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, 2024

☐ **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	**46-0408024**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

(626) 304-3400
177 E. Colorado Blvd, Suite 700
Pasadena, California 91105
(Address and telephone number of principal executive offices)

Securities registered pursuant to 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 the 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

The aggregate market value of issuer's voting and non-voting outstanding common stock held by non-affiliates was approximately $3.0 billion based upon the closing stock price of issuer's common stock on March 31, 2024. 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, 2024, 124,434,442 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 2025 Annual Meeting of Stockholders are incorporated by reference into Part III hereof.

PART I

PART II

PART III

PART IV

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, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, 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," "might," "will," "expect," "believe," "anticipate," "goal," "endeavor," "strive," "intend," "plan," "project," "could," "estimate," "target," "might," "forecast," or "continue" or the negative of these words 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 business, or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our expectations regarding regulatory approval for and commercial launch of plozasiran our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future; our beliefs and expectations regarding the amount and timing of future milestone, royalty or other payments that could be due to or from third parties under existing agreements; and our estimates regarding future revenues, research and development expenses, capital requirements and payments to third parties.

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 and timing of certain events may differ materially from the results discussed, projected, anticipated or indicated in any forward-looking statements. Forward-looking statements are not guarantees of future performance and our actual results of operations, financial condition and cash flows may differ materially. 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 (the "SEC"). 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. Statements made herein are as of the date of the filing of this Annual Report on Form 10-K with the SEC and should not be relied upon as of any subsequent date. 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.

PART I

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 to Arrowhead Madison Inc. ("Arrowhead Madison"), Arrowhead Australia Pty Ltd ("Arrowhead Australia"), and Visirna Therapeutics Inc. ("Visirna") (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

A. Overview

The Company 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, the Company's therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes.

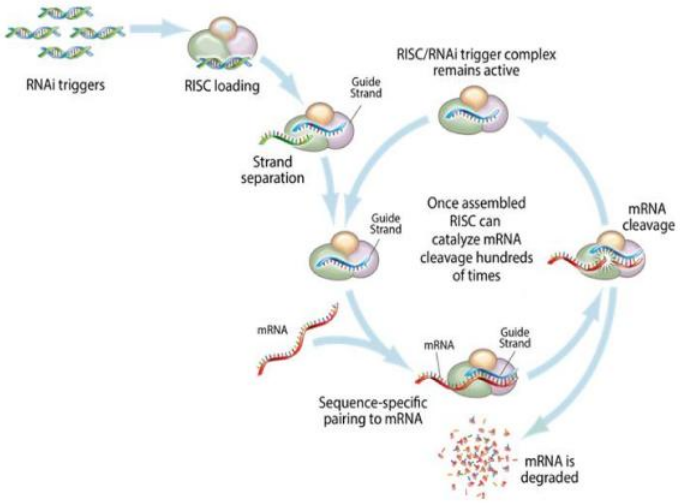
The Company's most advanced candidate, plozasiran, has completed a Phase 3 study in patients with familial chylomicronemia syndrome (FCS) and expects to have its first commercial launch in 2025, provided the United States Food and Drug Administration (the "FDA") accepts the New Drug Application ("NDA") for filing and after a successful review and subsequent approval. The Company's pipeline of 16 clinical stage investigational medicines range in development stage from Phase 1 to Phase 3. In addition, the Company has a robust discovery stage pipeline which is capable of generating multiple new clinical candidates each year.

The Company endeavors to serve unmet medical needs and change lives leveraging the versatility of its proprietary RNAi-based technology. The Company is acutely aware of the urgent need to develop solutions for the many diseases that have genetic targets that are otherwise undruggable by small molecules or biologics. To that end, the Company embraced its bold goal and strives to have 20 individual drugs, either partnered or wholly owned, in clinical trials or on the market in 2025.

RNA Interference and the Benefits of RNAi Therapeutics

RNA interference ("RNAi") is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. 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 are 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 Benefits of RNAi as a Therapeutic Modality:

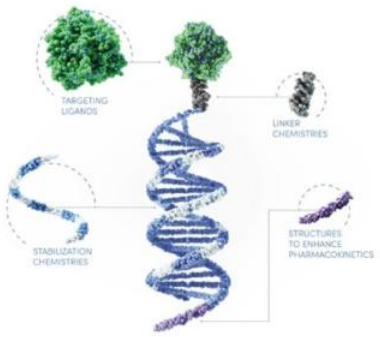
- Silences the expression of disease associated genes;
- Potential to address any target in the transcriptome including previously "undruggable" targets;
- Rapid lead identification;
- High specificity;
- Opportunity to use multiple RNA sequences in one drug product for synergistic silencing of related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

Targeted RNAi Molecule (TRiM™) Platform

The Company'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 the Company's development philosophy and the TRiM™ platform builds on more than a decade of work on actively targeted drug delivery vehicles. The Company's scientists have discovered ways to progressively "TRiM" away extraneous features and chemistries and retain optimal pharmacologic activity.

The TRiM™ platform is comprised of a highly potent RNA trigger identified using the Company'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 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. The Company also believes that for RNAi to reach its true potential, it must target organs outside the liver. The Company is leading this expansion with the TRiM™ platform, which has shown the potential to reach multiple tissues, including liver, lung, central nervous system (CNS), muscle, and adipose tissue.



TRiM™ – *Targeting the gene, to Silence the disease*

- ***Activity*** characterized by depth & duration of effect
  - Ability to unlock previously undruggable targets
- ***Specificity*** to maximize activity and innate stability with the potential for reduced off-target effects
- ***Versatility*** in formulation & ligand design offers multiple routes of administration, and access to multiple tissues
  - Facilitates rapid drug development and speed to patients
- ***Simplicity*** in design translates to relatively lower costs, and production at scale

RNA Chemistries

The structure and chemistries of the oligonucleotide molecules used to trigger the RNAi mechanism can be tailored for optimal activity. The Company'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, the Company'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.

B. Pipeline

The Company 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 the Company's RNAi technologies enables the Company to potentially address conditions in virtually any therapeutic area and pursue disease targets that are not otherwise addressable by small molecules and biologics. The Company is focused on bringing the promise of RNAi to address diseases outside of the liver, and its pipeline now includes disease targets in the liver, lung, central nervous system (CNS), muscle and adipose tissue.

Plozasiran (ARO-APOC3)

Plozasiran (formerly ARO-APOC3) is designed to reduce production of Apolipoprotein C-III (apoC-III), a component of triglyceride rich lipoproteins (TRLs) including Very Low Density Lipoprotein (VLDL) and chylomicrons, a key regulator of triglyceride metabolism. The Company believes 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. The Company is currently investigating plozasiran in one Phase 2 clinical trial and four Phase 3 clinical trials. In the Phase 3 PALISADE trial in patients with familial chylomicronemia syndrome (FCS), plozasiran has met its primary endpoint of triglyceride reduction as well as all of its key (alpha controlled) secondary endpoints. The Company is currently in the process of seeking regulatory approval for plozasiran for the treatment of FCS.

Hypertriglyceridemia: Elevated triglyceride levels are an independent risk factor for cardiovascular disease. Severely elevated triglycerides in patients with severe hypertriglyceridemia (SHTG) or familial chylomicronemia syndrome (FCS), a rare genetic disorder, can result in potentially fatal acute pancreatitis.

Study Name: Study of ARO-APOC3 in Adults With Dyslipidemia
A Phase 2 Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of ARO-APOC3 in Adults With Dyslipidemia
ClinicalTrials.gov Identifier: NCT05413135

Study Name: Study of ARO-APOC3 in Adults With FCS (PALISADE)
A Phase 3 Study to Evaluate the Efficacy and Safety of ARO-APOC3 in Adults With Familial Chylomicronemia Syndrome
ClinicalTrials.gov Identifier: NCT05089084

Study Name: Study of Plozasiran (ARO-APOC3) in Adults With Severe Hypertriglyceridemia (SHASTA-3)
Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Plozasiran in Adults With Severe Hypertriglyceridemia
ClinicalTrials.gov Identifier: NCT06347003

Study Name: Study of Plozasiran in Adults With Severe Hypertriglyceridemia (SHASTA-4)
Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Plozsiran in Adults With Severe Hypertriglyceridemia
ClinicalTrials.gov Identifier: NCT06347016

Study Name: Phase 3 Study of Plozasiran in Adults With Hypertriglyceridemia (MUIR-3)
Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Plozasiran in Adults With Hypertriglyceridemia
ClinicalTrials.gov Identifier: NCT06347133

Zodasiran (ARO-ANG3)

Zodasiran (formerly 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. The Company is currently investigating zodasiran in two Phase 2b clinical trials.

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

Study Name: Study of ARO-ANG3 in Adults With Mixed Dyslipidemia (ARCHES-2)
A Double-blind, Placebo-controlled Phase 2b Study to Evaluate the Efficacy and Safety of ARO-ANG3 in Adults With Mixed Dyslipidemia
ClinicalTrials.gov Identifier: NCT04832971

Study Name: Study of ARO-ANG3 in Participants With Homozygous Familial Hypercholesterolemia (HoFH) (GATEWAY)
Phase 2 Study to Evaluate the Safety and Efficacy of ARO-ANG3 in Subjects with Homozygous Familial Hypercholesterolemia (HoFH)
ClinicalTrials.gov Identifier: NCT05217667

ARO-PNPLA3

ARO-PNPLA3 (formerly JNJ-75220795) is an investigational RNAi therapeutic designed to reduce liver expression of patatin-like phospholipase domain containing 3 (PNPLA3) as a potential treatment for patients with metabolic-dysfunction associated steatohepatitis (MASH). PNPLA3 has strong genetic and preclinical validation as a driver of fat accumulation and damage in the livers of patients who carry the common I148M mutation. Former licensee Janssen Pharmaceuticals, Inc. investigated ARO-PNPLA3 in two Phase 1 clinical trials.

MASH: MASH is a subgroup of steatotic liver disease (MASLD) in which hepatic cell injury and inflammation has developed over background steatosis. The I148M genetic variant in the PNPLA3 gene is involved with the underlying pathophysiology and is a known risk factor for hepatic steatosis, steatohepatitis, elevated plasma liver enzyme levels, hepatic fibrosis and cirrhosis. The rising prevalence of MASH presents a significant health burden in many developed countries.

ARO-INHBE

ARO-INHBE is designed to reduce the hepatic expression of the INHBE gene and its secreted gene product, Activin E. INHBE is a promising genetically validated target in which loss-of-function INHBE variants in humans are associated with lower risk of obesity and metabolic diseases, such as type 2 diabetes. The Company has filed for regulatory clearance to initiate a Phase 1/2a clinical trial of ARO-INHBE.

ARO-RAGE

ARO-RAGE is designed to reduce production of the Receptor for Advanced Glycation End products (RAGE) as a potential treatment for various inflammatory pulmonary diseases. The Company is currently investigating ARO-RAGE in a Phase 1/2a clinical trial.

Study Name: Study of ARO-RAGE in Healthy Subjects and Patients With Inflammatory Lung Disease
A Phase 1/2a Study Evaluating the Effects of ARO-RAGE in Healthy Subjects and Patients With Inflammatory Lung Disease
ClinicalTrials.gov Identifier: NCT05276570

ARO-MUC5AC

ARO-MUC5AC is designed to reduce production of mucin 5AC (MUC5AC) as a potential treatment for various muco-obstructive pulmonary diseases. The Company is currently investigating ARO-MUC5AC in a phase 1/2a clinical trial.

Study Name: Study of ARO-MUC5AC in Healthy Subjects and Patients With Muco-Obstructive Lung Disease
A Phase 1/2a Study to Evaluate the Effects of ARO-MUC5AC in Healthy Subjects and Patients with Muco-Obstructive Lung Disease
ClinicalTrials.gov Identifier: NCT05292950

ARO-MMP7

ARO-MMP7 is designed to reduce expression of matrix metalloproteinase 7 (MMP7) as a potential treatment for Idiopathic Pulmonary Fibrosis (IPF). The Company is currently investigating ARO-MMP7 in a Phase 1/2a clinical trial.

Study Name: Study of ARO-MMP7 Inhalation Solution in Healthy Subjects and Patients With Idiopathic Pulmonary Fibrosis
A Phase 1/2a Study Evaluating the Effects of ARO-MMP7 Inhalation Solution in Healthy Subjects and Patients With Idiopathic Pulmonary Fibrosis
ClinicalTrials.gov Identifier: NCT05537025

ARO-DUX4

ARO-DUX4 is designed to target the gene that encodes human double homeobox 4 (DUX4) protein as a potential treatment for patients with facioscapulohumeral muscular dystrophy.

Facioscapulohumeral Muscular Dystrophy: Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant disease associated with the failure to maintain complete epigenetic suppression of DUX4 expression in differentiated skeletal muscle, leading to overexpression of DUX4, which is myotoxic and can lead to muscle degeneration. As DUX4 expression is recognized as the cause of muscle pathology in FSHD patients, the Company believes that the selective targeting and knockdown of DUX4 using RNAi may prevent or reverse downstream myotoxicity and lead to muscle repair and improvement in muscle function in patients. There are currently no effective treatments specifically for FSHD.

Study Name: Study of ARO-DUX4 in Adult Patients With Facioscapulohumeral Muscular Dystrophy Type 1
A Phase1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARO-DUX4 in Adult Patients With Facioscapulohumeral Muscular Dystrophy Type 1.
ClinicalTrials.gov Identifier: NCT06131983

ARO-DM1

ARO-DM1 is designed to reduce expression of the dystrophia myotonica protein kinase (DMPK) gene. There is currently no approved disease-modifying therapy for type 1 myotonic dystrophy (DM1). Treatments have focused on symptomatic management, including physical therapy, exercise, ankle-foot orthoses, wheelchairs, and other assistive devices. The Company is currently investigating ARO-DM1 in a Phase 1/2a clinical trial.

Type 1 Myotonic Dystrophy: Type 1 myotonic dystrophy is an autosomal dominant, debilitating, chronic progressive multisystem disorder characterized by an expansion of a highly unstable CUG^{exp} in the DMPK gene. Patients with DM1 have muscle weakness and wasting, myotonia, cataracts, and often have cardiac conduction abnormalities, and may become physically disabled and have a shortened life span.

Study Name: Study of ARO-DM1 in Subjects With Type 1 Myotonic Dystrophy
A Phase 1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARO-DM1 in Subjects With Type 1 Myotonic Dystrophy Who Are ≥18 to ≤ 65 Years
ClinicalTrials.gov Identifier: NCT06138743

ARO-ATXN2

ARO-ATXN2 is designed to reduce the expression of the ATXN2 gene as a potential treatment for spinocerebellar ataxia 2 (SCA2). SCA2 is a progressive cerebellar ataxia with instability of stance, speech and swallow disorder, pain, spasticity, and ocular signs, caused by gain of function of mutant expanded polyQ ATXN2 protein. The Company is currently investigating ARO-ATXN2 in a Phase 1 clinical trial.

Study Name: Study of ARO-ATXN2 Injection in Adults With Spinocerebellar Ataxia Type 2
A Phase 1 Placebo-Controlled Dose Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARO-ATXN2 in Adult Subjects With Spinocerebellar Ataxia Type 2
ClinicalTrials.gov Identifier: NCT06672445

ARO-C3

ARO-C3 is designed to reduce production of complement component 3 (C3) as a potential therapy for patients with various complement mediated or complement associated renal diseases. The Company is currently investigating ARO-C3 in a Phase 1/2a clinical trial.

Complement-Mediated Renal Disease: A number of rare renal diseases result from uncontrolled activation of the alternative pathway of complement, leading to progressive glomerular damage, proteinuria, hematuria, and impaired kidney function, and often resulting in end-stage renal disease (ESRD). In addition, dysregulation of the alternative

complement pathway has been shown to play a role in the pathogenesis and progression of disease in some of the more common glomerulopathies. Silencing C3 may be a therapeutic approach for treatment of these conditions.

Study Name: Study of ARO-C3 in Adult Healthy Volunteers and Patients With Complement-Mediated Renal Disease
A Phase 1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and/or Pharmacodynamics of ARO-C3 in Adult Healthy Volunteers and in Adult Patients With Complement-Mediated Renal Disease
ClinicalTrials.gov Identifier: NCT05083364

ARO-CFB

ARO-CFB is designed to reduce hepatic expression of complement factor B (CFB), which plays an important regulatory role in amplifying complement alternative pathway activation and has been identified as a promising therapeutic target. ARO-CFB is being developed as a potential treatment for complement mediated kidney diseases such as immunoglobulin A nephropathy (IgAN), which is the most common glomerular disease worldwide and carries a high lifetime risk of progression to end-stage renal disease. Additionally, ARO-CFB may have clinical applications in non-renal diseases involving complement activation. The Company is currently investigating ARO-CFB in a Phase 1/2a clinical trial.

Complement-Mediated Disease: A number of rare renal diseases result from uncontrolled activation of the alternative pathway of complement, leading to progressive glomerular damage, proteinuria, hematuria, and impaired kidney function, and often resulting in end-stage renal disease (ESRD). In addition, dysregulation of the alternative complement pathway has been shown to play a role in the pathogenesis and progression of disease in some of the more common glomerulopathies. Silencing CFB may be a therapeutic approach for treatment of these conditions.

Study Name: Study of ARO-CFB in Adult Healthy Volunteers and Patients With Complement-Mediated Kidney Disease
A Phase 1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single and Multiple Doses of ARO-CFB in Adult Healthy Volunteers and Adult Patients With Complement-Mediated Kidney Disease
ClinicalTrials.gov Identifier: NCT06209177

Collaboration and License Agreements

Glaxosmithkline Intellectual Property (No. 3) Limited ("GSK")

GSK-HSD License Agreement

On November 22, 2021, GSK and the Company entered into an Exclusive License Agreement (the "GSK-HSD License Agreement"). Under the GSK-HSD License Agreement, GSK has received an exclusive license for GSK-4532990 (formerly ARO-HSD). The exclusive license is worldwide with the exception of greater China. GSK is wholly responsible for all clinical development and commercialization of GSK-4532990 in its territory. GSK dosed the first patient in a Phase 2b trial in March 2023.

GSK-4532990

GSK-4532990 (formerly 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 metabolic-dysfunction associated steatohepatitis (MASH) cirrhosis and alcoholic hepatitis and cirrhosis. GSK is conducting Phase 2b clinical trials in patients with MASH and alcohol-related liver disease (ALD).

Metabolic-Dysfunction Associated Steatohepatitis: MASH is liver inflammation and damage caused by a buildup of fat in the liver. This can cause scarring of the liver and in advanced cases can lead to cirrhosis. Alcochol-related liver disease (ALD) represents a spectrum of liver injury resulting from alcohol use, ranging from hepatic steatosis to more advances forms including alcoholic hepatitis (AH), alcohol-associated cirrhosis (AC), and acute AH presenting as acute-on-chronic liver failure.

Study Name: Phase 2b Study of GSK4532990 in Adults With MASH (HORIZON)
17 β-Hydroxysteroid Dehydrogenase Type 13 Minimization for the Treatment of MASH (HORIZON): A Double-Blind, Placebo-Controlled Phase 2b Study to Evaluate the Efficacy and Safety of GSK4532990 in Adults With Pre-Cirrhotic Metabolic-Dysfunction Associated Steatohepatitis
ClinicalTrials.gov Identifier: NCT05583344

GSK-HBV Agreement

On December 11, 2023, the Company entered into an Amended and Restated License Agreement with GSK (the "GSK-HBV Agreement") pursuant to which GSK received a worldwide, exclusive license to develop and commercialize daplusiran/tomligisiran (GSK5637608, formerly JNJ-3989), the Company's third-generation subcutaneously administered RNAi therapeutic candidate being developed as a potential therapy for patients with chronic hepatitis B virus infection. GSK5637608 had previously been licensed to Janssen Pharmaceuticals, Inc. ("Janssen") in October 2018. GSK is currently in the process of initiating a Phase 2 study of daplusiran/tomligisiran followed by bepirovirsen in patients with chronic hepatitis B.

Study Name: A Study of Sequential Therapy With Daplusiran/Tomligisiran (DAP/TOM) Followed by Bepirovirsen in Participants Living With Chronic Hepatitis B (CHB) (B-UNITED)
A Phase 2b, Multi-centre, Randomized, Partially Placebo-controlled, Double-blind Study to Investigate the Safety and Efficacy of Sequential Therapy With Daplusiran/Tomligisiran Followed by Bepirovirsen in Participants With Chronic Hepatitis B Virus on Background Nucleos(t)Ide Analogue Therapy (B-United)
ClinicalTrials.gov Identifier: NCT06537414

Takeda Pharmaceutical Company Limited ("Takeda")

On October 7, 2020, Takeda and the Company entered into an Exclusive License and Co-Funding Agreement (the "Takeda License Agreement"). Under the Takeda License Agreement, Takeda and the Company co-develop the Company's Fazirsiran program (formerly TAK-999 and ARO-AAT), the Company's second-generation subcutaneously administered RNAi therapeutic candidate being developed as a treatment for liver disease associated with alpha-1 antitrypsin deficiency. Within the United States, fazirsiran, if approved, will be co-commercialized under a 50/50 profit sharing structure. Outside the United States, Takeda received an exclusive license to commercialize fazirsiran and will lead the global commercialization strategy, while the Company will be eligible to receive tiered royalties of 20% to 25% on net sales.

Fazirsiran

Fazirsiran is a 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. Fazirsiran 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.

Goal of Fazirsiran Treatment: The goal of Fazirsiran 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 protease to protect healthy lung 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 treatment.

Clinical Trials:

Study Name: Study to Check the Safety of Fazirsiran and Learn if Fazirsiran Can Help People With Liver Disease and Scarring (Fibrosis) Due to an Abnormal Version of Alpha-1 Antitrypsin Protein (REDWOOD)
REDWOOD – A Randomized, Double-blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency-Associated Liver Disease With METAVIR Stage F2 to F4 Fibrosis
ClinicalTrials.gov Identifier: NCT05677971

Study Name: An Extension Study to Learn About the Long-Term Safety of Fazirsiran and if Fazirsiran Can Help People With Alpha-1 Antitrypsin Liver Disease
A Phase 3, Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of fazirsiran in Participants With Alpha-1 Antitrypsin Deficiency-Associated Liver Disease
ClinicalTrials.gov Identifier: NCT05899673

Study Name: Study to Learn About the Safety of Fazirsiran and if it Can Help People With Alpha-1 Antitrypsin Liver Disease With Mild Liver Scarring (Fibrosis)
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Evaluate the Safety and Efficacy of Fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency-Associated Liver Disease With METAVIR Stage F1 Fibrosis
ClinicalTrials.gov Identifier: NCT06165341

Amgen Inc. ("Amgen")

On September 28, 2016, Amgen and the Company entered into two collaboration and license agreements and a common stock purchase agreement. Under the Second Collaboration and License Agreement (the "Olpasiran Agreement"), Amgen received a worldwide, exclusive license to the Company's novel RNAi olpasiran (previously referred to as AMG 890 or 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 Olpasiran Agreement, Amgen is wholly responsible for clinical development and commercialization.

In November 2022, Royalty Pharma Investments 2019 ICAV ("Royalty Pharma") and the Company entered into a Royalty Purchase Agreement (the "Royalty Pharma Agreement"). In consideration for the payments under the Royalty Pharma Agreement, Royalty Pharma is entitled to receive all royalties otherwise payable by Amgen to the Company under the Olpasiran Agreement. The Company remains eligible to receive up to an additional $485.0 million in remaining development, regulatory and sales milestone payments payable from Amgen and Royalty Pharma.

Olpasiran

Olpasiran is designed to reduce production of apolipoprotein A, a key component of lipoprotein(a), which has been genetically linked with increased risk of cardiovascular diseases, independent of cholesterol and LDL levels. Amgen completed a Phase 2 clinical study evaluating the efficacy, safety, and tolerability of olpasiran in subjects with elevated levels of lipoprotein(a). Amgen reported Phase 2 clinical results at the American Heart Association (AHA) Scientific Sessions in November 2022 and simultaneously published in the New England Journal of Medicine. Amgen began evaluating olpasiran in a Phase 3 study to assess the impact of olpasiran on major cardiovascular events in participants with atherosclerotic cardiovascular disease and elevated lipoprotein(a), in a double-blind, randomized, placebo-controlled, multi center study in December 2022.

Study Name: Olpasiran Trials of Cardiovascular Events and Lipoprotein(a) Reduction (OCEAN(a)) - Outcomes Trial
A Double-blind, Randomized, Placebo-controlled, Multicenter Study Assessing the Impact of Olpasiran on Major Cardiovascular Events in Participants With Atherosclerotic Cardiovascular Disease and Elevated Lipoprotein(a)
ClinicalTrials.gov Identifier: NCT05581303

C. Intellectual Property and Other Key Agreements

The Company controls approximately 667 issued patents (including 427 directed to RNAi trigger molecules; 144 directed to targeting groups or targeting compounds; and one for hydrodynamic gene delivery), including European validations, and approximately 745 currently pending patent applications worldwide from 92 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, Lebanon, Mexico, New Zealand, OAPI (African Intellectual Property Organization), Peru, Philippines, Russian Federation, South Africa, Saudi Arabia, Singapore, South Korea, Thailand, Taiwan, Uruguay, Venezuela, and Vietnam.

***RNAi Triggers*:** The Company owns issued patents or has filed patent applications directed to RNAi trigger molecules, which serve as the foundation of the Company's TRiM™ platform, and are targeted to reduce expression of various gene targets. However, the Company cannot guarantee that issued patents will be enforceable or provide adequate protection for the Company, or that pending patent applications will result in issued patents. These patents and patent applications include the following:

Patent Group	Estimated Year(s) of Expiration*
AAT	2035, 2038
ANGPTL3	2038
APOC3	2035, 2038
ATXN2	2044
C3	2043
CFB	2044
COVID	2043
Cx43	2029
DM1	2043
DUX4	2041
Factor 12	2036, 2038
FRP-1	2026
HBV	2032, 2036, 2037
HIF1A	2026
HIF2α	2034, 2036, 2040
HRH1	2027
HSD17B13	2039
HSF1	2030, 2032
KRAS	2033
LPA	2036
MARC1	2044
MMP7	2042
Mob-5	2027
MUC5AC	2042
P2X3	2027
PCSK9	2044
PDtype4	2026
PI4Kinase	2028
PNPLA3	2041
RAGE (AGER)	2042
RRM2	2031
SOD1	2043
SYK	2027
TNF-α	2027, 2028
TSLP	2044
XDH	2042
α-ENaC	2028, 2038
β-Catenin	2033
β-ENaC	2031, 2040

*Assuming issuance of any pending patent applications, and excluding any patent term adjustments or patent term extensions.

***Delivery Technologies*:** The delivery technology-related patents and patent applications, which include components used in the Company'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 Africa, South Korea, Singapore,

Taiwan, and Uruguay. The Company also controls a patent directed to hydrodynamic nucleic acid delivery that issued in the United States. However, the Company cannot guarantee that issued patents will be enforceable or provide adequate protection for the Company, or that pending patent applications will result in issued patents. These various groups of patents and applications are set forth below:

Patent Group	Estimated Year(s) of Expiration*
Targeting ligands and other RNAi delivery and platform technologies	
CNS Intrathecal Delivery Platform	2043
Adipose Delivery Platform	2044
Biologically cleavable linkers	2036
LDLR targeting	2028
Muscle delivery platform	2041
Peptide targeting (CPP-Arg)	2028
Peptide targeting (YM3-10H)	2032
Physiologically labile linkers	2036
PK/PD lipid modifiers	2041
RNAi agent design (5′-phosphate mimic)	2037
Targeting groups (Galactose derivative ligands)	2037
Targeting groups (Galactose derivative trimer-PK)	2031
Targeting groups (αvβ3/αvβ5 integrin)	2034, 2038, 2039
Targeting groups (αvβ6 integrin)	2037, 2038, 2041
Transferrin targeting	2028
Trialkyne linkers	2039
Hydrodynamic delivery	
Third iteration	2024

*Assuming issuance of any pending patent applications, and excluding any patent term adjustments or patent term extensions.

The RNAi and drug delivery patent landscapes are complex and rapidly evolving. As such, the Company may need to obtain additional patent licenses prior to commercialization of its candidates. Please see "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K.

Acquisition of Assets from Novartis

On March 3, 2015, Novartis and the Company entered into an Asset Purchase and Exclusive License Agreement (the "RNAi Purchase Agreement") pursuant to which the Company acquired Novartis's 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 Pharmaceuticals, Inc. ("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.

Non-Exclusively Licensed Patent Rights from Roche

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

- Broad freedom to operate with respect to key patents directed to the primary RNAi-trigger formats: canonical, unlocked nucleotide analogs ("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 the Company its entire rights under certain licenses including: the License and Collaboration Agreement between Roche and Alnylam dated July 8, 2007; 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 (collectively the "RNAi Licenses").

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 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.

D. 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 ("EU"), 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 the Company's current product candidates are expected to be regulated as drugs. The processes for obtaining regulatory approval in the United States 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 the Company's products and its R&D activities and require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

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 United States 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 United States must typically undertake the following:

(1) completion of preclinical laboratory tests, which may include animal and *in vitro* studies, and formulation studies in compliance with the FDA's good laboratory practice ("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 an 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 National Institutes of Health 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.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval or licensure, including that the study was conducted in accordance with cGCP, including review and approval by an independent ethics committee and use of proper procedures for obtaining informed consent from subjects, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems such inspection necessary. The cGCP requirements encompass both ethical and data integrity standards for clinical studies.

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 approximately $4.3 million for fiscal year 2025, for applications requiring clinical data, and the sponsor of an approved NDA is also subject to an annual program fee, currently approximately $0.4 million for fiscal year 2025. These fees are adjusted 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 United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States 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.

The FDA's interpretation of the scope of orphan drug exclusivity may change. The FDA's longstanding interpretation of the Orphan Drug Act is that exclusivity is specific to the orphan indication for which the drug was actually approved. As a result, the scope of exclusivity has been narrow and protected only against competition from the same "use or indication" rather than the broader "disease or condition." In the September 2021 case Catalyst Pharmaceuticals, Inc. v. FDA, a federal circuit court set aside the FDA's narrow interpretation and ruled that orphan drug exclusivity covers the full scope of the orphan-designated disease or condition regardless of whether the drug obtains approval only for a narrower use. The decision concerned amifampridine, a drug used to treat Lambert-Eaton myasthenic syndrome (LEMS). Depending on how the FDA applies the decision beyond this case, it may limit which drugs can receive exclusivity orphan drug.

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. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. The FDA also has increased authority for expedited procedures to withdraw approval of a product or indication approved under accelerated approval if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In addition, the Food and Drug Administration Safety and Innovation Act of 2012 ("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, untitled, or it has come to our attention 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 ("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. However, an applicant may submit an ANDA suitability petition to request the FDA's prior permission to submit an abbreviated application for a drug that differs from the RLD in route of administration, dosage form, or strength, or for a drug that has one different active ingredient in a fixed combination drug product (i.e., a drug product with multiple active ingredients).

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 NDAs 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 referenced 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 for 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 after the receipt of the Paragraph IV certification, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

505(b)(2) New Drug Applications

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant, and for which the applicant has not obtained a right of reference. If the 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional bridging studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new drug candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) 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.

Patent Term Restoration and Extension

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.

Review and Approval of Drugs in the European Union and United Kingdom

In order to market any pharmaceutical product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions governing, among other things, research and development, testing, manufacturing, quality control, safety, efficacy, labeling, clinical trials, marketing authorization, packaging, storage, record keeping, reporting, export and import, advertising, marketing and other promotional practices involving pharmaceutical products, as well as commercial sales, distribution, authorization, approval and post-approval monitoring and reporting of its products. Whether or not a company obtains FDA approval for a pharmaceutical 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 pharmaceutical 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.

The United Kingdom ("UK") formally left the EU on January 31, 2020 ("Brexit") and EU laws now only apply to the UK in respect of Northern Ireland as laid out in the Protocol on Ireland and Northern Ireland. The EU and the UK have agreed on a trade and cooperation agreement ("TCA") which includes provisions affecting the life sciences sector (including on customs and tariffs). There are some specific provisions concerning pharmaceuticals, including the mutual recognition of Good Manufacturing Practice ("GMP") and issued GMP documents. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards.

The UK government has enacted the Medicines and Medical Devices Act 2021. The purpose of the act is to enable the existing regulatory frameworks in relation to human medicines and clinical trials of human medicines, among others, to be updated. The powers under the act may only be exercised in relation to specified matters and must safeguard public health.

The Medicines and Medical Devices Act 2021 supplements the UK Medical Devices Regulations 2002 ("UK Regulations"), which are based on the EU Medical Devices Directive as amended to reflect the UK's post-Brexit regulatory regime. Notably, the UK Regulations do not include any of the revisions that have been made by the EU Medical Devices Regulation (EU) 2017/745, which, since May 26, 2021, applies in all EU member states.

The UK's Medicines and Healthcare products Regulatory Agency ("MHRA") conducted a comprehensive consultation in 2021 on proposals to develop a new UK regime for medical devices in the UK. The proposals include more closely aligning definitions for medical devices and in vitro medical devices with internationally recognized definitions and changing the classification of medical devices according to levels or risk. The proposals are intended to improve patient and public safety and increase the appeal of the UK market. Core aspects of the new regime are planned to come into force on July 1, 2025, with strengthened post-market surveillance proposals to be introduced ahead of this in 2023.

Under the Medical Devices (Amendment) (Great Britain) Regulations 2023, CE marked European medical devices will continue to be accepted for sale in the UK until 2028 or 2030 (depending on the type of device).

Drug and Biologic Development Process

The conduct of clinical trials in the EU is governed by the EU Clinical Trials Regulation (EU) No. 536/2014 ("CTR") which entered into force on January 31, 2022. The CTR replaced the Clinical Trials Directive 2001/20/EC, (Clinical Trials Directive) and introduced a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU.

Under the former regime, which will expire after a transition period of one or three years, respectively, as outlined below in more detail, before a clinical trial can be initiated, it must be approved in each EU member state where there is a site at which the clinical trial is to be conducted. The approval must be obtained from two separate entities: the National Competent Authority ("NCA"), and one or more Ethics Committees. The NCA of the EU member states in which the clinical trial will be conducted must authorize the conduct of the trial, and the independent Ethics Committee must grant a

positive opinion in relation to the conduct of the clinical trial in the relevant EU member state before the commencement of the trial. Any substantial changes to the trial protocol or other information submitted with the Clinical Trial Applications ("CTA") must be submitted to or approved by the relevant NCA and Ethics Committees. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the NCA and to the Ethics Committees of the EU member state where they occur.

A more unified procedure applies under the new CTR. A sponsor is able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal, the Clinical Trials Information System ("CTIS"). One national regulatory authority (the reporting EU member state proposed by the applicant) takes the lead in validating and evaluating the application, and consults and coordinates with the other concerned EU member states. If an application is rejected, it may be amended and resubmitted through the CTIS. If an approval is issued, the sponsor may start the clinical trial in all concerned EU member states. However, a concerned EU member state may in limited circumstances declare an "opt-out" from an approval and prevent the clinical trial from being conducted in such EU member state. The CTR 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 CTIS. The CTR includes a three-year transition period. Member states will work in CTIS immediately after the system has gone live. Since January 31, 2023, submission of initial CTA via CTIS is mandatory and CTIS serves as the single entry point for submission of clinical trial-related information and data. By January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive will need to comply with the CTR and have to be transitioned to CTIS.

Under both the former regime and the new CTR, national laws, regulations, and the applicable GCP and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines on GCP, and the ethical principles that have their origin in the Declaration of Helsinki.

During the development of a medicinal product, the European Medicines Agency ("EMA") and national regulators within the EU provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Committee for Medicinal Products for Human Use ("CHMP") on the recommendation of the Scientific Advice Working Party ("SAWP"). A fee is incurred with each scientific advice procedure, but is significantly reduced for designated orphan medicines. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future Marketing Authorization Application ("MAA") of the product concerned.

Marketing Authorization Procedures

In the EU and in Iceland, Norway and Liechtenstein (together the European Economic Area or "EEA"), after completion of all required clinical testing, pharmaceutical products may only be placed on the market after obtaining a Marketing Authorization ("MA"). To obtain an MA of a drug under EU regulatory systems, an applicant can submit a MAA through, amongst others, a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single MA by the European Commission ("EC") that is valid for all EU member states and, after respective national implementing decisions which must be rendered within 30 days, in the three additional member states of the EEA. The centralized procedure is compulsory for specific pharmaceutical products, including for medicines developed by means of certain biotechnological processes, products designated as orphan pharmaceutical products, advanced therapy pharmaceutical products and pharmaceutical products with a new active substance indicated for the treatment of certain diseases (AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). For pharmaceutical products containing a new active substance not yet authorized in the European Economic Area before May 20, 2004 and indicated for the treatment of other diseases, pharmaceutical products that constitute significant therapeutic, scientific or technical innovations or for which the grant of a MA through the centralized procedure would be in the interest of public health at EU level, an applicant may voluntarily submit an application for a marketing authorization through the centralized procedure.

Under the centralized procedure, the CHMP established at the 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, the timeframe for the evaluation of an MAA by the EMA's CHMP is, in principle, 210 days from receipt of a valid MAA. However, this timeline excludes clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, so the overall process typically takes a year or more, unless the application is eligible for an accelerated assessment. Accelerated assessment might be granted by the CHMP in exceptional cases when a pharmaceutical product is expected to be of major public health interest, particularly from the point of therapeutic innovation. On request, the CHMP can reduce the time frame to 150 days if the applicant provides sufficient justification

for an accelerated assessment. The CHMP will provide a positive opinion regarding the application only if it meets certain quality, safety and efficacy requirements. However, the EC has final authority for granting the MA within 67 days after receipt of the CHMP opinion.

The decentralized procedure permits companies to file identical MA applications for a pharmaceutical product to the competent authorities in various EU member states simultaneously if such pharmaceutical product has not received marketing approval in any EU member state before. This procedure is available for pharmaceutical products not falling within the mandatory scope of the centralized procedure. The competent authority of a single EU member state, known as the reference EU member state, is appointed to review the application and provide an assessment report. 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 EU member state and concerned EU member states. The reference EU member state prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. Subsequently, each concerned EU member state must decide whether to approve the assessment report and related materials.

If an EU 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 EC, whose decision is binding for all EU member states.

All new MAAs must include a Risk Management Plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. New RMPs are required to be submitted (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. Since October 20, 2023, all RMPs for centrally authorized products are published by the EMA subject to only limited redactions.

Marketing Authorizations have an initial duration of five years. After these five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

Data and Market Exclusivity in the European Union

As in the United States, it may be possible to obtain a period of market and / or data exclusivity in the EU that would have the effect of postponing the entry into the marketplace of a competitor's generic, hybrid or biosimilar product (even if the pharmaceutical product has already received an MA) and prohibiting another applicant from relying on the MA holder's pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining MA or placing the product on the market. New Chemical Entities ("NCE") approved in the EU qualify for eight years of data exclusivity and ten years of marketing exclusivity. The overall ten-year period can 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 deemed to bring a significant clinical benefit in comparison with existing therapies.

The data exclusivity period begins on the date of the product's first MA in the EU. After eight years, a generic product application may be submitted and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product), or three years later (or a total of 11 years after the first MA in the EU of the innovator product) if the MA holder obtains MA for a new indication with significant clinical benefit within the eight-year data exclusivity period. Additionally, another noncumulative one-year period of data exclusivity can be added to the eight years of data exclusivity where an application is made for a new indication for a well-established substance, provided that significant preclinical or clinical studies were carried out in relation to the new indication. Another year of data exclusivity may be added to the eight years, where a change of classification of a pharmaceutical product has been authorized on the basis of significant pre-trial tests or clinical trials (when examining an application by another applicant for or holder of market authorization for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial change was authorized).

Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the EU's regulatory authorities to include an NCE. Even if a compound is considered to be an NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of

the pharmaceutical product if such company can complete a full MAA with their own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its pharmaceutical product.

On April 26, 2023, the EC submitted a proposal for the reform of the European pharmaceutical legislation. The current draft envisages e.g., a shortening of the periods of data exclusivity, however, there is currently neither a final version of this draft nor a date for its entry into force. Although the European Parliament adopted its approving position on the reform on April 10, 2024, no further required legislative steps have since been taken.

Orphan Designation and Exclusivity

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the United States. The EMA's Committee for Orphan Medicinal Products ("COMP") evaluates applications for orphan drug designation within 90 days and will issue a recommendation if the medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the EU (prevalence criterion). In addition, Orphan Drug Designation can be granted if, for economic reasons, the medicinal product would be unlikely to be developed without incentives and if there is no other satisfactory method approved in the EU of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed medicinal product is a significant benefit to patients affected by the condition. Orphan drug designations are granted by the EC. An application for orphan drug designation (which is not a marketing authorization, as not all orphan-designated medicines reach the authorization application stage) must be submitted first before an application for marketing authorization of the medicinal product is submitted. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted, and sponsors must submit an annual report to EMA summarizing the status of development of the medicine. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Designated orphan medicines are eligible for conditional marketing authorization.

COMP reassesses the orphan drug designation of a product in parallel with the review for a marketing authorization; for a product to benefit from market exclusivity it must maintain its orphan drug designation at the time of marketing authorization review by the EMA and approval by the EC. Additionally, any marketing authorization granted for an orphan medicinal product must only cover the therapeutic indication(s) that are covered by the orphan drug designation. Upon the grant of a marketing authorization, orphan drug designation provides up to ten years of market exclusivity in the orphan indication.

During the 10-year period of market exclusivity, with a limited number of exceptions, the regulatory authorities of the EU member states and the EMA may not accept applications for marketing authorization, accept an application to extend an existing marketing authorization or grant marketing authorization for other similar medicinal products for the same therapeutic indication. A similar medicinal product is defined as a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan medicinal product can also obtain an additional two years of market exclusivity for an orphan-designated condition when the results of specific studies are reflected in the Summary of Product Characteristics ("SmPC"), addressing the pediatric population and completed in accordance with a fully compliant Pediatric Investigation Plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, i.e. the condition prevalence or financial returns criteria under Article 3 of Regulation (EC) No. 141/2000 on orphan medicinal products. When the period of orphan market exclusivity for an indication ends, the orphan drug designation for that indication expires as well. Orphan exclusivity runs in parallel with normal rules on data exclusivity and market protection. Additionally, a marketing authorization may be granted to a similar medicinal product (orphan or not) for the same or overlapping indication subject to certain requirements.

Pediatric Development

In the EU, companies developing a new pharmaceutical product are obligated to study their product in children and must therefore submit a PIP together with a request for agreement to the EMA. The EMA issues a decision on the PIP based on an opinion of the EMA's Pediatric Committee ("PDCO"). Companies must conduct pediatric clinical trials in accordance with the PIP approved by the EMA, unless a deferral (*e.g.* until enough information to demonstrate its effectiveness and safety in adults is available) or waiver (*e.g.* because the relevant disease or condition occurs only in adults) has been granted by the EMA. The MAA for the pharmaceutical product must include the results of all pediatric clinical trials performed and details of all information collected in compliance with the approved PIP, unless a waiver or a deferral has been granted, in which case the pediatric clinical trials may be completed at a later date. Pharmaceutical products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with

the approved PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the approved PIP are developed and submitted. An approved PIP is also required when a marketing authorization holder wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized and covered by intellectual property rights.

Post-Approval Regulation

Similar to the United States, both MA holders and manufacturers of pharmaceutical products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the EU member states. This oversight applies both before and after grant of manufacturing licenses and marketing authorizations. It includes control of compliance with EU good manufacturing practices rules, manufacturing authorizations, pharmacovigilance rules and requirements governing advertising, promotion, sale, and distribution, recordkeeping, importing and exporting of pharmaceutical products.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials, manufacturing approval, MA of pharmaceutical products and marketing of such products, both before and after grant of MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The holder of an EU MA for a pharmaceutical product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of pharmaceutical products.

These pharmacovigilance rules can impose on holders of MAs the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed pharmaceutical products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies or post-authorization safety studies to obtain further information on a medicine's safety, or to measure the effectiveness of risk-management measures, which may be time consuming and expensive and could impact our profitability. MA holders must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of Periodic Safety Update Reports ("PSURs") in relation to pharmaceutical products for which they hold MAs. The EMA reviews PSURs for pharmaceutical products authorized through the centralized procedure. If the EMA has concerns that the risk-benefit profile of a product has varied, it can adopt an opinion advising that the existing MA for the product be suspended, withdrawn or varied. The agency can advise that the MA holder be obliged to conduct post-authorization Phase 4 safety studies. If the EC agrees with the opinion, it can adopt a decision varying the existing MA. Failure by the MA holder to fulfill the obligations for which the European Commission's decision provides can undermine the on-going validity of the MA.

More generally, non-compliance with pharmacovigilance obligations can lead to the variation, suspension or withdrawal of the marketing authorization for the pharmaceutical product or imposition of financial penalties or other enforcement measures.

The manufacturing process for pharmaceutical products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice ("GMP"). These requirements include compliance with EU GMP standards when manufacturing pharmaceutical products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Amendments or replacements of Directive 2001/83/EC and Regulation (EC) No 726/2004 are part of the reform proposal for European pharmaceutical legislation.

Similarly, the distribution of pharmaceutical products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU member states. The manufacturer or importer must have a qualified person who is responsible for certifying that each batch of product has been manufactured in accordance with

GMP, before releasing the product for commercial distribution in the EU or for use in a clinical trial. Manufacturing facilities are subject to periodic inspections by the competent authorities for compliance with GMP.

Advertising and Promotion

The advertising and promotion of our products is also subject to EU laws concerning promotion of pharmaceutical products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other national legislation of individual EU member states may apply to the advertising and promotion of pharmaceutical products and may differ from one country to another. These laws require that promotional materials and advertising in relation to pharmaceutical products comply with the product's SmPC as approved by the competent regulatory authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the pharmaceutical product. It forms an intrinsic and integral part of the marketing authorization granted for the pharmaceutical product. Promotion of a pharmaceutical product that does not comply with the SmPC is considered to constitute off-label promotion. All advertising and promotional activities for the product must be consistent with the approved SmPC and therefore all off-label promotion of pharmaceutical products is prohibited in the EU. Direct-to-consumer advertising of prescription-only pharmaceutical products is prohibited in the EU. Violations of the rules governing the promotion of pharmaceutical products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on its promotional activities with healthcare professionals.

Pricing and Reimbursement Environment

Even if a pharmaceutical product obtains a marketing authorization in the EU, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. The EU member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. An EU member state may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of our product candidates, if any, to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, pharmaceutical products launched in the EU do not follow price structures of the United States and generally published and actual prices tend to be significantly lower. Publication of discounts by third-party payers or authorities and public tenders may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries.

The so-called health technology assessment ("HTA") of pharmaceutical products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including France, Germany, Ireland, Italy and Sweden. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact, and the economic and societal impact of use of a given pharmaceutical product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual pharmaceutical products as well as their potential implications for the healthcare system. Those elements of pharmaceutical products are compared with other treatment options available on the market. The outcome of HTA regarding specific pharmaceutical products will often influence the pricing and reimbursement status granted to pharmaceutical products by the regulatory authorities of individual EU member states. A negative HTA of one of our products by a leading and recognized HTA body could not only undermine our ability to obtain reimbursement for such product in the EU member state in which such negative assessment was issued, but also in other EU member states. For example, EU member states that have not yet developed HTA mechanisms could rely to some extent on the HTA performed in other countries with a developed HTA framework, when adopting decisions concerning the pricing and reimbursement of a specific pharmaceutical product.

On January 31, 2018, the European Commission adopted Regulation (EU) 2021/2282 on health technology assessment ("HTAR"). HTAR entered into force on January 11, 2022 and applies from January 12, 2025 onwards, followed by a further three-year transitional period during which EU member states must fully adapt to the new system. HTAR intends to boost EU level cooperation among EU member states in assessing health technologies, including new pharmaceutical products, and to provide the basis for cooperation at the EU level for joint clinical assessments in these areas. Under HTAR, EU member states will be able to use common HTA tools, methodologies and procedures across the

EU, working together in four main areas: the joint clinical assessment of the innovative health technologies with the most potential impact for patients; joint scientific consultations whereby developers can seek advice from HTA authorities; identification of emerging health technologies to identify promising technologies early; and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (*e.g.*, economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement. While EU member states can choose to delay participation in the joint network until three years after the rules enter into force, it will become mandatory after six years. The European Commission has stated that the role of the HTA regulation is not to influence pricing and reimbursement decisions in the individual EU member states, but there can be no assurance that the HTA regulation will not have effects on pricing and reimbursement decisions.

To obtain reimbursement or pricing approval in some countries, including the EU member states, we may be required to conduct studies that compare the cost-effectiveness of our product candidates to other therapies that are considered the local standard of care. There can be no assurance that any country will allow favorable pricing, reimbursement and market access conditions for any of our products, or that we will be feasible to conduct additional cost-effectiveness studies, if required.

In certain EU member states, pharmaceutical products designated as orphan pharmaceutical products may be exempted or waived from having to provide certain clinical, cost-effectiveness and other economic data in connection with their filings for pricing/reimbursement approval.

Data Privacy and Security Laws

There are numerous U.S. federal, state, and local laws and regulations, as well as foreign legislation, in particular in the EU and UK, which regulate personal information, including how that information may be used, processed, and disclosed. These regulations also cover sensitive personal information, including medical and health information, and impose requirements on entities that handle such information to implement certain privacy and security measures. We and/or our partners may be subject to these laws.

In the United States, at the federal level, the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH Act"), and the regulations promulgated thereunder, impose data privacy, security and data breach reporting obligations with respect to protected health information ("PHI") on covered entities—which include health plans, healthcare clearinghouses and certain healthcare providers—and business associates—which include persons or entities that perform certain functions or activities that involve the use or disclosure of PHI on behalf of, or in connection with providing a service for, a covered entity.

There are also a number of U.S. state privacy laws, such as the California Consumer Privacy Act of 2018 ("CCPA"), as amended by the California Privacy Rights Act of 2020 ("CPRA"), that govern the privacy and security of personal information in certain circumstances. The CCPA/CPRA applies to personal data of consumers (which is defined to include business representatives and employees) who are California residents, imposes obligations on certain businesses that do business in California, including to provide specific disclosures in privacy notices, and affords rights to California residents in relation to their personal information. Health information falls under the CCPA/CPRA's definition of personal information where it identifies, relates to, describes, is reasonably capable of being associated with or could reasonably be linked, directly or indirectly, with a particular consumer or household and is considered "sensitive personal information," which is offered greater protection. However, the CCPA/CPRA, like other U.S. state privacy laws, does not apply to PHI, and other U.S. state entities exempt covered entities and business associates altogether. Some of these laws and regulations impose different, and in certain instances, more stringent requirements than HIPAA. Failing to comply with these laws and regulations can result in significant civil and/or criminal penalties, as well as, in some cases, exposure to private litigation, all of which can result in financial and reputational risks.

The collection and use of personal health data and other personal data in the EU is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 ("GDPR"), which came into force in May 2018, and by related implementing laws in the individual EU member states. The GDPR has a number of significant practical consequences, in particular for international data transfers, competent supervisory authorities and enforcement of the GDPR. The GDPR increased responsibility and liability in relation to personal data that we process.

The GDPR imposes a number of strict obligations and restrictions on the ability to process (processing includes collection, analysis and transfer of) personal data of individuals in the EEA, including health data from clinical trials and adverse event reporting. The GDPR also includes requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals prior to processing their personal data or personal health data, notification obligations to the national data protection authorities and the security and confidentiality of the personal

data. EU member states may also impose additional requirements in relation to health, genetic and biometric data through their national implementing legislation.

The GDPR also imposes specific restrictions on the transfer of personal data to countries outside of the EEA that are not considered by the European Commission to provide an adequate level of data protection. Appropriate safeguards are required to enable such transfers. Among the appropriate safeguards that can be used, the data exporter may use the standard contractual clauses ("SCCs"). In this respect, on June 4, 2021, the EU Commission has issued a new set of SCCs which replace the old sets of SCCs that were adopted under the previous European Data Protection Directive 95/46. In addition, when relying on SCCs, the data exporters are required to conduct a transfer risk assessment to verify if anything in the law and/or practices of the third country may impinge on the effectiveness of the SCCs in the context of the transfer at stake and, if so, to identify and adopt supplementary measures that are necessary to bring the level of protection of the data transferred to the EU standard of essential equivalence. Where no supplementary measure is suitable, the data exporter should avoid, suspend or terminate the transfer. On June 18, 2021, the European Data Protection Board adopted recommendations to assist data exporters with such assessment and their duty to identify and implement supplementary measures where they are needed to ensure compliance with the EU level of protection to the personal data they transfer to third countries. With regard to the transfer of data from the EEA to the US, on July 10, 2023, the European Commission adopted its adequacy decision for the EU-US Data Privacy Framework. On the basis of the new adequacy decision, personal data can flow from the EEA to US companies participating in the framework.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU member states may result in significant monetary fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company — whichever is greater — other administrative penalties, and a number of criminal offenses (punishable by uncapped fines) for organizations and in certain cases their directors and officers as well as civil liability claims from individuals whose personal data was processed. Data protection authorities from the different EU member states may still implement certain variations, enforce the GDPR and national data protection laws differently, and introduce additional national regulations and guidelines, which adds to the complexity of processing personal data in the EU. Guidance developed at both EU level and at the national level in individual EU member states concerning implementation and compliance practices are often updated or otherwise revised.

There is, moreover, a growing trend towards required public disclosure of clinical trial data in the EU which adds to the complexity of obligations relating to processing health data from clinical trials. Such public disclosure obligations are provided in the EU Clinical Trials Regulation, EMA disclosure initiatives and voluntary commitments by industry. Failing to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results. The uncertainty regarding the interplay between different regulatory frameworks, such as the Clinical Trials Regulation and the GDPR, further adds to the complexity that we face with regard to data protection regulation.

With regard to the transfer of data from the EEA to the UK, on June 28, 2021 the European Commission adopted two adequacy decisions for the UK: one under the GDPR and the other for the Law Enforcement Directive. Personal data may now freely flow from the EU to the UK since the UK is deemed to have an adequate data protection level for the purposes of the EU regime. However, the adequacy of decisions are subject to a 'sunset clause' which entails that the decisions will automatically expire four years after their entry into force, unless renewed. Additionally, following the UK's withdrawal from the EEA, companies also have to comply with the UK's data protection laws (including the GDPR as incorporated into UK national law), the latter regime having the ability to impose fines up to the greater of £17.5 million or 4% of global turnover. Furthermore, transfers from the UK to other countries, including to the EEA, are subject to specific transfer rules under the UK regime; personal data may freely flow from the UK to the EEA, since the EEA is deemed to have an adequate data protection level for purposes of the UK regime. These UK international transfer rules broadly mirror the EU GDPR rules. On February 2, 2022, the UK Secretary of State laid before the UK Parliament the international data transfer agreement (IDTA) and the international data transfer addendum to the European Commission's standard contractual clauses for international data transfers (Addendum) and a document setting out transitional provisions. The IDTA and Addendum came into force on March 21, 2022 and replaced the old EU SCCs for the purposes of the UK regime.

With regard to the transfer of data from the UK to the US, the UK government has adopted an adequacy decision for the US, the UK-US Data Bridge, which came into force on October 12, 2023. The UK-US Data Bridge recognizes the US as offering an adequate level of data protection where the transfer is to a US company participating in the EU-US Data Privacy Framework and the UK Extension.

Promotional Activities

In the EU, interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and in

the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of pharmaceutical products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of the EU member states. Violation of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, their regulatory professional organization, and/or the competent authorities of the individual EU member states. These requirements are provided in the national laws, industry codes, or professional codes of conduct, applicable in the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

While the UK has left the EU, as mentioned above, it should be noted that the UK still has the strictest anti-bribery regime in Europe, the UK Bribery Act 2010. The Act is applicable English law and continues to apply to any company incorporated in or "carrying on business" in the UK, irrespective of where in the world the alleged bribery activity occurs.

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 EU exists as regulations and directives, while the implementing acts and guidelines based on these may vary in each EU member state. In addition, the respective national provisions of the member states, as well as self-committed codes of the pharmaceutical industry, must be observed. Such regulations and directives include 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 EU 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"); repealed by Directive 2017/1572 on January 31, 2022; this directive also lays out standards and principles for manufacturing practices of medicinal products for human use and investigational medicinal products for human use.
- 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").
- Directives 2004/9/EC and 2004/10/EC laying down principles of GLP including on the organizational process under which non-clinical health and safety studies are performed.
- Directive 2010/84/EU and Regulation (EU) 1235/2010 on pharmacovigilance laying down procedures for the authorization and supervision of medicinal products for human and veterinary use.
- Directive 2006/114/EC concerning misleading and comparative advertising.
- Directive 2005/29/EC regulating unfair business-to-consumer commercial practices that occur before, during and after a business-to-consumer transaction.
- Regulation (EC) 1223/2009 on Cosmetic Products, setting mandatory requirements for cosmetics which are available on the market within the EU.
- Regulation (EC) 1901/2006 on Pediatric Use, laying down rules to ensure that medicines for use in children are researched, developed and authorized appropriately.

- Directive (2004/109/EC) on Transparency laying down rules to improves the harmonization of information duties of issuers, whose securities are listed at a regulated market at a stock exchange within the EU; amended by Directive (EU) 2022/2464 with effect from May 1, 2023 as regards corporate sustainability reporting.

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. Recently, the U.S. government passed the Inflation Reduction Act ("IRA"), which authorizes the U.S. Department of Health and Human Services to negotiate prices of certain drugs with participating manufacturers in federal healthcare programs. 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 EU, pricing and reimbursement schemes vary widely between member states. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some member states may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the EU 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. EU 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 play important roles 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 the Company markets, sells and distributes products for which it obtains marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully 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 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 who bring civil actions (qui tam actions) on behalf of the federal government, imposes civil penalties, as well as liability for treble 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 U.S. Department of Health and Human Services' Civil Monetary Penalty authorities, which imposes administrative sanctions for, among other things, presenting or causing to be presented false claims for government payment and providing remuneration to government health program beneficiaries to influence them to order or receive healthcare items or services;
- 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 HITECH 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 imposes criminal liability for knowingly and willfully 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 various healthcare professionals including physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, certified nurse-midwives 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 (e.g., in the EU, where the implementation of EU-wide regulations as well as independent national legislation may vary for each EU member state) to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers; and
- certain state laws require pharmaceutical companies to comply with voluntary compliance guidelines promulgated by a pharmaceutical industry association and relevant compliance guidance issues by the U.S. Department of Health and Human Services 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.

E. Facilities and Resources

The Company's principal executive offices are located in Pasadena, California. The Company further recently expanded its footprint with a new manufacturing and laboratory facility to manufacture drug substance (API) under current Good Manufacturing Practices (GMP) in Verona, Wisconsin.

Research and Development Facilities

The Company operates research laboratory facilities in San Diego, California and Madison, Wisconsin, where its pre-clinical research and development activities, including the discovery and early development of RNAi therapeutics, take place. A summary is provided below:

- State-of-the-art laboratories with supporting office space that comprise more than 251,000 total square feet;
- Cell culture laboratories;
- Complete animal facilities;
- Animal efficacy models for numerous diseases, including cardio metabolic, viral, liver, skeletal muscle, ocular, central nervous system (CNS), metabolic, obesity and lung diseases;
- Animal safety screening and assessment;
- Clinical pathology laboratories and in-house histopathology capabilities;
- Drug metabolism and pharmacokinetics (DMPK), bioanalytical, biodistribution, and clearance assessment and methodology capabilities;
- Primate colony housed at the Wisconsin National Primate Research Center, an affiliate of the University of Wisconsin, and at other contract research organizations (CROs);
- Pharmacodynamic method development and analysis and translational biomarker development capabilities;
- Conventional and confocal microscopy, flow cytometry, Luminex platform, qRT-PCR and clinical chemistry analytics; and
- Oligonucleotide, peptide, antibody, and small molecule discovery, synthesis, and analytics capabilities (for example, HPLC, NMR, and LCMS).

GMP Manufacturing and Related Development Laboratory Facility

The Company also recently expanded into a new, state-of-the-art GMP manufacturing facility in Verona, Wisconsin that includes related laboratories and office space to support chemistry, manufacturing, and controls (CMC) and quality activities. A summary is provided below:

- State-of-the-art, custom-designed GMP oligonucleotide manufacturing facility with related support laboratories for process development and analytical development, comprising approximately 300,000 total square feet;
- Full certificate of occupancy for laboratory, office & manufacturing spaces obtained August 2024;
- Full analytical chemistry capabilities including method development and validation, transfer of methods, and support of in-process and final product analysis;
- Drug product formulation development capabilities;
- In-house capabilities to release GMP drug substance and finished drug product;
- Multiple equipment scales for oligonucleotide manufacturing with maximum capacity to manufacture hundreds of kilograms of GMP drug substance annually; and
- Drug substance manufacturing capabilities to produce and release GMP material (API) and capabilities to release finished drug product pending ongoing commissioning, qualification, and validation (CQV) activities, which are scheduled to allow for the manufacture of GMP drug substance at the facility which is currently anticipated to begin by December 2024.

F. Human Capital Management

As of September 30, 2024, the Company employed 609 full-time employees based at four facilities in the United States, including Pasadena and San Diego, California, and Madison and Verona, Wisconsin. The following table presents the total number of employees as of September 30 by location.

Site	2024	2023
Pasadena, CA	141	137
San Diego, CA	135	104
Madison, WI	202	284
Verona, WI	131	—
Total	609	525

In fiscal year 2024, the Company continued to expand its workforce, focusing on increasing in-house manufacturing capacity, as well as enhancing expertise and throughput in clinical and preclinical research and development and commercialization preparation. The Company continually evaluates the business need and opportunity and balances in-house expertise and capacity with outsourced expertise and capacity. Currently, the Company outsources substantial clinical trial work to clinical research organizations and certain drug manufacturing to contract manufacturers.

Drug development is a complex endeavor which requires deep expertise and experience across a broad array of disciplines. Pharmaceutical companies both large and small compete for a limited number of qualified applicants to fill specialized positions. To attract qualified applicants to the Company, it offers a total compensation package consisting of base salary and cash target bonus targeting the 50th to 75th percentile of market, and offers a comprehensive benefit package and equity compensation to every employee. Bonus opportunity and equity compensation increase as a percentage of total compensation based on level of responsibility. Actual bonus payout is based on performance.

A significant portion of the Company's employees have obtained advanced degrees in their professions. The Company supports its employees' further development with individualized development plans, mentoring, coaching, group training, conference attendance and financial support including tuition reimbursement.

Diversity and Inclusion

The Company is dedicated to fostering a welcoming, healthy and equitable environment where all employees can thrive and contribute to its mission of delivering safe and effective medicine to patients in need. Ongoing efforts include formal training programs and processes that promote awareness of inclusion and diversity, such as anti-bias training and employee engagement initiatives. The Company's Diversity, Equity, and Inclusion (DEI) committee, comprised of a diverse group of employees across each of its worksites, meets regularly to provide well-attended education and outreach opportunities. The DEI committee also advises its senior management on building a more diverse, equitable, and inclusive workplace.

G. Investor Information

The Company's website address is http://www.arrowheadpharma.com. The Company's website address is not intended to function as a hyperlink and the information contained on its website is not, and should not be considered part of, and is not incorporated by reference into, this Annual Report on Form 10-K. The Company's reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), including its Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, Proxy Statements, and amendments to such periodic reports and Proxy Statements, are accessible through its 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 the Company's website.

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding the Company and other issuers that file electronically with the SEC. The SEC's Internet website address is http://www.sec.gov.

ITEM 1A. RISK FACTORS

The Company's business involves various risks and uncertainties in addition to the normal risks of business, some of which are discussed in this section. It should be noted that the Company's business may be adversely affected by general economic conditions and other forces beyond the Company's control. In addition, other risks and uncertainties not presently known or that the Company currently believes to be immaterial may also adversely affect the Company's business. Any such risks or uncertainties, or any of the following risks or uncertainties, that develop into actual events could result in a material and adverse effect on the Company's business, financial condition, results of operations, or liquidity.

The information discussed below should be considered carefully with the other information contained in this Annual Report on Form 10-K and the other documents and materials filed by the Company with the SEC, as well as news releases and other information publicly disseminated by the Company from time to time.

Risk Factors Summary

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

- Our prospects substantially depend on the success of our clinical-stage product candidates. If we and our licensees are unable to obtain approval for and commercialize these product candidates, our business could be materially harmed.
- 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 product candidates are in clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. There can be no assurance that our product candidates will obtain regulatory approval, which is necessary before they can be commercialized.
- Our clinical trials may not yield successful results for the product candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory approval and commercialization.
- Our clinical trials may reveal significant adverse events, toxicities or other side effects and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.
- Results of earlier studies or clinical trials may not be predictive of future clinical trial results, and initial studies or clinical trials may not establish an adequate safety or efficacy profile for our product candidates to justify proceeding to advanced clinical trials or an application for regulatory approval.
- 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 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.
- Our commercialization, collaborative and other arrangements may give rise to disputes over commercial terms, contract interpretation and ownership or protection of our intellectual property and may adversely affect the commercial success of our products.

Risks Related to Regulatory Review and Approval of Our Candidates

- A Fast Track product designation may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.
- We and our licensees conduct clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.
- Even if we obtain FDA approval for products in the United States, we may never obtain approval to commercialize any product candidates outside of the United States, which would limit our ability to realize their full market potential.
- Even if our product candidates are approved for commercialization, failure to comply with regulatory requirements or unanticipated problems with our products may result in various adverse actions such as the suspension or withdrawal of one or more of our products, closure of a facility or enforcement of substantial penalties or fines.
- Pharmaceutical and biological product marketing is subject to substantial regulation in the U.S. and any failure by us or our commercial and collaborative partners to comply with applicable statutes or regulations can adversely affect our business.

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 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 could be seriously and adversely affected.

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 various stages of development and we have no approved products based on RNA interference and our delivery technologies. Accordingly, there is a limited amount of information about us upon which you can evaluate our business and prospects.
- We may need to establish additional relationships with strategic and development partners to fully develop our drug candidates and market any approved products.
- 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.
- 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.
- We will need to achieve commercial acceptance of our drug candidates to generate revenues and achieve profitability.
- If the market opportunities for our approved product candidates, if any, are smaller than we expect, it could materially adversely affect our financial condition and results of operations.
- 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 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 face competition from various entities including large pharmaceutical companies, small biotech companies, private companies, and research institutions.
- We may have difficulty expanding our operations successfully as we evolve our pipeline and move toward commercializing drugs.
- 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 operations, including our relationships with healthcare providers, physicians and third-party payers, are subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which, in the event of a violation, exposes us to liability for criminal sanctions, civil penalties, and contractual damages, and reputational harm and diminished profits and future earnings.
- The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors and specialty pharmacies could adversely affect our revenues, financial condition, or results of operations.

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 will require substantial additional funds to complete our research and development activities.
- The terms of our Sixth Street Financing Agreement and our indebtedness could adversely affect our operations and limit our ability to plan for or respond to changes in our business. If we are unable to comply with restrictions in our Sixth Street Financing Agreement, the repayment of our existing indebtedness could be accelerated.
- 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 operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.
- The investment of our cash, cash equivalents and fixed income securities is subject to risks which may cause losses and affect the liquidity of these investments.
- Our ability to utilize net operating loss carryforwards and other tax benefits may be limited.

Risks Related to Investment and Securities

- 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 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.
- 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.

Economic and Industry Risks

- Drug development is time consuming, expensive and risky.
- 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.

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

Our prospects substantially depend on the success of our clinical-stage product candidates. If we and our licensees are unable to obtain approval for and commercialize these product candidates, our business could be materially harmed.

Our future success is substantially dependent on the ability of our company and our licensees to timely complete clinical trials and obtain marketing approval for, and then successfully commercialize our clinical-stage product candidates. We are not permitted to market or promote our product candidates before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of developing and commercializing our product candidates will depend on several factors, including the following:

- obtaining positive data that supports demonstration of efficacy, safety and tolerability profiles and durability of effect for our product candidates that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval;
- successful and timely enrollment of appropriate patients for the indications included in our current and future clinical trials;
- potential variability of patient outcomes;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- the establishment of and maintenance of sufficient internal manufacturing capabilities;
- the maintenance of existing or the establishment of new supply arrangements with third-party drug product suppliers and manufacturers for clinical development and, if approved, commercialization of our product candidates;
- the maintenance of existing or the establishment of new scaled production arrangements with third-party manufacturers to obtain finished products that are appropriately packaged for sale;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting our rights in our intellectual property portfolio, including our licensed intellectual property;
- establishing sales, marketing and distribution capabilities and the successful launch of commercial sales of our product candidates if and when approved for marketing, whether alone or in collaboration with others;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any collaborator or licensee. For development programs that are licensed to third parties, we generally do not have control over the design or conduct of clinical trials and will not have discretion over marketing decisions. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates from our lead programs, which would materially harm our business. If we do not receive marketing approvals for such product candidates, we may not be able to continue our operations.

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.

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. Because we use platform technology to develop drug candidates, toxicology signals that may emerge in the course of testing of one particular candidate may apply broadly across our drug candidate platform. Further, certain underlying premises in our development programs are not proven and many of the drug targets that we are pursuing have not yet been validated clinically. For instance, ARO-RAGE has demonstrated the ability to reduce the expression of RAGE in the lung, however it has not been established that this will have an anti-inflammatory effect sufficient for a meaningful clinical benefit in patients with inflammatory lung disease. Further, it is also unknown at this time what may be required to gain favorable reimbursement. With respect to fazirsiran, 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.

Our product candidates are in clinical development, which is a lengthy and expensive process with uncertain outcomes and the potential for substantial delays. There can be no assurance that our product candidates will obtain regulatory approval, which is necessary before they can be commercialized.

The sale of human therapeutic products in the United States 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, preclinical and clinical data; and
- adherence to cGMP regulations during production and storage.

Since 2011, we have focused substantially all of our efforts and financial resources on identifying, acquiring and developing our product candidates, including conducting lead optimization, nonclinical studies, preclinical studies and clinical trials, and providing general administrative support for these operations. And, the clinical-stage product candidates we currently have under development will require significant development, preclinical and clinical testing and investment of significant funds to gain regulatory approval before they can be approved for commercialization. The results of our research and human clinical testing of our products may not meet regulatory requirements. Some of our product candidates, if approved, may 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 several years and require the use of substantial resources. For instance, we currently plan to study plozasiran in a cardiovascular outcomes trial, and cardiovascular outcomes trials are expensive clinical trials performed in a large number of subjects over several years. 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.

Our clinical trials may not yield successful results for the product candidates that we may identify and pursue for their intended uses, which would prevent, delay or limit the scope of regulatory approval and commercialization.

We must demonstrate our product candidates' safety and efficacy in humans for each target indication through extensive clinical testing. 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 preclinical 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.

We cannot be certain that current clinical trials or any future clinical trials, whether conducted by us or our licensees, will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have

a material adverse effect on our business, financial condition and results of operation. Success in clinical trials in a particular indication does not ensure that a product candidate will be successful in other indications. Similarly, approval of a product candidate in a particular indication does not ensure that the product candidate will be successful in other indications. For instance, although plozasiran's Phase 3 PALISADE trial for patients with FCS was successful in achieving its primary endpoint and all multiplicity-controlled key secondary endpoints, and we filed an NDA with the FDA on November 16, 2024 and sought regulatory approval with additional global regulatory authorities thereafter, there can be no guarantee that the FDA or another regulatory authority approves plozasiran for the treatment of FCS, and plozasiran may not succeed in achieving its clinical trial endpoints or be approved for the treatment of larger indications such as sHTG or ASCVD because the endpoints and clinical data required for approval in a rare disease indication are different from what is required for a broader patient population. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or comparable foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for a product candidate, the terms of such approval may limit the scope and use of the specific product candidate, which may also limit its commercial potential.

Our clinical trials may reveal significant adverse events, toxicities or other side effects and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.

In order to obtain marketing approval for any of our product candidates, we must demonstrate the safety and efficacy of the product candidate for the relevant clinical indication or indications through preclinical studies and clinical trials as well as additional supporting data. As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events ("AEs") associated with the use of our products or product candidates. If our product candidates are associated with undesirable side effects in preclinical studies or clinical trials, or have unexpected characteristics, we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective.

If further significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, the EMA, other applicable regulatory authorities or an institutional review board may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage studies have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the drug from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability relative to other therapies. Any of these developments could materially harm our business, financial condition and prospects.

Clinical trials of our product candidates may not uncover all possible adverse events that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population, which may have significant variability. By design, clinical trials are based on a limited number of subjects and are of limited duration of exposure to the product, to determine whether the product candidate demonstrates the substantial evidence of efficacy and safety necessary to obtain regulatory approval. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered. It may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration may a more complete safety profile be identified. Further, even larger clinical trials may not identify rare significant AEs, and the duration of such studies may not be sufficient to identify when those events may occur. Other products have been approved by the regulatory authorities for which safety concerns have been uncovered following approval. Such safety concerns have led to labeling changes, restrictions on distribution through use of a REMS, or withdrawal of products from the market, and any of our product candidates may be subject to similar risks.

Although to date our current drug candidates have generally evidenced an acceptable safety profile in clinical trials, patients treated with our products, if approved, may experience previously unreported adverse reactions or minor incidences of adverse reactions may manifest with greater frequency in subsequent larger trials, and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If toxicities, adverse events or any other safety problems occur or are identified after our products, if any, reach the market, we may make the decision or be required by regulatory authorities to

conduct additional clinical safety trials, amend the labeling of our products or add additional warnings to the labeling, recall our products, or even withdraw approval for our products.

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 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.

Results of earlier studies or clinical trials may not be predictive of future clinical trial results, and initial studies or clinical trials may not establish an adequate safety or efficacy profile for our product candidates to justify proceeding to advanced clinical trials or an application for regulatory approval.

The results of nonclinical and preclinical studies and clinical trials may not be predictive of the results of later-stage clinical trials, and interim results of clinical trials do not necessarily predict final results. The results of preclinical studies and clinical trials in one set of patients or disease indications, or from preclinical studies or clinical trials that we did not lead, may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. In addition, preclinical and clinical data are often susceptible to various interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through nonclinical studies and initial clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, or after achieving positive results in pivotal trials, and we cannot be certain that we will not face similar setbacks. Even if early-stage clinical trials are successful, we may need to conduct additional clinical trials of our product candidates in additional patient populations or under different treatment conditions before we are able to seek approvals from the FDA and regulatory authorities outside the United States to market and sell these product candidates. Our failure to obtain marketing approval for our product candidates for commercially viable indications, or at all, would substantially harm our business, prospects, financial condition and results of operations.

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. The 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.

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, healthcare 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 adequate 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. With respect to our partnered product candidates, we will 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. For example, the IRA includes several measures intended to lower the cost of prescription drugs and related healthcare reforms, including limits on price increases and subjecting an escalating number of drugs to annual price negotiations with CMS (The Centers for Medicare & Medicaid Services). We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, or what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future. There also may be future changes unrelated to the IRA 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 designations.

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 the 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 that 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. Further, orphan drug exclusivity can be lost if the FDA later determines that the request for designation was materially defective or if the applicant is unable to assure the availability of sufficient quantities of the drug to meet the needs of patients with the disease or condition for which the drug was designated.

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, management and other employees. This will depend in part on our ability to create and maintain a desirable workplace culture, which may be impacted by employee preferences for remote working. In addition, the market for qualified employees in the pharmaceutical industry is experiencing labor shortages and inflationary pressures are causing salaries and wages to increase, all of which exacerbates these competitive dynamics. 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.

Our commercialization, collaborative and other arrangements may give rise to disputes over commercial terms, contract interpretation and ownership or protection of our intellectual property and may adversely affect the commercial success of our product candidates.

We have in the past and may again in the future enter into collaboration or license arrangements, including commercialization or collaborative arrangements, some of which may be based on less definitive agreements, such as memoranda of understanding, material transfer agreements, options or feasibility agreements.

Commercialization and collaborative relationships are generally complex and can give rise to disputes regarding the relative rights, obligations and revenues of the parties, including the ownership of intellectual property and associated rights and obligations, especially when the applicable collaborative provisions have not been fully negotiated and documented. Such disputes have arisen in the past from time to time and, if they arise again could delay collaborative research, development or commercialization of potential product candidates, and can lead to lengthy, expensive litigation or arbitration. The terms of such arrangements may also limit or preclude us from commercializing products or technologies developed pursuant to such collaborations. Additionally, the commercialization or collaborative partners under these arrangements might breach the terms of their respective agreements or fail to maintain, protect or prevent infringement of the licensed patents or our other intellectual property rights by third parties. Moreover, negotiating commercialization and collaborative arrangements often takes considerably longer to conclude than the parties initially anticipate, which could cause us to enter into less favorable agreement terms that delay or defer recovery of our development costs and reduce the funding available to support key programs. Any failure by our commercialization or collaborative partners to abide by the terms of their respective agreements with us (including their failure to accurately calculate, report or pay any royalties payable to either us or a third party or their failure to repay, in full or in part, either any outstanding receivables or any other amounts for which we are entitled to reimbursement) may adversely affect our results of operations.

We are not always able to enter into commercialization or collaborative arrangements on acceptable terms, which can harm our ability to develop and commercialize our current and potential future products and technologies. Other factors relating to collaborations that may adversely affect the commercial success of our product candidates include:

- any parallel development by a commercialization or collaborative partner of competitive technologies or products;
- arrangements with commercialization or collaborative partners that limit or preclude us from developing products or technologies;
- premature termination of a commercialization or collaboration agreement or the inability to renegotiate existing agreements on favorable terms; or
- failure by a commercialization or collaborative partner to devote sufficient resources to the development and commercial sales of products using our current and potential future products and technologies.

Our commercialization or collaborative arrangements do not necessarily restrict our commercialization or collaborative partners from competing with us or restrict their ability to market or sell competitive products. Our current and any future commercialization or collaborative partners may pursue existing or other development-stage products or alternative technologies in preference to those being commercialized or developed in collaboration with us.

In addition, contract disputes with customers or other third parties may arise from time to time. Our commercialization or collaborative partners, or customers or other third parties, may also terminate their relationships with us or otherwise decide not to proceed with the development, commercialization or purchase of our product candidates.

Risks Related to Regulatory Review and Approval of Our Product Candidates

Breakthrough Therapy designation for Plozasiran and/or Fazirsiran (formerly ARO-AAT) may not lead to a faster development or review process.

We have been granted a Breakthrough Therapy designation for plozasiran in the United States for the treatment of FCS and fazirsiran in the United States for the treatment of liver disease associated with AATD. Breakthrough Therapy 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 and additional drug development guidance with the FDA and its senior managers. Breakthrough Therapy designation applies to the combination of the drug candidate and the specific indication for which it is being studied. Product candidates that receive Breakthrough Therapy 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 Breakthrough Therapy designation, plozasiran and/or fazirsiran may not actually benefit from 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 plozasiran or fazirsiran will receive marketing approval in the United States. The FDA may also rescind Breakthrough Therapy designation if it determines that plozasiran or fazirsiran no longer meets the relevant criteria.

A Fast Track product designation may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We have received a Fast Track product designation for plozasiran in the United States for the treatment of FCS, and we may seek Fast Track designation for other of our current or future product candidates. The Fast Track designation is a program offered by the FDA designed to facilitate drug development and to expedite the review of new drugs that are intended to treat serious or life-threatening conditions. Compounds selected must demonstrate the potential to address unmet medical needs. The FDA's Fast Track designation allows for close and frequent interaction with the FDA. A designated Fast Track drug may also be considered for priority review with a shortened review time, rolling submission, and accelerated approval if applicable.

A Fast Track designation does not, however, guarantee FDA approval or expedited approval of any application for the product candidate. The receipt of such a designation for a product candidate may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate marketing approval by the FDA. In addition, the FDA may later decide that the products no longer meet the designation conditions.

We intend to deliver some of our product candidates via drug delivery devices that will have their own regulatory, development, supply and other risks.

We intend to deliver some of our product candidates via drug delivery devices, such as an autoinjector or nebulizer. There may be unforeseen technical complications related to the development activities required to bring such a product to market, including container compatibility and/or dose volume requirements. If our product candidates are intended to be used with drug delivery devices, we expect to utilize drug delivery devices authorized for marketing under clearances of approvals held by third parties. Our product candidates may not be approved or may be substantially delayed in receiving approval if the devices do not gain and/or maintain their own regulatory approvals or clearances. Where approval of the drug product and device is sought under a single application, the increased complexity of the review process may delay approval. In addition, some drug delivery devices are provided by single-source unaffiliated third-party companies. We may be dependent on the sustained cooperation and effort of those third-party companies both to supply the devices and, in some cases, to conduct the studies required for approval or other regulatory clearance of the devices. Even if approval is obtained for our products, we may also be dependent on those third-party companies continuing to maintain such approvals or clearances, if required, for their drug delivery devices once they have been received. Failure of third-party companies to supply the devices, to successfully complete studies on the devices in a timely manner, or to obtain or maintain required approvals or clearances of the devices could result in increased development costs, delays in or failure to obtain regulatory

approval and delays in product candidates reaching the market or in gaining approval or clearance for expanded labels for new indications.

We and our licensees conduct clinical trials for product candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We and our licensees currently conduct clinical trials outside the United States. The acceptance by the FDA or comparable foreign regulatory authority of study data from clinical trials conducted outside the United States or another jurisdiction may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such as inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. Most of our clinical trials involve study subjects outside of the United States, including most of our phase 1 clinical trials (which often enroll study subjects in Australia and New Zealand), and our Phase 3 clinical trials of plozasiran, for which we have enrolled (with respect to FCS and sHTG) and plan to enroll (with respect to ASCVD) cohorts outside the United States. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in product candidates that we may develop not receiving approval or clearance for commercialization in the applicable jurisdiction.

Even if we obtain FDA approval for products in the United States, we may never obtain approval to commercialize any product candidates outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and effectiveness. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional or different administrative review periods from those in the United States, including additional preclinical studies or clinical trials. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval before a product can be marketed in that jurisdiction, even after establishing safety and efficacy in a clinical setting.

Seeking foreign regulatory approval could result in difficulties and costs and require additional nonclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates in those countries. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We do not have any product candidates approved for sale in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approval in international markets is delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

Even if our product candidates are approved for commercialization, failure to comply with regulatory requirements or unanticipated problems with our products may result in various adverse actions such as the suspension or withdrawal of one or more of our products, closure of a facility or enforcement of substantial penalties or fines.

If regulatory approval to sell any of our product candidates is received, regulatory agencies will subject any marketed product(s) and the facilities where they are manufactured to continual review and periodic inspection. If previously unknown problems with a product, manufacturing and laboratory facilities or regulatory requirements are discovered, such as adverse events of unanticipated severity or frequency, problems with a manufacturing process or laboratory facility, or failure to comply with applicable regulatory approval requirements, a regulatory agency may impose restrictions or penalties on that product or on us. Such restrictions or penalties may include, among other things:

- restrictions on the marketing or manufacturing of the product, the withdrawal of the product from the market or product recalls;
- warning, untitled, or it has come to our attention letters, or holds on clinical trials;

- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- closure of the facility, enforcement of substantial fines, injunctions, or the imposition of civil or criminal penalties.

Pharmaceutical and biological product marketing is subject to substantial regulation in the U.S. and any failure by us or our commercial and collaborative partners to comply with applicable statutes or regulations can adversely affect our business.

Any marketing activities associated with our product candidates, if approved for commercialization, will be subject to numerous federal and state laws governing the marketing and promotion of pharmaceutical and biological products. The FDA regulates post-approval promotional labeling and advertising to ensure that they conform to statutory and regulatory requirements. In addition to FDA restrictions, the marketing of prescription drugs is subject to laws and regulations prohibiting fraud and abuse under government healthcare programs. Similarly, many states have similar statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, and, in some states, such statutes or regulations apply regardless of the payor. In addition, government authorities may also seek to hold us responsible for any failure of our commercialization or collaborative partners to comply with applicable statutes or regulations. If we, or our commercial or collaborative partners, fail to comply with applicable FDA regulations or other laws or regulations relating to the marketing of our product candidates, if approved for commercialization, we could be subject to criminal prosecution, civil penalties, seizure of products, injunctions and exclusion of our product candidates from reimbursement under government programs, as well as other regulatory or investigatory actions against our future product candidates, our commercial or collaborative partners or us. See also "*Our operations, including our relationships with healthcare providers, physicians and third-party payers, are subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which, in the event of a violation, exposes us to liability for criminal sanctions, civil penalties, and contractual damages, and reputational harm and diminished profits and future earnings.*"

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 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. In addition, the laws of some foreign countries in which we do business, including through our joint ventures, do not protect intellectual property rights to the same extent or in the same manner as the laws of the United States. Moreover, if we or our licensors fail to maintain the patents and patent applications covering our product candidates or technologies, including as a result of geopolitical events such as civil or political unrest (including the ongoing conflicts between Ukraine and Russia and Israel and Palestine), we may not be able to use such patents and patent applications or stop a competitor from marketing products that are the same as or similar to our product candidates. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to adequately protect our owned intellectual property or derive sufficient value from our licensed or owned intellectual property, the value of your investment may decline.

In addition, patent grant standards by the USPTO and its foreign counterparts are not always uniform or predictable, and subject to change. For example, the America Invents Act enacted a number of changes to U.S. patent laws, which may prevent us from adequately protecting our inventions and discoveries, including our ability to seek injunctive relief, pursue infringement claims, and obtain substantial damage awards. An example of a major provision of the America Invents Act is the change in the U.S. patent policy from a first-to-invent to a first-to-file practice. Additionally, the USPTO and patent offices in other jurisdictions have often required that patent applications directed to pharmaceutical and/or biotechnology-related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting the scope of protection against competitive challenges. Accordingly, even if we or our

licensors are able to obtain patents, the patents might be substantially narrower than anticipated. Thus, there is no assurance as to the degree and range of protections any of our patents, if issued, may afford us or whether patents will be issues. Foreign counterparts to this law are also not uniform, and there is no worldwide policy governing the subject matter and scope of claims granted in a pharmaceutical or biotechnology patent. Uncertainty, arising from changing laws, can impact our ability to protect our patents and other proprietary rights.

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 could be seriously and adversely affected.

We are party to license agreements to incorporate third-party proprietary technologies into our drug products under development or our manufacturing processes. 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 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 may 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. As our organization grows, so does the risk of unauthorized disclosure of confidential information. In addition, while we undertake efforts to protect our 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. Enforcing a claim that a party illegally obtained and is using our trade secrets is challenging and the outcome is unpredictable. In addition, courts outside of the U.S. may be less willing to protect trade secrets. 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 also compete with a substantial number of other companies that are working to develop novel drugs using technology that compete directly with us. We are aware of several other companies that are working to develop RNAi therapeutic products and any one of these companies may develop its RNAi technology more rapidly and more effectively than us 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 or to otherwise effectively compete. 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.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents covering our current and any future product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we or our licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents, and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing. Issued patents may be challenged by third parties in the courts or patent offices in various countries throughout the world. Invalidation proceedings may result in patent claims being narrowed, invalidated or held unenforceable. Uncertainties regarding the outcome of such proceedings, as well as any resulting losses of patent protection, could harm our business.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. Some countries do not enforce patents related to medical treatments, or limit enforceability in the case of a public emergency. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

The intellectual property systems in other countries can be destabilized or unpredictable as a result of geopolitical events such as civil or political unrest (including the ongoing conflicts between Ukraine and Russia and Israel and Palestine). Therefore, during such geopolitical events, the ability to obtain, retain and enforce intellectual property protection in the affected countries may be uncertain and evolve during the course of such geopolitical event. The U.S. government's response to geopolitical events may also negatively affect our ability to obtain, retain and enforce intellectual property protection in the affected countries. Uncertainties regarding geopolitical events, as well as any resulting losses of intellectual property protection, could harm our business.

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 various stages of development and we have no approved products based on RNA interference and our delivery technologies. Accordingly, 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 product candidates. Because no drug candidates generated with our product platform have been approved, we 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 technologies that have not yet generated an approved product;
- 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.

Over the past several years we have entered into license and collaboration agreements with Takeda, Janssen, Amgen, Horizon, GSK and Visirna. Our business strategy includes securing 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 all of the products that may result from our technologies. Unless we expand our own product development capacity and enhance our own internal marketing capability, we may need to make arrangements with other 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, particularly as partnered programs progress and our licensees may elect to assume greater control over these programs. 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.

Under our licensing and collaboration agreements with Amgen, Takeda, GSK and Visirna, our partners substantially control clinical development and commercialization for all of the candidates covered under those agreements in their relevant territories. To the extent that (i) our partners' interests in advancing these candidates or targets changes, (ii) unforeseen scientific issues with the candidates arise, or (iii) the pace at which our partners move 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 in getting regulatory approval of our drug candidates, 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.

Moreover, as no drug candidates generated with our product platform has been approved for commercialization, we have not generated any revenue from product sales. Our ability to generate significant revenue and achieve profitability depends on our ability, alone or with potential strategic collaboration partners, to complete the development of and obtain the regulatory and marketing approvals necessary to commercialize our drug candidates and introduce products that will be accepted by the medical community. The commercial success of our products, if approved, will depend on many factors, including, but not limited to:

- the availability of coverage and adequate and timely reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid and similar foreign authorities) and other third-party payors for our products;
- patients' ability and willingness to pay out-of-pocket for our products in the absence of coverage and/or adequate reimbursement from third-party payors;
- patient demand for our products;
- our ability to establish and enforce intellectual property rights in and to our products; and
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims.

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.

If the market opportunities for our approved product candidates, if any, are smaller than we expect, it could materially adversely affect our financial condition and results of operation.

If the market opportunity for our products, if approved, is smaller than we expect, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business even if we obtain significant market share for them. The potentially addressable patient population for our products may be limited or may not be amenable to treatment with our products, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business.

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. For instance, many of our pulmonary drug candidates are administered using a proprietary delivery device which can only be sourced from a single manufacturer. 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, particularly as a result of recent labor market and global supply chain constraints.

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.

Although we have developed our own internal manufacturing capabilities which allow us to manufacture oligonucleotide drug substance for our clinical product candidates, we do not currently have internal manufacturing capabilities beyond such clinical-stage oligonucleotide drug substance. We rely, and expect to continue to rely, on third-party manufacturers for the production of our drug product candidates for clinical trials and potential future commercialization. We may choose to utilize third-party manufacturers to produce some or all of our development candidates, even if we have internal manufacturing capabilities to do so. Further, we have not developed the ability to manufacture drug product ourselves, nor have we developed the capabilities to manufacture biologics. If we were to experience an unexpected loss or interruption of supply for any of our product candidates, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. Further, our drug candidates are composed of multiple components and require specific formulations for which scale-up and manufacturing could be difficult. For certain products, we have limited experience in such scale-up and manufacturing which may require 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. We anticipate an increase in our GMP drug substance manufacturing capacity following the successful completion and integration of our manufacturing facility in Verona, Wisconsin. 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, if any of our product candidates become approved for commercial sale, we will need to establish either internal or third-party manufacturing and analytic capacity. For example, while we are still seeking regulatory approval, we intend to enter into third-party agreements for the manufacturing of plozasiran, in anticipation of a commercial launch in 2025. Further, some manufacturing partners 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 or additional 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. While we are exploring alternative suppliers for certain critical materials, there can be no assurance that our efforts will be successful.

If any of our drug candidates is approved by a regulatory authority, manufacturers of our approved products (including us, if we chose to internally manufacture) must comply with cGMP requirements relating to methods, facilities and controls used in the manufacturing, processing and packaging of the product, which are intended to ensure that drug products are safe and that they consistently meet applicable requirements and specifications. These requirements include quality control, quality assurance, and the maintenance of records and documentation. These manufacturers (including us, if we chose to internally manufacture) may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. These requirements are enforced by the FDA and other health authorities through periodic announced and unannounced inspections of manufacturing facilities. A failure to comply with these requirements or to provide adequate and timely corrective actions in response to deficiencies identified in an inspection may result in enforcement action, including warning letters, fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, plant shutdown, or the delay, withholding, 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 (CROs) 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. We rely on these parties to carry out our clinical trials in compliance with GCP and other relevant requirements. 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, GCP, or other regulatory requirements or if such third parties otherwise fail to meet deadlines or quality requirements, 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 various stages of preclinical and clinical 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 our pipeline and move toward commercializing drugs.

Our future financial performance and our ability to commercialize products and compete effectively will depend, in part, on our ability to effectively manage future growth. 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 and information technology systems. 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. We are currently establishing a sales and marketing infrastructure, and although we have hired individuals with significant experience in the sales, marketing, or distribution of pharmaceutical products, we have never done so as a company. To achieve commercial success for any approved product for which we retain sales and marketing rights, we must continue to develop a sales and marketing organization or outsource these functions to third parties. If we or our collaborators are unable to establish sales, marketing and distribution capabilities or enter into or maintain agreements with third parties to market and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved. Further, 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, information technology and management controls, reporting systems and procedures. We may not be able to effectively manage the expansion of our operations or 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 a cybersecurity incident or other 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 preclinical 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 or other cybersecurity incidents may allow hackers access to our preclinical compounds, strategies, discoveries, trade secrets, and/or other confidential information. Additionally, sensitive data could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel's, vendors' or partners' use of generative AI technologies. To the extent that any disruption or cybersecurity incident 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 protected health information and other personal data, 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 cybersecurity incident 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, and certain of the third parties for which we depend on to operate our business, 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 facilities in Madison, Wisconsin, Verona, Wisconsin, and San Diego, California 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.

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.

Our operations, including our relationships with healthcare providers, physicians and third-party payers, are subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which, in the event of a violation, exposes us to liability for criminal sanctions, civil penalties, and contractual damages, and reputational harm and diminished profits and future earnings.

Our operations, including any arrangements that we enter into with healthcare providers, physicians, and third-party payers, are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such laws and

regulations, including applicable U.S. federal and state healthcare laws and regulations, as well as foreign laws, such as the federal Anti-Kickback Statute, the False Claims Act, the Health Insurance Portability and Accountability Act of 1996, or the Foreign Corrupt Practices Act, may constrain our operation and the business or financial arrangements through which we can market, sell and distribute any drug candidates for which we obtain marketing approval.

Efforts to confirm that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may become subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors and specialty pharmacies could adversely affect our revenues, financial condition, or results of operations.

We have an exclusive agreement with Vanscoy Rare Pharmacy for drug delivery services, and we expect to rely on this pharmacy for a considerable portion of our sales for plozasiran, if approved. The financial failure of Vanscoy Rare Pharmacy could adversely affect our revenues, financial condition or results of operations. Our revenues, financial condition or results of operations may also be affected by fluctuations in their buying or distribution patterns. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors.

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 efforts and prepare for the potential commercialization of our product candidates. 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 preclinical 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, including the progression of our clinical trials, with late-stage trials generally requiring greater capital than early-stage trials;
- Regulatory requirements for our clinical trials;
- The extent to which our research and development and clinical efforts are successful;

- Expenditures to build out or contract for sales, marketing and distribution capabilities as we prepare for the potential commercialization of our product candidates, if any;
- 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 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.

The terms of our financing agreement with Sixth Street Lending Partners and our indebtedness could adversely affect our operations and limit our ability to plan for or respond to changes in our business. If we are unable to comply with restrictions in the financing agreement, the repayment of our existing indebtedness could be accelerated.

On August 7, 2024, we entered into a financing agreement with Sixth Street Lending Partners, as the administrative agent and collateral agent for several lenders. The financing agreement establishes a senior secured term loan facility of $500.0 million (the "Credit Facility"), consisting of $400.0 million funded on the closing date and an additional $100.0 million available at the our option, subject to mutual agreement with Sixth Street, over the seven-year term. We have incurred a substantial amount of debt under the financing agreement which could adversely affect our business.

The financing agreement requires us to make certain payments over time and contains several other negative covenants that, subject to certain exceptions, restrict indebtedness, liens, investments (including acquisitions), fundamental changes, asset sales and licensing transactions, dividends, modifications to material agreements, payment of subordinated indebtedness, and other matters customarily restricted in such agreements. Among other requirements of the financing agreement, we and our subsidiaries party to the financing agreement must maintain certain liquidity thresholds based on our market capitalization. We are also subject to restrictions on sales and licensing transactions with respect to our core intellectual property and product assets, including, but not limited to, olpasiran, plozasiran, zodasiran, fazirsiran, GSK4532990, and daplusiran/tomligisiran, subject to certain exceptions. These and other terms in the financing agreement could restrict our ability to grow our business or enter into transactions that we believe would be beneficial to our business.

Our indebtedness could affect our business in the following ways, among other things: make it more difficult for us to satisfy our contractual and commercial commitments; require us to use a substantial portion of our cash flow subject to mandatory prepayments to pay interest and principal when due, which would reduce funds available for working capital, capital expenditures and other general corporate purposes; limit our ability to obtain additional financing for working capital, capital expenditures, acquisitions and other investments or general corporate purposes; heighten our vulnerability to downturns in our business, our industry or in the general economy; place us at a disadvantage compared to those of our competitors that may have proportionately less debt; limit management's discretion in operating our business; and limit our flexibility in planning for, or reacting to, changes in our business, the industry in which we operate or the general economy.

Our business may not generate cash flows from operations in the future that are sufficient to service our debt and support our growth strategies. In addition, our ability to generate sufficient cash flows to meet our debt obligations depends upon several factors, such as the ability of our Company and our licensees to timely complete clinical trials and obtain marketing approval for our clinical-stage product candidates, to successfully commercialize our clinical-stage product candidates, our receipt of regulatory approval for plozasiran for treatment of FCS, and our future performance, which is subject to financial, business, and other impacts on our operations, many of which are beyond our control. If we are unable to generate sufficient cash flows, we may be required to adopt one or more alternatives, such as obtaining additional equity capital on terms that may be onerous or highly dilutive, selling assets, or restructuring debt. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in

any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

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. 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.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results have fluctuated and may continue to fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, may of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our current and any future product candidates, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of manufacturing our current and any future product candidates, which may vary depending on FDA guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers and other suppliers;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies;
- the timing and outcomes of clinical trials for product candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products that compete with any of our product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of any of our product candidates;
- the level of demand for any of our product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future products that compete with our product candidates;
- our ability to commercialize any of our product candidates, if approved, inside and outside of the United States, either independently or working with third parties;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our

revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

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

At September 30, 2024, we had $681.0 million in cash, cash equivalents, restricted cash and available-for-sale securities. Our investments may also include commercial paper, securities issued by the U.S. government obligations, 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 (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, 2024, we had federal, state, and foreign NOL carryforwards of $223.1 million, $693.2 million, and $38.3 million, respectively. As a result of the Coronavirus Aid, Relief, and Economic Security Act of 2020 ("CARES Act") and legislation commonly referred to as the Tax Cuts and Jobs Act of 2017 ("2017 Tax Act"), NOLs arising before January 1, 2018, and NOLs arising after January 1, 2018, are subject to different rules. Under the CARES Act and 2017 Tax Act, federal NOLs incurred in 2018, 2019 and 2020 can generally be carried back five years, carried forward indefinitely and can offset 100% of future taxable income for tax years before January 1, 2021 and up to 80% of future taxable income for tax years after December 31, 2020. Any NOLs arising on or after January 1, 2021, cannot be carried back, but can generally be carried forward indefinitely and can offset up to 80% of future taxable income. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. These NOL carryforwards could expire unused before offsetting potential future income tax liabilities.

In addition, under Section 382 and 383 of the Code 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.

We could be subject to additional tax liabilities.

We are subject to U.S. federal, state, and local taxes in the United States and other countries. 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. For instance, beginning in 2022, the 2017 Tax Act eliminated the option of expensing all research and development expenditures in the current year, instead requiring amortization over five years for expenditures in the U.S. and over fifteen years for foreign-based expenditures. There is no assurance that the requirement will be deferred, repealed, or otherwise modified. This change in law increased our tax liability for the fiscal year. We continue to monitor new tax legislation or other developments since significant changes in tax legislation, or in the interpretation of existing legislation, could materially and adversely affect our financial condition and operating results.

Additionally, 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.

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 The Nasdaq Global Select Market. Any such action could adversely affect our financial results and the market price of our common stock.

Risks Related to Investment and Securities

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. 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 still a clinical-stage pharmaceutical company and have not yet commercialized a drug, 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, antisense technologies, gene editing technologies 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.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation and mass arbitration demands; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.

In the ordinary course of business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share confidential, proprietary, and sensitive information, including personal information, business data, trade secrets, intellectual property, information we collect about trial participants in connection with clinical trials, sensitive third-party data, business plans, transactions, and financial information.

These activities may subject us to numerous data privacy and security obligations governing the collection, use, disclosure, protection, and other processing of personal data, such as various laws, regulations, guidance, industry standards, external and internal data privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

In the United States, there are both state and federal data privacy and security laws, including data breach notification laws, data privacy laws (including biometric privacy laws), consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), the Health Insurance Portability and Accountability Act ("HIPPA"), and other similar laws (e.g., wiretapping laws). For example, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020 (together, the "CCPA") applies to personal data of consumers, business representatives, and employees, and requires businesses to provide specific disclosures in privacy notices and certain rights to California residents with respect to their personal data. The CCPA provides for civil penalties of up to $7,500 per intentional violation

and $2,500 per unintentional violation and allows private litigants affected by certain data breaches to recover significant statutory damages.

Outside the United States there are additional laws, regulations, and industry standards governing data privacy and security. For example, the General Data Protection Regulation ("GDPR") and the GDPR as incorporated into UK law pursuant to the European Union (Withdrawal) Act 2018 (the "UK GDPR") impose strict requirements for processing personal data, including health-related information. Under the GDPR and UK GDPR, companies may face fines of up to 20 million Euros or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data. In addition, the GDPR and UK GDPR impose specific restrictions on the transfer of personal data to countries outside of the EEA and UK. Although there are currently various mechanisms that may be used to make such transfers in compliance with law, such as the EEA and UK's standard contractual clauses, these mechanisms are subject to legal challenges. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions are subject to scrutiny from regulators, individual litigants, and activities groups.

Preparing for and complying with these obligations requires us to devote resources and may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf.

If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data; and orders to destroy or not use personal data. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

Economic and Industry Risks

Unfavorable global economic conditions, whether brought about by material global crises, health epidemics, military conflicts or war, geopolitical and trade disputes or other factors, may adversely affect our business and financial results.

Our business is sensitive to global economic conditions, which can be adversely affected by epidemics and other public health crises (such as the COVID-19 pandemic), political and military conflict, trade and other international disputes, significant natural disasters (including as a result of climate change) or other events that disrupt macroeconomic conditions. Adverse macroeconomic conditions, including inflation, slower growth or recession, new or increased tariffs and other barriers to trade, changes to fiscal and monetary policy or government budget dynamics (particularly in the pharmaceutical and biotech areas), tighter credit, higher interest rates, volatility in financial markets, high unemployment, labor availability constraints, currency fluctuations and other challenges in the global economy have in the past adversely affected, and may in the future adversely affect, us and our business partners and suppliers.

For example, trade policies and geopolitical disputes (including as a result of China-Taiwan relations) and other international conflicts can result in tariffs, sanctions and other measures that restrict international trade, and can materially adversely affect our business, particularly if these measures occur in regions where we source our components or raw materials. For example, tensions between the United States and China have led to a series of tariffs being imposed by the United States on imports from China mainland, as well as other business restrictions. Tariffs increase the costs of the components and raw materials we source. Countries may also adopt other measures, such as controls on imports or exports of goods, technology or data, that could adversely impact the Company's operations and supply chain. These geopolitical risks could also adversely affect Visirna.

Further, military conflicts or wars (such as the ongoing conflicts between Russia and Ukraine and in the Middle East) can cause exacerbated volatility and disruptions to various aspects of the global economy. The uncertain nature, magnitude, and duration of hostilities stemming from such conflicts, including the potential effects of sanctions and counter-sanctions, or retaliatory cyber-attacks on the world economy and markets, have contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic factors that affect our business and operations, such as worldwide supply chain issues. Additionally, the ongoing conflict between Russia and Ukraine has impacted our business decisions with respect to potential clinical trial sites in Europe. For example, a number of our clinical trial sites we had previously planned to use in Russia, Ukraine and Belarus were shut down and we had to seek alternatives in other geographies. We cannot be certain of the overall impact of the conflict between Russia and Ukraine on our ability to conduct and complete our clinical trials as planned, and any interruptions of our clinical trials can result in significant delays or termination of the research, development or commercialization of our drug candidates, which could impair our ability to generate revenues and harm our business and financial condition. Moreover, the conflict between

Israel and Palestine could impact future business decisions to locate potential clinical trials in Israel. It is not possible to predict the short and long-term implications of military conflicts or wars or geopolitical tensions which could include further sanctions, uncertainty about economic and political stability, increases in inflation rate and energy prices, cyber-attacks, supply chain challenges and adverse effects on currency exchange rates and financial markets.

Additionally, our operations and facilities, as well as operations of our suppliers and manufacturers, may be located in areas that are prone to earthquakes, wildfires and other natural disasters. Such operations and facilities are also subject to the risk of interruption by drought, power shortages, nuclear power plant accidents and other industrial accidents, terrorist attacks and other hostile acts, ransomware and other cybersecurity attacks, labor disputes, public health crises, and other events beyond the Company's control. Global climate change is resulting in certain types of natural disasters occurring more frequently or with more intense effects. Such events can create delays or interruptions to the Company's development efforts and inefficiencies in the Company's supply and manufacturing chain. 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. Further, because the Company relies on single or limited sources for the supply and manufacture of many critical components, a business interruption affecting such sources would exacerbate any negative consequences to the Company.

Any future public health crises, may affect our operations and those of third parties on which we rely, including our business partners and suppliers. We may in the future experience:

- delays in receiving authorization from regulatory authorities to initiate any planned clinical trials, inspections, reviews and approvals of products;
- delays or difficulties enrolling patients in our clinical trials;
- delays in or disruptions to the conduct of preclinical programs and clinical trials;
- constraints on the movement of products and supplies through the supply chain, which can disrupt our ability to conduct clinical trials and develop our products;
- price increases in raw materials and capital equipment, as well as increasing price competition in our markets;
- adverse impacts on our workforce and/or key employees; and
- increased risk that counterparties to our contractual arrangements will become insolvent or otherwise unable to fulfill their contractual obligations.

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 FDA, may not approve our potential product for the intended use, or at all; and/or
- Manufacturing and distribution may be uneconomical.

For example, any positive preclinical results in animals may not be replicated in human clinical studies. These programs may be also found to be unsafe in humans, particularly if higher doses are 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 preclinical 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. Many federal and state legislatures have considered, and adopted, healthcare policies intended to curb rising healthcare costs, such as the Inflation Reduction Act of 2022. These cost-containment measures may include, among other measures: requirements for pharmaceutical companies to negotiate prescription drug prices with government healthcare programs; controls on government-funded reimbursement for drugs; new or increased requirements to pay prescription drug rebates to government healthcare programs, including if drug prices increase at a higher rate than inflation; controls on healthcare providers; challenges to or limits on the pricing of drugs, including pricing controls or limits or prohibitions on reimbursement for specific products through other means; requirements to try less expensive products or generics before a more expensive branded product; and public funding for cost effectiveness research, which may be used by government and private third-party payors to make coverage and payment decisions. Political, economic and regulatory developments may further complicate developments in healthcare systems and pharmaceutical drug pricing. These developments could, for example, impact our potential licensing agreements as commercial and collaborative partners may also consider the impact of these pressures on their licensing strategies.

Any new laws or regulations that have the effect of imposing additional costs or regulatory burden on pharmaceutical manufacturers, or otherwise negatively affect the industry, could adversely affect our ability to successfully commercialize our product candidates. The implementation of any price controls, caps on prescription drugs or price transparency requirements could adversely affect our business, operating results and financial condition.

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 1C. CYBERSECURITY

The Company maintains a cybersecurity program, with direct oversight from senior management and the Board of Directors (the "Board"), to manage information, data, and technology security. The cybersecurity program is informed in part by the National Institute of Standards and Technology Cybersecurity Framework (NIST CSF) and is designed to help identify, assess, and manage cybersecurity risks relevant to the Company's business. The Company's cybersecurity program has been developed in light of the nature of the Company's business, resource availability, requirements from stakeholders, and industry trends. The Company has formed an internal cross-functional Technology Risk Management Committee comprised of representative leaders from various aspects of the Company's business to broadly implement its cybersecurity program.

The Company's cybersecurity program prioritizes vulnerability management, risk reduction, detection, and prevention to help protect against material risks from cybersecurity threats to its information systems. The Company routinely conducts internal and third-party cybersecurity risk assessments and penetration tests and incorporates relevant findings and recommendations into its overall cybersecurity strategy, as appropriate. Through these assessments, the Company develops targeted strategies intended to address the most significant cybersecurity risks and conducts at least one annual cybersecurity incident tabletop exercise to refine response plans.

The Company's cybersecurity program emphasizes defense, rapid detection, and remediation of cybersecurity threats and incidents, including the use of various security tools and systems based on defense-in-depth and zero-trust principles that are intended to meet control requirements. The cybersecurity program also encompasses crisis incident response guidelines that detail the processes for the detection, response, mitigation, and remediation of cybersecurity incidents, in order to support the effective management of, response to, communication during, and recovery from any such incidents.

A key element of the Company's strategy is fostering training and awareness through annual cybersecurity training and role-based phishing tests for employees and certain third parties having access to the Company's information systems. The Company also utilizes a third-party cybersecurity operations monitoring center to help identify threats and incidents to the Company's servers and computers. The Company's cybersecurity preparedness program includes specific requirements and guidelines for the information security team relating to the Company's computer emergency response preparedness, intrusion response preparedness, and incident response preparedness.

When a potential cybersecurity threat or incident is identified, our processes require that the Senior Director of Information Security be promptly notified of the incident, who then is to conduct an initial investigation to determine the probability and potential of the threat or incident to have a material impact on key business systems and processes. If there is a reasonable possibility for a material impact to the Company's business or information systems, the cybersecurity program requires that the Technology Risk Management Committee be promptly notified, which then assigns a risk level to the threat or incident. All threats and incidents identified as high-risk are promptly escalated to Company leadership and the legal department, who are tasked with activating and implementing a high-risk information security incident mitigation and response plan, which details the roles, responsibilities, and strategies to respond. Our cybersecurity program also requires that high-risk cybersecurity incidents or threats be reported to the Company's Materiality Committee and the Audit Committee of the Board within 24 hours of their designation as high-risk by the Technology Risk Management Committee.

Cybersecurity risks are incorporated into our overall risk management program. If a cybersecurity risk is identified as high-risk, a response and mitigation plan is developed, and progress updates on the plan are routinely reported to the Technology Risk Management Committee and tracked by the Audit Committee of the Board as part of our overall risk management process.

The Company is not aware of any cybersecurity threats or incidents in the last fiscal year, including as a result of any prior cybersecurity incidents, that have had a material impact on our Company, including its business strategy, operations, or financial condition. However, we face certain ongoing cybersecurity risks and threats that, if realized, are reasonably likely to materially affect us. Additional information on cybersecurity risks we face is discussed in Part I, Item 1A "Risk Factors," under the heading "Our business and operations could suffer in the event of a cybersecurity incident or other information technology system failures."

Execution of the Company's cybersecurity program is delegated by the Board to the Senior Director of Information Security, who has nearly 25 years of relevant experience in information security, including 13 years at the Company, and is further supported by a team of security professionals within the Information Systems & Informatics department. The Senior Director of Information Security reports to the Vice President of Information Systems & Informatics, and they meet periodically with senior leadership and the Board to review metrics on cybersecurity preparedness, incidents, mitigations and remediation efforts. In addition, the Company's internal audit team conducts periodic audits of its systems and cybersecurity processes, with findings reported to the Audit Committee and senior management.

The Company has also established a management-level Technology Risk Committee, which includes leaders from finance, legal, operations, quality & compliance, and information systems & informatics, who are responsible for overseeing the execution of high-risk incident response and mitigation plans. This committee actively reviews technology strategies, physical and cybersecurity threat assessment, and emerging issues and related initiatives. It is also responsible for evaluating the materiality of information for SEC filings and, as required or as otherwise appropriate, coordinates with the Company's Materiality Committee to support timely disclosure of relevant information.

ITEM 2. PROPERTIES

The following table summarizes the Company's leased facilities as of November 20, 2024.

	Approximate Square Footage	Primary Use	Lease Expiration	Remaining Lease Term (year)
Pasadena, California	49,000	Corporate Headquarters	April 2027	2.5
Madison, Wisconsin	107,000	Research Facility	September 2031	6.9
San Diego, California	144,000	Research and Office Facility	April 2038	13.5

The Company owns land in the Verona Technology Park in Verona, Wisconsin, which has been developed into an approximately 160,000 square foot drug manufacturing facility and an approximately 140,000 square foot laboratory and office facility which will support the Company's manufacturing process development and analytical activities. During fiscal year 2024, the Company completed the build out of one of its laboratory and office facilities and plans to finalize the manufacturing facility by the end of the first quarter of fiscal year 2025.

ITEM 3. LEGAL PROCEEDINGS

Legal Proceedings are set forth in the Company's financial statement schedules in Part IV, Item 15 of this Annual Report on Form 10-K 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

Market Information

Shares of the Company's common stock are traded on The Nasdaq Global Select Market under the symbol "ARWR." There were 89 holders of record of the Company's common stock as of November 20, 2024.

Dividends

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

Recent Sales of Unregistered Securities

To the extent required by Form 10-K, the disclosures set forth in Part II, Item 9B of this Annual Report on Form 10-K under the headings "Stock Purchase Agreement" and "Securities Purchase Agreement" are incorporated herein by reference.

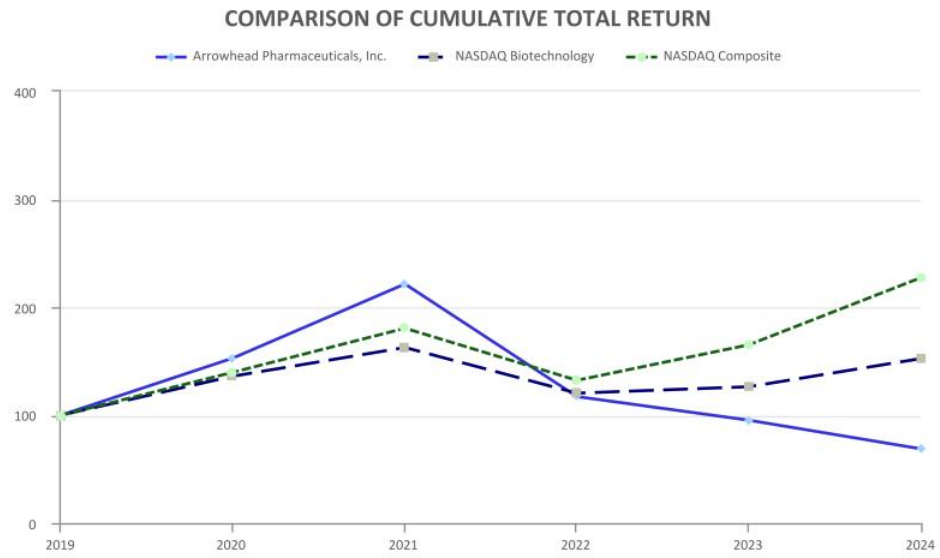
Repurchases of Equity Securities

None.

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 stockholders on the Company's common stock relative to the cumulative total returns of the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The Company selected the Nasdaq Biotechnology Index because it believes the index reflects the market conditions within the industry in which the Company primarily operates. 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, 2019, in each of the Company's 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 the Company's common stock.



$100 investment in stock or index	Ticker	2019	2020	2021	2022	2023	2024
Arrowhead Pharmaceuticals, Inc.	ARWR	$ 100.00	$ 152.80	$ 221.54	$ 117.28	$ 95.35	$ 68.74
NASDAQ Biotechnology Index	^NBI	$ 100.00	$ 136.10	$ 162.58	$ 120.46	$ 126.41	$ 152.44
NASDAQ Composite Index	^IXIC	$ 100.00	$ 139.61	$ 180.62	$ 132.21	$ 165.26	$ 227.38

ITEM 6. RESERVED

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

OVERVIEW

The Company 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, the Company's therapies trigger the RNAi interference mechanism to induce rapid, deep and durable knockdown of target genes. RNAi is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. RNAi-based therapeutics may leverage this natural pathway of gene silencing to target and shut down specific disease-causing genes.

The Company believes that TRiM™ enabled therapeutics offer several potential advantages over prior generation and competing technologies, including: simplified manufacturing and reduced costs; multiple routes of administration including subcutaneous injection and inhaled administration; the ability to target multiple tissue types including liver, lung, central nervous system (CNS), muscle, and adipose tissue; and the potential for improved safety and reduced risk of intracellular buildup, because there are fewer metabolites from smaller, simpler molecules.

The Company's pipeline includes:

- Hypertriglyceridemia - plozasiran (formerly ARO-APOC3)
- Dyslipidemia - zodasiran (formerly ARO-ANG3)
- Cardiovascular disease - olpasiran (formerly AMG 890 or ARO-LPA, out-licensed to Amgen)
- Muco-obstructive or inflammatory pulmonary conditions - ARO-MUC5AC and ARO-RAGE
- Idiopathic pulmonary fibrosis - ARO-MMP7
- Metabolic-dysfunction associated steatohepatitis (MASH) - GSK-4532990 (formerly ARO-HSD, out licensed to GSK);
- Alpha-1 antitrypsin deficiency (AATD) - fazirsiran (formerly ARO-AAT, a collaboration with Takeda)
- Chronic hepatitis B virus - daplusiran/tomligisiran (GSK5637608, formerly JNJ-3989, out-licensed to GSK)
- Complement mediated diseases - ARO-C3
- Metabolic-dysfunction associated steatohepatitis (MASH) - ARO-PNPLA3 (formerly JNJ-75220795 or ARO-JNJ1);
- Facioscapulohumeral muscular dystrophy - ARO-DUX4;
- Dystrophia myotonica protein kinase (DMPK) - ARO-DM1;
- Hepatic expression of complement factor B (CFB) - ARO-CFB
- Obesity - ARO-INHBE; and
- Spinocerebellar ataxia 2 - ARO-ATXN2

The Company operates lab facilities in California and Wisconsin, where its research and development activities, including the development of RNAi therapeutics, take place. The Company's principal executive offices are located in Pasadena, California.

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 manufactured internally or contracted to third-party manufacturers. 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, including toxicology/efficacy testing and manufacturing costs, as well as the preparation for and administration of clinical trials, are referred to as "candidate costs." As clinical candidates progress through clinical development, candidate costs will increase.

2024 Business Highlights

During fiscal year 2024, the Company continued to develop and advance its pipeline and partnered candidates and expand its facilities to support its growing programs. The bullets below highlight some of these key developments; however, this list is not all-inclusive and is meant to be read in conjunction with the entirety of management's discussion and analysis, the Company's Consolidated Financial Statements and notes thereto, and all other items contained within this Annual Report on Form 10-K.

- Presented new pivotal Phase 3 Data from PALISADE study of plozasiran in patients with familial chylomicronemia syndrome (FCS) at the European Society of Cardiology (ESC) Congress 2024 and simultaneously published in The New England Journal of Medicine. The Company filed a New Drug Application on November 16, 2024;

- Presented preclinical data and detailed plans to advance two next generation RNAi-based candidates, ARO-INHBE and ARO-ALK7, into upcoming clinical studies for the treatment of obesity and metabolic diseases. In preclinical studies to date, these candidates demonstrated the potential to reduce body weight and fat mass with a novel mechanism of action that may lead to improved preservation of lean muscle mass compared to currently approved obesity therapies. On September 23, 2024, the Company filed for regulatory clearance to initiate a Phase 1/2a clinical trial of ARO-INHBE and plans to file for regulatory clearance before the end of 2024 to initiate a clinical trial for its second obesity candidate, ARO-ALK7;
- Announced successful top-line results from the pivotal Phase 3 PALISADE study of investigational plozasiran in patients with familial chylomicronemia syndrome (FCS). The Company highlighted recent data for its cardiometabolic pipeline at its June 25, 2024, Cardiometabolic event;
- Announced results from the Phase 2b double blind, randomized ARCHES-2 study of investigational zodasiran in patients with mixed hyperlipidemia;
- Announced that new interim clinical data on ARO-RAGE achieves high level of gene knockdown in patients with asthma;
- Amgen completed enrollment in Amgen's Phase 3 OCEAN(a) - outcomes trial of olpasiran, triggering a $50.0 million milestone payment to the Company from Royalty Pharma, which was paid in the third quarter of fiscal 2024;
- Presented final data from the double-blind treatment period of the Company's Phase 2 SHASTA-2 study of investigational plozasiran in patients with severe Hypertriglyceridemia. Results from the SHASTA-2 study showed dramatic, consistent, and sustained reductions in Apolipoprotein C-III (APOC3) and triglycerides and improvement in multiple atherogenic lipoprotein levels;
- Announced an Expanded Access Program ("EAP") to make investigational plozasiran available outside of a clinical trial for qualifying patients with familial chylomicronemia syndrome (FCS);
- Initiated a Phase 1/2a clinical trial of ARO-DM1, being developed as a potential treatment for type 1 myotonic dystrophy (DM1), the most common adult-onset muscular dystrophy;
- Filed an application for clearance to initiate a Phase 1/2a clinical trial of ARO-CFB, being developed as a potential treatment for complement mediated renal disease;
- Entered into an Amended and Restated License Agreement with GSK, pursuant to which GSK received a worldwide, exclusive license to develop and commercialize daplusiran/tomligisiran (GSK5637608, formerly JNJ-3989). Daplusiran/tomligisiran had previously been licensed to Janssen Pharmaceuticals, Inc.

2024 Financial Performance Summary

Net loss attributable to Arrowhead Pharmaceuticals, Inc. was $599.5 million for the year ended September 30, 2024 as compared to $205.3 million for the year ended September 30, 2023. Net loss per share – diluted was $5.00 for the year ended September 30, 2024 as compared to $1.92 for the year ended September 30, 2023. The change in net loss for the year ended September 30, 2024 was mainly due to a decrease in revenue from the Company's license and collaboration agreements, in conjunction with increased research and development expenses, which have continued to increase as the Company's pipeline of candidates has expanded and progressed through clinical trial phases.

The Company entered into an underwriting agreement with Jefferies LLC, BofA Securities, Inc., and Cowen and Company, LLC, as representatives of the several underwriters. The Company issued 15,790,000 shares of common stock at a price of $28.50 per share. The aggregate purchase price paid by investors was $450.0 million and the Company received net proceeds of $429.3 million after deducting advisory fees and offering expenses.

Further, the Company entered into a financing agreement with Sixth Street Lending Partners, as representatives of the several lenders. The financing agreement provides for a senior secured term loan facility of $500.0 million, which includes $400.0 million funded on the closing date with an additional $100.0 million at the Company's option during the seven-year term of the agreement. The Company received net proceeds of $388.9 million, after issuance costs as of September 30, 2024. This is discussed further in Note 14, Financing Agreements of the Notes to the Company's Consolidated Financial Statements in Part IV, "Item 15. Exhibits and Financial Statement Schedules."

The Company had $102.7 million of cash, cash equivalents and restricted cash and $578.3 million in available-for-sale securities as of September 30, 2024, as compared to $110.9 million of cash, cash equivalents and restricted cash and $292.7 million in available-for-sale securities as of September 30, 2023. 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 from the date of the issuance of these consolidated financial statements.

Critical Accounting Estimates

Management makes certain judgments and uses certain estimates and assumptions when applying U.S. generally accepted accounting principles ("GAAP") in the preparation of the Company's Consolidated Financial Statements. On an ongoing basis, the Company evaluates its estimates, judgments and assumptions. The Company bases its estimates on historical experience and on various other assumptions that it believes are reasonable, the results of which form the basis for making judgments about the carrying values of assets, liabilities and equity and the amount of revenue and expense. Actual results may vary from what the Company anticipates and different assumptions or estimates about the future could change its reported results. The Company believes the following accounting policies are the most critical to it, in that they require its most difficult, subjective or complex judgments in the preparation of the Company's Consolidated Financial Statements. For further information, see Note 1, Organization and Significant Accounting Policies of the Notes to the Company's Consolidated Financial Statements in Part IV, "Item 15. Exhibits and Financial Statement Schedules."

Revenue Recognition—The Company has adopted Financial Accounting Standards Board ("FASB") Topic 606 – *Revenue for Contracts from Customers.* The Company has not yet achieved commercial sales of its drug candidates to date, however, this standard is applicable to its licensing and collaboration agreements. This is discussed further in Note 2, Collaboration and License Agreements of the Notes to the Company's Consolidated Financial Statements in Part IV, "Item 15. Exhibits and Financial Statement Schedules."

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 it 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 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 its 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 the Company's consolidated statements of operations and comprehensive 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 preclinical 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 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 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 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 we determine 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 input method. Labor hours, costs incurred or patient visits in clinical trials 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.

Collaborative Arrangements—The Company analyzes its collaborative arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards, and therefore an appropriate recognition method is determined and applied consistently, either by analogy to appropriate accounting literature or by applying a reasonable accounting policy election. For collaborative arrangements that are within the scope of FASB Topic 808—*Collaborative Arrangements*, the Company evaluates the income statement classification for presentation of amounts due to or owed from other participants associated with multiple units of account in a collaborative arrangement based on the nature of each activity. Payments or reimbursements that are the result of a collaborative relationship instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as increases or decreases to research and development expense or general and administrative expense, as appropriate.

Clinical Accruals—The Company accrues liabilities for products received or services incurred, particularly for ongoing clinical trials, where service providers have not yet billed or where billing terms do not align with the timing of the work performed as of the period-end. These costs mainly include third-party clinical management or clinical research organization (CRO), laboratory analysis, and investigator fees. Accrual estimates may be based on vendor communications to obtain pending invoices and/or estimates for services performed during the period. In some cases, these estimates require judgment, drawing on an understanding of research and development programs, services provided during the period, prior experience, and, where applicable, the expected duration of third-party contracts. Actual costs upon settlement may differ significantly from the accrued amounts in the Company's consolidated financial statements, though historical estimates have not differed materially from actual costs.

Liability Related to the Sale of Future Royalties—Based on its evaluation of the agreement terms, the Company classifies the liability related to the sale of future royalties as a debt financing. The Company records the obligations at their carrying value using the effective interest method. In order to amortize the sale of future royalties, the Company utilizes the prospective method to estimate the future royalties to be paid by the Company to the counterparty over the life of the arrangement. Under the prospective method, a new effective interest rate is determined based on the revised estimate of remaining cash flows. The new rate is the discount rate that equates the present value of the revised estimate of remaining cash flows with the carrying amount of the debt, and it will be used to recognize non-cash interest expense for the remaining periods. The Company periodically assesses the amount and the timing of expected royalty payments using a combination of internal projections and forecasts from external sources. The estimates of future net product sales (and resulting royalty payments) are based on key assumptions including population, penetration, probability of success and sales price, among others. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is different than its original estimates, the Company will prospectively adjust the amortization of the royalty financing obligations and the effective interest rate.

RESULTS OF OPERATIONS

The following data summarizes the Company's results of operations for the following periods indicated:

	Year Ended September 30,		
	2024	2023	2022
	(in thousands, except per share amounts)		
Revenue	$ 3,551	$ 240,735	$ 243,231
Operating loss	$ (601,080)	$ (205,002)	$ (178,507)
Net loss attributable to Arrowhead Pharmaceuticals, Inc.	$ (599,493)	$ (205,275)	$ (176,063)
Net loss per share (diluted) attributable to Arrowhead Pharmaceuticals, Inc.	$ (5.00)	$ (1.92)	$ (1.67)

Year Ended September 30, 2024 Compared to Year Ended September 30, 2023

Revenue

Total revenue for the year ended September 30, 2024 decreased to $3.6 million, 98.5%, from the same period of 2023. The changes were primarily driven by decreased revenue recognition associated with the Company's license and collaboration agreements during the year ended September 30, 2024. The Company has evaluated each agreement in accordance with FASB Topic 808–*Collaborative Arrangements* and Topic 606-*Revenue for Contracts from Customers*. See Note 2 — Collaboration and License Agreements of the Notes to Consolidated Financial Statements of Part IV, "Item 15. Exhibits and Financial Statement Schedules."

Takeda: In October 2020, Takeda and the Company entered into the Takeda License Agreement. The Company determined that they key deliverables included the license and specific R&D services. Given the specialized and unique nature of the R&D services, the Company concluded that these deliverables represent one combined performance obligation. The Company allocated the total $300.0 million initial transaction price to its one distinct performance obligation for the fazirsiran license and the associated Takeda R&D Services. Revenue was recognized using the input method (based on actual patient visits completed versus total estimated visits completed for the ongoing SEQUOIA and AROAAT2002 clinical studies). The Phase 2 study visits for patients in the SEQUOIA and AROAAT2002 studies concluded by December 31, 2023, and the Company has substantially completed its performance obligation under the Takeda License Agreement. As such, all revenue has been fully recognized as of December 31, 2023.

During the fiscal year of 2023, the Company recorded $162.5 million of revenue, including a $40.0 million milestone payment by dosing the first patient in the Phase 3 REDWOOD clinical study of fazirsiran.

GSK: On December 11, 2023, GSK and the Company entered into the GSK-HBV Agreement. Under the GSK-HBV Agreement, GSK received a worldwide, exclusive license to develop and commercialize daplusiran/tomligisiran (GSK5637608, formerly JNJ-3989). Daplusiran/tomligisiran had previously been licensed to Janssen in October 2018. Under the terms of the GSK-HBV Agreement, the Company received $2.7 million during fiscal year 2024 upon signing the GSK-HBV Agreement.

On November 22, 2021, GSK and the Company entered into the GSK-HSD License Agreement. Under the GSK-HSD License Agreement, GSK has received an exclusive license for GSK-4532990. The Company has completed its performance obligation related to this agreement, and the upfront payment of $120.0 million was fully recognized in the year ended September 30, 2022. Further, during fiscal year 2023, the Company recorded a $30.0 million milestone payment by dosing the first patient in a Phase 2b trial under GSK-HSD License Agreement.

Horizon/Amgen: During the fiscal year of 2023, the Company recognized $6.7 million of the total $40.0 million upfront payment received in July 2021, which was recognized on a straight-line basis over the timeframe for completing the Horizon R&D Services, concluding in the first quarter of 2023. There was also $1.5 million of reimbursable costs. Horizon enrolled the first subject in December 2022 in a Phase 1 randomized, placebo-controlled trial to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of HZN-457, triggering a $15.0 million milestone payment to the Company which was paid in the second quarter of fiscal 2023. Further, Amgen enrolled the first subject in its Phase 3 trial of olpasiran, which triggered a $25.0 million milestone payment to the Company which was paid in the second quarter of fiscal 2023. On October 6, 2023, Amgen Inc. completed its acquisition of Horizon and subsequently notified the Company of Amgen's intent to terminate the HZN-457 license. Horizon exercised its right to terminate the Horizon License Agreement for convenience, which took effect on December 21, 2023.

Operating Expenses

The analysis below details the operating expenses and discusses the expenditures of the Company within the major expense categories. For purposes of comparison, the amounts for the years ended September 30, 2024 and 2023 are shown in the tables below.

Research and Development (R&D) Expenses

R&D expenses are related to the Company's research and development discovery efforts and related candidate 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 discovery operations at the Company's research facilities in California and Wisconsin, including facility costs and laboratory-related expenses. The Company does not separately track R&D expenses by individual research and development projects, or by individual drug candidates. The Company operates in a cross-functional manner across projects and does not separately allocate facilities-related costs, candidate costs, discovery costs, compensation expenses, depreciation and amortization expenses, and other expenses related to research and development activities.

The following table provides details of research and development expenses:

(in thousands)	Year Ended September 30, 2024	% of Expense Category	Year Ended September 30, 2023	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Candidate costs	$ 259,280	51 %	$ 162,459	46 %	$ 96,821	60 %
R&D discovery costs	74,150	15 %	55,586	15 %	18,564	33 %
Salaries	96,418	19 %	73,668	21 %	22,750	31 %
Facilities related	25,782	5 %	16,267	5 %	9,515	58 %
Total research and development expense, excluding non-cash expense	$ 455,630	90 %	$ 307,980	87 %	$ 147,650	48 %
Stock compensation	33,586	7 %	34,332	10 %	(746)	(2)%
Depreciation and amortization	16,654	3 %	10,876	3 %	5,778	53 %
Total research and development expense	$ 505,870	100 %	$ 353,188	100 %	$ 152,682	43 %

Candidate costs increased $96.8 million, or 60%, for the year ended September 30, 2024 compared to the same period of 2023. This increase was primarily due to the additional progression of the Company's pipeline of candidates into and through clinical trials, which resulted in higher manufacturing, outsourced clinical trial, and toxicity study costs.

R&D discovery costs increased $18.6 million, or 33%, for the year ended September 30, 2024 compared to the same period of 2023. This increase was primarily driven by the growth of the Company's discovery efforts and continued advancement into novel therapeutic areas and tissue types, along with rising costs associated with central nervous system (CNS) studies and lab supplies.

Salaries consist of salary, bonuses, payroll taxes, and related benefits for the Company's R&D personnel. Salaries expense increased $22.8 million, or 31%, for the year ended September 30, 2024 compared to the same period of 2023. The increase was primarily due to an increase in R&D headcount that has occurred as the Company has expanded its pipeline of candidates, in addition to annual salary increases.

Facilities-related expense includes lease costs for the Company's research and development facilities in San Diego, California and in Madison and Verona, Wisconsin. These expenses increased $9.5 million, or 58%, for the year ended September 30, 2024 compared to the same period of 2023. The increase was primarily due to full-year expenses such as utilities and repair and maintenance charges associated with the new facilities in San Diego, California and Verona, Wisconsin

Stock compensation expense, a non-cash expense, is based upon the valuation of stock options and restricted stock units granted to employees. Stock compensation expense decreased $0.7 million, or 2%, for the year ended September 30, 2024 compared to the same period of 2023. The decrease was primarily due to the cancellation of awards upon the departure of employees.

Depreciation and amortization expense, a non-cash expense, relates to depreciation on building, lab equipment and leasehold improvements. Depreciation and amortization expense increased $5.8 million, or 53% for the year ended September 30, 2024 compared to the same period of 2023. The increase was primarily attributed to higher leasehold improvements due to completion of the development of the San Diego facility. Additionally, as of December 31, 2023, the Company completed the build out of one of its laboratory and office facilities in Verona, Wisconsin, and commenced depreciation.

The Company anticipates these R&D expenses to continue to increase as its pipeline of candidates grows and progresses to later phase clinical trials, in addition to inflationary pressure on goods and services and the labor market.

General & Administrative Expenses

The following table provides details of general and administrative expenses:

(in thousands)	Year Ended September 30, 2024	% of Expense Category	Year Ended September 30, 2023	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Salaries	$ 27,589	28 %	$ 22,999	25 %	$ 4,590	20 %
Professional, outside services, and other	24,733	25 %	20,720	22 %	4,013	19 %
Facilities related	4,116	4 %	3,415	4 %	701	21 %
Total general & administrative expense, excluding non-cash expense	$ 56,438	57 %	$ 47,134	51 %	$ 9,304	20 %
Stock compensation	40,382	41 %	43,798	47 %	(3,416)	(8)%
Depreciation/amortization	1,941	2 %	1,617	2 %	324	20 %
Total general & administrative expense	$ 98,761	100 %	$ 92,549	100 %	$ 6,212	7 %

Salaries expense increased $4.6 million, or 20%, for the year ended September 30, 2024 compared to the same period of 2023. The increase was driven by the combination of annual salary increases and increased headcount required to support the Company's growth.

Professional, outside services, and other expenses include costs related to legal, audit, consulting, patent filings, business insurance, other external services, as well as travel, communication, and technology expenses. This expense increased $4.0 million, or 19%, for the year ended September 30, 2024 compared to the same period of 2023. The increase was primarily driven by legal services associated with patent applications and intellectual property matters, as well as other professional services.

Facilities related expense primarily includes rental costs and other facilities-related costs for the Company's corporate headquarters in Pasadena, California.

Stock compensation expense, a non-cash expense, is based on the valuation of stock options and restricted stock units granted to employees. This expense decreased by $3.4 million, or 8%, for the year ended September 30, 2024 compared to the same period of 2023. The decrease was mainly due to lower compensation costs related to performance awards, as the timing of these expenses can vary based on the achievement of related performance targets.

Depreciation and amortization expense, a noncash expense, was primarily related to amortization of leasehold improvements for the Company's corporate headquarters.

Other than with respect to the stock compensation costs described above, the Company anticipates these general and administrative expenses to increase as its pipeline of candidates grows and progresses to later phase clinical trials including commercialization efforts, in addition to inflationary pressure on goods and services and the labor market.

Other Income (Expense)

Other income (expense) is primarily related to interest income and expense. Other expense increased $9.9 million for the year ended September 30, 2024 compared to the same period of 2023. The increase was mainly due to non-cash interest expense associated with the liability related to the sale of future royalties and the Credit Facility, partially offset by higher income from increased investment yields due to higher average cash balance.

Year Ended September 30, 2023 Compared to Year Ended September 30, 2022

See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" of the Company's Form 10-K for the year ended September 30, 2023 for a discussion of changes in its results of operations from the year ended September 30, 2023 to the year ended September 30, 2022.

LIQUIDITY AND CAPITAL RESOURCES

The Company has historically financed its operations through the sale of its equity securities, credit facility, revenue from its licensing and collaboration agreements, and the sale of certain future royalties. Research and development activities have required significant investment since the Company's inception and are expected to continue to require significant cash expenditure as the Company's pipeline continues to expand and matures into later stage clinical trials, including commercialization efforts. Additionally, the Company expanded its facilities in Verona, Wisconsin and leased additional facilities in San Diego, California. Each of these expansions is designed to increase the Company's internal manufacturing and discovery capabilities and requires significant capital investment. For further information on the Company's capital needs, see the section titled "Risks Related to Our Financial Condition" in "Item 1A. Risk Factors" of this Annual Report on Form 10-K.

The Company's cash, cash equivalents and restricted cash was $102.7 million at September 30, 2024 compared to $110.9 million at September 30, 2023. Cash invested in available-for-sale securities was $578.3 million at September 30, 2024 compared to $292.7 million at September 30, 2023.

On December 2, 2022, the Company entered into an open market sale agreement ("the Open Market Sale Agreement"), pursuant to which the Company may, from time to time, sell up to $250.0 million in shares of the Company's common stock through Jefferies LLC, acting as the sales agent and/or principal, in an at-the-market offering. As of September 30, 2024, no shares have been issued under the Open Market Sale Agreement.

On January 2, 2024, the Company entered into an underwriting agreement with Jefferies LLC, BofA Securities, Inc., and Cowen and Company, LLC, as representatives of the several underwriters. The Company issued 15,790,000 shares of common stock at an offering price of $28.50 per share. The aggregate purchase price paid by investors was $450.0 million and the Company received net proceeds of $429.3 million after deducting advisory fees and offering expenses.

Further, the Company entered into the Credit Facility, which provides for a senior secured term loan facility of $500.0 million, which includes $400.0 million funded on the closing date with an additional $100.0 million at the Company's option during the seven-year term of the agreement. The Company received net proceeds of $388.9 million, after issuance costs as of September 30, 2024. This is discussed further in Note 14, Financing Agreements of the Notes to the Company's Consolidated Financial Statements in Part IV, "Item 15. Exhibits and Financial Statement Schedules." If the Company repays in full the aggregate principal outstanding under the Credit Facility and such payment in full occurs on or prior to August 7, 2028, the Company will be required to make an additional payment to the lenders under the Credit Facility on such date in an amount necessary for the lenders to achieve a multiple of two times on invested capital of the aggregate principal amount funded on the Closing Date. If such payment in full occurs after August 7, 2028, the Company will be required to make an additional payment to the lenders under the Credit Facility on such date in an amount necessary for the lenders to achieve the greater of the multiple of two times on invested capital of the aggregate principal amount funded on the Closing Date and the present value of all interest payments that would have been payable from such date through the maturity date of the Credit Facility.

The Company believes its current financial resources are sufficient to fund its operations through at least the next twelve months from the date of the issuance of these consolidated financial statements.

The following table presents a summary of cash flows:

	Year Ended September 30,		
	2024	2023	2022
	(in thousands)		
Cash Flow from:			
Operating activities	$ (462,851)	$ (153,890)	$ (136,131)
Investing activities	(420,072)	(96,155)	(5,417)
Financing activities	870,520	253,053	65,186
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (12,403)	$ 3,008	$ (76,362)
Cash, cash equivalents and restricted cash at end of period	$ 102,685	$ 110,891	$ 108,005

During the year ended September 30, 2024, cash flow used in operating activities was $462.9 million, which was primarily due to the ongoing expenses related to the Company's research and development programs and general and administrative expenses. Cash used in investing activities amounted to $420.1 million, which was primarily attributable to capital expenditures of $141.5 million and investment purchases of $720.9 million, offset by proceeds from sales and maturities of investments of $442.3 million. Cash provided by financing activities of $870.5 million was related to cash

received from the issuance of common stock, the Credit Facility, a milestone payment from Royalty Pharma, and stock option exercises. (See Note 13 — Liability Related to the Sale of Future Royalties and Note 14 — Financing Agreement of Notes to Consolidated Financial Statements of Part IV, "Item 15. Exhibits and Financial Statement Schedules.").

During the year ended September 30, 2023, cash flow used in operating activities was $153.9 million, which was primarily due to the ongoing expenses related to the Company's research and development programs and general and administrative expenses, partially offset by the receipt of the $110.0 million from collaboration and license agreements. Cash used in investing activities was $96.2 million, which was primarily related to the purchase of property and equipment of $176.7 million, offset by net proceeds of $80.6 million from maturities of securities. Cash provided by financing activities of $253.1 million was primarily related to the $250.0 million payment from Royalty Pharma as well as cash received from stock option exercises.

See "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" of the Company's Form 10-K for the year ended September 30, 2023 for a discussion of cash flows from the year ended September 30, 2022.

Contractual Obligations

Based on the Company's current operating plan, it believes that cash, cash equivalents and short-term investments as of September 30, 2024 will be sufficient to satisfy its near-term capital and operating needs. Recent and expected working and other capital requirements include the items described below.

- For information related to the Company's future commitments for its collaboration and licensing agreements, see Note 2 of Notes to the Company's Consolidated Financial Statements of Part IV, "Item 15. Exhibits and Financial Statement Schedules."
- Amounts related to future lease payments for operating lease obligations at September 30, 2024 totaled $117.4 million, with $6.3 million expected to be paid within the next 12 months.
- Cash outflows for capital expenditures related to the manufacturing facility build-out at Verona, Wisconsin were $136.9 million in 2024 and $134.8 million in 2023. The Company expects to spend an additional $8.0 million to complete the build out of the facilities.
- A secured term loan facility of $500.0 million, which includes $400.0 million funded on the closing date with an additional $100.0 million at the Company's option during the seven-year term of the agreement. The Company does not expect to make payments within the next 12 months. See Note 14 of Notes to the Company's Consolidated Financial Statements of Part IV, "Item 15. Exhibits and Financial Statement Schedules."
- The liability related to the sale of future royalties were $341.4 million at September 30, 2024, for which the Company does not expect to make payments within the next 12 months. See Note 13 of Notes to the Company's Consolidated Financial Statements of Part IV, "Item 15. Exhibits and Financial Statement Schedules."
- Commitments related to the Company's clinical, manufacturing and business operation related agreements totaled $471.9 million as of September 30, 2024. However, many of these agreements are cancellable.
- The Company has not entered into, nor does it currently have, any off-balance sheet arrangements (as defined under SEC rules).

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The Company is subject to market risk exposures primarily due to its investing activities. The primary market risk exposure is change in interest rates. Adverse changes to rates may occur due to changes in the liquidity of a market or to changes in market perceptions of creditworthiness and risk tolerance.

The Company's investment criteria are governed by its Investment Policy. The Company primarily invests its excess cash in securities of reputable financial institutions, corporations, and US government agencies with strong credit ratings. On September 30, 2023, the Company changed the classification of its investment securities from held-to-maturity to available-for-sale. This change enables the Company to sell securities to diversify its portfolio, reduce exposure to market risks, and provide flexibility to meet cash flow needs and new investment opportunities. Due to the relatively short-term nature of the investments that the Company holds, it does 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 its 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

Evaluation of Disclosure Controls and Procedures

The Company maintains disclosure controls and procedures designed to ensure that information required to be disclosed in its reports filed under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC rules and forms, and that such information is accumulated and communicated to its management, including its Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily was required to apply its judgment in evaluating the cost benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) of the Exchange Act, the Company carried out an evaluation, under the supervision and with the participation of its management, including its Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of the Company's disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on the foregoing, the Company's Chief Executive Officer and Chief Financial Officer concluded that the Company's disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. The Company's internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of its Consolidated Financial Statements for external purposes in accordance with GAAP.

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 the Company's assets;

(ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that receipts and expenditures are being made only in accordance with authorizations of the Company's management and directors; and

(iii) 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 Company's 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 controls may become inadequate because either conditions change or the degree of compliance with policies or procedures may deteriorate.

Management has assessed the effectiveness of the Company's internal control over financial reporting as of September 30, 2024. In making this assessment, the Company used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013). Based on this assessment, management concluded that the Company's internal control over financial reporting was effective as of September 30, 2024.

KPMG LLP, the independent registered public accounting firm that audited the Consolidated Financial Statements included in this 2024 Annual Report on Form 10-K, has issued an audit report on the effectiveness of the Company's internal control over financial reporting as of September 30, 2024, which is included herein.

Changes in Internal Control Over Financial Reporting

There has been no change in the Company's internal control over financial reporting during the Company's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting. The Company regularly evaluates its controls and procedures and makes improvements in the design and effectiveness of established controls and procedures and the remediation of any deficiencies which may be identified during this process.

ITEM 9B. OTHER INFORMATION

(a) ***License and Collaboration Agreement***

On November 25, 2024, the Company entered into an Exclusive License and Collaboration Agreement (the "Collaboration Agreement") with Sarepta Therapeutics, Inc. ("Sarepta") for the co-development and commercialization of multiple clinical and preclinical programs in rare, genetic diseases of the muscle, central nervous system, and the lungs.

Under the Collaboration Agreement, Sarepta has received an exclusive worldwide license to the Company's ARO-DUX4, ARO-DM1, ARO-MMP7, and ARO-ATXN2 clinical stage programs. Sarepta has also received an exclusive sublicensable worldwide license to the Company's ARO-HTT, ARO-ATXN1, and ARO-ATXN3 preclinical stage programs.

Pursuant to the Collaboration Agreement, Sarepta will be able to select up to six new targets for which the Company will perform discovery, optimization and preclinical development. Upon completion of the Company's preclinical activities, Sarepta will receive an exclusive license to the Company's product-specific intellectual property rights covering those compounds and be wholly responsible for clinical development and commercialization of each compound.

Under the terms of the Collaboration Agreement, the Company expects to receive $500.0 million as an upfront payment and $250.0 million to be paid in annual installments of $50.0 million over 5 years. The Company is also eligible to receive $300.0 million in near-term payments associated with the continued enrollment of certain cohorts of a Phase 1/2 study, which the Company is on track to achieve.

Further, for each of the 13 programs, the Company is eligible to receive development milestone payments between $110.0 million and $180.0 million per program and sales milestone payments between $500.0 million and $700.0 million per program. The Company is also eligible to receive tiered royalties on net sales of licensed products of up to the low double digits.

Closing of the Collaboration Agreement is subject to clearance under the Hart-Scott Rodino Antitrust Improvements Act.

The foregoing description of the Collaboration Agreement does not purport to be complete and is qualified in its entirety by reference to the Collaboration Agreement, a copy of which will be filed with the Company's Quarterly Report on Form 10-Q for the quarter ended December 31, 2024.

Stock Purchase Agreement

In connection with the Collaboration Agreement, on November 25, 2024, the Company entered into a Stock Purchase Agreement (the "Stock Purchase Agreement") with an affiliate of Sarepta (the "Purchaser") for a private placement of shares of common stock of the Company (the "Private Placement"). Pursuant to the Stock Purchase Agreement, the Company sold 11,926,301 shares of common stock (the "Shares"), at a price per Share of $27.2507, for an aggregate value of approximately $325.0 million. The Private Placement is expected to close concurrently with the Collaboration Agreement (the "Closing").

The Stock Purchase Agreement contains customary representations and warranties of the Company, on the one hand, and the Purchaser, on the other hand, and customary conditions to closing. The Stock Purchase Agreement provides that at any time following the Closing, the Purchaser may elect to exchange any or all of its Shares for pre-funded warrants to purchase shares of common stock of the Company, substantially in the form attached to the Stock Purchase Agreement.

At the Closing, the Company will enter into an Investor Rights Agreement (the "Investor Rights Agreement") with the Purchaser, which provides that the Company will appoint Doug Ingram to the board of directors of the Company effective as of the Closing. In addition, the Company will register the resale of the Shares pursuant to the Investor Rights Agreement. The Company is required to prepare and file a registration statement with the Securities and Exchange Commission no later than 30 days following the Closing.

The Company has also agreed to, among other things, indemnify the Purchaser, their officers, directors, members, employees, partners, managers, stockholders, affiliates, investment advisors and agents under the registration statement

from certain liabilities and pay certain fees and expenses incident to the Company's obligations under the Investor Rights Agreement.

The securities to be issued and sold to Purchaser under the Stock Purchase Agreement will not be registered under the Securities Act of 1933, as amended (the Securities Act) in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act and/or Rule 506 of Regulation D promulgated thereunder, or under any state securities laws. The Company relied on this exemption from registration based in part on representations made by the Purchaser. The securities may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements. This Annual Report on Form 10-K is not an offer to sell or the solicitation of an offer to buy the securities described herein.

The foregoing descriptions of the Stock Purchase Agreement and the form of Investor Rights Agreement do not purport to be complete and are qualified in their entirety by reference to the Stock Purchase Agreement and the form of Investor Rights Agreement, copies of which are filed as Exhibits 10.48 and 4.6 to this Annual Report on Form 10-K, respectively, and are incorporated by reference herein.

Amendment to Credit Facility

Also on November 26, 2024, the Company entered into an amendment to the Credit Facility (the "Amendment") to modify, subject to certain conditions, amongst other things, the requirements to make prepayments of the loans under the Credit Facility with respect to the transactions contemplated by the Collaboration Agreement and the Stock Purchase Agreement.

The foregoing description of the Amendment does not purport to be complete and is qualified in its entirety by reference to the Amendment, a copy of which will be filed with the Company's Quarterly Report on Form 10-Q for the quarter ending December 31, 2024.

Securities Purchase Agreement

On November 25, 2024, the Company entered into a Securities Purchase Agreement (the "Securities Purchase Agreement") with an institutional and accredited investor (the "Warrant Purchaser") for a private placement of pre-funded warrants to purchase shares of common stock with an exercise price of $0.001 per share. Pursuant to the Securities Purchase Agreement, the Company sold pre-funded warrants to purchase up to 917,441 shares of common stock at a purchase price of $27.2497 per pre-funded warrant, for an aggregate value of approximately $25.0 million. The transaction is expected to close on or about November 27, 2024 (the "Warrant Closing").

The Securities Purchase Agreement contains customary representations and warranties of the Company, on the one hand, and the Purchasers, on the other hand, and customary conditions to closing. At the Warrant Closing, the Company will enter into a Registration Rights Agreement (the Registration Rights Agreement) with the Warrant Purchaser, which provides that the Company will register the resale of the shares of common stock underlying the pre-funded warrants pursuant to the Registration Rights Agreement. The Company is required to prepare and file a registration statement with the Securities and Exchange Commission no later than 30 days following the Warrant Closing.

The Company has also agreed to, among other things, indemnify the Purchaser, their officers, directors, members, employees, partners, managers, stockholders, affiliates, investment advisors and agents under the registration statement from certain liabilities and pay certain fees and expenses incident to the Company's obligations under the Registration Rights Agreement.

The securities to be issued and sold to Warrant Purchaser under the Securities Purchase Agreement will not be registered under the Securities Act in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act and/or Rule 506 of Regulation D promulgated thereunder, or under any state securities laws. The Company relied on this exemption from registration based in part on representations made by the Warrant Purchaser. The securities may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements. This Annual Report on Form 10-K is not an offer to sell or the solicitation of an offer to buy the securities described herein.

The foregoing descriptions of the Securities Purchase Agreement, the form of Registration Rights Agreement and the form of Pre-Funded Warrant do not purport to be complete and are qualified in their entirety by reference to the Securities Purchase Agreement, the form of Registration Rights Agreement and the form of Pre-Funded Warrant, copies of which are filed as Exhibits 10.49, 4.7 and 4.8 to this Annual Report on Form 10-K, respectively, and are incorporated by reference herein.

(b) Trading Plans

During the fiscal quarter ended September 30, 2024, the following directors and officers (as defined in Exchange Act Rule 16a-1(f)) adopted certain trading plans intended to satisfy Rule 10b5-1(c):

Name	Title	Adoption or Termination Date	Plan Start Date	Plan End Date	Shares Vesting and Subject to Sell-To-Cover [1]	Other Shares Being Sold (Subject to Certain Conditions)
Adeoye Olukotun	Board Member	09/24/2024	12/24/2024	06/24/2025	n/a	5,465
Christopher Anzalone	President and Chief Executive Officer	08/16/2024	03/03/2025	12/31/2025	n/a	351,726
Christopher Anzalone	President and Chief Executive Officer	08/22/2024	12/04/2024	12/31/2026	2,082,892	n/a
Christopher Anzalone	President and Chief Executive Officer	09/16/2024	01/02/2025	12/31/2026	96,566	n/a
Douglass Given	Board Member	09/12/2024	12/16/2024	12/31/2024	n/a	5,547
James Hamilton	Chief of Discovery and Translational Medicine	08/19/2024	12/04/2024	11/28/2025	n/a	30,000

(1) This column indicates the total number of shares vesting, but the 10b5-1 Plan provides for the sale of only those shares necessary to satisfy payment of applicable withholding taxes.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information called for by this Item will be incorporated by reference from the Company's Definitive Proxy Statement, under the headings Proposal One — Election of Directors, Equity Compensation Plan Information, Corporate Governance, Environmental and Social Commitment, Executive Compensation, and, if applicable, Delinquent Section 16(a) Reports — to be filed for the Company's 2025 Annual Meeting of Stockholders (the "Definitive Proxy Statement").

ITEM 11. EXECUTIVE COMPENSATION

The information called for by this Item will be incorporated by reference from the Definitive Proxy Statement, under the heading Executive Compensation.

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 the Definitive Proxy Statement, under the heading Voting Securities of Principal Stockholders and Management.

ITEM 13. CERTAIN RELATIONSHIPS, RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

The information called for by this Item will be incorporated by reference from the Definitive Proxy Statement, under the headings Review and Approval of Related-Party Transactions and Certain Relationships and Related Transactions, and Director Independence.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information called for by this Item will be incorporated by reference from the Definitive Proxy Statement, under the heading Audit Fees.

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:

		Incorporated by Reference Herein	
Exhibit Number	**Description**	**Form**	**Date**
1.1	Open Market Sale Agreement, dated as of December 2, 2022, by and between Arrowhead Pharmaceuticals, Inc. and Jefferies LLC	Current Report on Form 8-K as Exhibit 1.1	December 2, 2022
2.1†	Stock and Asset Purchase Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011	Annual Report on Form 10-K 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 (incorporated by reference from Exhibit 3.3 of the Company's Form 8-K filed on April 6, 2016)	Current Report on Form 8-K as Exhibit 3.3	April 6, 2016
3.2	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Arrowhead Pharmaceuticals, Inc. (incorporated by reference from Exhibit 3.2 of the Company's Form 10-Q filed on May 2, 2023)	Quarterly Report on Form 10-Q, as Exhibit 3.2	May 2, 2023
3.3	Second Amended and Restated Bylaws (incorporated by reference from Exhibit 3.1 of the Company's Form 8-K filed on January 30, 2023)	Current Report on Form 8-K as Exhibit 3.2	January 30, 2023
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, as Exhibit 4.2	December 2, 2019
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	Annual Report on Form 10-K, as Exhibit 4.4	November 25, 2019
4.5	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
4.6*	Form of Investor Rights Agreement by and between Company and Sarepta Therapeutics Investments, Inc. (included as Exhibit A in Exhibit 10.48)		

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
4.7*	Form of Registration Rights Agreement by and between Company and Avoro Life Sciences Fund LLC (included as Exhibit B in Exhibit 10.49)		
4.8*	Form of Pre-Funded Warrant for Avoro Life Sciences Fund LLC		
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**	Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan	Schedule 14A, as Exhibit A	January 28, 2021
10.6**	Form of RSU Agreement for Officers and Certain Other Employees (Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan- Inducement Award)	Registration Statement on Form S-8, as Exhibit 99.1	December 22, 2021
10.7**	Form of RSU Agreement for Officers and Certain Other Employees (Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan)	Registration Statement on Form S-8, as Exhibit 99.1	February 28, 2024
10.8**	Form of RSU Agreement for Employees (Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan - Inducement Award)	Registration Statement on Form S-8, as Exhibit 99.2	December 22, 2021
10.9**	Form of RSU Agreement for Employees (Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan)	Registration Statement on Form S-8, as Exhibit 99.2	February 28, 2024
10.10**	Form of Stock Option Grant (Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan- Inducement Award)	Registration Statement on Form S-8, as Exhibit 99.3	December 22, 2021
10.11**	Form of Stock Option Grant (Arrowhead Pharmaceuticals, Inc. 2021 Incentive Plan)	Annual Report on Form 10-K, as Exhibit 10.11	November 29, 2023
10.12**	Executive Incentive Plan, adopted December 12, 2006	Annual Report on Form 10-K, as Exhibit 10.11	December 14, 2006
10.13**	Arrowhead Pharmaceuticals, Inc. Inducement Plan	Quarterly Report on Form 10-Q, as Exhibit 10.1	May 9, 2024
10.14**	Employment Agreement between Arrowhead and Dr. Christopher Anzalone, dated June 11, 2008	Current Report on Form 8-K, as Exhibit 10.1	June 13, 2008
10.15**	Amendment to Employment Agreement between Arrowhead and Dr. Christopher Anzalone, effective May 12, 2009	Annual Report on Form 10-K, as Exhibit 10.8	December 22, 2009
10.16†	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, as Exhibit 10.36	December 20, 2011
10.17†	Non-Exclusive License Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011†	Annual Report on Form 10-K, as Exhibit 10.33	December 20, 2011
10.18†	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
10.19†	Second Collaboration and Licensing Agreement between Arrowhead Pharmaceuticals, Inc. and Amgen Inc., dated September 28, 2016†	Annual Report on Form 10-K, as Exhibit 10.19	December 14, 2016

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
10.20	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, as Exhibit 10.1)	November 25, 2016
10.21†	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
10.22†	Amendment No. 1 to License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated December 18, 2018†	Annual Report on Form 10-K, as Exhibit 10.19	November 25, 2019
10.23†	Amendment No. 2 to License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Janssen Pharmaceuticals, Inc., dated February 4, 2019†	Annual Report on Form 10-K, as Exhibit 10.20	November 25, 2019
10.24†	Amended and Restated License Agreement by and between Arrowhead Pharmaceuticals, Inc. and GlaxoSmithKline Intellectual Property (No. 3) Limited, dated December 11, 2023	Quarterly Report on Form 10-Q, as Exhibit 10.1	August 8, 2024
10.25	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
10.26†	Exclusive License and Co-Funding Agreement by and between Arrowhead Pharmaceuticals, Inc. and Takeda Pharmaceuticals U.S.A., Inc., dated October 7, 2020†	Quarterly Report on Form 10-Q, as Exhibit 10.1	February 4, 2021
10.27	First Amendment to Exclusive License and Co-Funding Agreement by and between Arrowhead Pharmaceuticals, Inc. and Takeda Pharmaceuticals U.S.A., Inc. dated March 15, 2022	Quarterly Report on Form 10-Q, as Exhibit 10.1	May 10, 2022
10.28†	Collaboration and License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Horizon Therapeutics Ireland DAC, dated June 18, 2021†	Quarterly Report on Form 10-Q, as Exhibit 10.4	August 5, 2021
10.29	Collaboration and License Agreement by and between Arrowhead Pharmaceuticals, Inc. and Glaxosmithkline Intellectual Property, dated November 22, 2021	Quarterly Report on Form 10-Q, as Exhibit 10.1	February 2, 2022
10.30	Royalty Purchase Agreement, dated as of November 9, 2022, by and between Arrowhead Pharmaceuticals, Inc. and Royalty Pharma Investments 2019 ICAV	Quarterly Report on Form 10-Q, as Exhibit 10.1	February 6, 2023
10.31	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
10.32	Amendment No. 1 to Lease Agreement between Arrowhead Madison, Inc. and University Research Park, Incorporated, dated October 22, 2018	Annual Report on Form 10-K, as Exhibit 10.23	November 23, 2020
10.33	Amendment No. 2 to Lease Agreement between Arrowhead Madison, Inc. and University Research Park, Incorporated, dated January 10, 2019	Annual Report on Form 10-K, as Exhibit 10.24	November 23, 2020
10.34	Amendment No. 3 to Lease Agreement between Arrowhead Madison, Inc. and University Research Park, Incorporated, dated January 11, 2019	Annual Report on Form 10-K, as Exhibit 10.25	November 23, 2020
10.35	Amendment No. 4 to Lease Agreement between Arrowhead Madison, Inc. and University Research Park, Incorporated, dated September 19, 2019	Annual Report on Form 10-K, as Exhibit 10.26	November 23, 2020
10.36	Amendment No. 5 to Lease Agreement between Arrowhead Madison, Inc. and University Research Park, Incorporated, dated May 14, 2020	Annual Report on Form 10-K, as Exhibit 10.27	November 23, 2020
10.37	Amendment No. 6 to Lease Agreement by and between Arrowhead Madison, Inc. and University Research Park, dated November 23, 2020	Quarterly Report on Form 10-Q, as Exhibit 10.3	February 4, 2021

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
10.38	Amendment No. 7 to Lease Agreement by and between Arrowhead Madison, Inc. and University Research Park, dated December 9, 2020	Quarterly Report on Form 10-Q, as Exhibit 10.4	February 4, 2021
10.39*	Amendment No. 8 to Lease Agreement by and between Arrowhead Madison, Inc. and University Research Park, dated August 26, 2022		
10.40*	Amendment No. 9 to Lease Agreement by and between Arrowhead Madison, Inc. and University Research Park, dated April 3, 2023		
10.41*	Amendment No. 10 to Lease Agreement by and between Arrowhead Madison, Inc. and University Research Park, dated June 28, 2023		
10.42*	Amendment No. 11 to Lease Agreement by and between Arrowhead Madison, Inc. and University Research Park, dated September 13, 2024		
10.43	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
10.44	First Amendment to Office Lease by and between Arrowhead Pharmaceuticals, Inc. and 177 Colorado Owner LLC., dated October 23, 2020	Quarterly Report on Form 10-Q, as Exhibit 10.2	February 4, 2021
10.45	Lease Agreement by and between Arrowhead Pharmaceuticals, Inc. and ARE-SD Region No. 72, LLC, dated November 19, 2021	Quarterly Report on Form 10-Q, as Exhibit 10.2	February 2, 2022
10.46	First Amendment to Lease Agreement by and between Arrowhead Pharmaceuticals, Inc. and ARE-SD Region No. 72, LLC, dated September 26, 2023	Annual Report on Form 10-K, as Exhibit 10.39	November 29, 2023
10.47*†	Financing Agreement by and between Company and Sixth Street Lending Partners, dated August 7, 2024		
10.48*	Stock Purchase Agreement by and between Company and Sarepta Therapeutics Investments, Inc., dated November 25, 2024		
10.49*	Securities Purchase Agreement by and between Company and Avoro Life Sciences Fund LLC, dated November 25, 2024		
16.1	Letter from Rose, Snyder & Jacobs LLP, dated December 4, 2023	Current Report on Form 8-K, as Exhibit 16.1	December 5, 2023
19.1*	Arrowhead Pharmaceuticals, Inc. Insider Trading Policy		
21.1*	List of Subsidiaries		
23.1*	Consent of Independent Public Registered Accounting Firm		
23.2*	Consent of Independent Public Registered Accounting Firm		
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		
97**	Arrowhead Pharmaceuticals, Inc. Compensation Recoupment (Clawback) Policy, dated November 20, 2023	Annual Report on Form 10-K, as Exhibit 97	November 29, 2023
101.INS*	Inline XBRL Taxonomy Extension Instance Document		

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
101.SCH*	Inline XBRL Taxonomy Extension Schema Document		
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document		
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document		
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document		
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document		
104*	The cover page from the Company's Annual Report on Form 10-K for the year ended September 30, 2024, formatted in Inline XBRL (included as Exhibit 101)		

* Filed herewith

** Indicates compensation plan, contract or arrangement.

*** Furnished herewith

† Certain portions of this exhibit were redacted by means of marking such portions with asterisks because the identified portions are (i) not material and (ii) treated as private or confidential by the Company.

ITEM 16. FORM 10-K SUMMARY

None.

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.

Dated: November 26, 2024

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
/s/ Christopher Anzalone **Christopher Anzalone**	Chief Executive Officer, President and Director (Principal Executive Officer)	November 26, 2024
/s/ Kenneth A. Myszkowski **Kenneth A. Myszkowski**	Chief Financial Officer (Principal Financial and Accounting Officer)	November 26, 2024
/s/ Douglass Given **Douglass Given**	Director, Chairman of the Board of Directors	November 26, 2024
/s/ Mauro Ferrari **Mauro Ferrari**	Director	November 26, 2024
/s/ Michael S. Perry **Michael S. Perry**	Director	November 26, 2024
/s/ William Waddill **William Waddill**	Director	November 26, 2024
/s/ Adeoye Olukotun **Adeoye Olukotun**	Director	November 26, 2024
/s/ Victoria Vakiener **Victoria Vakiener**	Director	November 26, 2024
/s/ Hongbo Lu **Hongbo Lu**	Director	November 26, 2024

Exhibit 21.1

Subsidiary	Jurisdiction
Arrowhead Madison Inc.	Delaware
Arrowhead Australia Pty Ltd	Australia

Exhibit 31.1

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 26, 2024

/s/ Christopher Anzalone

Christopher Anzalone

Chief Executive Officer

Exhibit 31.2

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 26, 2024

/s/ Kenneth A. Myszkowski

Kenneth A. Myszkowski,
Chief Financial Officer

Exhibit 32.1

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, 2024, 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 26, 2024

/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.

Exhibit 32.2

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, 2024, 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 26, 2024

/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.

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 14A
(Rule 14a-101)

INFORMATION REQUIRED IN PROXY STATEMENT

SCHEDULE 14A INFORMATION

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934

Filed by the Registrant ☒ Filed by a Party other than the Registrant ☐

Check the appropriate box:

- ☐ Preliminary Proxy Statement
- ☐ Confidential, For Use of the Commission Only (as permitted by 14a-6(e)(2))
- ☒ Definitive Proxy Statement
- ☐ Definitive Additional Materials
- ☐ Soliciting Material Pursuant To §240.14a-12

ARROWHEAD PHARMACEUTICALS, INC.

(Name of Registrant as Specified in Its Charter)

(Name of Person(s) Filing Proxy Statement if other than the Registrant)

Payment of filing fee (Check all boxes that apply):

- ☒ No fee required.
- ☐ Fee paid previously with preliminary materials.
- ☐ Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11.

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Notice of Annual Meeting of Stockholders

To Be Held on Wednesday, March 12, 2025

Your vote is important, whether or not you expect to attend the Annual Meeting of Stockholders. Stockholders of record are urged to vote via the Internet or telephone as instructed, or if you are voting by mail, to mark, sign and date and promptly return the proxy in the postage-prepaid return envelope provided.

Voting promptly will help avoid the additional expense of further solicitation to assure a quorum at the meeting.

Important Notice Regarding the Availability of Proxy Materials for the Stockholder Meeting to be Held on Thursday, March 12, 2025:

You may access the following proxy materials at www.proxyvote.com before the meeting and www.virtualshareholdermeeting.com/ARWR2025 during the meeting.

- Notice of the 2025 Annual Meeting of Stockholders;
- Company's 2025 Proxy Statement;
- Company's Annual Report on Form 10-K for the year ended September 30, 2024; and
- Form of Proxy Card

TO THE STOCKHOLDERS OF ARROWHEAD PHARMACEUTICALS, INC.:

NOTICE IS HEREBY GIVEN that the 2025 Annual Meeting of Stockholders of Arrowhead Pharmaceuticals, Inc., a Delaware corporation (the "Company" or "Arrowhead"), will be held on Wednesday, March 12, 2024, at 10:00 a.m., Pacific time (the "Annual Meeting"). This year's meeting will be a completely "virtual" meeting of stockholders. You can attend the Annual Meeting online, vote your shares electronically, and submit your questions during the Annual Meeting by visiting www.virtualshareholdermeeting.com/ARWR2025. Prior to the Annual Meeting, you will be able to vote at www.proxyvote.com. The Annual Meeting will be held for the purpose of considering and voting upon the following proposals, as more fully described in the accompanying Proxy Statement:

1. To elect the eight directors named in the Proxy Statement to serve as members of the Company's Board of Directors until the next Annual Meeting or until their successors are elected;
2. To conduct an advisory (non-binding) vote to approve executive compensation;
3. To conduct an advisory (non-binding) vote on the frequency of future advisory votes to approve executive compensation;
4. To ratify the selection of KPMG LLP as independent auditors of the Company for the fiscal year ending September 30, 2025; and
5. To transact any other matters that may properly come before the Annual Meeting or any adjournments or postponements thereof.

The foregoing items of business are more fully described in the Proxy Statement accompanying this Notice. Proposal No. 1 relates solely to the election of the eight directors nominated by the Board of Directors and does not include any other matters relating to the election of directors, including, without limitation, the election of directors nominated by any stockholder of the Company.

All stockholders of record are cordially invited to attend the Annual Meeting by visiting www.virtualshareholdermeeting.com/ARWR2025. Instructions for accessing the virtual Annual Meeting are provided in the Proxy Statement. In the event of a technical malfunction or other situation that the meeting chair determines may affect the ability of the Annual Meeting to satisfy the requirements for a meeting of stockholders to be held by means of remote communication under the Delaware General Corporation Law, or that otherwise makes it advisable to adjourn the Annual Meeting, the chair or secretary of the Annual Meeting will convene the meeting at 10:30 a.m., Pacific Time on the date specified above and at the Company's address specified below solely for the purpose of adjourning the meeting to reconvene at a date, time and physical or virtual location announced by the meeting chair. Under either of the foregoing circumstances, we will post information regarding the announcement on the Investors page of the Company's website at ir.arrowheadpharma.com.

If you prefer to receive paper copies of our proxy materials, please follow the instructions included in the Notice of Internet Availability. To ensure your representation at the meeting, you are urged to vote via the Internet or telephone as instructed in the Notice of Internet Availability, or to mark, sign, date and return the proxy card as promptly as possible in the postage-prepaid envelope enclosed for that purpose. Any stockholder of record attending the Annual Meeting may vote at the Annual Meeting even if such stockholder has previously returned a proxy.

/s/ Patrick O'Brien
Patrick O'Brien
Secretary

Pasadena, California
January 28, 2025

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

PROXY STATEMENT FOR ANNUAL MEETING OF STOCKHOLDERS

To be held on Wednesday, March 12, 2025

General Information Concerning Solicitation and Voting

The enclosed Proxy is solicited on behalf of Arrowhead Pharmaceuticals, Inc. (the "**Company**" or "**Arrowhead**") for use at the 2025 Annual Meeting of Stockholders (the "**Annual Meeting**") to be held on Wednesday, March 12, 2025 at 10:00 a.m., Pacific time, and at any adjournment(s) or postponement(s) thereof, for the purposes set forth herein and in the accompanying Notice of Annual Meeting of Stockholders (the "**Notice**"). The Company anticipates that the Notice Regarding the Availability of Proxy Materials (the "**Notice of Internet Availability**") in connection with these proxy solicitation materials will first be mailed on or about January 28, 2024 to all stockholders entitled to vote at the Annual Meeting and we will post our proxy materials on the website referenced in the Notice of Internet Availability. As more fully described in the Notice of Internet Availability, all stockholders may choose to access our proxy materials on the website referred to in the Notice of Internet Availability or may request to receive a printed set of our proxy materials.

This year's meeting will be a completely "virtual" meeting of stockholders. If you were a stockholder as of the close of business on the Record Date (as defined below), you can attend the Annual Meeting online, vote your shares electronically, and submit your questions and view our list of stockholders as of the Record Date during the Annual Meeting, by visiting www.virtualshareholdermeeting.com/ARWR2025. You will need to have your 16-digit Control Number included on your Notice of Internet Availability or your proxy card (if you received a printed copy of the proxy materials) to join the Annual Meeting. If your shares are held in street name and your voting instruction form or Notice of Internet Availability indicates that you may vote those shares through www.proxyvote.com, then you may access, participate in, and vote at the Annual Meeting with the 16-digit access code indicated on that voting instruction form or Notice. Otherwise, stockholders who hold their shares in street name should contact their bank, broker or other nominee (preferably at least five days before the Annual Meeting) and obtain a "legal proxy" in order to be able to attend, participate in or vote at the Annual Meeting.

The meeting webcast will begin promptly at 10:00 a.m. Pacific Time. Online check-in will begin approximately 15 minutes before then and we encourage you to allow ample time for check-in procedures. If you experience technical difficulties during the check-in process or during the meeting, please call the number listed on the meeting website for technical support.

We will endeavor to answer as many stockholder-submitted questions as time permits that comply with the Annual Meeting rules of conduct. We reserve the right to edit profanity or other inappropriate language and to exclude questions regarding topics that are not pertinent to meeting matters or Company business. If we receive substantially similar questions, we may group such questions together and provide a single response to avoid repetition. Additional information regarding the rules and procedures for participating in the Annual Meeting will be set forth in our meeting rules of conduct, which stockholders can view during the meeting at the meeting website.

By hosting the Annual Meeting virtually, we believe we can expand access, improve communication and lower costs while reducing the environmental impact of the meeting.

Record Date

Only holders of record of our common stock at the close of business on January 17, 2025 (the "**Record Date**") are entitled to notice of the Annual Meeting and to vote at the Annual Meeting. On that date, the Company had outstanding 125,073,046 shares of common stock ("**Common Stock**").

Revocability of Proxies

Any proxy given by a stockholder of record pursuant to this solicitation may be revoked by the person giving it at any time before its use by delivering to the Secretary of the Company, at or before the taking of the vote at the Annual Meeting, a written notice of revocation or a duly executed proxy bearing a later date or by attending the Annual Meeting and voting electronically. Stockholders may also revoke their proxy by entering a new vote over the Internet or by telephone.

Voting and Solicitation

Each share of the Company's Common Stock is entitled to one vote on all matters presented at the Annual Meeting. Each stockholder may appoint only one proxy holder or representative to attend the Annual Meeting on his or her behalf. Stockholders do not have the right to cumulate their votes in the election of directors. Shares of Common Stock represented by properly executed proxies will, unless such proxies have been previously revoked, be voted in accordance with the instructions indicated thereon. In the absence of specific instructions to the contrary, properly executed proxies will be voted FOR the Proposals 1, 2, and 4 and "1 Year" on Proposal 3 and submitted to a vote of stockholders at the Annual Meeting pursuant to this proxy statement. No business other than that set forth in the accompanying Notice of Annual Meeting of Stockholders is expected to come before the Annual Meeting. Should any other matter requiring a vote of stockholders properly arise, the persons named in the enclosed form of proxy will vote in accordance with their best judgment.

If you cannot attend the Annual Meeting to vote, you may vote your shares via the Internet, telephone or by mail as set forth in the Notice.

The Company has engaged a proxy solicitor, Okapi Partners, LLC, to encourage voting by our stockholders. The total cost for the solicitation campaign is estimated at about $15,000. Proxies may also be solicited by certain of the directors, officers and employees of the Company, without additional compensation. The Company will bear the costs of solicitation. In addition, the Company expects to reimburse brokerage firms and other persons representing beneficial owners of shares for their expenses in forwarding solicitation materials to such beneficial owners.

If your shares are held in a street name, the voting instruction form sent to you by your broker, bank or other nominee should indicate whether the institution has a process for beneficial holders to provide voting instructions over the Internet or by telephone. If your bank or brokerage firm gives you this opportunity, the voting instructions from the bank or brokerage firm that accompany this proxy statement will tell you how to use the Internet or telephone to direct the vote of shares held in your account. If your voting instruction form does not include Internet or telephone information, please complete, and return the voting instruction form in the self-addressed, postage-paid envelope provided by your broker. Stockholders who vote by proxy over the Internet or by telephone need not return a proxy card or voting instruction form by mail.

Quorum; Abstentions; Broker Non-Votes

The required quorum for the transaction of business at the Annual Meeting is a majority of the votes eligible to be cast by holders of shares of Common Stock issued and outstanding on the Record Date. Shares that are voted "FOR," "AGAINST" or "ABSTAIN" on a matter are treated as being present at the meeting for purposes of establishing a quorum with respect to such matter. If you are the beneficial owner and do not direct your broker, fiduciary, or custodian how to vote your shares, your broker, fiduciary, or custodian will only be able to vote your shares with respect to proposals considered to be "routine." Your broker, fiduciary, or custodian is not entitled to vote your shares with respect to "non-routine" proposals (resulting in "**broker non-votes**" for the matters on which the broker, fiduciary, or custodian does not vote). Whether a proposal is considered routine or non-routine is subject to stock exchange rules. Even with respect to routine matters, some brokers are choosing not to exercise discretionary voting authority.

As a result, we urge you to direct your broker, fiduciary, or custodian how to vote your shares on all proposals to ensure that your vote is counted. Shares subject to a broker non-vote will be counted as present for the purpose of determining the presence or absence of a quorum for the transaction of business at the Annual Meeting; the effect of abstentions and broker non-votes on the proposals presented herein is discussed below.
With regard to the election of directors, votes may be cast "FOR," "AGAINST" or "ABSTAIN" for each director nominee. Because directors are elected by a majority of votes cast in an uncontested election, abstentions from voting and broker non-votes, if any, will have no effect on the outcome of the election of directors. If a quorum is present at the meeting, the nominees receiving more "FOR" votes than "AGAINST" votes will be elected. Because Proposal Nos. 2, 3 and 4 must be approved by the affirmative vote of a majority of the shares of Common Stock entitled to vote thereon and present in person or by proxy at the Annual Meeting (the "**Required Vote**"), abstentions will have the same effect as a vote "AGAINST" the proposal, whereas broker non-votes, if any, will have no effect on its outcome.

Deadline for Receipt of Stockholder Proposals and Nominations

To be considered for inclusion in the proxy statement and proxy card for the Company's 2026 Annual Meeting of Stockholders, proposals of stockholders pursuant to Rule 14a-8 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and stockholder director nominations pursuant to the proxy access provisions of the Company's Amended and Restated Bylaws ("**Bylaws**"), must be submitted in writing to our Corporate Secretary at the address set forth on the first page of this Proxy Statement. Such proposals and nominations must be received by us not later than our close of business (5:00 p.m. Pacific Time) on September 30, 2025, and, in the case of a proxy access nomination, no earlier than August 31, 2025, and must satisfy the requirements of Rule 14a-8 and our Bylaws, as applicable. The submission of a stockholder proposal or proxy access nomination does not guarantee that it will be included in our proxy materials.

Additionally, our Bylaws provide for advance notice procedures to nominate a person for director (other than pursuant to our Bylaws' proxy access provisions) or to propose business to be considered by stockholders at a meeting (other than pursuant to Rule 14a-8). To be considered timely under these provisions, the stockholder's notice must provide the information set forth in the Bylaws (which includes information required under Rule 14a-19 of the Exchange Act) and be received by the Corporate Secretary at our principal executive offices at the address set forth on the first page of this Proxy Statement between November 12, 2025 and our close of business (5:00 p.m. Pacific Time) on December 12, 2025; *provided, however*, that if the 2025 Annual Meeting date is advanced by more than 30 days before or delayed by more than 60 days after the anniversary date of the 2025 Annual Meeting, then stockholders must provide notice within time periods specified in our Bylaws. Our Bylaws also specify requirements as to the form and content of a stockholder's notice. If a stockholder fails to meet these deadlines and fails to satisfy the requirements of Rule 14a-4 under the Exchange Act, we may exercise discretionary voting authority under proxies we solicit to vote on any such proposal as we determine appropriate.

We reserve the right to reject, rule out of order, or take other appropriate action regarding any nomination or proposal that does not comply with these and other applicable requirements.

Proposal One — Election of Directors

The Company's Board of Directors (the "Board") has nominated the following eight persons as directors to serve until the 2026 Annual Meeting or until their successors have been duly elected. All but one of the nominees is currently a director of Arrowhead and six were elected most recently by stockholders at the 2024 Annual Meeting. Hongbo Lu was appointed to the Arrowhead Board in February 2024 and was initially recommended to the Board by several non-management directors. Douglas Ingram is expected to be appointed to the board before our 2025 Annual Meeting and was initially recommended to the Board by our CEO and, other executive officers. Douglass Given resigned as director of the Company as of December 31, 2024.

None of the nominees is related by blood, marriage or adoption to any other nominee or any executive officer of the Company. The nominees receiving more "FOR" votes than "AGAINST" votes at the Annual Meeting will be elected. Unless otherwise instructed, the proxy holders will vote the proxies received by them for the nominees named below. Under Delaware law, a director not receiving a majority of votes cast in an uncontested election would continue to serve as a "holdover director" until the director resigns or is replaced. Under the Company's director resignation policy, a director who is not reelected by a majority of the votes cast in an uncontested election will be required to tender his or her resignation to the Board, and the Board will then decide whether to accept or reject the resignation, or whether other action is required. The table below sets forth, with respect to each nominee for election, the nominee's age, and current position with Arrowhead. The director nominees have indicated that they are willing and able to serve as directors. However, if any of the director nominees becomes unable or, for good cause, unwilling to serve, proxies may be voted for the election of such other person as shall be designated by our Board, or the Board may decrease the size of the Board.

Nominees for Election as Directors. The Board unanimously adopted a resolution proposing the nominees set forth below for election as Directors of the Company for the next year.

OUR BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" EACH OF THE NOMINEES LISTED BELOW.

Christopher Anzalone, PhD
Chief Executive Officer, President, Director & Board Chair

Age: 55

Director since: 2007

Experience & Expertise
Dr. Anzalone has been President, Chief Executive Officer and Director of the Company since December 1, 2007 and has led the Company's business and technical development since then. Prior to joining Arrowhead, Dr. Anzalone formed and served as CEO of the Benet Group LLC, a private equity firm focused on creating and building new nano-biotechnology companies from university-generated science. Before his tenure at the Benet Group, from 1999 to 2003, he was a partner at the Washington, DC-based private equity firm Galway Partners, LLC, where he was responsible for sourcing, structuring and building new business ventures. Dr. Anzalone holds a PhD. in Biology from UCLA and a B.A. in Government from Lawrence University.

Qualifications
Dr. Anzalone's qualifications to serve on the Board include his deep understanding of the business through his role as Chief Executive Officer; in addition, Dr. Anzalone has extensive experience in business development, biotechnology, drug development, company-building and venture capital.

Mauro Ferrari, PhD
Independent Director

Age: 65

Director since: 2010

Serves on:
- Science Committee (Co-Chair)
- Audit Committee
- Nomination Committee

Experience & Expertise
Dr. Ferrari currently serves as Affiliate Professor of Pharmaceutics at the University of Washington in Seattle, Washington and as President, CEO, and Board Member of BrYet US, Inc., a biotech company, in Houston, Texas. He also serves as Chairman of the Board of BrYet Europe, a wholly-owned subsidiary of BrYet US, based in Italy. From 2010 to 2019, Dr. Ferrari served in several different capacities at the Houston Methodist Hospital, including President and CEO of The Houston Methodist Hospital Research Institute (TMHRI), Executive Vice President of Houston Methodist Hospital, and Senior Associate Dean of the hospital's academic affiliate, Weill Cornell Medical College in New York. Dr. Ferrari is an internationally recognized expert in cancer therapeutics, nanomedicine and biomedical nanotechnology. His previous academic appointments include tenured professorships at his graduate Alma Mater UC Berkeley, The Ohio State University, as Professor and Chair of The Department of NanoMedicine and Biomedical Engineering at The University of Texas Health Science Center, Professor of Experimental Therapeutics at the MD Anderson Cancer Center, as Adjunct Professor of Bioengineering at Rice University, and as Adjunct Professor of Business at the University of Saint Thomas. From 2003 to 2005, Dr. Ferrari served as Special Expert on Nanotechnology and Eminent Scholar at The National Cancer Institute. He has received many National and International awards and recognitions.

Qualifications:
Dr. Ferrari's qualifications to serve on the Board include his extensive training and experience in the fields of nanotechnology, biotechnology and biomedical applications. Dr. Ferrari has significant technical training, several academic appointments, over 500 published articles, over 30 issued patents, and is the recipient of most prestigious academic awards in nanomedicine and drug delivery technology. Additionally, Dr. Ferrari has extensive experience in developmental stage organizations having founded several startup companies.

Douglas Ingram
Independent Director

Age: 62

Director since: New Nominee

Other Public Company Boards:
- Sarepta Therapeutics, Inc.
- Relay Therapeutics, Inc.

Experience & Expertise

Mr. Ingram has served as the President and Chief Executive Officer of Sarepta Therapeutics, Inc. (Nasdaq: SRPT), a biopharmaceutical company for rare diseases, since June,2017. Prior to joining Sarepta, Mr. Ingram served as a Chief Executive Officer, President and Director of Chase Pharmaceuticals Corporation, a clinical-stage biopharmaceutical company from December 2015 until November 2016. Prior to joining Chase Pharmaceuticals, Mr. Ingram served as the President of Allergan, Inc., a pharmaceutical company, from July 2013 until it was acquired by Actavis in early 2015. At Allergan, he also served as President, Europe, Africa and Middle East from August 2010 to June 2013, and Executive Vice President, Chief Administrative Officer, and Secretary from October 2006 to July 2010, where he led Allergan's Global Legal Affairs, Compliance, Internal Audit and Internal Controls, Human Resources, Regulatory Affairs and Safety, and Global Corporate Affairs and Public Relations departments. Mr. Ingram also served as General Counsel of Allergan from January 2001 to June 2009 and as Secretary and Chief Ethics Officer from July 2001 to July 2010. With the acquisition of Allergan by Actavis, Mr. Ingram consulted as a special advisor to the Chief Executive Officer of Actavis. Mr. Ingram served as a director of Pacific Mutual Holding Company, a parent company for subsidiaries engaged in a variety of insurance, financial services and other investment-related businesses, from March 2015 to May 2018. Mr. Ingram received his J.D. from the University of Arizona and his Bachelor of Science degree from Arizona State University.

Qualifications:
Mr. Ingram's qualifications to serve on the Board include his deep understanding of the business through his role as President and Chief Executive Officer of Sarepta Therapeutics, Inc., which gives him an extensive understanding of our business and operations. Additionally, Mr. Ingram has extensive experience in business development, biotechnology, drug development, company-building and venture capital.

Hongbo Lu
Independent Director

Age: 54

Director since: 2024

Serves on:
- Science Committee
- Nomination Committee
- Compensation Committee

Other Public Company Boards:
- Terns Pharmaceuticals, Inc.
- Zenas Biopharma Inc

Experience & Expertise

Hongbo Lu, Ph.D., has served as a member of our board of directors since March 2024. Dr. Lu is the founding member of NEXTBio Capital, a newly launched biotech investment firm. Dr. Lu has over 20 years of healthcare investment management experience in both public securities and private companies, including prior roles previously served as Managing Partner at Vivo Capital LLC ("Vivo Capital"), a Palo Alto-based investment firm, a position she has held since December 2020, Managing Partner at Lilly Asia Ventures (LAV), a venture capital firm, from January 2017 to December 2020, and Managing Director at OrbiMed Advisors. Over her investment career, Dr. Lu served on the boards of over 20 healthcare companies, including Turning Point Therapeutics, Crown Bioscience Inc (6554.TT), Avedro, Inc., Rgenta, Ronovo Surgical, Avistone, and BlossomHill Therapeutics Inc. Dr. Lu currently serves on the board of directors for, Terns Pharmaceuticals Inc. (Nasdaq: TERN), where she has served as director since 2020, Zenas BioPharma (Nasdaq: ZBIO), where she has served as director since 2022, Ribox Therapeutics, where she has served as director since 2021, Visirna Therapeutics, where she has served as director since 2021, and Createrna Science and Technology. Dr. Lu started her Wall Street career as a biotechanalyst at Piper Jaffray & Co. and was involved in biotech start-up Zyomyx in the San Francisco Bay Area previously. Dr. Lu earned a Ph.D. in Bioengineering from the University of Washington, an M.B.A.

Qualifications: Dr. Lu's qualifications to serve on the Board include her deep experience in international business and the pharmaceutical industry, her expertise with venture and capital markets, and her executive leadership experience.

Adeoye Olukotun, MD, MPH
Independent Director

Age: 80

Director since: 2020

Serves on:
- Science Committee (Co-Chair)
- Nomination Committee

Other Public Company Boards:
- Tonix Pharmaceuticals Holding Corp.

Experience & Expertise
Dr. Olukotun is a Mayo Clinic trained cardiologist who has served as Chief Executive Officer of CR Strategies, LLC, which consults on clinical trial design and FDA strategy for pharmaceutical development, since 2001. Dr. Olukotun currently serves on the board of directors of Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceuticals company. He served as CEO of Epigen Pharmaceuticals, Inc., a discovery phase biotechnology company, from 2014 to 2017, and Vice Board Chair of CardioVax, Inc., a clinical-stage biopharmaceutical company, from 2012 to 2016. He spent the first 20 years of his career in roles of increasing responsibility in clinical development, including multiple product approvals, at Pfizer, Bristol-Myers Squibb, and Mallinckrodt. He has over 35 years of experience in the pharmaceutical industry and has been instrumental in the approval and success of numerous cardiology and metabolic medicines, including the first daily beta blocker and the first approved ACE inhibitor, among others. Dr. Olukotun received his Medical Doctor degree from the Albert Einstein College of Medicine in New York, and a Masters in Public Health from Harvard University School of Public Health.

Qualifications
Dr. Olukotun's qualifications to serve on the Board include his extensive background in biopharmaceutical development, particularly in the cardiometabolic field, his scientific and public health expertise, and his board and executive leadership experience.

Michael S. Perry, DVM, PhD

Independent Director

Age: 65

Director since: 2011

Serves on:

- Compensation Committee (Chair)
- Nomination Committee
- Science Committee

Experience and Expertise

Dr. Perry is currently a Venture Partner with Bioscience Managers, a global venture capital firm. He also serves as Chairman and board member of 7 Hills Pharma, a private clinical stage pharmaceutical company. Dr. Perry was Chief Executive Officer of Avita Medical, Inc., a regenerative medicine company based in Valencia, CA (Nasdsaq: RCEL) from 2017 to 2022. From 2014 to 2017, he served as Chief Scientific Officer of Novartis' Cell and Gene Therapy Unit, and from 2012 to 2014 he served as Vice President and Global Head of Stem Cell Therapy for Novartis Pharmaceuticals Corp, the US affiliate of Switzerland-based Novartis AG, a global pharmaceutical company. Dr. Perry has also served as SVP and Global Head of R&D at Baxter Healthcare, President and as CEO of Cell & Gene Therapy at Novartis AG. Earlier in his career he served as VP Regulatory Affairs at Novartis, Sandoz Pharmaceuticals, and Syntex Corporation. He also served as Director of Regulatory Affairs at Schering-Plough Corporation. Dr. Perry also served as a Venture Partner with Bay City Capital, LLC for eight years. Dr. Perry has previously served as a board member for the following companies: Ampliphi Bioscience Corp, Gamida Cell Ltd, Targeted Genetics, Inc., American Xeno, Inc., BioTransplant, Inc., Itamar Biomedical Ltd, Systemix, Inc., Genetic Therapy, Inc., Extropy Pharmaceuticals, Inc, and Pharsight Corporation. Dr. Perry holds an Honors Bachelor of Science in Physics and Engineering and a PhD in Biomedical Pharmacology from the University of Guelph. He also holds a Doctor of Veterinary Medicine & Surgery from Ontario Veterinary College and is a graduate of the International Advanced Management Program at Harvard Business School. Dr. Perry currently serves as Adjunct Professor at the Gates Center for Regenerative Medicine at the University of Colorado Anschutz Medical Campus and as Faculty at Houston Methodist and Chair of the Translational Medicine Advisory Board of the Houston Methodist Research Institute.

Qualifications

Dr. Perry's qualifications to serve on the board include his medical expertise and his extensive experience in preclinical and clinical drug development, including executive level leadership roles and directorships in several publicly held biotech companies.

Victoria Vakiener
Independent Director

Age: 61

Director since: 2022

Serves on:
- Nomination Committee (Chair)
- Audit Committee

Other Public Company Boards:
- Chimerix, Inc.

Experience & Expertise
Ms. Vakiener currently serves on the board of directors of Chimerix (Nasdaq: CMRX), a clinical-stage biopharmaceutical company. From November 2018 through September 2021, she served as Chief Commercial Officer of Epizyme, Inc., a biopharmaceutical company that was acquired in 2022, where she built the commercial organization and launched TAZVERIK for two indications within six months. Prior to joining Epizyme, Ms. Vakiener was an executive at Johnson & Johnson (NYSE: JNJ) for more than twenty years where she held positions of leadership with increasing responsibility across the company's pharmaceutical and diagnostics businesses. Ms. Vakiener began her pharmaceutical career at Schering-Plough, where she spent nine years in both scientific and commercial roles. Ms. Vakiener received a BS in Biochemistry from Albright College.

Qualifications
Ms. Vakiener's qualifications to serve on the Board include her deep commercial experience and expertise, her scientific development experience, and her board and executive leadership experience.

William Waddill
Lead Independent Director

Age: 67

Director since: 2018

Serves on:
- Audit Committee (Chair)
- Compensation Committee
- Nomination Committee

Other Public Company Boards:
- Protagonist Therapeutics, Inc.
- Annexon Biosciences

Experience & Expertise
Mr. Waddill began his career over 35 years ago in commercial banking and public accounting and has been in the biotechnology industry for over 30 years. He currently serves on the boards of Protagonist Therapeutics (Nasdaq: PTGX), Annexon Biosciences (Nasdaq: ANNX) and Turnstone Biologics (Nasdaq: TSBX), all clinical-stage biopharmaceutical companies. Mr. Waddill was Senior Vice President and CFO of Calithera Bioscience (Nasdaq: CALA), from 2014 to 2016 and Senior Vice President and CFO at OncoMed Pharmaceuticals from 2007 to 2014, both of which were public clinical-stage biopharmaceutical companies. Prior to that, he served as the Senior Vice President and CFO of Ilypsa, Inc., a biotechnology company that was acquired in 2007 by Amgen, Inc. Before joining Ilypsa, he served as the founder and principal at Square One Finance, a financial consulting business. Mr. Waddill received a BS in accounting from the University of Illinois, Chicago, and certification as a public accountant (inactive) after working at PriceWaterhouseCoopers and Deloitte in Boston.

Qualifications
Mr. Waddill's qualifications to serve on the Board include his extensive background in the biopharma industry, his financial and audit expertise, executive leadership roles and experience as a director of other public companies.

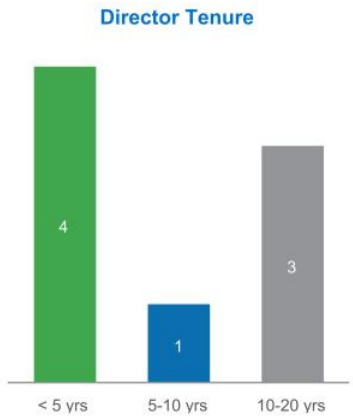
Board Composition and Nominating Process

The Nomination Committee of the Board annually considers the size, composition and needs of the Board and, as appropriate, recommends the nominees for directors to the Board for approval. The Nomination Committee considers and evaluates suggestions from many sources regarding possible candidates for directors. Below are general criteria for the evaluation of current and proposed directors:

- The highest ethical character and shared values with our Code of Corporate Conduct
- Reputation, both personal and professional, consistent with our image and reputation
- Accomplishment within a candidate's field, with superior credentials and recognition
- Relevant expertise and experience and the ability to offer advice and guidance to the Chief Executive Officer based on such expertise and experience
- Independence, without the appearance of any conflict in serving as a Director, and independence of any particular constituency with the ability to represent all stockholders
- Ability to exercise sound business judgment
- Diversity, reflecting differences in skills, regional and industry experience, backgrounds, ages, and other unique characteristics, such as race, gender and ethnicity

The Nomination Committee considers the mix of skills and experience among current and prospective directors with a goal of assembling a Board with complementary skills for the benefit of the Company. Listed below are selected key contributions of each current Board member. The table is not intended to be an exhaustive summary of all the contributions of each Board member.

Expertise	Given	Perry	Anzalone	Ferrari	Olukotun	Vakiener	Waddill	Lu	Ingram
Biopharma Research & Development	X	X	X	X	X	X	X	X	X
Healthcare	X	X	X	X	X	X	X	X	X
Drug Development	X	X	X	X	X	X			X
Executive Leadership	X	X	X	X	X	X	X	X	X
Public Company Governance	X	X	X	X	X	X	X	X	X
Accounting/Audit				X		X	X	X	
Capital Markets	X	X	X				X	X	X
Commercial	X	X			X	X			X



Board Diversity

The Nomination Committee believes that the Board should represent a diverse mix of skills, regional and industry experience, backgrounds, ages, and other unique characteristics, such as race, gender, and ethnicity. In furtherance of this goal, the Committee is committed to actively seeking out highly qualified diverse candidates (including women and minority candidates) to include in the pool from which Board nominees are chosen.

Board Diversity Matrix (As of January 28, 2025)				
Total Number of Directors		#8		
	Female	Male	Non-Binary	Did Not Disclose Gender
Part I: Gender Identity				
Directors	2	6	0	0
Part II: Demographic Background				
African American or Black	0	1	0	0
Alaskan Native or Native American	0	0	0	0
Asian	1	0	0	0
Hispanic or Latinx	0	0	0	0
Native Hawaiian or Pacific Islander	0	0	0	0
White	1	5	0	0
Two or More Races or Ethnicities	0	0	0	0
LGBTQ+			0	
Did Not Disclose Demographic Background			0	

Corporate Governance, Environmental and Social Commitment

The following is a summary of our corporate governance, environmental, and social commitment policies and practices:

- **Lead Independent Director:** Because our CEO serves as the Board Chair, we have elected a Lead Independent Director to lead discussions and decision-making of the Board when it would not be appropriate for the CEO to do so, including during executive sessions of the independent members of the Board.
- **Combined Chair and CEO:** Following Douglass Given's retirement from the Board, including as Board Chair, Mr. Anzalone currently serves as Board Chair and Chief Executive Officer. Our Bylaws do not require that our Board Chair and Chief Executive Officer positions be separate, and our Board believes that having a combined CEO and Chair is the appropriate leadership structure for us at this time as it helps promote unified leadership and direction and provide management a single, clear focus to execute our strategy and business plans.
- **Majority Independent Board:** A majority of the members of the Board are independent directors, as defined by Nasdaq Marketplace Rules. The Board has determined that all of the Company's directors and director nominees are independent, except Dr. Anzalone, due to his employment relationship with the Company. Douglass Given was independent during the period he served on the Board. Non-employee directors do not receive consulting or other fees from the Company, other than Board and Committee compensation.
- **Board Oversight of Risk:** The Board has overall responsibility for the oversight of the Company's risk management process, which is designed to support the achievement of organizational objectives, including strategic objectives, to improve long-term organizational performance and enhance stockholder value. Risk management includes not only understanding company-specific risks and the steps management implements to manage those risks, but also what level of risk is acceptable and appropriate for the Company. Management is responsible for establishing our business strategy, identifying and assessing the related risks and implementing appropriate risk management practices. The Board regularly reviews our business strategy and management's assessment of the related risk and discusses with management the appropriate level of risk for the Company.
- **Corporate Code of Conduct:** All of the Company's employees, officers, and directors are subject to the Company's Corporate Code of Conduct, which is available on the Company's website at www.arrowheadpharma.com. The code meets the requirements of Nasdaq Marketplace Rules, as well as the code of ethics requirements of the SEC. We intend to disclose future amendments to certain provisions of the Corporate Code of Conduct, and waivers of the Corporate Code of Conduct granted to officers and directors, on the Company's website within four business days following the date of the amendment or waiver.
- **Independent Committees:** The Audit, Compensation, and Nomination Committees consist entirely of independent directors.
- **Regularly Held Executive Sessions:** The independent directors meet separately in executive session on a regular basis to discuss matters relating to the Company and the Board, without members of the management team present.
- **Proxy Access:** Stockholders have a proxy access right with market-standard terms (3% for 3 years, up to 20% of the Board).
- **Board Oversight of Strategy:** The Board reviews at least annually the Company's business initiatives, capital projects and budget matters.
- **Environmental and Social Responsibility Oversight:** The Board has designated one of its members, Adeoye Olukotun, with responsibility for confirming the Company's environmental and social programs align with the Board's expectations in these matters.
- **Cybersecurity:** The Company maintains a cybersecurity program, with direct oversight from senior management and the Board of Directors, to manage information, data, and technology security. The Company has formed an internal cross-functional Technology Risk Management Committee comprised of representative leaders from various aspects of the Company's business to broadly implement its cybersecurity program.
- **Related Party Transaction Oversight:** The Audit Committee is responsible for reviewing and approving all disclosable related-party transactions or, if the size and nature of the transaction warrants, a special committee of non-related Board members is formed to negotiate and approve the transaction.

- **Sustainability:** The Company continues to assess its environmental impact and ways in which it can operate more responsibly and sustainably. The Company completed building its research and development facilities in San Diego, California and Verona, Wisconsin. Both research and development facilities were built to meet LEED certification standards. The Company has contracted with a third party to operate a solar power generation plant at our San Diego facility with a generating capacity of approximately 1,406kW, which is comprised of a rooftop system, parking lot solar canopies, and a 1,200 kW battery storage system to supply power to the building. Additionally, the Company has continued its efforts to minimize use of paper records in favor of electronic records and has a robust recycling program for paper, batteries, and electronic equipment.
- **Human Capital Management:** Arrowhead has a vibrant and growing culture and we are committed to the health and welfare of our employees. Our important work developing advanced drugs for patients requires a specialized and dedicated workforce. Arrowhead supports the development of our employees with a competitive compensation and benefits package, internal advancement, and individualized development opportunities. We are committed to training young scientists and businesspeople and offer multiple internships and entry level positions each year.
- **Workforce Diversity:** As of September 30, 2024, women comprise 51% of our employee workforce and 45% of our employee leaders at the level of director or above. People self-identifying as a minority under the categories established by the Equal Employment Opportunity Commission comprise 27% of our employee workforce and 39% of our employee leaders at the level of director or above. One of our executive officers is a member of the LGBTQ+ community.

Stockholder Communications with Directors

Stockholders who wish to communicate with the Board or any individual director can write to: Patrick O'Brien, Corporate Secretary, Arrowhead Pharmaceuticals, Inc., 177 E. Colorado, Suite 700, Pasadena, CA 91105. Your letter should indicate that you are an Arrowhead stockholder. Depending on the subject matter, management will:

- Forward the communication to the director or directors to whom it is addressed;
- Forward the communication to the Board Chair, if addressed to the board of directors; or
- If not addressed to, or otherwise appropriate for, any director or directors, attempt to handle the inquiry directly (for example, requests for information or stock-related matters).

Board Meetings and Committees

The Board held a total of five meetings during the fiscal year ended September 30, 2024. The Board has three standing committees: Audit Committee, Compensation Committee, and Nomination Committee. The functions of the Audit Committee are to select and oversee the independent registered public accounting firm, to review the scope and results of the year-end audit with management and the independent auditors, to review the Company's accounting principles and its system of internal accounting controls, to review the Company's annual and quarterly reports before filing with the SEC and to review any related-party transactions. The Audit Committee met four times during fiscal 2024. The members of the Audit Committee for fiscal 2024 were William Waddill (Committee Chair), Mauro Ferrari, and Victoria Vakiener. The current members of the Audit Committee for fiscal 2025 are William Waddill (Committee Chair), Mauro Ferrari, and Victoria Vakiener. The Board has determined that all members of the Audit Committee who served during 2024 were independent directors under the rules of the Securities and Exchange Commission ("**SEC**") and the listing standards of Nasdaq Marketplace Rules and are financially literate. The Board has determined that Mr. Waddill is an "audit committee financial expert" in accordance with the applicable regulations, based on his experience as noted above. The Audit Committee Charter is available on the Company's website at www.arrowheadpharma.com.

The functions of the Compensation Committee are to review the goals and achievements of the Company and the Chief Executive Officer for the prior year and approve the goals of the Company and the Chief Executive Officer for the next year, to review and approve salaries, bonuses, equity awards, and other benefits payable to the Company's executive officers and to administer the Company's equity incentive compensation plans. The Compensation Committee is specifically responsible for determining the compensation of the Chief Executive Officer and the other executive officers. The Compensation Committee reviews compensation recommendations made by the Chief Executive Officer for other senior executives of the Company and the compensation of the Chief Executive Officer at least annually; the Chief Executive Officer is not present during discussions or deliberations regarding his compensation. In fiscal 2024, the Compensation Committee engaged Compensia, Inc. ("**Compensia**"), a national

compensation consulting firm, to provide advice and guidance with regard to compensation for our NEOs. The decision to engage the consultant was not made or recommended by management and the Compensation Committee has the sole discretion to engage or change the consultant. The Compensation Committee met four times during fiscal 2024. The members of the Compensation Committee for fiscal 2024 were William Waddill (Committee Chair), Mauro Ferrari, and Michael Perry. The current members of the Compensation Committee for fiscal 2025 are Michael Perry (Committee Chair), Hongbo Lu, and William Waddill . The Board has determined that all members of the Compensation Committee are independent directors under the listing rules of Nasdaq Marketplace Rules. The Compensation Committee's charter is available on the Company's website at www.arrowheadpharma.com. The Compensation Committee has not delegated any of its responsibilities or authorities granted under its charter.

The Nomination Committee is responsible for proposing a slate of directors for election by the stockholders at each annual meeting and for proposing candidates to fill any vacancies. The Nomination Committee met three times during fiscal 2024. The members of the Nomination Committee for fiscal 2024 were Michael Perry (Committee Chair) Mauro Ferrari, Adeoye Olukotun, Victoria Vakiener, and William Waddill. The current members of the Nomination Committee for fiscal 2025 are Victoria Vakiener (Committee Chair), Mauro Ferrari, Adeoye Olukotun, Michael Perry, Hongbo Lu, and William Waddill. The Board has determined that all members of the Nomination Committee are independent directors under the listing rules of Nasdaq Marketplace Rules. The Nomination Committee's charter is available on the Company's website at www.arrowheadpharma.com. The Nomination Committee manages the process for evaluating current Board members at the time they are considered for re-nomination. After considering the appropriate skills and characteristics required on the Board, the current makeup of the Board, the results of the evaluations and the wishes of the Board members to be re-nominated, the Nomination Committee recommends to the Board whether those individuals should be re-nominated.

On at least an annual basis, the Nomination Committee reviews with the Board whether it believes the Board would benefit from adding new members and, if so, the appropriate skills and characteristics required for any new members. If the Board determines that a new member would be beneficial, the Nomination Committee solicits and receives recommendations for candidates and manages the process for evaluating candidates. All potential candidates, regardless of their source, are reviewed under the same process. The Nomination Committee (or the Committee Chair) screens the available information about the potential candidate(s). Based on the results of the initial screening, interviews with candidates are scheduled with Nomination Committee members, other members of the Board and senior members of management. Upon completion of these interviews and other due diligence, the Nomination Committee may recommend a candidate to the Board for appointment.

Candidates for independent Board member positions are identified through recommendations from directors or others associated with the Company, as well as through a formal search process managed by a third-party search firm. Arrowhead stockholders may also recommend candidates by sending the candidate's name and resume to the Nomination Committee pursuant to the procedures, set forth above, for communication with the Board. The Nomination Committee evaluates director candidates recommended by stockholders in the same way that it evaluates candidates recommended by its members, other members of the Board, or other persons. As described above, our Bylaws also provide for separate notice procedures to recommend a person for nomination as a director to be considered by stockholders at a meeting, including requirements as to the timing, form and content of a stockholder's notice.

The Nomination Committee has no predefined minimum criteria for selecting Board nominees, although it believes that all directors should share qualities such as governance and business experience at the corporate level, relevant non-competitive experience, and strong communication and analytical skills. Independent directors must meet the criteria for independence set forth by Nasdaq and, as applicable, the SEC. In any given search, the Nomination Committee may also define particular characteristics for candidates to balance the overall mix of skills, backgrounds and characteristics of the Board and the needs of the Company. During any search, the Nomination Committee reserves the right to modify its stated search criteria for exceptional candidates.

The Nomination Committee assesses its effectiveness in achieving its goal of building a diverse board as part of its annual assessment of the composition of the Board.

In 2018, the Board established a Science Committee to review and advise on science topics of interest to the Company. The members of the Science Committee for fiscal 2024 were Mauro Ferrari (Committee Co-Chair), Adeoye Olukotun (Committee Co-Chair), Douglass Given, and Michael Perry. The current members of the Science Committee for fiscal 2025 are Mauro Ferrari (Committee Co-Chair), Adeoye Olukotun (Committee Co-Chair), Hongbo Lu, and Michael Perry.

Each of our incumbent directors attended 100% of the aggregate of (i) the total number of meetings of the Board held during fiscal 2024, and (ii) the total number of meetings held by all committees of the Board during fiscal 2024 on which such person served, in each case during the period in which such person served on the Board or committee.

In addition, all of the directors then serving on the Board and standing for re-election attended the virtual 2024 Annual Meeting of Stockholders. It is the Company's policy to encourage, but not require, that all directors attend our annual stockholder meetings.

Director Compensation

Directors who are also employees of the Company receive no separate compensation from the Company for their service as members of the Board. For 2024, the Company maintained the structure of director compensation it adopted in 2019 to provide a base retainer for each director with higher base retainers for service by the Board Chair and committee leadership. The average total compensation paid to the Company's non-executive directors for service in 2024 is at or below the 60th percentile of the total compensation paid to non-executive directors of its peer group as described later in this proxy statement. The Compensation Committee believes the structure aligns compensation according to the level of service contributions by each director. The fees payable to directors for service on the Board and for service on each committee of the Board on which the director serves are as follows:

Board of Directors:	2023 Annual Retainer:	2024 Annual Retainer:
All non-employee directors	$80,000	$80,000
Additional retainer for Non-Executive Chairman of the Board	$15,000	$15,000
Audit Committee:		
Chairman	$5,000	$5,000
Compensation Committee:		
Chairman	$5,000	$5,000

The following table sets forth the total compensation paid to our non-employee directors in fiscal 2024. Dr. Anzalone's compensation is set forth in the discussion of Executive Compensation and in the Summary Compensation Table.

Name	Fee Earned or Paid in Cash ($)	Stock Awards ($) (1) (2)	Total ($)
Douglass Given (3)	$95,000	$380,833	$475,833
Michael S. Perry	$80,000	$380,833	$460,833
Mauro Ferrari	$80,000	$380,833	$460,833
William Waddill	$90,000	$380,833	$470,833
Hongbo Lu (4)(5)	$43,333	$761,666	$804,999
Adeoye Olukotun	$80,000	$380,833	$460,833
Victoria Vakiener	$80,000	$380,833	$460,833

(1) This column represents the total grant date fair value, computed in accordance with ASC 718, of RSUs granted during fiscal year 2024 to each director. The assumptions used to calculate the value of the stock underlying the RSU awards are set forth in Note 9 of the Notes to the Consolidated Financial Statements included with the Company's Annual Report on Form 10-K.

(2) The RSUs granted to non-employee directors vest one year from the date of grant, subject to continued service through the vesting date, with the exception of the RSUs granted to Dr. Lu in connection with her appointment to the Board, which vest in three equal installments on each anniversary of the date of grant , subject to continued service through each such vesting date.

(3) Douglass Given retired from the Board effective as of December 31, 2024.

(4) Dr. Lu joined the Board during fiscal year 2024 and her cash compensation was pro-rated for such fiscal year.

(5) In connection with her appointment, Dr. Lu received a sign-on grant of restricted stock units valued at $761,666.

As of the last day of fiscal year 2024, the directors held the following outstanding restricted stock unit ("**RSU**") grants in the aggregate: Douglass Given — — 19,583; Michael S. Perry — 19,583; Mauro Ferrari —19,583; William Waddill — 19,583; Adeoye Olukotun — 19,583; Victoria Vakiener — 24,722; and Hongbo Lu — 24,080 RSUs.

As of the last day of fiscal year 2024, the directors held the following outstanding option ("Options") grants in the aggregate: Douglass Given — 4,593; Michael S. Perry — 4,593; Mauro Ferrari —4,593; William Waddill — 4,593; Adeoye Olukotun — 4,593; Victoria Vakiener — 4,593 Options; and Hongbo Lu — 0.

Vote Required; Recommendation of the Board

The nominees listed above receiving more "FOR" votes than "AGAINST" votes, assuming a quorum is present, will be elected as directors to serve until their terms expire or until their successors have been duly elected and qualified. Because directors are elected by a majority of votes cast, abstentions from voting and broker non-votes, if any, will be excluded from the vote and will have no effect on its outcome.

THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" EACH OF THE NOMINEES FOR DIRECTOR IN PROPOSAL ONE.

Proposal Two — Advisory Vote to Approve Executive Compensation

The compensation paid to our Named Executive Officers ("**NEOs**") is described below in the Compensation Discussion and Analysis of this proxy statement for the year ended September 30, 2024. The Board is asking stockholders to cast a non-binding, advisory vote FOR the following resolution:

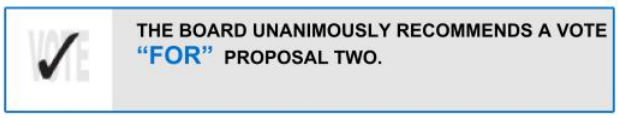
> "RESOLVED, that the compensation paid to the Company's named executive officers, as disclosed pursuant to Item 402 of Regulation S-K, as set forth in the compensation tables and narrative discussion, is hereby APPROVED."

Although the vote we are asking you to cast is non-binding, the Compensation Committee and the Board value the views of our stockholders and will consider the outcome of the vote when determining future compensation arrangements for our NEOs.

The Board has adopted a policy providing for annual advisory votes to approve executive compensation. Unless stockholders approve a different frequency in Proposal Three or the Board modifies its policy on the frequency of holding advisory votes to approve executive compensation, the next such advisory vote will occur in 2026.

Vote Required; Recommendation of the Board

Proposal Two must be approved by the Required Vote, assuming a quorum is present. For this purpose, abstentions will be counted as a vote "AGAINST" the proposal, while broker non-votes, if any, will have no effect on the outcome of the vote.



Proposal Three —Advisory Vote on Frequency of Executive Compensation Advisory Votes

In Proposal Two, we are asking stockholders to cast an advisory vote to approve the compensation disclosed in this proxy statement that we paid in fiscal 2024 to our named executive officers. This advisory vote is referred to as a "Say-on-Pay" vote. In this Proposal Three, the Board is asking stockholders to cast a non-binding, advisory vote on how frequently we should have Say-on-Pay votes in the future. Stockholders will be able to mark the enclosed proxy card or voting instruction form on whether to hold say-on-pay votes every one, two or three years. Alternatively, you may indicate that you are abstaining from voting.

> "RESOLVED, that the stockholders of the Company recommend, in a non-binding vote, whether an advisory vote to approve the compensation of the Company's named executive officers should occur every one, two or three years."

This vote, like the Say-on-Pay vote itself, is not binding on the Board. Although the Board and the Compensation Committee recognize the potential benefits of having less frequent advisory votes to approve executive compensation (including allowing the Company additional time to effectively evaluate the relationship between the executive compensation and long-term Company performance and stockholder return), we recognize that the widely adopted standard is to hold Say-on-Pay votes annually. The Board and Compensation Committee also acknowledge current stockholder expectations regarding having the opportunity to express their views on the Company's executive compensation on an annual basis. In light of investor expectations and prevailing market practice, our Board and the Compensation Committee recommend that the advisory vote to approve executive compensation occur every year.

Vote Required; Recommendation of the Board

Proposal Three must be approved by the Required Vote, assuming a quorum is present. For this purpose, abstentions will be counted as a vote against the proposal, while broker non-votes will have no effect on the outcome of the vote. Because Proposal Three has three possible substantive responses (every one, two or three years), if none of the frequency alternatives receives the Required Vote, then we will consider stockholders to have approved the frequency that receives the greatest number of the votes cast.

THE BOARD UNANIMOUSLY RECOMMENDS THAT STOCKHOLDERS SELECT "1 YEAR" ON THE PROPOSAL CONCERNING THE FREQUENCY OF FUTURE ADVISORY VOTES TO APPROVE

Executive Compensation

COMPENSATION DISCUSSION AND ANALYSIS

The following compensation discussion and analysis contains statements regarding future individual and Company performance targets and goals. These targets and goals are disclosed in the limited context of Arrowhead's executive compensation program and should not be understood to be statements of management's expectations or guidance. Arrowhead cautions investors not to apply these statements to other contexts. Fiscal years are denoted as fiscal years, all other year references refer to calendar years.

This Compensation Discussion and Analysis describes the compensation program for our NEOs. During fiscal 2024, these individuals were:

- Christopher Anzalone, our President and Chief Executive Officer (our "**CEO**");
- James Hamilton, our Chief of Discovery and Translational Medicine (our "**CDTM**");
- Kenneth Myszkowski, our Chief Financial Officer (our "**CFO**");
- Patrick O'Brien, our Chief Operating Officer and General Counsel (our "**COO**" and "**GC**");
- Tracie Oliver, our former Chief Commercial Officer (our "**CCO**"); and
- Javier San Martin, our former Chief Medical Officer (our "**CMO**").

This Compensation Discussion and Analysis describes the material elements of our executive compensation program during fiscal 2024. It also provides an overview of our executive compensation philosophy and objectives and summarizes our executive compensation policies and practices. Finally, it analyzes how and why the Compensation Committee of our Board arrived at the specific compensation decisions for our executive officers, including our NEOs, for fiscal 2024, including the key factors that the Compensation Committee considered in determining their compensation.

Our Company

We develop medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, our 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.

Arrowhead is focused on developing innovative drugs for diseases with a genetic basis, typically characterized by the overproduction of one or more proteins. The depth and versatility of our RNAi technologies enable us to potentially address conditions in virtually any therapeutic area and pursue disease targets that are not otherwise addressable by small molecules and Biologics.

2024 Business Highlights

- Presented new pivotal Phase 3 Data from PALISADE study of plozasiran in patients with familial chylomicronemia syndrome (FCS) at the European Society of Cardiology (ESC) Congress 2024 and simultaneously published in The New England Journal of Medicine.
- The Company submitted a New Drug Application to the U.S. Food and Drug Administration (FDA) on November 16, 2024, which was accepted for filing on January 17, 2025. The FDA provided a Prescription Drug User Fee Act (PDUFA) action date of November 18, 2025, and indicated it is not currently planning to hold an advisory committee meeting.
- Entered into a global and collaboration agreement with Sarepta Therapeutics, Inc. Upon closing, Arrowhead will receive $825 million, consisting of $500 million cash and $325 million as an equity investment. Arrowhead will also receive $250 million to be paid in equal installments over five years and is eligible to receive an additional

$300 million in near-term payments. Additionally, Arrowhead is eligible to receive royalties on commercial sales and up to approximately $10 billion in future potential milestone payments.

- Presented preclinical data and detailed plans to advance two next generation RNAi-based candidates, ARO-INHBE and ARO-ALK7, into upcoming clinical studies for the treatment of obesity and metabolic diseases. In preclinical studies to date, these candidates demonstrated the potential to reduce body weight and fat mass with a novel mechanism of action that may lead to improved preservation of lean muscle mass compared to currently approved obesity therapies. On September 23, 2024, the Company filed for regulatory clearance to initiate a Phase 1/2a clinical trial of ARO-INHBE and subsequently on December 3, 2024, filed for regulatory clearance to initiate a Phase 1/2a clinical trial of ARO-ALK7.
- Announced successful top-line results from the pivotal Phase 3 PALISADE study of investigational plozasiran in patients with familial chylomicronemia syndrome (FCS). The Company highlighted recent data for its cardiometabolic pipeline at its June 25, 2024, Cardiometabolic event.
- Announced results from the Phase 2b double blind, randomized ARCHES-2 study of investigational zodasiran in patients with mixed hyperlipidemia.
- Announced that new interim clinical data on ARO-RAGE achieves high level of gene knockdown in patients with asthma.
- Amgen completed enrollment in Amgen's Phase 3 OCEAN(a) - outcomes trial of olpasiran, triggering a $50.0 million milestone payment to the Company from Royalty Pharma, which was paid in the third quarter of fiscal 2024.
- Presented final data from the double-blind treatment period of the Company's Phase 2 SHASTA-2 study of investigational plozasiran in patients with severe Hypertriglyceridemia. Results from the SHASTA-2 study showed dramatic, consistent, and sustained reductions in Apolipoprotein C-III (APOC3) and triglycerides and improvement in multiple atherogenic lipoprotein levels.
- Announced an Expanded Access Program ("EAP") to make investigational plozasiran available outside of a clinical trial for qualifying patients with familial chylomicronemia syndrome (FCS).
- Initiated a Phase 1/2a clinical trial of ARO-DM1, being developed as a potential treatment for type 1 myotonic dystrophy (DM1), the most common adult-onset muscular dystrophy.
- Filed an application for clearance to initiate a Phase 1/2a clinical trial of ARO-CFB, being developed as a potential treatment for complement mediated renal disease.
- Entered into an Amended and Restated License Agreement with GSK, pursuant to which GSK received a worldwide, exclusive license to develop and commercialize daplusiran/tomligisiran (GSK5637608, formerly JNJ-3989). Daplusiran/tomligisiran had previously been licensed to Janssen Pharmaceuticals, Inc.

Business Development

Sarepta Therapeutics, Inc.

On November 25, 2024, the Company entered into an Exclusive License and Collaboration Agreement (the "Sarepta Collaboration") with Sarepta Therapeutics, Inc. ("Sarepta") for the co-development and commercialization of ARO-DUX4, ARO-DM1, ARO-MMP7, and ARO-ATXN2 clinical stage programs. Sarepta has also received an exclusive sublicensable worldwide license to the Company's ARO-HTT, ARO-ATXN1, and ARO-ATXN3 preclinical stage programs.

Pursuant to the Sarepta Collaboration, Sarepta may select up to six gene targets for which the Company will perform discovery, optimization and preclinical development activities to identify RNAi compounds against each selected target. Upon completion of the Company's preclinical activities, Sarepta will receive an exclusive license to the Company's intellectual property rights to exploit those compounds and be wholly responsible for clinical development and commercialization of each compound.

Closing of the Sarepta Collaboration is subject to clearance under the Hart-Scott Rodino Antitrust Improvements Act.

In connection with the Sarepta Collaboration, on November 25, 2024, the Company entered into a Stock Purchase Agreement (the "Stock Purchase Agreement") with an affiliate of Sarepta for a private placement of shares of

common stock of the Company (the "Private Placement"). Pursuant to the Stock Purchase Agreement, the Company sold 11,926,301 shares of common stock, at a price per share of $27.25, for an aggregate value of approximately $325.0 million. The Private Placement is expected to close concurrently with the Sarepta Collaboration.

Under the terms of the agreements taken together, the Company expects to receive $500.0 million as an upfront payment under the Sarepta Collaboration, $325.0 million in the form of an equity investment under the Stock Purchase Agreement, and $250.0 million to be paid in annual installments of $50.0 million over 5 years. The Company is also eligible to receive $300.0 million in near-term payments associated with the continued enrollment of certain cohorts of a Phase 1/2 study, which the Company is on track to achieve. Further, for each of the 13 programs, the Company is eligible to receive development milestone payments between $110.0 million and $180.0 million per program and sales milestone payments between $500.0 million and $700.0 million per program. The Company is also eligible to receive tiered royalties on net sales of licensed products of up to the low double digits.

Platform

In fiscal 2024, the Company continued to develop and deploy its Targeted RNAi Molecule platform ("**TRiM**™") to identify and develop new therapeutics. TRiM™ utilizes ligand-mediated delivery and is designed to enable tissue-specific targeting, while being structurally simple. Targeting has been core to the Company's development philosophy and the TRiM™ platform builds on more than a decade of work on actively targeted drug delivery vehicles. The TRiM™ platform is designed to offer several potential competitive advantages including:

- A more sophisticated RNAi trigger selection and screening process that identifies potent sequences rapidly in locations that RNAi competitors may miss;
- Multiple routes of administration including subcutaneous, intravenous and inhaled;
- Faster time to clinical candidates;
- Optimal pharmacologic activity and long duration-of-effect;
- Potentially wide safety margins;
- Simplified manufacturing at reduced cost; and
- The ability to take RNAi to tissues beyond the liver.

Pipeline

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 Arrowhead's RNAi technologies enables Arrowhead 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 focused on bringing the promise of RNAi to address diseases outside of the liver, and its pipeline now includes disease targets in the liver, lung, muscle and CNS.

*The timing of our planned and already filed clinical trial applications ("**CTA**") discussed below are based on calendar years, not fiscal years.*

Arrowhead Proprietary Clinical Stage Candidates

Plozasiran (ARO-APOC3) is designed to reduce production of Apolipoprotein C-III (apoC-III), a component of triglyceride rich lipoproteins (TRLs) including Very Low Density Lipoprotein (VLDL) and chylomicrons, a key regulator of triglyceride metabolism. The Company believes 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. The Company is currently investigating plozasiran in one Phase 2 clinical trial and four Phase 3 clinical trials. In the Phase 3 PALISADE trial in patients with familial chylomicronemia syndrome (FCS), plozasiran has met its primary endpoint of triglyceride reduction as well as all of its key (alpha controlled) secondary endpoints. The Company is currently in the process of seeking regulatory approval for plozasiran for the treatment of FCS.

- **Study Name: Study of ARO-APOC3 in Adults With Dyslipidemia**
  A Phase 2 Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of ARO-APOC3 in Adults With Dyslipidemia

  ClinicalTrials.gov Identifier: NCT05413135
- **Study Name: Study of ARO-APOC3 in Adults With FCS (PALISADE)**
  A Phase 3 Study to Evaluate the Efficacy and Safety of ARO-APOC3 in Adults With Familial Chylomicronemia Syndrome

  ClinicalTrials.gov Identifier: NCT05089084
- **Study Name: Study of Plozasiran (ARO-APOC3) in Adults With Severe Hypertriglyceridemia (SHASTA-3)**
  Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Plozasiran in Adults With Severe Hypertriglyceridemia
- ClinicalTrials.gov Identifier: NCT06347003
- **Study Name: Study of Plozasiran in Adults With Severe Hypertriglyceridemia (SHASTA-4)**
  Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Plozsiran in Adults With Severe Hypertriglyceridemia
- ClinicalTrials.gov Identifier: NCT06347016
- **Study Name: Phase 3 Study of Plozasiran in Adults With Hypertriglyceridemia (MUIR-3)**
  Double-blind, Placebo-controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Plozasiran in Adults With Hypertriglyceridemia
- ClinicalTrials.gov Identifier: NCT06347133

Zodasiran (*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 zodasiran in two Phase 2b clinical trials.

- **Dyslipidemia and Hypertriglyceridemia**: Dyslipidemia and hypertriglyceridemia are risk factors for atherosclerotic coronary heart disease and cardiovascular events.
- **Study Name: Study of ARO-ANG3 in Adults With Mixed Dyslipidemia (ARCHES-2)**
  A Double-blind, Placebo-controlled Phase 2b Study to Evaluate the Efficacy and Safety of ARO-ANG3 in

Adults With Mixed Dyslipidemia

ClinicalTrials.gov Identifier: NCT04832971

- **Study Name: Study of ARO-ANG3 in Participants With Homozygous Familial Hypercholesterolemia (HoFH) (GATEWAY)**
  Phase 2 Study to Evaluate the Safety and Efficacy of ARO-ANG3 in Subjects with Homozygous Familial Hypercholesterolemia (HoFH)

  ClinicalTrials.gov Identifier: NCT05217667

ARO-INHBE is designed to reduce the hepatic expression of the INHBE gene and its secreted gene product, Activin E. INHBE is a promising genetically validated target in which loss-of-function INHBE variants in humans are associated with lower risk of obesity and metabolic diseases, such as type 2 diabetes. The Company has filed for regulatory clearance to initiate a Phase 1/2a clinical trial of ARO-INHBE.

- **Study Name: ARO-INHBE in Adults With Obesity With and Without Diabetes Mellitus**
  Phase 2 Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARO-INHBE in Adult Volunteers With Obesity With and Without Diabetes Mellitus

  ClinicalTrials.gov Identifier: NCT06700538

ARO-ALK7 is designed to silence adipocyte expression of the ACVR1C gene to reduce production of Activin receptor-like kinase 7 (ALK7), which acts as a receptor in a pathway that regulates energy homeostasis in adipose tissue. In large genetic datasets, reduced ACVR1C expression has been associated with healthier adipose distribution and reduced risk of obesity-related metabolic complications. Treatment with investigational ARO-ALK7 has the potential to reduce visceral adiposity and improve lipid and glycemic parameters.

ARO-C3 is designed to reduce production of complement component 3 ("**C3**") as a potential therapy for patients with various complement mediated or complement associated renal. Arrowhead is currently investigating ARO-C3 in a Phase 1/2a clinical trial.

- **Complement-Mediated Renal Disease:** A number of rare renal diseases result from uncontrolled activation of the alternative pathway of complement, leading to progressive glomerular damage, proteinuria, hematuria, and impaired kidney function, and often resulting in end-stage renal disease (ESRD). In addition, dysregulation of the alternative complement pathway has been shown to play a role in the pathogenesis and progression of disease in some of the more common glomerulopathies. Silencing C3 may be a therapeutic approach for treatment of these conditions.

- **Study Name: Study of ARO-C3 in Adult Healthy Volunteers and Patients With Complement-Mediated Renal Disease**
  A Phase 1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and/or Pharmacodynamics of ARO-C3 in Adult Healthy Volunteers and in Adult Patients With Complement-Mediated Renal Disease

  ClinicalTrials.gov Identifier: NCT05083364

ARO-CFB is designed to reduce hepatic expression of complement factor B (CFB), which plays an important regulatory role in amplifying complement alternative pathway activation and has been identified as a promising therapeutic target. ARO-CFB is being developed as a potential treatment for complement mediated kidney diseases such as immunoglobulin A nephropathy (IgAN), which is the most common glomerular disease worldwide and carries a high lifetime risk of progression to end-stage renal disease. Additionally, ARO-CFB may have clinical applications in non-renal diseases involving complement activation. The Company is currently investigating ARO-CFB in a Phase 1/2a clinical trial.

- **Complement-Mediated Disease:** A number of rare renal diseases result from uncontrolled activation of the alternative pathway of complement, leading to progressive glomerular damage, proteinuria, hematuria, and impaired kidney function, and often resulting in end-stage renal disease (ESRD). In addition, dysregulation of the alternative complement pathway has been shown to play a role in the pathogenesis and progression of disease in some of the more common glomerulopathies. Silencing CFB may be a therapeutic approach for treatment of these conditions.

- **Study Name: Study of ARO-C3 in Adult Healthy Volunteers and Patients With Complement-Mediated Kidney Disease**
  A Phase 1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Single and Multiple Doses of ARO-CFB in Adult Healthy Volunteers and Adult

Patients With Complement-Mediated Kidney Disease

ClinicalTrials.gov Identifier: NCT06209177

ARO-RAGE is designed to reduce production of the Receptor for Advanced Glycation End products ("**RAGE**") as a potential treatment for various inflammatory pulmonary diseases. Arrowhead is currently investigating ARO-RAGE in a Phase 1/2a clinical trial.

- **Study Name: Study of ARO-RAGE in Healthy Subjects and Patients With Inflammatory Lung Disease**
  A Phase 1/2a Study Evaluating the Effects of ARO-RAGE in Healthy Subjects and Patients With Inflammatory Lung Disease

  ClinicalTrials.gov Identifier: NCT05276570

ARO-PNPLA3 (formerly JNJ-75220795) is an investigational RNAi therapeutic designed to reduce liver expression of patatin-like phospholipase domain containing 3 (PNPLA3) as a potential treatment for patients with metabolic-dysfunction associated steatohepatitis (MASH). PNPLA3 has strong genetic and preclinical validation as a driver of fat accumulation and damage in the livers of patients who carry the common I148M mutation. Former licensee Janssen Pharmaceuticals, Inc. investigated ARO-PNPLA3 in two Phase 1 clinical trials.

- **MASH**: MASH is a subgroup of steatotic liver disease (MASLD) in which hepatic cell injury and inflammation has developed over background steatosis. The I148M genetic variant in the PNPLA3 gene is involved with the underlying pathophysiology and is a known risk factor for hepatic steatosis, steatohepatitis, elevated plasma liver enzyme levels, hepatic fibrosis and cirrhosis. The rising prevalence of MASH presents a significant health burden in many developed countries.

Partnered Programs

Sarepta Therapeutics, Inc.

ARO-DUX4 is designed to target the gene that encodes human double homeobox 4 (DUX4) protein as a potential treatment for patients with facioscapulohumeral muscular dystrophy.
Facioscapulohumeral Muscular Dystrophy: Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant disease associated with the failure to maintain complete epigenetic suppression of DUX4 expression in differentiated skeletal muscle, leading to overexpression of DUX4, which is myotoxic and can lead to muscle degeneration. As DUX4 expression is recognized as the cause of muscle pathology in FSHD patients, the Company believes that the selective targeting and knockdown of DUX4 using RNAi may prevent or reverse downstream myotoxicity and lead to muscle repair and improvement in muscle function in patients. There are currently no effective treatments specifically for FSHD.

- **Study Name: Study of ARO-DUX4 in Adult Patients With Facioscapulohumeral Muscular Dystrophy Type 1**
  A Phase1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARO-DUX4 in Adult Patients With Facioscapulohumeral Muscular Dystrophy Type 1.

  ClinicalTrials.gov Identifier: NCT06131983

ARO-DM1 is designed to reduce expression of the dystrophia myotonica protein kinase (DMPK) gene. There is currently no approved disease-modifying therapy for type 1 myotonic dystrophy (DM1). Treatments have focused on symptomatic management, including physical therapy, exercise, ankle-foot orthoses, wheelchairs, and other assistive devices. The Company is currently investigating ARO-DM1 in a Phase 1/2a clinical trial.

Type 1 Myotonic Dystrophy: Type 1 myotonic dystrophy is an autosomal dominant, debilitating, chronic progressive multisystem disorder characterized by an expansion of a highly unstable CUGexp in the DMPK gene. Patients with DM1 have muscle weakness and wasting, myotonia, cataracts, and often have cardiac conduction abnormalities, and may become physically disabled and have a shortened life span.

- **Study Name: Study of ARO-DM1 in Subjects With Type 1 Myotonic Dystrophy**
  A Phase 1/2a Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ARO-DM1 in Subjects With Type 1 Myotonic Dystrophy Who Are ≥18 to ≤ 65 Years

  ClinicalTrials.gov Identifier: NCT06138743

ARO-MMP7 is designed to reduce expression of matrix metalloproteinase 7 (MMP7) as a potential treatment for idiopathic Pulmonary Fibrosis (IPF). The Company is currently investigating ARO-MMP7 in a Phase 1/2a clinical trial.

- **Study Name: Study of ARO-MMP7 Inhalation Solution in Healthy Subjects and Patients With Idiopathic Pulmonary Fibrosis**
  A Phase 1/2a Study Evaluating the Effects of ARO-MMP7 Inhalation Solution in Healthy Subjects and Patients With Idiopathic Pulmonary Fibrosis

  ClinicalTrials.gov Identifier: NCT05537025

ARO-ATXN2 is designed to reduce the expression of the ATXN2 gene as a potential treatment for spinocerebellar ataxia 2 (SCA2). SCA2 is a progressive cerebellar ataxia with instability of stance, speech and swallow disorder, pain, spasticity, and ocular signs, caused by gain of function of mutant expanded polyQ ATXN2 protein. The Company is currently investigating ARO-ATXN2 in a Phase 1 clinical trial.

- **Study Name: Study of ARO-ATXN2 Injection in Adults With Spinocerebellar Ataxia Type 2**
  A Phase 1 Placebo-Controlled Dose Escalating Study to Evaluate the Safety, Tolerability,Pharmacokinetics, and Pharmacodynamics of ARO-ATXN2 in Adult Subjects With Spinocerebellar AtaxiaType 2

ClinicalTrials.gov Identifier: NCT06672445

ARO-HTT is designed to reduce the expression of the Huntingtin gene as a potential treatment for Huntington's disease.

ARO-ATXN1 is designed to reduce the expression of the ATXN1 gene as a potential treatment for spinocerebellar ataxia 1 (SCA1).

ARO-ATXN3 is designed to reduce the expression of the ATXN3 gene as a potential treatment for spinocerebellar ataxia 3 (SCA3).

Takeda Pharmaceuticals U.S.A., Inc.

Fazirsiran (formerly ARO-AAT) is a clinical-stage RNAi therapeutic candidate for the treatment of liver disease associated with alpha-1 antitrypsin deficiency. ARO-AAT is designed to knock down the Alpha-1 antitrypsin ("**AAT**") gene transcript and reduce the hepatic production of the mutant AAT protein.

- **Study Name: Study to Check the Safety of Fazirsiran and Learn if Fazirsiran Can Help People With Liver Disease and Scarring (Fibrosis) Due to an Abnormal Version of Alpha-1 Antitrypsin Protein**
  A Randomized, Double-blind, Placebo-Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency-Associated Liver Disease With METAVIR Stage F2 to F4 Fibrosis

  ClinicalTrials.gov Identifier: NCT05677971

- **Study Name: An Extension Study to Learn About the Long-Term Safety of Fazirsiran and if Fazirsiran Can Help People With Alpha-1 Antitrypsin Liver Disease**
  A Phase 3, Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of fazirsiran in Participants With Alpha-1 Antitrypsin Deficiency-Associated Liver Disease
  ClinicalTrials.gov Identifier: NCT05899673

- **Study Name: Study to Learn About the Safety of Fazirsiran and if it Can Help People With Alpha-1 Antitrypsin Liver Disease With Mild Liver Scarring (Fibrosis)**
  A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study to Evaluate the Safety and Efficacy of Fazirsiran in the Treatment of Alpha-1 Antitrypsin Deficiency-Associated Liver Disease With METAVIR Stage F1 Fibrosis

  ClinicalTrials.gov Identifier: NCT06165341

Amgen Inc.

Olpasiran (formerly AMG 890 and ARO-LPA) is designed to reduce production of apolipoprotein A, a key component of lipoprotein(a), which has been genetically linked with increased risk of cardiovascular diseases, independent of cholesterol and LDL levels.

- **Study Name: Olpasiran Trials of Cardiovascular Events and Lipoprotein(a) Reduction (OCEAN(a)) - Outcomes Trial**

A Double-blind, Randomized, Placebo-controlled, Multicenter Study Assessing the Impact of Olpasiran on Major Cardiovascular Events in Participants With Atherosclerotic Cardiovascular Disease and Elevated Lipoprotein(a)

ClinicalTrials.gov Identifier: NCT05581303

GlaxoSmithKline Intellectual Property (No. 3) Limited ("GSK")

GSK-4532990 (**formerly ARO-HSD**) is designed to reduce production of HSDPublished human genetic data indicate that a loss of function mutation in HSD17B13 provides strong protection against metabolic-dysfunction associated steatohepatitis (MASH) cirrhosis and alcoholic hepatitis and cirrhosis. GSK is conducting Phase 2b clinical trials in patients with MASH and alcohol-related liver disease (ALD).

Metabolic-Dysfunction Associated Steatohepatitis: MASH is liver inflammation and damage caused by a buildup of fat in the liver. This can cause scarring of the liver and in advanced cases can lead to cirrhosis. Alcochol-related liver disease (ALD) represents a spectrum of liver injury resulting from alcohol use, ranging from hepatic steatosis to more advances forms including alcoholic hepatitis (AH), alcohol-associated cirrhosis (AC), and acute AH presenting as acute-on-chronic liver failure.

- **Study Name: Phase 2b Study of GSK4532990 in Adults With MASH (HORIZON)**
  17 β-Hydroxysteroid Dehydrogenase Type 13 Minimization for the Treatment of MASH (HORIZON): A Double-Blind, Placebo-Controlled Phase 2b Study to Evaluate the Efficacy and Safety of GSK4532990 in Adults With Pre-Cirrhotic Metabolic-Dysfunction Associated Steatohepatitis

  ClinicalTrials.gov Identifier: NCT05583344

GSK5637608 (formerly JNJ-3989 and ARO-HBV) 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.

- **Study Name: A Study of Sequential Therapy With Daplusiran/Tomligisiran (DAP/TOM) Followed by Bepirovirsen in Participants Living With Chronic Hepatitis B (CHB) (B-UNITED)**
  A Phase 2b, Multi-centre, Randomized, Partially Placebo-controlled, Double-blind Study to Investigate the Safety and Efficacy of Sequential Therapy With Daplusiran/Tomligisiran Followed by Bepirovirsen in Participants With Chronic Hepatitis B Virus on Background Nucleos(t)Ide Analogue Therapy (B-United)

  ClinicalTrials.gov Identifier: NCT05583344

Financial Results

- ***Revenue*** — Generated revenue of $3.6 million, compared to revenues of $240.7 million in fiscal 2023 and $243.2 million in fiscal 2022;
- ***Net Loss attributable to Arrowhead Pharmaceuticals, Inc.*** — Recorded net loss of $599.5 million, compared to net losses of $205.3 million in fiscal 2023 and $176.1 million in fiscal 2022;
- ***Net Loss Per Share attributable to Arrowhead Pharmaceuticals, Inc.*** — Recorded net loss per share (diluted) of ($5.00), compared to net loss per share (diluted) of ($1.92) in fiscal 2023 and ($1.67) in fiscal 2022;
- ***Cash at end of fiscal 2024*** — Cash and investments of cash totaled $681.0 million at September 30, 2024; and
- ***Total Stockholder Return*** — Achieved a three-year total stockholder return ("**TSR**") at the 28th percentile of our peer group as measured in September 2024.

The comparisons in the above graph are based on historical data and are not intended to forecast the possible future performance of our common stock.

Executive Compensation Highlights

Say-on-Pay Vote and Ongoing Response to Stockholder Feedback

At our 2024 Annual Meeting of Stockholders, 94% of the stockholder votes cast on our non-binding, advisory proposal (the "**Say-on-Pay**" vote) on the executive compensation program were in favor of the program. Our Board of Directors was pleased with this result.

We value the opinions of our stockholders and will continue to consider the outcome of future Say-on-Pay votes, as well as feedback received throughout the year, when making compensation decisions for our executive officers. The Compensation Committee is committed to being responsive to stockholder feedback regarding our executive compensation program, policies, and practices, including concerns expressed through the Say-on-Pay vote.

Stockholder Engagement

During the summer and fall of 2023, our Corporate Secretary and Mr. Waddill, the Compensation Committee Chair, requested meetings with our top 10 stockholders to discuss our executive compensation program. On the basis of that feedback, and the stockholder vote during our 2024 Annual Meeting of Stockholders, we believe stockholders are pleased with our current compensation approach.

Aggressive Performance Fueled by Incentives

The Compensation Committee expects and has observed aggressive performance from the entire executive management team. Our philosophy has been to foster this expectation with reasonably aggressive incentive compensation. Based on our overall operating environment, feedback from our stockholders, and stockholder return results, the Compensation Committee took the following key actions and maintained key policies with respect to the compensation of all of our NEOs for fiscal 2024:

- ***Base Salary*** **—** Approved base salary increases for our current NEOs based on performance and market adjustments.

- ***Annual Incentive Compensation*** — Certified performance and Approved annual cash bonuses for our NEOs for fiscal 2024 in amounts of up to 140% of their target annual cash incentive compensation opportunities, including an annual cash bonus for our CEO in the amount of $1,152,000, equal to 120% of his target annual cash incentive compensation opportunity.
- ***Equity Compensation*** — The Compensation Committee granted our our CEO entirely performance-based restricted stock unit awards ("PRSUs") due to and granted our other NEOs long-term incentive compensation opportunities in the form of time-based RSU awards that may be settled for shares of our common stock with grant date values described below in the Compensation Tables section of this Proxy. The awards vest in four equal annual installments beginning in 2025.
- ***Clawback Policy*** — Maintained our clawback policy which allows Arrowhead to recover incentive compensation from our executive officers, on a non-fault basis, in the event a financial restatement is required to correct any accounting errors made by any such executive officer.
- ***Stock Ownership Guidelines*** — Maintained guidelines mandating ownership of Arrowhead stock in amounts equal to, for our CEO, six times annual base salary and, for our CFO, two times annual base salary.
- ***"Double Trigger" Feature for Acceleration of Equity Awards*** — Maintained the agreements for outstanding equity awards granted to our CEO pursuant to our 2013 and 2021 Incentive Plans to provide that, upon a change in control of Arrowhead, the vesting of such awards will accelerate only in the event of a subsequent involuntary termination of employment (i.e., on a "double-trigger" basis).

Pay-for-Performance Analysis

We believe our executive compensation program is reasonable, competitive, and appropriately balances the goals of attracting, motivating, rewarding, and retaining our executive officers with the objective of aligning their interests with those of our stockholders. To ensure this alignment and to motivate and reward individual initiative and effort, a significant portion of our executive officers' target total direct compensation opportunity is both performance-based and "at-risk."

We emphasize performance-based compensation that appropriately rewards our executive officers, including our NEOs, through two separate compensation elements:

- First, we provide the opportunity to participate in our annual incentive compensation plan which provides cash payments if executive officers produce short-term financial, operational, and strategic results that meet or exceed the objectives set forth each year in our annual operating plan.
- In addition, we grant equity awards as long-term incentive compensation. These require substantial performance and are themselves substantial awards, designed to drive our financial and operational performance and long-term growth. In the case of our CEO, these awards are heavily performance weighted, and in the case of our other executive officers, are either dependent on the future appreciation in value of our common stock or are subject to the risk of fluctuations in the value of our common stock and, therefore, are "at risk."

We believe that, ultimately, the creation of sustainable long-term stockholder value will depend on our ability to successfully bring to market the products we develop or our success in partnering with strategic collaborators to bring them to market. Consequently, the Compensation Committee strives to incent our executive officers to create that value through the discovery and development of a robust and attractive pipeline of drug candidates. To achieve that end, our executive compensation program is designed to provide incentives that facilitate these efforts. Particularly for our CEO, the Compensation Committee has awarded 100% of his long term incentive compensation for fiscal 2024 as performance-based equity awards designed to produce stockholder value. The Compensation Committee closely tracks the progress against these objectives and, in conjunction with the independent members of our Board, ensures the objectives are met using sound, ethical business practices before certifying performance achievement of the awards.

To ensure that we remain faithful to our compensation philosophy, the Compensation Committee regularly evaluates the relationship between the reported values of the equity awards granted to our executive officers, the amount of compensation realizable (and, ultimately, realized) from such awards in subsequent years, and our total stockholder return over this period.

Executive Compensation Policies and Practices

We endeavor to maintain sound governance standards consistent with our executive compensation policies and practices. The Compensation Committee evaluates our executive compensation program on a regular basis to ensure that it is consistent with our short-term and long-term goals given the dynamic nature of our business and the market in which we compete for executive talent. The following summarizes our executive compensation and related policies and practices:

WHAT WE DO	WHAT WE DON'T DO
✓ ***Maintain an Independent Compensation Committee.*** The Compensation Committee consists solely of independent directors.	✗ ***No Executive Retirement Plans.*** We do not offer pension arrangements or retirement plans or arrangements to our executive officers that are different from or in addition to those offered to our other employees.
✓ ***Retain an Independent Compensation Advisor.*** The Compensation Committee engaged its own compensation advisor to provide information and analysis with its fiscal 2024 compensation review, and other advice on executive compensation independent of management. This consultant performed no consulting or other services for us in fiscal 2024.	✗ ***No Perquisites.*** We do not provide perquisites or other personal benefits to our executive officers.
✓ ***Annual Executive Compensation Review.*** The Compensation Committee conducts an annual review and approval of our compensation strategy, including a review and determination of our compensation peer group and a review of our compensation-related risk profile to ensure that our compensation programs do not encourage excessive or inappropriate risk-taking.	✗ ***No Special Welfare or Health Benefits.*** Our executive officers participate in broad-based Company-sponsored health and welfare benefits programs generally on the same basis as our other full-time, salaried employees.
✓ ***Compensation At-Risk.*** Our executive compensation program is designed so that a significant portion of compensation is "at risk" based on our performance, as well as short-term cash and long-term equity incentives to align the interests of our executive officers and stockholders.	✗ ***No Post-Employment Tax Payment Reimbursement.*** We do not provide any tax reimbursement payments (including "gross-ups") on any severance or change-in-control payments or benefits.
✓ ***CEO Annual Incentive Compensation Cap.*** Our CEO's annual cash incentive compensation opportunity is capped at 150% of his base salary.	✗ ***No Hedging and Limit on Pledging of Our Equity Securities.*** We prohibit our employees, executive officers and the non-employee members of our Board from hedging our equity securities. Our board members and executive officers may pledge up to 75% of owned and vested shares with the approval of our Board.
✓ ***Stock Ownership Policy.*** We maintain a stock ownership policy that requires our CEO and CFO to maintain a minimum ownership level of our common stock.	✗ ***No Dividends or Dividend Equivalents Payable on Unvested Equity Awards.*** We do not pay dividends or dividend equivalents on unvested RSU awards or PRSU awards.
✓ ***Compensation Recovery ("Clawback") Policy.*** We maintain a clawback policy to allow Arrowhead to recover incentive compensation from our executive officers, on a non-fault basis, in the event a financial restatement is required to correct any accounting errors made by any such executive officer.	✗ ***No Stock Option Re-pricing.*** Our employee stock plan does not permit options to purchase shares of our common stock to be repriced to a lower exercise or strike price without the approval of our stockholders.
✓ ***Conduct an Annual Stockholder Advisory Vote on NEO Compensation.*** We conduct an annual stockholder advisory vote on the compensation of our NEOs.	
✓ ***Use a Pay-for-Performance Philosophy.*** The majority of our CEO's compensation is directly linked to achievement of milestones to the benefit of all stakeholders; we also structure target total direct compensation opportunities with a significant long-term equity component, thereby making a substantial portion of our CEO's and each additional executive officer's target total direct compensation dependent upon our stock price and/or total stockholder return.	
✓ ***"Double Trigger" Feature for Acceleration of CEO Equity Awards*** — The outstanding equity awards granted to our CEO pursuant to our 2013 Incentive Plan and 2021 Incentive Plan provide that, upon a change in control of the Company, the vesting of such awards will accelerate only in the event of a subsequent involuntary termination of employment (a "double-trigger" arrangement).	

Executive Compensation Philosophy

Our executive compensation philosophy reflects our two fundamental objectives:

- to attract, motivate and retain a highly skilled team of executives; and
- to align our executive officers' interests with those of our stockholders by rewarding short-term and long-term performance and aligning compensation to increases in stockholder value.

We believe that the compensation of our executive officers should be directly linked to the achievement of specific objectives that are expected to increase stockholder value. In furtherance of this goal, the Compensation Committee has established the following guidelines as a foundation for compensation decisions:

- provide a competitive total compensation package that enables us to attract, retain and motivate highly-qualified executives with the skills and experience required for the achievement of business goals;
- promote the achievement of key strategic and financial performance measures by linking short-term and long-term compensation to the achievement of measurable goals;
- reward significant achievements outside of pre-established goals;
- recognize that pharmaceutical research, development and commercialization require sustained and focused effort over many years, and involve a high degree of risk and therefore balance incentives for short-term and long-term compensation;
- employ external compensation expertise and market data from industry peers to help assure that our compensation policies and practices are consistent with industry practice and meet our goals for our compensation program;
- consider our cash resources and cost of capital to balance cash and equity compensation; and
- align our executives' incentives with the creation of stockholder value.

Executive Compensation Program Design

Our practice is to combine a mixture of compensation elements that balance achievement of our short-term goals with our longer-term performance. Currently, our executive compensation program consists of three principal elements:

- base salary;
- an annual cash incentive compensation opportunity; and
- long-term incentive compensation in the form of equity awards.

We believe that cash compensation in the form of base salary and an annual incentive compensation opportunity provides our executive officers with short-term rewards for success in operations, and that long-term incentive compensation in the form of RSU and PRSU awards that may be settled for shares of our common stock, and options to purchase shares of our common stock, align the objectives of our executive officers with those of our stockholders with respect to long-term performance and success.

The Compensation Committee takes into consideration, among other things, our financial and working capital condition when approving performance objectives and making compensation decisions for our executive officers. Since we seek to invest our cash prudently and do not have marketed products, overall target total direct compensation opportunities are weighted more heavily toward long-term incentive compensation in the form of equity awards. Thus, a significant portion of each executive officer's target total direct compensation opportunity is "at risk," and dependent on the increase in the value of our common stock. The Compensation Committee periodically reassesses the appropriate weighting of cash and equity compensation.

In the case of long-term incentive compensation, typically the Compensation Committee designs these awards to vest, or be earned, over a multi-year period, meaning that long-term value creation, contrasted with short-term gain, presents the best opportunity for our executive officers to benefit from their awards.

We do not maintain a specific policy on the percentage allocation between short-term and long-term incentive compensation elements.

Governance of Executive Compensation Program

Role of the Compensation Committee

The Compensation Committee discharges many of the responsibilities of our Board relating to the compensation of our executive officers, including our NEOs, and the non-employee members of our Board. The Compensation Committee has overall responsibility for overseeing our compensation and benefits philosophy and policies generally, overseeing and evaluating the compensation plans, policies and practices applicable to our CEO and our other executive officers, and ensuring that the target total direct compensation opportunities of our executive officers, including our NEOs, are consistent with our compensation philosophy, policies and objectives.

The members of the Compensation Committee are appointed by our Board, and each member is an independent director (as "independence" is currently defined in Rule 5605(a)(2) of Nasdaq listing standards). Currently, the members of the Compensation Committee are Michael Perry (Committee Chair), Hongbo Lu, and William Waddill .

The Compensation Committee reviews our executive compensation program annually on a calendar year basis, generally in December. The Compensation Committee draws on a number of resources to assist in the evaluation of the various elements of our executive compensation program including, but not limited to, feedback from our stockholders, input from our CEO, the advice of an external compensation consultant (as identified below) retained by the Compensation Committee, information provided in the public filings of industry peers and industry data compiled yearly by Radford in its Global Life Sciences Survey, which represents a nationally-based assessment of executive compensation widely used within the pharmaceutical and biotechnology industry sectors.

The Compensation Committee relies upon the judgment of its members in making compensation decisions. In addition, the Compensation Committee incorporates its members' judgment in the assessment process to respond to and adjust for the evolving business environment. The members of the Compensation Committee have extensive experience in executive management, as well as compensation practices and policies.

Compensation-Setting Process

The Compensation Committee develops recommendations for the target total direct compensation opportunities for our executive officers, including our NEOs. The Compensation Committee does not use a single method or measure in making its compensation decisions, nor does it ordinarily position compensation levels based upon a specific or target level relative to a compensation peer group or other companies. Nonetheless, the pay practices at other companies are an important factor that the Compensation Committee considers in assessing the reasonableness of compensation and ensuring that our compensation practices are competitive in the marketplace.

Generally, the Compensation Committee evaluates the compensation of our executive officers relative to the median of the competitive market. However, as discussed hereafter, various other factors are taken into consideration in determining our executive officers' compensation and the Compensation Committee does not target compensation at any specific level relative to the competitive market. When reviewing our current executive compensation arrangements and approving each compensation element and the target total direct compensation opportunity for our executive officers, the Compensation Committee considers the following factors:

- Our performance against the financial and operational objectives established by the Compensation Committee and our Board;
- Each individual executive officer's skills, experience and qualifications relative to other similarly-situated executives at the companies in our compensation peer group and in selected broad-based compensation surveys;
- The scope of each executive officer's role compared to other similarly-situated executives at the companies in our compensation peer group and in selected broad-based compensation surveys;
- The performance of each individual executive officer, based on a subjective assessment of his or her contributions to our overall performance, ability to lead his or her business unit or function and work as part of a team, all of which reflect our core values;
- The compensation practices of our compensation peer group and the companies in selected broad-based compensation surveys and the positioning of each executive officer's compensation in a ranking of peer company compensation levels; and

- The recommendations provided by our CEO with respect to the compensation of our other executive officers.

These factors provide the framework for compensation decision-making and final decisions regarding the compensation opportunity for each executive officer. No single factor is determinative in setting pay levels, nor was the impact of any factor on the determination of pay levels quantifiable.

Role of Chief Executive Officer

In discharging its responsibilities, the Compensation Committee works with members of our management, including our CEO. Our management assists the Compensation Committee by providing information on corporate and individual performance, market compensation data and management's perspective on compensation matters. The Compensation Committee solicits and reviews our CEO's recommendations with respect to the compensation levels for individual executive officers other than himself based on his performance evaluation of each executive officer.

The Compensation Committee reviews and discusses these recommendations and proposals with our CEO and considers them as one factor in determining the compensation for our executive officers, including our other NEOs. Our CEO recuses himself from all discussions and recommendations regarding his own compensation.

Role of Compensation Consultant

The Compensation Committee engages an external compensation consultant to assist it by providing information, analysis and other advice relating to our executive compensation program and the decisions resulting from its annual executive compensation review. The Compensation Committee has the final authority to engage and terminate the engagement of any compensation consultant that it retains.

Since October 2018, the Compensation Committee has engaged Compensia as its external compensation consultant. Compensia assisted the Compensation Committee in its review of executive officer and non-employee director compensation practices for fiscal 2024, including the competitiveness of compensation levels, executive compensation design, comparisons with our industry peers, and other technical considerations. Such assistance included:

- Reviewing and updating our compensation peer group;
- Reviewing and analyzing the compensation arrangements for our executive officers, including our NEOs;
- Reviewing and analyzing the compensation arrangements for the non-employee members of our Board;
- Reviewing and updating of the Compensation Discussion and Analysis section of our proxy statement for our 2025 Annual Meeting of Stockholders; and
- Supporting on other ad hoc matters.

The terms of Compensia's engagement include reporting directly to the Compensation Committee and to the Compensation Committee Chair.

In fiscal 2024, Compensia did not provide any services to us other than those described above. The Compensation Committee has evaluated Compensia's independence pursuant to the listing standards of Nasdaq and the relevant SEC rules and has determined that no conflict of interest has arisen as a result of the work performed by Compensia.

Competitive Positioning

For each of the past ten years, the Compensation Committee has directed its external compensation consultant to conduct a comparative study and report on compensation levels and practices relative to industry peers, including a competitive assessment of our executive compensation program as compared to the market data for base salaries, target total cash compensation, long-term incentive compensation and target total direct compensation. Typically, the findings of this study are presented to the Compensation Committee by the compensation consultant in conjunction with the Compensation Committee's annual review of our executive compensation program.

Because the biotechnology sector is dynamic, the comparator group used by the Compensation Committee to assess the competitive positioning of the compensation of our executive officers is updated annually to ensure that peer companies continue to meet the established criteria. For purposes of its review of our executive compensation

program in fiscal 2024, the Compensation Committee directed Compensia to update the compensation peer group reflecting the competitive market for executive talent based on the following criteria:

- Publicly-held, U.S. biotechnology companies;
- Companies with lead assets that are in mid to late clinical stage or early commercialization stage;
- Companies with market capitalizations between 0.25x to 4.0x our market capitalization at the time of the peer selection; and
- Companies with between 92 to 1,311 employees.

The compensation peer group was selected in such a manner that our market capitalization was very near the median for all peer companies. Consideration was also given to the frequency or infrequency with which a company was identified as a peer with other peer companies.

For fiscal 2024, the compensation peer group was generated in the first quarter of fiscal 2024 and consisted of the following companies:

ACADIA Pharmaceuticals, Inc.	Insmed
Amicus Therapeutics	Intellia Therapeutics
Apellis Pharmaceuticals	Ionis Pharmaceuticals
Arcus Biosciences	Ironwood Pharmaceuticals
BioCryst Pharmaceuticals	Mirati Therapeutcis
Blueprint Medicines	Madrigal Pharmaceuticals
BridgeBio Pharma	REGENXBIO
CRISPR Therapeutics AG	Sarepta Therapeutics
Deciphera Pharmaceuticals	Ultragenyx Pharmaceuticals
Denali Therapeutics	Vir Biotechnology
Halozyme Therapeutics	

BioCryst Pharmaceuticals, Deciphera Pharmaceuticals, Ironwood Pharmaceuticals, and Madrigal Pharmaceuticals were added to the compensation peer group and Chemo Centryx, FibroGen, Novavax, amd Reata Pharmaceuticals were removed from the compensation peer group due to changes in our business complexity, employee base and market capitalization, as well as mergers, changes to business complexity, employee base and market capitalization among our prior peer group.

The compensation study prepared by Compensia and presented in October 2023 provided an assessment of our compensation practices as compared to industry peers. Compensation levels for our executive officers, in the aggregate, were determined to be within the range of compensation provided to similarly placed executives and consistent with our compensation philosophy.

Individual Compensation Elements

In 2024, the principal elements of our executive compensation program were as follows:

- base salary;
- an annual cash incentive compensation opportunity;
- long-term incentive compensation in the form of equity awards;
- welfare and health benefits; and
- post-employment compensation arrangements.

Base Salary

Base salary represents the fixed portion of the compensation of our executive officers, including our NEOs, and is an important element of compensation intended to attract and retain highly-talented individuals.

The initial base salaries for our executive officers were negotiated on an individual basis at the time of hire. Thereafter, using the competitive market data provided by its external compensation consultant, the Compensation Committee reviews and determines adjustments to the base salaries for each of our executive officers, including our NEOs, as part of its annual executive compensation review. In addition, the base salaries of our executive officers may be adjusted by the Compensation Committee in the event of a promotion or significant change in responsibilities. Generally, the Compensation Committee sets base salaries with reference to the competitive range of the market median of our compensation peer group and applicable executive compensation survey data, as well as its assessment of the factors described in "Governance of Executive Compensation Program — Compensation-Setting Process" above.

The base salaries of our NEOs for fiscal 2024 and fiscal 2023 were as follows:

Named Executive Officer	Fiscal 2024 Base Salary	Fiscal 2023 Base Salary	Percentage Adjustment
Christopher Anzalone President & CEO	$960,000	$913,868	5%
Kenneth Myszkowski Chief Financial Officer	$582,400	$560,000	4%
Patrick O'Brien Chief Operating Officer and General Counsel	$600,000	$560,000	7%
James Hamilton Chief of Discovery and Translational Medicine	$582,400	$525,000	11%
Javier San Martin (1) Former Chief Medical Officer	$582,400	$560,000	4%
Tracie Oliver (2) Former Chief Commercial Officer	$488,880	$470,000	4%

(1) Dr. San Martin left the Company on February 1, 2024.
(2) Ms. Oliver served as the Company's Chief Commercial Officer until October 2024.

The actual base salaries paid to our NEOs in fiscal 2024 are set forth in the "Fiscal 2024 Summary Compensation Table" below.

Annual Cash Incentive Compensation

We provide our executive officers, including our NEOs, with the opportunity to earn performance-based annual incentive awards, payable in cash, which are designed to reward them for our overall corporate performance as well as their individual performance. Generally, our executive officers are evaluated each year for eligibility to receive an annual cash incentive compensation opportunity. Through a collaborative planning process involving our Board and management, corporate performance objectives are established at the beginning of each year and evaluated regularly by our Board for their continued relevance to our status.

Target Annual Cash Incentive Award Opportunities

For purposes of the fiscal 2024 performance-based incentive awards, each of our NEOs was assigned a target annual cash incentive award opportunity based upon a percentage of his or her base salary. The target annual cash incentive award opportunities for our executive officers, including our NEOs, were recommended by our CEO (except with respect to his own target annual cash incentive award opportunity) based on each executive officer's accountability, scope of responsibilities, and potential impact on our performance, and approved by the Compensation Committee. The determination of target annual cash incentive award opportunities was also based on the factors described in "Governance of Executive Compensation Program — Compensation-Setting Process" above. Our NEOs' target annual cash incentive award opportunities did not change from fiscal 2023.

The target cash annual incentive award opportunities for our NEOs were as follows:

Named Executive Officer	Fiscal 2024 Target Annual Incentive Award Opportunity (as a percentage of base salary)	Fiscal 2023 Target Annual Incentive Award Opportunity (as a percentage of base salary)
Dr. Anzalone (1)	100%	100%
Mr. Myszkowski	45%	45%
Mr. O'Brien	45%	45%
Dr. Hamilton	45%	45%
Dr. San Martin	45%	45%
Ms. Oliver	40%	40%

(1) Dr. Anzalone' annual cash incentive compensation opportunity is capped at 150% of his base salary.

Performance Objectives

In determining the amount of the annual cash incentive award for each of our executive officers, including each of our NEOs, the Compensation Committee evaluated the corporate performance objectives that had been established at the beginning of the calendar year (as set forth below) as well as other corporate and individual achievements and performance throughout the year. These performance objectives addressed milestones for our lead products, research and development milestones for our drug pipeline and business development objectives. In December 2024, the Compensation Committee determined our performance against our primary business objectives set for calendar 2024, as described below.

Goal	Achievement Highlights
Corporate/ Business Development - Weight: 40% *Meet certain goals related to business development, capitalization, long-term financial planning, preparation for commercialization, and utilization of recent capital improvements*	Met Substantial business development transaction leading to significant recapitalization. Manufacturing supply commitments, utilizing our Verona manufacturing facility, for commercial product. Fully deployed a medical affairs field force and other commercially oriented operations.
Clinical Development and Regulatory Affairs - Weight: 40% *Meet certain goals relating to Phase 3 studies in our clinical Cardiometabolic programs.*	Met Launched three Phase 3 studies for plozasiran. Established an Early Access Program for plozasiran in patients with FCS. Submitted a New Drug Application with the U.S. Food and Drug Administration
Discovery and Early Development - Weight: 20% *Meet certain goals with regard to progress on our pre-clinical and early clinical programs*	Met. Achieved clinical milestone timelines for seven Phase 1 clinical assets Filed three new clinical trial applications Nominated six new drug candidates

Annual Incentive Award Payments

The actual annual cash incentive award payments earned by our incumbent NEOs totaled 127% of the respective target award opportunities. Except for the annual incentive award for our CEO, these awards were recommended by our CEO and approved by the Compensation Committee based on the overall achievement of our goals, their contributions to the goals and the overall performance of each executive officer during the year. The following table sets forth the target annual cash incentive award opportunities, the target award expressed as a percentage of each

NEO's base salary and the actual award payment made in cash or cash equivalents to each of our NEOs based on their performance in fiscal 2024:

Named Executive Officer	Target Annual Incentive Award Opportunity (as a percentage of base salary)	Achievement target bonus	Actual Annual Incentive Award ($)
Dr. Anzalone (1)	100%	120%	$1,152,000
Mr. Myszkowski	45%	120%	$314,496
Mr. O'Brien	45%	140%	$378,000
Dr. Hamilton	45%	120%	$314,496
Dr. San Martin (2)	45%	—%	$—
Ms. Tracie Oliver (3)	40%	—%	$—

(1) Dr. Anzalone received an initial bonus of $960,000, which was paid in December 2024 and an additional bonus of $192,000 which will be paid upon receipt of Hart Scott Rodino clearance of the Sarepta transaction.
(2) Dr. San Martin left the Company on February 1, 2024 and did not receive an annual incentive award.
(3) Ms. Oliver served as the Company's Chief Commercial Officer until October 2024 and did not receive an annual incentive award.

The annual cash incentive award payments made to our NEOs for fiscal 2024 are set forth in the "Fiscal 2024 Summary Compensation Table" below.

Long-Term Incentive Compensation

We view long-term incentive compensation in the form of equity awards as a critical element of our executive compensation program. The realizable value of these equity awards over time bears a direct relationship to our stock price, and, therefore, these awards are an incentive for our executive officers, including our NEOs, to create value for our stockholders. Equity awards also help us retain qualified executive officers in a competitive market.

Long-term incentive compensation opportunities in the form of equity awards are granted to our executive officers by the Compensation Committee. The amount and forms of such equity awards are determined by the Compensation Committee after considering the factors described in "Governance of Executive Compensation Program — Compensation-Setting Process" above.

2024 Long-Term Incentive Awards

Performance-Based RSU Award for Chief Executive Officer

Annual equity awards granted to our executive officers are solely in the form of RSU awards that may be settled for shares of our common stock.

Our CEO's fiscal 2024 award was designed entirely as a performance-based award consisting of 340,000 PRSUs that will only vest upon the completion of a single performance trigger of a cash inflow to the Company of $1 billion by June 30, 2025. The CEO's fiscal 2024 award was also designed with the intention that the Compensation Committee would not certify performance prior to December 21, 2024 ,without good reasons, in accordance with the Company's 2021 Incentive Compensation Plan.

Results from PRSU Awards Previously Granted

In fiscal 2024, the Compensation Committee certified achievement of the performance milestones relating to the following PRSU awards:

Performance Goal	Achievement	No. of Shares Certified as Vested
Maintain clinical trials concurrently in four different tissue types (hepatic, pulmonary, and two others). *Issued 12/2022*	Certified in October 2023	46,805 shares pursuant to a PRSU award

RSU Awards for Other Named Executive Officers

The Compensation Committee approved the following aggregate RSU awards for our other NEOs for 2024:

Named Executive Officer	Restricted Stock Unit Awards (number of shares)	Restricted Stock Unit Awards ($)
Mr. Myszkowski	75,000	$2,589,750
Mr. O'Brien	85,000	$2,935,050
Dr. Hamilton	75,000	$2,589,750
Dr. San Martin	75,000	$2,589,750
Ms. Tracie Oliver	75,000	$2,589,750

RSUs granted to our NEOs in fiscal 2024 vest over four years in equal annual installments, subject to the NEO's continued employment on each applicable vesting date. Dr. San Martin and Ms. Oliver forfeited their fiscal 2024 equity awards upon their respective departures.

The equity awards granted to our NEOs in fiscal 2024 are set forth in the "Fiscal 2024 Summary Compensation Table" and the "Fiscal 2024 Grants of Plan-Based Awards Table" below.

Welfare and Health Benefits

Our executive officers, including our NEOs, are eligible to participate in all of our employee benefit plans, including medical, dental, vision, life and disability insurance, in each case on the same basis as our other employees, subject to applicable law. In addition, we provide an additional life insurance benefit to our CEO for the benefit of his heirs. We also provide vacation and other paid holidays to all our employees, including our executive officers, all of which we believe to be comparable to those provided the companies in our compensation peer group. These benefit programs are designed to enable us to attract and retain our workforce in a competitive marketplace. Our health, welfare and vacation benefits are designed to ensure that we have a productive and focused workforce through reliable and competitive health and other benefits.

Our retirement savings plan ("401(k) plan") is a tax-qualified retirement savings plan, pursuant to which qualified employees, including our NEOs, are able to contribute certain amounts of their annual compensation, subject to limits prescribed by the Internal Revenue Service. Historically, we have made matching contributions of 100% of the first 3% of base salary and of 50% of the next 2% of base salary contributed to the plan. The value of these benefits for each of our NEOs is reflected in the "All Other Compensation" column of the "Fiscal 2024 Summary Compensation Table" below.

Perquisites and Other Personal Benefits

Currently, we do not view perquisites or other personal benefits as a significant component of our executive compensation program. Accordingly, we do not provide significant perquisites or other personal benefits to our executive officers, including our NEOs, except as generally made available to our employees, or in situations where we believe it is appropriate to assist an individual in the performance of his or her duties, to make our executive officers more efficient and effective and for recruitment and retention purposes.

In the future, we may provide perquisites or other personal benefits in limited circumstances, such as those described in the preceding paragraph. All future practices with respect to perquisites or other personal benefits will be approved and subject to periodic review by the Compensation Committee.

Employment Arrangements

We have entered into a written employment agreement with our CEO and have written employment offer letters with our other executive officers. In filling each of our executive positions, we recognized the need to develop competitive compensation packages to attract qualified candidates in a dynamic labor market. At the same time, in formulating these compensation packages, we were sensitive to the need to integrate new executive officers into the executive compensation structure that we were seeking to develop, balancing both competitive and internal equity considerations. Each of these arrangements provides for "at will" employment.

For detailed descriptions of the employment arrangements we maintained with our NEOs during fiscal 2024, see "Termination Benefits — Potential Payments Upon Termination or Change in Control" below.

Post-Employment Compensation Arrangements

We have entered into a written employment agreement with our CEO, and we also have agreements with our CFO and Chief Operating Officer & General Counsel that provide for certain payments and benefits in the event of certain involuntary terminations of employment. We believe that having in place reasonable and competitive post-employment compensation arrangements are essential to attracting and retaining highly-qualified executive officers. These agreements are designed to provide reasonable compensation these to executive officers if they were to leave our employ under certain circumstances to facilitate their transition to new employment. Further, in some instances we seek to mitigate any potential employer liability and avoid future disputes or litigation by requiring a departing executive officer to sign a separation and release agreement acceptable to us as a condition to receiving post-employment compensation payments or benefits.

The Compensation Committee does not consider the specific amounts payable under these agreements when establishing annual compensation. We do believe, however, that these arrangements are necessary to offer compensation packages that are competitive.

In addition, our 2013 Incentive Plan and our 2021 Incentive Plan each provides for the acceleration of vesting of outstanding and unvested equity awards in the event of a change in control of the Company, as defined in the plans, except as otherwise determined by our Board. However, the agreements for equity awards granted to our CEO pursuant to our 2013 Incentive Plan and our 2021 Incentive Plan provide that, upon a change in control of the Company, the vesting of such awards will accelerate only in the event of a subsequent involuntary termination of employment (a "double-trigger" arrangement).

For detailed descriptions of the post-employment compensation arrangements we maintained with our NEOs during fiscal 2024, as well as an estimate of the potential payments and benefits payable under these arrangements, see "Termination Benefits — Potential Payments Upon Termination or Change in Control" below.

Other Compensation Policies and Practices

Equity Awards Grant Policy

We do not have any program, plan, or obligation that requires us to grant equity awards on specified dates, although historically we have granted such awards to our existing executive officers and employees at least annually and to newly-hired employees upon the commencement of their employment. We do not have any program, plan or practice to grant equity awards of our common stock to our executive officers in coordination with the release of material nonpublic information. Equity awards may occasionally be granted following a significant change in job responsibilities or to meet other special retention or performance objectives.

Authority to grant equity awards to our employees rests with the Compensation Committee, although the Compensation Committee has delegated authority to our CEO to grant equity awards to non-executive employees within prescribed limits set by the Compensation Committee. With respect to our executive officers, except for our CEO, recommendations for equity awards are made by our CEO and reviewed and approved by the Compensation Committee.

Under the terms of our 2021 Incentive Plan, pursuant to which new equity awards are granted, the exercise price of any option to purchase shares of our common stock awarded under the plan must be equal to at least 100% of the

fair market value of our common stock (which is determined based on the closing sales price of our common stock on the Nasdaq Global Market) on the date of grant.

Stock Ownership Policy

We maintain a stock ownership policy for our CEO and CFO to further align their respective interests with the interests of our stockholders, and to further promote our commitment to sound corporate governance. This policy requires our CEO to own a minimum number of shares of our common stock equal to a value of six times his annualized base salary and our CFO to own a minimum number of shares of our common stock equal to a value of twice his annualized base salary. Our CEO and CFO have each achieved the respective required ownership level.

Compensation Recovery ("Clawback") Policy

In November 2023, we updated our compensation recovery ("Clawback") policy, in accordance with new Nasdaq listing rules. The updated policy allows for the Company to recover incentive compensation from our executive officers, on a non-fault basis, in the event a financial restatement is required to correct any accounting errors made by any such executive officer.

Additionally, our 2013 Incentive Plan and our 2021 Incentive Plan each provides for the recovery of awards made under the plan in accordance with any applicable compensation recovery or recoupment policy, including as required by law, regulation or national securities exchange rule.

Insider Trading Policy

Our insider trading policy governs the purchase, sale and other transactions in our securities by our directors, officers and employees, and other covered persons, as well as the Company itself, and is designed to promote compliance with insider trading laws, rules and regulations, and Nasdaq listing rules, as applicable. As part of this policy, we prohibit our directors, officers, and employees from engaging in (a) short-term trading; (b) short sales; (c) options trading; (d) trading on margin; (e) pledging our common stock as collateral (except as noted below); and (f) all hedging transactions with respect to our securities. Subject to approval of our Board, directors and executive officers may pledge up to 75% owned and vested stock as collateral for a loan.

Tax and Accounting Considerations

Deductibility of Executive Compensation

Section 162(m) of the Internal Revenue Code limits the federal income tax deductibility of certain compensation amounts in excess of $1 million paid to certain executive officers. While the Compensation Committee generally seeks to pay compensation that is tax-deductible, it reserves the right to pay non-deductible compensation to the extent it deems appropriate.

Accounting for Stock-Based Compensation

We follow the Financial Accounting Standard Board's Accounting Standards Codification Topic 718 ("FASB ASC Topic 718") for our stock-based compensation awards. FASB ASC Topic 718 requires us to measure the compensation expense for all share-based payment awards made to our employees and non-employee members of our Board, including options to purchase shares of our common stock and other stock awards, based on the grant date "fair value" of these awards. This calculation is performed for accounting purposes and reported in the executive compensation tables required by the federal securities laws, even though the recipient of the awards may never realize any value from their awards.

Compensation Risk Assessment

In reviewing our various compensation programs, the Compensation Committee considers how our compensation policies and practices may affect our risk profile and whether such policies and practices may encourage undue risk-taking by our employees. More specifically, the Compensation Committee considers the general design philosophy of our policies and practices for our employees whose conduct would be most affected by incentives established pursuant to these compensation policies. In considering these issues, the Compensation Committee concluded that the use of a performance-based annual incentive compensation plan and long-term incentive compensation opportunities in the form of equity awards did not appear to create undue risks for us or encourage excessive risk-taking behavior on the part of our NEOs.

With respect to the annual incentive awards for our executive officers, the amount of an individual's award depends principally on overall Company performance, as determined by the Compensation Committee, which reduces the ability and incentive for an individual to take undue risks at the expense of our performance in an effort to increase the amount of his or her annual incentive award. Our performance objectives are reviewed regularly by the Compensation Committee and our Board and are considered to be generally of the nature that promote the steady progression of our development programs and would not encourage or reward excessive risk-taking. In addition, our Board has the ability to intervene in instances where actions by our executive officers vis-à-vis Company performance objective attainment would be considered unduly risky to prevent or penalize such actions.

Compensation Committee Report

The Compensation Committee of the Company has reviewed and discussed with management the Compensation Discussion and Analysis required by Item 402(b) of Regulation S-K. Based on this review and discussion, the Compensation Committee recommended to our Board that the foregoing Compensation Discussion and Analysis be included in this proxy statement.

Submitted by the Compensation
Committee of the Board of Directors

Michael Perry, Committee Chair
Hongbo Lu
William Waddill

Compensation Committee Interlocks and Insider Participation

During fiscal year 2024, Mr. Waddill, Dr. Ferrari, and Dr. Perry, served on the Compensation Committee. During fiscal year 2024 and through December 2024, there were no compensation committee interlocks between the Company and other entities involving the Company's executive officers and directors. For information regarding a transaction involving the brother of Dr. Douglass Given, the Company's former Director and Chairman of the Board,which is required to be disclosed under Item 404 of Regulation S-K, see "Certain Relationships and Related Transactions, and Director Independence" below.

Fiscal 2024 Summary Compensation Table

The following table summarizes compensation earned for services rendered during fiscal 2024, 2023, and 2022 by our Chief Executive Officer, our Chief Financial Officer, our Chief Operating Officer and General Counsel, our Chief of Discovery and Translational Medicine, and our former Chief Medical Officer and former Chief Commercial Officer, collectively our "Named Executive Officers":

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards (1) ($)	Non-Equity Incentive Plan Compensation (2) ($)	All Other Compensation (3) ($)	Total ($)
Christopher Anzalone	2024	951,012	—	10,319,000 (4)	1,152,000	1,461	12,423,473
President and Chief Executive Officer	2023	902,522	—	8,314,056 (5)	700,000	1,515	9,918,093
	2022	863,417	—	10,382,549 (7)	783,315 (6)	2,688	12,031,969
Kenneth Myszkowski	2024	592,369	—	2,589,750	314,496	15,761	3,512,376
Chief Financial Officer	2023	568,128	—	2,284,800	252,000	14,215	3,119,143
	2022	509,648	—	3,978,000	238,106	13,798	4,739,552
Patrick O'Brien	2024	605,259	—	2,935,050	378,000	15,261	3,933,570
Chief Operating Officer and General Counsel	2023	568,422	—	2,475,200	252,000	14,715	3,310,337
	2022	500,466	—	3,978,000	235,599	13,798	4,727,863
James Hamilton	2024	567,937	—	2,589,750	314,496	15,261	3,487,444
Chief of Discovery and Translational Medicine	2023	511,178	—	2,284,800	236,250	14,715	3,046,943
	2022	450,436	—	3,646,500	212,580	13,798	4,323,314
Javier San Martin (8)	2024	260,529	—	2,589,750	—	606,285	3,456,564
Former Chief Medical Officer	2023	544,467	—	2,284,800	252,000	14,715	3,095,982
	2022	479,170	—	—	225,574	—	704,744
Tracie Oliver (8)	2024	484,065	—	2,589,750	—	2,965	3,076,780
Former Chief Commercial Officer	2023	647,261	—	19,040	188,000	19,521	873,822
	2022	111,154	16,344	2,517,200	94,874	4,899	2,744,471

(1) This column represents the total grant date fair value, computed in accordance with ASC 718, of RSUs granted during fiscal years 2024, 2023 and 2022. The assumptions used to calculate the value of the stock underlying the RSU awards are set forth in Note 9 of the Notes to the Consolidated Financial Statements included with the Company's Annual Report on Form 10-K.

(2) These bonus amounts represent the amounts earned for performance under the Company's Annual Bonus Incentive Plan during calendar years 2024, 2023 and 2022 and paid in fiscal years 2025, 2024 and 2023, respectively. The Annual Bonuses are described in more detail in the "Bonus Incentive" section.

(3) Amounts consist of 401(k) matching contribution, as well as life insurance premiums for the benefit of each executive officer.

(4) The amount reported for Christopher Anzalone in the Stock Awards column includes the grant date fair value of a fiscal 2024 RSU award that is subject to vesting upon the achievement of a specific performance condition. We determined the performance condition was 100% probable of being achieved as of the grant date, as defined under applicable accounting guidance, and assigned a grant date fair value of $10,319,000 based on this evaluation. The amount reported in the Summary Compensation Table for this award may not represent the amount that Christopher Anzalone will realize from the award. Whether, and to what extent, an NEO realizes the value will depend on our actual operating performance, stock price fluctuations and the NEO's continued employment.

(5) The amount reported for Christopher Anzalone in the Stock Awards column includes the grant date fair value of a fiscal 2023 RSU award that is subject to vesting upon the achievement of specific performance conditions. We determined the performance conditions that were probable and not probable of being achieved as of the grant date, as defined under applicable accounting guidance, and assigned a grant date fair value of $4,625,270 based on this evaluation. If we had determined that as of the date of the grant it was probable that 100% of the performance conditions would be achieved, we would have assigned a grant date fair value of $8,314,056 for the performance-based RSUs. The amount reported in the Summary Compensation Table for this award may not represent the amount that Christopher Anzalone will realize from the award. Whether, and to what extent, an NEO realizes the value will depend on our actual operating performance, stock price fluctuations and the NEO's continued employment.

(6) Dr. Anzalone's Fiscal Year 2022 bonus, totaling $783,315, was paid as $200,000 cash and the remaining balance as immediately vested Arrowhead stock.

(7) In July of 2022, our CEO's fiscal 2022 compensation was revised by reducing his equity award and re-formulating the equity award to consist 60% of performance-based RSUs and 40% of time-based RSUs. The CEO's Stock Awards are described in more detail in the "Our CEO's Fiscal 2022 Equity Award" section in our 2023 proxy statement. The amounts reported for Christopher Anzalone in the Stock Awards column reflect the grant date fair value of a July 2022 RSU award that is subject to vesting upon the achievement of specific performance conditions, as described in the Compensation Discussion and Analysis section in our 2023 proxy statement. We determined the performance conditions that were probable and not probable of being achieved as of the grant date, as defined under applicable accounting guidance, and assigned a grant date fair value of $6,229,538 based on this evaluation. The amounts reported in the Summary Compensation Table for these awards may not represent the amounts that Christopher Anzalone will realize from the awards. Whether, and to what extent, an NEO realizes value will depend on our actual operating performance, stock price fluctuations and the NEO's continued employment.

(8) Dr. San Martin left the Company on February 1, 2024 and Ms. Oliver served as the Company's Chief Commercial Officer until October 2024.

Fiscal 2024 Grants of Plan Based Awards Table

The following table sets forth cash bonus and equity grants made to the NEOs in fiscal 2024:

Name	Grant Date	Estimated Future Payouts Under Non-Equity Incentive Plan Awards (1)		Estimated Future Payouts Under Equity Incentive Plan Awards (2)	All Other Stock Awards: Number of Shares of Stock or Units (#) (3)	Grant Date Fair Value
		Target ($)	Maximum ($)	Target (#)		
Christopher Anzalone						
Cash Bonus		$960,000	$1,440,000	—	—	—
PRSUs	12/22/2023	—		340,000	—	$10,319,000
Kenneth Myszkowski						
Cash Bonus		$262,080		—	—	—
RSUs	01/04/2024	—		—	75,000	$2,589,750
Patrick O'Brien						
Cash Bonus		$270,000		—	—	—
RSUs	01/04/2024	—		—	85,000	$2,935,050
James Hamilton						
Cash Bonus		$262,080		—	—	—
RSUs	01/04/2024	—		—	75,000	$2,589,750
Javier San Martin (4)						
Cash Bonus		$262,080		—	—	—
RSUs	01/04/2024	—		—	75,000	2,589,750
Tracie Oliver (4)						
Cash Bonus		$195,552		—	—	—
RSUs	01/04/2024	—		—	75,000	$2,589,750

(1) Amounts listed represent cash award targets for our NEOs in fiscal 2024. Actual payments were made in fiscal 2025 and the amounts are reported in the Summary Compensation Table above. There are no thresholds or maximum levels applicable under our annual cash incentive awards except with respect to Dr. Anzalone, whose target opportunity is capped at 150%.

(2) These PRSUs are described above in the "Compensation Discussion and Analysis" under the heading "Equity Compensation".

(3) RSUs granted in fiscal 2024 vest in four equal annual installments beginning 1 year from the grant date.

(4) Dr. San Martin and Ms. Oliver forfeited their fiscal 2024 equity awards upon their respective departures.

Fiscal 2024 Outstanding Equity Awards at Fiscal Year End Table

The following table provides information, with respect to the NEOs, concerning the outstanding equity awards covering shares of the Company's common stock as of September 30, 2024.

		Stock Awards			
Name	Grant Date	Number of Shares or Units of Stock That Have Not Vested (#) (1)	Market Value of Shares or Units of Stock That Have Not Vested ($) (2)	Equity Incentive Plan Awards: Number of Unearned Shares or Units of Stock That Have Not Vested (#) (3)	Equity Incentive Plan Awards: Market Value of Unearned Shares or Units of Stock That Have Not Vested ($) (2)
Christopher Anzalone	01/01/2020	—	—	700,000	13,559,000
	01/01/2021	—	—	800,000	15,496,000
	07/08/2022	49,761	963,871	149,282	2,891,592
	12/20/2022	70,208	1,359,929	93,610	1,813,226
	12/22/2023	—	—	340,000	6,585,800
Kenneth Myszkowski	01/01/2021	15,000	290,550	—	—
	01/01/2022	30,000	581,100	—	—
	01/04/2023	45,000	871,650	—	—
	01/04/2024	75,000	1,452,750	—	—
Patrick O'Brien	01/01/2021	15,000	290,550	—	—
	01/01/2022	30,000	581,100	—	—
	01/04/2023	48,750	944,288	—	—
	01/04/2024	85,000	1,646,450	—	—
James Hamilton	01/01/2021	12,500	242,125	—	—
	01/01/2022	27,500	532,675	—	—
	01/04/2023	45,000	871,650	—	—
	01/04/2024	75,000	1,452,750	—	—
Javier San Martin	01/04/2024	—	—	—	—
Tracie Oliver	07/01/2022	35,000	677,950	—	—
	01/04/2023	375	7,264	—	—
	01/04/2024	75,000	1,452,750	—	—

(1) RSUs have various vesting parameters but generally vest in four equal annual installments beginning one year from the grant date.
(2) Value is based on our Company's Common Stock closing price of $19.37 on September 30, 2024.
(3) The amounts reported for Christopher Anzalone in this column reflect the January 2020, January 2021, July 2022, December 2022, and December 2023 awards that contain performance-based vesting conditions. These awards and their vesting conditions are described above in the "Compensation Discussion and Analysis" under the heading "Equity Compensation" in this year's proxy statement and in prior proxy statements, as applicable.

Fiscal 2024 Options Exercises and Stock Vested Table

The following table provides information, with respect to the NEOs, concerning options exercised or RSUs or PRSUs vested during fiscal 2024.

	Option Awards		Stock Awards	
Name	Number of Shares Acquired on Exercise	Value Realized on Exercise (1)	Number of Shares Acquired on Vesting	Value Realized on Vesting (2)
Christopher Anzalone	57,499	$ 1,024,000	95,087	$ 2,603,325
Kenneth Myszkowski	—	—	66,250	$ 2,212,813
Patrick O'Brien	—	—	63,750	$ 2,139,688
James Hamilton	—	—	52,500	$ 1,773,225
Javier San Martin	—	—	52,500	1,570,200
Tracie Oliver	—	—	17,625	$ 460,191

(1) Value is calculated as the price of our Common Stock upon exercise, less the exercise price, multiplied by the number of shares exercised.

(2) Value is calculated as the price of our Common Stock upon vesting, multiplied by the number of shares vested.

Termination Benefits — Potential Payments Upon Termination or Change in Control

The Company has the following severance or change of control arrangements with its NEOs:

Dr. Anzalone's employment agreement with the Company provides that, if the Company terminates Dr. Anzalone's employment without Cause or if Dr. Anzalone terminates his employment for Good Reason, on his date of termination, Dr. Anzalone will receive a one-time lump sum payment equal to the sum of: (i) one month of base salary and (ii) premiums for thirty (30) days of medical and dental benefits. To receive such payments Dr. Anzalone is required to execute a general release in favor of the Company.

For purposes of Dr. Anzalone's employment agreement:

"**Cause**" means (i) the conviction (by trial or upon a plea of nolo contendere) of a felony or other crime involving moral turpitude or the commission of any other material act or omission involving dishonesty, disloyalty or fraud with respect to the Company or any of its subsidiaries or any of their customers or suppliers, (ii) reporting to work under the influence of alcohol or illegal drugs, the use of illegal drugs (whether or not at the workplace) or other repeated conduct causing the Company or any of its subsidiaries substantial public disgrace or disrepute or economic harm, (iii) the engaging of gross misconduct and the failure to cease such conduct and rectify any harm to the Company resulting therefrom within 30 days after written demand therefor by the Company identifying with reasonable particularity such conduct and harm, or (iv) any other material breach by Dr. Anzalone of his employment agreement and the failure to cease such breach and rectify any harm to the Company within 30 days after written demand by the Company identifying with reasonable particularity such breach and harm; and

"**Good Reason**" means (i) Dr. Anzalone's duties, responsibilities, titles or offices are diminished as compared to those described in his employment agreement without his written consent, and the Company fails to reinstate such duties, responsibilities, titles or offices within 30 days after written demand by Dr. Anzalone

identifying with reasonable particularity the diminishment, (ii) the relocation of Dr. Anzalone's base office to an office that is more than thirty (30) highway miles from Pasadena, CA, (iii) the failure of the Company to obtain a satisfactory agreement from any successor to assume and agree to perform the obligations under the employment agreement and (iv) any other material breach of Dr. Anzalone's employment agreement by the Company and the failure to cease such breach and rectify any harm to Dr. Anzalone resulting within 30 days after written demand by Dr. Anzalone identifying with reasonable particularity the breach and harm.

Pursuant to his offer of employment by the Company, Mr. Myszkowski is entitled to severance pay equal to three months' base salary plus an amount equal to the premiums on his medical and dental benefits for the same period upon termination of his employment without cause.

Pursuant to his offer of employment by the Company, Mr. O'Brien is entitled to severance pay equal to six months' base salary upon a qualifying termination of his employment without cause only upon change of control as defined in the Company's 2013 Incentive Plan.

The Company has not entered into a severance arrangement with Dr. San Martin or Dr. Hamilton or Ms. Oliver.

Additionally, pursuant to the 2004 Equity Incentive Plan, the 2013 Incentive Plan, and the 2021 Incentive Plan, any unvested awards held by plan participants, including the NEOs, become fully vested upon a change of control of the Company, except as otherwise determined by the Board and except with respect to the outstanding awards held by the CEO whose awards will only become fully vested if he experiences a qualifying termination of employment following a change of control.

The following tables set forth information regarding potential termination and change of control arrangements with our executive officers had their employment been terminated or a change in control of the Company taken place on September 30, 2024:

Termination Payments

Triggering Event	Salary ($)	Benefits ($)	Stock Awards (1)($)	Option Awards (1)($)	Total
Termination by Employer without Cause					
Christopher Anzalone (2)	80,000	2,307	—	—	82,307
Kenneth Myszkowski	140,000	8,848	—	—	148,848
Patrick O'Brien	—	—	—	—	—
James Hamilton	—	—	—	—	—
Change in Control					—
Christopher Anzalone (2)	—	—	—	—	—
Kenneth Myszkowski	140,000	8,848	3,196,050	—	3,344,898
Patrick O'Brien	—	—	3,462,388	—	3,462,388
James Hamilton	—	—	3,099,200	—	3,099,200
Involuntary Termination Following a Change in Control					—
Christopher Anzalone	80,000	2,307	42,669,418	—	42,751,725
Patrick O'Brien	280,000	—	—	—	280,000

(1) For stock awards the value is calculated as the number of unvested shares multiplied by the Company's closing stock price at September 30, 2024 of $19.37.

(2) Dr. Anzalone's employment contract also provides for payment of the values set forth above upon his resignation for "good reason" as defined in his employment agreement.

Dr. San Martin entered into a standard separation and release of claims agreement with the Company, under which he received a one-time payment of $603,200 in exchange for the release claims. Ms. Oliver did not receive any payments or benefits in connection with her departure from the Company.

CEO Pay Ratio

Pursuant to Item 402(u) of Regulation S-K, we are required to calculate and disclose the median of the annual total compensation of all of our employees (excluding our CEO, Dr. Anzalone), the annual total compensation of Dr. Anzalone, and the ratio of these two amounts.

Based on the fact that we had a significant number of new hires during fiscal 2024, we did not elect to use the same median employee as the prior year. Our median employee was identified using the entire population of our employees as of September 30, 2024 based on a consistently applied compensation measure, or CACM, that reasonably reflects the annual compensation of our employees. The CACM selected by us for our disclosure included annual base salary, the cash bonus amount for fiscal 2024, the grant-date fair value for stock-based awards (calculated in accordance with requirements for the Summary Compensation Table), and welfare and health benefits for fiscal 2024.

Based on the CACM methodology described above, we identified the median employee and calculated the fiscal 2024 compensation for this selected employee in the same manner we determine the annual total compensation of our NEOs for purposes of the Summary Compensation Table. The median of the annual total compensation of all our employees was $174,364.00. Dr. Anzalone's fiscal 2024 annual total compensation as disclosed in the Fiscal 2024 Summary Compensation Table was $ 12,423,473. As a result, our CEO to median employee pay ratio for fiscal 2024 is 70:1.

This pay ratio is a reasonable estimate calculated by a method consistent with the SEC requirements, described above, based on our payroll and employment records. As a result of a variety of factors, including employee populations, potential differences in the components used for the CACM, compensation philosophies and certain assumptions, pay ratios reported by other companies may not be comparable to our pay ratio. The pay ratio is not utilized by our management or our compensation committee for compensation-related decisions.

Pay Versus Performance

As required by Section 953(a) of the Dodd-Frank Wall Street Reform and Consumer Protection Act, and Item 402(v) of Regulation S-K, we are providing the following information about the relationship between executive "compensation actually paid" and certain financial performance of the Company. This information has been prepared in accordance with Item 402(v) and does not necessarily reflect the actual amount of compensation earned by or paid to our named executive officers ("NEOs") for the applicable year. Please refer to the Compensation Discussion and Analysis section of this proxy statement for a discussion of our executive compensation program objectives and the ways in which we align executive compensation with performance.

					Value of Initial Fixed $100 Investment Based On:		(in thousands)	
Year (a)	Summary Compensation Table Total for PEO (1)(b)	Compensation Actually Paid to PEO (2)(c)	Average Summary Compensation Table Total for Non-PEO NEOs (1)(d)	Average Compensation Actually Paid to Non-PEO NEOs (2) (e)	Total Shareholder Return (3)(f)	Peer Group Total Shareholder Return (4)(g)	Net Loss (5) (h)	Company Selected Measure (6)(i)
2024	$12,423,473	($5,232,848)	$3,493,347	$2,614,573	$31	$94	($599,493)	$ —
2023	$9,918,093	($2,160,939)	$3,143,102	$2,298,902	$62	$49	($205,275)	$ —
2022	$12,031,969	($40,073,641)	$4,133,800	($386,119)	$77	$67	($176,063)	$ —
2021	$24,703,855	$69,061,855	$3,324,746	$6,080,786	$145	$116	($140,848)	$ —

(1) The dollar amounts reported are the amounts reported for Christopher Anzalone (the Company's Chief Executive Officer) for each of the corresponding years in the "Total" column in our Summary Compensation Table. The dollar amounts reported in column (d) represent the average of the amounts reported for the Company's named executive officers (NEOs) as a group (excluding Christopher Anzalone) in the "Total" column of the Summary Compensation Table in each applicable year. The names of each of the NEOs included for these purposes in each applicable year are as follows: (i) for fiscal year 2024, Kenneth Myszkowski, Patrick O'Brien, James Hamilton, Javier San Martin and Tracie Oliver, (ii) for fiscal year 2023, Kenneth Myszkowski, Patrick O'Brien, James Hamilton, and Javier San Martin; (iii) for fiscal year 2022, Kenneth Myszkowski, Patrick O'Brien, James Hamilton, and Tracie Oliver; and (iv) for fiscal year 2021, Kenneth Myszkowski, Patrick O'Brien, James Hamilton, Javier San Martin, and James Hassard.

(2) The dollar amounts reported in column (c) represent the amount of "compensation actually paid" to Christopher Anzalone, and the dollar amounts reported in column (e) represent the average amount of "compensation actually paid" to our other NEOs as a group, each as computed in accordance with Item 402(v) of Regulation S-K and do not reflect the total compensation actually realized or received by Christopher Anzalone or the other NEOs on average, as applicable. In accordance with these rules, these amounts reflect "Total Compensation" as set forth in the Summary Compensation Table for each year, adjusted as shown below. Equity values are calculated in accordance with FASB ASC Topic 718, and the valuation assumptions used to calculate fair values did not materially differ from those disclosed at the time of grant.

Compensation Actually Paid	2024		2023		2022		2021	
	PEO	Other NEOs*	PEO	Other NEOs*	PEO	Other NEOs*	PEO	Other NEOs*
Summary Compensation Table Total	$ 12,423,473	$ 3,493,347	$ 9,918,093	$ 3,143,102	$ 12,031,969	$ 4,133,800	$ 24,703,855	$ 3,324,746
Less, value of "Stock Awards" and "Option Awards" reported in Summary Compensation Table	$ (10,319,000)	$ (2,658,810)	$ (8,314,056)	$ (2,332,400)	$ (10,382,549)	$ (3,529,925)	$ (23,019,000)	$ (2,608,820)
Plus, year-end fair value of outstanding and unvested equity awards granted in the year	$ 6,585,800	$ 1,501,175	$ 6,288,252	$ 1,645,788	$ 8,222,939	$ 1,578,138	$ 49,944,000	$ 3,537,700
Plus, fair value as of vesting date of equity awards granted and vested in the year	$ —	$ —	$ 595,920	$ —	$ —	$ —	$ —	$ —
Plus (less), year over year change in fair value of outstanding and unvested equity awards granted in prior years	$ (13,971,458)	$ (570,234)	$ (10,653,844)	$ (492,469)	$ (49,946,000)	$ (2,754,375)	$ 17,433,000	$ 2,015,691
Plus (less), change in fair value from last day of prior fiscal year to vesting date for equity awards granted in prior years that vested in the year	$ 48,337	$ 849,095	$ 4,696	$ 334,881	$ —	$ 186,244	$ —	$ (188,531)
Compensation Actually Paid	$ (5,232,848)	$ 2,614,573	$ (2,160,939)	$ 2,298,902	$ (40,073,641)	$ (386,118)	$ 69,061,855	$ 6,080,786

* Amounts presented are averages for the entire group of Other NEOs in each respective year.

(3) Total Shareholder Return (TSR) is calculated by dividing (a) the sum of (i) the cumulative amount of dividends for the measurement period, assuming dividend reinvestment, and (ii) the difference between the Company's share price at the end of each fiscal year shown and the beginning of the measurement period, and the beginning of the measurement period by (b) the Company's share price at the beginning of the measurement period. The beginning of the measurement period for each year in the table is September 30, 2020.

(4) The peer group used for this purpose is the Nasdaq Biotechnology Index.

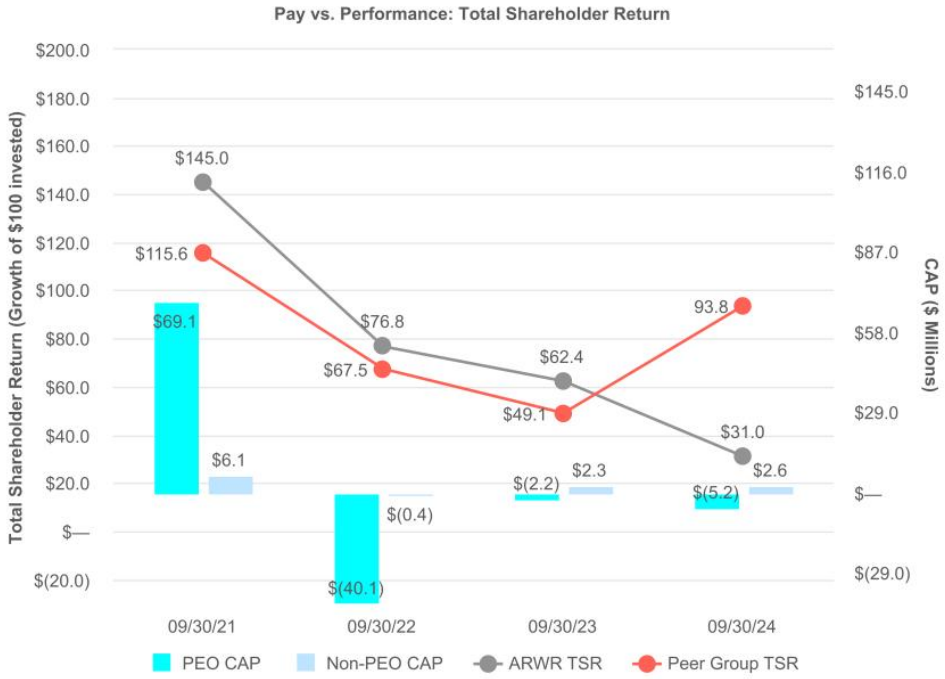
(5) The dollar amounts reported represent the amount of net income reflected in the Company's audited financial statements for the applicable year.

(6) The Company does not use any financial performance measures to link executive compensation actually paid to company performance. Consequently, no "Company Selected Measure" is included in the table above.

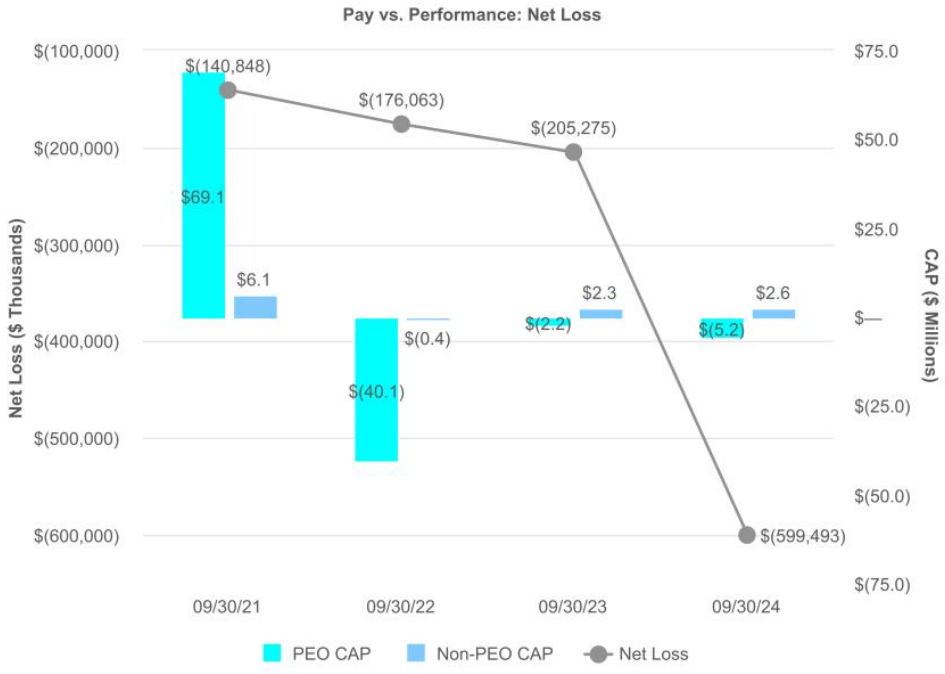
Analysis of Information Presented in the Pay versus Performance Table

As described in more detail in the Compensation Discussion and Analysis section, the Company's executive compensation program reflects a variable pay-for-performance philosophy. While the Company utilizes several performance measures to align executive compensation with Company performance, all of those Company measures are not presented in the Pay versus Performance table. Moreover, the Company generally seeks to incentivize long-term performance, and therefore does not specifically align the Company's performance measures with compensation that is actually paid (as computed in accordance with SEC rules) for a particular year. In accordance with SEC rules, the Company is providing the following descriptions of the relationships between information presented in the Pay versus Performance table.

Compensation Actually Paid, Cumulative TSR and Peer Group TSR



Compensation Actually Paid and Net Loss



Financial Performance Measures

As described in greater detail in the Compensation Discussion and Analysis section, the Company's executive compensation program reflects a variable pay-for-performance philosophy. The metrics that the Company uses for both our long-term and short-term incentive awards are selected based on an objective of incentivizing our NEOs to increase the value of our enterprise for our shareholders. The Company does not currently use any financial performance measures to link executive compensation actually paid to our performance. However, the most important performance measures used by the Company to link executive compensation actually paid to the Company's NEOs, for the most recently completed fiscal year, to the Company's performance are as follows:

- Corporate goals related to meeting certain objectives with respect to business development, market capitalization, preparation for commercialization, and and utilization of recent capital improvements;
- Discovery and early development goals related to meeting certain goals with regard to progress on our pre-clinical and early clinical programs; and
- Clinical development goals involving meeting certain goals relating to Phase 2 and 3 studies in our clinical programs;

All information provided above under the "Item 402(v) Pay Versus Performance" heading will not be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing, except to the extent the Company specifically incorporates such information by reference.

Proposal Four — Ratification of Appointment of Independent Auditors

Our Audit Committee, with the ratification of our Board, selected the accounting firm of KPMG LLP ("**KPMG**") as the Company's independent auditors for the fiscal year ending September 30, 2025, and that selection is now being submitted to the stockholders.

A representative of KPMG is expected to be available at the Annual Meeting to respond to appropriate stockholder questions or make any other statements such representative deems appropriate.

Stockholders are not required to ratify the appointment of KPMG as our independent auditor. However, we are submitting the appointment for ratification as a matter of good corporate practice. If stockholders fail to ratify the appointment, the Audit Committee will consider whether or not to retain KPMG. Even if the appointment is ratified, the Audit Committee may direct the appointment of a different independent auditor at any time during the year if it determines that such a change would be in the best interests of the Company and our stockholders.

The Company's former independent auditor for the fiscal year 2023 was Rose, Snyder & Jacobs, LLP ("RS&J"). As previously reported on the Company's Current Report on Form 8-K, filed on December 5, 2023, the Audit Committee approved the engagement of KPMG as the Company's independent registered public accounting firm for the fiscal year ending September 30, 2024. RS&J continued as the Company's independent registered public accounting firm for the interim period through December 1, 2023, at which time the Audit Committee approved the dismissal of RS&J as the Company's independent registered public accounting firm, effective immediately.

RS&J's audit report on the financial statements for the fiscal years ended September 30, 2023 and September 30, 2022 did not contain an adverse opinion or a disclaimer of opinion, and was not qualified or modified as to uncertainties, audit scope or accounting principles. In addition, during the two fiscal years ended September 30, 2023 and September 30, 2022, and the subsequent interim period through December 1, 2023, there were no: (1) "disagreements" (as defined by Item 304(a)(1)(iv) of Regulation S-K and related instructions) between the Company and RS&J on any matter of accounting principles or practices, financial statement disclosure or auditing scope and procedures, which if not resolved to the satisfaction of RS&J, would have caused RS&J to make reference in connection with their opinion to the subject matter of the disagreement, or (2) reportable events (as defined by Item 304(a)(1)(v) of Regulation S-K).

During the years ended September 30, 2023 and September 30, 2022, and the subsequent interim period through December 1, 2023, neither the Company, nor anyone on its behalf, consulted KPMG regarding either (i) the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on the financial statements of the Company, and neither a written report nor oral advice was provided to the Company that KPMG concluded was an important factor considered by the Company in reaching a decision as to any accounting, auditing or financial reporting issue; or (ii) any matter that was the subject of a "disagreement" (as defined in Item 304(a)(1)(iv) of Regulation S-K and the related instructions) or a "reportable event" (as described in Item 304(a)(1)(v) of Regulation S-K).

Vote Required; Recommendation of the Board

In order to be ratified, Proposal Four must be approved by the Required Vote, assuming a quorum is present. For this purpose, abstentions and broker non-votes, if any, will be counted as a vote "AGAINST" the proposal.

THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" PROPOSAL FOUR.

Audit Fees

The Audit Committee regularly reviews and determines whether specific projects or expenditures with our independent auditors may potentially affect their independence. The Audit Committee's policy is to pre-approve all audit and permissible non-audit services provided by our independent auditors. Pre-approval is generally provided by the Audit Committee for up to one year, detailed to the particular service or category of services to be rendered and is generally subject to a specific budget. The Audit Committee may also pre-approve additional services of specific engagements on a case-by-case basis. All engagements of our independent registered public accounting firm in 2024 and 2023 were pre-approved by the audit committee.

The following table sets forth the aggregate audit fees and other services provided during the indicated fiscal years. These include amounts billed and expected to be billed by our current independent auditors, KPMG, for fiscal year 2024, and by our former independent auditors, RS&J, for fiscal year 2023:

	Year Ended September 30,	
	2024	2023
Audit fees (1)	$860,000	$414,250
Audit-related fees (2)	150,000	226,100
Tax Fees	—	—
All other fees	—	—
Total	$1,010,000	$640,350

(1) Fees invoiced by KPMG and RS&J include year-end audit and periodic reviews of Forms 10-Q and 10-K.

(2) Fees invoiced by KPMG and RS&J related to Comfort Letters and Consents for financings and registration statements, and other agreed-upon procedures.

Report of the Audit Committee

The following is the report of the Audit Committee with respect to the Company's audited financial statements for fiscal 2024, which include the consolidated balance sheets of the Company as of September 30, 2024 and September 30, 2023, and the related consolidated statements of operations, stockholders' equity and cash flows for the fiscal years ended September 30, 2024, September 30, 2023 and September 30, 2022, and the notes thereto.

Composition. At September 30, 2024, the Audit Committee of the Board was comprised of three directors and operated under a written charter adopted by the Board. The members of the Audit Committee for fiscal 2024 were William Waddill, Victoria Vakiener, and Maura Ferrari. All members of the Audit Committee were "independent," as defined in Rule 10A-3 under the Exchange Act and Rule 5605(c) of the Nasdaq Marketplace Rules, and are financially literate.

Responsibilities. The responsibilities of the Audit Committee include engaging an accounting firm as the Company's independent registered public accounting firm. Management has primary responsibility for the Company's internal controls and financial reporting process. The independent registered public accounting firm is responsible for performing an independent audit of the Company's consolidated financial statements in accordance with generally accepted auditing standards and for issuing a report thereon. The Audit Committee's responsibility is to oversee these processes.

Review with Management and independent registered public accounting firm. The Audit Committee met separately to review the Company's consolidated audited financial statements and held discussions with management and KPMG. Management represented to the Audit Committee that the Company's consolidated financial statements were prepared in accordance with generally accepted accounting principles. The members of the Audit Committee discussed with KPMG matters required to be discussed under the applicable standards of the Public Company Accounting Oversight Board ("PCAOB") and the SEC. The Company's independent registered public accounting firm also provided to the Audit Committee the written disclosures and the letter required by the PCAOB regarding the independent registered public accounting firm's communications with the Audit Committee concerning independence and the Audit Committee discussed the firm's independence with KPMG.

Conclusion. Based upon the Audit Committee's review of the financial statements and discussions with management and KPMG, the Audit Committee's review of the representations of management and the report of KPMG to the Audit Committee, the Audit Committee recommended that the Board include the audited consolidated financial statements in the Company's Annual Report on Form 10-K for the fiscal year ended September 30, 2024, as filed with the SEC.

This report is submitted by the Audit Committee of the Board.

William Waddill, Committee Chair
Victoria Vakiener
Mauro Ferrari

Voting Securities of Principal Stockholders and Management

The following table sets forth the beneficial ownership of the Company's Common Stock as of January 17, 2025, by (i) each of the NEOs named in the table under "Executive Compensation and Related Information," (ii) each director and nominee, (iii) all current directors and executive officers as a group, and (iv) the holders of greater than 5% of our total shares outstanding known to us. Unless otherwise specified in the footnotes to the table below, the persons and entities named in the table have sole voting and investment power with respect to all shares beneficially owned, subject to community property laws, where applicable, and the address of each stockholder is c/o Arrowhead Pharmaceuticals, Inc., 177 E. Colorado Blvd, Suite 700, Pasadena, CA, 91105 unless otherwise indicated.

	Number and Percentage of Shares Beneficially Owned (1)	
	Shares	Percentage
5% Beneficial Owners		
BlackRock Inc (2) 55 East 52nd Street, New York, NY 10055	13,303,281	12.4%
The Vanguard Group (3) 100 Vanguard Blvd., Malvern, PA 19355	12,404,050	10.0%
Avoro Capital Advisors LLC (4) 110 Greene Street, Suite 800, New York, NY 10012	8,888,888	7.2%
State Street Corporation (5) One Congress Street, Suite 1, Boston MA 02114	6,354,331	5.1%
Named Executive Officers and Directors		
Christopher Anzalone (4)	3,764,252	3.0%
Patrick O'Brien	527,201	*
Kenneth Myszkowski	455,433	*
James Hamilton	272,122	*
Javier San Martin	198,497	*
Tracie Oliver	127,107	*
Michael S. Perry	131,490	*
Mauro Ferrari	77,514	*
William Waddill	57,111	*
Hongbo Lu	47,163	
Victoria Vakiener	37,944	*
Adeoye Olukotun	36,740	*
Douglas Ingram	0	*
All Executive Officers and Directors as a group (10 persons)	5,406,970	4.3%

* Less than 1%

(1) Based on 125,073,049 shares of Common Stock issued and outstanding as of January 17, 2024. Shares not outstanding but deemed beneficially owned by virtue of the right of a person to acquire them as of January 17, 2024, or within sixty days of such date are treated as outstanding only when determining the percentage owned by such individual and when determining the percentage owned by a group.

(2) Based on Amendment No. 2 to Schedule 13G/A filed January 23, 2024 by BlackRock Inc. According to Amendment No. 2, BlackRock Inc. has sole voting power and sole dispositive power over 13,160,327 shares and 13,303,281 shares, respectively,.

(3) Based on Amendment No. 7 to Schedule 13G/A filed April 10, 2024. According to Amendment No. 7, The Vanguard Group has sole dispositive power over 12,062,313 shares, respectively, and has shared voting power and shared dispositive power over 211,103 shares and 341,737 shares, respectively.

(4) Based on Schedule 13G filed November 14, 2024. According to Schedule 13G, Avoro Capital Advisors LLC and Behzad Aghazadeh, who serves as the portfolio manager and controlling person of Avoro Capital Advisors LLC, have sole voting power and sole dispositive power over 8,888,888 and 8,888,888 shares, respectively.

(5) Based on Schedule 13G/A filed October 16, 2024. According to Schedule 13G, State Street Corporation has shared voting power and shared dispositive power over 5,936,957 shares and 6,354,331 shares, respectively.

Equity Compensation Plan Information

The following table provides information as of September 30, 2024 with respect to shares of our Common Stock that may be issued under our equity compensation plans.

	Equity Compensation Plan Information		
	Number of shares to be issued upon exercise of outstanding options, warrants and rights	Weighted average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders (1)	6,600,427	$41.75	4,600,465
Equity compensation plans not approved by security holders (2)	291,401	$49.61	510,600
Total	6,891,828	$42.08	5,111,065

(1) Includes options outstanding representing 1,290,720 and 32,151 shares of Common Stock under the 2013 Incentive Plan and the 2021 Incentive Plan, respectively. Also includes 1,608,510 and 2,768,776 RSUs subject to the 2013 Incentive Plan and the 2021 Incentive Plan, respectively. There is no exercise price associated with a RSU award. Accordingly, these have been excluded from the column in the table reporting the weighted-average exercise price of outstanding awards.

(2) Includes 655,645 inducement option grants and 244,625 inducement RSU grants issued to newly hired employees granted outside of the Company's Inducement Plan and 0 inducement option grants and 291,401 inducement RSU grants issued to newly hired employees pursuant to the Company's Inducement Plan.

Material Features of the Inducement Plan and Stand-Alone Inducement Awards

The Company's Inducement Plan was established by the Board during fiscal year 2024 to advance the interests of the Company by providing for the grant of stock-based awards. The Company has also granted inducement awards outside of the inducement plan. In accordance with Nasdaq rules, this plan and the stand-alone awards are used to offer equity awards as material inducements for new employees to join the Company. Subject to adjustment for certain changes in our capitalization, the maximum aggregate number of shares that may be issued under the inducement plan is 832,950. The equity awards granted as inducement awards both under and outside of the inducement plan are typically in the form of stock options with exercise prices equal to the fair market value of our common stock on the date of grant and/or restricted stock units. The inducement plan also provides for the granting of other types of equity awards, including stock appreciation rights and restricted stock awards.

Current Executive Officers of the Registrant

The names, ages, and positions of our current executive officers serving as of January 28, 2025 are provided below. Biographical information regarding these officers is set forth under the following table, except for Dr. Anzalone, whose biography is set forth above with our other directors. Each executive officer holds office until the first meeting of the Board of Directors after the annual meeting of stockholders next succeeding their election, and until his/her successor is elected and qualified or until his/her earlier resignation or removal.

Name	Age	Position with Arrowhead
Christopher Anzalone	55	Chief Executive Officer & President and Director
Kenneth A. Myszkowski	58	Chief Financial Officer
James Hamilton	47	Chief of Discovery and Translational Medicine
Patrick O'Brien	61	Chief Operating Officer and General Counsel

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

Patrick C. O'Brien, Chief Operating Officer and General Counsel, joined the Company in December 2014, where he has served as Chief Operating Officer since July 2022 and as General Counsel since 2014. Mr. O'Brien has practiced in the healthcare legal field for over 30 years. Before joining the Company, from 2012 to 2014, Mr. O'Brien was with Shire, a global pharmaceutical company, where he was Group Vice President, Law. Immediately prior to working with Shire he was a partner with the international law firm of Holland & Knight LLP in its Washington, DC office. In 2010, Mr. O'Brien co-founded the law firm O'Brien Gould PLLC which joined Holland & Knight in 2011. From 2009 to 2010, Mr. O'Brien was a partner in Burke O'Neil LLC. From 2001 to 2009, Mr. O'Brien served in several legal roles with Johnson & Johnson, including serving as Vice President of Law for J&J's Centocor Ortho-Biotech unit. Mr. O'Brien previously served as Regulatory Counsel with the United States Food & Drug Administration. Mr. O'Brien was awarded a BS in Pharmacy and a PharmD from the University of Arizona before completing a residency in Clinical Pharmacy with the University of Illinois at Chicago Hospital. He was also awarded his JD from the University of Arizona.

James Hamilton, Chief of Discovery & Translational Medicine, joined the Company in 2014. He is responsible for target discovery as well as non-clinical and early clinical development. Previously, Dr. Hamilton served as Vice President, Clinical Development, responsible for clinical strategy, clinical trial design and execution including early translational and mid-stage development of all Arrowhead programs. He is experienced in multiple disease areas including virology, hepatology, cardiovascular disease, rare disease and oncology. Dr. Hamilton led the clinical development of ARO-HBV (now JNJ-3989), which was licensed to Janssen Pharmaceuticals. In parallel, Dr. Hamilton served as Head of Corporate Development and led Arrowhead's in-licensing transaction of Novartis's RNAi assets, as well as the out-licensing of ARO-LPA (now AMG890) to Amgen and the ARO-AAT partnership with Takeda. Dr. Hamilton started his employment at Arrowhead as Medical Director and Head of Corporate development. He holds both MD and MBA degrees from The Ohio State University. He is a licensed physician and completed residency training with board certification in emergency medicine.

Review and Approval of Related-Party Transactions

Our Board has adopted written policies and procedures for the review and approval of related-party transactions and has delegated to the Audit Committee the authority to review and approve the material terms of any proposed related-party transactions. To the extent that a proposed related-party transaction may involve a non-employee director or nominee for election as a director and may be material to a consideration of that person's independence, the matter may also be considered by the other disinterested directors.

Pursuant to our Corporate Code of Conduct and our Nomination Committee Charter, each of our officers, directors and employees must disclose related-party transactions to our Board. In order to avoid conflicts of interest, our executive officers and directors may not acquire any ownership interest in any supplier, customer or competitor (other than nominal amounts of stock in publicly traded companies), enter into any consulting or employment relationship with any customer, supplier or competitor, or engage in any outside business activity that is competitive with any of our businesses, without first disclosing the proposed transaction. After the proposed transaction has been disclosed, a determination will be made by our Board or Audit Committee as to what course to follow, depending on the nature or extent of the conflict. Furthermore, our executive officers and directors may not serve on any board of directors of any customer, supplier or competitor unless such board service has been disclosed to us and approved by our Board.

In determining whether to approve or ratify a related-party transaction, the Board and/or Audit Committee may consider, among other factors it deems appropriate, the potential benefits to the Company, the impact on a director's or nominee's independence or an executive officer's relationship with or service to the Company, whether the related-party transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances, and the extent of the related party's interest in the transaction. In deciding to approve a transaction, the Board or Audit Committee may, in its sole discretion, impose such conditions as it deems appropriate on us or the related party in connection with its approval of any transaction. Any transactions involving the compensation of executive officers, however, are reviewed and approved by the Compensation Committee. If a related-party transaction will be ongoing, the Audit Committee may establish guidelines to be followed in our ongoing dealings with the related party. Thereafter, the Audit Committee reviews and assesses the ongoing relationship with each related party to see that it is in compliance with the Audit Committee's guidelines and that the related-party transaction remains appropriate.

Certain Relationships and Related Transactions, and Director Independence

As of September 30, 2024, a majority of the members of the Board are independent directors, as defined by the Nasdaq Marketplace Rules. The Board has determined that all of the Company's directors are independent, except Dr. Anzalone, the Company's Chief Executive Officer. Non-employee directors do not receive consulting, legal or other fees from the Company, other than Board compensation.

Dr. Bruce Given is the Company's Chief Medical Scientist and the brother of Dr. Douglass Given, the Company's former Director and Chairman of the Board, who stepped down effective as of December 31, 2024. Dr. Bruce Given earned base salary and bonus of $582.400 during fiscal year 2024. His current base salary is $605,696. In January 2025, Dr. Bruce Given was awarded 100,000 RSUs, and this award vests in four annual tranches from the grant date. The grant date fair value of this award is $1,979,000.

Vincent Anzalone is the Company's Vice President, Investor Relations and the brother of Christopher Anzalone, the Company's Chief Executive Officer. Vincent Anzalone earned base salary and bonus of $382,955 during fiscal year 2024. His current base salary is $340,240. In January 2025, Vincent Anzalone was awarded 25,000 RSUs, and this award vests in four annual tranches from the grant date. The grant date fair value of this award is $494,750.

Annual Report on Form 10-K

The Company will mail, without charge to any stockholder upon written request, a copy of the Company's Annual Report on Form 10-K for the year ended September 30, 2024 including the financial statements, schedules and a list of exhibits. Requests should be sent to Arrowhead Pharmaceuticals, Inc., 177 E. Colorado Blvd., Suite 700, Pasadena, CA 91105, Attn: Corporate Secretary, Phone (626) 304-3400.

Stockholders Sharing the Same Address

We may satisfy SEC rules regarding delivery of proxy statements including the proxy statement, annual report and Notice, by delivering a single Notice and, if applicable, a single set of proxy materials to an address shared by two or more of our stockholders. This delivery method can result in meaningful cost savings for us. To take advantage of this opportunity, we may deliver only one Notice, and if applicable, a single set of proxy materials to multiple stockholders who share an address, unless contrary instructions are received prior to the mailing date. Similarly, if you share an address with another stockholder and have received multiple copies of our Notice and/or other proxy materials, you may write or call us at the address and phone number below to request delivery of a single copy of these materials in the future. We undertake to deliver promptly upon written or oral request a separate copy of the Notice and/or other proxy materials to a stockholder at a shared address to which a single copy of these documents was delivered. If you hold stock as a record stockholder and prefer to receive separate copies of a Notice, and if applicable, other proxy materials either now or in the future, please contact us at the address provided below. If your stock is held through a brokerage firm or bank and you prefer to receive separate copies of a Notice and, if applicable, other proxy materials either now or in the future, please contact your brokerage firm or bank.

Arrowhead Pharmaceuticals, Inc.
177 E. Colorado Blvd., Suite 700
Pasadena CA 91105
Attn: Corporate Secretary
Phone (626) 304-3400

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, executive officers, and greater-than-10% stockholders to file forms with the SEC to report their ownership of Company shares and any changes in ownership. We have reviewed all forms filed electronically with the SEC. Based on that review and on written information given to us by our executive officers and directors, we believe that all of our directors and executive officers filed the required reports on a timely basis under Section 16(a) during fiscal 2024, except for the inadvertent late filing of one Form 5 reporting one transaction for Dr. Lu.

Other Matters

The Company knows of no other matters to be submitted at the Annual Meeting. If any other matters properly come before the meeting, it is the intention of the persons named in the proxy card to vote on such matters in accordance with their best judgment.

BY ORDER OF THE BOARD OF DIRECTORS

/s/ Patrick O'Brien
Patrick O'Brien,
Secretary

Pasadena, California
January 28, 2025

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ARROWHEAD PHARMACEUTICALS, INC.
177 EAST COLORADO BLVD, SUITE 700
PASADENA, CA 91105

SCAN TO VIEW MATERIALS & VOTE

VOTE BY INTERNET - www.proxyvote.com or scan the QR Barcode above
Use the Internet to transmit your voting instructions and for electronic delivery of information. Vote by 11:59 P.M. ET on March 11, 2025. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.
During the meeting - Go to **www.virtualshareholdermeeting.com/ARWR2025**
You may attend the meeting via the Internet and vote during the meeting. Have the information that is printed in the box marked by the arrow available and follow the instructions.
VOTE BY PHONE - 1-800-690-6903
Use any touch-tone telephone to transmit your voting instructions. Vote by 11:59 P.M. ET on March 11, 2025. Have your proxy card in hand when you call and then follow the instructions.
VOTE BY MAIL
Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

KEEP THIS PORTION FOR YOUR RECORDS
THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED. DETACH AND RETURN THIS PORTION ONLY

The Board of Directors recommends you vote FOR the following:

1. Election of Directors

Nominees	For	Against	Abstain
1a. Hongbo Lu	☐	☐	☐
1b. Michael S. Perry	☐	☐	☐
1c. Christopher Anzalone	☐	☐	☐
1d. Mauro Ferrari	☐	☐	☐
1e. Adeoye Olukotun	☐	☐	☐
1f. William Waddill	☐	☐	☐
1g. Victoria Vakiener	☐	☐	☐
1h. Douglas Ingram	☐	☐	☐

The Board of Directors recommends you vote FOR the following proposal:

	For	Against	Abstain
2. Advisory Vote to Approve Executive Compensation.	☐	☐	☐

The Board of Directors recommends you vote 1 YEAR on the following proposal:

	1 year	2 years	3 years	Abstain
3. Advisory Vote on Frequency of Executive Compensation Advisory Votes.	☐	☐	☐	☐

The Board of Directors recommends you vote FOR the following proposal:

	For	Against	Abstain
4. To ratify the selection of KPMG LLP as independent auditors of the Company for the fiscal year ending September 30, 2025.	☐	☐	☐

NOTE: Such other business as may properly come before the meeting or any adjournment thereof.

Please sign exactly as your name(s) appear(s) hereon. When signing as attorney, executor, administrator, or other fiduciary, please give full title as such. Joint owners should each sign personally. All holders must sign. If a corporation or partnership, please sign in full corporate or partnership name by authorized officer.

Signature [PLEASE SIGN WITHIN BOX] Date

Signature (Joint Owners) Date

C000256842_1 R1.0.0.2

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting:
The Notice and Proxy Statement and Form 10-K are available at www.proxyvote.com

ARROWHEAD PHARMACEUTICALS, INC.
Annual Meeting of Stockholders
March 12, 2025 10:00 AM PT
This proxy is solicited by the Board of Directors

The stockholder(s) hereby appoint(s) Christopher Anzalone and Patrick O'Brien or either of them, as proxies, each with the power to appoint his substitute, and hereby authorize(s) them to represent and to vote, as designated on the reverse side of this ballot, all of the shares of Common Stock of ARROWHEAD PHARMACEUTICALS, INC. that the stockholder(s) is/are entitled to vote at the Annual Meeting of Stockholders to be held at 10:00 AM, PT on March 12, 2025, online at www.virtualshareholdermeeting.com/ARWR2025, and any adjournment or postponement thereof.

This proxy, when properly executed, will be voted in the manner directed herein. If no such direction is made, this proxy will be voted in accordance with the Board of Directors' recommendations.

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Continued and to be signed on reverse side