

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

FORM 10-K

(Mark One)

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

For the fiscal year ended **September 30, 2019**.

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

For the transition period from _____ to _____

Commission file number **001-38042**

ARROWHEAD PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State of incorporation)

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

**177 E. Colorado Blvd, Suite 700
Pasadena, California 91105
(626) 304-3400**

(Address and telephone number of principal executive offices)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.001 par value	ARWR	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Exchange Act: None

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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

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

Large accelerated filer Accelerated filer Non-accelerated filer Smaller Reporting Company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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 voting and non-voting outstanding Common Stock held by non-affiliates was approximately \$1.7 billion based upon the closing stock price of issuer's Common Stock on March 31, 2019. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding Common Stock have been excluded in that such persons may be deemed to be affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of November 20, 2019, 95,708,027 shares of the issuer's Common Stock were issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Definitive Proxy Statement to be filed for Arrowhead Pharmaceuticals Inc.'s 2020 Annual Meeting of Stockholders are incorporated by reference into Part III hereof.

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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 disclaim any intent 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.

Unless otherwise noted, (1) the term “Arrowhead” refers to Arrowhead Pharmaceuticals, Inc., a Delaware corporation and its Subsidiaries, (2) the terms “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. (“Arrowhead Madison”), Arrowhead Australia Pty Ltd (“Arrowhead Australia”) and Ablaris Therapeutics, Inc. (“Ablaris”), (4) the term “Common Stock” refers to Arrowhead’s Common Stock, (5) the term “Preferred Stock” refers to Arrowhead’s Preferred Stock and (6) the term “Stockholder(s)” refers to the holders of Arrowhead Common Stock.

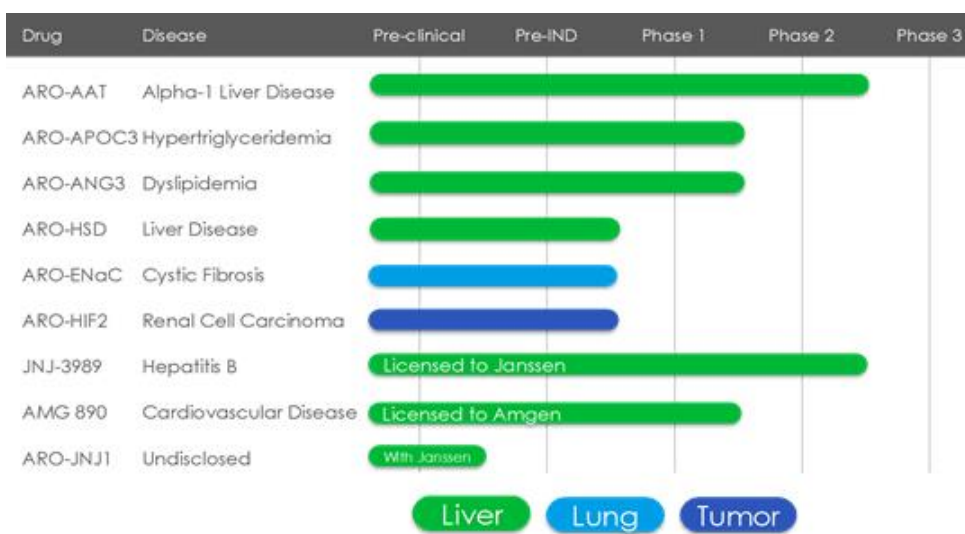
ITEM 1. BUSINESS

Description of Business

Arrowhead develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. 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 a Nobel Prize in 2006 for their work. Arrowhead’s RNAi-based therapeutics leverage this natural pathway of gene silencing.

Pipeline Overview

Arrowhead is focused on developing innovative drugs for diseases with a genetic basis, typically characterized by the overproduction of one or more proteins that are involved with disease. The depth and versatility of our RNAi technologies enables us to potentially address conditions in virtually any therapeutic area and pursue disease targets that are not otherwise addressable by small molecules and biologics. Arrowhead is leading the field in bringing the promise of RNAi to address diseases outside of the liver, and our pipeline now includes disease targets in the liver, lung, and solid tumors.



ARO-AAT

ARO-AAT is the company's second generation subcutaneously administered RNAi therapeutic being developed as a treatment for liver disease associated with alpha-1 antitrypsin deficiency (AATD), which is a rare genetic disorder that severely damages the liver and lungs of affected individuals. ARO-AAT is designed to reduce production of the mutant Z-AAT protein by silencing the AAT gene in order to prevent accumulation of Z-AAT in the liver, allow clearance of the accumulated Z-AAT protein, prevent repeated cycles of cellular damage, and possibly prevent or even reverse the progression of liver fibrosis.

Arrowhead is currently investigating ARO-AAT in two clinical studies:

1. SEQUOIA (AROAAT2001), which is a potentially pivotal multi-center, multi-dose, placebo-controlled, adaptive Phase 2/3 study to evaluate the safety, efficacy and tolerability of ARO-AAT, administered subcutaneously to patients with alpha-1 antitrypsin deficiency.
2. AROAAT2002, which is a pilot open-label, multi-dose, Phase 2 study to assess changes in a novel histological activity scale in response to ARO-AAT over time in patients with alpha-1 antitrypsin deficiency associated liver disease.

Initial results from AROAAT1001, a randomized, double-blind, placebo controlled single-ascending dose and multiple-ascending dose Phase 1 study to evaluate the safety, tolerability, pharmacokinetics, and effect of subcutaneous doses of ARO-AAT on serum alpha-1 antitrypsin levels in healthy adult volunteers, were presented in November 2018 at The Liver Meeting®. In the AROAAT1001 study, 45 normal healthy volunteers received a single dose of ARO-AAT (n=16), three monthly doses of ARO-AAT (n=12), or placebo (n=17). Key data presented include the following:

- ARO-AAT at single and multiple doses produced robust and consistent reductions in serum AAT levels
 - Single-doses of 200 mg and 300 mg resulted in greater than 91% serum AAT reduction with 3 of 4 subjects having concentrations below the level of quantitation (BLQ)
 - In 200 mg and 300 mg single-dose cohorts, an average serum AAT reduction of greater than 90% was sustained for 6 weeks
 - In the multiple-dose cohorts of 200 and 300 mg, for subjects receiving all 3 doses, an average of greater than 90% reduction in serum AAT was sustained for longer than 14 weeks
 - The maximum NADIR reduction is 94%
- Monthly serum AAT follow up is ongoing with 9 of 10 subjects at BLQ in the multiple-dose cohorts, including 100% of subjects from the 300 mg cohort
- Duration of response indicates that quarterly or less frequent dosing appears feasible
- ARO-AAT has been well-tolerated at all doses tested (up to 300 mg) given three times every 28 days
 - The most common adverse events were upper respiratory tract infection (39%) and headache (32%)

Goal of ARO-AAT Treatment

The goal of ARO-AAT treatment is prevention and potential reversal of Z-AAT accumulation-related liver injury and fibrosis. Reduction of inflammatory Z-AAT protein, which has been clearly defined as the cause of progressive liver disease in AATD patients, is important as it is expected to halt the progression of liver disease and allow fibrotic tissue repair.

Alpha-1 Antitrypsin Deficiency (AATD)

AATD is a genetic disorder associated with liver disease in children and adults, and pulmonary disease in adults. AAT is a circulating glycoprotein protease inhibitor that is primarily synthesized and secreted by liver hepatocytes. Its physiologic function is the inhibition of neutrophil proteases to protect healthy tissues during inflammation and prevent tissue damage. The most common disease variant, the Z mutant, has a single amino acid substitution that results in improper folding of the protein. The mutant protein cannot be effectively secreted and accumulates in globules in the hepatocytes. This triggers continuous hepatocyte injury, leading to fibrosis, cirrhosis, and increased risk of hepatocellular carcinoma.

Current Treatments

Individuals with the homozygous PiZZ genotype have severe deficiency of functional AAT leading to pulmonary disease and hepatocyte injury and liver disease. Lung disease in this patient population is frequently treated with AAT augmentation therapy. However, augmentation therapy does nothing to treat liver disease, and there is no specific therapy for hepatic manifestations. There is a significant unmet need as liver transplant, with its attendant morbidity and mortality, is currently the only available cure.

Clinical Trials

Study Name: Study of ARO-AAT in Normal Adult Volunteers

A Phase 1 Single and Multiple Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Effect of ARO-AAT on Serum Alpha-1 Antitrypsin Levels in Normal Adult Volunteers
ClinicalTrials.gov Identifier: NCT03362242

Study Name: Assessment of Changes in a Novel Histological Activity Scale in Response to ARO-AAT

A Pilot Open Label, Multi-dose, Phase 2 Study to Assess Changes in a Novel Histological Activity Scale in Response to ARO-AAT in Patients With Alpha-1 Antitrypsin Deficiency Associated Liver Disease (AATD)
ClinicalTrials.gov Identifier: NCT03946449

Study Name: Safety, Tolerability and Effect on Liver Histologic Parameters of ARO-AAT (SEQUOIA)

A Placebo-Controlled, Multi-dose, Phase 2/3 Study to Determine the Safety, Tolerability and Effect on Liver Histologic Parameters in Response to ARO-AAT in Patients With Alpha-1 Antitrypsin Deficiency (AATD)
ClinicalTrials.gov Identifier: NCT03945292

ARO-APOC3

ARO-APOC3 is designed to reduce production of Apolipoprotein C-III (apoC-III), a component of triglyceride rich lipoproteins (TRLs) including VLDL and chylomicrons and a key regulator of triglyceride metabolism. We believe that knocking down the hepatic production of apoC-III may result in reduced VLDL synthesis and assembly, enhanced breakdown of TRLs, and better clearance of VLDL and chylomicron remnants. Arrowhead is currently investigating ARO-APOC3 in a Phase 1 clinical trial.

Initial topline results from the Phase 1 study (ARO-APOC31001) were presented at The 2019 Global Summit on Cardiology and Heart Diseases. The data demonstrated that ARO-APOC3 reduced plasma apoC-III and reduced triglycerides without drug-related serious or severe adverse events. A single dose of 100 mg of ARO-APOC3 in healthy volunteers achieved mean maximal reductions of plasma triglycerides of 63% and apoC-III protein of 94%. In November 2019, we presented additional data at the American Heart Association meeting. The data demonstrated in 40 subjects (24 active, 16 placebo) dose dependent reduction in serum APOC3, including a mean maximum reduction from baseline in serum APOC3 levels which ranged from 72% (10 mg dose) to 94% (100 mg dose). A reduction in serum APOC3 levels was maintained through the end of the study with week 16 mean reductions of 70% (25 mg dose) to 91% (100 mg dose). Mean maximum reduction from baseline in serum triglycerides ranged from 53% (77 mg/dL) (10 mg dose) to 64% (92 mg/dL) (100 mg dose). Mean maximum reduction from baseline in serum VLDL-C ranged from 53% (16 mg/dL) (10 mg dose) to 68% (19 mg/dL) (50 mg dose). Reduction in serum triglycerides and VLDL-C was maintained through the end of study, with week 16 mean reductions of 41%-55% for triglycerides and 42-53% for VLDL-C. Mean maximum reduction from baseline in serum LDL-C ranged from 12% (19 mg/dL) (25 mg dose) to 25% (35 mg/dL) (100 mg dose). A dose dependent increase in serum HDL-C was seen with a mean maximum increase from baseline in serum HDL-C ranging from 30% (13 mg/dL) 10 mg dose to 69% (32 mg/dL) 100 mg dose. Serum HDL-C increases were maintained through the end of study, with week 16 mean increases of 28% (12 mg/dL) (10 mg dose) to 52% (22 mg/dL) (100 mg dose). No serious or severe adverse events were reported. There was one adverse event of moderate transit ALT elevation (peak of 210 U/L on Day 22) in a subject receiving ARO-APOC3 who had elevated ALT at baseline (65 U/L). The ALT in that subject returned to baseline by Day 85 (61 U/L). There were eight local injection site reactions reported, more commonly at higher doses, all of which were rated mild.

Hypertriglyceridemia

Elevated triglyceride levels are an independent risk factor for cardiovascular disease. Severely elevated triglycerides (often over 2,000 mg/dL) in patients with familial chylomicronemia syndrome (FCS), a rare genetic disorder, can result in potentially fatal acute pancreatitis.

Clinical Trials

Study Name: Study of ARO-APOC3 in Healthy Volunteers, Hypertriglyceridemic Patients and Patients With Familial Chylomicronemia Syndrome (FCS)

A Phase 1 Single and Multiple Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamic Effects of ARO-APOC3 in Adult Healthy Volunteers as Well as in Severely Hypertriglyceridemic Patients and Patients With Familial Chylomicronemia Syndrome
ClinicalTrials.gov Identifier: NCT03783377

ARO-ANG3

ARO-ANG3 is designed to reduce production of angiopoietin-like protein 3 (ANGPTL3), a liver synthesized inhibitor of lipoprotein lipase and endothelial lipase. ANGPTL3 inhibition has been shown to lower serum LDL, serum and liver triglyceride and has genetic validation as a novel target for cardiovascular disease. Arrowhead is currently investigating ARO-ANG3 in a Phase 1 clinical trial.

Initial topline results from the Phase 1 study (AROANG1001) were presented at the 2019 Global Summit on Cardiology and Heart Diseases. The data demonstrated that ARO-ANG3 reduced plasma ANGPTL3 and reduced triglycerides without drug-related serious or severe adverse events. A single dose of 200 mg of ARO-ANG3 in healthy volunteers demonstrated mean maximal reductions of plasma triglycerides of 66% and ANGPTL3 protein of 79%. In November 2019, we presented additional data at the American Heart Association meeting. The data demonstrated dose dependent reduction in serum ANGPTL3. The mean reduction from baseline in ANGPTL3 ranged from 55% (50 ng/mL) (35 mg) to 83% (63 ng/mL) 300 mg, and reduction in ANGPTL3 were maintained through the end of the study, with week 16 mean reductions of 43% (42 ng/mL) (35 mg) to 75% (57 ng/mL) (300 mg). Dose dependent reduction in triglycerides and VLDL-C were also observed. Mean maximum triglyceride reduction from baseline ranged from 31% (38 mg/dL) (35 mg) to 66% (167 mg/dL) (200 mg). Mean maximum VLDL-C reduction from baseline ranged from 30% (8 mg/dL) (35 mg) to 65% (33 mg/dL) (200 mg). The reduction in triglyceride and VLDL-C maintained through end of study in 200 mg and 300 mg cohorts, with week 16 mean reductions of 47% to 53% for triglycerides, and 49% to 51% for VLDL-C. Mean maximum HDL-C were reduction ranged from 8% (4 mg/dL) (35 mg) to 26% (12 mg/dL) (300 mg) and there were HDL-C mean reductions at week 16 of up to 16% ((7mg/dL) (200 mg). The mean maximum LDL-C reduction ranged from 9% (16 mg/dL) (200 mg) to 30% (48 mg/dL) (300 mg) and LDL-C mean reductions at week 16 were up to 28% (46 mg/dL) (100 mg) after a single dose. The mean maximum reduction in LDL-C with a single dose of 200 mg was blunted by two subjects in the cohort with increasing LDL-C post-dose. Multiple dose healthy volunteer data at a 200 mg dose demonstrated similar reductions to 100 mg and 300 mg doses of 33%-46% reduction in LDL-C from baseline two weeks after a second dose. There were no drug related severe or serious adverse events. Two adverse events of mild transient elevations in ALT occurred, one on active drug and one on placebo. ALT elevation in one subject on ARO-ANG3 was confounded by concomitant ingestion of an herbal supplement with known liver toxicity. In that subject, the peak ALT was 192 U/L at day 99, and within normal limits by study day 113. One patient had a mild local injection site reaction.

Dyslipidemia and Hypertriglyceridemia

Dyslipidemia and hypertriglyceridemia are risk factors for atherosclerotic coronary heart disease and cardiovascular events.

Study Name: Study of ARO-ANG3 in Healthy Volunteers and in Dyslipidemic Patients

A Phase 1 Single and Multiple Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamic Effects of ARO-ANG3 in Adult Healthy Volunteers and in Dyslipidemic Patients
ClinicalTrials.gov Identifier: NCT03747224

ARO-HSD

ARO-HSD is designed to reduce production of HSD17B13, a hydroxysteroid dehydrogenase involved in the metabolism of hormones, fatty acids and bile acids. Published human genetic data indicate that a loss of function mutation in HSD17B13 provides strong protection against nonalcoholic steatohepatitis (NASH) cirrhosis and alcoholic hepatitis and cirrhosis. Improvements in NASH and fibrosis were seen with HSD17B13 knockdown in the CDAA diet mouse model, a commonly used NASH model. Arrowhead expects to file a clinical trial application (CTA) before calendar year end 2019.

ARO-ENaC

ARO-ENaC is designed to reduce production of the epithelial sodium channel alpha subunit (α ENaC) in the airways of the lung. In cystic fibrosis patients, increased ENaC activity contributes to airway dehydration and reduced mucociliary transport. Arrowhead expects to file a CTA in the first half of calendar year 2020.

Cystic Fibrosis

Cystic fibrosis (CF) is a rare disease caused by a genetic mutation that leads to mucus buildup in the lungs and pancreas. In CF lung disease, patients can have difficulty breathing and experience frequent and persistent lung infections.

ARO-HIF2

ARO-HIF2 is being developed for the treatment of clear cell renal cell carcinoma (ccRCC). ARO-HIF2 is designed to inhibit the production of HIF-2 α , which has been linked to tumor progression and metastasis in ccRCC. Arrowhead believes it is an attractive target for intervention because over 90% of ccRCC tumors express a mutant form of the Von Hippel-Landau protein that is unable to degrade HIF-2 α , leading to its accumulation during tumor hypoxia and promoting tumor growth. Arrowhead expects to file a CTA before calendar year end 2019.

Renal Cell Carcinoma

Renal Cell Carcinoma is a type of kidney cancer that originates in the cells that line the small tubes that filter waste material from the blood. RCC is the most common type of kidney cancer accounting for more than 90% of cases with approximately 50,000 diagnoses in the U.S. each year. Unfortunately, patients with advanced stages of RCC have a 5-year survival rate of only 12-25%. Surgical resection is the mainstay of current treatment while chemotherapy and radiation have not been successful at prolonging survival. The treatment options for patients with metastatic disease are extremely limited.

Partnered Programs

Janssen Pharmaceuticals, Inc.

Arrowhead entered into a license agreement in October 2018 with Janssen Pharmaceuticals, Inc. (“Janssen”), part of the Janssen Pharmaceutical Companies of Johnson & Johnson, to develop and commercialize ARO-HBV. In addition, Arrowhead entered into a research collaboration and option agreement with Janssen to potentially collaborate for up to three additional RNAi therapeutics against new targets to be selected by Janssen.

Under the terms of the license agreement, Arrowhead received \$175 million as an upfront payment. Separately, Johnson & Johnson Innovation – JJDC, Inc. (JJDC) made a \$75 million equity investment in Arrowhead at a price of \$23.00 per share of Arrowhead common stock.

Arrowhead is eligible to receive up to approximately \$1.6 billion in milestone payments for the license agreement. Arrowhead is also eligible to receive approximately \$1.9 billion in option and milestone payments for the collaboration and option agreement related to up to three additional targets. Arrowhead is further eligible to receive tiered royalties up to mid teens under the license agreement and up to low teens under the collaboration and option agreement on product sales. During the year ended September 30, 2019, Arrowhead received two \$25 million developmental milestone payments from Janssen.

JNJ-3989 (formerly ARO-HBV)

JNJ-3989, formerly ARO-HBV, is being developed in collaboration with Janssen to be a potentially curative therapy for patients with chronic hepatitis B infection, when used in combination with other therapeutic modalities. JNJ-3989 is a sub-cutaneous, RNAi therapy candidate which is designed to silence all HBV gene products and intervenes upstream of the reverse transcription process where current standard-of-care nucleotide and nucleoside analogues act. The company believes this, especially the elimination of hepatitis B surface antigen (HBsAg), may allow the body’s natural immune defenses to clear the virus and potentially lead to a functional cure. JNJ-3989 (ARO-HBV) is being investigated in multiple Phase 2 clinical trials being conducted by Janssen.

Clinical Trials

Study Name: Study of ARO-HBV in Normal Adult Volunteers and Patients With Hepatitis B Virus (HBV)

A Phase 1/2a Single Dose-Escalating Study to Evaluate the Safety, Tolerability and Pharmacokinetic Effects of ARO-HBV in Normal Adult Volunteers and Multiple Escalating Doses Evaluating Safety, Tolerability and Pharmacodynamic Effects in HBV Patients
ClinicalTrials.gov Identifier: NCT03365947

Study Name: A Study of JNJ-73763989 in Healthy Japanese Adult Participants

A Double-blind, Placebo-controlled, Randomized, Parallel, Single Dose Study to Investigate Pharmacokinetics, Safety, and Tolerability of JNJ-73763989 in Healthy Japanese Adult Participants
ClinicalTrials.gov Identifier: NCT04002752

Study Name: A Study of Different Combination Regimens Including JNJ-73763989 and/or JNJ-56136379 for the Treatment of Chronic Hepatitis B Virus Infection (REEF-1)

A Phase 2b, Multicenter, Double-blind, Active-controlled, Randomized Study to Investigate the Efficacy and Safety of Different Combination Regimens Including JNJ-73763989 and/or JNJ-56136379 for the Treatment of Chronic Hepatitis B Virus Infection
ClinicalTrials.gov Identifier: NCT03982186

Study Name: A Study of JNJ 73763989+JNJ 56136379+Nucleos(t)Ide Analog (NA) Regimen Compared to NA Alone in e Antigen Negative Virologically Suppressed Participants With Chronic Hepatitis B Virus Infection

A Randomized, Double Blind, Placebo-controlled Phase 2b Study to Evaluate Efficacy, Pharmacokinetics, and Safety of 48-week Study Intervention With JNJ 73763989+JNJ 56136379+Nucleos(t)Ide Analog (NA) Regimen Compared to NA Alone in e Antigen Negative Virologically Suppressed Participants With Chronic Hepatitis B Virus Infection
ClinicalTrials.gov Identifier: NCT04129554

ARO-JNJ1

ARO-JNJ1 is being developed against an undisclosed liver-expressed target as part of Arrowhead's Research Collaboration and Option Agreement with Janssen .

Amgen Inc.

Amgen Inc. ("Amgen") acquired a worldwide, exclusive license in September 2016 to develop and commercialize ARO-LPA (now referred to as AMG 890). Under the terms of the agreements taken together for AMG 890 (ARO-LPA) and ARO-AMG1, the Company received \$35 million in upfront payments, \$21.5 million in the form of an equity investment by Amgen in the Company's Common Stock, and the Company was eligible to receive up to \$617 million in option payments and development, regulatory and sales milestone payments. The Company remains eligible to receive up to \$420 million in development, regulatory and sales milestone payments under the AMG-890 (ARO-LPA) agreement. The Company is further eligible to receive up to low double-digit royalties for sales of products under the AMG-890 (ARO-LPA) agreement.

AMG 890 (formerly ARO-LPA)

AMG 890 (ARO-LPA) is designed to reduce production of apolipoprotein A₁, a key component of lipoprotein(a), which has been genetically linked with increased risk of cardiovascular diseases, independent of cholesterol and LDL levels. Amgen started a Phase 1 clinical study of AMG 890 (ARO-LPA) designed to assess its safety in volunteers and patients with elevated levels of lipoprotein(a) in August 2018. The initiation of this Phase 1 clinical study triggered a \$10 million milestone payment from Amgen to Arrowhead in 2018. Amgen expects to initiate a Phase 2 clinical study in the first half of calendar year 2020.

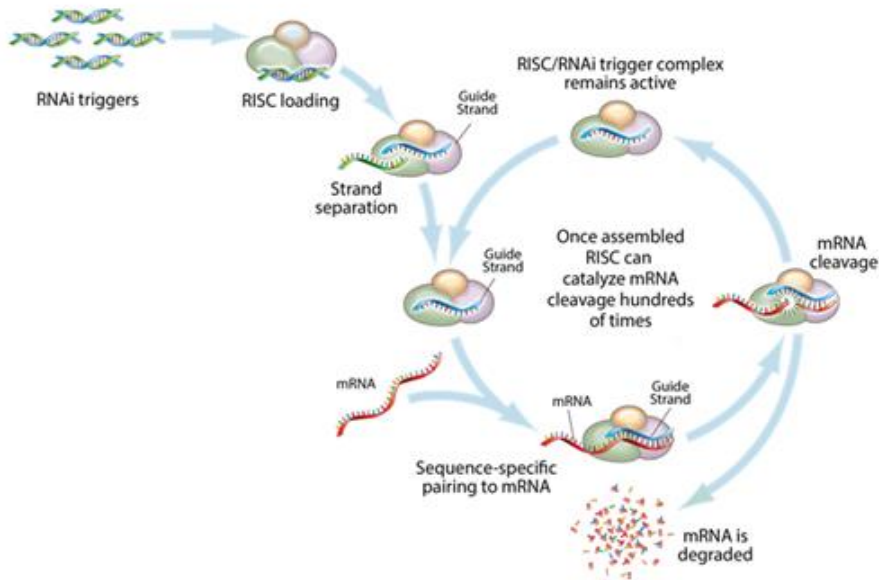
ARO-AMG1

In August 2018, Arrowhead delivered to Amgen a candidate that met or exceeded the activity and safety requirements stipulated in the ARO-AMG1 collaboration agreement. The option period expired on August 7, 2019, and Amgen advised Arrowhead that it did not intend to exercise its option.

RNA Interference & the Benefits of RNAi Therapeutics

RNAi is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. 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 a Nobel Prize in 2006 for their work. RNAi-based therapeutics may leverage this natural pathway of gene silencing to target and shut down specific disease-causing genes.

Small molecule and antibody drugs have proven effective at inhibiting certain cell surface, intracellular, and extracellular targets. However, other drug targets have proven difficult to inhibit with traditional drug-based and biologic therapeutics. Developing effective drugs for these targets would have the potential to address large underserved markets for the treatment of many diseases. Using the ability to specifically silence any gene, RNAi therapeutics may be able to address previously “undruggable” targets, unlocking the market potential of such targets.



This figure depicts the mechanism by which gene silencing occurs. Double stranded RNAi triggers are introduced into a cell and get loaded into the RNA-induced silencing complex, (RISC). The strands are then separated, leaving an active RISC/RNAi trigger complex. This complex can then pair with and degrade the complementary messenger RNAs (mRNA) and stop the production of the target proteins. RNAi is a catalytic process, so each RNAi trigger can degrade mRNA hundreds of times, which results in a relatively long duration of effect for RNAi therapeutics.

Key Advantages of RNAi as a Therapeutic Modality

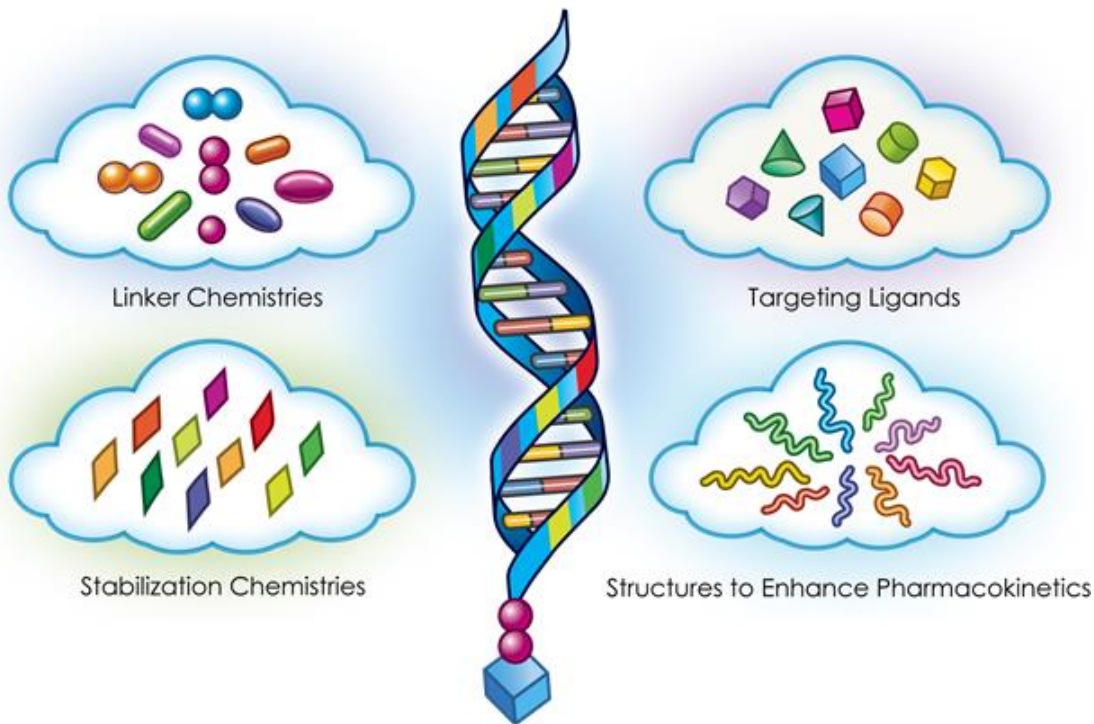
- Silences the expression of disease associated genes;
- Potential to address any target in the transcriptome including previously "undruggable" targets;
- Rapid lead identification;
- High specificity;
- Opportunity to use multiple RNA sequences in one drug product for synergistic silencing of related targets; and
- RNAi therapeutics are uniquely suited for personalized medicine through target and cell specific delivery and gene knockdown.

Targeted RNAi Molecule (TRiM™) Platform

Arrowhead's Targeted RNAi Molecule (TRiM™) platform utilizes ligand-mediated delivery and is designed to enable tissue-specific targeting while being structurally simple. Targeting has been core to Arrowhead's development philosophy and the TRiM™ platform builds on more than a decade of work on actively targeted drug delivery vehicles. Arrowhead scientists have discovered ways to progressively "TRiM" away extraneous features and chemistries and retain optimal pharmacologic activity.

The TRiM™ platform comprises a highly potent RNA trigger identified using Arrowhead's proprietary trigger selection rules and algorithms with the following components optimized, as needed, for each drug candidate: a high affinity targeting ligand; various linker and chemistries; structures that enhance pharmacokinetics; and highly potent RNAi triggers with sequence specific stabilization chemistries.

Therapeutics developed with the TRiM™ platform offer several advantages: simplified manufacturing and reduced costs; multiple routes of administration; and potential for improved safety because there are less metabolites from smaller molecules, thereby reducing the risk of intracellular buildup. At Arrowhead, we also believe that for RNAi to reach its true potential, it must target organs outside the liver. Arrowhead is leading this expansion with the TRiM™ platform, which has shown the potential to reach multiple tissues, including liver, lung, tumor, muscle and others.



RNA Chemistries

The structure and chemistries of the oligonucleotide molecules used to trigger the RNAi mechanism can be tailored for optimal activity. Arrowhead's broad portfolio of RNA trigger structures and chemistries, including some proprietary structures, enable the company to optimize each drug candidate on a target-by-target basis and utilize the combination of structure and chemical modifications that yield the most potent RNAi trigger.

As a component of the TRiM™ platform, Arrowhead's design philosophy for RNA chemical modifications is to start with a structurally simple molecule and add only selective modification and stabilization chemistries as necessary to achieve the desired level of target knockdown and duration of effect. The conceptual framework for the stabilization strategy starts with a more sophisticated RNAi trigger screening and selection process that identifies potent sequences rapidly in locations that others may miss.

Intellectual Property and Key Agreements

The Company controls approximately 383 issued patents (including 239 directed to RNAi trigger molecules; 30 directed to targeting groups or targeting compounds; and 7 for hydrodynamic gene delivery), including European validations, and approximately 397 currently pending patent applications worldwide from 49 different patent families. The Company's patent applications have been filed throughout the world, including, in the United States, Argentina, ARIPO (Africa Regional Intellectual Property Organization), Australia, Brazil, Canada, Chile, China, Eurasian Patent Organization, Europe, GCC (Gulf Cooperation Council), Hong Kong, Israel, India, Indonesia, Iraq, Jordan, Japan, Republic of Korea, Lebanon, Mexico, New Zealand, OAPI (African Intellectual Property Organization), Peru, Philippines, Russian Federation, Saudi Arabia, Singapore, Thailand, Taiwan, Uruguay, Venezuela, Vietnam, and South Africa.

RNAi Triggers

The Company owns issued patents or has filed patent applications directed to RNAi trigger molecules, which serve as the foundation of Arrowhead's TRiM™ platform, and are targeted to reduce expression of various gene targets, including the following:

Patent Group	Estimated Year(s) of Expiration*
RNAi Triggers Gene Target	
HBV	2032, 2036, 2037
AAT	2035, 2038
LPA	2036
Factor 12	2036, 2038
HIF2 α	2034, 2036
RRM2	2031
APOC3	2035, 2038
ANGPTL3	2038
α -ENaC	2028, 2038
β -ENaC	2031
β -Catenin	2033
Cx43	2029
HCV	2023
HIF1A	2026
HRH1	2027
HSF1	2030, 2032
FRP-1	2026
KRAS	2033
PDtype4	2026
PI4Kinase	2028
SYK	2027
TNF- α	2027, 2028

*Assuming issuance of any pending patent applications.

Delivery Technologies

The delivery technology-related patents and patent applications, which include components used in Arrowhead's TRiM™ platform, have been filed and/or issued in various jurisdictions worldwide including the United States, Argentina, Australia, Brazil, Canada, China, Eurasian Patent Organization, Europe (including validations in France, Germany, Italy, Spain, Switzerland, United Kingdom), GCC (Gulf Cooperation Council), Israel, India, Japan, Lebanon, Mexico, New Zealand, Philippines, Russia, South Korea, Singapore, Taiwan, Uruguay, and South Africa. The Company also controls a number of patents directed to hydrodynamic nucleic acid delivery, which issued in the United States, Australia and Europe (validated in Austria, Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, the United Kingdom, Hungary, Ireland, Italy, Netherlands and Sweden). The approximate year of expiration for each of these various groups of patents are set forth below:

Patent Group	Estimated Year(s) of Expiration*
Targeting ligands and other RNAi delivery technologies	
Targeting groups (Galactose derivative trimer-PK)	2031
Targeting groups ($\alpha v\beta 3$ integrin)	2034, 2039, 2039
Targeting groups ($\alpha v\beta 6$ integrin)	2037, 2038
Targeting groups (Galactose derivative ligands)	2037, 2037
RNAi agent design (5'-phosphate mimic)	2037
Physiologically labile linkers	2036
Biologically cleavable linkers	2036
Trialkyne linkers	2039
Transferrin targeting	2028
LDLR targeting	2028
Peptide targeting (CPP-Arg)	2028
Peptide targeting (YM3-10H)	2032
Hydrodynamic delivery	
Second iteration	2020
Third iteration	2024

*Assuming issuance of any pending patent applications.

The RNAi and drug delivery patent landscapes are complex and rapidly evolving. As such, we may need to obtain additional patent licenses prior to commercialization of our candidates. You should review the factors identified in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K.

Non-Exclusively Licensed Patent Rights obtained from Roche

On October 21, 2011, Arrowhead acquired the RNAi therapeutics business of Hoffmann-La Roche, Inc. and F. Hoffmann-La Roche Ltd. (collectively, “Roche”). The acquisition provided us with two primary sources of value:

- Broad freedom to operate with respect to key patents directed to the primary RNAi-trigger formats: canonical, UNA, meroduplex, and dicer substrate structures; and
- A large team of scientists experienced in RNAi and oligonucleotide delivery.

Pursuant to this acquisition, Roche assigned to Arrowhead its entire rights under certain licenses including: the License and Collaboration Agreement between Roche and Alnylam Pharmaceuticals, Inc. (“Alnylam”) dated July 8, 2007 (the “Alnylam License”); the Non-Exclusive Patent License Agreement between Roche and MDRNA, Inc. dated February 12, 2009 (“MDRNA License”); and the Non-Exclusive License Agreement between Roche and City of Hope dated September 19, 2011 (the “COH License”) (Collectively the “RNAi Licenses”). The RNAi Licenses have provided the Company with non-exclusive, worldwide, perpetual, irrevocable, royalty-bearing rights and the right to sublicense a broad portfolio of intellectual property relating to the discovery, development, manufacture, characterization, and use of therapeutic products that function through the mechanism of RNA interference for specified targets.

The RNAi Licenses include licenses to patents related to modifications of double-stranded oligonucleotides, including modifications to the base, sugar, or internucleoside linkage, nucleotide mimetics, and end modifications, which do not abolish the RNAi activity of the double-stranded oligonucleotides. Also included are patents relating to modified double-stranded oligonucleotides, such as meroduplexes described in U.S. Patent No. 9,074,205 assigned to Marina Biotech (f/k/a MDRNA, Inc.), as well as U.S. Patent Nos. 8,314,227, 9,051,570, and 9,303,260 related to unlocked nucleotide analogs (UNA). The UNA patents were assigned by Marina Biotech to Arcturus Therapeutics, Inc., but remain part of the MDRNA License. The RNAi Licenses further include patents related to dicer substrates and uses of the double-stranded oligonucleotides that function through the mechanism of RNA interference, such as described in City of Hope’s U.S. Patent Nos. 8,084,599, 8,658,356, 8,691,786, 8,796,444, 8,809,515, and 9,518,262.

2012 License to Alnylam

In consideration for licenses obtained from Alnylam to certain RNAi intellectual property, in January 2012 we granted Alnylam a worldwide non-exclusive, sublicensable royalty-bearing license under our broad and target-specific DPC intellectual property rights

to research, develop and commercialize RNAi-based products against a single undisclosed target in combination with DPC technology. Under the license to Alnylam, Alnylam may be obligated to pay us development and sales milestone payments of up to the low double-digit millions of dollars for each licensed product that progresses through clinical trials, receives marketing approval and is the subject of a first commercial sale. Additionally, Alnylam may be obligated to pay us low single-digit percentage royalties on sales of such products.

Acquisition of Assets from Novartis

On March 3, 2015, the Company entered into an Asset Purchase and Exclusive License Agreement (the “RNAi Purchase Agreement”) with Novartis pursuant to which the Company acquired Novartis’ RNAi assets and rights thereunder. Pursuant to the RNAi Purchase Agreement, the Company acquired or was granted a license to certain patents and patent applications owned or controlled by Novartis related to RNAi therapeutics, was assigned Novartis’s rights under a license from Alnylam (the “Alnylam-Novartis License”) and acquired a license to certain additional Novartis assets (the “Licensed Novartis Assets”). The patents acquired from Novartis include multiple patent families covering delivery technologies and RNAi-trigger design rules and modifications. The Licensed Novartis Assets include an exclusive, worldwide right and license, solely in the RNAi field, with the right to grant sublicenses through multiple tiers under or with respect to certain patent rights and know how relating to delivery technologies and RNAi-trigger design rules and modifications. Under the assigned Alnylam-Novartis License, the Company acquired a worldwide, royalty-bearing, exclusive license with limited sublicensing rights to existing and future Alnylam intellectual property (including intellectual property that came under Alnylam’s control on or before March 31, 2016), excluding intellectual property concerning delivery technology, to research, develop and commercialize 30 undisclosed gene targets.

We see the Roche and Novartis acquisitions as a powerful combination of intellectual property, R&D infrastructure, and RNAi experts. This foundation and substantial progress made by Arrowhead scientists over the last several years enable us to develop what we think are optimal RNAi therapeutics.

Cardiovascular Collaboration and License Agreements with Amgen

On September 28, 2016, the Company entered into two Collaboration and License agreements and a Common Stock Purchase Agreement with Amgen. Under the First Collaboration and License Agreement, Amgen received an option to a worldwide, exclusive license to ARO-AMG1, an RNAi therapy for an undisclosed genetically validated cardiovascular target. Under the Second Collaboration and License, Amgen received a worldwide, exclusive license to Arrowhead’s novel, RNAi AMG-980 (ARO-LPA) program. The AMG-890 (ARO-LPA) RNAi molecules are designed to reduce elevated lipoprotein(a), which is a genetically validated, independent risk factor for atherosclerotic cardiovascular disease. In both agreements, Amgen is wholly responsible for clinical development and commercialization. Under the terms of the agreements taken together, the Company has received \$35 million in upfront payments, \$21.5 million in the form of an equity investment by Amgen in the Company’s Common Stock. The Company was eligible to receive up to \$617 million in option payments and development, regulatory and sales milestone payments. In August 2018, the Company received a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. The Company remains eligible to receive up to \$420 million in development, regulatory and sales milestone payments under the AMG-890 (ARO-LPA) agreement. The Company is further eligible to receive up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) agreement.

In August 2018, Arrowhead delivered to Amgen a candidate that met or exceeded the activity and safety requirements stipulated in the ARO-AMG1 collaboration agreement. The option period expired on August 7, 2019, and Amgen advised Arrowhead that it did not intend to exercise its option.

License and Research Collaboration Agreements with Janssen Pharmaceuticals, Inc.

On October 3, 2018, the Company entered into a License Agreement (“Janssen License Agreement”) and a Research Collaboration and Option Agreement (“Janssen Collaboration Agreement”) with Janssen Pharmaceuticals, Inc. (“Janssen”), part of the Janssen Pharmaceutical Companies of Johnson & Johnson. The Company also entered into a Stock Purchase Agreement (“JJDC Stock Purchase Agreement”) with Johnson & Johnson Innovation-JJDC, Inc. (“JJDC”), a New Jersey corporation.

Under the Janssen License Agreement, Janssen will receive a worldwide, exclusive license to the Company’s JNJ-3989 (ARO-HBV) program, the Company’s third-generation subcutaneously administered RNAi therapeutic candidate being developed as a potentially curative therapy for patients with chronic hepatitis B virus infection. Beyond the Company’s ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV) (which will remain the responsibility of the Company), Janssen will be wholly responsible for clinical development and commercialization.

Under the Janssen Collaboration Agreement, Janssen will be able to select up to three new targets against which the Company will develop clinical candidates. These candidates are subject to certain restrictions and will not include candidates in the Company's current pipeline. The Company will perform discovery, optimization and preclinical development on selected targets, entirely funded by Janssen, sufficient to allow the filing of a U.S. Investigational New Drug application or equivalent, at which time Janssen will have the option to take an exclusive license to the Company's intellectual property rights covering that compound. If the option is exercised, Janssen will be wholly responsible for clinical development and commercialization of each optioned compound.

Under the terms of the agreements taken together, the Company has received (i) \$175 million as an upfront payment, (ii) \$75 million in the form of an equity investment by JJDC in the Company's common stock at a price of \$23.00 per share, and may receive (iii) up to \$1.6 billion in development and sales milestones payments for the Janssen License Agreement, and (iv) up to \$1.9 billion in development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the Janssen License agreement and up to low teens under the Janssen Collaboration Agreement on product sales. During the year ended September 30, 2019, the Company received two \$25 million developmental milestones from Janssen.

Research and Development Facility

Arrowhead's research and development operations are primarily located in Madison, Wisconsin. Substantially all of the Company's assets are located either in this facility or in our corporate headquarters in Pasadena. A summary of our research and development resources in Madison is provided below:

- 93 R&D personnel as of September 30, 2019;
- State-of-the-art laboratories consisting of 74,000 total sq. ft.;
- Complete small animal facility;
- Primate colony housed at the Wisconsin National Primate Research Center, an affiliate of the University of Wisconsin;
- In-house histopathology capabilities;
- Animal models for cardio metabolic, viral, lung, and oncologic diseases;
- Animal efficacy and safety assessment;
- In-house drug manufacturing capabilities to produce first-in-human GMP (phase appropriate) material;
- Polymer, peptide, oligonucleotide and small molecule synthesis and analytics capabilities (HPLC, NMR, MS, etc.);
- Polymer, peptide and oligonucleotide PK, biodistribution, clearance methodologies; and
- Conventional and confocal microscopy, flow cytometry, Luminex platform, qRT-PCR, clinical chemistry analytics.

Research and Development Expenses

Research and development (R&D) expenses consist of costs incurred in discovering, developing and testing our clinical and preclinical candidates and platform technologies. R&D expenses also include costs related to clinical trials, including costs of contract research organizations to recruit patients and manage clinical trials. Other costs associated with clinical trials include manufacturing of clinical supplies, as well as good laboratory practice ("GLP") toxicology studies necessary to support clinical trials, both of which are currently outsourced to cGMP-compliant manufacturers and GLP-compliant laboratories. Total research and development expense for fiscal 2019, 2018 and 2017 was \$81.0 million, \$53.0 million and \$50.9 million, respectively.

At September 30, 2019, we employed 109 employees in an R&D function, primarily working from our facility in Madison, Wisconsin. These employees are engaged in various areas of research on Arrowhead candidate and platform development including synthesis and analytics, PK/biodistribution, formulation, CMC and analytics, tumor and extra-hepatic targeting, bioassays, live animal research, toxicology/histopathology, clinical and regulatory operations, and other areas. Salaries and payroll-related expenses and stock compensation for our R&D activities were \$19.0 million, \$15.1 million, and \$14.6 million in fiscal 2019, 2018 and 2017, respectively. Costs related to the manufacture of clinical supplies, GLP toxicology studies and clinical trial costs were \$47.1 million, \$23.6 million, and \$22.2 million in fiscal 2019, 2018, and 2017, respectively. Facility-related costs, primarily rental costs for our leased laboratory in Madison, Wisconsin were \$2.6 million, \$2.3 million, and \$2.3 million in fiscal 2019, 2018, and 2017, respectively. Depreciation and amortization expenses primarily for our lab equipment and leasehold improvements in our leased laboratory in Madison, Wisconsin were \$4.4 million, \$4.7 million and \$4.7 million in fiscal 2019, 2018 and 2017, respectively. Licensing, royalties and milestones expenses were \$0, \$0, and \$0 million in fiscal 2019, 2018 and 2017, respectively. These expenses are primarily related to milestone payments, which can vary from period to period depending on the nature of our various license agreements, and the timing of reaching various development milestones requiring payment. Other research and development expenses

were \$7.9 million, \$7.3 million, and \$7.2 million in fiscal 2019, 2018 and 2017, respectively. These expenses primarily relate to laboratory supply costs and animal-related costs for in-vivo studies.

Government Regulation

Government authorities in the United States, at the federal, state, and local levels, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, product approval, manufacture, quality control, manufacturing changes, packaging, storage, recordkeeping, labeling, promotion, advertising, sales, distribution, marketing, and import and export of drugs and biologic products. All of our foreseeable product candidates are expected to be regulated as drugs. The processes for obtaining regulatory approval in the U.S. and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities both pre- and post-commercialization, are a significant factor in the production and marketing of our products and our R&D activities and require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the U.S., the FDA and other government entities regulate drugs under the Federal Food, Drug, and Cosmetic Act (the “FDCA”), the Public Health Service Act, and the regulations promulgated under those statutes, as well as other federal and state statutes and regulations. Failure to comply with applicable legal and regulatory requirements in the U.S. at any time during the product development process, approval process, or after approval, may subject us to a variety of administrative or judicial sanctions, such as a delay in approving or refusal by the FDA to approve pending applications, withdrawal of approvals, delay or suspension of clinical trials, issuance of warning letters and other types of regulatory letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil monetary penalties, refusals of or debarment from government contracts, exclusion from the federal healthcare programs, restitution, disgorgement of profits, civil or criminal investigations by the FDA, U.S. Department of Justice, State Attorneys General, and/or other agencies, False Claims Act suits and/or other litigation, and/or criminal prosecutions.

An applicant seeking approval to market and distribute a new drug in the U.S. must typically undertake the following:

- (1) completion of pre-clinical laboratory tests, animal studies, and formulation studies in compliance with the FDA’s GLP regulations;
- (2) submission to the FDA of an Investigational New Drug Application (“IND”) for human clinical testing, which must become effective without FDA objection before human clinical trials may begin;
- (3) approval by an independent institutional review board (“IRB”), representing each clinical site before each clinical trial may be initiated;
- (4) performance of adequate and well-controlled human clinical trials in accordance with the FDA’s current good clinical practice (“cGCP”) regulations, to establish the safety and effectiveness of the proposed drug product for each indication for which approval is sought;
- (5) preparation and submission to the FDA of a New Drug Application (“NDA”);
- (6) satisfactory review of the NDA by an FDA advisory committee, where appropriate or if applicable,
- (7) satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the drug product, and the active pharmaceutical ingredient or ingredients thereof, are produced to assess compliance with current good manufacturing practice (“cGMP”) regulations and to assure that the facilities, methods, and controls are adequate to ensure the product’s identity, strength, quality, and purity;
- (8) payment of user fees, as applicable, and securing FDA approval of the NDA; and
- (9) compliance with any post-approval requirements, such as any Risk Evaluation and Mitigation Strategies (“REMS”) or post-approval studies required by the FDA.

Preclinical Studies and an IND

Preclinical studies can include *in vitro* and animal studies to assess the potential for adverse events and, in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including

GLP regulations. Other studies include laboratory evaluation of the purity, stability and physical form of the manufactured drug substance or active pharmaceutical ingredient and the physical properties, stability and reproducibility of the formulated drug or drug product. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some preclinical testing, such as longer-term toxicity testing, animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Following commencement of a clinical trial under an IND, the FDA may place a clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with cGCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

Phase 2: The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2, and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites in late-stage clinical trials to assure compliance with cGCP and the integrity of the clinical data submitted.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications.

Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently \$2.9 million for applications requiring clinical data, and the sponsor of an approved NDA is also subject to an annual program fee, currently \$325,000. These fees are typically increased annually.

Under certain circumstances, the FDA will waive the application fee for the first human drug application that a small business, defined as a company with less than 500 employees, including employees of affiliates, submits for review. An affiliate is defined as a business entity that has a relationship with a second business entity if one business entity controls, or has the power to control, the other business entity, or a third-party controls, or has the power to control, both entities. In addition, an application to market a prescription drug product that has received orphan designation is not subject to a prescription drug user fee unless the application includes an indication for other than the rare disease or condition for which the drug was designated.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

The FDA also may require submission of a REMS plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. After approval, the FDA may seek to prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. Some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

The product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of

some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety and effectiveness of drug products.

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 entitles the applicant to incentives such as grant funding towards clinical study costs, tax advantages, and waivers of FDA user fees. Orphan drug designation must be requested before submitting an NDA, and both the drug and the disease or condition must meet certain criteria specified in the Orphan Drug Act and FDA's implementing regulations at 21 C.F.R. Part 316. The granting of an orphan drug designation does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and effectiveness of a drug must be established through adequate and well-controlled studies.

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. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of NDAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition and data demonstrate its potential to address unmet medical needs for the disease or condition. The key benefits of Fast Track Designation are the eligibility for priority review, rolling review (submission of portions of an application before the complete marketing application is submitted), and accelerated approval, if relevant criteria are met. The FDA may grant the NDA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

The FDA may approve an NDA under the accelerated approval program if the drug treats a serious condition, provides a meaningful advantage over available therapies, and demonstrates an effect on either (1) a surrogate endpoint that is reasonably likely to predict clinical benefit, or (2) on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit.

In addition, the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, established the Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If a drug is designated as breakthrough therapy, FDA will provide more intensive guidance on the drug development program and expedite its review.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations

from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events or problems with manufacturing processes of unanticipated severity or frequency, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly referred to as the “Hatch-Waxman Amendments”) amending the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application (ANDA) to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD. To reference that information, however, the ANDA applicant must demonstrate, and the FDA must conclude, that the generic drug does, in fact, perform in the same way as the RLD it purports to copy. Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug.

At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the RLD.” Upon approval of an ANDA, the FDA indicates that the generic product is “therapeutically equivalent” to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider the therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of a therapeutic equivalence rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of nonpatent exclusivity for the RLD has expired. The FDCA provides a period of five years of data exclusivity for new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30 Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that a Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With the enactment of FDASIA, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application.

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Amendments. Those Amendments permit a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of a NDA, plus the time between the submission date of a NDA and ultimate approval. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Legislative Developments

The 21st Century Cures Act (Cures Act), which was signed into law in December 2016, includes provisions to accelerate the development and delivery of new treatments. For example, the Cures Act requires the FDA to establish a program to evaluate the potential use of real world evidence to help to support the approval of a new indication for an approved drug and to help to support or satisfy post-approval study requirements, to issue guidance on adaptive and novel clinical trial designs for new drugs, and to establish a process for qualifying drug development tools used to support FDA approval for marketing or investigational use of a drug. The Cures Act also permits the FDA to rely on qualified data summaries to support the approval of a supplemental application for an already approved drug. The FDA is in the process of implementing the Cures Act requirements.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Pursuant to the EU Clinical Trial Directive 2001/20/EC, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. CTAs must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

In 2014, a new Clinical Trial Regulation 536/2014, replacing the EU Clinical Trials Directive, was adopted. The new Regulation will become directly applicable in all European Union member states (without national implementation) once the relevant EU portal and database are fully functional. It is expected that this will occur in calendar year 2020. The new Regulation seeks to simplify and streamline the approval of clinical trials in the European Union, in particular through a harmonised electronic submission and assessment process for clinical trials conducted in multiple Member States. As part of the application process, the sponsor shall propose a reporting Member State, who will coordinate the validation and evaluation of the application. The reporting member state shall consult and coordinate with the other concerned member states. If an application is rejected, it can be amended and resubmitted through the EU portal. If an approval is issued, the sponsor can start the clinical trial in all concerned member states. However, a concerned member state can in limited circumstances declare an "opt-out" from an approval. In such a case, the clinical trial cannot be conducted in that member state. The Regulation also aims to streamline and simplify the rules on safety reporting and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU database. Information stored in the EU database will be made publicly available subject to transparency rules.

To obtain marketing approval of a drug under European Union regulatory systems, an applicant must submit a marketing authorization application (MAA) either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases (AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). For products with a new active substance indicated for the treatment of other diseases and

products that are highly innovative or for which a centralized process is in the interest of patients, an applicant may voluntarily submit an application for a centralized marketing authorization to the EMA.

Under the centralized procedure, the Committee for Medicinal Products for Human Use (CHMP) established at the European Medicines Agency (EMA) is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member state before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one-member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Data and Market Exclusivity in the European Union

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the drug if such company can complete a full MAA with a complete database of pharmaceutical test, preclinical tests and clinical trials and obtain marketing approval of its product.

Other legislation regarding marketing, authorization and pricing of pharmaceutical products in the European Union

Other core legislation relating to the marketing, authorization and pricing of pharmaceutical products in the European Union includes the following:

- Directive 2001/83/EC, establishing the requirements and procedures governing the marketing authorization for medicinal products for human use, as well as the rules for the constant supervision of products following authorization. This Directive has been amended several times, most recently by Directive 2012/26/EU regarding pharmacovigilance, and the Falsified Medicines Directive 2011/62/EU.
- Regulation (EC) 726/2004, as amended, establishing procedures for the authorization, supervision and pharmacovigilance of medicinal products for human and veterinary use and establishing the EMA.
- Regulation (EC) 469/2009, establishing the requirements necessary to obtain a Supplementary Protection Certificate, which extends the period of patent protection applicable to medicinal products at the EU-level.
- Directive 89/105/EEC, ensuring the transparency of measures taken by the European Union member states to set the prices and reimbursements of medicinal products. Specifically, while each member state has competence over the pricing and reimbursement of medicines for human use, they must also comply with this Directive, which establishes procedures to ensure that member state decisions and policies do not obstruct trade in medicinal products. The European Commission proposed to repeal and replace Directive 89/105/EEC, but this proposal was withdrawn in 2015.

- Directive 2003/94/EC, laying down the principles of good manufacturing practice in respect of medicinal products and investigational medicinal products for human use (the "GMP Directive").
- Directive 2005/28/EC of April 8 2005, laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorization of the manufacturing or importation of such products" (the "GCP Directive").

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in the European Union, its member states and other states of Europe that could significantly change the statutory provisions governing the testing, approval, manufacturing, marketing, coverage and reimbursement of pharmaceutical products. In addition to new legislation, pharmaceutical regulations and policies are often revised or interpreted by the EMA and national agencies in ways that may significantly affect our business and our products.

On March 29, 2017, the United Kingdom triggered Article 50 of the Treaty of the Functioning of the European Union in order to formally leave the European Union (the so-called "Brexit"). As of the date of this filing, we cannot predict the regulatory implications of Brexit in the (i) enforcement of EU law in the UK before the effective date of Brexit (which might be less stringent); and / or (ii) the post-Brexit UK regime on market authorizations.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as, in the United States, Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not necessarily imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider a product to be cost effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, risk sharing, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals. As a result, the marketability of any product which receives regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement.

In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements for any of our products.

Healthcare Laws and Regulations

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with healthcare providers, physicians, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare Anti-Kickback Statute prohibits, among other things, persons from soliciting, offering, receiving or providing any remuneration (in cash or in kind), directly or indirectly, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any item, facility or service for which payment may be made in whole or in part under a federal healthcare program such as Medicare and Medicaid;
- the federal Foreign Corrupt Practices Act (FCPA) prohibits, among other things, U.S. corporations and persons acting on their behalf from offering, promising, authorizing or making payments to any foreign government official (including certain healthcare professionals in many countries), political party, or political candidate in an attempt to obtain or retain business or otherwise seek preferential treatment abroad;
- the federal False Claims Act, which may be enforced by the U.S. Department of Justice or private whistleblowers to bring civil actions (qui tam actions) on behalf of the federal government, imposes civil penalties, as well as liability for damages and for attorneys' fees and costs, on individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent, making a false statement material to a false or fraudulent claim, or improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) imposes criminal and civil liability for, among other conduct, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes criminal and civil liability and penalties on those who violate requirements, including mandatory contractual terms, intended to safeguard the privacy, security, transmission and use of individually identifiable health information;
- the federal false statements statute relating to healthcare matters prohibits falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal Physician Payment Sunshine Act requires manufacturers of drugs (among other products) to report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals, as well as physician ownership and investment interests in the reporting manufacturers;
- similar state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers;
- certain state laws require pharmaceutical companies to comply with voluntary compliance guidelines promulgated by a pharmaceutical industry association and relevant compliance guidance issues by HHS Office of Inspector General; bar drug manufacturers from offering or providing certain types of payments or gifts to physicians and other health care providers; and/or require disclosure of gifts or payments to physicians and other healthcare providers.

Various state and foreign laws also govern the privacy and security of health information in some circumstances; many of these laws differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Certain Financial Information

The financial information required in this Item 1 is included in Part II, Item 6 and Part IV, Item 15 of this Annual Report on Form 10-K.

Corporate Information

Arrowhead was originally incorporated in South Dakota in 1989 and was reincorporated in Delaware in 2000. In April 2016, Arrowhead changed its name from Arrowhead Research Corporation to Arrowhead Pharmaceuticals, Inc. The Company's principal executive offices are located at 177 E. Colorado Blvd, Suite 700, Pasadena, California 91105, and its telephone number is (626) 304-3400. We also operate a research and development facility in Madison, Wisconsin. As of September 30, 2019, Arrowhead had 134 full-time employees.

Investor Information

Our website address is <http://www.arrowheadpharmaceuticals.com>. Our reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, including our annual reports on Form 10-K, our quarterly reports on Form 10-Q and our current reports on Form 8-K, and amendments to those reports, are accessible through our website, free of charge, as soon as reasonably practicable after these reports are filed electronically with, or otherwise furnished to, the SEC. These SEC reports can be accessed through the "Investors" section of our website.

You may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy and information statements, and other information regarding Arrowhead and other issuers that file electronically with the SEC. The SEC's Internet website address is <http://www.sec.gov>.

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 have accrued net losses annually since inception given the stage of our drug development. 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 Company

Risks Related to Our Discovery, Development, and Commercialization of Medicines

There are substantial risks inherent in attempting to commercialize our new drugs, and, as a result, we may not be able to successfully develop products for commercial use.

Our research and development efforts involve therapeutics based on RNA interference and our delivery systems, which are largely unproven technologies. Our scientists and engineers are working on developing technology in the early 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 it can be achieved at all. To date, our research and development projects have not produced commercially viable drugs and may never do so. During the research and development process, we may experience technological barriers that we may be unable to overcome. Further, certain underlying premises in our development programs are not proven. For instance, the reduction of the production of mutant alpha-1 antitrypsin in the liver may not lead to a reduction of globules in the liver, and even if it leads to a reduction in such globules, this may not lead to other beneficial hepatic changes. It is also unknown at this time what changes in the liver may be required to gain regulatory approval and/or favorable reimbursement for a drug that reduces the production of mutant alpha-1 antitrypsin in the liver. Similar uncertainties and risks exist that are specific to each of our development programs. Because of these and similar uncertainties, it is possible that no commercial products will be successfully developed. If we are unable to successfully develop commercial products, we will be unable to generate revenue or build a sustainable or profitable business.

There can be no assurance that our product candidates will obtain regulatory approval.

The sale of human therapeutic products in the U.S. and foreign jurisdictions is subject to extensive and time consuming regulatory approval which requires, among other things:

- controlled research and human clinical testing;
- establishment of the safety and efficacy of the product;
- government review and approval of a submission containing manufacturing, pre-clinical and clinical data; and
- adherence to cGMP regulations during production and storage.

The product candidates we currently have under development will require significant development, pre-clinical and clinical testing and investment of significant funds to gain regulatory approval before they can be commercialized. The results of our research and human clinical testing of our products may not meet regulatory requirements. Some of our product candidates, if approved, will require the completion of post-market studies. There can be no assurance that any of our products will be further developed and approved. The process of completing clinical testing and obtaining required approvals will take a number of years and require the use of substantial resources. Further, there can be no assurance that product candidates employing a new technology will be shown to be safe and effective in clinical trials or receive applicable regulatory approvals. If we fail to obtain regulatory approvals for any or all of our products, we will not be able to market such product and our operations may be adversely affected.

If testing of a particular product candidate does not yield successful results, then we will be unable to commercialize that product candidate.

We must demonstrate our product candidates' safety and efficacy in humans through extensive clinical testing. Our research and development programs are at an early stage of development. We may experience numerous unforeseen events during, or as a result of, the testing process that could delay or prevent commercialization of any products, including the following:

- the results of pre-clinical studies may be inconclusive, or they may not be indicative of results that will be obtained in human clinical trials;

- safety and efficacy results attained in early human clinical trials may not be indicative of results that are obtained in later clinical trials;
- after reviewing test results, we may abandon projects that we might previously have believed to be promising;
- we or our regulators may suspend or terminate clinical trials because the participating subjects or patients are being exposed to unacceptable health risks; and
- our product candidates may not have the desired effects or may include undesirable side effects or other characteristics that preclude regulatory approval or limit their commercial use if approved.

Topline data may not accurately reflect the complete results of a particular study or trial.

We may publicly disclose topline or interim data from time to time, which is based on a preliminary analysis of then-available efficacy and safety data such as the data reported from the AROAAT1001, AROANG31001, and AROAPOC31001 clinical studies which are based on preliminary analysis of key efficacy and safety data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or drug and our company in general. In addition, the information we may publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the topline data that we report differ from a future analysis of results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects or financial condition may be harmed.

It may take us longer than we project to complete clinical trials, and we may not be able to complete them at all.

Although for planning purposes, we project the commencement, continuation and completion of our clinical trials, a number of factors, including scheduling conflicts with participating clinicians and clinical institutions, and difficulties in identifying or enrolling patients who meet trial eligibility criteria, may cause significant delays. Enrollment of clinical trials may be particularly difficult in orphan diseases or limited-sized patient populations. FDA or other regulatory bodies may require additional, longer, or broader clinical trials to establish safety and effectiveness, notwithstanding guidance the Company may have received from those bodies during clinical trial planning and execution. Further, the cost for conducting clinical trials is significant and if our cash resources become limited we may not be able to commence, continue, and/or complete our clinical trials. We may not commence or complete clinical trials involving any of our product candidates as projected or may not conduct them successfully.

Fast Track designation for ARO-AAT may not lead to a faster development or review process.

We have been granted a Fast Track designation for ARO-AAT in the United States for the treatment of liver disease associated with AATD. Fast Track designation is intended to facilitate the development and expedite the review of new therapies to treat serious conditions with unmet medical needs by providing sponsors with the opportunity for frequent interactions with the FDA. Fast Track designation applies to the combination of the drug candidate and the specific indication for which it is being studied. Product candidates that receive Fast Track designation may receive more frequent interactions with the FDA regarding the product candidate's development plan and clinical trials and may be eligible for the FDA's Rolling Review.

Despite receiving Fast Track designation, ARO-AAT may not actually receive faster clinical development or regulatory review or approval any sooner than other product candidates that do not have such designation, or at all. Furthermore, such a designation does not increase the likelihood that ARO-AAT will receive marketing approval in the United States. The FDA may also withdraw Fast Track if it determines that ARO-AAT no longer meets the relevant criteria.

Even if our clinical studies are successful and we achieve regulatory approval, the approved product label may be more limited than we or other parties anticipate, which could limit the commercial opportunity for our product candidates.

At the time drugs are approved for commercialization, they are given a "product label" from the FDA or other regulatory body. In most countries this label sets forth the approved indication for marketing and identifies potential safety concerns for prescribing

physicians and patients. While we intend to seek as broad a product label as possible for our product candidates, we may receive a narrower label than is expected by either us or third parties, such as stockholders and securities analysts. For example, any approved products may only be indicated to treat refractory patients (i.e., those who have failed some other first-line therapy). Similarly, it is possible that only a specific sub-set of patients safely responds to one or more of our drug candidates. As a result, our product candidates, even if successful in clinical trials, could be approved only for a subset of patients. Additionally, safety considerations may result in contraindications that could further limit the scope of an approved product label. Any of these or other safety and efficacy considerations could limit the commercial opportunity for our product candidates.

Even if our product candidates are approved for commercialization, future regulatory reviews or inspections may result in the suspension or withdrawal of one or more of our products, closure of a facility or enforcement of substantial fines.

If regulatory approval to sell any of our product candidates is received, regulatory agencies will subject any marketed product(s), as well as the manufacturing facilities, to continual review and periodic inspection. If previously unknown problems with a product or manufacturing and laboratory facility are discovered, or we fail to comply with applicable regulatory approval requirements, a regulatory agency may impose restrictions on that product or on us. The agency may require the withdrawal of the product from the market, closure of the facility or enforcement of substantial fines.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for a product candidate and may have to limit its commercialization.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. Product liability claims might be brought against us by clinical trial participants, consumers, health-care providers, pharmaceutical companies, or others selling our products. If we cannot successfully defend ourselves against these claims, we may incur substantial liabilities. Regardless of merit or eventual outcomes of such claims, product liability claims may result in:

- decreased demand for our product candidates;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs of litigation;
- substantial monetary awards to patients or other claimants; and
- loss of revenues.

Our insurance coverage may not be sufficient to reimburse us for all expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

The successful commercialization of our product candidates, if approved, will depend in part on the extent to which government authorities and health insurers establish adequate reimbursement levels and pricing policies.

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, who are increasingly challenging the price of medical products and services. Accordingly, coverage and reimbursement may be uncertain. Adoption of any drug by the medical community may be limited if third-party payers will not offer coverage. Additionally, significant uncertainty exists as to the reimbursement status of newly approved drugs. Cost control initiatives may decrease coverage and payment levels for any drug and, in turn, the price that we will be able to charge and/or the volume of our sales. 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. If we partner with third parties with respect to any of our product candidates, we may be reliant on that partner to obtain reimbursement from government and private payors for the drug, if approved, and any failure of that partner to establish adequate reimbursement could have a negative impact on our revenues and profitability.

In addition, both the federal and state governments in the United States and foreign governments continue to propose and pass new legislation, regulations, and policies affecting coverage and reimbursement rates, which are designed to contain or reduce the cost of health care. 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 potential 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.

If future reimbursement for approved product candidates, if any, is substantially less than we project, or rebate obligations associated with them are substantially greater than we expect, our future net revenue and profitability could be materially diminished.

We may not enjoy the market exclusivity benefits of our orphan drug designation.

Although we may obtain orphan designations in the treatment of certain diseases our products are intended to treat, the designation may not be applicable to any particular product we might get approved and that product may not be the first product to receive approval for that indication. Under the Orphan Drug Act, the first product with an orphan designation receives market exclusivity, which prohibits FDA from approving the “same” drug for the same indication. The FDA has stated that drugs can be the “same” even when they are not identical but has not provided guidance with respect to how it will determine “sameness” for RNAi drugs. It is possible that another RNAi drug could be approved for the treatment of a disease one of our orphan products is intended to treat before our product is approved, which means that we may not obtain orphan drug exclusivity and could also potentially be blocked from approval until the first product’s orphan drug exclusivity period expires or we demonstrate, if we can, that our product is superior. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved and granted orphan drug exclusivity, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care.

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

Our future success depends to a significant extent on the continued services of our key employees, including our senior scientific, technical and managerial personnel. We do not maintain key person life insurance for any of our executives and we do not maintain employment agreements with many senior employees. Competition for qualified employees in the pharmaceutical industry is high, and our ability to execute our strategy will depend in part on our ability to continue to attract and retain qualified scientists and management. If we are unable to find, hire and retain qualified individuals, we will have difficulty implementing our business plan in a timely manner, or at all.

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.

We have licensed rights to pending patents and have filed and expect to continue to file patent applications. Researchers sponsored by us may also file patent applications that we may need to license. Such patent applications may not be available for licensing or may not be economically feasible to license. Certain of our patents may not be granted or may not contain claims of the necessary breadth because, for example, prior patents exist. 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 ultimately successful, efforts to enforce our patent rights could be expensive, distracting for management, cause our patents to be invalidated or held unenforceable, and thus frustrate commercialization of products. Even if patents are issued and are enforceable, others may develop similar, superior or parallel technologies to any technology developed by us and not infringe on our patents. Our technology may prove to infringe upon patents or rights owned by others. Patent prosecution and maintenance is expensive, and we may be forced to curtail prosecution or maintenance if our cash resources are limited. 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.

We are party to 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.

We are party to license agreements to incorporate third party proprietary technologies into our drug products under development. These license agreements require us to pay royalties and satisfy other conditions. If we fail to satisfy our obligations under these agreements, the terms of the licenses may be materially modified, such as by rendering currently exclusive licenses non-exclusive, or it may give our licensors the right to terminate their respective agreement with us, which could limit our ability to implement our current business plan and harm our business and financial condition.

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 intellectual property landscape in the fields in which we participate is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate without infringing on third party rights. However, if granted marketing approval, 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 drug candidates infringing. If a claim should be brought and is successful, we may be required to pay substantial damages, be forced to abandon any affected drug candidates 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 will not be challenged, potentially successfully, by others.

In addition, if our product candidates are found to infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our customers, licensees, and other parties with whom we have business relationships and we may be required to indemnify those parties 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, licensees, and other parties regardless of the merits of these claims. If any of these claims succeed, we may be forced to pay damages on behalf of those parties 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.

We license patent rights from third-party owners and we rely on such owners to obtain, maintain and enforce the patents underlying such licenses.

We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary or useful for our business. We also expect to enter into additional licenses to third-party intellectual property in the future.

Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents are issued in respect of these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects.

Our technology licensed from various third parties may be subject to retained rights.

Our licensors 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 licensors 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.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers, and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, while the company undertakes efforts to protect its trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

Our future success may require that we acquire patent rights and know-how to 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.

Risks Related to Our Business Model

Our business model assumes we will generate revenue by, among other activities, marketing or out-licensing the products we develop. Our drug candidates are in the early stages of development and because we have a short development history with both

RNA interference and our delivery technologies, there is a limited amount of information about us upon which you can evaluate our business and prospects.

We have no approved drugs and thus have not begun to market or generate revenues from the commercialization of any products. We have only a limited history upon which one can evaluate our RNAi therapeutic business as our drug candidates are still at an early stage of development. Thus, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- Execute product development activities using unproven technologies;
- Build, maintain, and protect a strong intellectual property portfolio;
- Demonstrate safety and efficacy of our drug candidates in multiple human clinical studies;
- Receive FDA approval and approval from similar foreign regulatory bodies;
- Gain market acceptance for the development and commercialization of any drugs we develop;
- Ensure our products are reimbursed by commercial and/or government payors at a rate that permits commercial viability;
- Develop and maintain successful strategic relationships with suppliers, distributors, and commercial licensing partners;
- Manage our spending and cash requirements as our expenses will increase in the near term if we add programs and additional preclinical and clinical trials; and
- Effectively market any products for which we obtain marketing approval.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop products, raise capital, expand our business or continue our operations.

We may need to establish additional relationships with strategic and development partners to fully develop our drug candidates and market any approved products.

In October 2018, we entered into a license agreement and research and collaboration agreement with Janssen Pharmaceuticals, Inc. and during fiscal year 2016, we entered into two collaboration and license agreements with Amgen Inc. Our business strategy includes obtaining additional collaborations with other pharmaceutical and biotech companies to support the development of our RNAi therapeutics and other drug candidates. We do not possess all of the financial and development resources necessary to develop and commercialize products that may result from our technologies. Unless we expand our product development capacity and enhance our internal marketing capability, we may need to make appropriate arrangements with strategic partners to develop and commercialize any drug candidates that may be approved. 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. 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 will be beyond our control. In addition, in the event we pursue our commercialization strategy through collaboration or licenses to third parties, there are a variety of technical, business and legal risks, including:

- 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 drug 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 drug 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 could impair our ability to generate revenues and harm our business and financial condition.

Our ability to generate milestone and royalty payments under our current and potential future licensing and collaboration agreements is substantially controlled by our partners, and as such, we will likely need other sources of financing to continue to develop our internal drug candidates.

For instance, under our licensing and collaboration agreements with Amgen and Janssen, both Amgen and Janssen substantially control all clinical development and commercialization for all of the candidates discussed, and the potential future targets. To the extent that i) either of these partners interests in advancing these candidates or targets changes, ii) unforeseen scientific issues with the candidates arise or iii) the pace at which either moves the candidates through clinical trials toward commercialization slows, our ability to collect milestones and royalties may be significantly diminished. This would further cause us to rely upon other sources of financing to continue to develop our other internal drug candidates.

We may lose a considerable amount of control over our intellectual property and may not receive anticipated revenues in strategic transactions, 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 utilize the intellectual property created through the research and development process to develop commercially successful products. If the acquirers of our technologies fail to achieve performance milestones, we may not receive a significant portion of the total value of any sale, license or other strategic transaction.

We will need to achieve commercial acceptance of our drug candidates to generate revenues and achieve profitability.

Even if our research and development efforts yield technologically feasible applications, we may not successfully develop commercial products. Drug development takes years of study in human clinical trials prior to regulatory approval, and, even if we are successful, it may not be on a timely basis. During our drug 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 the medical community and consumers will adopt any product we develop is uncertain. The rate and degree of market acceptance of our products will depend on a number of factors, including the establishment and demonstration in the medical community of the clinical efficacy and safety of our products, their potential advantage over alternative treatments, and the costs to patients and third-party payors, including insurance companies and Medicare. Recent efforts in the United States and abroad to reduce overall healthcare spending has put significant pressure on the price of prescription drugs and certain companies have been publicly criticized for the relatively high cost of their therapies. These pressures may force us to sell any approved drugs at a lower price than we or analysts may anticipate or may result in lower levels of reimbursement and coverage from third parties.

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 consistent profitability will depend substantially on our ability to introduce products that will be accepted by the medical community. 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 rely on outside sources for various components and processes for our products.

We rely on third parties for various components and processes for our product candidates. 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. There may be a disruption or delay in the performance of our third-party contractors, suppliers or collaborators which is beyond our control. If such third parties are unable to satisfy their commitments to us, the development of our products would be adversely affected. Therefore, it is possible that our development 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 have limited manufacturing capability and must rely on third-party manufacturers to manufacture our clinical supplies and commercial products, if and when approved, and if they fail to meet their obligations, the development and commercialization of our products could be adversely affected.

We have limited manufacturing capabilities and experience. Our drug candidates are composed of multiple components and require specialized formulations for which scale-up and manufacturing could be difficult. We have limited experience in such scale-up and manufacturing requiring us to depend on a limited number of third parties, who may not be able to deliver in a timely manner, or at all. In order to develop products, apply for regulatory approvals, and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. Our internal manufacturing capabilities are limited to small-scale production of material for use in *in vitro* and *in vivo* experiments that is not required to be produced under cGMP standards beyond those applicable to active pharmaceutical ingredients used in some early phase studies. There are a limited number of manufacturers that supply synthetic oligonucleotides. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our contract manufacturers to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are synthesis and purification failures and contamination during the manufacturing process, which could result in unusable product and cause delays in our development process, as well as additional expense to us.

Additionally, our product candidates have not yet been manufactured for commercial use. If any of our product candidates become approved for commercial sale, we will need to establish either internal or third-party manufacturing capacity. Manufacturing partner requirements may require us to fund capital improvements, perhaps on behalf of third parties, to support the scale-up of manufacturing and related activities. We may not be able to establish scaled manufacturing capacity for an approved product in a timely or economic manner, if at all. If we or our third-party manufacturers are unable to provide commercial quantities of such an approved product, we will have to successfully transfer manufacturing technology to a different manufacturer. Engaging a new manufacturer for such an approved product could require us to conduct comparative studies or utilize other means to determine bioequivalence of the new and prior manufacturers' products, which could delay or prevent our ability to commercialize such an

approved product. If we or any of these manufacturers is unable or unwilling to increase its manufacturing capacity or if we are unable to establish alternative arrangements on a timely basis or on acceptable terms, the development and commercialization of such an approved product may be delayed or there may be a shortage in supply. Any inability to manufacture our product candidates or future approved drugs in sufficient quantities when needed would seriously harm our business.

Manufacturers of our approved products, if any, must comply with cGMP requirements enforced by the FDA and foreign health authorities through facilities inspection programs. These requirements include quality control, quality assurance, and the maintenance of records and documentation. Manufacturers of our approved products, if any, may be unable to comply with these cGMP requirements and with other FDA, state, and foreign regulatory requirements. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any quantities supplied is compromised due to a manufacturer's failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, which would seriously harm our business.

We rely on third parties to conduct our clinical trials, and if they fail to fulfill their obligations, the development of our products may be adversely affected.

We rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our clinical trials. We contract with certain third-parties to provide certain services, including site selection, enrollment, monitoring and data management services. Although we depend heavily on these parties, we do not control them and therefore we cannot be assured that these third-parties will adequately perform all of their contractual obligations to us. If our third-party service providers cannot adequately and timely fulfill their obligations to us, or if the quality and accuracy of our clinical trial data is compromised due to failure by such third parties to adhere to our protocols or regulatory requirements or if such third-parties otherwise fail to meet deadlines, our development plans may be delayed or terminated. Further, if clinical study results are compromised, then we may need to repeat the affected studies, which could result in significant additional costs and delays to us.

We face competition from various entities including large pharmaceutical companies, small biotech companies, private companies, and research institutions.

Many of our competitors have greater financial resources and may have more experience in research and development, manufacturing, managing clinical trials and/or regulatory compliance than we do. Our competitors may compete with us for lead clinical trial investigators, clinical trial site locations and patient enrollment. These competitors may also compete with us on recruiting scientific and management personnel. Because our products are in the early stages of development, along with many of the competing products, and given unpredictability inherent in drug development, it is difficult to predict which third parties may provide the most competition, and on what specific basis that competition may be based.

We may have difficulty expanding our operations successfully as we evolve from a company primarily involved in discovery and pre-clinical testing into one that develops and commercializes drugs.

We expect that as we increase the number of product candidates we are developing we will also need to expand our operations. This expected growth may place a strain on our administrative and operational infrastructure. As product candidates we develop enter and advance through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing, and sales capabilities or contract with other organizations to provide these capabilities for us. As our operations expand due to our development progress, we expect that we will need to manage additional relationships with various collaborators, suppliers, and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

Our business and operations could suffer in the event of information technology system failures.

Our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, ransomware and other cyber-attacks, human error, natural disasters, terrorism, war, and telecommunication and electrical failures. Such events could cause interruption of our operations and loss of intellectual property. For example, the loss of pre-clinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts and significantly increase our costs. Further, cybersecurity breaches may allow hackers access to our preclinical compounds, strategies, discoveries, trade secrets, and/or other confidential information. To the extent that any disruption or security breach were to result in a loss of or damage to our data, or inappropriate disclosure of confidential, proprietary or private information, we could incur liability or regulatory penalties, including under laws and regulations governing the protection of health and other personally identifiable information, we could lose valuable trade secret rights, the development of our

product candidates could be delayed, and we could suffer reputational damage and damage to key business relationships. The risk of a cyber-security breach or other informational technology disruption, particularly through cyber-attacks, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We have experienced cyber-security attacks in the past, which to date have not had a material impact on our operations or development programs; however, there is no assurance that such impacts will not be material in the future.

Because we use biological materials, hazardous materials, chemicals and radioactive compounds, if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research, development and manufacturing activities involve the use of potentially harmful biological materials as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. We store most of these materials and various wastes resulting from their use at our facility in Madison, Wisconsin pending ultimate use and disposal. We cannot completely eliminate the risk of contamination, which could cause: interruption to our research and development and manufacturing efforts, injury to our employees and others, environmental damage, and liabilities under federal, state and local law. In such an event, we may be held liable for any resulting damages, and any liability could exceed our resources. Although we carry insurance in amounts and types that we consider commercially reasonable, we do not have insurance coverage for losses relating to an interruption of our research, development or manufacturing efforts caused by contamination, and the coverage or coverage limits of our insurance policies may not be adequate. If our losses exceed our insurance coverage, our financial condition would be affected.

If a natural or man-made disaster strikes our research and development facility or otherwise affects our business, it could delay our progress developing our product candidates.

We conduct research and development in a facility in Madison, Wisconsin. The facilities and the equipment we use are costly to replace and require substantial lead time to repair or replace. Our facilities may be harmed by natural or man-made disasters, including, without limitation, earthquakes, floods, fires and acts of terrorism; and if our facilities are affected by a disaster, our development efforts would be delayed. Significant delays in our development efforts could materially impact our ability to obtain regulatory approval and to commercialize our products. Any insurance we maintain against damage to our property and the disruption of our business due to disaster may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all. In addition, our development activities could be harmed or delayed by a shutdown of the U.S. government, including the FDA.

Litigation claims may result in financial losses or harm our reputation and may divert management resources.

When the market price of a stock is volatile, holders of that stock have often initiated securities class action litigation against the company that issued the stock. We cannot predict with certainty the eventual outcome of such litigation, arbitration or third-party inquiry. We may not be successful in defending ourselves or asserting our rights in current or future lawsuits, investigations, or claims that have been or may be brought against us and, as a result, our business could be materially harmed. These lawsuits, arbitrations, investigations or claims may result in large judgments or settlements against us, any of which could have a negative effect on our financial performance and business. Additionally, lawsuits, arbitrations and investigations can be expensive to defend, whether or not the lawsuit, arbitration or investigation has merit, and the defense of these actions may divert the attention of our management and other resources that would otherwise be engaged in running our business.

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 and we expect that our operating losses will continue for the foreseeable future as we continue our drug development and discovery efforts. To achieve profitability, we must, either directly or through licensing and/or partnering relationships, meet certain milestones, successfully develop and obtain regulatory approval for one or more drug candidates 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 consistent profitability.

We will require substantial additional funds to complete our research and development activities.

Our business currently does not generate the cash that is necessary to finance our operations. Subject to the success of the research and development programs of our company and our partners, and potential licensing or partnering transactions, we may need to raise additional capital to:

- Fund research and development infrastructure and activities relating to the development of our drug candidates, including pre-clinical and clinical trials and manufacturing to support these efforts;
- Fund a commercialization infrastructure and activities related to the sale, marketing, customer support, and distribution of our drug products if and when they become approved;
- Fund our general and administrative infrastructure and activities;
- Pursue business development opportunities for our technologies;
- Add to and protect our intellectual property; and
- Retain our management and technical staff.

Our future capital needs depend on many factors, including:

- The scope, duration, and expenditures associated with our research and development;
- Regulatory requirements for our clinical trials;
- The extent to which our research and development and clinical efforts are successful;
- The outcome of potential partnering or licensing transactions, if any, and the extent to which our business development efforts result in the acquisition of new programs or technologies;
- Competing technological developments;
- Our intellectual property positions, if any, in our products; and
- The regulatory approval process and regulatory standards for our drug candidates.

We will need to raise additional funds through public or private equity offerings, debt financings or additional strategic alliances and licensing arrangements in the future to continue our operations. We may not be able to obtain additional financing on terms favorable to us, if at all. General market conditions may make it very difficult for us to seek financing from the capital markets, and the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our stockholders will result, which may substantially dilute the value of your investment. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants that could limit our flexibility in conducting future business activities and, in the event of insolvency, would be paid before holders of equity securities received any distribution of corporate assets. In order to raise additional funds through alliance, joint venture or licensing arrangements, we may be required to relinquish rights to our technologies or drug candidates or grant licenses on terms that are not favorable to us. If adequate funds are not available, we may have to further delay, reduce or eliminate one or more of our planned activities. These actions would likely reduce the market price of our common stock.

If the estimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements prove inaccurate, our actual results may vary from those reflected in our accruals.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

The investment of our cash, cash equivalents and fixed income marketable securities is subject to risks which may cause losses and affect the liquidity of these investments.

At September 30, 2019, we had \$81.1 million in fixed income marketable securities. These investments are in corporate bonds, but our investments may also include commercial paper, securities issued by the U.S. government obligations, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, and market and interest rate risks, particularly in the current economic environment. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

Our ability to utilize net operating loss carryforwards and other tax benefits may be limited.

We have historically incurred net losses. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses (NOLs) carried forward from a prior taxable year. Under that provision, we can carryforward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. As of September 30, 2019, we had federal, and state NOL carryforwards of approximately \$314.8 million and \$211.5 million, respectively. The federal NOL carryforwards will begin to expire, if not utilized, beginning in 2039. These NOL carryforwards could expire unused before offsetting potential future income tax liabilities. Under the Tax Cut and Jobs Act of 2017, or the Tax Act, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50 percent change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. It is possible that we have experienced an ownership change limitation. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our NOL carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

Our business is subject to changing regulations for corporate governance and public disclosure that has increased both our costs and the risk of noncompliance.

Each year we are required to evaluate our internal controls systems in order to allow management to report on and our Independent Registered Public Accounting Firm to attest to, our internal controls as required by Section 404 of the Sarbanes-Oxley Act. As a result, we continue to incur additional expenses and divert our management’s time to comply with these regulations. In addition, if we cannot continue to comply with the requirements of Section 404 in a timely manner, we might be subject to sanctions or investigation by regulatory authorities, such as the SEC, the Public Company Accounting Oversight Board, or PCAOB, or The Nasdaq Global Select Market. Any such action could adversely affect our financial results and the market price of our common stock.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

The Tax Act significantly revises the Internal Revenue Code of 1986, as amended. The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35 percent to a flat rate of 21 percent, limitation of the tax deduction for interest expense to 30 percent of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80 percent of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

We could be subject to additional tax liabilities.

We are subject to U.S. federal, state, local and sales taxes in the U.S. and Australia. Significant judgment is required in evaluating our tax positions. During the ordinary course of business, there are many activities and transactions for which the ultimate tax determination is uncertain. In addition, our tax obligations and effective tax rates could be adversely affected by changes in the relevant tax, accounting and other laws, regulations, principles and interpretations, including those relating to income tax nexus, by recognizing tax losses or lower than anticipated earnings in jurisdictions where we have lower statutory rates and higher than anticipated earnings in jurisdictions where we have higher statutory rates, by changes in foreign currency exchange rates, or by changes in the valuation of our deferred tax assets and liabilities. We may be audited in various jurisdictions, and such jurisdictions may assess additional taxes, sales taxes and value-added taxes against us. Although we believe our tax estimates are reasonable, the final determination of any tax audits or litigation could be materially different from our historical tax provisions and accruals, which could have a material adverse effect on our operating results or cash flows in the period for which a determination is made.

Investment and Securities Risks

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. For example, 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. These factors could also reduce the price that certain investors might be willing to pay for shares of our Common Stock and result in the market price being lower than it would be without these provisions.

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.

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. Currently, coverage of our Company by industry and securities analysts is limited. Investors have many investment opportunities and may limit their investments to companies that receive greater coverage from analysts. If additional industry or securities analysts do not commence coverage of the Company, the trading price of our stock could be negatively impacted. 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 fail 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. Further, incorrect judgments, estimates or assumptions made by research analysts may adversely affect our stock price, particularly if subsequent performance falls below the levels that were projected by the research analyst(s), even if we did not set or endorse such expectations. Any of these events could cause further volatility in our stock price and could result in substantial declines in the value of our stock.

The market for purchases and sales of our Common Stock may be 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 Global Select Market, at various times our securities are relatively thinly traded. Investor trading patterns could serve to exacerbate the volatility of the price of our 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. 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 result in major fluctuations in the price of the stock.

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 early in the stage of our drug development, there are few objective metrics by which our progress may be measured. Consequently, we expect that the market price of our Common Stock will continue to fluctuate significantly. We may not continue to 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, including clinical trial results;
- Market perception and/or investor sentiment regarding our technology;
- Announcements of actions taken by regulatory authorities, such as the U.S. Food and Drug Administration;
- Announcements regarding developments in the RNA interference or biotechnology fields in general;
- Announcements regarding clinical trial results with our products or competitors’ products;
- Market perception and/or announcements regarding other companies developing products in the field of biotechnology generally or specifically RNA interference;

- The issuance of competitive patents or disallowance or loss of our patent rights;
- The addition or departure of key executives; 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 such volatility could result in the loss of all or part of your investment.

Stockholder equity interest may be substantially diluted in any additional equity issuances.

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. The following serves as a summary of share issuance activity during the fiscal year ended September 30, 2019:

- 3,260,869 shares of Common Stock issued as part of the Stock Purchase Agreement with JJDC Inc. in October 2018 that generated \$75 million of net proceeds to the Company; and
- 3,740,100 shares of Common Stock pursuant to the exercise of stock options and the vesting of restricted stock units.

As of September 30, 2019, we had 95,506,271 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 could 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.

Risks Inherent in Our Industry

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 animal and early 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, or at all; and
- Manufacturing and distribution may be uneconomical.

For example, any positive pre-clinical results in animals for our pre-clinical programs may not be replicated in human clinical studies. These programs may be also found to be unsafe in humans, particularly at higher doses needed to achieve the desired levels of efficacy. Also, the positive safety results from single dose human clinical studies may not be replicated in other human studies, including multiple dose studies. Clinical and pre-clinical study 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 many years to complete, including the process of study design, clinical site selection and the recruitment of patients. As a result, we can experience significant delays in completing clinical studies, which can increase the cost of developing a drug candidate and shorten the time that an approved product may be protected by patents. If our drug candidates are not successful in human clinical trials, we may be forced to curtail or abandon certain development programs. 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.

The healthcare system is under significant financial pressure to reduce costs, which could reduce payment and reimbursement rates for drugs.

Throughout the world and particularly in the United States the healthcare system is under significant financial pressure to reduce costs. The price of pharmaceuticals has been a topic of considerable public discussion that could lead to price controls or other price-limiting strategies by payors that have the effect of lowering payment and reimbursement rates for drugs or otherwise making the commercialization of pharmaceuticals less profitable. These effects could reduce or eliminate our ability to return value to our shareholders.

Regulatory standards are subject to change over time, making it difficult to accurately predict the likelihood of marketing approval even when clinical trials meet their endpoints.

Regulatory standards are promulgated by various government entities and are subject to change based on factors such as scientific developments, public perceptions of risk, and political forces. Because clinical trials often take years to complete, it is sometimes possible for standards that exist during the conception and initiation of a clinical trial to change before the clinical trial is completed or reviewed by government regulators. For example, we may initiate clinical trials that are designed to show benefits on relatively short-term endpoints, but ultimately be required to show benefits in longer-term outcome studies. While some government entities have safeguards intended to ensure standards agreed upon by sponsors and regulators at the outset of a clinical trial are applied during regulatory review processes, those safeguards generally permit regulators to apply more rigorous standards where regulators believe doing so is necessary. As such, there can be no assurance that regulatory standards that are appropriate at the outset of a clinical trial program will not become more rigorous during the regulatory approval process and could potentially result in a delayed approval or denial of marketing authorization.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

The Company does not own any real property. The following table summarizes the Company’s leased facilities as of September 30, 2019.

	Office Space	Monthly Expenses	Primary Use	Lease Expiration	Lease Term
Pasadena, California	24,000 sq. ft.	\$ 65,700	Corp. Headqtrs. Research Facility	April 2027	7.5 years
Madison, Wisconsin	74,000 sq. ft.	\$ 135,800		September 2029	13 years

ITEM 3. LEGAL PROCEEDINGS

Legal Proceedings are set forth in our financial statement schedules in Part IV, Item 15 of this Annual Report and are incorporated herein by reference. See Note 7 — *Commitments and Contingencies* of Notes to Consolidated Financial Statements of Part IV, Item 15. *Exhibits and Financial Statement Schedules*.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

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 Global Select 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.

	Fiscal Year Ended September 30,			
	2019		2018	
	High	Low	High	Low
1st Quarter	\$ 20.31	\$ 10.41	\$ 4.54	\$ 3.01
2nd Quarter	20.60	11.67	8.09	3.57
3rd Quarter	28.84	17.30	14.24	6.26
4th Quarter	36.80	25.68	22.39	12.25

Shares Outstanding

At November 20, 2019, 95,708,027 shares of the Company's Common Stock were issued and outstanding, and were owned by 112 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 of Part III of 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 the years ended September 30, 2019, 2018 and 2017.

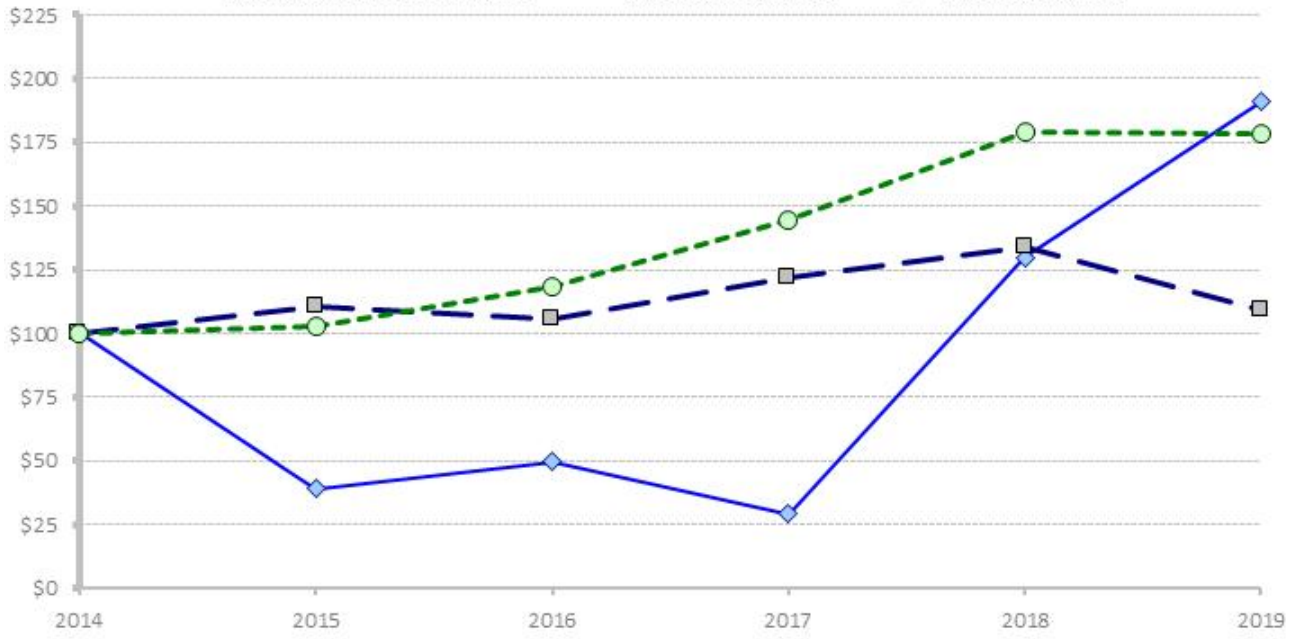
Performance Graph

The following performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing. The graph compares the cumulative 5-year total return to shareholders on our Common Stock relative to the cumulative total returns of the Nasdaq Composite Index and the Nasdaq Biotechnology Index. We selected the Nasdaq Biotechnology Index because we believe the index reflects the market conditions within the industry in which we primarily operate. The comparison of total return on investment, defined as the change in year-end stock price plus reinvested dividends, for each of the periods assumes that \$100 was invested on September 30, 2014, in each of our Common Stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index, with investment weighted on the basis of market capitalization.

The comparisons in the following graph are based on historical data and are not intended to forecast the possible future performance of our Common Stock.

COMPARISON OF CUMULATIVE TOTAL RETURN

—◇— Arrowhead Pharmaceuticals, Inc. -■- NASDAQ Biotechnology -○- NASDAQ Composite



ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data has been derived from our audited consolidated financial statements and should be read in conjunction with the consolidated financial statements, the related notes thereto and the independent auditors' report thereon, and "Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this Form 10-K and in previously filed annual reports on Form 10-K of Arrowhead Pharmaceuticals, Inc.

	Year Ended September				
	2019	2018	2017	2016	2015
OPERATING SUMMARY					
REVENUE	\$ 168,795,577	\$ 16,142,321	\$ 31,407,709	\$ 158,333	\$ 382,000
OPERATING EXPENSES					
Research and development	81,048,686	52,968,505	50,904,466	62,117,818	64,035,385
Acquired in-process research and development	-	-	-	-	10,142,786
General and administrative expenses	26,556,257	19,110,051	17,499,152	23,594,888	20,286,272
Impairment expense	-	-	-	2,050,817	-
Contingent consideration - fair value adjustments	-	-	-	(5,862,464)	1,891,533
TOTAL OPERATING EXPENSES (a)	107,604,943	72,078,556	68,403,618	81,901,059	96,355,976
OPERATING INCOME (LOSS)	61,190,634	(55,936,235)	(36,995,909)	(81,742,726)	(95,973,976)
NET INCOME (LOSS)	67,974,849	(54,450,478)	(34,380,295)	(81,723,002)	(91,940,882)
NET INCOME (LOSS) PER SHARE:					
Net Income (Loss) Per Share - Basic	\$ 0.72	\$ (0.65)	\$ (0.47)	\$ (1.34)	\$ (1.60)
Net Income (Loss) Per Share - Diluted	\$ 0.69	\$ (0.65)	\$ (0.47)	\$ (1.34)	\$ (1.60)
Weighted average shares outstanding – basic	93,858,857	83,638,469	73,898,598	61,050,880	57,358,442
Weighted average shares outstanding – diluted	98,607,815	83,638,469	73,898,598	61,050,880	57,358,442
CASH DIVIDEND PAID PER COMMON SHARE	\$ -	\$ -	\$ -	\$ -	\$ -

	September 30,				
	2019	2018	2017	2016	2015
FINANCIAL POSITION SUMMARY					
CASH AND CASH EQUIVALENTS (b)	\$ 221,804,128	\$ 30,133,213	\$ 24,838,567	\$ 85,366,448	\$ 81,214,354
SHORT- AND LONG-TERM INVESTMENTS (b)	81,075,887	46,400,176	40,769,539	-	17,539,902
TOTAL ASSETS (b)	349,845,437	111,609,951	104,022,280	128,176,505	132,267,914
CAPITAL LEASE OBLIGATIONS	-	-	-	-	758,340
OTHER LONG-TERM OBLIGATIONS	8,738,506	4,003,999	4,454,070	7,508,452	6,204,917

- (a) The increase in our Total Operating Expenses during the year ended September 30, 2019 is primarily due to the expansion of our pipeline of clinical candidates, as we began to incur clinical study costs for our ARO-ANG3 and ARO-APOC3 candidates during the year ended September 30, 2019. We expect research and development expenses to continue to increase as our other pipeline candidates progress toward the clinic.
- (b) The Company's Cash, Cash Equivalents, Short- and Long-Term Investments and Total Assets increased from September 30, 2018 to September 30, 2019 due primarily due to the upfront payment, equity investment and milestone payments totaling \$300 million received from Janssen during the year ended September 30, 2019. These cash inflows were partially offset by cash used in research and development expenditures and investing activities.

Description of Business

Unless otherwise noted, (1) the term "Arrowhead" refers to Arrowhead Pharmaceuticals, Inc., a Delaware corporation, (2) the terms "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. ("Arrowhead Madison"), Arrowhead Australia Pty Ltd ("Arrowhead Australia") and Ablaris Therapeutics, Inc. ("Ablaris"), (4) the term "Common Stock" refers to Arrowhead's Common Stock, (5) the term "Preferred Stock" refers to Arrowhead's Preferred Stock and (6) the term "Stockholder(s)" refers to the holders of Arrowhead Common Stock.

Overview

Arrowhead Pharmaceuticals, Inc. develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing. The company's pipeline includes ARO-AAT for liver disease associated with alpha-1 antitrypsin deficiency (AATD), ARO-APOC3 for hypertriglyceridemia, ARO-ANG3 for dyslipidemia, ARO-HSD for liver disease, ARO-ENaC for cystic fibrosis, and ARO-HIF2 for renal cell carcinoma. ARO-JNJ1 is being developed for an undisclosed liver-expressed target under a license and collaboration agreement with Janssen Pharmaceuticals, Inc. ARO-HBV (JNJ-3989) for chronic hepatitis B virus was out-licensed to Janssen Pharmaceuticals, Inc. ("Janssen") in October 2018. ARO-LPA (AMG 890) for cardiovascular disease was out-licensed to Amgen Inc. ("Amgen") in 2016.

Arrowhead operates a lab facility in Madison, Wisconsin, where the Company's research and development activities, including the development of RNAi therapeutics, are based. The Company's principal executive offices are located in Pasadena, California.

During fiscal 2019, the Company has continued to develop its pipeline and partnered candidates. In April 2019, the Company presented clinical data for JNJ-3989 (ARO-HBV) and ARO-AAT at the International Liver Congress, and in April 2019, the Company received FDA clearance to commence a Phase 2/3 study of ARO-AAT that has the potential to serve as a pivotal registrational study. In June 2019, the Company received the Fast Track Designation for ARO-AAT from the FDA. In December 2018 and January 2019, Clinical Trial Applications (CTAs) were filed for ARO-ANG3 and ARO-APOC3, respectively, and dosing has commenced for both trials. In June 2019 and July 2019, the Company received the Orphan Drug Designations for ARO-APOC3 and ARO-ANG3, respectively, from the FDA. In September 2019, the Company presented clinical and preclinical data on ARO-APOC3 and ARO-ANG3 at the Global Summit on Cardiology and Heart Diseases. The Company also continues to work on optimizing its other extra-hepatic preclinical pipeline candidates including ARO-ENaC and ARO-HIF2, its hepatic preclinical pipeline candidate, ARO-HSD, and its partnered pipeline candidate, ARO-JNJ1. Amgen is currently progressing its phase 1 clinical study of AMG-890 (ARO-LPA) and Janssen is currently progressing its phase 2b clinical study of JNJ-3989 (ARO-HBV).

The Company also made significant progress on the business development front. In October 2018, the Company entered into a License Agreement ("Janssen License Agreement") and a Research Collaboration and Option Agreement ("Janssen Collaboration Agreement") with Janssen Pharmaceuticals, Inc. ("Janssen") part of the Janssen Pharmaceutical Companies of Johnson & Johnson. The Company also entered into a Stock Purchase Agreement ("JJDC Stock Purchase Agreement") with Johnson & Johnson Innovation-JJDC, Inc. ("JJDC"), a New Jersey corporation. Under the Janssen License Agreement, Janssen has received a worldwide, exclusive license to the Company's JNJ-3989 (ARO-HBV) program, the Company's third-generation subcutaneously administered RNAi therapeutic candidate being developed as a potentially curative therapy for patients with chronic hepatitis B virus infection. Beyond the Company's ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV), Janssen will be wholly responsible for clinical development and commercialization. Under the Janssen Collaboration Agreement, Janssen will be able to select three new targets against which Arrowhead will develop clinical candidates. These candidates are subject to certain restrictions and will not include candidates in the Company's current pipeline. The Company will perform discovery, optimization and preclinical development, entirely funded by Janssen, sufficient to allow the filing of a U.S. Investigational New Drug application or equivalent, at which time Janssen will have the option to take an exclusive license. If the option is exercised, Janssen will be wholly responsible for clinical development and commercialization. Under the JJDC Stock Purchase Agreement, in October 2018 the Company sold 3,260,869 shares of common stock to JJDC at a price of \$23.00 per share. Under the terms of the agreements taken together, the Company has received \$175 million as an upfront payment, \$75 million in the form of an equity investment by JJDC in Arrowhead common stock, and may receive up to \$1.6 billion in development and sales milestones payments for the Janssen License Agreement, and up to \$1.9 billion in development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the Janssen License Agreement and up to low teens under the Janssen Collaboration Agreement on product sales. In April 2019, the Company earned a \$25 million milestone payment from Janssen following the initiation of dosing in a new triple combination cohort (cohort 12) in the Company's ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV). In August 2019, the Company earned an additional \$25 million milestone

payment from Janssen following the initiation of dosing in its phase 2b study of JNJ-3989 (ARO-HBV). The revenue recognition for these milestone payments and the Janssen License Agreement and the Janssen Collaboration Agreement are discussed further below.

The Company's license agreement with Amgen for AMG 890 (ARO-LPA) continues to progress. The Company has received \$35 million in upfront payments and \$21.5 million in the form of an equity investment by Amgen in the Company's Common Stock. Upon signing the collaboration agreements with Amgen, the Company was eligible to receive up to \$617 million in option payments and development, regulatory and sales milestone payments. The Company remains eligible to receive up to \$420 million in development, regulatory and sales milestone payments under the AMG-890 (ARO-LPA) agreement. The Company is further eligible to receive up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement. On August 1, 2018, the Company announced that it had earned a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. This milestone payment was recognized as Revenue in its entirety during the year ended September 30, 2018. In July 2019, Amgen informed the Company that it would not be exercising its option to an exclusive license for ARO-AMG1, and as such, there will be no further milestone or royalty payments under the ARO-AMG1 Agreement.

The Company continues to develop other clinical candidates for future clinical trials. Clinical candidates are tested internally and through GLP toxicology studies at outside laboratories. Drug materials for such studies and clinical trials are either contracted to third-party manufacturers or manufactured internally. The Company engages third-party contract research organizations (CROs) to manage clinical trials and works cooperatively with such organizations on all aspects of clinical trial management, including plan design, patient recruiting, and follow up. These outside costs, relating to the preparation for and administration of clinical trials, are referred to as "program costs". If the clinical candidates progress through human testing, program costs will increase.

Net income was \$68.0 million during the year ended September 30, 2019 as compared to net losses of \$54.5 million and \$34.4 million during the years ended September 30, 2018 and 2017, respectively. Diluted income per share was \$0.69 during the year ended September 30, 2019 as compared to diluted losses per share of \$0.65 and \$0.47 during the years ended September 30, 2018 and 2017, respectively. An increase in revenue in 2019 from the license and collaboration agreements with Janssen is the driver of the increases in net income and diluted income per share, as discussed further below.

The Company strengthened its liquidity and financial position during the year ended September 30, 2019 with \$300 million in upfront, milestone and equity investment payments received from Janssen. These cash proceeds secure the funding needed to continue to advance our preclinical candidates. The Company had \$221.8 million of cash and cash equivalents, \$36.9 million in short-term investments, \$44.2 million in long-term investments and \$349.8 million of total assets as of September 30, 2019, as compared to \$30.1 million, \$46.4 million, \$0 and \$111.6 million as of September 30, 2018, respectively. Based upon the Company's current cash and investment resources and operating plan, the Company expects to have sufficient liquidity to fund operations for at least the next twelve months.

Critical Accounting Policies and Estimates

Management makes certain judgments and uses certain estimates and assumptions when applying GAAP 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 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.

Revenue Recognition

On October 1, 2018, the Company adopted FASB Topic 606 – Revenue for Contracts from Customers which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The Company's adoption of the new revenue standard did not have a material impact on its Consolidated Financial Statements. The Company has not yet achieved commercial sales of its drug candidates to date, however, the new standard is applicable to the Company's ongoing licensing and collaboration agreements, including those with Amgen and Janssen, and the analysis of the impact of this guidance on those agreements is discussed further below.

The new revenue standard provides a five-step framework for recognizing revenue as control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those

goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of the new revenue standard, the Company performs the following five steps: (i) identify the contract; (ii) identify the performance obligations; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. At contract inception, the Company assesses whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation, or whether they are not distinct and are combined with other goods and services until a distinct bundle is identified. The Company then determines the transaction price, which typically includes upfront payments and any variable consideration that the Company determines is probable to not cause a significant reversal in the amount of cumulative revenue recognized when the uncertainty associated with the variable consideration is resolved. The Company then allocates the transaction price to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied.

The Company recognizes the transaction price allocated to upfront license payments as revenue upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license, if the license is determined to be distinct from the other performance obligations identified in the contract. These other performance obligations are typically to perform research and development services for the customer, often times relating to the candidate that the customer is licensing. If the license is not considered to be distinct from other performance obligations, the Company assesses the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied at a point in time or over time. If the performance obligation is satisfied over time, the Company then determines the appropriate method of measuring progress for purposes of recognizing revenue from license payments. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the related revenue recognition.

Typically, the Company's collaboration agreements entitle it to additional payments upon the achievement of milestones or royalties on sales. The milestones are generally categorized into three types: development milestones, generally based on the initiation of toxicity studies or clinical trials; regulatory milestones, generally based on the submission, filing or approval of regulatory applications such as a Clinical Trial Application (CTA) or a New Drug Application (NDA) in the United States; and sales-based milestones, generally based on meeting specific thresholds of sales in certain geographic areas. The Company evaluates whether it is probable that the consideration associated with each milestone or royalty will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are excluded from the transaction price until they meet this threshold. At the end of each subsequent reporting period, the Company re-evaluates the probability of a significant reversal of the cumulative revenue recognized for our milestones and royalties, and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and net income in our Consolidated Statement of Operations and Comprehensive Income (Loss). Typically, milestone payments and royalties are achieved after the Company's performance obligations associated with the collaboration agreements have been completed and after the customer has assumed responsibility for the respective clinical or pre-clinical program. Milestones or royalties achieved after the Company's performance obligations have been completed are recognized as revenue in the period the milestone or royalty was achieved. If a milestone payment is achieved during the performance period, the milestone payment would be recognized as revenue to the extent performance had been completed at that point, and the remaining balance would be recorded as deferred revenue.

The new revenue standard requires the Company to assess whether a significant financing component exists in determining the transaction price. The Company performs this assessment at the onset of its licensing or collaboration agreements. Typically, a significant financing component does not exist because the customer is paying for a license or services in advance with an upfront payment. Additionally, future royalty payments are not substantially within the control of the Company or the customer.

The new revenue standard requires the Company to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the new revenue standard as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which the Company has sold the same performance obligation separately are not available, the Company estimates the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever the Company determines that goods or services promised in a contract should be accounted for as a combined performance obligation over time, the Company determines the period over which the performance obligations will be performed and revenue will be recognized. Revenue is recognized using the proportional performance method. Labor hours are typically used as the measure of performance. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations. If the Company determines that the performance obligation is satisfied over time, any upfront payment received is initially recorded as deferred revenue on the Company's Consolidated Balance Sheets.

Certain judgments affect the application of the Company's revenue recognition policy. For example, the Company records short-term and long-term deferred revenue based on its best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months, and long-term deferred revenue consists of amounts that the Company does not expect will be recognized in the next 12 months. This estimate is based on the Company's current operating plan and, if the Company's operating plan should change in the future, the Company may recognize a different amount of deferred revenue over the next 12-month period.

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 the 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.

Impairment of Intangible assets

Intangible assets consist of a license agreement and patents acquired in conjunction with a business or asset acquisition. Intangible assets are monitored for potential impairment whenever events or circumstances indicate that the carrying amount may not be recoverable and are also reviewed annually to determine whether any impairment is necessary. Based on ASC 350, the annual review of intangible assets is performed via a two-step process. First, a qualitative assessment is performed to determine if it is more likely than not that the intangible asset is impaired. If required, a quantitative assessment is performed and, if necessary, impairment is recorded.

Stock-Based Compensation

We account for stock-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. The Company uses the Black-Scholes option valuation model to estimate the fair value of its 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. For restricted stock units, the value of the award is based on the Company's stock price at the grant date. For performance-based restricted stock unit awards, the value of the award is based on the Company's stock price at the grant date. The Company uses historical data and other information to estimate the expected price volatility for stock option awards and the expected forfeiture rate for all awards. Expense is recognized over the vesting period for all awards and commences at the grant date for time-based awards and upon the Company's determination that the achievement of such performance conditions is probable for performance-based awards. This determination requires significant judgement by management.

Contingent Consideration

The consideration for our acquisitions often includes future payments that are contingent upon the occurrence of a particular event. For example, milestone payments might be based on progress of clinical development, the achievement of various regulatory approvals or future sales milestones, and royalty payments might be based on drug product sales levels. The Company records a contingent consideration obligation for such contingent payments at fair value on the acquisition date. The Company estimates the fair value of contingent consideration obligations through valuation models designed to estimate the probability of the occurrence of such contingent payments based on various assumptions and incorporating estimated success rates. Estimated payments are discounted using present value techniques to arrive at estimated fair value at the balance sheet date. Changes in the fair value of our contingent consideration obligations are recognized within our Consolidated Statements of Operations. Changes in the fair value of the contingent consideration obligations can result from changes to one or multiple inputs, including adjustments to the discount rates, changes in the amount or timing of expected expenditures associated with product development, changes in the amount or timing of cash flows from products upon commercialization, changes in the assumed achievement or timing of any development milestones, changes in the probability of certain clinical events and changes in the assumed probability associated with regulatory approval. These fair value measurements are based on significant inputs not observable in the market. Substantial judgment is employed in determining the appropriateness of these assumptions as of the acquisition date and for each subsequent period. Accordingly, changes in assumptions could have a material impact on the amount of contingent consideration expense the Company records in any given period.

Results of Operations

The following data summarizes our results of operations for the following periods indicated:

Year ended September 30,

	2019	2018	2017
Revenue	\$ 168,795,577	\$ 16,142,321	\$ 31,407,709
Operating Income (Loss)	61,190,634	(55,936,235)	(36,995,909)
Net Income (Loss)	67,974,849	(54,450,478)	(34,380,295)
Net Income (Loss) per Share - Diluted	\$ 0.69	\$ (0.65)	\$ (0.47)

The increase in our Revenue during the year ended September 30, 2019 was driven by recognition of Revenue associated with our license and collaboration agreements with Janssen discussed further below. This increase in Revenue was also the key driver of the increase in our Operating Income, Net Income and Net Income per Share. Research and Development expenses increased during fiscal 2019 due to the progress and expansion of our clinical candidate pipeline as both ARO-ANG3 and ARO-APOC3 entered the clinic, and ARO-AAT progressed to a phase 2 clinical study.

Results of Operations Comparison for 2019 and 2018

Revenues

Total revenue was \$168,795,577 for the year ended September 30, 2019 and \$16,142,321 for the year ended September 30, 2018. Revenue in the current period is primarily related to the recognition of a portion of the \$252.6 million initial transaction price associated with our agreements with Janssen and JJDC as we achieved progress toward completing our performance obligation within those agreements. Revenue in the prior period was primarily related to a \$10 million milestone payment received from Amgen in August 2018, which was earned following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study.

Amgen Inc.

On September 28, 2016, the Company entered into two Collaboration and License agreements, and a Common Stock Purchase Agreement with Amgen Inc., a Delaware corporation (“Amgen”). Under one of the license agreements (the “Second Collaboration and License Agreement” or “AMG 890 (ARO-LPA) Agreement”), Amgen has received a worldwide, exclusive license to Arrowhead’s novel, RNAi ARO-LPA program. These RNAi molecules are designed to reduce elevated lipoprotein(a), which is a genetically validated, independent risk factor for atherosclerotic cardiovascular disease. Under the other license agreement (the “First Collaboration and License Agreement” or “ARO-AMG1 Agreement”), Amgen received an option to a worldwide, exclusive license for ARO-AMG1, an RNAi therapy for an undisclosed genetically validated cardiovascular target. In both agreements, Amgen is wholly responsible for clinical development and commercialization. Under the Common Stock Purchase Agreement, the Company has sold 3,002,793 shares of Common Stock to Amgen at a price of \$7.16 per share. Under the terms of the agreements taken together, the Company has received \$35 million in upfront payments, \$21.5 million in the form of an equity investment by Amgen in the Company’s Common Stock. Upon signing the collaboration agreements with Amgen, the Company was eligible to receive up to \$617 million in option payments, and development, regulatory and sales milestone payments. The Company remains eligible to receive up to \$420 million in development, regulatory and sales milestone payments. The Company is eligible to receive up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement.

The Company has evaluated these agreements in accordance with the new revenue recognition standard that became effective for the Company on October 1, 2018. The adoption of the new revenue standard did not have a material impact on the balances reported when evaluated under the superseded revenue standard. During the year ended September 30, 2018, the Company substantially completed its performance obligations under the AMG 890 (ARO-LPA) Agreement and the ARO-AMG1 Agreement. Future milestones and royalties achieved will be recognized in their entirety when earned. During the years ended September 30, 2019, 2018 and 2017, the Company recognized \$0.3 million, \$16.1 million and \$31.3 million of Revenue associated with its agreements with Amgen, respectively. As of September 30, 2019, there were \$0 contract assets recorded as Accounts Receivable, and \$0 contract liabilities recorded as Deferred Revenue on the Company’s Consolidated Balance Sheets.

Regarding the ARO-AMG1 Agreement, in August 2018, the Company delivered to Amgen a candidate that met or exceeded the activity and safety requirements stipulated in the ARO-AMG1 Agreement. The option period expired on August 7, 2019, and Amgen advised the Company that it did not intend to exercise its option. As such, there will be no further milestone or royalty payments under the ARO-AMG1 Agreement.

Janssen Pharmaceuticals, Inc.

On October 3, 2018, the Company entered into a License Agreement (“Janssen License Agreement”) and a Research Collaboration and Option Agreement (“Janssen Collaboration Agreement”) with Janssen Pharmaceuticals, Inc. (“Janssen”) part of the Janssen Pharmaceutical Companies of Johnson & Johnson. The Company also entered into a Stock Purchase Agreement (“JJDC Stock Purchase Agreement”) with Johnson & Johnson Innovation-JJDC, Inc. (“JJDC”), a New Jersey corporation. Under the Janssen License Agreement, Janssen has received a worldwide, exclusive license to the Company’s ARO-HBV program, the Company’s third-generation subcutaneously administered RNAi therapeutic candidate being developed as a potentially curative therapy for patients with chronic hepatitis B virus infection. Beyond the Company’s ongoing Phase 1 / 2 study of ARO-HBV, Janssen will be wholly

responsible for clinical development and commercialization. Under the Janssen Collaboration Agreement, Janssen will be able to select three new targets against which Arrowhead will develop clinical candidates. These candidates are subject to certain restrictions and will not include candidates in the Company's current pipeline. The Company will perform discovery, optimization and preclinical development, entirely funded by Janssen, sufficient to allow the filing of a U.S. Investigational New Drug application or equivalent, at which time Janssen will have the option to take an exclusive license. If the option is exercised, Janssen will be wholly responsible for clinical development and commercialization. Under the JJDC Stock Purchase Agreement, in October 2018 the Company sold 3,260,869 shares of common stock to JJDC at a price of \$23.00 per share. Under the terms of the agreements taken together, the Company has received \$175 million as an upfront payment, \$75 million in the form of an equity investment by JJDC in Arrowhead common stock, and may receive up to \$1.6 billion in development and sales milestones payments for the Janssen License Agreement, and up to \$1.9 billion in development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the license agreement and up to low teens under the collaboration and option agreement on product sales.

The Company has evaluated these agreements in accordance with the new revenue recognition requirements that became effective for the Company on October 1, 2018. The adoption of the new revenue standard did not have a material impact on the balances reported when evaluated under the superseded revenue standard. At the inception of these agreements, the Company has identified one distinct performance obligation. Regarding the Janssen License Agreement, the Company determined that the key deliverables included the license and certain R&D services including the Company's responsibility to complete the ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV) and the Company's responsibility to ensure certain manufacturing of JNJ-3989 (ARO-HBV) drug product is completed and delivered to Janssen (the "Janssen R&D Services"). Due to the specialized and unique nature of these Janssen R&D services, and their direct relationship with the license, the Company determined that these deliverables represent one distinct bundle and thus, one performance obligation. The Company also determined that Janssen's option to require the Company to develop up to three new targets is not a material right, and thus, not a performance obligation at the onset of the agreement. The consideration for this option will be accounted for when it is exercised.

The Company determined the transaction price totaled approximately \$252.6 million which includes the upfront payment, the premium paid by JJDC for its equity investment in the Company, the two \$25 million milestone payments earned and estimated payments for reimbursable Janssen R&D services to be performed. The Company has allocated the total \$252.6 million initial transaction price to its one distinct performance obligation for the ARO-HBV license and the associated Janssen R&D Services. This revenue will be recognized using a proportional performance method (based on actual labor hours versus estimated total labor hours) beginning in October 2018 and ending as the Company's efforts in overseeing the ongoing phase 1 / 2 clinical trial are completed. During the year ended September 30, 2019, the Company recognized approximately \$167.5 million of Revenue associated with this performance obligation. As of September 30, 2019 there were \$0 contract assets recorded as Accounts Receivable, \$77.8 million of contract liabilities recorded as current Deferred Revenue, and \$5.0 million of contract liabilities recorded as long-term Deferred Revenue on the Company's Consolidated Balance Sheets. The \$77.8 million of current Deferred Revenue and \$5.0 million of long-term Deferred Revenue is driven by the upfront payment and premium paid by JJDC for its equity investment in the Company as well as the two \$25 million milestones paid by Janssen, net of revenue recognized in the period.

During the year ended September 30, 2019, Janssen selected the first of the three targets under the Janssen Collaboration Agreement, now referred to as ARO-JNJ1, and the Company has begun to conduct its discovery, optimization and preclinical development of ARO-JNJ1. All costs and labor hours spent by the Company will be entirely funded by Janssen. During the year ended September 30, 2019, the Company recognized \$1.0 million of Revenue associated with its efforts on the ARO-JNJ1 candidate. As of September 30, 2019 there were \$0.7 million of contract assets recorded as Accounts Receivable, and \$0 of contract liabilities.

Operating Expenses

The analysis below details the operating expenses and discusses the expenditures of the Company within the major expense categories. Certain reclassifications have been made to prior-period operating expense categories to conform to the current period presentation. For purposes of comparison, the amounts for the years ended September 30, 2019 and 2018 are shown in the tables below.

Research and Development Expenses

R&D expenses are related to the Company's research and development efforts, and related program costs which are comprised primarily of outsourced costs related to the manufacturing of clinical supplies, toxicity/efficacy studies and clinical trial expenses. Internal costs primarily relate to operations at our research facility in Madison, Wisconsin, including facility costs and laboratory-related expenses. Salaries and stock compensation expense consist of salary, bonuses, payroll taxes and related benefits and stock compensation for our R&D personnel. Depreciation and amortization expense relates to depreciation on lab equipment and leasehold improvements at our Madison research facility. The following table provides details of research and development expense for the periods indicated:

(in thousands)

	Twelve Months Ended September 30, 2019		Twelve Months Ended September 30, 2018		Increase (Decrease)	
	\$	% of Expense Category	\$	% of Expense Category	\$	%
Salaries	\$ 15,502	19%	\$ 12,721	24%	\$ 2,781	22%
Stock compensation	3,515	4%	2,396	5%	1,119	47%
In Vivo studies	2,526	3%	2,705	5%	(179)	-7%
Drug manufacturing	22,069	27%	14,336	27%	7,733	54%
Toxicity/efficacy studies	11,251	14%	6,294	12%	4,957	79%
Clinical trials	13,742	17%	2,935	6%	10,807	368%
License, royalty & milestones	-	0%	32	0%	(32)	N/A
Facilities related	2,649	3%	2,280	4%	369	16%
Depreciation/amortization	4,420	6%	4,672	9%	(252)	-5%
Other R&D	5,375	7%	4,598	9%	777	17%
Total	\$ 81,049	100%	\$ 52,969	100%	\$ 28,080	53%

Salaries expense increased by \$2,781,000 from \$12,721,000 during the year ended September 30, 2018 to \$15,502,000 during the current period. The increase in the expense is primarily due to an increase in R&D headcount that has occurred as the Company expands its pipeline of candidates.

Stock compensation expense, a non-cash expense, increased by \$1,119,000 from \$2,396,000 during the year ended September 30, 2018 to \$3,515,000 during the current period. Stock compensation expense is based upon the valuation of stock options and restricted stock units granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company's stock price on the date of the grant, as well as other assumptions. The increase in the expense is primarily due to the increased headcount discussed above and a mix of higher grant date fair values of awards amortizing during the periods due to the Company's stock price at the time of the grants.

In vivo studies expense decreased by \$179,000 from \$2,705,000 during the year ended September 30, 2018 to \$2,526,000 during the current period. In vivo studies expense can vary depending on the stage of preclinical candidates, the nature and amount of testing required and the cost variation of different in vivo testing models. The decrease in in vivo studies expense is the result of the timing of discovery studies being completed between periods.

Drug manufacturing expense increased by \$7,733,000 from \$14,336,000 during the year ended September 30, 2018 to \$22,069,000 during the current period. The increase in the expense primarily relates to the timing of manufacturing campaigns for JNJ-3989 (ARO-HBV), ARO-ANG3 and ARO-APOC3 clinical trials and toxicology studies. We anticipate this expense to increase as the volume of candidates in our pipeline increases and as each candidate progresses through clinical trial phases.

Toxicity/efficacy studies expense increased by \$4,957,000 from \$6,294,000 during the year ended September 30, 2018 to \$11,251,000 during the current period. This category includes IND-enabling toxicology studies as well as post-IND toxicology studies, such as long-term toxicology studies, and other efficacy studies. The increase in the expense primarily relates to toxicology studies for ARO-AAT, JNJ-3989 (ARO-HBV), ARO-ANG3 and ARO-APOC3 as each candidate progresses through and into clinical trials. We anticipate this expense to increase as we prepare to enter clinical trials with our other drug candidates.

Clinical trials expense increased by \$10,807,000 from \$2,935,000 during the year ended September 30, 2018 to \$13,742,000 during the current period. The increase in the expense is primarily due to the ongoing ARO-AAT and JNJ-3989 (ARO-HBV) clinical trials, and the start up of the ARO-ANG3 and ARO-APOC3 clinical trials. We anticipate this expense to increase as our current clinical candidates progress through clinical trials and as we enter clinical trials with our other drug candidates.

License, royalty and milestones expense was relatively minor in both periods. This category includes milestone payments which can vary from period to period depending on the nature of our various license agreements, and the timing of reaching various development milestones requiring payment. No significant milestones were achieved in either period.

Facilities expense increased by \$369,000 from \$2,280,000 during the year ended September 30, 2018 to \$2,649,000 during the current period. This category includes rental costs for our research and development facility in Madison, Wisconsin. The increase in the expense is primarily due to increased rental and common area maintenance expenses for our research and development facility.

Depreciation and amortization expense, decreased by \$252,000 from \$4,672,000 during the year ended September 30, 2018 to \$4,420,000 during the current period. The majority of depreciation and amortization expense relates to depreciation on lab equipment at our Madison research facility. In addition, the Company records depreciation on leasehold improvements at its Madison research facility, and the decrease in depreciation and amortization expense relates to the timing of amortization of these leasehold improvements in each period as the length of our lease has been extended.

Other research expense increased by \$777,000 from \$4,598,000 during the year ended September 30, 2018 to \$5,375,000 during the current period. This category includes the following costs to support discovery efforts and the advancement of current drug candidates: in-house laboratory supplies, outsourced labs services, and other miscellaneous research and development expenses. The increase in other research expense is due to additional in-house laboratory supplies for our increased headcount.

General & Administrative Expenses

The following table provides details of our general and administrative expenses for the periods indicated:

(in thousands)

	Twelve Months Ended September 30, 2019	% of Expense Category	Twelve Months Ended September 30, 2018	% of Expense Category	Increase (Decrease)	
					\$	%
Salaries	\$ 8,288	31%	\$ 6,382	33%	\$ 1,906	30%
Stock compensation	8,878	33%	6,059	32%	2,819	47%
Professional/outside services	5,605	21%	4,331	23%	1,274	29%
Facilities related	1,434	5%	727	4%	707	97%
Depreciation/amortization	19	0%	27	0%	(8)	-30%
Other G&A	2,332	9%	1,584	8%	748	47%
Total	\$ 26,556	100%	\$ 19,110	100%	\$ 7,446	39%

Salaries expense increased by \$1,906,000 from \$6,382,000 during the year ended September 30, 2018 to \$8,288,000 during the current period. The increase in the expense is primarily driven by annual merit increases, performance bonuses and increased headcount.

Stock compensation expense increased by \$2,819,000 from \$6,059,000 during the year ended September 30, 2018 to \$8,878,000 during the current period. Stock compensation expense is based upon the valuation of stock options and restricted stock units granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company's stock price on the date of the grant, as well as other assumptions. The increase in the expense is primarily due to the timing of the achievement of certain performance-based awards in each period.

Professional/outside services include legal, accounting, consulting, patent expenses, business insurance expenses and other outside services retained by the Company. Professional/outside services expense increased by \$1,274,000 from \$4,331,000 during the year ended September 30, 2018 to \$5,605,000 during the current period. The increase in the expense is primarily related to recruiting fees for increased headcount.

Facilities-related expense increased \$707,000 from \$727,000 during the year ended September 30, 2018 to \$1,434,000 during the current period. This category primarily includes rental costs for our corporate headquarters in Pasadena, California. The increase in the expense is primarily due to furniture and office supply purchases as the Company moved to a new corporate headquarters in September and October 2019.

Depreciation and amortization expense, a noncash expense, was relatively minor in each of the periods. The majority of general and administrative depreciation and amortization expense relates to depreciation on leasehold improvements at our Pasadena headquarters. This expense will increase as we anticipate spending approximately \$3.5 million, net of tenant improvement allowances, on leasehold improvements for our new corporate headquarters in Pasadena, California.

Other G&A expense increased by \$748,000 from \$1,584,000 during the year ended September 30, 2018 to \$2,332,000 during the current period. This category consists primarily of travel, communication and technology, office expenses, and franchise and property tax expenses. The increase in the expense was due to various travel and communication and technology expenses as our headcount has increased.

Other Income / Expense

Other income / expense was income of \$1,488,157 during the year ended September 30, 2018 as compared to income of \$6,957,768 during the current period. The largest component of other income / expense in both period was interest income of \$7.0 million and \$1.0 million for the years ended September 30, 2019 and 2018, respectively. This interest income was earned on the Company's portfolio of short-term and long-term investments, money market accounts and cash and cash equivalents which increased significantly due to the cash received from Janssen during the year ended September 30, 2019.

Provision for Income Taxes

The Provision for Income Taxes increased by \$171,153 from \$2,400 during the year ended September 30, 2018 to \$173,553 during the current period. The increase in the expense is due to alternative minimum state taxes due in the current year based on our net income earned.

Results of Operations Comparison for 2018 and 2017

For a discussion of our results of operations comparison for 2018 and 2017, refer to our Annual Report on Form 10-K for the fiscal year ended September 30, 2018 filed on December 11, 2018.

Liquidity and Cash Resources

Arrowhead has historically financed its operations through the sale of its equity securities. Research and development activities have required significant capital investment since the Company's inception and are expected to continue to require significant cash expenditure in the future.

At September 30, 2019, the Company had cash and cash equivalents on hand of approximately \$221.8 million as compared to \$30.1 million at September 30, 2018. Excess cash invested in short-term and long-term fixed income securities was \$81.1 million at September 30, 2019, compared to \$46.4 million at September 30, 2018. The Company believes its current financial resources are sufficient to fund its operations through at least the next twelve months.

A summary of cash flows for the years ended September 30, 2019, 2018, and 2017 is as follows:

	2019	Year ended September 30, 2018	2017
Cash Flow from:			
Operating Activities	\$ 173,034,923	\$ (47,223,417)	\$ (23,938,972)
Investing Activities	(47,746,007)	(7,434,963)	(48,644,218)
Financing Activities	66,381,999	59,953,026	12,055,309
Net increase (decrease) in cash and cash equivalents	191,670,915	5,294,646	(60,527,881)
Cash and cash equivalents at beginning of period	30,133,213	24,838,567	85,366,448
Cash and cash equivalents at end of period	<u>\$ 221,804,128</u>	<u>\$ 30,133,213</u>	<u>\$ 24,838,567</u>

During the year ended September 30, 2019, the Company generated \$173.0 million in cash from operating activities, which was primarily related to the \$175.0 million upfront payment and the two \$25.0 million milestone payments received from Janssen, and the premium JJDC paid on the Company's common stock during the period. These inflows were partially offset by approximately \$66.5 million of cash used for the ongoing expenses of the Company's research and development programs and general and administrative expenses. Cash used in investing activities was \$47.7 million, which was primarily related to purchases of fixed-income investments of \$90.3 million partially offset by maturities of fixed-income investments of \$54.5 million. Cash provided by financing activities of \$66.4 million was driven by the equity investment the Company received from JJDC during the period.

During the year ended September 30, 2018, the Company used \$47.2 million in cash from operating activities, which was primarily related to \$57.2 million used for the on-going expenses of its research and development programs and general and administrative expenses, offset by the \$10 million milestone payment for the AMG 890 (ARO-LPA) Agreement with Amgen. Cash used in investing activities was \$7.4 million, which was primarily related to maturities of fixed-income investments of \$46.1 million offset by purchases of fixed-income securities of \$52.1 million. Cash provided by financing activities of \$60.0 million was driven by the \$56.6 million of cash generated from the underwritten public offering in January 2018.

During the year ended September 30, 2017, the Company used \$23.9 million in cash from operating activities, primarily driven by \$53.9 million of cash used for the on-going expenses of its research and development programs and general and administrative expenses, partially offset by the \$30 million upfront payment received from Amgen. Cash used in investing activities was \$48.6 million, which was primarily related to investments in short-term fixed-income securities of \$45.0 million and \$7.9 million of capital expenditures primarily for leasehold improvements on the Company's Madison, Wisconsin research facility and lab equipment purchases. Cash generated by financing activities of \$12.1 million was driven by the \$12.5 million equity investment received from Amgen and was partially offset by cash paid for employee taxes on net share settlements of restricted stock units that vested during the period.

Contractual Obligations

In the table below, we set forth our enforceable and legally binding obligations and future commitments at September 30, 2019 for the categories shown, as well as obligations related to contracts in such categories that we are likely to continue. Some of the figures that we include in this table are based on management's estimates and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties and other factors. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table. The following table does not include any future obligations that may be owed under existing license agreements, as the certainty of achieving the relevant milestones that would trigger these payments is currently unknown.

	Total	Payments due by Period			
		Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Long-Term Debt	-	-	-	-	-
Capital Leases	-	-	-	-	-
Operating Leases	22,385,552	1,521,451	4,777,825	5,252,070	10,834,206
Purchase Obligations	60,200,000	50,900,000	9,300,000	-	-
Other Long-Term Liabilities	8,738,506	415,608	5,866,358	831,216	1,625,324
Total	\$ 91,324,058	\$ 52,837,059	\$ 19,944,183	\$ 6,083,286	\$ 12,459,530

Off-Balance Sheet Arrangements

As of September 30, 2019, we did not have any off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of SEC Regulation S-K.

Recent Accounting Pronouncements

See Note 1 to our Consolidated Financial Statements of this annual report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risk related to changes in interest rates, which could adversely affect the value of our interest rate-sensitive assets and liabilities. We do not hold any instruments for trading purposes and investment criteria are governed by the Company's Investment Policy. As of September 30, 2019 and 2018, we had cash and cash equivalents of \$221.8 million and \$30.1 million, respectively, and short-term and long-term investments of \$81.1 million and \$46.4 million, respectively. At times, we have invested our cash reserves in corporate bonds typically with maturities of less than 2 years, and we have historically classified these investments as held-to-maturity. Due to the relatively short-term nature of the investments that we hold, we do not believe that the results of operations or cash flows would be affected to any significant degree by a sudden change in market interest rates relative to our investment portfolio.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this item is included in Item 15 of this Annual Report on 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.

No change in the Company's internal controls over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) of the Exchange Act) occurred during the Company's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Management conducted an assessment of the effectiveness of the Company's internal control over financial reporting based on the criteria set forth in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on the Company's assessment, management

has concluded that its internal control over financial reporting was effective as of September 30, 2019 to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with GAAP. The Company's independent registered public accounting firm, Rose, Snyder and Jacobs LLP, has issued an audit report on the Company's internal control over financial reporting, which appears in Item 15 of this Form 10-K.

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, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2020 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2020.

We have adopted a Code of Ethics, as part of our Code of Corporate Conduct, that applies to all of our directors, officers and employees, including our principal executive, principal financial and principal accounting officers, or persons performing similar functions. Our Code of Ethics is posted on our website located at <https://arrowheadpharma.com/code-corporate-conduct/>. We intend to disclose future amendments to certain provisions of the Code of Ethics, and waivers of the Code of Ethics granted to executive officers and directors, on the website within four business days following the date of the amendment or waiver.

ITEM 11. EXECUTIVE COMPENSATION

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2020 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2020.

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

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2020 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2020.

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

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2020 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2020.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2020 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2020.

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.

(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†	Annual Report on Form 10-K for the fiscal year ended September 30, 2011, as Exhibit 2.1	December 20, 2011
2.2	Asset Purchase and Exclusive License Agreement between Arrowhead Research Corporation and Novartis Institutes for BioMedical Research, Inc., dated March 3, 2015†	Quarterly Report on Form 10-Q, as Exhibit 2.1	May 11, 2015
3.1	Amended and Restated Certificate of Incorporation of Arrowhead Research Corporation, a Delaware corporation, filed with the Secretary of State of the State of Delaware on April 5, 2016	Current Report on Form 8-K as Exhibit 3.3	April 6, 2016
3.2	Amended and Restated Bylaws of Arrowhead Pharmaceuticals, Inc.	Current Report on form 8-K as Exhibit 3.4	April 6, 2016
4.1	Form of Common Stock Certificate of Arrowhead Pharmaceuticals, Inc.	Current Report on Form 8-K, as Exhibit 4.1	April 6, 2016
4.2	Form of Indenture	Registration Statement on Form S-3 (File No. 333-214315) as Exhibit 4.2	October 28, 2016
4.3	Rights Agreement dated as of March 21, 2017, between the Company and Computershare Trust Company, N.A., as rights agent, which includes as Exhibit B the Form of Rights Certificate	Current Report on Form 8-K, as Exhibit 4.1	March 23, 2017
4.4	Description of Registrant's Securities*		
10.1**	Arrowhead Research Corporation 2004 Equity Incentive Plan, as amended	Schedule 14C, as Annex B	January 12, 2012
10.2**	Arrowhead Research Corporation 2013 Incentive Plan	Schedule 14C, as Annex A	December 20, 2013
10.3**	Form of Stock Option Agreement for use with the 2013 Incentive Plan	Current Report on Form 8-K, as Exhibit 10.1	February 12, 2014
10.4**	Form of Restricted Stock Unit Agreement for use with the 2013 Incentive Plan	Current Report on Form 8-K, as Exhibit 10.2	February 12, 2014
10.5**	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
10.6**	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

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
10.7**	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
10.8	Non-Exclusive License Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011†	Annual Report on Form 10-K for the fiscal year ended September 30, 2011, as Exhibit 10.33	December 20, 2011
10.9	Collaboration Agreement by and among Alnylam Pharmaceuticals, Inc. and F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc., dated October 29, 2009 †	Annual Report on Form 10-K for the fiscal year ended September 30, 2011, as Exhibit 10.36	December 20, 2011
10.10	License Agreement by and between Alnylam Pharmaceuticals, Inc., Arrowhead Research Corporation and Arrowhead Madison, Inc.†	Quarterly Report on Form 10-Q, as Exhibit 10.1	August 12, 2014
10.11	Lease Agreement between University Research Park, Incorporated and Arrowhead Madison, Inc., dated January 8, 2016	Quarterly Report on Form 10-Q, as Exhibit 10.1	February 9, 2016
10.12	First Collaboration and Licensing Agreement between Arrowhead Pharmaceuticals, Inc. and Amgen Inc., dated September 28, 2016†	Annual Report on Form 10-K for the fiscal year ended September 30, 2016, as Exhibit 10.18	December 14, 2016
10.13	Second Collaboration and Licensing Agreement between Arrowhead Pharmaceuticals, Inc. and Amgen Inc., dated September 28, 2016†	Annual Report on Form 10-K for the fiscal year ended September 30, 2016, as Exhibit 10.19	December 14, 2016
10.14	Common Stock Purchase Agreement between the Company and Amgen Inc., dated September 28, 2016	Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-214311)	November 25, 2016
10.15	License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated October 3, 2018†	Quarterly Report on Form 10-Q, as Exhibit 10.1	February 7, 2019
10.16	Research Collaboration and Option Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated October 3, 2018†	Quarterly Report on Form 10-Q, as Exhibit 10.2	February 7, 2019
10.17	Stock Purchase Agreement by and between Johnson & Johnson Innovation-JJDC, Inc. and Arrowhead Pharmaceuticals, Inc., dated October 3, 2018	Quarterly Report on Form 10-Q, as Exhibit 10.3	February 7, 2019
10.18	Registration Rights Agreement by and between Arrowhead Pharmaceuticals, Inc. and Johnson & Johnson Innovation-JJDC, Inc., dated October 3, 2018	Quarterly Report on Form 10-Q, as Exhibit 10.4	February 7, 2019
10.19	Amendment No. 1 to License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated December 18, 2018*†		
10.20	Amendment No. 2 to License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated February 4, 2019*†		
10.21	Amendment No. 1 to Research Collaboration and Option Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated November 14, 2019*†		

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
10.22	Office Lease by and between 177 Colorado Owner LLC and Arrowhead Pharmaceuticals, Inc., dated April 17, 2019	Quarterly Report on Form 10-Q, as Exhibit 10.1	August 5, 2019
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*		
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*		

* Filed herewith

** Indicates compensation plan, contract or arrangement.

*** Furnished herewith

† Certain confidential portions of this exhibit were omitted by means of marking such portions with asterisks because the identified confidential portions (i) are not material and (ii) would be competitively harmful if publicly disclosed.

SIGNATURE

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, on this 25th day of November 2019.

Dated: November 25, 2019

ARROWHEAD PHARMACEUTICALS, INC.

By: /s/ Christopher Anzalone
Christopher Anzalone
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report on Form 10-K has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

Signature	Title	Date
<u>/s/ Christopher Anzalone</u> Christopher Anzalone	Chief Executive Officer, President and Director (Principal Executive Officer)	November 25, 2019

Signature	Title	Date
<u>/s/ Kenneth A. Myszkowski</u> Kenneth A. Myszkowski	Chief Financial Officer (Principal Financial and Accounting Officer)	November 25, 2019
<u>/s/ Douglass Given</u> Douglass Given	Director, Chairman of the Board of Directors	November 25, 2019
<u>/s/ Mauro Ferrari</u> Mauro Ferrari	Director	November 25, 2019
<u>/s/ Michael S. Perry</u> Michael S. Perry	Director	November 25, 2019
<u>/s/ William Waddill</u> William Waddill	Director	November 25, 2019

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To the Board of Directors and
Stockholders of Arrowhead Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Arrowhead Pharmaceuticals, Inc. and subsidiaries (the Company) as of September 30, 2019 and 2018, and the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the years in the three-year period ended September 30, 2019, and the related notes (collectively referred to as the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of September 30, 2019 and 2018, and the results of its operations and its cash flows for each of the years in the three-year period ended September 30, 2019, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of September 30, 2019, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated November 25, 2019, expressed an unqualified opinion.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Revenue Recognition – Contract cost estimates

Description of the Matter

As discussed in Note 1 to the Consolidated Financial Statements, the Company adopted Accounting Standards Codification 606 ("ASC 606"): Revenue from Contracts with Customers as of October 1, 2018. As discussed in Note 1 and Note 2 to the Consolidated Financial Statements, the Company earns its revenue through license and collaboration agreements. For performance obligations related to services that are required to be recognized over time, the Company generally measures its progress to completion using an input measure of total labor costs incurred divided by total labor costs expected to be incurred.

Auditing revenue recognition is complex and highly judgmental due to the variability and uncertainty associated with the Company's assessment of measure of progress. Changes in these estimates would have a significant effect on the amount of revenue recognized.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls that address the risk of material misstatement of license and collaboration agreement revenue including those associated with cost to complete estimates. We tested controls over management's process to collect, review, and approve the data used in assessing revenue recognized over time.

To test the measures of progress used for performance obligations related to services that are required to be recognized over time, our audit procedures included, among others, evaluating the appropriateness of the Company's accounting policy for each type of arrangement, testing the identified measure of performance by reading contracts with customers, including all amendments, and reviewing the contract analyses prepared by management. We evaluated whether the selected measures of progress towards satisfaction of performance obligations were applied consistently. We also tested the completeness and accuracy of the underlying data used for the measure of progress by testing the underlying cost data and conducting interviews of project personnel.

Rose, Snyder & Jacobs LLP

We have served as the Company's auditor since 2004.

Encino, California

November 25, 2019

To the Board of Directors and
Stockholders of Arrowhead Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Arrowhead Pharmaceuticals, Inc. and subsidiaries (the Company's) internal control over financial reporting as of September 30, 2019, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of September 30, 2019, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets as of September 30, 2019 and the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows for each of the three years in the period ended September 30, 2019 and related notes, and our report dated November 25, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process 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. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) 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 of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

Rose, Snyder & Jacobs LLP
Encino, CA
November 25, 2019

ITEM 1. FINANCIAL STATEMENTS

Arrowhead Pharmaceuticals, Inc.
Consolidated Balance Sheets

	September 30, 2019	September 30, 2018
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	\$ 221,804,128	\$ 30,133,213
Accounts receivable	661,361	327,375
Prepaid expenses	3,317,999	1,267,717
Other current assets	2,563,435	640,117
Short-term investments	36,899,894	46,400,176
TOTAL CURRENT ASSETS	265,246,817	78,768,598
Property and equipment, net	23,214,899	13,935,425
Intangible assets, net	17,063,580	18,764,010
Long-term investments	44,175,993	-
Other assets	144,148	141,918
TOTAL ASSETS	\$ 349,845,437	\$ 111,609,951
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	\$ 7,649,921	\$ 2,806,098
Accrued expenses	6,504,729	5,043,087
Accrued payroll and benefits	4,955,887	3,937,605
Deferred rent	173,952	307,334
Deferred revenue	77,769,629	600
Note payable	-	223,820
Other current liabilities	16,561	46,407
TOTAL CURRENT LIABILITIES	97,070,679	12,364,951
LONG-TERM LIABILITIES		
Deferred rent, net of current portion	3,703,364	1,702,801
Deferred revenue, net of current portion	5,035,142	-
Note payable, net of current portion	-	2,101,198
Other non-current liabilities	-	200,000
TOTAL LONG-TERM LIABILITIES	8,738,506	4,003,999
Commitments and contingencies (Note 7)		
STOCKHOLDERS' EQUITY		
Arrowhead Pharmaceuticals, Inc. stockholders' equity:		
Common stock, \$0.001 par value; 145,000,000 shares authorized; 95,506,271 and 88,505,302 shares issued and outstanding as of September 30, 2019 and September 30, 2018, respectively	187,876	180,875
Additional paid-in capital	664,086,155	582,902,694
Accumulated other comprehensive income (loss)	(391,624)	(21,564)
Accumulated deficit	(419,290,967)	(487,265,816)
Total Arrowhead Pharmaceuticals, Inc. stockholders' equity	244,591,440	95,796,189
Noncontrolling interest	(555,188)	(555,188)
TOTAL STOCKHOLDERS' EQUITY	244,036,252	95,241,001
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	\$ 349,845,437	\$ 111,609,951

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

Arrowhead Pharmaceuticals, Inc.
Consolidated Statements of Operations and Comprehensive Income (Loss)

	Year Ended September 30		
	2019	2018	2017
REVENUE	\$ 168,795,577	\$ 16,142,321	\$ 31,407,709
OPERATING EXPENSES			
Research and development	81,048,686	52,968,505	50,904,466
General and administrative expenses	26,556,257	19,110,051	17,499,152
TOTAL OPERATING EXPENSES	107,604,943	72,078,556	68,403,618
OPERATING INCOME (LOSS)	61,190,634	(55,936,235)	(36,995,909)
OTHER INCOME (EXPENSE)			
Interest income (expense), net	6,957,768	1,048,523	415,128
Change in value of derivatives	-	432,141	890,362
Other income (expense)	-	7,493	1,312,524
TOTAL OTHER INCOME (EXPENSE)	6,957,768	1,488,157	2,618,014
INCOME (LOSS) BEFORE INCOME TAXES	68,148,402	(54,448,078)	(34,377,895)
Provision for income taxes	(173,553)	(2,400)	(2,400)
NET INCOME (LOSS)	67,974,849	(54,450,478)	(34,380,295)
NET INCOME (LOSS) PER SHARE - BASIC	\$ 0.72	\$ (0.65)	\$ (0.47)
NET INCOME (LOSS) PER SHARE - DILUTED	\$ 0.69	\$ (0.65)	\$ (0.47)
Weighted average shares outstanding - basic	93,858,857	83,638,469	73,898,598
Weighted average shares outstanding - diluted	98,607,815	83,638,469	73,898,598
OTHER COMPREHENSIVE INCOME (LOSS), NET OF TAX:			
Foreign Currency Translation Adjustments	(370,060)	(54,796)	25,783
COMPREHENSIVE INCOME (LOSS)	\$ 67,604,789	\$ (54,505,274)	\$ (34,354,512)

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

Arrowhead Pharmaceuticals, Inc.
Consolidated Statement of Stockholders' Equity

	Preferred Stock	Amount (\$)	Common Stock	Amount (\$)	Additional Paid-In Capital	Accumulated Other Comprehensive Income (loss)	Accumulated Deficit	Non-controlling Interest	Totals
Balance at September 30, 2016	15,652	\$ 16	69,746,685	\$ 162,116	\$ 493,844,909	\$ 7,449	\$ (398,435,043)	\$ (555,188)	\$ 95,024,259
Stock-based compensation	-	-	-	-	7,891,595	-	-	-	7,891,595
Exercise of stock options	-	-	135,730	136	271,795	-	-	-	271,931
Common stock- Restricted Stock Units vesting	-	-	481,212	481	(403,742)	-	-	-	(403,261)
Common stock issued to Amgen at \$7.16 per share	-	-	1,745,810	1,746	12,418,254	-	-	-	12,420,000
Preferred stock converted to common stock	(15,652)	(16)	2,670,989	2,671	(2,655)	-	-	-	-
Exchange rights exercised	-	-	5,000	5	17,145	-	-	-	17,150
Foreign currency translation adjustments	-	-	-	-	-	25,783	-	-	25,783
Net loss for the year ended September 30, 2017	-	-	-	-	-	-	(34,380,295)	-	(34,380,295)
Balance at September 30, 2017	-	\$ -	74,785,426	\$ 167,155	\$ 514,037,301	\$ 33,232	\$ (432,815,338)	\$ (555,188)	\$ 80,867,162
Stock-based compensation	-	-	-	-	8,454,607	-	-	-	8,454,607
Exercise of stock options	-	-	604,611	605	2,656,105	-	-	-	2,656,710
Exercise of warrants	-	-	288,473	288	1,237,141	-	-	-	1,237,429
Common stock- Restricted Stock Units vesting	-	-	1,326,792	1,327	(55,995)	-	-	-	(54,668)
Common stock issued at \$5.25 per share	-	-	11,500,000	11,500	56,573,535	-	-	-	56,585,035
Foreign currency translation adjustments	-	-	-	-	-	(54,796)	-	-	(54,796)
Net loss for the year ended September 30, 2018	-	-	-	-	-	-	(54,450,478)	-	(54,450,478)
Balance at September 30, 2018	-	\$ -	88,505,302	\$ 180,875	\$ 582,902,694	\$ (21,564)	\$ (487,265,816)	\$ (555,188)	\$ 95,241,001
Stock-based compensation	-	-	-	-	12,393,323	-	-	-	12,393,323
Exercise of stock options	-	-	1,542,795	1,543	8,273,867	-	-	-	8,275,410
Common stock- Restricted Stock Units vesting	-	-	2,197,305	2,197	(2,197)	-	-	-	-
Common stock issued at \$23.00 per share	-	-	3,260,869	3,261	60,518,468	-	-	-	60,521,729
Foreign currency translation adjustments	-	-	-	-	-	(370,060)	-	-	(370,060)
Net income for the year ended September 30, 2019	-	-	-	-	-	-	67,974,849	-	67,974,849
Balance at September 30, 2019	-	\$ -	95,506,271	\$ 187,876	\$ 664,086,155	\$ (391,624)	\$ (419,290,967)	\$ (555,188)	\$ 244,036,252

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

Arrowhead Pharmaceuticals, Inc.
Consolidated Statements of Cash Flows

	Year ended September 30,		
	2019	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net income (loss)	\$ 67,974,849	\$ (54,450,478)	\$ (34,380,295)
Change in value of derivatives	-	(432,141)	(890,362)
Stock-based compensation	12,393,323	8,454,607	7,891,595
Depreciation and amortization	4,439,144	4,699,275	4,690,440
Amortization/(accretion) of note premiums	1,069,070	383,075	(43,519)
Changes in operating assets and liabilities:			
Accounts receivable	(333,986)	(259,578)	7,203
Prepaid expenses and other current assets	(3,710,515)	319,166	2,814,509
Deferred revenue	82,804,171	(5,269,140)	157,981
Accounts payable	4,843,825	(1,270,416)	(3,509,995)
Accrued expenses	2,450,079	1,016,506	(401,777)
Other	1,104,963	(414,293)	(274,752)
NET CASH PROVIDED BY (USED IN) OPERATING ACTIVITIES	173,034,923	(47,223,417)	(23,938,972)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(12,001,225)	(1,421,252)	(7,918,198)
Purchases of marketable securities	(90,266,001)	(52,083,131)	(44,974,736)
Proceeds from sale of marketable securities	54,521,219	46,069,420	4,248,716
NET CASH PROVIDED BY (USED IN) INVESTING ACTIVITIES	(47,746,007)	(7,434,963)	(48,644,218)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Principal payments on notes payable	(2,415,150)	(208,506)	(197,790)
Payments of taxes for net share settled restricted stock unit issuances	-	(54,667)	(438,838)
Proceeds from the exercises of warrants and stock options	8,275,410	3,631,164	272,818
Proceeds from the issuance of common stock	60,521,739	56,585,035	12,419,119
NET CASH PROVIDED BY (USED IN) FINANCING ACTIVITIES	66,381,999	59,953,026	12,055,309
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	191,670,915	5,294,646	(60,527,881)
CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD	30,133,213	24,838,567	85,366,448
CASH AND CASH EQUIVALENTS AT END OF PERIOD	\$ 221,804,128	\$ 30,133,213	\$ 24,838,567
Supplementary disclosures:			
Interest Paid	\$ (27,437)	\$ (173,381)	\$ (187,647)
Income Tax Credits Refunded	\$ -	\$ -	\$ 3,635,016
Income Tax Paid	\$ (302,400)	\$ (2,400)	\$ (2,400)

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

Arrowhead Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements

Unless otherwise noted, (1) the term “Arrowhead” refers to Arrowhead Pharmaceuticals, Inc., a Delaware corporation and its Subsidiaries, (2) the terms “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. (“Arrowhead Madison”), Arrowhead Australia Pty Ltd (“Arrowhead Australia”) and Ablaris Therapeutics, Inc. (“Ablaris”), (4) the term “Common Stock” refers to Arrowhead’s Common Stock, (5) the term “Preferred Stock” refers to Arrowhead’s Preferred Stock and (6) the term “Stockholder(s)” refers to the holders of Arrowhead Common Stock.

NOTE 1. ORGANIZATION AND SIGNIFICANT ACCOUNTING POLICIES

Nature of Business and Recent Developments

Arrowhead Pharmaceuticals, Inc. develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead’s RNAi-based therapeutics leverage this natural pathway of gene silencing. The company’s pipeline includes ARO-AAT for liver disease associated with alpha-1 antitrypsin deficiency (AATD), ARO-APOC3 for hypertriglyceridemia, ARO-ANG3 for dyslipidemia, ARO-HSD for liver disease, ARO-ENaC for cystic fibrosis, and ARO-HIF2 for renal cell carcinoma. ARO-JNJ1 is being developed for an undisclosed liver-expressed target under a license and collaboration agreement with Janssen Pharmaceuticals, Inc. ARO-HBV (JNJ-3989) for chronic hepatitis B virus was out-licensed to Janssen Pharmaceuticals, Inc. (“Janssen”) in October 2018. ARO-LPA (AMG 890) for cardiovascular disease was out-licensed to Amgen Inc. (“Amgen”) in 2016.

Arrowhead operates a lab facility in Madison, Wisconsin, where the Company’s research and development activities, including the development of RNAi therapeutics, are based. The Company’s principal executive offices are located in Pasadena, California.

During fiscal 2019, the Company has continued to develop its pipeline and partnered candidates. In April 2019, the Company presented clinical data for JNJ-3989 (ARO-HBV) and ARO-AAT at the International Liver Congress, and in April 2019, the Company received FDA clearance to commence a Phase 2/3 study of ARO-AAT that has the potential to serve as a pivotal registrational study. In June 2019, the Company received the Fast Track Designation for ARO-AAT from the FDA. In December 2018 and January 2019, Clinical Trial Applications (CTAs) were filed for ARO-ANG3 and ARO-APOC3, respectively, and dosing has commenced for both trials. In June 2019 and July 2019, the Company received the Orphan Drug Designations for ARO-APOC3 and ARO-ANG3, respectively, from the FDA. In September 2019, the Company presented clinical and preclinical data on ARO-APOC3 and ARO-ANG3 at the Global Summit on Cardiology and Heart Diseases. The Company also continues to work on optimizing its other extra-hepatic preclinical pipeline candidates including ARO-ENaC and ARO-HIF2, its hepatic preclinical pipeline candidate, ARO-HSD, and its partnered pipeline candidate, ARO-JNJ1. Amgen is currently progressing its phase 1 clinical study of AMG-890 (ARO-LPA) and Janssen is currently progressing its phase 2b clinical study of JNJ-3989 (ARO-HBV).

The Company also made significant progress on the business development front. In October 2018, the Company entered into a License Agreement (“Janssen License Agreement”) and a Research Collaboration and Option Agreement (“Janssen Collaboration Agreement”) with Janssen Pharmaceuticals, Inc. (“Janssen”) part of the Janssen Pharmaceutical Companies of Johnson & Johnson. The Company also entered into a Stock Purchase Agreement (“JJDC Stock Purchase Agreement”) with Johnson & Johnson Innovation-JJDC, Inc. (“JJDC”), a New Jersey corporation. Under the Janssen License Agreement, Janssen has received a worldwide, exclusive license to the Company’s JNJ-3989 (ARO-HBV) program, the Company’s third-generation subcutaneously administered RNAi therapeutic candidate being developed as a potentially curative therapy for patients with chronic hepatitis B virus infection. Beyond the Company’s ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV), Janssen will be wholly responsible for clinical development and commercialization. Under the Janssen Collaboration Agreement, Janssen will be able to select three new targets against which Arrowhead will develop clinical candidates. These candidates are subject to certain restrictions and will not include candidates in the Company’s current pipeline. The Company will perform discovery, optimization and preclinical development, entirely funded by Janssen, sufficient to allow the filing of a U.S. Investigational New Drug application or equivalent, at which time Janssen will have the option to take an exclusive license. If the option is exercised, Janssen will be wholly responsible for clinical development and commercialization. Under the JJDC Stock Purchase Agreement, in October 2018 the Company sold 3,260,869 shares of common stock to JJDC at a price of \$23.00 per share. Under the terms of the agreements taken together, the Company has received \$175 million as an upfront payment, \$75 million in the form of an equity investment by JJDC in Arrowhead common stock, and may receive up to \$1.6 billion in development and sales milestones payments for the Janssen License Agreement, and up to \$1.9 billion in development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the Janssen License Agreement and up to low teens under the Janssen Collaboration Agreement on product sales. In April 2019, the Company earned a \$25 million milestone payment from Janssen following the initiation of dosing in a new triple combination cohort (cohort 12) in the Company’s

ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV). In August 2019, the Company earned an additional \$25 million milestone payment from Janssen following the initiation of dosing in its phase 2b study of JNJ-3989 (ARO-HBV). The revenue recognition for these milestone payments and the Janssen License Agreement and the Janssen Collaboration Agreement are discussed further in Note 2 below.

The Company's license agreement with Amgen for AMG 890 (ARO-LPA) continues to progress. The Company has received \$35 million in upfront payments and \$21.5 million in the form of an equity investment by Amgen in the Company's Common Stock. Upon signing the collaboration agreements with Amgen, the Company was eligible to receive up to \$617 million in option payments and development, regulatory and sales milestone payments. The Company remains eligible to receive up to \$420 million in development, regulatory and sales milestone payments. The Company is further eligible to receive up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement. On August 1, 2018, the Company announced that it had earned a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. This milestone payment was recognized as Revenue in its entirety during the year ended September 30, 2018. In July 2019, Amgen informed the Company that it would not be exercising its option to an exclusive license for ARO-AMG1, and as such, there will be no further milestone or royalty payments under the ARO-AMG1 Agreement.

Liquidity

The Consolidated Financial Statements have been prepared in conformity with the accounting principles generally accepted in the United States of America, which contemplate the continuation of the Company as a going concern. Historically, the Company's primary source of financing has been through the sale of its securities. Research and development activities have required significant capital investment since the Company's inception. The Company expects its operations to continue to require cash investment to pursue its research and development goals, including clinical trials and related drug manufacturing.

At September 30, 2019, the Company had \$221.8 million in cash and cash equivalents, \$36.9 million in short-term investments, and \$44.2 million in long-term investments to fund operations. During the year ended September 30, 2019, the Company's cash and investments balance increased by \$226.3 million, which was primarily the result of the \$75 million equity investment from JJDC and the \$175 million upfront payment and \$50 million of milestone payments from Janssen, respectively, as discussed further in Note 2 below. These cash inflows were partially offset by cash outflows related to operating activities and investing activities.

Summary of Significant Accounting Policies

Principles of Consolidation—The Consolidated Financial Statements include the accounts of Arrowhead and its Subsidiaries. Arrowhead's primary operating subsidiary is Arrowhead Madison, which is located in Madison, Wisconsin, where the Company's research and development facility is located. All significant intercompany accounts and transactions are eliminated in consolidation.

Basis of Presentation and Use of Estimates—The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could materially differ from those estimates. Additionally, certain reclassifications have been made to prior period financial statements to conform to the current period presentation.

Cash and Cash Equivalents—The Company considers all liquid debt instruments purchased with a maturity of three months or less to be cash equivalents. Included within Cash and cash equivalents on the Consolidated Balance Sheets is \$1.0 million and \$0 restricted cash at September 30, 2019 and September 30, 2018, respectively. Amounts included in restricted cash are primarily held as collateral associated with a letter of credit for the Company's new lease for its corporate headquarters in Pasadena, California.

Concentration of Credit Risk—The Company maintains several bank accounts primarily at two financial institutions for its operations. These accounts are insured by the Federal Deposit Insurance Corporation (FDIC) for up to \$250,000 per institution. Management believes the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which these deposits are held.

Investments—The Company may invest excess cash balances in short-term and long-term marketable debt securities. Investments may consist of certificates of deposit, money market accounts, government-sponsored enterprise securities, corporate bonds and/or commercial paper. The Company accounts for its investment in marketable securities in accordance with FASB ASC 320, Investments – Debt and Equity Securities. This statement requires debt securities to be classified into three categories:

Held-to-maturity—Debt securities that the entity has the positive intent and ability to hold to maturity are reported at amortized cost.

Trading Securities—Debt securities that are bought and held primarily for the purpose of selling in the near term are reported at fair value, with unrealized gains and losses included in earnings.

Available-for-Sale—Debt securities not classified as either securities held-to-maturity or trading securities are reported at fair value with unrealized gains or losses excluded from earnings and reported as a separate component of shareholders' equity.

The Company classifies its investments in marketable debt securities based on the facts and circumstances present at the time of purchase of the securities. During the years ended September 30, 2019, 2018 and 2017, respectively, all of the Company's investments were classified as held-to-maturity.

Held-to-maturity investments are measured and recorded at amortized cost on the Company's Consolidated Balance Sheet. Discounts and premiums to par value of the debt securities are amortized to interest income/expense over the term of the security. No gains or losses on investment securities are realized until they are sold or a decline in fair value is determined to be other-than-temporary.

Property and Equipment—Property and equipment are recorded at cost, which may equal fair market value in the case of property and equipment acquired in conjunction with a business acquisition. 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. Long-lived assets, including property and equipment are reviewed for impairment whenever events or circumstances indicate that the carrying amount of these assets may not be recoverable.

Intangible Assets Subject to Amortization—Intangible assets subject to amortization include certain patents and license agreements. 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 and are also reviewed annually to determine whether any impairment is necessary.

Contingent Consideration - The consideration for the Company's acquisitions may include future payments that are contingent upon the occurrence of a particular event. For example, milestone payments might be based on the achievement of various regulatory approvals or future sales milestones, and royalty payments might be based on drug product sales levels. The Company records a contingent consideration obligation for such contingent payments at fair value on the acquisition date. The Company estimates the fair value of contingent consideration obligations through valuation models designed to estimate the probability of such contingent payments based on various assumptions and incorporating estimated success rates. Estimated payments are discounted using present value techniques to arrive at an estimated fair value at the balance sheet date. Changes in the fair value of the contingent consideration obligations are recognized within the Company's Consolidated Statements of Operations and Comprehensive Income (Loss). Changes in the fair value of the contingent consideration obligations can result from changes to one or multiple inputs, including adjustments to the discount rates, changes in the amount or timing of expected expenditures associated with product development, changes in the amount or timing of cash flows from products upon commercialization, changes in the assumed achievement or timing of any development milestones, changes in the probability of certain clinical events and changes in the assumed probability associated with regulatory approval. These fair value measurements are based on significant inputs not observable in the market. Substantial judgment is employed in determining the appropriateness of these assumptions as of the acquisition date and for each subsequent period. Accordingly, changes in assumptions could have a material impact on the amount of contingent consideration expense the Company records in any given period. The Company determined the fair value of its contingent consideration obligation to be \$0 at September 30, 2019 and September 30, 2018.

Revenue Recognition— On October 1, 2018, the Company adopted FASB Topic 606 – Revenue for Contracts from Customers which amended revenue recognition principles and provides a single, comprehensive set of criteria for revenue recognition within and across all industries. The Company's adoption of the new revenue standard did not have a material impact on its Consolidated Financial Statements. The Company has not yet achieved commercial sales of its drug candidates to date, however, the new standard is applicable to the Company's ongoing licensing and collaboration agreements, including those with Amgen and Janssen, and the analysis of the impact of this guidance on those agreements is discussed further in Note 2 below.

The new revenue standard provides a five-step framework for recognizing revenue as control of promised goods or services is transferred to a customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of the new revenue standard, the Company performs the following five steps: (i) identify the contract; (ii) identify the performance obligations; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. At contract inception, the Company assesses whether the goods or services promised within each contract are distinct and, therefore, represent a separate performance obligation, or whether they are not distinct and are combined with other goods and services until a distinct bundle is identified. The Company then determines the transaction price, which typically includes upfront payments and any variable consideration that the Company determines is probable to not cause a significant reversal in the amount of cumulative revenue recognized when the uncertainty associated with the variable

consideration is resolved. The Company then allocates the transaction price to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied.

The Company recognizes the transaction price allocated to upfront license payments as revenue upon delivery of the license to the customer and resulting ability of the customer to use and benefit from the license, if the license is determined to be distinct from the other performance obligations identified in the contract. These other performance obligations are typically to perform research and development services for the customer, often times relating to the candidate that the customer is licensing. If the license is not considered to be distinct from other performance obligations, the Company assesses the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied at a point in time or over time. If the performance obligation is satisfied over time, the Company then determines the appropriate method of measuring progress for purposes of recognizing revenue from license payments. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the related revenue recognition.

Typically, the Company's collaboration agreements entitle it to additional payments upon the achievement of milestones or royalties on sales. The milestones are generally categorized into three types: development milestones, generally based on the initiation of toxicity studies or clinical trials; regulatory milestones, generally based on the submission, filing or approval of regulatory applications such as a Clinical Trial Application (CTA) or a New Drug Application (NDA) in the United States; and sales-based milestones, generally based on meeting specific thresholds of sales in certain geographic areas. The Company evaluates whether it is probable that the consideration associated with each milestone or royalty will not be subject to a significant reversal in the cumulative amount of revenue recognized. Amounts that meet this threshold are included in the transaction price using the most likely amount method, whereas amounts that do not meet this threshold are excluded from the transaction price until they meet this threshold. At the end of each subsequent reporting period, the Company re-evaluates the probability of a significant reversal of the cumulative revenue recognized for our milestones and royalties, and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and net income in our Consolidated Statement of Operations and Comprehensive Income (Loss). Typically, milestone payments and royalties are achieved after the Company's performance obligations associated with the collaboration agreements have been completed and after the customer has assumed responsibility for the respective clinical or pre-clinical program. Milestones or royalties achieved after the Company's performance obligations have been completed are recognized as revenue in the period the milestone or royalty was achieved. If a milestone payment is achieved during the performance period, the milestone payment would be recognized as revenue to the extent performance had been completed at that point, and the remaining balance would be recorded as deferred revenue.

The new revenue standard requires the Company to assess whether a significant financing component exists in determining the transaction price. The Company performs this assessment at the onset of its licensing or collaboration agreements. Typically, a significant financing component does not exist because the customer is paying for a license or services in advance with an upfront payment. Additionally, future royalty payments are not substantially within the control of the Company or the customer.

The new revenue standard requires the Company to allocate the arrangement consideration on a relative standalone selling price basis for each performance obligation after determining the transaction price of the contract and identifying the performance obligations to which that amount should be allocated. The relative standalone selling price is defined in the new revenue standard as the price at which an entity would sell a promised good or service separately to a customer. If other observable transactions in which the Company has sold the same performance obligation separately are not available, the Company estimates the standalone selling price of each performance obligation. Key assumptions to determine the standalone selling price may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Whenever the Company determines that goods or services promised in a contract should be accounted for as a combined performance obligation over time, the Company determines the period over which the performance obligations will be performed and revenue will be recognized. Revenue is recognized using the proportional performance method. Labor hours are typically used as the measure of performance. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company is expected to complete its performance obligations. If the Company determines that the performance obligation is satisfied over time, any upfront payment received is initially recorded as deferred revenue on the Company's Consolidated Balance Sheets.

Certain judgments affect the application of the Company's revenue recognition policy. For example, the Company records short-term and long-term deferred revenue based on its best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next 12 months, and long-term deferred revenue consists of amounts that the Company does not expect will be recognized in the next 12 months. This estimate is based on the Company's current operating plan and, if the Company's operating plan should change in the future, the Company may recognize a different amount of deferred revenue over the next 12-month period.

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. Included in research and development costs are operating costs, facilities, supplies, external services, clinical trial and manufacturing costs, overhead directly related to the Company's research and development operations, and costs to acquire technology licenses.

Net Income (Loss) per Share—Basic net income (loss) per share is computed using the weighted-average number of common shares outstanding during the period. Diluted net income (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 and restricted stock units issued to employees. During the years ended September 30, 2019, 2018 and 2017, the calculation of the effect of dilutive stock options and restricted stock units was 4,748,958 shares, 0 shares and 0 shares, respectively. During the year ended September 30, 2019, the calculation of the effect of dilutive stock options and restricted stock units excluded 1,007,500 stock options and 11,500 restricted stock units due to their anti-dilutive effect. During the years ended September 30, 2018 and 2017, the calculation of the effect of dilutive stock options and restricted stock units excluded all stock options and restricted stock units granted and outstanding during the period due to their anti-dilutive effect.

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. The Company uses the Black-Scholes option valuation model to estimate the fair value of its 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. For restricted stock units, the value of the award is based on the Company's stock price at the grant date. For performance-based restricted stock unit awards, the value of the award is based on the Company's stock price at the grant date, with consideration given to the probability of the performance condition being achieved. The Company uses historical data and other information to estimate the expected price volatility for stock option awards and the expected forfeiture rate for all awards. Expense is recognized over the vesting period for all awards and commences at the grant date for time-based awards and upon the Company's determination that the achievement of such performance conditions is probable for performance-based awards. This determination requires significant judgment by management.

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.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09 Revenue from Contracts with Customers (Topic 606), which will supersede nearly all existing revenue recognition guidance under GAAP. ASU No. 2014-09 provides that an entity recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. This update also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments, and assets recognized from costs incurred to obtain or fulfill a contract. ASU No. 2014-09 allows for either full retrospective or modified retrospective adoption and became effective for the Company in the first quarter of fiscal 2019. In April 2016, the FASB issued an amendment to ASU No. 2014-09 with update ASU 2016-10 which provided more specific guidance around the identification of performance obligations and licensing arrangements. On October 1, 2018, the Company adopted this standard using the modified retrospective method. The Company's implementation approach included reviewing the status of each of its ongoing license agreements and collaboration agreements and designing appropriate internal controls to enable the preparation of financial information. The Company completed its assessment of the impact of the new revenue recognition guidance and determined that there will be no material impact. The Company's existing performance obligations under its ongoing license and collaboration agreements as of October 1, 2018 and prior were substantially completed prior to September 30, 2018. For these agreements that were ongoing as of October 1, 2018, any future option, milestone or royalty payments received will be accounted for under the sales-based royalty exception provided for under this new revenue recognition guidance. Additionally, there will be no impact to cash from or used in operating, financing or investing activities on the Company's Consolidated Statement of Cash Flows as a result of the adoption of the new standard.

In March 2016, the FASB issued ASU No. 2016-02, Leases. Under ASU 2016-02, lessees will be required to recognize a right-of-use asset and a lease liability for virtually all of their leases (other than leases that meet the definition of a short-term lease). For income statement purposes, a dual model was retained, requiring leases to be classified as either operating or finance. Operating leases will result in straight-line expense (similar to current operating leases) while finance leases will result in a front-loaded expense pattern (similar to current capital leases). ASU 2016-02 becomes effective for the Company in the first quarter of fiscal 2020. The Company is assessing the impact of the adoption of this update and it expects the adoption to have a material effect on its Consolidated Balance Sheets, including classification and disclosure of its leased facilities.

In May 2017, the FASB issued ASU No. 2017-09, which is an update to Topic 718, Compensation - Stock Compensation. The update provides guidance on determining which changes to the terms and conditions of share-based payment awards, including stock options, require an entity to apply modification accounting under Topic 718. ASU 2017-09 became effective for the Company in the first quarter of fiscal 2019. The adoption of this update has not had a material impact on the Company's results of operations and Consolidated Financial Statements.

In November 2018, the FASB issued ASU No. 2018-18 Collaborative Arrangements (Topic 808). This update provides clarification on the interaction between Revenue Recognition (Topic 606) and Collaborative Arrangements (Topic 808) including the alignment of unit of account guidance between the two topics/ ASU 2018-18 becomes effective for the Company in the first quarter of fiscal 2021 with early adoption permitted. The Company does not expect the adoption of this update to have a material effect on its Consolidated Financial Statements.

NOTE 2. COLLABORATION AND LICENSE AGREEMENTS

Amgen Inc.

On September 28, 2016, the Company entered into two Collaboration and License agreements, and a Common Stock Purchase Agreement with Amgen Inc., a Delaware corporation ("Amgen"). Under one of the license agreements (the "Second Collaboration and License Agreement" or "AMG 890 (ARO-LPA) Agreement"), Amgen has received a worldwide, exclusive license to Arrowhead's novel, RNAi ARO-LPA program. These RNAi molecules are designed to reduce elevated lipoprotein(a), which is a genetically validated, independent risk factor for atherosclerotic cardiovascular disease. Under the other license agreement (the "First Collaboration and License Agreement" or "ARO-AMG1 Agreement"), Amgen received an option to a worldwide, exclusive license for ARO-AMG1, an RNAi therapy for an undisclosed genetically validated cardiovascular target. In both agreements, Amgen is wholly responsible for clinical development and commercialization. Under the Common Stock Purchase Agreement, the Company has sold 3,002,793 shares of Common Stock to Amgen at a price of \$7.16 per share. Under the terms of the agreements taken together, the Company has received \$35 million in upfront payments and \$21.5 million in the form of an equity investment by Amgen in the Company's Common Stock. Upon signing the collaboration agreements with Amgen, the Company was eligible to receive up to \$617 million in Option payments, and development, regulatory and sales milestone payments. The Company remains eligible to receive up to \$420 million in development, regulatory and sales milestone payments. The Company is further eligible to receive up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement.

The Company has evaluated these agreements in accordance with the new revenue recognition standard that became effective for the Company on October 1, 2018. The adoption of the new revenue standard did not have a material impact on the balances reported when evaluated under the superseded revenue standard. During the year ended September 30, 2018, the Company substantially completed its performance obligations under the AMG 890 (ARO-LPA) Agreement and the ARO-AMG1 Agreement. Future milestones and royalties achieved will be recognized in their entirety when earned. During the years ended September 30, 2019, 2018 and 2017, the Company recognized \$0.3 million, \$16.1 million and \$31.3 million of Revenue associated with its agreements with Amgen, respectively. As of September 30, 2019, there were \$0 contract assets recorded as Accounts Receivable, and \$0 contract liabilities recorded as Deferred Revenue on the Company's Consolidated Balance Sheets associated with these agreements.

Regarding the ARO-AMG1 Agreement, in August 2018, the Company delivered to Amgen a candidate that met or exceeded the activity and safety requirements stipulated in the ARO-AMG1 Agreement. The option period expired on August 7, 2019, and Amgen advised the Company that it did not intend to exercise its option. As such, there will be no further milestone or royalty payments under the ARO-AMG1 Agreement.

Janssen Pharmaceuticals, Inc.

On October 3, 2018, the Company entered into a License Agreement ("Janssen License Agreement") and a Research Collaboration and Option Agreement ("Janssen Collaboration Agreement") with Janssen Pharmaceuticals, Inc. ("Janssen") part of the Janssen Pharmaceutical Companies of Johnson & Johnson. The Company also entered into a Stock Purchase Agreement ("JJDC Stock Purchase Agreement") with Johnson & Johnson Innovation-JJDC, Inc. ("JJDC"), a New Jersey corporation. Under the Janssen License Agreement, Janssen has received a worldwide, exclusive license to the Company's ARO-HBV program, the Company's third-

generation subcutaneously administered RNAi therapeutic candidate being developed as a potentially curative therapy for patients with chronic hepatitis B virus infection. Beyond the Company's ongoing Phase 1 / 2 study of ARO-HBV, Janssen will be wholly responsible for clinical development and commercialization. Under the Janssen Collaboration Agreement, Janssen will be able to select three new targets against which Arrowhead will develop clinical candidates. These candidates are subject to certain restrictions and will not include candidates in the Company's current pipeline. The Company will perform discovery, optimization and preclinical development, entirely funded by Janssen, sufficient to allow the filing of a U.S. Investigational New Drug application or equivalent, at which time Janssen will have the option to take an exclusive license. If the option is exercised, Janssen will be wholly responsible for clinical development and commercialization. Under the JJDC Stock Purchase Agreement, in October 2018 the Company sold 3,260,869 shares of common stock to JJDC at a price of \$23.00 per share. Under the terms of the agreements taken together, the Company has received \$175 million as an upfront payment, \$75 million in the form of an equity investment by JJDC in Arrowhead common stock, and may receive up to \$1.6 billion in development and sales milestones payments for the Janssen License Agreement, and up to \$1.9 billion in development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the license agreement and up to low teens under the collaboration and option agreement on product sales.

The Company has evaluated these agreements in accordance with the new revenue recognition requirements that became effective for the Company on October 1, 2018. The adoption of the new revenue standard did not have a material impact on the balances reported when evaluated under the superseded revenue standard. At the inception of these agreements, the Company has identified one distinct performance obligation. Regarding the Janssen License Agreement, the Company determined that the key deliverables included the license and certain R&D services including the Company's responsibility to complete the ongoing Phase 1 / 2 study of JNJ-3989 (ARO-HBV) and the Company's responsibility to ensure certain manufacturing of JNJ-3989 (ARO-HBV) drug product is completed and delivered to Janssen (the "Janssen R&D Services"). Due to the specialized and unique nature of these Janssen R&D services, and their direct relationship with the license, the Company determined that these deliverables represent one distinct bundle and thus, one performance obligation. The Company also determined that Janssen's option to require the Company to develop up to three new targets is not a material right, and thus, not a performance obligation at the onset of the agreement. The consideration for this option will be accounted for when it is exercised.

The Company determined the transaction price totaled approximately \$252.6 million which includes the upfront payment, the premium paid by JJDC for its equity investment in the Company, the two \$25 million milestone payments earned and estimated payments for reimbursable Janssen R&D services to be performed. The Company has allocated the total \$252.6 million initial transaction price to its one distinct performance obligation for the ARO-HBV license and the associated Janssen R&D Services. This revenue will be recognized using a proportional performance method (based on actual labor hours versus estimated total labor hours) beginning in October 2018 and ending as the Company's efforts in overseeing the ongoing phase 1 / 2 clinical trial are completed. During the year ended September 30, 2019, the Company recognized approximately \$167.5 million of Revenue associated with this performance obligation. As of September 30, 2019 there were \$0 contract assets recorded as Accounts Receivable, \$77.8 million of contract liabilities recorded as current Deferred Revenue, and \$5.0 million of contract liabilities recorded as and long-term Deferred Revenue on the Company's Consolidated Balance Sheets. The \$77.8 million of current Deferred Revenue and \$5.0 million of long-term Deferred Revenue is driven by the upfront payment and premium paid by JJDC for its equity investment in the Company as well as the two \$25 million milestones paid by Janssen, net of revenue recognized in the period.

During the year ended September 30, 2019, Janssen selected the first of the three targets under the Janssen Collaboration Agreement, now referred to as ARO-JNJ1, and the Company has begun to conduct its discovery, optimization and preclinical development of ARO-JNJ1. All costs and labor hours spent by the Company will be entirely funded by Janssen. During the year ended September 30, 2019, the Company recognized \$1.0 million of Revenue associated with its efforts on the ARO-JNJ1 candidate. As of September 30, 2019 there were \$0.7 million of contract assets recorded as Accounts Receivable, and \$0 of contract liabilities.

NOTE 3. PROPERTY AND EQUIPMENT

The following table summarizes the Company's major classes of property and equipment:

	September 30, 2019	September 30, 2018
Computers, office equipment and furniture	\$ 637,577	\$ 600,334
Research equipment	12,932,304	10,751,627
Software	147,254	152,676
Leasehold improvements	21,579,415	12,236,150
Total gross fixed assets	35,296,550	23,740,787
Less: Accumulated depreciation and amortization	(12,081,651)	(9,805,362)
Property and equipment, net	<u>\$ 23,214,899</u>	<u>\$ 13,935,425</u>

Depreciation and amortization expense for Property and Equipment for the years ended September 30, 2019, 2018 and 2017 was \$2,738,715, \$2,998,846, and \$2,990,010, respectively.

NOTE 4. INVESTMENTS

The Company invests a portion of its excess cash balances in short-term debt securities and may, from time to time, also invest in long-term debt securities. Investments at September 30, 2019 consisted of corporate bonds with maturities remaining of less than 36 months. The Company may also invest excess cash balances in certificates of deposits, money market accounts, government-sponsored enterprise securities, corporate bonds and/or commercial paper. The Company accounts for its investments in accordance with FASB ASC 320, Investments – Debt and Equity Securities. At September 30, 2019, all investments were classified as held-to-maturity securities.

The following tables summarize the Company's short-term and long-term investments as of September 30, 2019, and September 30, 2018.

	As of September 30, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial notes (due within one year)	\$ 36,899,894	\$ 222,584	\$ —	\$ 37,122,478
Commercial notes (due within three years)	\$ 44,175,993	\$ 875,258	\$ —	\$ 45,051,251
Total	\$ 81,075,887	\$ 1,097,842	\$ —	\$ 82,173,729

	As of September 30, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial notes (due within one year)	\$ 46,400,176	\$ —	\$ (429,050)	\$ 45,971,126
Commercial notes (due within three years)	\$ —	\$ —	\$ —	\$ —
Total	\$ 46,400,176	\$ —	\$ (429,050)	\$ 45,971,126

NOTE 5. INTANGIBLE ASSETS

Intangible assets subject to amortization include patents and a license agreement capitalized as part of the Novartis RNAi asset acquisition in March 2015. The license agreement associated with the Novartis RNAi asset acquisition is being amortized over the estimated life remaining at the time of acquisition, which was 21 years, and the accumulated amortization of the asset is approximately \$680,191. The patents associated with the Novartis RNAi asset acquisition are being amortized over the estimated life remaining at the time of acquisition, which was 14 years, and the accumulated amortization of the assets is \$7,113,443. Amortization expense for the years ended September 30, 2019, 2018 and 2017 was \$1,700,430, \$1,700,429 and \$1,700,429, respectively. Amortization expense is expected to be \$1,700,429 in 2020, \$1,700,429 in 2021, \$1,700,429 in 2022, \$1,700,429 in 2023, \$1,700,429 in 2024, and \$8,561,435 thereafter.

The following table provides details on the Company's intangible asset balances:

	Intangible assets subject to amortization
Balance at September 30, 2018	\$ 18,764,010
Impairment	-
Amortization	(1,700,430)
Balance at September 30, 2019	\$ 17,063,580

NOTE 6. STOCKHOLDERS' EQUITY

At September 30, 2019, 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 per share, and 5,000,000 shares of Preferred Stock, par value \$0.001 per share.

At September 30, 2019, 95,506,271 shares of Common Stock were outstanding. At September 30, 2019, 7,177,796 shares of Common Stock were reserved for issuance upon exercise of options and vesting of restricted stock units granted or available for grant under Arrowhead's 2004 Equity Incentive Plan and 2013 Incentive Plan, as well as for inducement grants made to new employees.

In October 2018 the Company sold 3,260,869 shares of Common Stock to JJDC at a price of \$23.00 per share as part of the JJDC Stock Purchase Agreement discussed further in Note 2 above. The Company received proceeds of \$75.0 million. The portion of these proceeds that were deemed to be a premium were recorded as deferred revenue as discussed further in Note 2 above.

NOTE 7. COMMITMENTS AND CONTINGENCIES

Leases

In April 2019, the Company entered a new lease for its corporate headquarters in Pasadena, California. The 91 month office building lease between the Company and 177 Colorado Owner, LLC is for approximately 24,000 square feet of office space located at 177 E. Colorado Blvd, Pasadena, California, and this lease will replace the Company's current corporate headquarters office lease. The increased capacity of this new office space compared to the Company's current corporate headquarters will accommodate increased personnel as the Company's pipeline of drug candidates expands and moves closer to market. Lease payments began on September 30, 2019 and are estimated to total approximately \$8.8 million over the term. The Company expects to pay approximately \$3.5 million for leasehold improvements, net of tenant improvement allowances. Monthly rental payments are approximately \$65,700 per month for the first year and will increase approximately 3% annually.

The Company also leases approximately 61,000 square feet of office and laboratory space for its research facility in Madison, Wisconsin. In January 2019, the Company amended its existing lease to add an additional 13,000 square feet of laboratory and office space to the facility. The amended lease will expire in September 2029. As part of this lease, the Company was provided a primary tenant improvement allowance of \$2.1 million which is accounted for as Deferred Rent and a secondary tenant improvement allowance of \$2.7 million which was accounted for as a Note Payable on the Company's Consolidated Balance Sheet. In October 2018, the Company paid off the remaining \$2.3 million balance on the note payable. Monthly rental payments are approximately \$135,800 per month and will increase approximately 2.5% annually.

Facility rent expense for the years ended September 30, 2019, 2018 and 2017 was \$1,654,800, \$1,288,000 and \$1,441,000, respectively.

As of September 30, 2019, future minimum lease payments due in fiscal years under operating leases are as follows:

2020	\$ 1,521,451
2021	2,256,379
2022	2,521,446
2023	2,590,558
2024	2,661,512
2025 and thereafter	10,834,206
Total	<u>\$ 22,385,552</u>

Litigation –

The Company and certain of its officers and directors were named as defendants in a putative consolidated class action in the United States District Court for the Central District of California regarding certain public statements in connection with the Company’s hepatitis B drug research. The consolidated class action, initially filed as *Wang v. Arrowhead Research Corp., et al.*, No. 2:14-cv-07890 (C.D. Cal., filed Oct. 10, 2014), and *Eskinazi v. Arrowhead Research Corp., et al.*, No. 2:14-cv-07911 (C.D. Cal., filed Oct. 13, 2014), asserted claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and sought damages in an unspecified amount. Additionally, three putative stockholder derivative actions captioned *Weisman v. Anzalone et al.*, No. 2:14-cv-08982 (C.D. Cal., filed Nov. 20, 2014), *Bernstein (Backus) v. Anzalone, et al.*, No. 2:14-cv-09247 (C.D. Cal., filed Dec. 2, 2014); and *Johnson v. Anzalone, et al.*, No. 2:15-cv-00446 (C.D. Cal., filed Jan. 22, 2015), were filed in the United States District Court for the Central District of California, alleging breach of fiduciary duty by the Company’s Board of Directors in connection with the alleged facts underlying the securities claims. An additional consolidated derivative action asserting similar claims was filed in Los Angeles County Superior Court, initially filed as *Bacchus v. Anzalone, et al.*, (L.A. Super., filed Mar. 5, 2015); and *Jackson v. Anzalone, et al.* (L.A. Super., filed Mar. 16, 2015). Each of these suits seeks damages in unspecified amounts and some seek various forms of injunctive relief. On October 7, 2016, the federal district court dismissed the consolidated class action with prejudice. Following the dismissal of the consolidated class action, the parties for the Weisman and Johnson actions jointly stipulated to dismiss the actions, with the parties bearing their own fees and costs. The parties to the Bernstein and consolidated derivative action agreed to stay the matters pending the resolution of the Ninth Circuit appeal of the dismissal of the consolidated class action. On February 15, 2018, the Ninth Circuit issued a memorandum affirming the district court’s dismissal of all claims. Plaintiffs in the consolidated derivative action voluntarily dismissed their case. The parties to the Bernstein action filed a stipulation to continue the stay of the action pending resolution of the Ninth Circuit appeal in *Meller v. Arrowhead Pharmaceuticals, Inc.*, Case No. 2:16-cv-08505 (C.D. Cal.). The Bernstein matter was dismissed on September 4, 2019. All actions relating to the Company’s hepatitis B drug research have been dismissed.

The Company and certain executive officers were named as defendants in a putative consolidated class action in the United States District Court for the Central District of California regarding certain public statements in connection with the Company’s drug research programs. The consolidated class action, initially filed as *Meller v. Arrowhead Pharmaceuticals, Inc., et al.*, No. 2:16-cv-08505 (C.D. Cal., filed Nov. 15, 2016), *Siegel v. Arrowhead Pharmaceuticals, Inc., et al.*, No. 2:16-cv-8954 (C.D. Cal., filed Dec. 2, 2016), and *Unz v. Arrowhead Pharmaceuticals, Inc., et al.*, No.2:17-cv-00310 (C.D. Cal., filed Jan. 13, 2017) asserts claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 regarding certain public statements in connection with the Company’s drug research programs and seek damages in an unspecified amount. Additionally, a putative stockholder derivative action captioned *Johnson v. Anzalone, et al.*, (Los Angeles County Superior Court, filed January 19, 2017) asserting substantially similar claims is pending in Los Angeles County Superior Court and is stayed pending the related consolidated class action. Two additional putative stockholder derivative actions, captioned *Lucas v. Anzalone, et al.*, No. 2:17-cv-03207 (C.D. Cal., filed April 28, 2017), and *Singh v. Anzalone, et al.*, No. 2:17-cv-03160 (C.D. Cal., filed April 27, 2017), alleging breach of fiduciary duty by the Company’s Board of Directors in connection with the alleged facts underlying the securities claims, are pending in the United States District Court for the Central District of California. The Lucas and Singh actions have been consolidated. On December 21, 2017, the federal district court dismissed the consolidated class action with prejudice. On July 23, 2019, the Ninth Circuit issued a memorandum affirming the district court’s dismissal of all claims in the consolidated class action. The Lucas and Singh actions have been voluntarily dismissed. The Johnson action was dismissed on November 13, 2019. All actions relating to public statements in connection with the Company’s drug research programs have been dismissed.

With regard to legal fees, such as attorney fees related to these matters or any other legal matters, the Company recognizes such costs as incurred.

Purchase Commitments

In the normal course of business, we enter into various purchase commitments for the manufacture of drug components, for toxicology studies, and for clinical studies. As of September 30, 2019, these future commitments were estimated at approximately \$60.2 million, of which approximately \$50.9 million is expected to be incurred in fiscal 2020, and \$9.3 is expected to be incurred beyond fiscal 2020.

Technology License Commitments

The Company has licensed from third parties the rights to use certain technologies for its research and development activities, as well as in any products the Company may develop using these licensed technologies. These agreements and other similar agreements often require milestone and royalty payments. Milestone payments, for example, may be required as the research and development process progresses through various stages of development, such as when clinical candidates enter or progress through clinical trials, upon NDA and upon certain sales level milestones. These milestone payments could amount to the mid to upper double-digit millions of dollars. During the years ended September 30, 2019, 2018 and 2017, the Company did not trigger any of these milestone payments. In certain agreements, the Company may be required to make mid to high single-digit percentage royalty payments based on a percentage of the sales of the relevant products.

NOTE 8. STOCK-BASED COMPENSATION

Arrowhead has two plans that provide for equity-based compensation. Under the 2004 Equity Incentive Plan and 2013 Incentive Plan, as of September 30, 2019, 1,099,337 and 5,226,948 shares, respectively, of Arrowhead's Common Stock are reserved for the grant of time-based vesting stock options, stock appreciation rights, restricted stock awards and performance unit/share awards to employees, consultants and others. No further grants may be made under the 2004 Equity Incentive Plan. As of September 30, 2019, there were options granted and outstanding to purchase 1,099,337 and 2,831,322 shares of Common Stock under the 2004 Equity Incentive Plan and the 2013 Incentive Plan, respectively, and there were 2,054,333 restricted stock units granted and outstanding under the 2013 Incentive Plan. Also, as of September 30, 2019, there were 843,011 shares reserved for options and 8,500 restricted stock units issued as inducement grants to new employees outside of equity compensation plans. During the year ended September 30, 2019, no options or restricted stock units were granted under the 2004 Equity Incentive Plan, 517,500 options and 1,406,888 restricted stock units were granted under the 2013 Incentive Plan, and 362,000 options and 8,500 restricted stock units were granted as inducement awards to new employees outside of equity incentive plans.

The following table summarizes information about stock options:

	Number of Options Outstanding	Weighted- Average Exercise Price Per Share	Weighted- Average Remaining Contractual Term	Aggregate Intrinsic Value
Balance At September 30, 2018	5,524,399	\$ 6.14		
Granted	879,500	16.05		
Cancelled	(87,434)	8.96		
Exercised	(1,542,795)	5.36		
Balance At September 30, 2019	4,773,670	\$ 8.16	6.0 years	\$ 95,727,301
Exercisable At September 30, 2019	3,515,379	\$ 6.58	4.9 years	\$ 75,931,836

Stock-based compensation expense related to stock options for the years ended September 30, 2019, 2018 and 2017 was \$3,955,216, \$3,265,348 and \$4,524,833, respectively. The Company does not recognize an income tax benefit as the Company has historically operated at a loss and an actual income tax benefit may not be realized. For non-qualified stock options, the expense creates a timing difference, resulting in a deferred tax asset, which is fully reserved by a valuation allowance.

The grant date fair value of the options granted by the Company for the years ended September 30, 2019, 2018 and 2017 was \$12,137,250, \$4,141,318 and \$849,816, respectively.

The intrinsic value of the options exercised during the years ended September 30, 2019, 2018 and 2017 was \$24,561,189, \$5,805,317 and \$35,512, respectively.

As of September 30, 2019, the pre-tax compensation expense for all outstanding unvested stock options in the amount of \$12,639,567 will be recognized in the Company's results of operations over a weighted average period of 3.2 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 the Company's 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:

	Years ended September 30,		
	2019	2018	2017
Dividend yield	—	—	—
Risk-free interest rate	1.50 – 3.11%	2.05 – 2.99%	1.34 – 2.31%
Volatility	115%	110%	79%
Expected life (in years)	6.25	6.25	5.85
Weighted average grant date fair value per share of options granted	\$13.80	\$5.04	\$1.33

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

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

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

Restricted Stock Units

Restricted stock units (RSUs), including time-based and performance-based awards, were granted under the Company's 2013 Incentive Plan and as inducement grants granted outside of the Plan. During the year ended September 30, 2019, the Company issued 1,406,888 RSUs under the 2013 Incentive Plan and 8,500 RSUs as an inducement award to a new employee outside of the equity incentive plans. At vesting, each outstanding RSU will be exchanged for one share of the Company's Common Stock. RSU recipients may elect to net share settle upon vesting, in which case the Company pays the employee's income taxes due upon vesting and withholds a number of shares of Common Stock of equal value. RSU awards generally vest subject to the satisfaction of service requirements or the satisfaction of both service requirements and achievement of certain performance targets.

The following table summarizes the activity of the Company's RSUs:

	Number of RSUs	Weighted- Average Grant Date Fair Value
Unvested at September 30, 2018	2,968,500	\$ 2.99
Granted	1,415,388	12.57
Vested	(2,197,305)	2.78
Forfeited	(123,750)	8.98
Unvested at September 30, 2019	2,062,833	\$ 9.43

During the years ended September 30, 2019, 2018 and 2017, the Company recorded \$8,438,107, \$5,189,259 and \$3,366,762 of expense related to RSUs, respectively. Such expense is included in stock-based compensation expense in the Company's Consolidated Statement of Operations and Comprehensive Income (Loss). The Company does not recognize an income tax benefit as the Company has historically operated at a loss and an actual income tax benefit may not be realized. For RSUs, the expense creates a timing difference, resulting in a deferred tax asset, which is fully reserved by a valuation allowance.

For RSUs, the grant date fair value of the award is based on the Company's closing stock price at the grant date, with consideration given to the probability of achieving performance conditions for performance-based awards.

As of September 30, 2019, the pre-tax compensation expense for all unvested RSUs in the amount of \$9,937,559 will be recognized in the Company's results of operations over a weighted average period of 2.6 years.

NOTE 9. FAIR VALUE MEASUREMENTS

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.

The following table summarizes fair value measurements at September 30, 2019 and September 30, 2018 for assets and liabilities measured at fair value on a recurring basis:

September 30, 2019:

	Level 1	Level 2	Level 3	Total
Cash and cash equivalents	\$ 221,804,128	\$ —	\$ —	\$ 221,804,128
Short-term investments	37,122,478	—	—	37,122,478
Long-term investments	45,051,251	—	—	45,051,251
Contingent Consideration	\$ —	\$ —	\$ —	\$ —

September 30, 2018:

	Level 1	Level 2	Level 3	Total
Cash and cash equivalents	\$ 30,133,213	\$ —	\$ —	\$ 30,133,213
Short-term investments	45,971,126	—	—	45,971,126
Long-term investments	—	—	—	—
Contingent Consideration	\$ —	\$ —	\$ —	\$ —

The Company had a liability for contingent consideration related to its acquisition of the Roche RNAi business completed in 2011. The fair value measurement of the contingent consideration obligations is determined using Level 3 inputs. The fair value of contingent consideration obligations is based on a discounted cash flow model using a probability-weighted income approach. The measurement is based upon unobservable inputs supported by little or no market activity based on the Company's assumptions and experience. Estimating timing to complete the development and obtain approval of products is difficult, and there are inherent uncertainties in developing a product candidate, such as obtaining U.S. Food and Drug Administration (FDA) and other regulatory approvals. In determining the probability of regulatory approval and commercial success, the Company utilizes data regarding similar milestone events from several sources, including industry studies and its own experience. These fair value measurements represent Level 3 measurements as they are based on significant inputs not observable in the market. Significant judgment is employed in determining the appropriateness of these assumptions as of the acquisition date and for each subsequent period. Accordingly, changes in assumptions could have a material impact on the amount of contingent consideration expense the Company records in any given period. In November 2016, the Company announced the discontinuation of its clinical trial efforts for ARC-520, ARC-AAT and ARC-521. Given this development, the Company assessed the fair value of its contingent consideration obligation to be \$0 at September 30, 2019 and September 30, 2018.

NOTE 10. - 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. 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.

Components of the net deferred tax asset (liability) at September 30, 2019 and 2018 are as follows:

	2019	2018
Deferred tax assets:		
Accrued compensation	\$ 1,310,466	\$ 1,085,908
Stock compensation	3,609,756	4,188,368
Capitalized research and development	926,026	1,227,137
Fixed Assets	438,882	404,836
Net operating losses	105,372,571	114,142,741
Intangible Assets	3,590,090	3,854,752
California Alternative Minimum Tax	173,553	—
Deferred Rent	821,317	566,535
Capital Loss	709,779	709,779
Total deferred tax assets	116,952,440	126,180,056
Valuation allowance	(108,232,402)	(116,875,075)
Deferred tax liabilities:		
State taxes	(8,720,038)	(9,304,981)
Total deferred tax liability	(8,720,038)	(9,304,981)
Net deferred tax assets (liabilities)	\$ —	\$ —

The Company has concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company may not realize the benefit of all of its deferred tax assets. Accordingly, 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. The Company has recorded a full valuation allowance related to all of its deferred tax assets. The Company has performed an assessment of positive and negative evidence regarding the realization of the net deferred tax asset in accordance with FASB 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.

As of September 30, 2019, the Company had available gross federal net operating loss (NOL) carry forwards of approximately \$314.8 million and gross state NOL carry forwards of \$211.5 million. The NOLs expire at various dates through 2039.

The provisions for income taxes for the years ended September 30, 2019 and 2018 are as follows:

	2019	2018
Federal:		
Current	\$ —	\$ —
Deferred	—	—
Total Federal	\$ —	\$ —
State:		
Current	\$ 173,553	\$ 2,400
Deferred	—	—
Total State	\$ 173,553	\$ 2,400
Provision from income taxes	\$ 173,553	\$ 2,400

The Company's effective income tax rate differs from the statutory federal income tax rate as follows for the years ended September 30, 2019 and 2018:

	2019	2018
At U.S. federal statutory rate	21.0%	21.0%
State taxes, net of federal effect	7.3	7.9
Stock compensation	(15.0)	2.6
Mark-to-market adjustments	0.0	0.2
Valuation allowance	(13.0)	36.2
Federal tax rate change in 2018	—	(67.9)
Effective income tax rate	0.3%	0.0%

In December 2017, the President of the United States signed into law the Tax Cuts and Jobs Act, or TCJA, tax reform legislation. The TCJA makes significant changes in U.S. tax law including a reduction in the corporate tax rates, changes to net operating loss

carryforwards and carrybacks, and a repeal of the corporate alternative minimum tax. The TCJA reduced the U.S. corporate tax rate from the current rate of 35 percent down to 21 percent starting on January 1, 2018. As a result of the TCJA, the Company was required to revalue deferred tax assets and liabilities at 21 percent during the year ended September 30, 2018. This revaluation resulted in a provision of \$37.0 million to income tax expense in continuing operations and a corresponding reduction in the valuation allowance during the year ended September 30, 2018. As a result, there was no impact to our Consolidated Statements of Comprehensive Income (Loss) as a result of the reduction in tax rates. The other provisions of the TCJA did not have a material impact on our Consolidated Financial Statements.

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. The Company's policy is to include interest and penalties related to unrecognized tax benefits in income tax expense. The Company has not recognized any unrecognized tax benefits and does not have any interest or penalties related to uncertain tax positions as of September 30, 2019 and 2018.

The Company files income tax returns with the Internal Revenue Service ("IRS"), the state of California, the Australia Tax Office ("ATO") and certain other taxing jurisdictions. The Company is subject to income tax examinations by the IRS and by state tax authorities until the net operating losses are settled. During the year ended September 30, 2016, the IRS commenced an audit for the tax year ended September 30, 2015. The IRS audit concluded without any material adjustments.

NOTE 11. EMPLOYEE BENEFIT PLANS

In January 2005, the Company adopted a defined contribution 401(k) retirement savings plan covering substantially all of its employees. The Plan is 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 allows 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.

For the years ended September 30, 2019, 2018, and 2017, we recorded expenses under this plan of \$545,698, \$451,623 and \$426,470, respectively.

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

NOTE 12. UNAUDITED QUARTERLY FINANCIAL DATA

The following table presents selected unaudited quarterly financial data for each full quarterly period of the years ended September 30, 2019 and 2018:

Year ended September 30, 2019	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	\$ 34,657,896	\$ 48,148,275	\$ 42,696,636	\$ 43,292,770
Operating Income (Loss)	\$ 10,946,144	\$ 22,010,692	\$ 18,595,749	\$ 9,638,049
Net Income (Loss)	\$ 12,037,253	\$ 23,896,982	\$ 20,335,708	\$ 11,704,906
Net Income (Loss) per share - BASIC	\$ 0.13	\$ 0.25	\$ 0.21	\$ 0.12
Net Income (Loss) per share - DILUTED	\$ 0.13	\$ 0.24	\$ 0.21	\$ 0.12

Year ended September 30, 2018	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenues	\$ 3,509,821	\$ 650,125	\$ 727,375	\$ 11,255,000
Operating Income (Loss)	\$ (13,813,348)	\$ (15,034,059)	\$ (15,919,719)	\$ (11,169,109)
Net Income (Loss)	\$ (13,198,878)	\$ (14,884,311)	\$ (15,606,017)	\$ (10,761,272)
Net Income (Loss) per share - BASIC	\$ (0.18)	\$ (0.18)	\$ (0.18)	\$ (0.12)
Net Income (Loss) per share - DILUTED	\$ (0.18)	\$ (0.18)	\$ (0.18)	\$ (0.12)

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following is a description of our common stock and a summary of our preferred stock. You should refer to our Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") and our Amended and Restated Bylaws (the "Bylaws"), each of which is filed as an exhibit to our Annual Report on Form 10-K for the year ended September 30, 2019, to which this exhibit is also appended (the "2019 Annual Report").

We are authorized to issue up to 145,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share. As of September 30, 2019, 95,506,271 shares of common stock and 0 shares of preferred stock were issued and outstanding.

Common Stock

Holders of our common stock are entitled to one vote for each share held on each matter to be voted on by stockholders. There is no cumulative voting in the election of directors. The holders of our common stock have no preemptive or conversion rights and are not subject to further calls or assessments. There are no redemption or sinking fund provisions applicable to our common stock. The rights of the holders of the Common Stock are subject to any rights that may be fixed for holders of preferred stock, if any. Holders of our common stock are entitled to receive ratably dividends out of funds legally available, if and when declared from time to time by our board of directors. In the event of liquidation, dissolution or winding up of the affairs of the Company, holders of our common stock are to share in all assets remaining after the payment of liabilities and any preferential distributions payable to preferred stockholders, if any.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "ARWR". The transfer agent and registrar for our common stock is Computershare Trust Company.

Preferred Stock

Under our Certificate of Incorporation, our board of directors has the authority, without further action by stockholders, to designate up to 5,000,000 shares of preferred stock, \$0.001 par value per share, in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including but not limited to dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of our common stock.

Delaware Anti-Takeover Law

We are subject to Section 203 of the General Corporation Law of the State of Delaware (the "DGCL"). Section 203 of the DGCL generally prohibits a public Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
 - the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine whether shares held subject to the plan will be tendered in a tender or exchange offer; or
 - on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.
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Section 203 of the DGCL defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 of the DGCL defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

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AMENDMENT NO. 1 TO LICENSE AGREEMENT

THIS AMENDMENT NO. 1 TO LICENSE AGREEMENT (this “Amendment”) is made and entered into as of 18 December 2018 (the “Amendment Effective Date”) and is by and between Arrowhead Pharmaceuticals, Inc., a Delaware corporation with a place of business at 225 South Lake Avenue, Suite 1050, Pasadena, California 91101, USA (“Arrowhead”), and Janssen Pharmaceuticals, Inc., a Pennsylvania corporation with a place of business at 1125 Trenton-Harbourton Road, Titusville, New Jersey 08560, USA (“Janssen”) and amends the License Agreement between the Parties dated October 3, 2018.

RECITALS:

WHEREAS, the Parties have entered into a License Agreement, dated as of October 3, 2018, pursuant to which Arrowhead granted Janssen an exclusive license to Develop and Commercialize Licensed Products (the “License Agreement”);

WHEREAS, under the License Agreement, Arrowhead is responsible for the conduct and completion of the Ongoing Phase 1/2 Study as described in the Clinical Plan;

WHEREAS, the Parties wish to make certain modifications to the Clinical Plan and the Ongoing Phase 1/2 Study to add a cohort that includes treatment with ARO-HBV, a nucleoside analog and a Janssen capsid assembly modulator;

WHEREAS, this Amendment modifies the License Agreement to address the changes in the Clinical Plan, a related change in the milestone payments and the supply of the Janssen capsid assembly modulator compound for Arrowhead’s use in the Ongoing Phase 1/2 Study;

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants of the Parties set forth in this Amendment, the Parties hereto agree as follows:

AGREEMENT:

1. Definitions. Capitalized terms used herein but not otherwise defined herein will have their respective meanings set forth in the License Agreement.

2. Amendments to the License Agreement.

2.1. Section 1.10 of the License Agreement is hereby replaced in its entirety with the following:

“1.10 “Ancillary Agreements” means, collectively, the Pharmacovigilance Agreement entered into in accordance with Section 5.6.4 and any supply agreement and quality agreement entered into in accordance with Section 7.1 or Section 7.2 of this Agreement or Section b.3 of Exhibit H.”

2.2. The following definitions are added between Sections 1.27 and 1.28 of the License Agreement:

“1.27bis “CAM” means the capsid assembly modulator known as JNJ-56136379.

1.27ter “CAM Cohort” means the cohort in the Ongoing Phase 1/2 Study to assess ARO-HBV in combination with a nucleoside analog and the CAM, as further specified in the Clinical Plan.”

2.3. The first sentence of Section 5.1 of the License Agreement is hereby replaced in its entirety with the following:

“Arrowhead shall be responsible for the conduct and completion of the Ongoing Phase 1/2 Study.”

2.4. The following sentences are added to Section 5.1 of the License Agreement:

*“Arrowhead shall bear [**] costs and expenses resulting from the conduct and completion of the Ongoing Phase 1/2 Study, except that (a) Janssen shall reimburse [**] conduct of the CAM Cohort on a quarterly basis; and (b) Janssen shall supply, [**], the CAM compound required for the conduct of the CAM Cohort in a form suitable for human administration. Such supply shall be governed by and the Parties agree to comply with the terms and conditions laid down in Exhibit H. Arrowhead shall provide Janssen with detailed [**] overviews of the [**] of the conduct of the CAM Cohort.”*

2.5. The following sentence is added to Section 5.1 of the License Agreement as the final sentence to that section:

“Notwithstanding anything herein to the contrary, Arrowhead’s diligence obligation with respect to the conduct and completion of the CAM Cohort is to use Commercially Reasonable Efforts until directed by the JSC, following a JSC decision in accordance with Section 3.6 of this Agreement, to stop such efforts.”

2.6. The following sentence is added to Section 5.6.4 of the License Agreement:

“In addition, the Parties shall, prior to dosing of the first patient in the CAM Cohort, agree on safety data exchange procedures concerning adverse events with respect to the CAM that arise during the CAM Cohort, which shall be attached to this Agreement as Exhibit I.”

2.7. The following section 5.13 is added to the License Agreement:

“5.13 CAM Cohort Data. *All data resulting from the CAM Cohort shall be deemed Confidential Information of both Parties.”*

2.8. The table in relation to the milestone payments in Section 8.3 of the License Agreement is hereby replaced in its entirety with the following:

Milestone Event	ARO-HBV Product Milestone Amount (USD)	Non-ARO-HBV Product Milestone Amount (USD)
[**]	[**]	[**]
Upon dosing of fifth patient in the CAM Cohort	[**]	[**]
[**]	[**]	[**]
[**]	[**]	[**]
[**]	[**]	[**]
[**]	[**]	[**]
[**]	[**]	[**]
[**]	[**]	[**]

2.9. The following sentence is added to Section 8.3 of the License Agreement following the table in relation to the milestone payments:

*“In the event that the JSC decides that the CAM Cohort will not be conducted or decides to terminate the CAM Cohort prior to [**], said [**]amount will be payable by Janssen to Arrowhead upon [**].”*

2.10. The Exhibit C to the License Agreement is hereby deleted in its entirety and replaced with the Appendix 1 (entitled ‘Exhibit C – Initial version of Clinical Plan’) which is attached to this Amendment.

2.11. The Appendix 2 (entitled ‘Exhibit H – Terms and conditions governing CAM supply’) which is attached to this Amendment is hereby added as Exhibit H to the License Agreement.

3. Term. This Amendment shall be effective as of the Amendment Effective Date.

4. No further changes. Except as specifically modified herein, no changes are made to the License Agreement and the License Agreement remains in full force and effect. This Amendment is subject to the terms of the License Agreement.

IN WITNESS WHEREOF, the Parties hereto have caused this Amendment to be executed by their duly authorized representatives as of the date first above written.

Arrowhead Pharmaceuticals, Inc.

By /s/ Christopher Anzalone

Christopher Anzalone, Ph.D.
Chief Executive Officer

Janssen Pharmaceuticals, Inc.

By /s/ Jeffrey Smith

Jeffrey Smith
Vice President

APPENDIX 1

Exhibit C

Current version of Clinical Plan

[**]

APPENDIX 2

Exhibit H

Terms and conditions for CAM supply.

- a. Definitions. For the purpose of this Exhibit H, the following terms, whether used in the singular or plural, have the respective meanings set forth below:
- a.1. “Batch” means a specific quantity of Clinical Product that is intended to be of uniform character and quality, tested and found to be within specified limits, and is produced during the same cycle of Manufacture as defined by the applicable Batch record.
 - a.2. “Certificate of Analysis” means a document, signed by an authorized representative of Janssen or any of its Affiliates, describing Specifications for, and testing methods applied to, the Clinical Product, and the results thereof.
 - a.3. “Certificate of Compliance” means a document, signed by an authorized representative of Janssen or any of its Affiliates, certifying that a particular Batch was Manufactured in accordance with GMP and the Specifications.
 - a.4. “Clinical Product” means the CAM compound to be supplied to Arrowhead or its Affiliate under this Exhibit H.
 - a.5. “Manufacture” or “Manufactured” or “Manufacturing” means all stages of the manufacture of a compound, including planning, purchasing, manufacture, processing, compounding, storage, filling, packaging, waste disposal, labeling, leafleting, testing, quality assurance, sample retention, dispatch and supply, as applicable.
 - a.6. “Quality Agreement” means the quality agreement which the Parties will enter into for the supply of the Clinical Product hereunder in accordance with Section b.3 below.
 - a.7. “Specifications” means the list of tests, references to any analytical procedures and appropriate acceptance criteria which are numerical limits, ranges or other criteria for tests as described in the Quality Agreement.
- b. Clinical Product Supply and Documentation.
- b.1. Subject to Section b.3 of this Exhibit H, Janssen will use Commercially Reasonable Efforts to Manufacture and ship (directly or through its Affiliates or any sublicensees) Clinical Product to Arrowhead, [**] in accordance with the terms of
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this Exhibit H and the Quality Agreement and in the quantities and by the dates as set forth below, for use by Arrowhead in the Ongoing Phase 1/2 Study.

Clinical Product	Quantity & presentation	Shipment date (i.e., date on which Clinical Product will be ready for shipment from Beerse)
JNJ-56136379, [**]	[**]	[**]
JNJ-56136379, [**]	[**]	[**]

* This shipment date is subject to Arrowhead's timely confirmation in writing to Janssen of the final packaging design and minimal expiry date for the Clinical Product to be supplied under this Exhibit H. In addition, the exact shipment date is to be confirmed between Janssen and Arrowhead prior to shipment and the Parties shall be in contact to coordinate shipment and delivery of the Clinical Product, through the Janssen Clinical Supply Chain group and an Arrowhead supply contact person to be appointed by Arrowhead.

- b.2. Janssen or its Affiliates will provide Arrowhead, at Janssen's discretion by granting Arrowhead a Right of Reference or otherwise, [**].
- b.3. Arrowhead and Janssen's Affiliate, Janssen Pharmaceutica NV, will enter into a Quality Agreement that sets forth the quality assurance provisions relating to the Manufacture and supply of Clinical Product. The Quality Agreement will be entered into prior to the supply of Clinical Product to Arrowhead.

c. Regulatory Matters.

- c.1. Subject to Janssen's obligation under Section 5.1 of this Agreement to reimburse certain [**], Arrowhead will be responsible for obtaining all regulatory and governmental approvals and permits necessary for Arrowhead's use of Clinical Product(s) in the Ongoing Phase 1/2 Study and for making the required payments, if any, in this respect. As reasonably requested by Arrowhead, Janssen (or its Affiliate) will provide Arrowhead, at Janssen's discretion by [**] which is necessary for obtaining such approvals and permits.
- c.2. Janssen (or its Affiliate) will provide Arrowhead reasonable advance written notice (to the extent reasonably practicable) of any visit or inspection by any Regulatory Authority of a Janssen facility (to the extent it relates to Clinical Product) and shall comply with all other regulatory obligations as set forth in the Quality Agreement.

- d. Testing and Acceptance Process. Upon QP release or other comparable quality review procedure of any Batch of Clinical Product by Arrowhead in accordance with Arrowhead's customary quality processes, Arrowhead shall notify Janssen in writing of (a) its acceptance
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of Clinical Product transferred hereunder or (b) its belief that such Batch of Clinical Product fails to conform to the Specifications or was not Manufactured in compliance with GMP and the Specifications. If the Parties determine that the Clinical Product is not in compliance with GMP or the Specifications, Arrowhead will not use the non-compliant Batch of Clinical Product in humans, and the Parties through the JSC will decide upon the course of action with respect to any non-conforming Clinical Product.

- e. Shipping and Delivery. Clinical Product(s) will be delivered to Arrowhead or its designee [**] PCI Pharma Services, 10/52 Wirraway Drive, Port Melbourne, Victoria, Australia (Incoterms 2010). Title and risk of loss on Clinical Product shall transfer to Arrowhead [**]. Notwithstanding anything to the contrary in this Exhibit H, [**] shall act as importer of record for the import of Clinical Product in Australia and Arrowhead shall be responsible for (i) custom clearance; and (ii) further transportation of Clinical Product from PCI Pharma Services. Each shipment shall be packed, marked and sealed in accordance with the product shipping requirements provided in the Quality Agreement and Specifications. Concurrent with each shipment of Clinical Product, Arrowhead will be provided with an electronic copy of the Certificate of Analysis confirming that such Batch meets the Specifications. Arrowhead shall provide Janssen with any information reasonable required by Janssen to ship and deliver Clinical Product in accordance with this Section e.
- f. Supporting data and information. The supporting data and information provided by Janssen in accordance with Sections b.2 and c.1 above shall be considered Confidential Information of Janssen. Arrowhead shall only be authorized to use such data and information to the extent required for the conduct of the Ongoing Phase 1/2 Study and nothing in this Exhibit H is intended to transfer ownership of such data and information.

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AMENDMENT NO. 2 TO LICENSE AGREEMENT

THIS **AMENDMENT NO. 2 TO LICENSE AGREEMENT** (this “Second Amendment”) is made and entered into as of February 4, 2019 (the “Second Amendment Effective Date”) and is by and between Arrowhead Pharmaceuticals, Inc., a Delaware corporation with a place of business at 225 South Lake Avenue, Suite 1050, Pasadena, California 91101, USA (“Arrowhead”), and Janssen Pharmaceuticals, Inc., a Pennsylvania corporation with a place of business at 1125 Trenton-Harbourton Road, Titusville, New Jersey 08560, USA (“Janssen”) and amends the License Agreement between the Parties dated October 3, 2018.

RECITALS:

WHEREAS, the Parties have entered into a License Agreement, dated as of October 3, 2018, pursuant to which Arrowhead granted Janssen an exclusive license to Develop and Commercialize Licensed Products (the “License Agreement”);

WHEREAS, the Parties now wish to amend the License Agreement to create a framework for Arrowhead to provide additional support to Janssen for certain activities in relation to the Licensed Product;

WHEREAS, under the License Agreement, Arrowhead is responsible for the conduct and completion of the Ongoing Phase 1/2 Study, which includes the CAM Cohort;

WHEREAS, the Parties now wish to agree on the safety data exchange procedures for the CAM Cohort;

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants of the Parties set forth in this Second Amendment, the Parties hereto agree as follows:

AGREEMENT:

1. Definitions. Capitalized terms used herein but not otherwise defined herein will have their respective meanings set forth in the License Agreement.
 2. Amendments to the License Agreement.
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2.1. The following definition is added between Sections 1.19 and 1.20 of the License Agreement:

*“1.19bis **“Arrowhead Services”** has the meaning set forth in Section 5.14.”*

2.2. Section 3.2.1 of the License Agreement is hereby replaced in its entirety with the following:

“3.2.1 serve as a forum to discuss and monitor the activities under the Clinical Plan and the Arrowhead Services and to approve changes to the Clinical Plan as provided for in Section 5.1.”

2.3. The following sentence is added to Section 5.3.2 of the License Agreement:

“Arrowhead shall use Commercially Reasonable Efforts to provide the Arrowhead Services.”

2.4. The last sentence of Section 5.6.4 of the License Agreement (which was added to the License Agreement by the Amendment No. 1 to the License Agreement entered into by the Parties on 18 December 2018) is hereby replaced in its entirety with the following two sentences:

“Notwithstanding the foregoing, the Parties shall not be required to enter into the Pharmacovigilance Agreement in the event that the Ongoing Phase 1/2 Study is fully terminated prior to the initiation of the first clinical study by Janssen for the Licensed Product. The Parties shall comply with the safety data exchange procedures laid down in Exhibit I for the CAM Cohort and Exhibit I shall serve as the pharmacovigilance agreement for the CAM Cohort for as long as Exhibit I has not been superseded by the Pharmacovigilance Agreement.”

2.5. The following section 5.14 is added to the License Agreement:

*“5.14 **Arrowhead Services.** Upon request by Janssen, the Parties may negotiate in good faith to enter into a Statement of Work, a template of which is attached to this Agreement as Exhibit J, under which Arrowhead would provide certain services to Janssen in relation to the [**] of any Licensed Product or Licensed Construct on [**] (the **“Arrowhead Services”**). The Arrowhead Services shall be governed by the terms and conditions of this Agreement, and the terms and conditions of the Statement of Work concerned. In the event of any conflict between the terms and conditions of this Agreement and the terms and conditions of a Statement of Work entered into between the Parties under this Section 5.14, the terms and conditions of the Statement of Work shall prevail.”*

2.6. The Appendix 1 (entitled ‘Exhibit I – Safety data exchange procedures for the CAM Cohort) which is attached to this Second Amendment is hereby added as Exhibit I to the License Agreement.

2.7. The Appendix 2 (entitled ‘Exhibit J – Statement of Work Template’) which is attached to this Second Amendment is hereby added as Exhibit J to the License Agreement.

3. Term. This Second Amendment shall be effective as of the Second Amendment Effective Date.

4. No further changes. Except as specifically modified herein, no changes are made to the License Agreement and the License Agreement remains in full force and effect. This Second Amendment is subject to the terms of the License Agreement.

IN WITNESS WHEREOF, the Parties hereto have caused this Second Amendment to be executed by their duly authorized representatives as of the date first above written.

Arrowhead Pharmaceuticals, Inc.

By /s/ Thomas Schluep

Print Name Thomas Schluep

Title Vice President, Program Management

Janssen Pharmaceuticals, Inc.

By /s/ Flavia Pease

Print Name Flavia Pease

Title Vice President Finance and Chief Financial Officer

APPENDIX 1

Exhibit I

Safety data exchange procedure for the CAM Cohort¹

[**]

APPENDIX 2

Exhibit J

Statement of Work Template

[**]

[***] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

**AMENDMENT #1 TO RESEARCH
COLLABORATION AND OPTION AGREEMENT**

This Amendment (hereinafter “Amendment #1”), is made, and effective, as of the date of execution by the last Party to sign below (the “Execution Date”), is to the Research Collaboration and Option Agreement having an Execution Date of **October 3, 2018** (the “Agreement”), by and between Arrowhead Pharmaceuticals, Inc., a Delaware corporation with a place of business at 225 South Lake Avenue, Suite 1050, Pasadena, California 91101, USA (“Arrowhead”), and Janssen Pharmaceuticals, Inc., a Pennsylvania corporation with a place of business at 1125 Trenton-Harbourton Road, Titusville, New Jersey 08560, USA (“Janssen”).

WHEREAS, Janssen and Arrowhead find it in their respective interests to modify the Agreement to include a process for conducting validation/preselection work on one or more targets to inform a Janssen decision on whether or not to propose such target(s) as Target(s) under the Agreement;

NOW THEREFORE, in consideration of the foregoing and the agreements below, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1 Definitions. Unless the context otherwise requires, the terms in this Amendment #1 with initial letters capitalized shall have the meanings described below or the meaning as designated in the indicated places throughout this Amendment #1. All other such terms not otherwise defined herein shall have the meanings ascribed thereto in the Agreement.

1.1 “Target Validation Costs” shall mean FTE Costs and Out-of-Pocket Costs (each analogously applied to work hereunder) incurred by the Parties and their Affiliates following the Effective Date of this Amendment #1, in each case to the extent incurred under the Target Validation Plan.

1.2 “Target Validation Plan” shall have the meaning as set for in section 2.2 below.

1.3 “Validation Compound Delivery Period” shall mean the period commencing upon the Parties’ mutual agreement in writing of the Target Validation Plan and ending [**] after such agreement.

1.4 “Validation Compounds” shall have the meaning as set for in section 2.2 below.

1.5 “Validation Data and Know-How” shall have the meaning as set forth in section 2.4 below.

1.6 “Validation Selection Period” shall mean the period commencing upon the Parties’ mutual agreement in writing of the Target Validation Plan and ending on the [**] anniversary of such agreement, except that if the agreed upon quantity of any Validation Compounds to be provided by Arrowhead are received by Janssen after the Validation Compound Delivery Period, then the Validation Selection Period shall be automatically extended by one day for each day past the end of the Validation Compound Delivery Period that the agreed upon quantity of such Validation Compound is received by Janssen.

1.7 “Validation Target” shall have the meaning as set for in section 2.1 below.

2. Target Validation/Selection.

2.1 Validation Targets. Promptly following execution of this Amendment #1, and continuing through the [**] anniversary of the Effective Date of the Agreement, Janssen may, at its own discretion, propose to Arrowhead targets for work under this Amendment #1. Arrowhead will accept or reject such proposed targets in a process analogous to the process for Target acceptance in Section 4.1.2 of the Agreement, except that Arrowhead shall have an additional right to reject a proposed target for work hereunder if Arrowhead has conducted rodent studies in an active research program against the proposed target. Such a proposed target that is accepted by Arrowhead will be a “Validation Target” for the purposes of this Amendment 1. Janssen may propose targets until up to [**] Validation Targets are identified. For clarity, the terms proposed herein relative to Validation Targets do not amend Janssen’s right to timely select any target that is not a Validation Target as a Target in accordance with Article 4 of the Agreement.

2.2 Target Validation Plan. Promptly following the acceptance of a Validation Target, the Parties shall mutually agree to a research plan to be conducted by Arrowhead and Janssen to generate data on such Validation Target to guide Janssen’s selection of Targets (“Target Validation Plan”). Such Target Validation Plan shall include, on behalf of Arrowhead, an obligation to identify, manufacture, and deliver [**] sRNAi compounds (“Validation Compounds”) to Janssen for each Validation Target, and on behalf of Janssen, a right to conduct model-specific studies to inform its Target selection. The Parties shall use Commercially Reasonable Efforts to complete the Target Validation Plan. Arrowhead will use its reasonable judgment, in consultation with Janssen, to select the Validation Compounds based on its determination of their potential effectiveness in modulating the Validation Targets. Arrowhead will manufacture and deliver to Janssen sufficient quantities of each of the Validation Compounds to complete the agreed model-specific studies.

2.3 Target Validation Plan Costs. Janssen will bear all Target Validation Costs for work under the Target Validation Plan. Such costs shall be reported by Arrowhead and paid by Janssen on a quarterly basis in accordance with a process analogous to that for Research Costs in Section 7.1 of the Agreement.

2.4 Validation Data and Know-How Sharing. The Parties will promptly and diligently share all material data and know-how generated in the course of completing work under the Target Validation Plan (“Validation Data and Know-How”) through the JSC or appropriate subcommittee. The Parties will promptly respond to any reasonable question of the other Party regarding such work or the Validation Data and Know-How. Validation Data and Know-How shall be deemed the Confidential Information of both Parties under the Agreement and subject to the licenses of each Party to the other under Section 2.1.3 except that the chemical identity of the Validation Compounds will be the Confidential Information of Arrowhead only and the licenses of Section 2.1.3 will not apply to the exploitation of the Validation Compounds.

2.5 Janssen Right to Select Validation Targets. At any time during the Validation Selection Period, in addition to the rights provided under the Agreement, Janssen shall have the right to: (a) select Validation Targets for inclusion as Targets under the Agreement, and/or (b) replace any Targets previously selected under the Agreement with Validation Targets, in each case, via a Target Proposal in accordance with Section 4.1.2 of the Agreement, with the exceptions under Section 4.1.2 that (i) the allowed time period is the Validation Selection Period and (ii) Arrowhead will not have the right to reject such a Target Proposal.

3. Inventions. During the Validation Selection Period, the reporting, ownership and patent rights with regard to any inventions arising from work under any Target Validation Plan shall be governed by Article X of the Agreement as if such work were under the Agreement and Validation Compounds were Licensed Constructs. Upon termination of the Validation Selection Period and as to the Validation Targets not made Targets under the Agreement, then Patents or Inventions subject to this Section will be treated as if such Validation Target was the basis of a Program and the Program is a terminated Program under Section 15.6.2 of the Agreement.

4. Arrowhead Limited Use of Validation Targets. Arrowhead shall not collaborate with any third party on any Validation Target during the Validation Selection Period. For clarity, after the expiration of the Validation Selection Period, this Amendment #1 shall not prevent or place any encumbrance on Arrowhead to develop compounds, including Validation Compounds, directed toward any Validation Target that is not selected as a Target under the Agreement for its own internal or external business purposes.

IN WITNESS WHEREOF, each Party has caused this Agreement to be duly executed by its authorized representative on the respective date written herein below.

Arrowhead Pharmaceuticals, Inc.

By:/s/ Christopher Anzalone

Name: Christopher
Anzalone
Title: Chief Executive Officer
Date: November 14, 2019

Janssen Pharmaceuticals, Inc.

By:/s/ Jeffrey N. Smith

Name: Jeffrey N. Smith
Title: Vice President
Date: November 14, 2019

Subsidiary	Jurisdiction
Ablaris Therapeutics, Inc.	Delaware
Arrowhead Madison Inc.	Delaware
Arrowhead Australia Pty Ltd	Australia

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Forms S-1 (Nos. 333-164039 and 333-161344), Forms S-3 (Nos. 333-228598, 333-214315, 333-214311, 333-213484, 333-202737, 333-191922, 333-188718, 333-178532, 333-178073, 333-178072, 333-144109, 333-137329, 333-132310, 333-124065, and 333-113065), and Forms S-8 (Nos. 333-230621, 333-223836, 333-210117, 333-202741, 333-198920, 333-194596, 333-190970, 333-180692, 333-170252, 333-136225, 333-124066, and 333-120072) of Arrowhead Pharmaceuticals, Inc. of our report dated November 25, 2019, with respect to the consolidated balance sheets of Arrowhead Pharmaceuticals, Inc. and Subsidiaries as of September 30, 2019 and September 30, 2018, and the related consolidated statements of operations and comprehensive income (loss), stockholders' equity and cash flows for each of the years in the three-year period ended September 30, 2019, and the effectiveness of internal control over financial reporting as of September 30, 2019, which reports appear in the September 30, 2019 annual report on Form 10-K of Arrowhead Pharmaceuticals, Inc.

/s/ Rose, Snyder & Jacobs LLP

Encino, California

November 25, 2019

**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 Pharmaceuticals, Inc., certify that:

1. I have reviewed this Annual Report on Form 10-K of Arrowhead Pharmaceuticals, Inc.;
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: November 25, 2019

/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 Pharmaceuticals, Inc., certify that:

1. I have reviewed this Annual Report on Form 10-K of Arrowhead Pharmaceuticals, Inc.;

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: November 25, 2019

/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 Pharmaceuticals, Inc. (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, 2019, 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: November 25, 2019

/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 Pharmaceuticals, Inc. and will be retained by Arrowhead Pharmaceuticals, Inc. 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 Pharmaceuticals, Inc. (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, 2019, 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: November 25, 2019

/s/ Kenneth A. Myszkowski

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 Pharmaceuticals, Inc. and will be retained by Arrowhead Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.