylam Collaboration Know-How” means any Know-How Controlled by Alnylam, patentable or otherwise, first identified, discovered or developed solely by employees of Alnylam or its Affiliates or other persons not employed by Roche or any of its Affiliates acting on behalf of Alnylam or any of its Affiliates in the conduct of the Collaboration. Alnylam Collaboration Know-How excludes Alnylam’s interest in Joint Collaboration Know-How.
9. “Alnylam Collaboration Patent Rights” means any Patent Rights that claim or cover Alnylam Collaboration Know-How and are Controlled by Alnylam. Alnylam Collaboration Patent Rights excludes Alnylam’s interest in Joint Collaboration Patent Rights.
10. “Alnylam Indemnitees” shall have the meaning set forth in Section 13.1.
11. “Alnylam Know-How” means Know-How Controlled by Alnylam as of the Effective Date or as to which Alnylam obtains Control during the Term that is necessary or reasonably useful for Roche and its Affiliates to perform their obligations or exploit their rights under this Agreement with respect to the Licensed Product(s), including their rights to Discover, Develop, Manufacture, or Commercialize Licensed Product (other than Alnylam’s rights in Joint Collaboration Know-How and Alnylam Collaboration Know-How); but excluding (a) Alnylam Platform Know-How and (b) Know-How to the extent specifically related to Blocked Targets.
12. “Alnylam Patent Rights” means those Patent Rights that are Controlled by Alnylam as of the Effective Date or as to which Alnylam obtains Control during the Term that are necessary or reasonably useful for Roche and its Affiliates to perform their obligations or exploit their rights under this Agreement with respect to the Licensed Product(s), including their rights to Discover, Develop, Manufacture, or Commercialize the Licensed Product(s) (other than Alnylam’s rights in Joint Collaboration Patent Rights and Alnylam Collaboration Patent Rights); but excluding (a) Alnylam Platform Patent Rights and (b) Patent Rights to the extent specifically related to Blocked Targets.
13. “Alnylam Platform Know-How” means the Licensed Know-How (as defined in the LCA).
14. “Alnylam Platform Patent Rights” means the Licensed Patent Rights (as defined in the LCA).
15. “Alnylam Pre-Existing Alliance Agreements” means the Pre-Existing Alliance Agreements (as defined in the LCA) and the agreements set forth on Exhibit B-1.
16. “Alnylam Pre-Existing Alliance Parties” means the Third Party counterparties to Alnylam Pre-Existing Alliance Agreements and their respective successors in interest.
17. “Alnylam Technology” means, collectively, Alnylam Know-How, Alnylam Patent Rights, Alnylam Collaboration IP and Alnylam’s interest in Joint Collaboration IP, and any Third Party Technology that is included in the definition of Alnylam Technology after the Effective Date in accordance with Section 10.6.

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18. “Alnylam Third Party Obligations” means Alnylam’s obligations to, and the rights of, Alnylam Pre-Existing Alliance Parties and Listed Alnylam Counterparties with respect to the Alnylam Technology under Alnylam Pre-Existing Alliance Agreements and Listed Alnylam Third Party Agreements or Manufacturing Agreements, as applicable.
19. “Annual Net Sales” means, with respect to a Licensed Product, the Net Sales of such Licensed Product during a Calendar Year.
20. “API Bulk Drug Substance” means siRNA in bulk form manufactured for use as an active pharmaceutical ingredient.
21. “Asia” means Brunei, Cambodia, China (including Hong Kong and Macao, but excluding Taiwan), Indonesia, Japan, Laos, Malaysia, Myanmar, North Korea, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam.
22. “Bankruptcy Code” shall have the meaning set forth in Section 15.14.
23. “Baseball Arbitration” shall have the meaning set forth in Exhibit G.
24. “Blocked Target” means any Target that is subject to a contractual obligation of an Alnylam Pre-Existing Alliance Agreement that would be breached by the inclusion of such Target as a Program Target under this Agreement.
25. “Business Day” means a day on which banking institutions in Boston, Massachusetts are open for business.
26. “Calendar Quarter” means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31; provided that the first Calendar Quarter of the Term shall begin on the Effective Date and end on September 30, 2009, and the last Calendar Quarter of the Term shall end on the last day of the Term.
27. “Calendar Year” means each successive period of twelve (12) months commencing on January 1 and ending on December 31; provided that the first Calendar Year of the Term shall begin on the Effective Date and end on December 31, 2009 and the last Calendar Year of the Term shall end on the last day of the Term.
28. “Candidate Selection Stage” means the earlier of (a) the Parties’ selection of a development candidate pursuant to Section 4.4, or (b) the completion of all activities pursuant to the Joint Research Plan.
29. “[\*\*]Agreement” shall have the meaning set forth in Section 3.1(f).
30. “cGMP” means current Good Manufacturing Practices and equivalent Laws outside the United States.

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31. “Change of Control” means, with respect to a Party (the “Acquired Party”), the occurrence of the closing of (a) a merger, reorganization or consolidation involving the Acquired Party in which its shareholders immediately prior to such transaction would hold less than fifty percent (50%) of the securities or other ownership or voting interests representing the equity of the surviving entity immediately after such merger, reorganization or consolidation, or (b) a sale to a Third Party of all or substantially all of the Acquired Party’s assets or business relating to this Agreement.
32. “Clinical Regulatory Filings” means data, filings or materials relating to Licensed Product submitted to the applicable Regulatory Authorities, including (a) data derived from Clinical Studies, (b) data derived from non-clinical studies, and (c) data, filings or materials relating to or contained in the CMC or a DMF.
33. “Clinical Study” means a Phase I Study, Phase II Study, or Phase III Study, as applicable, but excluding any Post-Approval Studies.
34. “CMC” means the chemistry, manufacturing and controls section of an IND or NDA in the United States, or the equivalent section of regulatory filings made outside the United States.
35. “Collaboration” means the collaboration of the Parties in the activities governed by this Agreement, including such activities relating to the Discovery, Development, Manufacture and Commercialization of the Licensed Product(s).
36. “Combination Product” means a Licensed Product combined with any other clinically active therapeutic or prophylactic ingredient, mechanism or device.
37. “Commercialization” or “Commercialize” means any and all activities directed to marketing, promoting, detailing, distributing, importing, having imported, exporting, having exported, selling or offering to sell, or seeking to obtain reimbursement for, a product, whether before or after Regulatory Approval for such product has been obtained.
38. “Commercialization Costs” shall have the meaning ascribed in Exhibit E.
39. “Commercialization Plan” shall have the meaning set forth in Section 5.3(a).
40. “Commercializing Party(ies)” means (a) Roche and Alnylam in the United States and Roche in the ROW Territory, if neither Party exercises its Opt-Out Right (unless otherwise mutually agreed by the Parties), or (b) the Continuing Party, if either Party exercises its Opt-Out Right or both Parties exercise their respective Opt-Out Rights, as the case may be.
41. “Competitive Infringement” shall have the meaning set forth in Section 10.4(a).
42. “Competitive Product” means any [\*\*].
43. “Confidential Information” means the terms of this Agreement and all Know-How or other information, including proprietary information and materials (whether or not patentable) regarding a Party’s technology, products, business information or objectives, that is treated as confidential by the disclosing Party in the regular course of business or is otherwise designated as confidential by the disclosing Party. For the avoidance of doubt, the identity of any Program Targets shall be deemed the Confidential Information of both Parties.

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44. “Continuing Party” means the Party that decides (or is decided by mutual agreement of the Parties, as the case may be) to unilaterally pursue the Development, Manufacture and Commercialization of Licensed Product(s) following (a) the other Party’s exercise of its Opt-Out Right or (b) the termination of this Agreement by the other Party pursuant to Section 14.2 or 14.3 (other than for a Diligence Breach).
45. “Control” or “Controlled” means, with respect to any intellectual property right or other intangible property, the possession by a Party (whether by ownership or license) (other than a license granted pursuant to this Agreement), or “control” (as defined in the definition of “Affiliate” above) over an Affiliate having possession (by ownership or license), of the ability to grant access to, or a license or sublicense of, such rights or property as contemplated under this Agreement, subject to the provisions of Section 10.6.
46. “Cover”, “Covered” or “Covering” means, with respect to a Patent Right, that, in the absence of a license granted to a Person under a Valid Claim included in such Patent Right, the practice by such Person of an invention claimed in such Patent Right would infringe such Valid Claim (or, in the case of a Patent Right that is a patent application, would infringe a Valid Claim in such patent application if it were to issue as a patent).
47. “CPI” means the Consumer Price Index — Urban Wage Earners and Clerical Workers, U.S. City Average, All Items, 1982-84 = 100, published by the United States Department of Labor, Bureau of Labor Statistics (or its successor equivalent index) in the United States.
48. “Debarred Party” shall have the meaning set forth in Section 7.5(a).
49. “Delivery Compound” means the chemical compound or compounds contained in either Alnylam’s proprietary lipid nanoparticle system (LNP) or Roche’s proprietary dynamic polyconjugate (DPC) system.
50. “Designated Target” shall have the meaning set forth in the LCA.
51. “[\*\*]” shall have the meaning set forth in the LCA.
52. “Develop” or “Development” means any and all preclinical and clinical drug development activities, including test method development and stability testing, toxicology, animal efficacy studies, formulation, quality assurance/quality control development, statistical analysis, clinical studies, clinical trials and testing, regulatory affairs, product approval and registration, chemical development and Manufacturing development, packaging development and Manufacturing and development documentation efforts in support of development activities anywhere in the world.
53. “Development Costs” shall have the meaning ascribed in Exhibit E.
54. “Development Plan” shall have the meaning set forth in Section 4.5(a).

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55. “Diligence Breach” means a breach of a Party’s diligence obligations under Section 8.1 or Section 8.2, as applicable.
56. “Diligence Breach Cure Period” shall have the meaning set forth in Section 14.2(c).
57. “Diligent Efforts” means, with respect to each Party’s obligations relating to the Licensed Product(s), the carrying out of such obligations in a diligent and sustained manner using efforts substantially similar to the efforts a biopharmaceutical company of comparable size and resources would typically devote to a product of similar market potential, profit potential, similar stage in development or commercialization, or strategic value resulting from its own research efforts, based on conditions then prevailing, and taking into account other relevant factors, including technical, medical, clinical efficacy, safety, manufacturing, and delivery considerations, product labeling or anticipated labeling, the patent and other proprietary position of the product, the regulatory environment and competitive market conditions.
58. “Discover” or “Discovery” means any and all research or discovery activities, including all activities pursuant to the Joint Research Plan, conducted anywhere in the world.
59. “DME” means a Drug Master File filed with the FDA, or an equivalent filing with any other Regulatory Authority.
60. “Effective Date” shall have the meaning set forth in the Preamble.
61. “EMA” means the European Medicines Agency or any successor agency thereto.
62. “European Union” or “EU” means the countries of the European Union, as it is constituted as of the Effective Date and as it may be expanded from time to time.
63. “Executive Officers” means the Chief Executive Officer of Alnylam (or a senior executive officer of Alnylam designated by Alnylam’s Chief Executive Officer) and the Global Head of Pharma Roche (or a senior executive officer of Roche designated by Roche’s Global Head of Pharma).
64. “FBMC” shall have the meaning ascribed in Exhibit E.
65. “FDA” means the United States Food and Drug Administration or any successor agency thereto.
66. “Field” means the treatment or prophylaxis of diseases in humans.
67. “Finished Product” means the finished product formulation of Licensed Product, containing API Bulk Drug Substance, filled into unit packages for final labeling and packaging, and as finally labeled and packaged in a form ready for administration.
68. “First Commercial Sale” means the first sale of a Licensed Product to a Third Party in a country following Regulatory Approval of such Licensed Product in that country or, if no such Regulatory Approval or similar marketing approval is required, the date upon which such Licensed Product is first commercially launched in such country.

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69. “First-in-Man Stage” means the earlier of (a) the issuance of a study report upon completion of GLP Toxicology Studies sufficient to file an IND in the United States or any Major Market Country, or (b) the first dosing of the first human patient in a Clinical Study.
70. “First Phase II Completion” means the issuance of a study report upon completion of the first Phase II Study for a Licensed Product under the Development Plan.
71. “Formulated Bulk” means the API Bulk Drug Substance which has been combined or conjugated with Delivery Compound, as the case may be, before being filled into unit packages.
72. “FTE” means the number of full-time-equivalent person-years of Development (each consisting of a total of [\*\*] hours, unless otherwise mutually agreed by the Parties), Manufacturing or Commercialization work by each Party’s personnel on or directly related to the applicable activity conducted hereunder.
73. “GAAP” means the Parties’ respective generally accepted accounting principles, for Alnylam, the United States generally accepted accounting principles applied on a consistent basis, or any successor accounting principles generally accepted for public companies in the United States (such as IFRS), and for Roche, the IFRS, or any successor accounting principles. Unless otherwise defined or stated, financial terms shall be calculated by the accrual method under GAAP.
74. “GLP Toxicology Study” means a toxicology study that is conducted in compliance with GLP and is required to meet the requirements for filing an IND.
75. “Good Clinical Practice” means the current good clinical practice applicable to the clinical Development of Licensed Product under applicable Law, to the extent such standards are not less stringent than the U.S. current good clinical practice, including the ICH guidelines.
76. “Good Laboratory Practice” or “GLP” means the current good laboratory practice applicable to the Development of Licensed Product under applicable Law, to the extent such standards are not less stringent than the U.S. current good laboratory practice, including 21 C.F.R. Part 58.
77. “Governmental Authority” means any United States federal, state or local or any foreign government, or political subdivision thereof, or any multinational organization or authority or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, any court or tribunal (or any department, bureau or division thereof), or any governmental arbitrator or arbitral body.
78. “ICH” means the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.
79. “IFRS” means International Financial Reporting Standards.

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80. "IND" means an application submitted to a Regulatory Authority to initiate human clinical trials, including (a) an Investigational New Drug application or any successor application or procedure filed with the FDA, (b) any non-U.S. equivalent of the foregoing, and (c) all supplements and amendments that may be filed with respect to any of the foregoing.
81. "Indemnified Party" shall have the meaning set forth in Section 13.4(a).
82. "Indemnifying Party" shall have the meaning set forth in Section 13.4(a).
83. "IND-Enabling Studies" means pharmacokinetic and toxicology studies required to meet the requirements for filing an IND, including any GLP Toxicology Study.
84. "Indication" means any disease or condition, or sign or symptom of a disease or condition.
85. "JCT" shall have the meaning set forth in Section 2.2(a).
86. "JFT" means the Joint Finance Team as set forth in Section 2.3.
87. "Joint Collaboration IP" means Joint Collaboration Know-How and Joint Collaboration Patent Rights.
88. "Joint Collaboration Know-How" means any Know-How, patentable or otherwise, first identified, discovered or developed jointly by the Parties or their Affiliates or others acting on behalf of Roche and Alnylam or their Affiliates in the conduct of the Collaboration.
89. "Joint Collaboration Patent Rights" means any Patent Rights which claim or cover Joint Collaboration Know-How.
90. "Joint Future Technology Committee" shall have the meaning set forth in the LCA.
91. "Joint Research Plan" means the written workplan and timetable attached hereto as Exhibit C, as updated or amended from time to time in accordance with this Agreement. The initial Joint Research Plan is expected to commence on the Effective Date and shall expire on or before August 9, 2012.
92. "JPDT" means the Joint Project Development Team as set forth in Section 2.3.
93. "JSC" shall have the meaning set forth in Section 2.1(a).
94. "JSC Chairperson" shall have the meaning set forth in Section 2.1(b).
95. "Know-How" means any information, inventions, trade secrets or technology, whether or not proprietary or patentable and whether stored or transmitted in oral, documentary, electronic or other form. Know-How shall include ideas, concepts, formulas, methods, procedures, designs, compositions, plans, documents, data, discoveries, developments, techniques, protocols, specifications, works of authorship, biological materials, and any information relating to research and development plans, experiments, results, compounds, therapeutic leads, candidates and products, clinical and preclinical data, clinical trial results, and Manufacturing information and plans (but excluding any scientific, regulatory, pre-clinical or clinical information or data regarding specific Indications and any marketing, financial, commercial, personnel and other business information and plans).

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96. "Law" means any law, statute, rule, regulation, ordinance or other pronouncement or requirement having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision, domestic or foreign.
97. "LCA" shall have the meaning set forth in the Recitals.
98. "Lead Regulatory Party:" shall have the meaning set forth in Section 7.1(a).
99. "Licensed Product" means an RNAi Product directed to a Program Target (or, subject to Section 4.3, to both Program Targets), in the form and formulation Developed (or to be Developed, as applicable) under the Program during the Research Term. All references to Licensed Product in this Agreement shall be deemed to include Combination Product, to the extent applicable.
100. "Licensee Partner" means, with respect to a Party, any Third Party to which a sublicense is granted by such Party in accordance with the terms of this Agreement, including without limitation a Third Party distributor whose obligations to such Party or such Party's Affiliates include responsibility for sales, marketing or distribution efforts in a country on behalf of such Party or such Party's Affiliates, excluding wholesale distributors who purchase Licensed Products from such Party or such Party's Affiliates in an arm's length transaction and who have no other obligation to such Party or such Party's Affiliates.
101. "Listed Alnylam Counterparties" means the Third Party counterparties to Listed Alnylam Third Party Agreements or to Manufacturing Agreements, as applicable, and their respective successors in interest.
102. "Listed Alnylam Third Party Agreement" means (a) the Listed Third Party Agreements (as defined in the LCA), (b) any agreement listed on Exhibit B-2, or (c) any other agreement between Alnylam and a Third Party executed during the Term, pursuant to which Alnylam has rights and obligations with respect to, or which otherwise Cover, a Licensed Product and where (i) the intellectual property that is the subject of such agreement is included within Alnylam Technology, and (ii) such Alnylam Technology is necessary or reasonably useful to Discover, Develop, Commercialize or Manufacture the Licensed Product(s).
103. "Listed Third Party Payment" shall have the meaning set forth in Section 9.3(g).
104. "Losses" shall have the meaning set forth in Section 13.1.
105. "Major EU Country(ies)" means Germany, France, the United Kingdom, Italy and Spain.
106. "Major Market Country:" means any of the United States, Germany, France, United Kingdom, Italy, Spain, and Japan.

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107. “Major Territory” means any of (a) the United States, (b) the EU, (c) Asia, and (d) all other territories not included within the foregoing clauses (a), (b) and (c).
108. “Manufacture” or “Manufacturing” means any and all activities and operations involved in or relating to the manufacturing, quality control testing (including in-process, release and stability testing), releasing or packaging, for pre-clinical, clinical or commercial purposes.
109. “Manufacturing Agreement” means any agreement listed on Exhibit B-3.
110. “Manufacturing Technology” shall have the meaning set forth in Section 6.4(b).
111. “NDA” means an application submitted to a Regulatory Authority for marketing approval of a product, including (a) a New Drug Application, Product License Application or Biologics License Application filed with FDA or any successor applications or procedures, (b) any non-U.S. equivalent of the foregoing, and (c) all supplements and amendments that may be filed with respect to the foregoing.
112. “Necessary Third Party Patents” shall be as defined in the definition of “Required Third Party Payments” below.
113. “Net Sales” means the amount calculated by subtracting from the amount of Adjusted Gross Sales (as defined below) the following:
- (a) With respect to Net Sales in the United States, a lump sum deduction of [\*\*] percent ([\*\*]%) of Adjusted Gross Sales in lieu of those sales-related deductions which are not accounted for by the Commercializing Party, its Affiliates and Licensee Partners on a product-by-product basis (e.g. outward freights, postage charges, transportation insurance, packaging materials for dispatch of goods, custom duties, bad debt expense, discounts granted later than at the time of invoicing);
  - (b) With respect to Net Sales in the Major Market Countries (other than the U.S.) and Canada, a lump sum deduction of [\*\*] percent ([\*\*]%) of Adjusted Gross Sales in lieu of those sales-related deductions which are not accounted for by the Commercializing Party, its Affiliates and Licensee Partners on a product-by-product basis (e.g. outward freights, postage charges, transportation insurance, packaging materials for dispatch of goods, custom duties, bad debt expense, discounts granted later than at the time of invoicing); and
  - (c) With respect to Net Sales in all territories other than those set forth in subsections (a) and (b) above, a lump sum deduction of [\*\*] percent ([\*\*]%) of Adjusted Gross Sales in lieu of those sales-related deductions which are not accounted for by the Commercializing Party, its Affiliates and Licensee Partners on a product-by-product basis (e.g. outward freights, postage charges, transportation insurance, packaging materials for dispatch of goods, custom duties, bad debt expense, discounts granted later than at the time of invoicing).

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For purposes of this definition of “Net Sales”, “Adjusted Gross Sales” shall mean the amount of gross sales of the Licensed Product invoiced by the Commercializing Party, its Affiliates and its Licensee Partners to Third Parties less deductions of returns and return reserves (including allowances actually given for spoiled, damaged, out-dated, rejected, returned Licensed Product sold, withdrawals and recalls), rebates and rebate reserves (to the extent consistently applied by the Commercializing Party to its products), price reductions, rebates to managed care organizations or social and welfare systems, charge backs or reserves for chargebacks, cash sales incentives (but only to the extent it is a sales related deduction which is accounted for within the Commercializing Party on a product-by-product basis), cash discounts, government mandated rebates and similar types of rebates (e.g., Pharmaceutical Price Regulation Scheme, Medicaid, each as consistently applied by Commercializing Party to its products), volume (quantity) discounts, taxes (value added or sales taxes, government mandated exceptional taxes and other taxes directly linked to the gross sales amount).

In the case where a Licensed Product is a Combination Product, the Parties shall meet approximately [\*\*] prior to commercial launch of such Combination Product to negotiate in good faith and agree to an appropriate adjustment to Net Sales to reflect the relative significance of the RNAi Compound and the other pharmaceutically active agent(s) contained in the Combination Product. If the Parties are unable to agree upon such adjustment to Net Sales, royalties with respect to a Combination Product in a country shall be equal to the rates set forth in Section 9.3(a), 9.3(b) or 9.3(c), as applicable, multiplied by a fraction whose numerator is the Commercializing Party’s published sales price in such country for an equivalent dosage of RNAi Compound contained in a given Combination Product, and whose denominator is the Commercializing Party’s published sale prices in such country for an equivalent dosage of all active pharmaceutical ingredients contained therein. If the numerator or denominator cannot be determined in the manner set forth above within ninety (90) days following the meeting between the Parties described in the first sentence of this paragraph, then such matter shall be determined by binding arbitration conducted by one (1) arbitrator in accordance with the rules of Judicial Arbitration and Mediation Services, Inc. (JAMS). The arbitration shall be held in the State of Delaware and shall not last for a period longer than six (6) months.

In such arbitration, the arbitrator shall be an independent expert in worldwide marketing in the pharmaceutical industry mutually acceptable to the Parties or, if the Parties are unable to agree upon such arbitrator, shall be selected by the President of the JAMS office located in the State of Delaware.

114. “Novartis” means Novartis Institutes for BioMedical Research, Inc.

115. “[\*\*]” shall have the meaning set forth in the LCA.

116. “Opt-Out Point” shall have the meaning set forth in Section 4.9(a).

117. “Opt-Out Product” shall have the meaning set forth in Section 4.9(a).

118. “Opt-Out Right” means a Party’s right to opt out of the Program pursuant to Section 4.9(a).

119. “Parties” means Alnylam and Roche; “Party” means either Alnylam or Roche.

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120. "Patent Expenses" shall have the meaning set forth in Section 10.3(g).
121. "Patent Rights" means all patents (including all reissues, extensions, substitutions, confirmations, re-registrations, re-examinations, invalidations, supplementary protection certificates and patents of addition) and patent applications (including all provisional applications, continuations, continuations-in-part and divisionals), and foreign equivalents of any of the foregoing.
122. "Person" means any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government, or any agency or political subdivisions thereof.
123. "Pharmacovigilance Agreement" shall have the meaning set forth in Section 7.2(b).
124. "Phase I Completion" means the issuance of a study report upon completion of all Phase I Studies for a Licensed Product under the Development Plan.
125. "Phase I Study" means a human clinical trial in any country that would satisfy the requirements of 21 C.F.R. § 312.21(a), as amended from time to time.
126. "Phase II Completion" means the issuance of a study report upon completion of all Phase II Studies for a Licensed Product under the Development Plan.
127. "Phase II Study" means a human clinical trial in any country, for which the primary endpoints include a determination of dose ranges or a preliminary determination of efficacy in patients being studied as described in 21 C.F.R. § 312.21(b), as amended from time to time.
128. "Phase III Completion" means the issuance of a study report upon completion of all Phase III Studies for a Licensed Product under the Development Plan.
129. "Phase III Study" means a human clinical trial in any country that is prospectively designed to demonstrate statistically whether a product is safe and effective for use in humans in a manner sufficient to obtain regulatory approval to market such product in patients having the disease or condition being studied as described in 21 C.F.R. § 312.21(c), as amended from time to time.
130. "Post-Approval Study" means a clinical study of Licensed Product that is initiated in a country in the Territory after receipt of Regulatory Approval for such Licensed Product in such country.
131. "Product Liability Claim" means, with respect to a product, any Third Party claim, suit, action, proceeding, liability or obligation involving any actual or alleged death or bodily injury arising out of or resulting from the use of such product, other than an Advertising Claim or any claim, suit, action, proceeding, liability or obligation resulting from the price and commercial terms of Licensed Product in the U.S., or any policy governing the handling of returns, recalls, order processing, invoicing and collection, distribution, and inventory and receivables for, Licensed Product(s) in the U.S.

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132. “Product Liability Costs” means costs associated with Product Liability Claims resulting from the Development, Manufacture, Commercialization, or use of the Licensed Product(s) under this Agreement in the United States and product liability insurance premiums for policies covering the Development, Manufacture, Commercialization, or use of the Licensed Product(s) in the United States (other than Losses entitled to indemnification under Section 13.1 or Section 13.2).
133. “Product Specific Know-How” means Know-How that is specific to a Licensed Product (and not broadly applicable to RNAi Products) or to particular sequences of a Licensed Product, including composition information and any preclinical and clinical test data related to any of the foregoing.
134. “Product Specific Patent Rights” means claim(s) contained in Patent Rights that Cover any Product Specific Know-How.
135. “Profit” means Net Sales of the Licensed Product(s) in the United States by the Commercializing Party and its Related Parties, minus (a) FBMC in the United States (as defined in Exhibit E).
136. “Program” means the Collaboration activities performed or to be performed by the Parties with respect to the Licensed Product(s) under this Agreement.
137. “Program Target” means (a) [\*\*] and (b) one (1) additional Target directed to the [\*\*] as may be mutually agreed by the Parties) as may be selected by mutual agreement of the Parties in accordance with Section 4.3. For purposes of clarity, [\*\*].
138. “Publishing Party” shall have the meaning set forth in Section 11.4.
139. “Regulatory Approval” means, with respect to a product in a country, the approval of the applicable Regulatory Authority necessary for the marketing and sale of such product in such country.
140. “Regulatory Authority” means any federal, national, multinational, state, provincial or local regulatory agency, department, bureau or other governmental entity with authority over the marketing, pricing or sale of a pharmaceutical product in a country, including the FDA.
141. “Related Party” means (a) with respect to Roche, any of Roche’s Affiliates or Licensee Partners, and, (b) with respect to Alnylam, any of Alnylam’s Affiliates or Licensee Partners.
142. “Required Third Party Payments” means royalty payments to a Third Party made by the Commercializing Party under Third Party agreements (other than Listed Alnylam Third Party Agreements and Alnylam Pre-Existing Alliance Agreements, if Alnylam is a Commercializing Party) to license Patent Rights Covering such Third Party’s technology if, in the absence of such license, the licensed use by the Commercializing Party of the Patent Rights licensed by such Commercializing Party from the other Party under Section 3.1 (if the Commercializing Party is Roche) or Section 3.2 (if the Commercializing Party is Alnylam) would infringe such Third Party Patent Rights (such Third Party Patent Rights,

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“Necessary Third Party Patents”); provided, however, that Required Third Party Payments shall not include any royalties or other amounts payable to obtain access to (a) a specific Target or Targets so that such Target or Targets can be the subject of research and development efforts, or (b) Third Party delivery technologies (other than Delivery Patent Rights (as defined in the LCA)) which may be necessary or useful for delivery of double-stranded oligonucleotide molecules, or manufacturing techniques for such delivery technologies.

143. “Research Term” means the period commencing on the Effective Date and ending on August 9, 2012 (as may be extended by mutual agreement of the Parties).
144. “RNAi Compound” means any compound that, in vitro or otherwise, functions through the mechanism of RNA interference and consists of or encodes double-stranded oligonucleotides, and which double-stranded oligonucleotides optionally may be chemically modified to contain modified nucleotide bases or non-RNA nucleotides, and optionally may be administered in conjunction with a delivery vehicle or vector.
145. “RNAi Product” means any product that contains one or more RNAi Compounds as an active ingredient.
146. “Roche” shall have the meaning set forth in the Preamble.
147. “Roche Basel” shall have the meaning set forth in the Preamble.
148. “Roche Nutley” shall have the meaning set forth in the Preamble.
149. “Roche Collaboration IP” means Roche Collaboration Know-How and Roche Collaboration Patent Rights.
150. “Roche Collaboration Know-How” means any Know-How Controlled by Roche, patentable or otherwise, first identified, discovered or developed solely by employees of Roche or its Affiliates or other persons not employed by Alnylam or any of its Affiliates acting on behalf of Roche or any of its Affiliates, in the conduct of the Collaboration. Roche Collaboration Know-How excludes Roche’s interest in Joint Collaboration Know-How.
151. “Roche Collaboration Patent Rights” means any Patent Rights which claim or cover Roche Collaboration Know-How and are Controlled by Roche. Roche Collaboration Patent Rights exclude Roche’s interest in Joint Collaboration Patent Rights.
152. “Roche Indemnities” shall have the meaning set forth in Section 13.2.
153. “Roche Know-How” means Know-How Controlled by Roche as of the Effective Date or as to which Roche obtains Control during the Term that is necessary or reasonably useful for Alnylam and its Affiliates to perform their obligations or exploit their rights under this Agreement with respect to the Licensed Product(s), including their rights to Discover, Develop, Manufacture, or Commercialize Licensed Product (other than Roche’s rights in Joint Collaboration Know-How and Roche Collaboration Know-How).

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154. “Roche Patent Rights” means those Patent Rights that are Controlled by Roche as of the Effective Date or as to which Roche obtains Control during the Term that are necessary or reasonably useful for Alnylam and its Affiliates to perform their obligations or exploit their rights under this Agreement with respect to the Licensed Product(s), including their rights to Discover, Develop, Manufacture, or Commercialize the Licensed Product(s) (other than Roche’s rights in Joint Collaboration Patent Rights and Roche Collaboration Patent Rights).
155. “Roche Technology” means, collectively, Roche Know-How and Roche Patent Rights, Roche Collaboration IP and Roche’s interest in Joint Collaboration IP, and any Third Party Technology that is included in the definition of Roche Technology after the Effective Date in accordance with Section 10.6.
156. “ROW Territory” means the entire Territory other than the United States.
157. “Royalty Term” means, separately with respect to each Licensed Product in each country, the period commencing on the First Commercial Sale of such Licensed Product in such country (provided that either (x) such Licensed Product is Covered by a Valid Claim of the Alnylam Platform Patent Rights, Alnylam Patent Rights, Roche Patent Rights, Alnylam Collaboration Patent Rights, Roche Collaboration Patent Rights or Joint Collaboration Patent Rights in such country at the time of such First Commercial Sale in such country, or (y) the Manufacture of such Licensed Product is Covered by a Valid Claim of the Alnylam Platform Patent Rights, Alnylam Patent Rights, Roche Patent Rights, Alnylam Collaboration Patent Rights, Roche Collaboration Patent Rights or Joint Collaboration Patent Rights in the country or countries in which such Licensed Product is Manufactured) and concluding on the expiration of the later of (a) the last to expire Alnylam Platform Patent Right, Alnylam Patent Right, Roche Patent Right, Alnylam Collaboration Patent Right, Roche Collaboration Patent Right or Joint Collaboration Patent Right containing a Valid Claim Covering the Development, Commercialization or Manufacture of such Licensed Product in that country, (b) the last to expire Alnylam Platform Patent Right, Alnylam Patent Right, Roche Patent Right, Alnylam Collaboration Patent Right, Roche Collaboration Patent Right or Joint Collaboration Patent Right containing a Valid Claim Covering the Manufacture of such Licensed Product in the country or countries in which such Licensed Product was Manufactured, or (c) ten (10) years from the date of First Commercial Sale of such Licensed Product in such country.
158. “[\*\*]” means [\*\*].
159. “Sales Representative” means an individual, who engages in or manages sales calls and other promotional efforts with respect to Licensed Product and who is employed by a Party or an Affiliate of a Party.
160. “Severed Clause” shall have the meaning set forth in Section 15.3.
161. “Supply Agreement” shall have the meaning set forth in Section 6.3.
162. “Supply Agreement Term Sheet” shall have the meaning set forth in Section 6.2(c).

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163. “Target” means (a) a polypeptide or entity comprising a combination of at least one polypeptide and other macromolecules, that is a site or potential site of therapeutic intervention by a therapeutic agent; or a nucleic acid which is required for expression of such polypeptide; (b) variants of a polypeptide (including any splice variant thereof), cellular entity or nucleic acid described in clause (a); or (c) a defined non-peptide entity, including a microorganism, virus, bacterium or single cell parasite; provided that the entire genome of a virus shall be regarded as a single Target.
164. “Term” shall have the meaning set forth in Section 14.1.
165. “Terminated Patent Right” shall have the meaning set forth in Section 9.3(i).
166. “Territory” means the entire world.
167. “Third Party” means any Person other than Alnylam or Roche and their respective Affiliates.
168. “Third Party Contractors” means Third Party contractors such as contract research organizations, contract employees, consultants, contract manufacturers and the like.
169. “Third Party Technology” shall have the meaning set forth in Section 10.6(a).
170. “UBC” means the University of British Columbia.
171. “UBC Sublicense Agreement” means the Sublicense Agreement between Tekmira Pharmaceuticals Corporation (formerly INEX Pharmaceuticals Corporation) and Alnylam Pharmaceuticals, Inc., dated January 8, 2007.
172. “United States” or “U.S.” means the United States of America and its territories and possessions.
173. “Valid Claim” means a claim (a) of any issued, unexpired patent that has not been revoked or held unenforceable or invalid by a decision of a court or governmental agency of competent jurisdiction from which no appeal can be taken, or with respect to which an appeal is not taken within the time allowed for appeal, and that has not been disclaimed or admitted to be invalid or unenforceable through reissue, disclaimer or otherwise, or (b) of any patent application that has not been cancelled, withdrawn or abandoned, or been pending for more than [\*\*] from the earliest priority date for such patent application.

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**EXHIBIT B-1**

**Alnylam Pre-Existing Alliance Agreements**

Copies of the following agreements, some in redacted form, have been, or shall be, made available to Roche as of the Effective Date:

1. Amended and Restated Strategic Collaboration and License Agreement between Isis Pharmaceuticals, Inc. and Alnylam Pharmaceuticals, Inc., dated April 28, 2009
2. Cross-License Agreement between Protiva Biotherapeutics Inc. and Alnylam Pharmaceuticals, Inc., dated August 14, 2007
3. Amended and Restated Cross-License Agreement between Protiva Biotherapeutics Inc. and Alnylam Pharmaceuticals, Inc., dated May 30, 2008
4. Amended and Restated License and Collaboration Agreement between Tekmira Pharmaceuticals Corporation and Alnylam Pharmaceuticals, Inc., dated May 30, 2008
5. License and Collaboration Agreement between Takeda Pharmaceutical Company Limited and Alnylam Pharmaceuticals, Inc., dated May 27, 2008, as supplemented by letter agreement dated May 27, 2008
6. Sponsored Research Agreement between the University of British Columbia, AlCana Technologies, Inc., and Alnylam Pharmaceuticals, Inc., dated July 27, 2009, as supplemented by the Supplemental Agreement between Tekmira Pharmaceuticals Corporation, Protiva Biotherapeutics Inc., the University of British Columbia, AlCana Technologies, Inc., and Alnylam Pharmaceuticals, Inc., dated July 27, 2009
7. Letter amendments dated July 11, 2008 and July 11, 2009 to the Research Collaboration and License Agreement, effective as of October 12, 2005, by and between Alnylam and Novartis, as amended by the Addendum Re: Influenza Program effective as of December 13, 2005, Amendment No. 1 to such Addendum effective as of March 14, 2006, and Amendment No. 2 to such Addendum effective as of May 5, 2006
8. Letter agreement dated January 31, 2008 to the Strategic Collaboration & License Agreement between Isis Pharmaceuticals, Inc., and Alnylam Pharmaceuticals, Inc., dated March 11, 2004, as supplemented or amended by letter agreements dated March 9, 2004 (as amended by letter agreement dated October 28, 2005), March 11, 2004, and June 10, 2005

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**EXHIBIT B-2**

**Listed Alnylam Third Party Agreements**

Copies of the following agreements, some in redacted form, have been, or shall be, made available to Roche as of the Effective Date:

1. License Agreement between Celo GmbH and Alnylam Pharmaceuticals, Inc., dated July 27, 2009
2. Licensing Agreement between ETH Zurich and Alnylam Pharmaceuticals, Inc., dated April 30, 2009
3. Amended and Restated Strategic Collaboration and License Agreement between Isis Pharmaceuticals, Inc. and Alnylam Pharmaceuticals, Inc., dated April 28, 2009
4. Cross-License Agreement between Protiva Biotherapeutics Inc. and Alnylam Pharmaceuticals, Inc., dated August 14, 2007
5. Amended and Restated Cross-License Agreement between Protiva Biotherapeutics Inc. and Alnylam Pharmaceuticals, Inc., dated May 30, 2008
6. Amended and Restated License and Collaboration Agreement between Tekmira Pharmaceuticals Corporation and Alnylam Pharmaceuticals, Inc., dated May 30, 2008
7. Exclusive License Agreement between The Regents of the University of California and Alnylam Pharmaceuticals, Inc., dated April 3, 2009
8. Waiver Amendment dated August 9, 2007 to the Co-Exclusive License Agreement between Max Planck Innovation GmbH (formerly Garching Innovation GmbH) and Alnylam Pharmaceuticals, Inc., dated December 20, 2002, as amended by Amendment dated July 2, 2003, and the Requirements Amendment effective June 15, 2005
9. Letter agreement dated January 31, 2008 to the Strategic Collaboration & License Agreement between Isis Pharmaceuticals, Inc., and Alnylam Pharmaceuticals, Inc., dated March 11, 2004, as supplemented or amended by letter agreements dated March 9, 2004 (as amended by letter agreement dated October 28, 2005), March 11, 2004, and June 10, 2005
10. Amendments dated May 7, 2008 and May 20, 2008 to the Amended and Restated Exclusive Patent License Agreement between Alnylam Pharmaceuticals, Inc., and Massachusetts Institute of Technology, dated May 9, 2007
11. License Agreement between Medical College of Georgia Research Institute, Inc., and Nucleonics, Inc., dated May 18, 2001, as amended on November 19, 2001, April 18, 2003, December 16, 2003, and July 20, 2004, and assigned from Nucleonics, Inc., to Alnylam Pharmaceuticals, Inc., on December 5, 2008

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12. License Agreement between Wyeth and Nucleonics, Inc, dated June 30, 2003, as amended on August 28, 2006, and assigned from Nucleonics, Inc., to Alnylam Pharmaceuticals, Inc., on December 5, 2008
13. License Agreement between Wyeth and Nucleonics, Inc., dated August 28, 2006, and assigned from Nucleonics, Inc., to Alnylam Pharmaceuticals, Inc., on December 5, 2008 [Wyeth as Licensor]
14. License Agreement between Wyeth and Nucleonics, Inc., dated August 28, 2006, and assigned from Nucleonics, Inc., to Alnylam Pharmaceuticals, Inc., on December 5, 2008 [Nucleonics as Licensor]
15. Sublicense Agreement between Wyeth and Nucleonics, Inc., dated June 30, 2003, and assigned from Nucleonics, Inc., to Alnylam Pharmaceuticals, Inc., on December 5, 2008
16. Assignment between Wyeth and Nucleonics, Inc., dated July 13, 2007, and assigned from Nucleonics, Inc., to Alnylam Pharmaceuticals, Inc., on December 5, 2008

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**EXHIBIT B-3**

**Manufacturing Agreements**

Copies of the following agreements, some in redacted form, have been, or shall be, made available to Roche as of the Effective Date:

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**EXHIBIT C**

**Joint Research Plan**

**Anylam-Roche [\*\*] Collaboration Workplan**

**September 9, 2009**

**FINAL**

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**Summary of Research Plan and Timeline:**

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A total of two pages were omitted pursuant to a request for confidential treatment.

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**EXHIBIT D**

**Supply Agreement Term Sheet**

Anylam and Roche shall use their respective Diligent Efforts to enter into a Supply Agreement which will be consistent with the terms of this Supply Agreement Term Sheet. From the Candidate Selection Stage until the effective date of the Supply Agreement, the terms of the Agreement and this Supply Agreement Term Sheet shall govern the Manufacture and supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) under the Agreement, including pre-clinical and clinical supply in the quantities and on the delivery terms set forth in the Development Plan (or as otherwise mutually agreed by the Parties); provided, however, that in the event of conflict between this Supply Agreement Term Sheet and the Agreement, the terms of the Agreement shall apply.

2. The Parties shall be responsible for establishing the specifications (the “Specifications”) and approving the master batch record, including the necessary documentation, certificates of analysis and test results, for the API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable), to be supplied under the Supply Agreement.

3. Unless agreed otherwise in writing by the Parties, [\*\*] before the commencement of each Calendar Quarter, each Party will give to the other Party (and to the JSC if the JSC remains in effect) a rolling [\*\*] Calendar Quarter forecast (“Forecast”) of the estimated quarterly requirements of API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) for which such other Party Controls the Manufacturing technology. Such Forecast will include quantity and unit requirements for API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) in the United States and the ROW Territory. [\*\*] percent ([\*\*]%) of forecasted requirements during the first [\*\*] Calendar Quarters of such Forecast shall be considered binding on the Parties. The purchasing Party will provide the supplying Party with binding purchase orders at least [\*\*] in advance of the requested delivery. If the purchasing Party requests any changes to the Forecast, the supplying Party shall (i) use its commercially reasonable efforts to accommodate such requests and (ii) use its commercially reasonable efforts to minimize any costs incurred as a result of such changes.

4. In the event of an anticipated shortage of supply of API Bulk Drug Substance, Delivery Compound, Formulated Bulk or Finished Product (as applicable), which a Party is responsible for supplying to the other Party hereunder, such supplying Party shall promptly notify the other Party and, unless otherwise agreed by the Parties, available supply shall be allocated between the United States and the ROW Territory on a pro-rata basis based on good faith forecasts of requirements. In addition, the supplying Party will use commercially reasonable efforts to engage a secondary source of supply and to resolve all anticipated failure to supply issues as promptly as possible in consultation with the other Party.

5. If and to the extent that a Failure to Supply (as hereinafter defined) occurs, the purchasing Party, if the purchasing Party is also the Commercializing Party, shall have the right to assume control of the Manufacture of the Licensed Product(s) by requesting a transfer of Manufacturing pursuant to Section 6.4. For purposes of this Supply Agreement Term Sheet, a “Failure to Supply” will be deemed to have occurred only after the supplying Party and all secondary

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sources of supply made available to the purchasing Party have failed to deliver [\*\*] percent ([\*\*]%) of the aggregate requirements for API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) for a given Calendar Quarter as described in the Forecast, in [\*\*] out of any [\*\*] consecutive Calendar Quarters.

6. Each Party agrees that all API Bulk Drug Substance, Delivery Compound, Formulated Bulk and Finished Product (as applicable) supplied to the other Party hereunder will, at the time of delivery to such other Party, have been Manufactured in accordance with the Specifications and the master batch record, and except for batches not intended for human use, with cGMP. The supplying Party will be solely responsible for all costs and expenses caused by failed batches, including batches which fail to meet the requirements of the previous sentence, as a result of the negligence or intentional misconduct of any employee of such supplying Party. The purchasing Party will be responsible for all costs and expenses caused by failed batches other than as a result of the negligence or intentional misconduct of any employee of the supplying Party.

7. In addition to more detailed terms regarding the matters specified above in this Supply Agreement Term Sheet, the Supply Agreement shall contain other customary supply agreement provisions, including indemnification provisions appropriate for a supply agreement. Furthermore, Alnylam and Roche will enter into a Technical and Quality Agreement with respect to the Licensed Product(s) governing, among other things, quality assurance requirements, documentation and procedures, audit and inspection rights and similar matters.

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## **EXHIBIT E**

### **FINANCIAL APPENDIX**

This Exhibit E sets forth the principles for capturing, reporting and consolidating Development Costs, Commercialization Costs, and Profit sharing. Roche shall be responsible for all other costs with respect to Licensed Product(s).

For such purpose, this Exhibit E sets forth the principles for reporting actual results and budgeted plans in the United States, the frequency of reporting, the use of a single "Functional Currency" (as defined under the heading "Foreign Exchange" below) and the methods of determining payments to the Parties, auditing of accounts and other matters.

This Exhibit E also provides agreed upon definitions of financial terms applicable to the Parties for any Licensed Product. Except for the term Licensed Product, all capitalized terms used herein without definition shall have the meanings ascribed thereto in the Agreement and, where applicable, the further definitions contained herein. The term "Product" in this Exhibit E shall mean Licensed Product. References in this Exhibit E to a "Party" or "Parties" shall be construed to mean Alnylam or Roche, as the case may be, and in every case shall be deemed to include a Party's Affiliates or Licensee Partners under the Agreement. Capitalized terms used herein, but not otherwise defined, shall have the meanings given them in the Agreement.

Notwithstanding anything in the Agreement to the contrary, no cost, expense, amount or sum allocable or chargeable to the Parties' activities under the Agreement shall be allocated or charged more than once. Unless otherwise specifically authorized by the Parties or the Agreement, all costs, expenses, amounts or sums to be charged or allocated by one Party to the other Party under the Agreement shall not be so chargeable or allocable unless they are both directly related to the Agreement and the activities to be performed under the Agreement and are reasonable and customary with respect to the global biopharmaceutical industry considering the respective size and activities of the two Parties as collaborators under the Agreement.

#### ARTICLE I

##### REPORTING AND CONSOLIDATION OF DEVELOPMENT COSTS AND COMMERCIALIZATION COSTS

Section 1.1 Preparation of Budgets. Preparation of annual budgets will be initiated in each July during such period and a preliminary budget will be presented for review by the JFT before [\*\*] during such period. The completed Development Plan budget or Commercialization Plan budget, as applicable, should be approved by the Parties by the end of each November during such period. Reporting by each Party will be performed as follows (with copies provided to the JPDT or JCT and to the other Party):

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<u>Reporting Event(calendar basis)</u>	<u>Submission</u>	<u>Frequency</u>	<u>Deadline</u>
Q1-Q3	Actuals	End of Calendar Quarter	[**]
Q4	Actuals	End of Calendar Quarter	[**]
Preliminary annual budget		Annually	[**]
Final annual budget		Annually	[**]
Forecasts for sales (current Calendar Year) for the United States		Quarterly, except Q4	[**]
Full profit and loss forecast for the United States (current Calendar Year)		Quarterly, except Q4	[**]

Responsibility for preparing the Development Plan budget and Commercialization Plan budget (other than the initial budget, which shall be determined by the Parties) will rest with the JPDT and JCT, respectively. Both JPDT and JCT budgets shall be reviewed and approved by the JFT and presented to the JSC for review (which shall then present to the Parties for approval)

Section 1.2 Reporting. Each Party shall report to the other Party and the JFT actual, budget and forecast results of operations related to the following, as applicable:

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The JFT shall be responsible for the preparation of consolidated reporting (actuals, budgets and forecasts) for the Development Costs, Commercialization Costs and Profit based upon the Commercialization Plan Reports, Development Plan Reports and Sales Reports provided by the Parties as specified below, as well as determination of the cash settlement.

Within [\*\*] days after the end of each Calendar Quarter (or for the last Calendar Quarter of each Calendar Year, within [\*\*] days after the end of such Calendar Quarter), each Party shall provide the other Party and the JFT with such Party's "Development Plan Report" for such Calendar Quarter. Such report shall be in writing and shall summarize the Development Program activities undertaken by such Party (or its relevant local Affiliates) during such Calendar Quarter in connection with the Development Plan, together with a detailed project-level statement of those expenses incurred by such Party during such Calendar Quarter that are specific to the Development Plan and satisfy those additional criteria necessary to qualify as Development Costs. Such report shall also address any necessary adjustments of Development Costs for previous Calendar Quarters.

Within [\*\*] days after the end of each Calendar Quarter (or for the last Calendar Quarter of each Calendar Year, within [\*\*] days after the end of such Calendar Quarter), each Party shall provide the other Party and the JFT with such Party's "Commercialization Plan Report" for such Calendar Quarter. Such report shall be in writing and shall summarize the marketing and promotional activities undertaken by such Party (or its relevant local Affiliates) during such

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Calendar Quarter in connection with the applicable Commercialization Plan, together with a detailed project-level statement of commercialization-related expenses incurred by such Party during such Calendar Quarter that are specific to the United States and satisfy those additional criteria necessary to qualify as Commercialization Costs. Such report shall also address any necessary adjustments of Commercialization Costs for previous Calendar Quarters. Within [\*\*] days after the end of each Calendar Quarter (or for the last Calendar Quarter of each Calendar Year, within [\*\*] days after the end of such Calendar Quarter), Roche shall provide Alnylam and the JFT with Roche's "Sales Report" for such Calendar Quarter. Such report shall be in writing and shall summarize the Product sales made by Roche in the United States in such Calendar Quarter and the calculation of Adjusted Gross Sales, Net Sales and Profit with respect to such sales. Such report shall also address any necessary adjustments of Adjusted Gross Sales, Net Sales and Profit for previous Calendar Quarters.

The JFT will be responsible for monitoring and agreeing upon appropriate controls to ensure reasonable and consistent calculation of Commercialization Costs, Development Costs and Profit under the Agreement, including in the Development Plan Reports, Commercialization Plan Reports and Sales Reports. More specifically, the JFT shall review the budgeted and forecasted versus actual FTEs and external expenses per quarter. In any event, the JFT shall review use of FTE resources on a quarterly basis. The Parties shall also use commercially reasonable efforts to provide access to available discounts and discount programs available from existing vendors for the benefit of the Parties under the Agreement. The Parties' actual results compared to budget and forecast will be calculated by the JFT and set forth in the Reconciliation Statement described below.

The Parties will work together to keep actual spending within the approved budget and forecast; provided, that, the Parties shall continue to share in Development Costs and Commercialization Costs that exceed the budget by up to [\*\*] percent ([\*\*]%). The Parties shall discuss in good faith the adoption of additional control measures to address deviations from the approved budget and forecast on an annual basis above [\*\*] percent ([\*\*]%). If a Party contemplates that any expenditure will increase the annual budget associated with the Commercialization Plan by more than [\*\*] percent ([\*\*]%), the Parties shall review the expenditure with the JCT prior to commitment to that expenditure. The JFT will meet as appropriate to review and approve the reporting events (actuals, budgets and forecasts) and any deviations from the approved budget.

Each Party shall report Development Costs and Commercialization Costs based on its project cost system (which shall in any event track FTEs by functional area and by month) or using such other system as such Party applies with respect to its internal programs and which system has been reviewed with the JFT. In general, these project cost systems shall report actual and/or allocable time spent on specific projects, apply the FTE rates, determined in the manner specified in Section 1.6 below.

Section 1.3 Reconciliation Statements. The financial representatives from each Party on the JFT shall be responsible for, within [\*\*] calendar days following the end of a Calendar Quarter (or, for the last Calendar Quarter in a Calendar Year, within [\*\*] days after the end of such Calendar Quarter), preparing and providing to the other Party (through the JFT) and to the JPDT and JCT, a statement ("Reconciliation Statement"), in a format agreed to by the Parties and based on the information contained in Development Plan Reports, Commercialization Plan

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Reports and Sales Report provided by Parties for such Calendar Quarter and any additional information obtained by the JFT from the Parties, that shows each Party's results, the calculations of Development Costs, Commercialization Costs, cost-sharing under the Agreement and any cash settlement required for such Calendar Quarter. The JPDT and JCT shall each promptly decide whether to approve those portions of the Reconciliation Statement that are under its jurisdiction. If there is a dispute within the JPDT or JCT (or both) regarding approval of a Reconciliation Statement, the JFT shall submit such dispute to the Executive Officers of each Party for resolution. The Executive Officers shall undertake good faith efforts to resolve such dispute and approve the Reconciliation Statement (or, if applicable, an amended Reconciliation Statement) no later than [\*\*] days after the end of the applicable Calendar Quarter (or, for the last Calendar Quarter in a Calendar Year, within [\*\*] days after the end of such Calendar Quarter).

Section 1.4 Foreign Exchange. The "Functional Currency" for accounting for Development Costs and Commercialization Costs will be U.S. dollars.

Section 1.5 Payments Between the Parties. Based upon the Reconciliation Statement, as prepared by the JFT and approved by the JPDT and JCT or the Executive Officers of each Party, as applicable, there shall be a cash settlement between the Parties of the amounts due under the Reconciliation Statement and each Party's share of the Profit. The Party that is owed any amount under the Reconciliation Statement will provide the other Party an invoice for such amount, and such other Party shall pay such invoice within [\*\*] days after approval of the applicable Reconciliation Statement and receipt of the applicable invoice. In the event any payment is made after the date specified in the preceding sentence and provided that such payment is not otherwise subject to good faith dispute, the paying Party shall pay interest as set forth in Section 9.7 of the Agreement. For clarity, the Parties shall separately identify, and make a separate payment for each of, the share of Profit provided for in Section 9.2 of the Agreement and the other payment (for Development Costs and Commercialization Costs) required pursuant to the Reconciliation Statement; however, both payments will take place on the same day.

Section 1.6 FTE Rates.

(a) The Parties have agreed on the Development FTE-rate, as set forth in clause (b) below, that will be charged for the resources allocated to the Development Plan activities from the functions directly operating the activities on a fractional Development FTE-basis. The Parties contemplate that this rate captures total actual personnel and fixed costs attributable to the performance of the Development Plan under this Agreement.

(b) All Development FTE expenditures shall be included in Development Costs based on a rate of US\$[\*\*] per Development FTE. For each Calendar Year after 2010, the Development FTE rate will be adjusted by the increase or decrease in CPI as published by the U.S. Bureau of Labor Statistics for the previous ..Calendar Year. All people within these functions will record the percent of time each month spent on the activities under the programs. For clarity, Development FTE time recording should be made on a fractional basis. Each Party will also use its respective project cost system with the purpose of tracking and reporting costs on a project/product indication/work package level.

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(c) FTE rates (i.e., Sales Force FTE Rate, G&A FTE Rate, Medical Affairs FTE Rate, Marketing FTE Rate) for purposes of determining Commercialization Costs hereunder shall be determined as set forth in Article II below.

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ARTICLE II

RELEVANT DEFINITIONS

Section 2.1 "Development Costs" shall mean the expenses incurred by a Party or for its account that are consistent with the Development Plan and specifically are attributable to the Development of a Product for a particular indication for approval in the U.S., commencing from the completion of activities under the Joint Research Plan onward until First Commercial Sale of the Product for such indication. Development Costs shall include amounts paid by a Party to Third Parties involved in the Development of Products, and all internal costs incurred by a Party in connection with the Development of Products. Notwithstanding anything to the contrary herein, Development Costs shall not include any expenses associated specifically for Development for a country other than the U.S.; except to the extent such expenses relate to Development activities specifically included in the Development Plan for the purpose of generating data or information to obtain expand and/or maintain Regulatory Approval in the United States.

Development Costs shall include the Fully Burdened Manufacturing Cost for clinical supplies for the Development Plan, the cost of the development plans and programs for the Development Plan, and the Required Third Party Payments payable prior to First Commercial Sale in the U.S., and the cost of Development pursued under the Development Plan through receipt of Regulatory Approval for such Product (including the cost of studies on the toxicological, pharmacokinetic, metabolic or clinical aspects of such Product conducted internally or by individual investigators or consultants necessary for the purpose of obtaining approval of such Product by a government organization in the U.S), and costs for preparing, submitting, reviewing or developing data or information for the purpose of a submission to a Regulatory Authority to obtain Regulatory Approval of the Product in a country within the Development Plan. For clarity, the cost of a human clinical trial conducted to support the filing of a Supplemental NDA, as defined in the FD&C Act and applicable regulations promulgated thereunder by the FDA, or equivalent application in any other regulatory jurisdiction within the Development Plan, or conducted to otherwise support a new Regulatory Approval of a Product in the U.S., shall be included within Development Costs, notwithstanding the fact that such trial is conducted after receipt of a Regulatory Approval for such Product. Development Costs shall not include Legal Expenses, Pre-Launch Marketing Expenses or Post-Approval Studies.

Section 2.2 "Fully Burdened Manufacturing Cost" or "FBMC" shall mean the manufacturing cost for a Product, as defined by Roche's or Alnylam's, as the case may be, standard cost accounting practices and policies, both in accordance with IFRS or GAAP, as applicable. In the event of any transfer of Product among Roche, Alnylam, its Affiliates or Licensee Partners, FBMC shall exclude any profit or other mark-up by any such parties.

Such FBMC shall include direct labor, materials, product testing costs (including quality control and quality assurance bulk testing and in-process testing e.g. adventitious virus and mycoplasma testing), direct Third Party contracting cost, Period Costs, cost of failed batches, and manufacturing overhead allocable to the Product (including information technology, human resources, manufacturing planning, manufacturing finance and control, energies, waste maintenance, insurance, custom & duties, shipment & logistic cost, warehousing and storage and

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distribution cost, to the extent that each is manufacturing and Product-specific), for manufacturing or contracting for each stage of the manufacturing process of the Product shipped. The Parties will discuss and agree annually between October and January the main drivers of FBMC for the up-coming Calendar Year. On or before October 31st of each Calendar Year, the parties will agree to an estimated FBMC to be charged for the subsequent Calendar Year, subject to annual true-up process, which will be agreed upon by the JFT.

Such FBMC shall not include any costs associated with process development, scale up costs, qualification lots and any other costs if they are included in Development Costs. If qualification lots are used for Product sale, then Alnylam's share of those Development Costs will be credited towards FBMC in the United States. This credit shall be a variance to FBMC based upon the unit pull-through of the qualification lots into Product Net Sales. The Parties shall discuss and agree upon cost-sharing principles for pre-launch investments, including but not limited to expanded production facilities and commitments to Third Parties, in case of unforeseen delay in launch.

Section 2.3 "Period Costs" shall be comprised of:

(a) Write offs and disposal cost of expired goods (raw materials, intermediates and Products valued at FBMC) (it being understood that the collaboration shall consider the Commercialization Plan requirements when establishing the manufacturing supply);

(b) Inventory valuation differences: The valuation difference for inventory in stock resulting from any change of standard FBMC at that respective point in time. At least annually, Roche will review and compare its standard FBMC for a Product when that particular material was produced to its new standard FBMC and make a retroactive adjustment to the inventory value;

(c) Start up costs to the extent not included in Development Costs;

(d) Excess capacity and idle plant cost to the extent associated with the Product and provided for in the Commercialization Plan with the consent of Alnylam. Except with the consent of Alnylam, FBMC shall not include excess capacity or idle plant cost that was not provided for in the Commercialization Plan in view of the anticipated needs and associated demand forecast of the Licensed Product. Period Costs will be credited for the costs of any idle plant that was earmarked for a different Roche product but actually used by a Product; and

(e) Normal yield losses and variances that could have reasonably been expected and/or justified in this area of technology.

Section 2.4 "Commercialization Costs" means those expenses incurred by a Party which are generally consistent with the Commercialization Plan (and associated budget) and are specifically attributable to Products in the United States, and shall consist of (i) Marketing Expenses, (ii) Medical Affairs Expenses, (iii) Out-of-Pocket Costs, (iv) Legal Expenses, (v) Third Party License Fees, (vi) General and Administrative Expenses, (vii) Post- Launch Product R&D Expenses, (viii) Sales Force Expenses, and (ix) Restructuring Expenses. Commercialization Costs shall exclude Development Costs. Notwithstanding the foregoing,

Legal Expenses need not be consistent with the Commercialization Plan (and associated budget) as long as they have been approved by the JCT. Each Party shall allocate its Commercialization Costs and each of the expenses based on reasonable accounting methodologies consistently applied throughout such Party's organization. The foregoing shall not include any Out-of-Pocket Costs or other costs which have been included in Development Costs. For clarity, it is the intent of the Parties that costs and headcount included in the foregoing will not be unfairly allocated to the Products (to the extent that any Commercialization Cost is attributable, in part, to products or activities other than the Products).

Section 2.5 "Marketing Expenses" means the costs incurred by a Party, excluding Sales Force Expenses, which are generally consistent with the Commercialization Plan (and associated budget) and are specifically attributable to the sale, promotion, and/or marketing of a Product in the United States. Marketing Expenses shall be the sum of Marketing Management, Market and Consumer Research, Pre-Launch Marketing Expenses, Advertising, Trade Promotion and Consumer Promotion (each of which is specified below). To the extent that Marketing Expenses consist of costs other than Third Party costs, it shall mean the product of (a) the number of FTEs directly involved in performing Marketing Management, Market and Consumer Research, Advertising, Trade Promotion, and Consumer Promotion and (b) the applicable Marketing FTE Rate. For purposes of calculating the number of FTEs, an allocated portion of the marketing staff directly involved in the management of and the performance of the marketing functions in the United States for such Product shall be included.

(a) "Marketing FTE Rate" shall mean, for the Calendar Year in which the First Commercial Sale in the United States occurs, a rate agreed upon by the Parties at least twelve (12) months prior to the anticipated date of Regulatory Approval in the United States, based on the fully burdened field force cost of major pharmaceutical companies in the United States.

(b) "Marketing Management" shall include product management and sales promotion management compensation and departmental expenses. This shall include costs associated with developing overall sales and marketing strategies and planning for Products. In addition, payments to Third Parties in connection with Product-specific trademark selection, filing, prosecution and enforcement shall be included in this category.

(c) "Market and Consumer Research" shall include compensation and departmental expenses for market and consumer research personnel and payments to Third Parties related to conducting and monitoring professional and consumer appraisals of existing, new or proposed Products such as market share services (e.g., IMS data), special research testing, and focus groups.

(d) "Advertising" shall include all media costs associated with Product advertising as follows: production expense/artwork including set up; design and art work for an advertisement; the cost of securing print space, air time, etc. in newspapers, magazines, trade journals, television, radio, billboards, etc.

(e) "Trade Promotion" shall include the allowances given to retailers, brokers, distributors, hospital buying groups, etc. for purchasing, promoting, and distribution of Products. This shall include purchasing, advertising, new distribution, and display allowances as well as

free goods, wholesale allowances and the cost of goods for reasonable field sales samples of Products and the cost of administering these programs. To the extent multiple products are involved and some of such products are not Products, then such allowances shall be allocated on a pro rata basis based upon net sales of each respective product by such operating unit during the most recent quarter.

(f) “Consumer Promotion” shall include the expenses associated with programs to promote Products directly to the end user. This category shall include expenses associated with promoting products directly to the professional community such as professional samples, professional literature, promotional material costs, patient aids and detailing aids. To the extent multiple products are involved and some of such products are not Products, then such allowances shall be allocated on a pro rata basis based upon net sales of each respective product by such operating unit during the most recent quarter.

(g) “Pre-Launch Marketing Expenses” shall include those Marketing Management, Market and Consumer Research, Advertising, Trade Promotion, and Consumer Promotion expenses incurred between the filing of a complete NDA for a Product and the First Commercial Sale of such Product.

Section 2.6 “Medical Affairs Expense” means (a) the product of (i) the number of field-and office-based FTEs supporting the coordination of pre-market authorization preparation as well as Post-Approval Studies in the United States related to a Product as agreed upon in the approved Commercialization Plan and its budget and (ii) the applicable Medical Affairs FTE Rate; (b) the cost of performing Post-Approval Studies in the United States; and (c) External Education Expenses (including journal clubs, congresses, and conferences, etc.). For purposes of calculating the number of FTEs, an allocated portion of the medical affairs staff directly involved in the coordination of pre-market authorization preparation for a Product or Post-Approval Studies in the United States for a Product shall be included. Each medical affairs staff member shall record the percent of time allocated to the Product and to all other products, and time allocated to other products shall be excluded in calculating the number of FTEs.

(a) The applicable “Medical Affairs FTE Rate” shall be a rate agreed upon by the Parties at the time the Commercialization Plan is agreed upon by the Parties based upon the fully burdened cost of medical affairs professionals reasonably appropriate for the United States. It is anticipated that the Medical Affairs FTE Rate will equal the Marketing FTE Rate agreed upon under “Marketing Expenses” above.

(b) “External Education Expenses” shall include expenses associated with professional education with respect to Products or AD/MCI in general through any means not covered above, including articles appearing in journals, newspapers, magazines or other media; seminars, scientific exhibits, and conventions; and symposia, advisory boards and opinion leader development activities.

Section 2.7 “Out-of-Pocket Costs” shall mean costs and expenses not included in any other category under Commercialization Costs that are paid to Third Parties (or payable to Third Parties and accrued in accordance with GAAP or IFRS) by either Party and/or its Affiliates in accordance with the applicable Development Plan or Commercialization Plan, other than Third Party License Fees.

Section 2.8 “Legal Expenses” means (a) the fees and expenses of outside counsel and payments to Third Parties incurred after the Effective Date in connection with the preparation, filing, prosecution, maintenance, interference, re-examination and re-issue of Product-specific trademarks in the United States, (b) Losses associated with Product Liability Claims in the United States, as provided in Section 13.3 of the Agreement (provided, that no internal legal costs shall be included in Legal Expenses), and (c) the fees and expenses, including without limitation reasonable fees for outside counsel, for any litigation or other action undertaken by a Party by mutual consent pursuant to Section 10.5(c)(iii) or 10.5(d) of the Agreement.

Section 2.9 “Third Party License Fees” means all Required Third Party Payments payable by either Party after First Commercial Sale.

Section 2.10 “General and Administrative Expenses” shall mean the product of (a) the number of FTEs allocated towards general and administrative functions as set forth in the approved Commercialization Plan and (b) the applicable G&A FTE Rate. For purposes of calculating the number of FTEs, an allocated portion of the general and administrative staffs directly involved in the management of and the performance of the general and administrative functions in the United States for such Product shall be included.

Section 2.11 “G&A FTE Rate” shall mean, for the Calendar Year in which the First Commercial Sale in the United States occurs, a rate agreed upon by the Parties at the time the Commercialization Plan is agreed upon by the Parties, based on the fully burdened general and administrative staff cost reasonably appropriate for the United States. For purposes of clarification, the G&A FTE Rate shall not include any items previously captured in the calculation of the Marketing FTE Rate, Medical Affairs FTE Rate or Sales Force FTE Rate.

Section 2.12 “Post-Launch Product R&D Expenses” shall include certain Development Costs incurred by a Party in relation to a Product after the First Commercial Sale in the United States and required to maintain Regulatory Approval in the United States and shall exclude (a) administrative expenses and costs that are included within Fully Burdened Manufacturing Costs and (b) Post-Approval Studies that are included within Medical Affairs Expenses.

Section 2.13 “Sales Force Expenses” shall mean the product of (a) the number of FTEs detailing and co-promoting Products in the United States as set forth in the approved Commercialization Plan and (b) the applicable fully burdened Sales Force FTE Rate. For purposes of calculating the number of FTEs, an allocated portion of the field sales forces, field sales offices, and home offices staffs directly involved in the management of and the performance of the selling functions in the United States for such Product shall be included, and any portion of staff time allocated to other products shall be excluded. If any members of the field sales force are detailing a Product and one or more other products, the Parties shall agree upon the relative value (on a percentage basis), based on the placement of and emphasis on each product in such detailing, of the detailing of such Product relative to the other products, and each such member of the field sales force shall record such percentage for those details that involve such Product, and the number of FTEs shall exclude that percent of total details that involve, in whole or in part, other products.

Section 2.14 "Sales Force FTE Rate" shall mean, for the Calendar Year in which the First Commercial Sale in the United States occurs, a rate agreed upon by the Parties at the time the Commercialization Plan is agreed upon by the Parties, based on the fully burdened field force cost reasonably appropriate for the United States.

Section 2.15 "Restructuring Expenses" shall mean any expenses related to re-organization or downsizing due to changes in the market environment of a Licensed Product. Such expenses shall be related to the organization and infrastructure that is promoting and selling Licensed Products. Such expenses shall include, but not be limited to, severance payments to dismissed employees, committed orders to third parties that can not be cancelled, termination costs for post-launch clinical marketing, and clinical studies. The Parties shall use Commercially Reasonable Efforts to minimize Restructuring Expenses, including, without limitation, by assigning employees to other products or organizations to be reviewed and approved by the Parties.

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**EXHIBIT F**

**Press Release**

**Contacts:**

**Alnylam Pharmaceuticals, Inc.**

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Yates Public Relations  
845-635-9828

*DRAFT — Not for Release*

**Alnylam and Roche Advance RNAi Therapeutic Collaboration  
Phase of Landmark 2007 Alliance**

*— Partners to Co-Develop and Co-Commercialize Certain RNAi Therapeutic Products  
in U.S. Market —*

*— Collaboration to Include Alnylam Lipid Nanoparticle and Roche Dynamic Polyconjugate Delivery  
Technologies —*

**CAMBRIDGE, Mass.**, November XX, 2009 — Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), a leading RNAi therapeutics company, announced today that it has advanced to the RNAi therapeutic collaboration stage of its landmark alliance with Roche formed in 2007. In this phase of the collaboration, the partners will jointly collaborate on the discovery and development of specific RNAi therapeutic products and each will contribute key delivery technologies in the new disease target-focused effort. New delivery technologies include Alnylam lipid nanoparticles and Roche Madison dynamic polyconjugate delivery technologies. Alnylam and Roche will co-develop and co-commercialize RNAi therapeutic products in the U.S. market and Alnylam is eligible to receive additional milestone and royalty payments for products developed in the rest of world.

“We are excited to advance to this phase of our 2007 agreement, as our joint efforts combine many strengths of the Alnylam and Roche platforms on specific disease target programs,” said Barry Greene, President and Chief Operating Officer of Alnylam. “Our partnership with Roche remains very strong and we look forward to working together to bring our innovation to patients.”

“Since the formation of our alliance with Alnylam and the establishment of Roche Kulmbach and Roche Madison as Centers of Excellence for RNA therapeutic research, we have made significant progress in advancing this technology as a potential new class of innovative medicines,” said Louis Renzetti, Ph.D., Vice President of RNA Therapeutics Research of Roche. “We continue to view RNAi as having true potential as a whole new class of differentiated drugs to benefit patients.”

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In July 2007, Alnylam granted to Roche a non-exclusive license providing access to broad Alnylam intellectual property (IP) and know-how, including fundamental, chemistry and delivery IP, in the fields of oncology, respiratory disease, metabolic disease, and certain liver diseases. In addition, Alnylam and Roche agreed to collaborate on RNAi therapeutics drug discovery for a defined number of disease targets, subject to certain Alnylam third party obligations. As part of the agreement, Roche also acquired Alnylam's Kulmbach-based research & development (R&D) organization which has now become Roche Kulmbach, a Roche Centre of Excellence for RNA therapeutics. In July 2008, Roche acquired Madison, WI-based Mirus Technologies, Inc., a pioneer in the discovery of a novel RNAi delivery technology known as dynamic polyconjugates. Mirus has become Roche Madison, an additional Roche Centre of Excellence for RNA therapeutics.

### **About RNA Interference (RNAi)**

RNAi (RNA interference) is a revolution in biology, representing a breakthrough in understanding how genes are turned on and off in cells, and a completely new approach to drug discovery and development. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today which was awarded the 2006 Nobel Prize for Physiology or Medicine. RNAi is a natural process of gene silencing that occurs in organisms ranging from plants to mammals. By harnessing the natural biological process of RNAi occurring in our cells, the creation of a major new class of medicines, known as RNAi therapeutics, is on the horizon. RNAi therapeutics target the cause of diseases by potently silencing specific messenger RNAs (mRNAs), thereby preventing disease-causing proteins from being made. RNAi therapeutics have the potential to treat disease and help patients in a fundamentally new way.

### **About Alnylam Pharmaceuticals**

Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is applying its therapeutic expertise in RNAi to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Alnylam is leading the translation of RNAi as a new class of innovative medicines with peer-reviewed research efforts published in the world's top scientific journals including *Nature*, *Nature Medicine*, and *Cell*. The company is leveraging these capabilities to build a broad pipeline of RNAi therapeutics; its most advanced program is in Phase II human clinical trials for the treatment of respiratory syncytial virus (RSV) infection and is partnered with Cubist and Kyowa Hakko Kirin. In addition, the company is developing RNAi therapeutics for the treatment of a wide range of disease areas, including liver cancers, hypercholesterolemia, Huntington's disease, and TTR amyloidosis. The company's leadership position in fundamental patents, technology, and know-how relating to RNAi has enabled it to form major alliances with leading companies including Medtronic, Novartis, Biogen Idec, Roche, Takeda, Kyowa Hakko Kirin, and Cubist. To reflect its outlook for key scientific,

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clinical, and business initiatives, Alnylam established “*RNAi 2010*” in January 2008 which includes the company’s plan to significantly expand the scope of delivery solutions for RNAi therapeutics, have four or more programs in clinical development, and to form four or more new major business collaborations, all by the end of 2010. Alnylam and Isis are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development, and commercialization of microRNA-based therapeutics. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit [www.alnylam.com](http://www.alnylam.com).

### **Alnylam Forward-Looking Statement**

Various statements in this release concerning Alnylam’s future expectations, plans and prospects, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the company’s ability to successfully research, develop, and commercialize RNAi therapeutics, and the company’s ability to successfully collaborate with Roche on these products, as well as those risks more fully discussed in the “Risk Factors” section of its most recent quarterly report on Form 10-Q on file with the Securities and Exchange Commission. In addition, any forward-looking statements represent Alnylam’s views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam does not assume any obligation to update any forward-looking statements.

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**EXHIBIT G**

**Baseball Arbitration Provisions**

1. General. In the event that the Parties are unable to agree upon the event payment amounts or royalty rates payable by the pursuing Party with respect to Licensed Product(s) in terminated Major Territory(ies) pursuant to Section 14.4(d)(i) (the "Financial Terms"), such Financial Terms shall be determined through binding arbitration in accordance with the provisions set forth below ("Baseball Arbitration").

(a) The Baseball Arbitration shall be held in a location mutually agreeable to the Parties, or if no such location can be agreed, in New York City, according to the then-current commercial arbitration rules of the American Arbitration Association ("AAA"), except to the extent such rules are inconsistent with this Exhibit G.

(b) The Baseball Arbitration will be conducted by one (1) arbitrator who shall be reasonably acceptable to the Parties and who shall be appointed in accordance with AAA rules. If the Parties are unable to select an arbitrator within [\*\*] days following the end of the negotiation period set forth in Section 14.4(d)(i), then the arbitrator shall be appointed in accordance with AAA rules. Any arbitrator chosen hereunder shall have the educational training and industry experience sufficient to demonstrate a reasonable level of scientific, financial, medical and industry knowledge relevant to the particular dispute.

(c) The (i) attorneys' fees of the Parties in the Baseball Arbitration, (ii) fees of the arbitrator and (iii) costs and expenses of the Baseball Arbitration shall be borne by the Parties as determined by the arbitrator.

(d) the proceedings and decisions of the arbitrator shall be confidential.

2. Exchange of Proposed Agreements. Within [\*\*] days after the designation of the arbitrator pursuant to Paragraph 1(b) above, the Parties shall exchange their proposed Financial Terms, substantially in the form of Appendix 1 attached hereto, together with a brief or other written memorandum supporting the merits of their proposed Financial Terms. Upon receipt of the proposed Financial Terms from each Party, the arbitrator shall provide copies of the same to the other Party. Within [\*\*] days after the arbitrator has delivered to each Party a copy of the Financial Terms proposed by the other Party (if any), each Party shall submit a written rebuttal of the other Party's proposed Financial Terms and may also amend and re-submit its original proposed Financial Terms. The Parties and the arbitrator shall meet within [\*\*] days thereafter, at which time each Party shall have one hour to argue in support of its final proposed Financial Terms. The Parties shall not call any witnesses in support of their arguments.

3. Selection of Proposed Agreement. The arbitrator shall be directed by the Parties to select, within [\*\*] days following the final hearing set forth in Paragraph 2 above, one of the final proposed Financial Terms so submitted by the Parties as the final Transition Agreement. In making such selection and ruling, the arbitrator shall not modify the terms or conditions of either Party's final proposed Financial Terms nor shall the arbitrator combine provisions from both proposed Financial Terms. However, the arbitrator may take into account the severity of the

Diligence Breach and the behavior of the breaching Party in selecting such Financial Terms. If a Party fails to submit to the arbitrator any proposal on Financial Terms in accordance with the terms of Paragraph 2 above, the arbitrator shall select the Financial Terms proposed by the other Party.

4. Effect of Decision. The Parties shall include, as part of the transition agreement to be executed by the Parties pursuant to Section 14.4(d)(i), the final Financial Terms selected by the arbitrator within [\*\*] days following the arbitrator's ruling; provided that the non-prevailing Party may elect not to accept such Financial Terms. If the non-prevailing Party elects to accept such Financial Terms within such [\*\*]-day period, the non-prevailing Party shall signify such election by executing a counterpart signature page to the Financial Terms selected by the arbitrator and providing such executed signature page to the prevailing Party within such [\*\*]-day period. If the non-prevailing Party does not provide such an executed signature page to the prevailing Party within such [\*\*]-day period, then thereafter this Agreement shall be terminated with respect to Licensed Product(s) in the Major Territory(ies) proposed to be terminated by the terminating Party, with neither Party having the right to Develop or Commercialize the Licensed Product(s) under a license from the other Party in any such terminated Major Territory(ies).

5. No Limitation. Nothing in this Exhibit G will preclude either Party from seeking equitable, interim or provisional relief from a court of competent jurisdiction, including a temporary restraining order, preliminary injunction or other interim equitable relief, either prior to or during any Baseball Arbitration if necessary to protect the interests of such Party or to preserve the status quo pending the Baseball Arbitration proceeding.

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Appendix 1

Form of Financial Terms

1. Development Event Payments with respect to terminated Major Territory(ies) (separately for each Terminated Territory):

<u>Development Event</u>	<u>Payments (In US\$ [**])</u>
(1) Initiation of the first Phase I Study for Licensed Product for the Terminated Territory	\$
(2) Initiation of the first Phase II Study for Licensed Product for the Terminated Territory	\$
(3) Initiation of the first Phase III Study for Licensed Product for the first (1st) Indication for the Terminated Territory	\$
(4) Initiation of the first Phase III Study for Licensed Product for a second (2nd) Indication for the Terminated Territory	\$
(5) First filing of an NDA in the Terminated Territory for Licensed Product for the first (1st) Indication	\$
(6) First filing of an NDA in the Terminated Territory for Licensed Product for the second (2nd) Indication	\$
(7) Regulatory Approval in the Terminated Territory for Licensed Product for the first (1st) Indication	\$
(8) Regulatory Approval in the Terminated Territory for Licensed Product for the second (2nd) Indication	\$
<b>Total Development Event Payments</b>	<b>\$</b>

2. Sales Event Payments with respect to terminated Major Territory(ies):

<u>Sales Event</u>	<u>Payments (In US\$ [**])</u>
Aggregate Worldwide Annual Net Sales of all Licensed Products in the Terminated Territory(ies) equal to or greater than \$[**]	\$
Aggregate Worldwide Annual Net Sales of all Licensed Products in the Terminated Territory(ies) equal to or greater than \$[**]	\$
<b>Total Sales Event Payments</b>	<b>\$</b>

3. Royalties Payable with respect to terminated Major Territory(ies):

<u>Annual Net Sales of a Licensed product in the Terminated Territory(ies) during the applicable Calendar Year</u>	<u>Incremental Royalty Rate Applicable to Such Annual Net Sales</u>
Less than or equal to \$[**]	%
Greater than \$[**], but less than or equal to \$[**]	%
Greater than \$[**], but less than or equal to \$[**]	%
Greater than \$[**], but less than or equal to \$[**]	%
Greater than \$[**], but less than or equal to \$[**]	%
Greater than \$[**], but less than or equal to \$[**]	%
Greater than \$[**]	%

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Acknowledged and agreed to by:

F. HOFFMANN-LA ROCHE LTD

By: \_\_\_\_\_  
Name:  
Title:

By: \_\_\_\_\_  
Name:  
Title:

HOFFMANN-LA ROCHE INC.

By: \_\_\_\_\_  
Name:  
Title:

ALNYLAM PHARMACEUTICALS, INC.

By: \_\_\_\_\_  
Name:  
Title:

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Subsidiary  
Calando Pharmaceuticals, Inc.  
Agonn Systems, Inc.  
Tego Biosciences Corporation  
Ablaris Therapeutics, Inc.  
Arrowhead Madison Inc.

Jurisdiction  
Delaware  
Delaware  
Delaware  
Delaware  
Delaware

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**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in this Annual Report on Form 10-K of Arrowhead Research Corporation for the year ended September 30, 2011 of our report dated December 16, 2011 included in its Registration Statements on Forms S-3 (Nos. 333-178532, 333-178073, 333-178072, 333-176159, 333-164039, 333-161344, 333-148218, 333-144109, 333-137329, 333-132310, 333-124065, and 333-113065) and Forms S-8 (Nos. 333-170252, 333-136225, 333-124066, and 333-120072) relating to the consolidated financial statements of Arrowhead Research Corporation and Subsidiaries for the year ended September 30, 2010.

Rose, Snyder & Jacobs  
A Corporation of Certified Public Accountants

Encino, California

/s/ Rose, Snyder & Jacobs

December 16, 2011

**CERTIFICATION OF CHIEF EXECUTIVE OFFICER  
PURSUANT TO RULE 13a-14(a) OR RULE 15d-14(a)  
OF THE SECURITIES EXCHANGE ACT OF 1934**

I, Christopher Anzalone, Chief Executive Officer of Arrowhead Research Corporation, certify that:

1. I have reviewed this Annual Report on Form 10-K of Arrowhead Research Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: December 20, 2011

/s/ CHRISTOPHER ANZALONE

**Christopher Anzalone**  
**Chief Executive Officer**

**CERTIFICATION OF CHIEF FINANCIAL OFFICER  
PURSUANT TO RULE 13a-14(a) OR RULE 15d-14(a)  
OF THE SECURITIES EXCHANGE ACT OF 1934**

I, Kenneth A. Myszkowski, Chief Financial Officer of Arrowhead Research Corporation, certify that:

1. I have reviewed this Annual Report on Form 10-K of Arrowhead Research Corporation;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: December 20, 2011

/s/ Kenneth A. Myszkowski

**Kenneth A. Myszkowski,  
Chief Financial Officer**

**CERTIFICATION OF CHIEF EXECUTIVE OFFICER  
PURSUANT TO RULE 13a-14(b) OR RULE 15d-14(b)  
OF THE SECURITIES EXCHANGE ACT OF 1934  
AND 18 U.S.C. SECTION 1350**

I, Christopher Anzalone, Chief Executive Officer of Arrowhead Research Corporation (the "Company"), certify, pursuant to Rule 13(a)-14(b) or Rule 15(d)-14(b) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, that (i) the Annual Report on Form 10-K of the Company for the year ended September 30, 2011, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and (ii) the information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition and results of operations of the Company.

Date: December 20, 2011

/s/ CHRISTOPHER ANZALONE

**Christopher Anzalone**  
**Chief Executive Officer**

A signed original of these written statements required by 18 U.S.C. Section 1350 has been provided to Arrowhead Research Corporation and will be retained by Arrowhead Research Corporation and furnished to the Securities and Exchange Commission or its staff upon request.

**CERTIFICATION OF CHIEF FINANCIAL OFFICER  
PURSUANT TO RULE 13a-14(b) OR RULE 15d-14(b)  
OF THE SECURITIES EXCHANGE ACT OF 1934  
AND 18 U.S.C. SECTION 1350**

I, Kenneth A. Myszkowski, Chief Financial Officer of Arrowhead Research Corporation (the "Company"), certify, pursuant to Rule 13(a)-14(b) or Rule 15(d)-14(b) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, that (i) the Annual Report on Form 10-K of the Company for the year ended September 30, 2011, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and (ii) the information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition and results of operations of the Company.

Date: December 20, 2011

/s/ Kenneth A. Myszkowski

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**Kenneth A. Myszkowski**  
**Chief Financial Officer**

A signed original of these written statements required by 18 U.S.C. Section 1350 has been provided to Arrowhead Research Corporation and will be retained by Arrowhead Research Corporation and furnished to the Securities and Exchange Commission or its staff upon request.