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

| Title of each class             | Name of each exchange on which registered |
|---------------------------------|---|
| Common Stock, \$0.001 par value | The NASDAQ 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

|  |  |  |  |
|--|--|--|--|
| <input type="checkbox"/> Large accelerated filer | <input type="checkbox"/> Accelerated filer | <input type="checkbox"/> Non-accelerated filer | <input type="checkbox"/> Smaller Reporting Company |
| <input type="checkbox"/> Emerging growth company |  |  |  |

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

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

The aggregate market value of issuer's voting and non-voting outstanding Common Stock held by non-affiliates was approximately \$619 million based upon the closing stock price of issuer's Common Stock on March 31, 2018. 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 December 7, 2018, 92,224,665 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 2019 Annual Meeting of Stockholders are incorporated by reference into Part III hereof.

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## FORWARD-LOOKING STATEMENTS

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

The forward-looking statements included herein are based on current expectations of our management based on available information and involve a number of risks and uncertainties, all of which are difficult or impossible to predict accurately and many of which are beyond our control. As such, our actual results may differ significantly from those expressed in any forward-looking statements. Factors that may cause or contribute to such differences include, but are not limited to, those discussed in more detail in Item 1 (Business) and Item 1A (Risk Factors) of Part I and Item 7 (Management’s Discussion and Analysis of Financial Condition and Results of Operations) of Part II of this Annual Report on Form 10-K. Readers should carefully review these risks, as well as the additional risks described in other documents we file from time to time with the Securities and Exchange Commission. In light of the significant risks and uncertainties inherent in the forward-looking information included herein, the inclusion of such information should not be regarded as a representation by us or any other person that such results will be achieved, and readers are cautioned not to place undue reliance on such forward-looking information. Except as may be required by law, we disclaim any intent to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

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## 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 collectively to Arrowhead Madison Inc. (“Arrowhead Madison”), Arrowhead Australia Pty Ltd (“Arrowhead Australia”) and Ablaris Therapeutics, Inc. (“Ablaris”), (4) the term “Common Stock” refers to Arrowhead’s Common Stock, (5) the term “Preferred Stock” refers to Arrowhead’s Preferred Stock and (6) the term “Stockholder(s)” refers to the holders of Arrowhead Common Stock.

### ITEM 1. BUSINESS

#### Description of Business

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

#### Pipeline Overview

Arrowhead is focused on developing innovative drugs for diseases with a genetic basis, typically characterized by the overproduction of one or more proteins. 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.

#### ARO-AAT

ARO-AAT is an RNAi therapeutic candidate for the treatment of liver disease associated with alpha-1 antitrypsin deficiency. ARO-AAT is a second-generation subcutaneously administered compound designed to knock down the Alpha-1 antitrypsin (AAT) gene transcript and reduce the hepatic production of the mutant AAT protein. Arrowhead completed AROAAT1001, a Phase 1 randomized, double-blind, placebo controlled single-ascending dose (SAD) and multiple-ascending dose (MAD) study to evaluate the safety, tolerability, pharmacokinetics, and effect of subcutaneous doses of ARO-AAT on serum alpha-1 antitrypsin levels in healthy adult volunteers in 2018 and plans to initiate a Phase 2 study in 2019.

Initial results from AROAAT1001 were presented in November 2018 at The Liver Meeting®, the Annual Meeting of the American Association for the Study of Liver Disease (AASLD). In the AROAAT1001 study, 45 normal healthy volunteers (NHV)

received a single dose of ARO-AAT (n=16), three monthly doses of ARO-AAT (n=12), or placebo (n=17). Key data presented include the following:

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

#### Goal of ARO-AAT Treatment

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

#### Alpha-1 Antitrypsin Deficiency (AATD)

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

#### Current Treatments

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

#### The Alpha-1 Project

Arrowhead has an agreement with The Alpha-1 Project (TAP), the venture philanthropy subsidiary of the Alpha-1 Foundation. TAP's mission is to support organizations in pursuit of cures and therapies for lung and liver disease caused by AATD. Under the terms of the agreement, TAP has partially funded development of ARO-AAT. In addition to the funding, TAP will make its scientific advisors available to Arrowhead, assist with patient recruitment for clinical trials with its Alpha-1 Foundation Patient Research Registry, and engage in other collaborative efforts that support development of ARO-AAT.

#### ARO-APOC3

ARO-APOC3 is designed to reduce production of Apolipoprotein C-III (apoC-III), a component of triglyceride rich lipoproteins (TRLs) including VLDL and chylomicrons and a key regulator of triglyceride metabolism. 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. A CTA is planned for the fourth calendar quarter of 2018.

#### Hypertriglyceridemia

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



### ARO-ANG3

ARO-ANG3 is designed to reduce production of angiopoietin-like protein 3 (ANGPTL3), a liver synthesized inhibitor of lipoprotein lipase and endothelial lipase. ANGPTL3 inhibition has been shown to lower serum LDL, serum and liver triglyceride and has genetic validation as a novel target for cardiovascular disease. A CTA was filed in October 2018 and Arrowhead intends to begin a Phase 1 study in 2019.

### Dyslipidemia and Hypertriglyceridemia

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

### ARO-ENaC

ARO-ENaC is designed to reduce production of the epithelial sodium channel alpha subunit ( ENaC) in the airways of the lung. In cystic fibrosis patients, increased ENaC activity contributes to airway dehydration and reduced mucociliary transport. A CTA is planned for 2019.

### Cystic Fibrosis

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

### ARO-HIF2

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

### Renal Cell Carcinoma

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

### Partnered Programs

#### Janssen Pharmaceuticals, Inc.

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

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

Arrowhead is eligible to receive up to approximately \$1.6 billion in milestone payments for the license agreement. Arrowhead is also eligible to receive approximately \$1.9 billion in option and milestone payments for the collaboration and option agreement related to up to three additional targets. Arrowhead is further eligible to receive tiered royalties up to mid teens under the license agreement and up to low teens under the collaboration and option agreement on product sales.

#### ARO-HBV

ARO-HBV is a third-generation subcutaneously administered RNAi therapeutic candidate being developed as a potential treatment for patients with chronic hepatitis B virus (HBV) infection. Arrowhead is conducting ARO-HBV1001, a Phase 1/2 clinical

study evaluating the safety, tolerability, and pharmacokinetic effects of single-ascending doses (SAD) of ARO-HBV in healthy adult volunteers, as well as the safety, tolerability, and pharmacodynamic effects of multiple-ascending doses (MAD) of ARO-HBV in patients with chronic HBV.

Initial results from AROHBV1001 were presented in November 2018 at The Liver Meeting®, the Annual Meeting of the American Association for the Study of Liver Disease (AASLD). The data in normal healthy volunteers (NHV) who received a single dose of ARO-HBV or placebo (n=30) and chronic hepatitis B patients who received three monthly doses of ARO-HBV in combination with entecavir or tenofovir (NUC) with greater than six weeks of available hepatitis B surface antigen (HBsAg) data (n=24) include the following:

- ARO-HBV administered subcutaneously appears to be well-tolerated at single or multiple monthly doses up to 400 mg
  - Mild injection site reactions were observed with approximately 12% of subcutaneous injections
- Strong HBsAg responses were observed in all HBV patients
  - Mean NADIR -1.9 Log<sub>10</sub> (-98.7%)
  - Range -1.3 (-95.0%) to -3.8 Log<sub>10</sub> (-99.98%)
- HBsAg reductions were similar in hepatitis B e-antigen (HBeAg) positive and HBeAg negative patients
  - Mean HBsAg NADIR in HBeAg positive (n=11) -2.1 Log<sub>10</sub>
  - Mean HBsAg NADIR in HBeAg negative (n=13) -1.8 Log<sub>10</sub>
- HBsAg reductions were similar for NUC naïve patients (cohort 8) and NUC experienced patients (cohort 9)
  - Mean HBsAg reduction on day 57 for cohort 8 (n=4) -1.7 Log<sub>10</sub>
  - Mean HBsAg reduction on day 57 for cohort 9 (n=4) -1.9 Log<sub>10</sub>
- This study highlighted an improvement over results with Arrowhead's first-generation compound ARC-520, which targeted only HBV transcripts derived from cccDNA (Wooddell, 2017)
- HBsAg responses observed with ARO-HBV are consistent with the ability of ARO-HBV to silence HBV mRNA from cccDNA and host-integrated viral DNA, a major source of HBsAg in certain patient populations (Wooddell, 2018)
- Responses were also observed in all other virologic parameters (HBV DNA, HBV RNA, HBeAg, HBcrAg)

Amgen Inc.

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

AMG 890 (ARO-LPA) and ARO-AMG1

AMG 890 (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. Amgen started a Phase 1 clinical study of AMG 890 (ARO-LPA) designed to assess its safety in volunteers with elevated levels of lipoprotein (a) (Lp(a)) in August 2018, triggering a \$10 million milestone payment to Arrowhead.

ARO-AMG1 is being developed against an undisclosed genetically-validated cardiovascular target under a license and collaboration agreement with Amgen.

#### RNA Interference & 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. Deemed to be one of the most important recent discoveries in life science with the potential to transform medicine, the discoverers of RNAi were awarded a Nobel Prize in 2006 for their work. RNAi-based therapeutics may leverage this natural pathway of gene silencing to target and shut down specific disease-causing genes.

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

### Figure 3: Mechanism of RNA interference

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

### Key Advantages of RNAi as a Therapeutic Modality

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

### Targeted RNAi Molecule (TRiM™) Platform

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

The TRiM™ platform comprises a highly potent RNA trigger identified using Arrowhead's proprietary trigger selection rules and algorithms with the following components optimized, as needed, for each drug candidate: a high affinity targeting ligand; various

linker and chemistries; structures that enhance pharmacokinetics; and highly potent RNAi triggers with sequence specific stabilization chemistries.

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

Figure 4: Targeted RNAi Molecule (TRiM™) Schematic

#### RNA Chemistries

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

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

#### Intellectual Property and Key Agreements

The Company controls approximately 356 issued patents (including 199 directed to RNAi trigger molecules; 23 directed to targeting groups or targeting compounds; and 17 for hydrodynamic gene delivery), including European validations, and approximately 316 currently pending patent applications worldwide from 51 different patent families. The Company's patent applications have been filed throughout the world, including, in the United States, Argentina, ARIPO (Africa Regional Intellectual Property Organization), Australia, Brazil, Canada, Chile, China, Eurasian Patent Organization, Europe, GCC (Gulf Cooperation Council), Hong Kong, Israel,

India, Indonesia, Iraq, Jordan, Japan, Republic of Korea, Lebanon, Mexico, New Zealand, OAPI (African Intellectual Property Organization), Peru, Philippines, Russian Federation, Saudi Arabia, Singapore, Thailand, Taiwan, Uruguay, Venezuela, Vietnam, and South Africa.

#### RNAi Triggers

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

#### Patent Group Estimated Year(s) of Expiration

##### RNAi Triggers Gene Target

|           |                  |
|-----------|------------------|
| HBV       | 2032, 2036, 2037 |
| AAT       | 2035, 2038       |
| LPA       | 2036             |
| Factor 12 | 2036, 2038       |
| HIF2      | 2034, 2036       |
| RRM2      | 2031             |
| APOC3     | 2035, 2038       |
| ANGPTL3   | 2038             |
| -ENaC     | 2028             |
| -ENaC     | 2031             |
| -Catenin  | 2033             |
| Cx43      | 2029             |
| HCV       | 2023             |
| HIF1A     | 2026             |
| HRH1      | 2027             |
| HSF1      | 2030, 2032       |
| FRP-1     | 2026             |
| KRAS      | 2033             |
| PDtype4   | 2026             |
| PI4Kinase | 2028             |
| SYK       | 2027             |
| TNF-      | 2027, 2028       |

#### Delivery Technologies

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

| Patent Group  | Estimated Year of Expiration |
|---|------------------------------|
| <b>Targeting ligands and other RNAi delivery technologies</b> |                              |
| Targeting groups (Galactose derivative trimer-PK)             | 2031                         |
| Targeting groups ( v 3 integrin)                              | 2035                         |
| Targeting groups ( v 6 integrin)                              | 2037                         |
| Targeting groups (Galactose derivative ligands)               | 2037, 2037                   |
| RNAi agent design (5'-phosphate mimic)                        | 2037                         |
| Physiologically labile linkers                                | 2036                         |
| Biologically cleavable linkers                                | 2036                         |
| Transferrin targeting   | 2028                         |
| LDLR targeting  | 2028                         |
| Peptide targeting (CPP-Arg)                                   | 2028                         |
| Peptide targeting (YM3-10H)                                   | 2032                         |

#### Hydrodynamic delivery

|                  |      |
|------------------|------|
| Second iteration | 2020 |
| Third iteration  | 2024 |

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

#### Non-Exclusively Licensed Patent Rights obtained from Roche

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

- Broad freedom to operate with respect to key patents directed to the primary RNAi-trigger formats: canonical, UNA, meroduplex, and dicer substrate structures; and

- A large team of scientists experienced in RNAi and oligonucleotide delivery.

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

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



2012 License to Alnylam

In consideration for licenses obtained from Alnylam to certain RNAi intellectual property, in January 2012 we granted Alnylam a worldwide non-exclusive, sublicensable royalty-bearing license under our broad and target-specific DPC intellectual property rights to research, develop and commercialize RNAi-based products against a single undisclosed target in combination with DPC technology. Under the license to Alnylam, Alnylam may be obligated to pay us development and sales milestone payments of up to the low double-digit millions of dollars for each licensed product that progresses through clinical trials, receives marketing approval

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and is the subject of a first commercial sale. Additionally, Alnylam may be obligated to pay us low single-digit percentage royalties on sales of such products.

#### Acquisition of Assets from Novartis

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

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

#### Cardiovascular Collaboration and License Agreements with Amgen

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

#### License and Research Collaboration Agreements with Janssen Pharmaceuticals, Inc.

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

Inc. (“JJDC”), a New Jersey corporation.

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

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

Under the terms of the agreements taken together, the Company has received (i) \$175 million as an upfront payment, (ii) \$75 million in the form of an equity investment by JJDC in the Company’s common stock at a price of \$23.00 per share, and may receive (iii) up to \$1.6 billion in development and sales milestones payments for the Janssen License Agreement, and (iv) up to \$1.9 billion in

development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the Janssen License agreement and up to low teens under the Janssen Collaboration Agreement on product sales.

#### Research and Development Facility

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

- Approximately 85 R&D personnel currently;

• State-of-the-art laboratories consisting of 60,000 total sq. ft.;

• Complete small animal facility;

• Primate colony housed at the Wisconsin National Primate Research Center, an affiliate of the University of Wisconsin;

• In-house histopathology capabilities;

• Animal models for cardio metabolic, viral, lung, and oncologic diseases;

• Animal efficacy and safety assessment;

• In-house drug manufacturing capabilities to produce first-in-human GMP (phase appropriate) material;

• Polymer, peptide, oligonucleotide and small molecule synthesis and analytics capabilities (HPLC, NMR, MS, etc.);

• Polymer, peptide and oligonucleotide PK, biodistribution, clearance methodologies; and

• Conventional and confocal microscopy, flow cytometry, Luminex platform, qRT-PCR, clinical chemistry analytics.

#### Research and Development Expenses

Research and development (R&D) expenses consist of costs incurred in discovering, developing and testing our clinical and preclinical candidates and platform technologies. R&D expenses also include costs related to clinical trials, including costs of contract research organizations to recruit patients and manage clinical trials. Other costs associated with clinical trials include manufacturing of clinical supplies, as well as good laboratory practice ("GLP") toxicology studies necessary to support clinical trials, both of which are outsourced to cGMP-compliant manufacturers and GLP-compliant laboratories. Total research and development expense for fiscal 2018, 2017 and 2016 was \$53.0 million, \$50.9 million and \$62.1 million, respectively.

At September 30, 2018, we employed approximately 95 employees in an R&D function, primarily working from our facility in Madison, Wisconsin. These employees are engaged in various areas of research on Arrowhead candidate and platform development including synthesis and analytics, PK/biodistribution, formulation, CMC and analytics, tumor and extra-hepatic targeting, bioassays, live animal research, toxicology/histopathology, clinical and regulatory operations, and other areas. Salaries and payroll-related expenses and stock compensation for our R&D activities were \$15.1 million, \$14.6 million, and \$17.4 million in fiscal 2018, 2017 and 2016, respectively. Costs related to the manufacture of clinical supplies, GLP toxicology studies and clinical trial costs were \$23.6 million, \$22.2 million, and \$32.3 million in fiscal 2018, 2017, and 2016, respectively. Facility-related costs, primarily rental costs for our leased laboratory in Madison, Wisconsin were \$2.3 million, \$2.3 million, and \$1.3 million in fiscal 2018, 2017, and 2016, respectively. Depreciation and amortization expenses primarily for our lab equipment and leasehold improvements in our leased laboratory in Madison, Wisconsin were \$4.7 million, \$4.7 million and \$3.2 million in fiscal 2018, 2017 and 2016, respectively. Licensing, royalties and milestones expenses were \$0, \$0, and \$3.1 million in fiscal 2018, 2017 and 2016, respectively. These expenses are primarily related to milestone payments, which can vary from period to period depending on the nature of our various license agreements, and the timing of reaching various development milestones requiring payment. Other research and development expenses were \$7.3 million, \$7.2 million, and \$4.8 million in fiscal 2018, 2017 and 2016, respectively. These expenses primarily relate to laboratory supply costs and animal-related costs for in-vivo studies.

## Government Regulation

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

significant factor in the production and marketing of our products and our R&D activities and require the expenditure of substantial time and financial resources.

#### Review and Approval of Drugs in the United States

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

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

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

#### Preclinical Studies and an IND

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

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

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

#### Human Clinical Studies in Support of an NDA

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

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

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

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

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

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

#### Submission of an NDA to the FDA



Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding \$2.6 million for applications requiring clinical data, and the sponsor of an approved NDA is also subject to an annual program fee, currently exceeding \$300,000. These fees are typically increased annually.

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

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

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

The FDA also may require submission of an 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 release, the

manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety and effectiveness of drug products.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a drug for this type of disease or condition will be recovered from sales in the U.S. for that drug. Orphan drug designation entitles the applicant to incentives such as grant funding towards clinical study costs, tax advantages, and waivers of FDA user fees. Orphan drug designation must be requested before submitting an NDA, and both the drug and the disease or condition must meet certain criteria specified in the Orphan Drug Act and FDA's implementing regulations at 21 C.F.R. Part 316. The granting of an orphan drug designation does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and effectiveness of a drug must be established through adequate and well-controlled studies.

After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other application to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition.

#### Expedited Review and Accelerated Approval Programs

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

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

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

#### Post-Approval Requirements

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

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

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

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

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

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

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

#### Abbreviated New Drug Applications for Generic Drugs

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

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

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

#### Hatch-Waxman Patent Certification and the 30 Month Stay

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

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

- the required patent information has not been filed;
- the listed patent has expired;

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

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

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

#### Pediatric Studies and Exclusivity

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

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

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

#### 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.

#### Legislative Developments

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

#### Review and Approval of Drug Products in the European Union

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

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

In 2014, a new Clinical Trial Regulation 536/2014, replacing the EU Clinical Trials Directive, was adopted. The new Regulation will become directly applicable in all European Union member states (without national implementation) once the relevant EU portal and database are fully functional. It is expected that this will occur in the second half of 2019. The new Regulation seeks to simplify and streamline the approval of clinical trials in the European Union, in particular through a harmonised electronic submission and assessment process for clinical trials conducted in multiple Member States. As part of the application process, the sponsor shall propose a reporting Member State, who will coordinate the validation and evaluation of the application. The reporting member state shall consult and coordinate with the other concerned member states. If an application is rejected, it can be amended and resubmitted through the EU portal. If an approval is issued, the sponsor can start the clinical trial in all concerned member states. However, a concerned member state can in limited circumstances declare an “opt-out” from an approval. In such a case, the clinical trial cannot be conducted in that member state. The Regulation also aims to streamline and simplify the rules on safety reporting and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU database. Information stored in the EU database will be made publicly available subject to transparency rules.

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

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products,

including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases (AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

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

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

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

#### Data and Market Exclusivity in the European Union

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

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

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

- Directive 2001/83/EC, establishing the requirements and procedures governing the marketing authorization for medicinal products for human use, as well as the rules for the constant supervision of products following authorization. This Directive has been amended several times, most recently by Directive 2012/26/EU regarding pharmacovigilance, and the Falsified Medicines Directive 2011/62/EU.

- Regulation (EC) 726/2004, as amended, establishing procedures for the authorization, supervision and pharmacovigilance of medicinal products for human and veterinary use and establishing the EMA.

- Regulation (EC) 469/2009, establishing the requirements necessary to obtain a Supplementary Protection Certificate, which extends the period of patent protection applicable to medicinal products at the EU-level.

- Directive 89/105/EEC, ensuring the transparency of measures taken by the European Union member states to set the prices and reimbursements of medicinal products. Specifically, while each member state has competence over the pricing and reimbursement of medicines for human use, they must also comply with this Directive, which establishes procedures to ensure that member state decisions and policies do not obstruct trade in medicinal products. The European Commission proposed to repeal and replace Directive 89/105/EEC, but this proposal was withdrawn in 2015.

- Directive 2003/94/EC, laying down the principles of good manufacturing practice in respect of medicinal products and investigational medicinal products for human use (the "GMP Directive").

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

#### New Legislation and Regulations

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

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

#### Pharmaceutical Coverage, Pricing and Reimbursement

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

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

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

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

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the

range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements for any of our products.

#### Healthcare Laws and Regulations

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with healthcare providers, physicians, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial

arrangements and relationships through which we market, sell and distribute products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

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

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

#### Certain Financial Information

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

#### Corporate Information

Arrowhead was originally incorporated in South Dakota in 1989 and was reincorporated in Delaware in 2000. In April 2016, Arrowhead changed its name from Arrowhead Research Corporation to Arrowhead Pharmaceuticals, Inc. The



Company's principal executive offices are located at 225 South Lake Avenue, Suite 1050, Pasadena, California 91101, and its telephone number is (626) 304-3400. We also operate a research and development facility in Madison, Wisconsin. As of September 30, 2018, Arrowhead had 116 full-time employees.

Investor Information

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

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

## ITEM 1A. RISK FACTORS

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

### Risks Related to Our Company

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

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

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

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

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

- controlled research and human clinical testing;

- establishment of the safety and efficacy of the product;

- government review and approval of a submission containing manufacturing, pre-clinical and clinical data; and

- adherence to cGMP regulations during production and storage.

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

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

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

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

- safety and efficacy results attained in early human clinical trials may not be indicative of results that are obtained in later clinical trials;

•after reviewing test results, we may abandon projects that we might previously have believed to be promising;

•we or our regulators may suspend or terminate clinical trials because the participating subjects or patients are being exposed to unacceptable health risks; and

•our product candidates may not have the desired effects or may include undesirable side effects or other characteristics that preclude regulatory approval or limit their commercial use if approved.

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. We may not commence or complete clinical trials involving any of our product candidates as projected or may not conduct them successfully.

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

At the time drugs are approved for commercialization, they are given a “product label” from the FDA or other regulatory body. In most countries this label sets forth the approved indication for marketing and identifies potential safety concerns for prescribing physicians and patients. While we intend to seek as broad a product label as possible for our product candidates, we may receive a narrower label than is expected by either us or third parties, such as stockholders and securities analysts. For example, any approved products may only be indicated to treat refractory patients (i.e., those who have failed some other first-line therapy). Similarly, it is possible that only a specific sub-set of patients safely responds to one or more of our drug candidates. As a result, our product candidates, even if successful in clinical trials, could be approved only for a subset of patients. Additionally, safety considerations may result in contraindications that could further limit the scope of an approved product label. Any of these or other safety and efficacy considerations could limit the commercial opportunity for our product candidates.

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

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

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

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

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

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

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

Sales of any approved drug candidate will depend in part on the availability of coverage and reimbursement from third-party payers such as government insurance programs, including Medicare and Medicaid, private health insurers, health maintenance organizations and other health care related organizations, who are increasingly challenging the price of medical products and services. Accordingly, coverage and reimbursement may be uncertain. Adoption of any drug by the medical community may be limited if third-party payers will not offer coverage. Additionally, significant uncertainty exists as to the reimbursement status of newly approved drugs. Cost control initiatives may decrease coverage and payment levels for any drug and, in turn, the price that we will be able to charge and/or the volume of our sales. We are unable to predict all changes to the coverage or reimbursement methodologies that will be applied by private or government payers. Any denial of private or government payer coverage or inadequate reimbursement could harm our business and reduce our revenue. If we partner with third parties with respect to any of our product candidates, we may be reliant on that partner to obtain reimbursement from government and private payors for the drug, if approved, and any failure of that partner to establish adequate reimbursement could have a negative impact on our revenues and profitability.

In addition, both the federal and state governments in the United States and foreign governments continue to propose and pass new legislation, regulations, and policies affecting coverage and reimbursement rates, which are designed to contain or reduce the cost of health care. Further federal and state proposals and healthcare reforms are likely, which could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunity. There may be future changes that result in reductions in potential coverage and reimbursement levels for our product candidates, if approved and commercialized, and we cannot predict the scope of any future changes or the impact that those changes would have on our operations.

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

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

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

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

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

### Risks Related to Our Intellectual Property

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

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



any meaningful competitive advantage. If we are unable to derive value from our licensed or owned intellectual property, the value of your investment may decline.

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

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

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

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

In addition, if our product candidates 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. In particular, we have obtained licenses from, among others, Novartis and Alnylam. We also expect to enter into additional licenses to third-party intellectual property in the future.

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

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

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

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

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers, and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of

unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information, and in such cases, we could not assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

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

#### Risks Related to Our Business Model

Our business model assumes we will generate revenue by, among other activities, marketing or out-licensing the products we develop. Our drug candidates are in the early stages of development and because we have a short development history with both RNA interference and our delivery technologies, there is a limited amount of information about us upon which you can evaluate our business and prospects.

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

Execute product development activities using unproven technologies;

Build, maintain, and protect a strong intellectual property portfolio;

Demonstrate safety and efficacy of our drug candidates in multiple human clinical studies;

Receive FDA approval and approval from similar foreign regulatory bodies;

Gain market acceptance for the development and commercialization of any drugs we develop;

Ensure our products are reimbursed by commercial and/or government payors at a rate that permits commercial viability;

Develop and maintain successful strategic relationships with suppliers, distributors, and commercial licensing partners;

Manage our spending and cash requirements as our expenses will increase in the near term if we add programs and additional preclinical and clinical trials; and

Effectively market any products for which we obtain marketing approval.

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

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

In October 2018, we entered in a license agreement and research and collaboration agreement with Janssen Pharmaceuticals, Inc. and during fiscal year 2016, we entered into two collaboration and license agreements with Amgen Inc. Our business strategy includes obtaining additional collaborations with other pharmaceutical and biotech companies to support the development of our therapeutic siRNA and other drug candidates. We do not possess all of the financial and development resources necessary to develop and commercialize products that may result from our technologies. Unless we expand our product development capacity and enhance our internal marketing capability, we may need to make appropriate arrangements with strategic partners to develop and commercialize any drug candidates that may be approved. We may not be able to attract such partners, and even if we are able to enter into such partnerships, the terms may be less favorable than anticipated. Further, entering into partnership agreements may limit our commercialization options and/or require us to share revenues and profits with our partners. If we do not find appropriate partners, or if our existing arrangements or future agreements are not successful, our ability to develop and commercialize products could be adversely affected. Even if we are able to find collaborative partners, the overall success of the development and commercialization of product candidates in those programs will depend largely on the efforts of other parties and will be beyond our control. In addition, in

the event we pursue our commercialization strategy through collaboration or licenses to third parties, there are a variety of technical, business and legal risks, including:

We may not be able to control the amount and timing of resources that our collaborators may be willing or able to devote to the development or commercialization of our drug candidates or to their marketing and distribution; and

Disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts our management's resources.

The occurrence of any of the above events or other related events could impair our ability to generate revenues and harm our business and financial condition.

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

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

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

Our business model has been to develop new technologies and to utilize the intellectual property created through the research and development process to develop commercially successful products. If the acquirers of our technologies fail to achieve performance milestones, we may not receive a significant portion of the total value of any sale, license or other strategic transaction.

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

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

We cannot predict whether significant commercial market acceptance for our products, if approved, will ever develop, and we cannot reliably estimate the projected size of any such potential market. Our revenue growth and achievement of profitability will depend substantially on our ability to introduce products that will be accepted by the medical community. If we are unable to cost-effectively achieve acceptance of our technology among the medical establishment and patients, or if the associated products do not achieve wide market acceptance, our business will be materially and adversely affected.

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

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

We have limited manufacturing capability and must rely on third-party manufacturers to manufacture our clinical supplies and commercial products, if and when approved, and if they fail to meet their obligations, the development and commercialization of our products could be adversely affected.

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

Additionally, our product candidates have not yet been manufactured for commercial use. If any of our product candidates become approved for commercial sale, we will need to establish either internal or third-party manufacturing capacity. Manufacturing partner requirements may require us to fund capital improvements, perhaps on behalf of third parties, to support the scale-up of manufacturing and related activities. We may not be able to establish scaled manufacturing capacity for an approved product in a timely or economic manner, if at all. If we or our third-party manufacturers are unable to provide commercial quantities of such an approved product, we will have to successfully transfer manufacturing technology to a different manufacturer. Engaging a new manufacturer for such an approved product could require us to conduct comparative studies or utilize other means to determine bioequivalence of the new and prior manufacturers' products, which could delay or prevent our ability to commercialize such an approved product. If we or any of these manufacturers is unable or unwilling to increase its manufacturing capacity or if we are unable to establish alternative arrangements on a timely basis or on acceptable terms, the development and commercialization of such an approved product may be delayed or there may be a shortage in supply. Any inability to manufacture our product candidates or future approved drugs in sufficient quantities when needed would seriously harm our business.

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

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

We rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our clinical trials. We contract with certain third-parties to provide certain services, including site selection, enrollment, monitoring and data management services. Although we depend heavily on these parties, we do not control them and therefore we cannot be assured that these third-parties will adequately perform all of their contractual obligations to us. If our third-party service

providers cannot adequately and timely fulfill their obligations to us, or if the quality and accuracy of our clinical trial data is compromised due to failure by such third parties to adhere to our protocols or regulatory requirements or if such third-parties otherwise fail to meet deadlines, our development plans may be delayed or terminated. Further, if clinical study results are compromised, then we may need to repeat the affected studies, which could result in significant additional costs and delays to us.

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

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



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

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

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

Our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. Such events could cause interruption of our operations and loss of intellectual property. For example, the loss of pre-clinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of or damage to our data, or inappropriate disclosure of confidential, proprietary or private information, we could incur liability, we could lose valuable trade secret rights, and the development of our product candidates could be delayed.

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

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

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

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

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

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

Risks Related to Our Financial Condition

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

We have incurred net losses since our inception, including net losses of \$54.5 million for the fiscal year ended September 30, 2018. We expect that our operating losses will continue for the foreseeable future as we continue our drug development and discovery efforts. To achieve profitability, we must, either directly or through licensing and/or partnering relationships, meet certain milestones, successfully develop and obtain regulatory approval for one or more drug candidates and effectively manufacture, market and sell any drugs we successfully develop. Even if we successfully commercialize drug candidates that receive regulatory approval, we may not be able to realize revenues at a level that would allow us to achieve or sustain profitability. Accordingly, we may never generate significant revenue and, even if we do generate significant revenue, we may never achieve 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 will likely need to raise additional capital to:

Fund research and development infrastructure and activities relating to the development of our drug candidates, including pre-clinical and clinical trials and manufacturing to support these efforts;

Fund a commercialization infrastructure and activities related to the sale, marketing, customer support, and distribution of our drug products if and when they become approved;

Fund our general and administrative infrastructure and activities;

Pursue business development opportunities for our technologies;

Add to and protect our intellectual property; and

Retain our management and technical staff.

Our future capital needs depend on many factors, including:

• The scope, duration, and expenditures associated with our research and development;

• Regulatory requirements for our clinical trials;

• The extent to which our research and development and clinical efforts are successful;

- The outcome of potential partnering or licensing transactions, if any, and the extent to which our business development efforts result in the acquisition of new programs or technologies;

Competing technological developments;

Our intellectual property positions, if any, in our products; and

The regulatory approval process and regulatory standards for our drug candidates.

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

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

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and

related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

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

At September 30, 2018, we had \$46.4 million in fixed income marketable securities. These investments are in corporate bonds nearing maturity, but our investments may also include commercial paper, securities issued by the U.S. government obligations, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, and market and interest rate risks, particularly in the current economic environment. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

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

We have historically incurred net losses. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses (NOLs) carried forward from a prior taxable year. Under that provision, we can carryforward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. As of September 30, 2017, we had federal, and state NOL carryforwards of approximately \$284.8 million and \$196.6 million, respectively. The federal NOL carryforwards will begin to expire, if not utilized, beginning in 2037. These NOL carryforwards could expire unused before offsetting potential future income tax liabilities. Under the Tax Cut and Jobs Act of 2017, or the Tax Act, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percent change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. It is possible that we have experienced an ownership change limitation. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our NOL carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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

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

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

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

We could be subject to additional tax liabilities.

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

#### Investment and Securities Risks

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

We have adopted and may in the future adopt certain measures that may have the effect of delaying, deferring or preventing a takeover or other change in control of the Company that a holder of our Common Stock might consider in its best interest. For example, our Board of Directors, without further action by our stockholders, currently has the authority to issue up to 5,000,000 shares of preferred stock and to fix the rights (including voting rights), preferences and privileges of these shares (“blank check” preferred). Such preferred stock may have rights, including economic rights, senior to our Common Stock. These factors could also reduce the price that certain investors might be willing to pay for shares of our Common Stock and result in the market price being lower than it would be without these provisions.

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

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

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

The trading market for our Common Stock can be influenced by the research and reports that industry or securities analysts publish about our business. Currently, coverage of our Company by industry and securities analysts is limited. Investors have many investment opportunities and may limit their investments to companies that receive greater coverage from analysts. If additional industry or securities analysts do not commence coverage of the Company, the trading price of our stock could be negatively impacted. If one or more of the analysts downgrade our stock or comment negatively on our prospects, our stock price may decline. If one or more of these analysts cease to cover our industry or us or fail to publish reports about the Company regularly, our Common Stock could lose visibility in the financial markets, which could also cause our stock price or trading volume to decline. Further, incorrect judgments, estimates or assumptions made by research analysts may adversely affect our stock price, particularly if subsequent performance falls below the levels that were projected by the research analyst(s), even if we did not set or endorse such expectations. Any of these events could cause further volatility in our stock price and

could result in substantial declines in the value of our stock.

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

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

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



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

Announcements of developments related to our business;

Our ability to enter into or extend investigation phase, development phase, commercialization phase and other agreements with new and/or existing partners;

Announcements regarding the status of any or all of our collaborations or products, including clinical trial results;

Market perception and/or investor sentiment regarding our technology;

Announcements of actions taken by regulatory authorities, such as the U.S. Food and Drug Administration;

Announcements regarding developments in the RNA interference or biotechnology fields in general;

Announcements regarding clinical trial results with our products or competitors' products;

Market perception and/or announcements regarding other companies developing products in the field of biotechnology generally or specifically RNA interference;

The issuance of competitive patents or disallowance or loss of our patent rights;

The addition or departure of key executives; and

Variations in our operating results.

We will not have control over many of these factors but expect that they may influence our stock price. As a result, our stock price may be volatile and such volatility could result in the loss of all or part of your investment.

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

Our certificate of incorporation authorizes the issuance of 145,000,000 shares of Common Stock and 5,000,000 shares of Preferred Stock, on such terms and at such prices as our Board of Directors may determine. The following serves as a summary of share issuance activity during the fiscal year ended September 30, 2018:

• 1,500,000 shares of Common Stock issued in an equity financing in January 2018 that generated \$56.6 million of net proceeds to the Company; and

2,219,876 shares of Common Stock pursuant to the exercise of stock options, warrants and exchange rights and the vesting of restricted stock units;

As of September 30, 2018, we had 88,505,302 shares of Common Stock issued and outstanding. The issuance of additional securities in financing transactions by us or through the exercise of options or warrants will dilute the equity interests of our existing stockholders, perhaps substantially, and could result in dilution in the tangible net book value of a share of our Common Stock, depending upon the price and other terms on which the additional shares are issued.

#### Risks Inherent in Our Industry

Drug development is time consuming, expensive and risky.

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

Clinical trial results may be unacceptable, even though preclinical trial results were promising;

Inefficacy and/or harmful side effects in humans or animals;

The necessary regulatory bodies, such as the U.S. Food and Drug Administration, may not approve our potential product for the intended use, or at all; and

Manufacturing and distribution may be uneconomical.

For example, any positive pre-clinical results in animals for our pre-clinical programs may not be replicated in human clinical studies. These programs may be also found to be unsafe in humans, particularly at higher doses needed to achieve the desired levels of efficacy. Also, the positive safety results from single dose human clinical studies may not be replicated in other human studies, including multiple dose studies. Clinical and pre-clinical study results are frequently susceptible to varying interpretations by scientists, medical personnel, regulatory personnel, statisticians and others, which often delays, limits, or prevents further clinical development or regulatory approvals of potential products. Clinical trials can take many years to complete, including the process of study design, clinical site selection and the recruitment of patients. As a result, we can experience significant delays in completing clinical studies, which can increase the cost of developing a drug candidate and shorten the time that an approved product may be protected by patents. If our drug candidates are not successful in human clinical trials, we may be forced to curtail or abandon certain development programs. If we experience significant delays in commencing or completing our clinical studies, we could suffer from significant cost overruns, which could negatively affect our capital resources and our ability to complete these studies.

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

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

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

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

#### ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

#### ITEM 2. PROPERTIES

The Company does not own any real property. The following table summarizes the Company's leased facilities as of September 30, 2018.

|                      | Office<br>Space | Monthly<br>Expenses | Primary Use       | Lease<br>Expiration | Lease Term |
|----------------------|-----------------|---------------------|-------------------|---------------------|------------|
| Pasadena, California | 8,500 sq. ft.   | \$28,000            | Corp. Headqtrs.   | September 2019      | 7 years    |
| Madison, Wisconsin   | 60,000 sq. ft.  | \$186,000           | Research Facility | September 2026      | 10 years   |

### ITEM 3. LEGAL PROCEEDINGS

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

### ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

## PART II

ITEM MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND  
5. ISSUER PURCHASES OF EQUITY SECURITIES

## Price Range of Common Stock

Our Common Stock is traded on the NASDAQ Global Select Market under the symbol "ARWR". The following table sets forth the high and low sales prices for a share of the Company's Common Stock during each period indicated.

|             | Fiscal Year Ended September 30, |        |        |        |
|-------------|---------------------------------|--------|--------|--------|
|             | 2018                            |        | 2017   |        |
|             | High                            | Low    | High   | Low    |
| 1st Quarter | \$4.54                          | \$3.01 | \$7.74 | \$1.20 |
| 2nd Quarter | 8.09                            | 3.57   | 2.45   | 1.42   |
| 3rd Quarter | 14.24                           | 6.26   | 2.04   | 1.42   |
| 4th Quarter | 22.39                           | 12.25  | 4.42   | 1.48   |

## Shares Outstanding

At December 7, 2018, 92,224,665 shares of the Company's Common Stock were issued and outstanding, and were owned by 120 stockholders of record, based on information provided by the Company's transfer agent.

## Dividends

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

## Securities Authorized for Issuance Under the Equity Compensation Plans

The disclosure required under this item related to equity compensation plans is incorporated by reference from Item 12 of Part III of this Annual Report on Form 10-K.

## Sales of Unregistered Securities

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

## Repurchases of Equity Securities

We did not repurchase any shares of our Common Stock during the years ended September 30, 2018, 2017 and 2016.

## Performance Graph

The following performance graph shall not be deemed "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities

Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing. The graph compares the cumulative 5-year total return to shareholders on our Common Stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. We selected the NASDAQ Biotechnology Index because we believe the index reflects the market conditions within the industry in which we primarily operate. The comparison of total return on investment, defined as the change in year-end stock price plus reinvested dividends, for each of the periods assumes that \$100 was invested on September 30, 2013, in each of our Common Stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index, with investment weighted on the basis of market capitalization.

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



## ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data has been derived from our audited consolidated financial statements and should be read

in conjunction with the consolidated financial statements, the related notes thereto and the independent auditors' report thereon, and

"Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this

Form 10-K and in previously filed annual reports on Form 10-K of Arrowhead Pharmaceuticals, Inc.

|   | Year Ended September   |                        |                        |                        |                        |
|---|------------------------|------------------------|------------------------|------------------------|------------------------|
|   | 2018                   | 2017                   | 2016                   | 2015                   | 2014                   |
| <b>OPERATING SUMMARY</b>  |                        |                        |                        |                        |                        |
| REVENUE   | \$ 16,142,321          | \$ 31,407,709          | \$ 158,333             | \$ 382,000             | \$ 175,000             |
| <b>OPERATING EXPENSES</b>                                       |                        |                        |                        |                        |                        |
| Research and development  | 52,968,505             | 50,904,466             | 62,117,818             | 64,035,385             | 33,738,674             |
| Acquired in-process research and development                    | -                      | -                      | -                      | 10,142,786             | -                      |
| General and administrative expenses                             | 19,110,051             | 17,499,152             | 23,594,888             | 20,286,272             | 15,164,567             |
| Impairment expense  | -                      | -                      | 2,050,817              | -                      | 2,172,387              |
| Contingent consideration - fair value adjustments               | -                      | -                      | (5,862,464 )           | 1,891,533              | 2,375,658              |
| <b>TOTAL OPERATING EXPENSES</b>                                 |                        |                        |                        |                        |                        |
| (a)   | 72,078,556             | 68,403,618             | 81,901,059             | 96,355,976             | 53,451,286             |
| <b>OPERATING LOSS</b>   | <b>(55,936,235 )</b>   | <b>(36,995,909 )</b>   | <b>(81,742,726 )</b>   | <b>(95,973,976 )</b>   | <b>(53,276,286 )</b>   |
| <b>NET LOSS</b>   | <b>(54,450,478 )</b>   | <b>(34,380,295 )</b>   | <b>(81,723,002 )</b>   | <b>(91,940,882 )</b>   | <b>(58,725,412 )</b>   |
| Net (gain) loss attributable to non-controlling interests       | -                      | -                      | -                      | -                      | 95,222                 |
| <b>NET LOSS ATTRIBUTABLE TO ARROWHEAD</b>                       | <b>\$(54,450,478 )</b> | <b>\$(34,380,295 )</b> | <b>\$(81,723,002 )</b> | <b>\$(91,940,882 )</b> | <b>\$(58,630,190 )</b> |
| <b>EARNINGS PER SHARE (BASIC AND DILUTED):</b>                  |                        |                        |                        |                        |                        |
| Net Income (Loss) attributable to Arrowhead common shareholders | \$(0.65 )              | \$(0.47 )              | \$(1.34 )              | \$(1.60 )              | \$(1.25 )              |
| <b>Weighted average shares outstanding – basic and diluted</b>  |                        |                        |                        |                        |                        |
|   | 83,638,469             | 73,898,598             | 61,050,880             | 57,358,442             | 46,933,030             |
| <b>CASH DIVIDEND PAID PER COMMON SHARE</b>                      |                        |                        |                        |                        |                        |
|   | \$-                    | \$-                    | \$-                    | \$-                    | \$-                    |
|   | September 30, 2018     | 2017                   | 2016                   | 2015                   | 2014                   |
| <b>FINANCIAL POSITION SUMMARY</b>                               |                        |                        |                        |                        |                        |
|   | \$30,133,213           | \$24,838,567           | \$85,366,448           | \$ 81,214,354          | \$ 132,510,610         |



|   |             |             |             |             |             |
|---|-------------|-------------|-------------|-------------|-------------|
| CASH AND CASH<br>EQUIVALENTS (b)        |             |             |             |             |             |
| SHORT- AND LONG-TERM<br>INVESTMENTS (b) | 46,400,176  | 40,769,539  | -           | 17,539,902  | 44,741,378  |
| TOTAL ASSETS (b)                        | 111,609,951 | 104,022,280 | 128,176,505 | 132,267,914 | 182,816,756 |
| CAPITAL LEASE OBLIGATIONS               | -           | -           | -           | 758,340     | 972,331     |
| OTHER LONG-TERM<br>OBLIGATIONS          | 4,003,999   | 4,454,070   | 7,508,452   | 6,204,917   | 4,226,137   |

- (a) The increase in our Total Operating Expenses during the year ended September 30, 2018 is primarily due to the progression of the ARO-HBV and ARO-AAT clinical trial candidates. We expect research and development expenses to continue to increase as our other pipeline candidates progress toward the clinic.
- (b) The Company's Cash and Cash Equivalents, Short- and Long-Term Investments and Total Assets increased from September 30, 2017 to September 30, 2018 due primarily to an equity financing completed in January 2018 which yielded net proceeds of \$56.6 million offset by cash used in research and development expenditures.

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

Description of Business

Unless otherwise noted, (1) the term "Arrowhead" refers to Arrowhead Pharmaceuticals, Inc., a Delaware corporation, (2) the terms "Company," "we," "us," and "our," refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term "Subsidiaries" refers collectively to Arrowhead Madison Inc. ("Arrowhead Madison"), Arrowhead Australia Pty Ltd ("Arrowhead Australia") and Ablaris Therapeutics, Inc. ("Ablaris"), (4) the term "Common Stock" refers to Arrowhead's Common Stock, (5) the term "Preferred Stock" refers to Arrowhead's Preferred Stock and (6) the term "Stockholder(s)" refers to the holders of Arrowhead Common Stock.

Overview

Arrowhead Pharmaceuticals, Inc. develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Deemed to be one of the most important recent discoveries in life science with the potential to transform medicine, the discoverers of RNAi were awarded a Nobel Prize in 2006 for their work. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing. The company's pipeline includes ARO-AAT for liver disease associated with alpha-1 antitrypsin deficiency (AATD), ARO-APOC3 for hypertriglyceridemia, ARO-ANG3 for dyslipidemia, ARO-ENaC for cystic fibrosis, and ARO-HIF2 for renal cell carcinoma. ARO-LPA (AMG 890) for cardiovascular disease was out-licensed to Amgen Inc. in 2016. ARO-AMG1 for an undisclosed genetically validated cardiovascular target is under a license and collaboration agreement with Amgen Inc. ARO-HBV for chronic hepatitis B virus was out-licensed to Janssen Pharmaceuticals, Inc. in October 2018.

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

Arrowhead has refocused its resources on therapeutics that exclusively utilize the company's Targeted RNAi Molecule (TRiM™) platform technology. Therapeutics built on the TRiM™ platform have demonstrated high levels of pharmacologic activity in multiple animal models spanning several therapeutic areas. 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, and tumors; and the potential for improved safety and reduced risk of intracellular buildup, because there are less metabolites from smaller, simpler molecules.

During fiscal 2018, the Company achieved substantial progress on its pipeline candidates. In the first half of fiscal 2018, Clinical Trial Applications (CTAs) were filed for ARO-AAT and ARO-HBV, and the associated phase 1 (ARO-AAT) and phase 1 / 2 (ARO-HBV) studies are ongoing. Dosing has completed for the ARO-AAT phase 1 clinical study. In October 2018, the Company also filed a CTA for ARO-ANG3 and, pending approval, the Company anticipates the startup of this study in 2019. The Company has also achieved substantial progress on its other preclinical candidates including ARO-APOC3, ARO-ENaC and ARO-HIF2, with planned CTA or equivalent filings planned in late calendar 2018 for ARO-APOC3 and in 2019 for ARO-ENaC and ARO-HIF2.

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

billion in development and sales milestones payments for the Janssen License Agreement, and up to \$1.9 billion in development and sales milestone payments for the three additional targets covered under the Janssen Collaboration Agreement. The Company is further eligible to receive tiered royalties up to mid teens under the Janssen License Agreement and up to low teens under the Janssen Collaboration Agreement on product sales.

The Company's collaboration agreements with Amgen also continue to progress as it relates to the AMG 890 (ARO-LPA) and ARO-AMG1 candidates. Under the terms of the agreements taken together, the Company has received \$35 million in upfront payments and \$21.5 million in the form of an equity investment by Amgen in the Company's Common Stock and could receive up to \$617 million in option payments and development, regulatory and sales milestone payments. The Company is further eligible to receive single-digit royalties for sales of products under the ARO-AMG1 agreement and up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement. On August 1, 2018, the Company announced that it had earned a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. This milestone payment was recognized as Revenue in its entirety during the year ended September 30, 2018.

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 contracted to third-party manufactures when cGMP production is required. The Company engages third-party contract research organizations (CROs) to manage clinical trials and works cooperatively with such organizations on all aspects of clinical trial management, including plan design, patient recruiting, and follow up. These outside costs, relating to the preparation for and administration of clinical trials, are referred to as "program costs". If the clinical candidates progress through human testing, program costs will increase.

Net losses were \$54.5 million, \$34.4 million and \$81.7 million during the years ended September 30, 2018, 2017 and 2016, respectively. Diluted losses per share were \$0.65, \$0.47 and \$1.34 during the years ended September 30, 2018, 2017 and 2016, respectively. A decrease in revenue in 2018 from the collaborations with Amgen is the driver of the increases in the net losses and diluted losses per share, as discussed further below.

The Company strengthened its liquidity and financial position through an equity offering completed in January 2018, which generated \$56.6 million of net cash proceeds for the Company, as well as the \$10 million milestone payment earned from Amgen under the AMG 890 (ARO-LPA) Agreement. Additionally, with the recent agreements made with Janssen, the Company has secured an additional \$250 million in cash proceeds in October 2018. These cash proceeds secure the funding needed to continue to advance our preclinical candidates. The Company had \$30.1 million of cash and cash equivalents, \$46.4 million in short-term investments and \$111.6 million of total assets as of September 30, 2018, as compared to \$24.8 million, \$40.8 million and \$104.0 million as of September 30, 2017, respectively. Based upon the Company's current cash and short-term investment resources and operating plan, the Company expects to have sufficient liquidity to fund operations for at least the next twelve months.

### Critical Accounting Policies and Estimates

Management makes certain judgments and uses certain estimates and assumptions when applying GAAP in the preparation of our Consolidated Financial Statements. We evaluate our estimates and judgments on an ongoing basis and base our estimates on historical experience and on assumptions that we believe to be reasonable under the circumstances. Our experience and assumptions form the basis for our judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may vary from what we anticipate and different assumptions or estimates about the future could change our reported results. We believe the following accounting policies are the most critical to us, in that they require our most difficult, subjective or complex judgments

in the preparation of our consolidated financial statements. For further information, see Note 1, Organization and Significant Accounting Policies, to our Consolidated Financial Statements, which outlines our application of significant accounting policies.

#### Revenue Recognition

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

The Company may generate revenue from technology licenses, collaborative research and development arrangements, research grants and product sales. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable and/or guaranteed technology license fees, collaborative research funding, manufacturing and development services and various milestone and future product royalty or profit-sharing payments. These agreements are generally referred to as “multiple element arrangements”.

The Company applies the accounting standard on revenue recognition for multiple element arrangements. The fair value of deliverables under the arrangement may be derived using a best estimate of selling price if vendor specific objective evidence and third-party evidence is not available. Deliverables under the arrangement will be separate units of accounting if a delivered item has value to the customer on a standalone basis and if the arrangement includes a general right of return for the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control.

The Company recognizes upfront license payments as revenue upon delivery of the license only if the license has standalone value from any undelivered performance obligations and that value can be determined. The undelivered performance obligations typically include manufacturing or development services or research and/or steering committee services. If the fair value of the undelivered performance obligations can be determined, then these obligations would be accounted for separately. If the license is not considered to have standalone value, then the license and other undelivered performance obligations would be accounted for as a single unit of accounting. In this case, the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed or deferred indefinitely until the undelivered performance obligation is determined.

Whenever the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company determines the period over which the performance obligations will be performed, and revenue will be recognized. Revenue is recognized using a proportional performance or straight-line method. The proportional performance method is used when the level of effort required to complete performance obligations under an arrangement can be reasonably estimated. The amount of revenue recognized under the proportional performance method is determined by multiplying the total payments under the contract, excluding royalties and payments contingent upon achievement of milestones, by the ratio of the level of effort performed to date to the estimated total level of effort required to complete performance obligations under the arrangement. If the Company cannot reasonably estimate the level of effort to complete performance obligations under an arrangement, the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. 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 under an arrangement.

The Company's collaboration agreements typically entitle the Company to additional payments upon the achievement of development, regulatory and sales performance-based milestones. If the achievement of a milestone is considered probable at the inception of the collaboration, the related milestone payment is included with other collaboration consideration, such as upfront fees and research funding, in the Company's revenue calculation. Typically, these milestones are not considered probable at the inception of the collaboration. As such, milestones will typically be recognized in one of two ways depending on the timing of when the milestone is achieved. If the milestone is achieved during the performance period, then the Company will only recognize revenue to the extent of the proportional performance achieved at that date, or the proportion of the straight-line basis achieved at that date, and the remainder will be recorded as deferred revenue to be amortized over the remaining performance period. If the milestone is achieved after the performance period has completed and all performance obligations have been delivered, then the Company will recognize the milestone payment as Revenue in its entirety in the period the milestone was achieved.

Deferred revenue will be classified as part of Current or Long-Term Liabilities in the accompanying Consolidated Balance Sheets based on the Company's estimate of the portion of the performance obligations regarding that revenue will be completed within the next 12 months divided by the total performance period estimate. This estimate is based on the Company's current operating plan and, if the Company's operating plan should change in the future, the Company may recognize a different amount of deferred revenue over the next 12-month period.

The new revenue recognition guidance (ASC 606) was effective as of October 1, 2018, and it will not have a material impact on our Consolidated Financial Statements. Please read Note 1 to our Consolidated Financial Statements included in Part II, Item 8, "Financial Statements and Supplementary Data," of this annual report on Form 10-K for our discussion of recent accounting pronouncements for the expected impact of this new accounting guidance.

#### Impairment of Long-lived Assets

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

#### Impairment of Intangible assets

Intangible assets consist of a license agreement and patents acquired in conjunction with a business or asset acquisition. Intangible assets are monitored for potential impairment whenever events or circumstances indicate that the carrying amount may not be recoverable and are also reviewed annually to determine whether any impairment is necessary. Based on ASU 2012-02, the annual review of intangible assets is performed via a two-step process. First, a qualitative assessment is performed to determine if it is more likely than not that the intangible asset is impaired. If required, a quantitative assessment is performed and, if necessary, impairment is recorded.

#### Stock-Based Compensation

We account for stock-based compensation arrangements in accordance with FASB ASC 718, which requires the measurement and recognition of compensation expense for all share-based payment awards to be based on estimated fair values. The Company uses the Black-Scholes option valuation model to estimate the fair value of its stock options at the date of grant. The Black-Scholes option valuation model requires the input of subjective assumptions to calculate the value of stock options. For restricted stock units, the value of the award is based on the Company's stock price at the grant date. For performance-based restricted stock unit awards, the value of the award is based on the Company's stock price at the grant date. The Company uses historical data and other information to estimate the expected price volatility for stock option awards and the expected forfeiture rate for all awards. Expense is recognized over the vesting period for all awards and commences at the grant date for time-based awards and upon the Company's determination that the achievement of such performance conditions is probable for performance-based awards. This determination requires significant judgement by management.

#### Contingent Consideration

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

#### Results of Operations

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

|         | Year ended September 30, |              |           |
|---------|--------------------------|--------------|-----------|
|         | 2018                     | 2017         | 2016      |
| Revenue | \$16,142,321             | \$31,407,709 | \$158,333 |



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|   |              |              |              |
|---|--------------|--------------|--------------|
| Operating Loss                                  | (55,936,235) | (36,995,909) | (81,742,726) |
| Net Loss  | (54,450,478) | (34,380,295) | (81,723,002) |
| Earnings (Losses) per Share (Basic and Diluted) | \$(0.65      | ) \$(0.47    | ) \$(1.34    |

The decrease in our Revenue during the year ended September 30, 2018 was driven by the timing of the recognition of the initial \$30 million payment associated with the AMG 890 (ARO-LPA) Agreement. This Revenue was recognized primarily in fiscal 2017 as performance was completed. This decrease in Revenue was also the key driver of the increase in our Operating Loss, Net Loss and Loss per Share. Research and Development expenses increased during fiscal 2018 due to the progress of ARO-AAT and ARO-HBV into phase 1 and phase 1 / 2 clinical studies.

Results of Operations Comparison for 2018 and 2017

Revenues

Total revenue was \$16,142,321 for the year ended September 30, 2018 and \$31,407,709 for the year ended September 30, 2017. Revenue in the current period is primarily related to the \$10 million milestone payment received from Amgen in August 2018, which

was earned following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. Revenue in the previous period was primarily related to the upfront payments received from Amgen in 2016 that we recognized as Revenue as performance was completed for the AMG 890 (ARO-LPA) and ARO-AMG1 Agreements. The decrease in our Revenue during the year ended September 30, 2018 was driven by a reduction in the amount of Revenue recognized associated with the \$30 million upfront payment received from Amgen associated with the AMG 890 (ARO-LPA) Agreement. We recognized Revenue from the ARO-LPA (AMG-890) Agreement on a straight-line basis as performance was completed from November 2016 thru October 2017.

Under the terms of the AMG 890 (ARO-LPA) Agreement, the Company has granted a worldwide, exclusive license to AMG 890 (ARO-LPA). The Company is also responsible for assisting Amgen in the oversight of certain development and manufacturing activities (the “AMG 890 (ARO-LPA) R&D Services”), most of which are to be covered at Amgen’s cost. The Company has determined that the significant deliverables under the AMG 890 (ARO-LPA) Agreement include the license and the AMG 890 (ARO-LPA) R&D Services. The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and the AMG 890 (ARO-LPA) R&D Services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. Therefore, the deliverables are not separable and, accordingly, the license and the AMG 890 (ARO-LPA) R&D Services are being treated as a single unit of accounting. The Company recognized revenue on a straight-line basis from November 18, 2016 (the Hart-Scott-Rodino clearance date), through October 31, 2017, which was the date where the AMG 890 (ARO-LPA) R&D Services were substantially completed. The Company received the upfront payment of \$30 million due under the AMG 890 (ARO-LPA) Agreement in November 2016. The upfront \$30 million payment was initially recorded as Deferred Revenue. During the years ended September 30, 2018 and 2017, \$2.7 million and \$27.3 million of this upfront payment were recognized into Revenue, respectively. This upfront payment has been recognized as Revenue in its entirety as of September 30, 2018.

On August 1, 2018, the Company announced that it had earned a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. The Company has recognized this payment as Revenue in its entirety during the year ended September 30, 2018 as the performance obligations had already been substantially completed.

Under the terms of the ARO-AMG1 Agreement, the Company has granted an option to a worldwide, exclusive license to ARO-AMG1, an undisclosed genetically validated cardiovascular target. The Company is also responsible for developing, optimizing and manufacturing the candidate through certain preclinical efficacy and toxicology studies to determine whether the candidate the Company has developed meets the required criteria as defined in the agreement (the “Arrowhead Deliverable”). The Company delivered the candidate in August 2018 and Amgen currently has the option to an exclusive license for the intellectual property generated through the Company’s development efforts. If Amgen exercises its option, it would likely assume all development, regulatory and commercialization efforts for the candidate. The Company determined that the significant deliverables under the ARO-AMG1 Agreement include the option to license and the development and manufacturing activities toward achieving the Arrowhead Deliverable (the “ARO-AMG1 R&D Services”). The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the option to license and ARO-AMG1 R&D Services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. Therefore, the deliverables are not separable and, accordingly, the option to license and ARO-AMG1 R&D Services are being treated as a single unit of accounting. The Company has recognized revenue on a straight-line basis from October 1, 2016, through September 30, 2018, as the Company completed the Arrowhead Deliverable during the three months ended September 30, 2018. The Company received an upfront payment of \$5 million due under this agreement in September 2016. The upfront \$5 million payment was initially recorded as Deferred Revenue. During the years ended September 30, 2018 and 2017, \$2.5 million and \$2.5 million of this upfront payment were recognized into Revenue, respectively. This upfront payment has been recognized as Revenue in its entirety as of September 30, 2018.

The Company also entered into a separate services agreement and separate statements of work with Amgen to provide certain services related to process development, manufacturing, materials supply, discovery studies, and other consulting services related to AMG 890 (ARO-LPA) and ARO-AMG1. During the years ended September 30, 2018 and 2017, these work orders generated approximately \$1.0 million and \$1.5 million of Revenue, respectively.

#### Operating Expenses

The analysis below details the operating expenses and discusses the expenditures of the Company within the major expense categories. Certain reclassifications have been made to prior-period operating expense categories to conform to the current period presentation. For purposes of comparison, the amounts for the years ended September 30, 2018 and 2017 are shown in the tables below.

## Research and Development Expenses

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

(in thousands)

|                               | Twelve<br>Months<br>Ended<br>September<br>30, 2018 | % of<br>Expense<br>Category |  | Twelve<br>Months<br>Ended<br>September<br>30, 2017 | % of<br>Expense<br>Category | Increase<br>(Decrease) |            |
|-------------------------------|--|-----------------------------|--|--|-----------------------------|------------------------|------------|
|                               |  |                             |  |  |                             | \$                     | %          |
| Salaries                      | \$ 12,721  | 24 %                        |  | \$ 11,722  | 23 %                        | \$ 999                 | 9 %        |
| Stock compensation            | 2,396  | 5 %                         |  | 2,840  | 6 %                         | (444 )                 | -16 %      |
| In Vivo studies               | 2,705  | 5 %                         |  | 2,513  | 5 %                         | 192                    | 8 %        |
| Drug manufacturing            | 14,336   | 27 %                        |  | 11,229   | 22 %                        | 3,107                  | 28 %       |
| Toxicity/efficacy studies     | 6,294  | 12 %                        |  | 1,768  | 4 %                         | 4,526                  | 256 %      |
| Clinical trials               | 2,935  | 6 %                         |  | 9,163  | 18 %                        | (6,228 )               | -68 %      |
| License, royalty & milestones | 32   | 0 %                         |  | 5  | 0 %                         | 27                     | N/A        |
| Facilities and related        | 2,280  | 4 %                         |  | 2,337  | 5 %                         | (57 )                  | -2 %       |
| Depreciation/amortization     | 4,672  | 9 %                         |  | 4,653  | 9 %                         | 19                     | 0 %        |
| Other R&D                     | 4,598  | 9 %                         |  | 4,674  | 9 %                         | (76 )                  | -2 %       |
| <b>Total</b>                  | <b>\$ 52,969</b>                                   | <b>100 %</b>                |  | <b>\$ 50,904</b>                                   | <b>100 %</b>                | <b>\$ 2,065</b>        | <b>4 %</b> |

Salaries expense increased by \$999,000 from \$11,722,000 during the year ended September 30, 2017 to \$12,721,000 during the current period. The increase in the expense is primarily due to an increase in R&D headcount that has occurred since the Company's reduction in force in late 2016 associated with the discontinuation of our previous clinical candidates.

Stock compensation expense, a non-cash expense, decreased by \$444,000 from \$2,840,000 during the year ended September 30, 2017 to \$2,396,000 during the current period. Stock compensation expense is based upon the valuation of stock options and restricted stock units granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company's stock price on the date of the grant, as well as other assumptions. The decrease in the expense is primarily due to a mix of lower grant date fair values of awards amortizing during the periods due to the Company's stock price at the time of the grants.

In vivo studies expense increased by \$192,000 from \$2,513,000 during the year ended September 30, 2017 to \$2,705,000 during the current period. In vivo studies expense can vary depending on the stage of preclinical candidates, the nature and amount of testing required and the cost variation of different in vivo testing models. The

increase in in vivo studies expense is a result of additional discovery studies being conducted for the Company's potential drug candidates.

Drug manufacturing expense increased by \$3,107,000 from \$11,229,000 during the year ended September 30, 2017 to \$14,336,000 during the current period. The increase in the expense primarily relates to the timing of manufacturing campaigns for ARO-AAT, ARO-HBV, ARO-ANG3 and ARO-APOC3 clinical trials and toxicology studies. We anticipate this expense to increase as the volume of candidates in our pipeline increases and as each candidate progresses through clinical trial phases.

Toxicity/efficacy studies expense increased by \$4,526,000 from \$1,768,000 during the year ended September 30, 2017 to \$6,294,000 during the current period. This category includes IND-enabling toxicology studies as well as post-IND toxicology studies, such as long-term toxicology studies, and other efficacy studies. The increase in the expense primarily relates to toxicology studies for ARO-AAT and ARO-HBV as each candidate progresses through clinical trials. We anticipate this expense to increase as we prepare to enter clinical trials with our other drug candidates.

Clinical trials expense decreased by \$6,228,000 from \$9,163,000 during the year ended September 30, 2017 to \$2,935,000 during the current period. The decrease in the expense is primarily due to the discontinuation of our previous clinical candidates, and the close out of those studies. We anticipate this expense to increase as ARO-AAT progresses through clinical trials and as we prepare to enter clinical trials with our other drug candidates.

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

Facilities expense decreased by \$57,000 from \$2,337,000 during the year ended September 30, 2017 to \$2,280,000 during the current period. This category includes rental costs for our research and development facility in Madison, Wisconsin. The decrease in the expense relates to reduced CAM costs.

Depreciation and amortization expense, was consistent at \$4,653,000 during the year ended September 30, 2017 and \$4,672,000 during the current period. The majority of depreciation and amortization expense relates to depreciation on lab equipment at our Madison research facility. In addition, the Company records depreciation on leasehold improvements at its Madison research facility.

Other research expense decreased by \$76,000 from \$4,674,000 during the year ended September 30, 2017 to \$4,598,000 during the current period. This category includes the following costs to support discovery efforts and the advancement of current drug candidates: in-house laboratory supplies, outsourced labs services, and other miscellaneous research and development expenses. The decrease in the expense primarily relates to a reduction in outsourced lab services as we have expanded our in-house manufacturing capabilities.

#### General & Administrative Expenses

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

(in thousands)

|                               | Twelve<br>Months<br>Ended<br>September<br>30, 2018 | % of<br>Expense<br>Category |  | Twelve<br>Months<br>Ended<br>September<br>30, 2017 | % of<br>Expense<br>Category | Increase<br>(Decrease) |            |
|-------------------------------|--|-----------------------------|--|--|-----------------------------|------------------------|------------|
|                               |  |                             |  |  |                             | \$                     | %          |
| Salaries                      | \$ 6,382   | 33 %                        |  | \$ 5,571   | 32 %                        | \$ 811                 | 15 %       |
| Stock compensation            | 6,059  | 32 %                        |  | 5,052  | 29 %                        | 1,007                  | 20 %       |
| Professional/outside services | 4,331  | 23 %                        |  | 4,660  | 27 %                        | (329 )                 | -7 %       |
| Facilities related            | 727  | 4 %                         |  | 890  | 5 %                         | (163 )                 | -18%       |
| Depreciation/amortization     | 27   | 0 %                         |  | 38   | 0 %                         | (11 )                  | -29%       |
| Other G&A                     | 1,584  | 8 %                         |  | 1,288  | 7 %                         | 296                    | 23 %       |
| <b>Total</b>                  | <b>\$ 19,110</b>                                   | <b>100 %</b>                |  | <b>\$ 17,499</b>                                   | <b>100 %</b>                | <b>\$ 1,611</b>        | <b>9 %</b> |

Salaries expense increased by \$811,000 from \$5,571,000 during the year ended September 30, 2017 to \$6,382,000 during the current period. The increase in the expense is primarily driven by annual merit increases, performance bonuses and increased headcount.

Stock compensation expense increased by \$1,007,000 from \$5,052,000 during the year ended September 30, 2017 to \$6,059,000 during the current period. Stock compensation expense is based upon the valuation of stock options and restricted stock units granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company's stock price on the date of the grant, as well as other assumptions. The increase in the expense is primarily due to the achievement of certain performance-based awards during the current period.

Professional/outside services include legal, accounting, consulting, patent expenses, business insurance expenses and other outside services retained by the Company. Professional/outside services expense decreased by \$329,000 from \$4,660,000 during the year ended September 30, 2017 to \$4,331,000 during the current period. The decrease in the expense is primarily related to reduced legal expenses on our outstanding litigation cases.

Facilities-related expense decreased \$163,000 from \$890,000 during the year ended September 30, 2017 to \$727,000 during the current period. This category primarily includes rental costs for our corporate headquarters in Pasadena, California. However, the decrease in the expense is primarily related to moving expenses incurred in the previous period associated with our research facility in Madison, Wisconsin.

Depreciation and amortization expense, a noncash expense, was relatively minor in each of the periods. The majority of general and administrative depreciation and amortization expense relates to depreciation on leasehold improvements at our Pasadena headquarters.

Other G&A expense increased by \$296,000 from \$1,288,000 during the year ended September 30, 2017 to \$1,584,000 during the current period. This category consists primarily of travel, communication and technology, office expenses, and franchise and property tax expenses. The increase in the expense was due to various travel and communication and technology expenses.

#### Other Income / Expense

Other income / expense was income of \$2,618,014 during the year ended September 30, 2017 as compared to income of \$1,488,157 during the current period. The largest component of other income / expense in the current period was interest income of \$1.0 million earned on the Company's short-term investments. The largest component of other income / expense in the previous period was \$1.3 million in other income due to an insurance settlement related to one of the Company's recent litigation cases. The settlement amount was received in fiscal 2017. The other significant component of other income / expense is related to the change in the value of derivative liabilities related to certain warrants with a price adjustment feature, which requires derivative accounting. The change in value of derivative liabilities was an income of approximately \$0.9 million in 2017 and an income of approximately \$0.4 million in the current period. The fluctuations in each period were primarily driven by changes in the Company's stock price, which had a corresponding impact on the valuation of the underlying warrant liability.

#### Results of Operations Comparison for 2017 and 2016

##### Revenues

Total revenue was \$31,407,709 for the year ended September 30, 2017 and \$158,333 for the year ended September 30, 2016. Revenue during the year ended September 30, 2017 is primarily related to the upfront payments received from Amgen that we are recognizing as performance is completed for the AMG 890 (ARO-LPA) and ARO-AMG1 agreements

Under the terms of the AMG 890 (ARO-LPA) Agreement, the Company has granted a worldwide, exclusive license to AMG 890 (ARO-LPA). The Company is also responsible for assisting Amgen in the oversight of certain development and manufacturing activities (the "AMG 890 (ARO-LPA) R&D Services"), most of which are to be covered at Amgen's cost. The Company has determined that the significant deliverables under the AMG 890 (ARO-LPA) Agreement include the license and the AMG 890 (ARO-LPA) R&D Services. The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and the AMG 890 (ARO-LPA) R&D Services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. Therefore, the deliverables are not separable and, accordingly, the license and the AMG 890 (ARO-LPA) R&D Services are being treated as a single unit of accounting. The Company recognized revenue on a straight-line basis from November 18, 2016 (the Hart-Scott-Rodino clearance date), through October 31, 2017, which was the date where the AMG 890 (ARO-LPA) R&D Services were substantially completed. The Company received the upfront payment of \$30 million due under this agreement in November 2016. The initial \$30 million payment was recorded as Deferred Revenue, and \$27.3 million of this was amortized into Revenue during the year ended September 30, 2017.

Under the terms of the ARO-AMG1 Agreement, the Company has granted an option to a worldwide, exclusive license to ARO-AMG1, an undisclosed genetically validated cardiovascular target. The Company is also responsible for developing, optimizing and manufacturing the candidate through certain preclinical efficacy and toxicology studies to determine whether the candidate the Company has developed meets the required criteria as defined in the agreement (the "Arrowhead Deliverable"). The Company delivered the candidate in August 2018 and Amgen currently has the option to an exclusive license for the intellectual property generated through the Company's development efforts. If Amgen exercises its option, it would likely assume all development, regulatory and commercialization efforts for the



candidate. The Company determined that the significant deliverables under the ARO-AMG1 Agreement include the option to license and the development and manufacturing activities toward achieving the Arrowhead Deliverable (the “ARO-AMG1 R&D Services”). The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the option to license and ARO-AMG1 R&D Services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. Therefore, the deliverables are not separable and, accordingly, the option to license and ARO-AMG1 R&D Services are being treated as a single unit of accounting. The Company has recognized revenue on a straight-line basis from October 1, 2016, through September 30, 2018, as the Company completed the Arrowhead Deliverable during the three months ended September 30, 2018. The Company received an upfront payment of \$5 million due under this agreement in September 2016. The upfront \$5 million payment was initially recorded as Deferred Revenue. The initial \$5 million payment was recorded as Deferred Revenue, and \$2.5 million of this was amortized into Revenue during the year ended September 30, 2017.

In January 2017, the Company also entered into a separate services agreement with Amgen to provide certain services related to process development, manufacturing, materials supply, discovery studies, and other consulting services related to AMG 890 (ARO-LPA). During the year ended September 30, 2017, work orders under this services agreement generated approximately \$1.5 million of Revenue.

## Operating Expenses

The analysis below details the operating expenses and discusses the expenditures of the Company within the major expense categories. Certain reclassifications have been made to prior-period operating expense categories to conform to the current period presentation. For purposes of comparison, the amounts for the years ended September 30, 2017 and 2016 are shown in the tables below.

## Research and Development Expenses

R&D expenses are related to the Company's on-going research and development efforts, primarily related to program costs, composed primarily of outsourced costs related to the manufacturing of clinical supplies, toxicity/efficacy studies and clinical trial expenses. Internal costs primarily relate to operations at our research and development facility in Madison, Wisconsin, including facility costs and laboratory-related expenses. The following table provides details of research and development expense for the periods indicated:

(in thousands)

|                               | Twelve<br>Months<br>Ended<br>September<br>30, 2017 | % of<br>Expense<br>Category | %        | Twelve<br>Months<br>Ended<br>September<br>30, 2016 | % of<br>Expense<br>Category | %        | Increase<br>(Decrease)<br>\$ | %            |
|-------------------------------|--|-----------------------------|----------|--|-----------------------------|----------|------------------------------|--------------|
| Salaries                      | \$ 11,722  | 23                          | %        | \$ 13,883  | 22                          | %        | \$(2,161 )                   | -16 %        |
| Stock compensation            | 2,840  | 6                           | %        | 3,548  | 6                           | %        | (708 )                       | -20 %        |
| In Vivo studies               | 2,513  | 5                           | %        | 1,631  | 3                           | %        | 882                          | 54 %         |
| Drug manufacturing            | 11,229   | 22                          | %        | 9,855  | 16                          | %        | 1,374                        | 14 %         |
| Toxicity/efficacy studies     | 1,768  | 3                           | %        | 7,766  | 12                          | %        | (5,998 )                     | -77 %        |
| Clinical trials               | 9,163  | 18                          | %        | 14,708   | 24                          | %        | (5,545 )                     | -38 %        |
| License, royalty & milestones | 2  | 0                           | %        | 3,057  | 5                           | %        | (3,055 )                     | N/A          |
| Facilities and related        | 2,337  | 5                           | %        | 1,315  | 2                           | %        | 1,022                        | 78 %         |
| Depreciation/amortization     | 4,653  | 9                           | %        | 3,232  | 5                           | %        | 1,421                        | 44 %         |
| Other R&D                     | 4,677  | 9                           | %        | 3,123  | 5                           | %        | 1,554                        | 50 %         |
| <b>Total</b>                  | <b>\$ 50,904</b>                                   | <b>100</b>                  | <b>%</b> | <b>\$ 62,118</b>                                   | <b>100</b>                  | <b>%</b> | <b>\$(11,214)</b>            | <b>-18 %</b> |

Salaries expense decreased by \$2,161,000 from \$13,883,000 during the year ended September 30, 2016 to \$11,722,000 during the year ended September 30, 2017. The decrease in the expense is primarily due to a reduction in force in late 2016 associated with the discontinuation of our previous clinical candidates.

Stock compensation expense, a non-cash expense, decreased by \$708,000 from \$3,548,000 during the year ended September 30, 2016 to \$2,840,000 during the year ended September 30, 2017. Stock compensation expense is based upon the valuation of stock options and restricted stock units granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company's stock price on the date of the grant, as well as other assumptions. The decrease in the expense is primarily due to a mix of lower grant date fair values of awards amortizing during the periods due to the Company's stock price at the time of the grants.

In vivo studies expense increased \$882,000 from \$1,631,000 during the year ended September 30, 2016 to \$2,513,000 during the year ended September 30, 2017. In vivo expense can vary depending on the stage of preclinical candidates, the nature and amount of testing required and the varying costs of different in vivo testing models. The increase in the expense is a result of additional discovery studies conducted for the Company's potential drug candidates.

Drug manufacturing expense increased \$1,374,000 from \$9,855,000 during the year ended September 30, 2016 to \$11,229,000 during the year ended September 30, 2017. The increase primarily relates to campaigns for the ARO-AAT and ARO-HBV candidates conducted during the year ended September 30, 2017 compared to campaigns ongoing for our previous clinical candidates to the previous period.

Toxicity/efficacy studies expense decreased \$5,998,000 from \$7,766,000 during the year ended September 30, 2016 to \$1,768,000 during the year ended September 30, 2017. This category includes IND-enabling toxicology studies, post-IND toxicology studies, such as long-term toxicology studies, and other efficacy studies. The decrease primarily relates to toxicology studies related to one of our discontinued drug candidates, ARC-521.

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Clinical trials expense decreased \$5,545,000 from \$14,708,000 during the year ended September 30, 2016 to \$9,163,000 during the year ended September 30, 2017. The decrease is primarily due to the discontinuation of our previous clinical candidates, and the close out of those studies.

License, royalty and milestones expense decreased \$3,055,000 from \$3,057,000 during the year ended September 30, 2016 to \$2,000 during the year ended September 30, 2017. This category can include milestone payments which can vary from period to period depending on the nature of our various license agreements and the timing of reaching various development milestones requiring payment. We reached milestones related to our clinical candidates that required a \$3 million payment in fiscal 2016 and did not reach any during fiscal 2017.

Facilities expense increased \$1,022,000 from \$1,315,000 during the year ended September 30, 2016 to \$2,337,000 during the year ended September 30, 2017. The increase relates to increased rental costs for our lease for a larger facility in Madison, Wisconsin, which we began occupying in October 2016.

Depreciation and amortization expense, a non-cash expense, increased \$1,421,000 from \$3,232,000 during the year ended September 30, 2016 to \$4,653,000 during the year ended September 30, 2017. The majority of depreciation and amortization expense relates to depreciation on lab equipment at our Madison research facility. In addition, the Company records depreciation on leasehold improvements at its Madison research facility. The increase in the expense is primarily due to the depreciation on leasehold improvements at the Company's new Madison, Wisconsin research facility.

Other research expense increased \$1,554,000 from \$3,123,000 during the year ended September 30, 2016 to \$4,677,000 during the year ended September 30, 2017. The increase primarily relates to additional miscellaneous supplies purchased to support efforts at our larger facility in Madison, Wisconsin.

#### General & Administrative Expenses

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

(in thousands)

|                               | Twelve<br>Months<br>Ended<br>September<br>30, 2017 | % of<br>Expense<br>Category |  | Twelve<br>Months<br>Ended<br>September<br>30, 2016 | % of<br>Expense<br>Category | Increase<br>(Decrease) |              |
|-------------------------------|--|-----------------------------|--|--|-----------------------------|------------------------|--------------|
|                               |  |                             |  |  |                             | \$                     | %            |
| Salaries                      | \$ 5,571   | 32 %                        |  | \$ 5,579   | 24 %                        | \$(8 )                 | 0 %          |
| Stock compensation            | 5,052  | 29 %                        |  | 8,048  | 34 %                        | (2,996)                | -37 %        |
| Professional/outside services | 4,660  | 27 %                        |  | 6,362  | 27 %                        | (1,702)                | -27 %        |
| Facilities related            | 890  | 5 %                         |  | 622  | 3 %                         | 268                    | 43 %         |
| Depreciation/amortization     | 38   | 0 %                         |  | 28   | 0 %                         | 10                     | 36 %         |
| Other G&A                     | 1,288  | 7 %                         |  | 2,956  | 13 %                        | (1,668)                | -56 %        |
| <b>Total</b>                  | <b>\$ 17,499</b>                                   | <b>100 %</b>                |  | <b>\$ 23,595</b>                                   | <b>100 %</b>                | <b>\$(6,096)</b>       | <b>-26 %</b> |

Salaries expense was consistent at \$5,579,000 for the year ended September 30, 2016 and \$5,571,000 for the year ended September 30, 2017.

Stock compensation expense, a non-cash expense, decreased by \$2,996,000 from \$8,048,000 during the year ended September 30, 2016 to \$5,052,000 during the year ended September 30, 2017. Stock compensation expense is based upon the valuation of stock options and restricted stock units granted to employees, directors, and certain consultants. Many variables affect the amount expensed, including the Company's stock price on the date of the grant, as well as other assumptions. The decrease in the expense is primarily due to a mix of lower grant date fair values of awards amortizing during the periods due to the Company's stock price at the time of the grants.

Professional/outside services include legal, accounting, consulting, patent expenses, business insurance expenses and other outside services retained by the Company Professional/outside services expense decreased \$1,702,000 from \$6,362,000 during the year ended September 30, 2016 to \$4,660,000 during the year ended September 30, 2017. The decrease in professional fees primarily related to legal fees related to previous litigation events.

Facilities-related expense increased \$268,000 from \$622,000 during the year ended September 30, 2016 to \$890,000 in the year ended September 30, 2017. This category primarily includes rental costs for our corporate headquarters in Pasadena, California. However, the increase in the expense is primarily related to moving expenses incurred in the previous period associated with our research facility in Madison, Wisconsin.

Depreciation and amortization expense, a noncash expense, was relatively minor in each of the periods. The majority of general and administrative depreciation and amortization expense relates to depreciation on leasehold improvements at our Pasadena headquarters.

Other expense decreased \$1,668,000 from \$2,956,000 during the year ended September 30, 2016 to \$1,288,000 during the year ended September 30, 2017. This category consists primarily of conference attendance fees, franchise and property tax expenses and marketing expenses. The decrease in other expense relates to litigation in the fiscal 2016 period that was settled.

#### Other Income / Expense

Other income / expense was income of \$22,124 during the year ended September 30, 2016 as compared to income of \$2,618,014 during the year ended September 30, 2017. The largest component of other income / expense in the year ended September 30, 2017 was \$1.3 million in other income due to an insurance settlement related to one of the Company's recent litigation cases. The settlement amount was received in fiscal 2017. The other significant component of other income / expense is related to the change in the value of derivative liabilities related to certain warrants with a price adjustment feature, which requires derivative accounting. The change in value of derivative liabilities was an expense of approximately \$0.3 million in 2016 and an income of approximately \$0.9 million in the year ended September 30, 2017. The fluctuations in each period were primarily driven by changes in the Company's stock price, which had a corresponding impact on the valuation of the underlying warrant liability

#### Liquidity and Cash Resources

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

At September 30, 2018, the Company had cash on hand of approximately \$30.1 million as compared to \$24.8 million at September 30, 2017. Excess cash invested in fixed income securities was \$46.4 million at September 30, 2018, compared to \$40.8 million at September 30, 2017. The Company believes its current financial resources are sufficient to fund its operations through at least the next twelve months.

A summary of cash flows for the years ended September 30, 2018, 2017, and 2016 is as follows:

|                                 | Year ended September 30, |                |                |
|---------------------------------|--------------------------|----------------|----------------|
|                                 | 2018                     | 2017           | 2016           |
| Cash Flow from:                 |                          |                |                |
| Operating Activities            | \$(47,223,417)           | \$(23,938,972) | \$(64,427,486) |
| Investing Activities            | (7,434,963 )             | (48,644,218)   | 13,447,763     |
| Financing Activities            | 59,953,026               | 12,055,309     | 55,131,817     |
| Net increase (decrease) in cash | 5,294,646                | (60,527,881)   | 4,152,094      |
| Cash at beginning of period     | 24,838,567               | 85,366,448     | 81,214,354     |
| Cash at end of period           | \$30,133,213             | \$24,838,567   | \$85,366,448   |

During the year ended September 30, 2018, the Company used \$47.2 million in cash from operating activities, which was primarily related to \$57.2 million used for the on-going expenses of its research and development programs and general and administrative expenses, offset by the \$10 million milestone payment for the AMG 890 (ARO-LPA) Agreement with Amgen. Cash used in investing activities was \$7.4 million, which was primarily related to maturities

of fixed-income investments of \$46.1 million offset by purchases of fixed-income securities of \$52.1 million. Cash provided by financing activities of \$60.0 million was driven by the \$56.6 million of cash generated from the underwritten public offering in January 2018.

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

During the year ended September 30, 2016, the Company used \$64.4 million in cash from operating activities, which represents the on-going expenses of its research and development programs and corporate overhead. Cash outlays were primarily composed of the following: research and development costs were \$42.6 million, salary and payroll-related expenses were \$16.4 million and general and administrative costs were \$9.9 million. These expenditures were partially offset by \$5 million received under the First Collaboration and License Agreement with Amgen. Cash provided by investing activities was \$13.4 million, primarily related to the maturity of certain marketable securities of \$17.3 million partially offset by capital expenditures of \$3.9 million. Cash provided by financing activities of \$55.1 million primarily includes an equity financing in August 2016, which yielded net proceeds of \$43.2 million to the Company, and \$9 million of equity investments from the Company's Common Stock Purchase Agreement with Amgen.

### Contractual Obligations

In the table below, we set forth our enforceable and legally binding obligations and future commitments at September 30, 2018 for the categories shown, as well as obligations related to contracts in such categories that we are likely to continue. Some of the figures that we include in this table are based on management's estimates and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties and other factors. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table. The following table does not include any future obligations that may be owed under existing license agreements, as the certainty of achieving the relevant milestones that would trigger these payments is currently unknown.

|                             | Payments due by Period |                  |              |             |                   |
|-----------------------------|------------------------|------------------|--------------|-------------|-------------------|
|                             | Total                  | Less than 1 Year | 1-3 Years    | 3-5 Years   | More than 5 Years |
| Long-Term Debt              | 2,101,198              | -                | 498,161      | 574,022     | 1,029,015         |
| Capital Leases              | -                      | -                | -            | -           | -                 |
| Operating Leases            | 9,316,831              | 1,435,409        | 2,114,927    | 2,221,613   | 3,544,882         |
| Purchase Obligations        | 27,500,000             | 20,051,000       | 7,449,000    | -           | -                 |
| Other Long-Term Liabilities | 1,902,801              | 307,335          | 424,319      | 424,319     | 746,828           |
| Total                       | \$40,820,830           | \$21,793,744     | \$10,486,407 | \$3,219,954 | \$5,320,725       |

### Off-Balance Sheet Arrangements

As of September 30, 2018, we did not have any off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of SEC Regulation S-K.

### Recent Accounting Pronouncements

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



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

We are exposed to market risk related to changes in interest rates, which could adversely affect the value of our interest rate-sensitive assets and liabilities. We do not hold any instruments for trading purposes and investment criteria are governed by the Company's Investment Policy. As of September 30, 2018 and 2017, we had cash and cash equivalents of \$30.1 million and \$24.8 million, respectively, and investments of \$46.4 million and \$40.8 million, respectively. At times, we have invested our cash reserves in corporate bonds typically with maturities of less than 2 years, and we have historically classified these investments as held-to-maturity. Due to the relatively short-term nature of the investments that we hold, we do not believe that the results of operations or cash flows would be affected to any significant degree by a sudden change in market interest rates relative to our investment portfolio.

## ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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

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

None.

## ITEM 9A. CONTROLS AND PROCEDURES.

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

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

Management's Annual Report on Internal Control over Financial Reporting

Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the United States. This process includes those policies and procedures that (i) pertain to the maintenance of records that, in

reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

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

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

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

has concluded that its internal control over financial reporting was effective as of September 30, 2018 to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with GAAP. The Company's independent registered public accounting firm, Rose, Snyder and Jacobs LLP, has issued an audit report on the Company's internal control over financial reporting, which appears in Item 15 of this Form 10-K.

#### Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting that occurred during the fourth quarter of the year ended September 30, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

#### ITEM 9B. OTHER INFORMATION

None.

### PART III

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

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2019 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2019.

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

#### ITEM 11. EXECUTIVE COMPENSATION

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2019 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2019.

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

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2019 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2019.

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

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2019 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2019.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information called for by this Item will be incorporated by reference from our Definitive Proxy Statement to be filed for our 2019 Annual Meeting of Stockholders, which proxy statement will be filed no later than January 28, 2019.

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.

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(2) Financial Statement Schedules.

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

(3) Exhibits.

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

| Exhibit Number | Description   | Incorporated by Reference Herein Form   | Date              |
|----------------|---|---|-------------------|
| 2.1            | <u>Stock and Asset Purchase Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011</u> †   | Annual Report on Form 10-K for the fiscal year ended September 30, 2011, as Exhibit 2.1 | December 20, 2011 |
| 2.2            | <u>Asset Purchase and Exclusive License Agreement between Arrowhead Research Corporation and Novartis Institutes for BioMedical Research, Inc., dated March 3, 2015</u> †                       | Quarterly Report on Form 10-Q, May 11, 2015 as Exhibit 2.1                              |                   |
| 3.1            | <u>Amended and Restated Certificate of Incorporation of Arrowhead Research Corporation, a Delaware corporation, filed with the Secretary of State of the State of Delaware on April 5, 2016</u> | Current Report on Form 8-K as Exhibit 3.3   | April 6, 2016     |
| 3.2            | <u>Amended and Restated Bylaws of Arrowhead Pharmaceuticals, Inc.</u>   | Current Report on form 8-K as Exhibit 3.4   | April 6, 2016     |
| 4.1            | <u>Form of Warrant to Purchase Shares of Common Stock expiring December 12, 2017</u>  | Current Report on Form 8-K, as exhibit 4.2  | December 12, 2012 |
| 4.2            | <u>Form of Warrant to Purchase Shares of Common Stock expiring January 30, 2018</u>   | Current Report on Form 8-K, as exhibit 4.2  | January 30, 2013  |
| 4.3            | <u>Form of Common Stock Certificate of Arrowhead Pharmaceuticals, Inc.</u>  | Current Report on Form 8-K, as Exhibit 4.1  | April 6, 2016     |
| 4.4            | <u>Form of Indenture</u>  | Registration Statement on Form S-3 (File No. 333-214315)                                | October 28, 2016  |
| 4.5            | <u>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</u>      | Current Report on Form 8-K, as Exhibit 4.1  | March 23, 2017    |
| 10.1**         | <u>Arrowhead Research Corporation (fka InterActive, Inc.) 2000 Stock Option Plan</u>  | Schedule 14C, as Exhibit D  | December 22, 2000 |

|        |   |   |                   |
|--------|---|---|-------------------|
| 10.2** | <u>Arrowhead Research Corporation 2004 Equity Incentive Plan, as amended</u>        | Schedule 14C, as Annex B                    | January 12, 2012  |
| 10.3** | <u>Arrowhead Research Corporation 2013 Incentive Plan</u>                           | Schedule 14C, as Annex A                    | December 20, 2013 |
| 10.4** | <u>Form of Stock Option Agreement for use with the 2013 Incentive Plan</u>          | Current Report on Form 8-K, as Exhibit 10.1 | February 12, 2014 |
| 10.5** | <u>Form of Restricted Stock Unit Agreement for use with the 2013 Incentive Plan</u> | Current Report on Form 8-K, as Exhibit 10.2 | February 12, 2014 |

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| Exhibit Number | Description  | Incorporated by Reference Herein Form   | Date              |
|----------------|--|---|-------------------|
| 10.6**         | <u>Executive Incentive Plan, adopted December 12, 2006</u>   | Annual Report on Form 10-K for the fiscal year ended September 30, 2006, as Exhibit 10.11 | December 14, 2006 |
| 10.7**         | <u>Employment Agreement between Arrowhead and Dr. Christopher Anzalone, dated June 11, 2008</u>  | Current Report on Form 8-K, as Exhibit 10.1   | June 13, 2008     |
| 10.8**         | <u>Amendment to Employment Agreement between Arrowhead and Dr. Christopher Anzalone, effective May 12, 2009</u>  | Annual Report on Form 10-K for the fiscal year ended September 30, 2009, as Exhibit 10.8  | December 22, 2009 |
| 10.9           | <u>Non-Exclusive License Agreement between Arrowhead Research Corporation and Roche entities, dated October 21, 2011†</u>                                  | Annual Report on Form 10-K for the fiscal year ended September 30, 2011, as Exhibit 10.33 | December 20, 2011 |
| 10.10          | <u>Collaboration Agreement by and among Alnylam Pharmaceuticals, Inc. and F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc., dated October 29, 2009 †</u> | Annual Report on Form 10-K for the fiscal year ended September 30, 2011, as Exhibit 10.36 | December 20, 2011 |
| 10.11          | <u>Office Lease Agreement between South Lake Avenue Investors LLC and the Company, dated April 12, 2012</u>  | Quarterly Report on Form 10-Q, as Exhibit 10.1  | May 8, 2012       |
| 10.12          | <u>License Agreement by and between Alnylam Pharmaceuticals, Inc., Arrowhead Research Corporation and Arrowhead Madison, Inc.†</u>                         | Quarterly Report on Form 10-Q, as Exhibit 10.1  | August 12, 2014   |
| 10.13          | <u>Lease Agreement between University Research Park, Incorporated and Arrowhead Madison, Inc., dated January 8, 2016</u>                                   | Quarterly Report on Form 10-Q, as Exhibit 10.1  | February 9, 2016  |
| 10.14          | <u>Securities Purchase Agreement between the Company and the purchasers listed thereon, dated August 8, 2016</u>   | Current Report on Form 8-K, as Exhibit 10.1   | August 10, 2016   |
| 10.15          | <u>First Collaboration and Licensing Agreement between Arrowhead Pharmaceuticals, Inc. and Amgen Inc., dated September 28, 2016†</u>                       | Annual Report on Form 10-K for the fiscal year ended September 30, 2016, as Exhibit 10.18 | December 14, 2016 |
| 10.16          | <u>Second Collaboration and Licensing Agreement between Arrowhead Pharmaceuticals, Inc. and Amgen Inc., dated September 28, 2016†</u>                      | Annual Report on Form 10-K for the fiscal year ended September 30, 2016, as Exhibit 10.19 | December 14, 2016 |
| 10.17          | <u>Common Stock Purchase Agreement between the Company and Amgen Inc., dated September 28, 2016</u>  | Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-214311)           | November 25, 2016 |
| 21.1           | <u>List of Subsidiaries*</u>   |   |                   |

23.1 Consent of Independent Public Registered Accounting Firm\*

24.1 Power of Attorney (contained on signature page)

31.1 Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002\*

31.2 Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002\*

32.1 Certification by Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002\*\*\*

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

\* Filed herewith

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

\*\*\*Furnished herewith

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

#### SIGNATURE

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, on this 11th day of December 2018.

Dated: December 11, 2018

ARROWHEAD  
PHARMACEUTICALS,  
INC.

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



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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<br>Christopher Anzalone   | Chief Executive Officer, President and<br>Director (Principal Executive Officer) | December<br>11, 2018 |
| /s/ Kenneth A. Myszkowski<br>Kenneth A. Myszkowski | Chief Financial Officer (Principal<br>Financial and Accounting Officer)          | December<br>11, 2018 |
| /s/ Douglass Given<br>Douglass Given               | Director, Chairman of the Board of Directors                                     | December<br>11, 2018 |
| /s/ Mauro Ferrari<br>Mauro Ferrari                 | Director   | December<br>11, 2018 |
| /s/ Michael S. Perry<br>Michael S. Perry           | Director   | December<br>11, 2018 |
| /s/ William Waddill<br>William Waddill             | Director   | December<br>11, 2018 |

INDEX TO FINANCIAL STATEMENTS AND SCHEDULE

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| <u>Consolidated Statements of Operations and Comprehensive Loss of Arrowhead Pharmaceuticals, Inc. for the years ended September 30, 2018, 2017 and 2016</u> | F-5 |
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| <u>Notes to Consolidated Financial Statements of Arrowhead Pharmaceuticals, Inc.</u>   | F-8 |

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Arrowhead Pharmaceuticals, Inc. and subsidiaries (the Company) as of September 30, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended September 30, 2018, and the related notes (collectively referred to as the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of September 30, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the three-year period ended September 30, 2018, in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of September 30, 2018, based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated December 11, 2018, expressed an unqualified opinion.

Basis for Opinion

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

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

Rose, Snyder &  
Jacobs LLP

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

Encino, California

December 11, 2018

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on Internal Control over Financial Reporting

We have audited Arrowhead Pharmaceuticals, Inc. and subsidiaries (the Company's) internal control over financial reporting as of September 30, 2018, based on criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of September 30, 2018, based on criteria established in Internal Control—Integrated Framework (2013) issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the balance sheet and the related statements of operations and comprehensive loss, stockholders' equity, and cash flows of the Company, and our report dated December 11, 2018 expressed an unqualified opinion.

Basis for Opinion

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

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

Definition and Limitations of Internal Control over Financial Reporting

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

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

Rose, Snyder &  
Jacobs LLP

Encino, California

December 11, 2018

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## PART I. FINANCIAL INFORMATION

## ITEM 1. FINANCIAL STATEMENTS

Arrowhead Pharmaceuticals, Inc.

## Consolidated Balance Sheets

|  | September 30,<br>2018 | September 30,<br>2017 |
|--|-----------------------|-----------------------|
| <b>ASSETS</b>  |                       |                       |
| <b>CURRENT ASSETS</b>  |                       |                       |
| Cash and cash equivalents  | \$30,133,213          | \$24,838,567          |
| Accounts receivable  | 327,375               | 67,797                |
| Prepaid expenses   | 1,267,717             | 867,363               |
| Other current assets   | 640,117               | 1,359,638             |
| Short term investments   | 46,400,176            | 40,769,539            |
| <b>TOTAL CURRENT ASSETS</b>  | <b>78,768,598</b>     | <b>67,902,904</b>     |
| Property and equipment, net  | 13,935,425            | 15,513,019            |
| Intangible assets, net   | 18,764,010            | 20,464,439            |
| Other assets   | 141,918               | 141,918               |
| <b>TOTAL ASSETS</b>  | <b>\$111,609,951</b>  | <b>\$104,022,280</b>  |
| <b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>  |                       |                       |
| <b>CURRENT LIABILITIES</b>   |                       |                       |
| Accounts payable   | \$2,806,098           | \$4,076,514           |
| Accrued expenses   | 5,043,087             | 4,564,507             |
| Accrued payroll and benefits   | 3,937,605             | 3,399,679             |
| Deferred rent  | 307,334               | 440,580               |
| Deferred revenue   | 600                   | 5,269,741             |
| Derivative liabilities   | -                     | 695,114               |
| Note Payable   | 223,820               | 208,506               |
| Other current liabilities  | 46,407                | 46,407                |
| <b>TOTAL CURRENT LIABILITIES</b>   | <b>12,364,951</b>     | <b>18,701,048</b>     |
| <b>LONG-TERM LIABILITIES</b>   |                       |                       |
| Deferred rent, net of current portion  | 1,702,801             | 1,929,052             |
| Note Payable, net of current portion   | 2,101,198             | 2,325,018             |
| Other non-current liabilities  | 200,000               | 200,000               |
| <b>TOTAL LONG-TERM LIABILITIES</b>   | <b>4,003,999</b>      | <b>4,454,070</b>      |
| Commitments and contingencies (Note 7)   |                       |                       |
| <b>STOCKHOLDERS' EQUITY</b>  |                       |                       |
| Arrowhead Pharmaceuticals, Inc. stockholders' equity:  |                       |                       |
| Common stock, \$0.001 par value; 145,000,000 shares authorized; 88,505,302 and 74,785,726 shares |                       |                       |
| issued and outstanding as of September 30, 2018 and September 30, 2017, respectively             | 180,875               | 167,155               |
| Additional paid-in capital   | 582,902,694           | 514,037,301           |
| Accumulated other comprehensive income (loss)  | (21,564)              | 33,232                |
| Accumulated deficit  | (487,265,816)         | (432,815,338)         |

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|  |                       |                       |
|--|-----------------------|-----------------------|
| Total Arrowhead Pharmaceuticals, Inc. stockholders' equity | 95,796,189            | 81,422,350            |
| Noncontrolling interest                                    | (555,188 )            | (555,188 )            |
| <b>TOTAL STOCKHOLDERS' EQUITY</b>                          | <b>95,241,001</b>     | <b>80,867,162</b>     |
| <b>TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY</b>          | <b>\$ 111,609,951</b> | <b>\$ 104,022,280</b> |

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

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Arrowhead Pharmaceuticals, Inc.

## Consolidated Statements of Operations and Comprehensive Loss

|   | Year Ended September 30 |                |                |
|---|-------------------------|----------------|----------------|
|   | 2018                    | 2017           | 2016           |
| REVENUE   | \$16,142,321            | \$31,407,709   | \$158,333      |
| OPERATING EXPENSES                                      |                         |                |                |
| Research and development                                | 52,968,505              | 50,904,466     | 62,117,818     |
| General and administrative expenses                     | 19,110,051              | 17,499,152     | 23,594,888     |
| Impairment expense                                      | -                       | -              | 2,050,817      |
| Contingent consideration - fair value adjustments       | -                       | -              | (5,862,464 )   |
| TOTAL OPERATING EXPENSES                                | 72,078,556              | 68,403,618     | 81,901,059     |
| OPERATING LOSS  | (55,936,235)            | (36,995,909)   | (81,742,726)   |
| OTHER INCOME (EXPENSE)                                  |                         |                |                |
| Interest income (expense), net                          | 1,048,523               | 415,128        | 265,794        |
| Change in value of derivatives                          | 432,141                 | 890,362        | (301,022 )     |
| Other income (expense)                                  | 7,493                   | 1,312,524      | 57,352         |
| TOTAL OTHER INCOME (EXPENSE)                            | 1,488,157               | 2,618,014      | 22,124         |
| LOSS BEFORE INCOME TAXES                                | (54,448,078)            | (34,377,895)   | (81,720,602)   |
| Provision for income taxes                              | (2,400 )                | (2,400 )       | (2,400 )       |
| NET LOSS  | (54,450,478)            | (34,380,295)   | (81,723,002)   |
| NET LOSS PER SHARE - BASIC & DILUTED                    | \$(0.65 )               | \$(0.47 )      | \$(1.34 )      |
| Weighted average shares outstanding - basic and diluted | 83,638,469              | 73,898,598     | 61,050,880     |
| OTHER COMPREHENSIVE INCOME (LOSS), NET OF TAX:          |                         |                |                |
| Foreign Currency Translation Adjustments                | (54,796 )               | 25,783         | 143,874        |
| COMPREHENSIVE LOSS                                      | \$(54,505,274)          | \$(34,354,512) | \$(81,579,128) |

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

Arrowhead Pharmaceuticals, Inc.

## Consolidated Statement of Stockholders' Equity

|  | Preferred<br>Stock | Amount<br>(\$) | Common<br>Stock | Amount<br>(\$) | Additional<br>Paid-In<br>Capital | Accumulated<br>Other<br>Comprehensive<br>Income<br>(loss) | Accumulated<br>Deficit | Non-controlling<br>Interest | Totals        |
|--|--------------------|----------------|-----------------|----------------|----------------------------------|---|------------------------|-----------------------------|---------------|
| Balance at<br>September 30,<br>2015  | 15,652             | \$16           | 59,544,677      | \$151,914      | \$426,873,358                    | \$(136,425)   | \$(316,712,041)        | \$(555,188)                 | \$109,621,634 |
| Exercise of<br>warrants  | -                  | -              | 852,532         | 853            | 3,690,545                        | -   | -                      | -                           | 3,691,398     |
| Exercise of<br>stock options   | -                  | -              | 37,187          | 37             | 133,832                          | -   | -                      | -                           | 133,869       |
| Stock-based<br>compensation  | -                  | -              | -               | -              | 11,595,816                       | -   | -                      | -                           | 11,595,816    |
| Common<br>stock-<br>Restricted<br>Stock Units<br>vesting                               | -                  | -              | 428,187         | 428            | (671,193 )                       | -   | -                      | -                           | (670,765 )    |
| Common<br>stock issued<br>for cash at<br>\$5.90 per<br>share, net of<br>offering costs | -                  | -              | 7,627,119       | 7,627          | 43,223,808                       | -   | -                      | -                           | 43,231,435    |
| Common<br>stock issued to<br>Amgen at<br>\$7.16 per<br>share                           | -                  | -              | 1,256,983       | 1,257          | 8,998,743                        | -   | -                      | -                           | 9,000,000     |
| Foreign<br>currency<br>translation<br>adjustments                                      | -                  | -              | -               | -              | -                                | 143,874   | -                      | -                           | 143,874       |
| Net loss for<br>the year ended<br>September 30,<br>2016                                | -                  | -              | -               | -              | -                                | -   | (81,723,002 )          | -                           | (81,723,002 ) |
| Balance at<br>September 30,<br>2016  | 15,652             | \$16           | 69,746,685      | \$162,116      | \$493,844,909                    | \$7,449   | \$(398,435,043)        | \$(555,188)                 | \$95,024,259  |
| Stock-based<br>compensation  | -                  | -              | -               | -              | 7,891,595                        | -   | -                      | -                           | 7,891,595     |

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|  |          |      |            |           |               |           |                 |             |               |
|--|----------|------|------------|-----------|---------------|-----------|-----------------|-------------|---------------|
| Exercise of stock options                        | -        | -    | 135,730    | 136       | 271,795       | -         | -               | -           | 271,931       |
| Common stock- Restricted Stock Units vesting     | -        | -    | 481,212    | 481       | (403,742 )    | -         | -               | -           | (403,261 )    |
| Common stock issued to Amgen at \$7.16 per share | -        | -    | 1,745,810  | 1,746     | 12,418,254    | -         | -               | -           | 12,420,000    |
| Preferred stock converted to common stock        | (15,652) | (16) | 2,670,989  | 2,671     | (2,655 )      | -         | -               | -           | -             |
| Exchange rights exercised                        | -        | -    | 5,000      | 5         | 17,145        | -         | -               | -           | 17,150        |
| Foreign currency translation adjustments         | -        | -    | -          | -         | -             | 25,783    | -               | -           | 25,783        |
| Net loss for the year ended September 30, 2017   | -        | -    | -          | -         | -             | -         | (34,380,295 )   | -           | (34,380,295 ) |
| Balance at September 30, 2017                    | -        | \$-  | 74,785,426 | \$167,155 | \$514,037,301 | \$33,232  | \$(432,815,338) | \$(555,188) | \$80,867,162  |
| Stock-based compensation                         | -        | -    | -          | -         | 8,454,607     | -         | -               | -           | 8,454,607     |
| Exercise of stock options                        | -        | -    | 604,611    | 605       | 2,656,105     | -         | -               | -           | 2,656,710     |
| Exercise of warrants                             | -        | -    | 288,473    | 288       | 1,237,141     | -         | -               | -           | 1,237,429     |
| Common stock- Restricted Stock Units vesting     | -        | -    | 1,326,792  | 1,327     | (55,995 )     | -         | -               | -           | (54,668 )     |
| Common stock issued at \$5.25 per share          | -        | -    | 11,500,000 | 11,500    | 56,573,535    | -         | -               | -           | 56,585,035    |
| Foreign currency translation adjustments         | -        | -    | -          | -         | -             | (54,796 ) | -               | -           | (54,796 )     |
| Net loss for the year ended                      | -        | -    | -          | -         | -             | -         | (54,450,478 )   | -           | (54,450,478 ) |

September 30,  
2018

|               |   |     |            |           |               |             |                 |             |              |
|---------------|---|-----|------------|-----------|---------------|-------------|-----------------|-------------|--------------|
| Balance at    |   |     |            |           |               |             |                 |             |              |
| September 30, |   |     |            |           |               |             |                 |             |              |
| 2018          | - | \$- | 88,505,302 | \$180,875 | \$582,902,694 | \$(21,564 ) | \$(487,265,816) | \$(555,188) | \$95,241,001 |

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

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Arrowhead Pharmaceuticals, Inc.

## Consolidated Statements of Cash Flows

|   | Year ended September 30, |                     |                     |
|---|--------------------------|---------------------|---------------------|
|   | 2018                     | 2017                | 2016                |
| <b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>  |                          |                     |                     |
| Net loss  | \$(54,450,478)           | \$(34,380,295)      | \$(81,723,002)      |
| Change in value of derivatives  | (432,141 )               | (890,362 )          | 301,022             |
| Contingent consideration - fair value adjustments                                     | -                        | -                   | (5,862,464 )        |
| Noncash impairment expense  | -                        | -                   | 2,050,817           |
| Stock-based compensation  | 8,454,607                | 7,891,595           | 11,595,816          |
| Depreciation and amortization   | 4,699,275                | 4,690,440           | 3,260,045           |
| Amortization/(accretion) of note premiums   | 383,075                  | (43,519 )           | 231,902             |
| <b>Changes in operating assets and liabilities:</b>                                   |                          |                     |                     |
| Accounts receivable   | (259,578 )               | 7,203               | (75,000 )           |
| Prepaid expenses and Other Current Assets   | 319,166                  | 2,814,509           | (1,020,734 )        |
| Deferred revenue  | (5,269,140 )             | 157,981             | 5,000,000           |
| Accounts payable  | (1,270,416 )             | (3,509,995 )        | 2,554,802           |
| Accrued expenses  | 1,016,506                | (401,777 )          | (871,833 )          |
| Other   | (414,293 )               | (274,752 )          | 131,143             |
| <b>NET CASH PROVIDED BY (USED IN) OPERATING ACTIVITIES</b>                            | <b>(47,223,417)</b>      | <b>(23,938,972)</b> | <b>(64,427,486)</b> |
| <b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>  |                          |                     |                     |
| Purchases of property and equipment   | (1,421,252 )             | (7,918,198 )        | (3,860,237 )        |
| Purchases of marketable securities  | (52,083,131)             | (44,974,736)        | -                   |
| Proceeds from sale of marketable securities   | 46,069,420               | 4,248,716           | 17,308,000          |
| <b>NET CASH PROVIDED BY (USED IN) INVESTING ACTIVITIES</b>                            | <b>(7,434,963 )</b>      | <b>(48,644,218)</b> | <b>13,447,763</b>   |
| <b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>  |                          |                     |                     |
| Principal payments on notes payable   | (208,506 )               | (197,790 )          | (217,549 )          |
| Payments of taxes for net share settled restricted stock unit issuances               | (54,667 )                | (438,838 )          | (634,187 )          |
| Proceeds from the exercises of warrants and stock options                             | 3,631,164                | 272,818             | 3,752,120           |
| Proceeds from the issuance of common stock  | 56,585,035               | 12,419,119          | 52,231,433          |
| <b>NET CASH PROVIDED BY (USED IN) FINANCING ACTIVITIES</b>                            | <b>59,953,026</b>        | <b>12,055,309</b>   | <b>55,131,817</b>   |
| <b>NET INCREASE (DECREASE) IN CASH</b>  | <b>5,294,646</b>         | <b>(60,527,881)</b> | <b>4,152,094</b>    |
| <b>CASH AT BEGINNING OF PERIOD</b>  | <b>24,838,567</b>        | <b>85,366,448</b>   | <b>81,214,354</b>   |
| <b>CASH AT END OF PERIOD</b>  | <b>\$30,133,213</b>      | <b>\$24,838,567</b> | <b>\$85,366,448</b> |
| <b>Supplementary disclosures:</b>   |                          |                     |                     |
| Interest Paid   | \$(173,381 )             | \$(187,647 )        | \$(11,287 )         |
| Property and equipment purchased through tenant improvement allowance financing       | \$-                      | \$-                 | \$(4,849,360 )      |
| Property and Equipment expenditures included in accounts payable and accrued expenses | \$-                      | \$-                 | \$(4,801,930 )      |
| Income Tax Credits Refunded   | \$-                      | \$3,635,016         | \$1,365,288         |
| Income Tax Paid   | \$(2,400 )               | \$(2,400 )          | \$(2,400 )          |

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

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Arrowhead Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

(unaudited)

Unless otherwise noted, (1) the term “Arrowhead” refers to Arrowhead Pharmaceuticals, Inc., a Delaware corporation and its Subsidiaries, (2) the terms “Company,” “we,” “us,” and “our,” refer to the ongoing business operations of Arrowhead and its Subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, (3) the term “Subsidiaries” refers collectively to Arrowhead Madison Inc. (“Arrowhead Madison”), Arrowhead Australia Pty Ltd (“Arrowhead Australia”) and Ablaris Therapeutics, Inc. (“Ablaris”), (4) the term “Common Stock” refers to Arrowhead’s Common Stock, (5) the term “Preferred Stock” refers to Arrowhead’s Preferred Stock and (6) the term “Stockholder(s)” refers to the holders of Arrowhead Common Stock.

## NOTE 1. ORGANIZATION AND SIGNIFICANT ACCOUNTING POLICIES

### Nature of Business and Recent Developments

Arrowhead Pharmaceuticals, Inc. develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Deemed to be one of the most important recent discoveries in life science with the potential to transform medicine, the discoverers of RNAi were awarded a Nobel Prize in 2006 for their work. Arrowhead’s RNAi-based therapeutics leverage this natural pathway of gene silencing. The company's pipeline includes ARO-AAT for liver disease associated with alpha-1 antitrypsin deficiency (AATD), ARO-APOC3 for hypertriglyceridemia, ARO-ANG3 for dyslipidemia, ARO-ENaC for cystic fibrosis, and ARO-HIF2 for renal cell carcinoma. ARO-LPA (AMG 890) for cardiovascular disease was out-licensed to Amgen Inc. in 2016. ARO-AMG1 for an undisclosed genetically validated cardiovascular target is under a license and collaboration agreement with Amgen Inc. ARO-HBV for chronic hepatitis B virus was out-licensed to Janssen Pharmaceuticals, Inc. in October 2018.

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

During fiscal 2018, the Company continued to develop its pipeline candidates. In the first half of fiscal 2018, Clinical Trial Applications (CTAs) were filed for ARO-AAT and ARO-HBV, and the associated phase 1 (ARO-AAT) and phase 1 / 2 (ARO-HBV) studies are ongoing. Dosing has completed for the ARO-AAT phase 1 clinical study. In October 2018, the Company also filed a CTA for ARO-ANG3 and, pending approval, the Company anticipates the startup of this study in 2019. The Company has also achieved substantial progress on its other preclinical candidates including ARO-APOC3, ARO-ENaC and ARO-HIF2, with planned CTA or equivalent filings planned in late calendar 2018 for ARO-APOC3 and in 2019 for ARO-ENaC and ARO-HIF2.

The Company also made significant progress on its business development and partnership collaboration efforts. In October 2018, the Company entered into a License Agreement (“Janssen License Agreement”) and a Research Collaboration and Option Agreement (“Janssen Collaboration Agreement” with Janssen Pharmaceuticals, Inc. (“Janssen”)

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

The Company’s collaboration agreements with Amgen also continue to progress as it relates to the AMG 890 (ARO-LPA) and ARO-AMG1 candidates. Under the terms of the agreements taken together, the Company has received \$35 million in upfront payments and \$21.5 million in the form of an equity investment by Amgen in the Company’s Common Stock and could receive up to

\$617 million in option payments and development, regulatory and sales milestone payments. The Company is further eligible to receive single-digit royalties for sales of products under the ARO-AMG1 agreement and up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement. On August 1, 2018, the Company announced that it had earned a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. This milestone payment was recognized as Revenue in its entirety during the year ended September 30, 2018.

## Liquidity

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

At September 30, 2018, the Company had \$30.1 million in cash and \$46.4 million in short-term investments to fund operations. During the year ended September 30, 2018, the Company's cash and investments balance increased by \$10.9 million, which was primarily the result of the \$56.6 million net proceeds received from a public offering of 11,500,000 of shares of Common Stock completed in January 2018, and a \$10 million milestone payment received from Amgen, discussed further below. These cash inflows were mostly offset by cash outflows related to operating activities.

On January 22, 2018, the Company sold 11,500,000 shares of Common Stock in a fully underwritten public offering, at a public offering price of \$5.25 per share. Net proceeds to the Company were approximately \$56.6 million after deducting underwriting commissions and discounts and other offering expenses payable by the Company. The Company believes its current financial resources are sufficient to fund its operations through at least the next twelve months.

In addition to the cash proceeds on hand, in October 2018, the Company entered into the Janssen License Agreement, the Janssen Collaboration Agreement and the JJDC Stock Purchase Agreement which yielded a \$175 million upfront payment received in November 2018 and a \$75 million equity investment received in October 2018. These agreements are discussed further in Note 2 below.

## Summary of Significant Accounting Policies

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

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

**Cash and Cash Equivalents**—The Company considers all liquid debt instruments purchased with a maturity of three months or less to be cash equivalents. The Company had no restricted cash at September 30, 2018 and September 30, 2017.

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

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

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

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

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

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

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

Property and Equipment—Property and equipment are recorded at cost, which may equal fair market value in the case of property and equipment acquired in conjunction with a business acquisition. Depreciation of property and equipment is recorded using the straight-line method over the respective useful lives of the assets ranging from three to seven years. Leasehold improvements are amortized over the lesser of the expected useful life or the remaining lease term. Long-lived assets, including property and equipment are reviewed for impairment whenever events or circumstances indicate that the carrying amount of these assets may not be recoverable.

Intangible Assets Subject to Amortization—Intangible assets subject to amortization include certain patents and license agreements. Intangible assets subject to amortization are reviewed for impairment whenever events or circumstances indicate that the carrying amount of these assets may not be recoverable.

Contingent Consideration - The consideration for the Company's acquisitions may include future payments that are contingent upon the occurrence of a particular event. For example, milestone payments might be based on the achievement of various regulatory approvals or future sales milestones, and royalty payments might be based on drug product sales levels. The Company records a contingent consideration obligation for such contingent payments at fair value on the acquisition date. The Company estimates the fair value of contingent consideration obligations through valuation models designed to estimate the probability of such contingent payments based on various assumptions and incorporating estimated success rates. Estimated payments are discounted using present value techniques to arrive at an estimated fair value at the balance sheet date. Changes in the fair value of the contingent consideration obligations are recognized within the Company's Consolidated Statements of Operations and Comprehensive Loss. Changes in the fair value of the contingent consideration obligations can result from changes to one or multiple inputs, including adjustments to the discount rates, changes in the amount or timing of expected expenditures associated with product development, changes in the amount or timing of cash flows from products upon commercialization, changes in the assumed achievement or timing of any development milestones, changes in the probability of certain clinical events and changes in the assumed probability associated with regulatory approval. These fair value measurements are based on significant inputs not observable in the market. Substantial judgment is employed in determining the appropriateness of these assumptions as of the acquisition date and for each subsequent period. Accordingly, changes in assumptions could have a material impact on the amount of contingent consideration expense the Company records in any given period. The Company determined the fair value of its contingent consideration obligation to be \$0 at September 30, 2018 and September 30, 2017.

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

The Company may generate revenue from technology licenses, collaborative research and development arrangements, research grants and product sales. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable and/or guaranteed technology license fees, collaborative research funding, manufacturing and development services and various milestone and future product royalty or profit-sharing payments. These agreements are generally referred to as multiple element arrangements.

The Company applies the accounting standard on revenue recognition for multiple element arrangements. The fair value of deliverables under the arrangement may be derived using a best estimate of selling price if vendor specific objective evidence and third-party evidence is not available. Deliverables under the arrangement will be separate units of accounting if a delivered item has value to the customer on a standalone basis, if the arrangement includes a general right of return for the delivered item, and if delivery or performance of the undelivered item is considered probable and substantially in the Company's control.

The Company recognizes upfront license payments as revenue upon delivery of the license only if the license is determined to be a separate unit of accounting from the other undelivered performance obligations. The undelivered performance obligations typically include manufacturing or development services or research and/or steering committee services. If the license is not considered to have standalone value, then the license and other undelivered performance obligations would be accounted for as a single unit of accounting. In this case, the license payments and payments for performance obligations are recognized as revenue

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over the estimated period of when the performance obligations are performed or deferred indefinitely until the undelivered performance obligation is determined.

Whenever the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company determines the period over which the performance obligations will be performed, and revenue will be recognized. Revenue is recognized using a proportional performance or straight-line method. The proportional performance method is used when the level of effort required to complete performance obligations under an arrangement can be reasonably estimated. The amount of revenue recognized under the proportional performance method is determined by multiplying the total payments under the contract, excluding royalties and payments contingent upon achievement of milestones, by the ratio of the level of effort performed to date to the estimated total level of effort required to complete performance obligations under the arrangement. If the Company cannot reasonably estimate the level of effort to complete performance obligations under an arrangement, the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. 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 under an arrangement.

The Company's collaboration agreements typically entitle the Company to additional payments upon the achievement of development, regulatory and sales performance-based milestones. If the achievement of a milestone is considered probable at the inception of the collaboration, the related milestone payment is included with other collaboration consideration, such as upfront fees and research funding, in the Company's revenue calculation. Typically, these milestones are not considered probable at the inception of the collaboration. As such, milestones will typically be recognized in one of two ways depending on the timing of when the milestone is achieved. If the milestone is achieved during the performance period, the Company will only recognize revenue to the extent of the proportional performance achieved at that date, or the proportion of the straight-line basis achieved at that date, and the remainder will be recorded as deferred revenue to be amortized over the remaining performance period. If the milestone is achieved after the performance period has completed and all performance obligations have been delivered, the Company will recognize the milestone payment as Revenue in its entirety in the period the milestone was achieved.

Deferred revenue will be classified as part of Current or Long-Term Liabilities in the accompanying Consolidated Balance Sheets based on the Company's estimate of the portion of the performance obligations regarding that revenue will be completed within the next 12 months divided by the total performance period estimate. This estimate is based on the Company's current operating plan and, if the Company's operating plan should change in the future, the Company may recognize a different amount of deferred revenue over the next 12-month period.

The new revenue recognition guidance (ASC 606) was effective as of October 1, 2018, and it will not have a material impact on the Company's Consolidated Financial Statements. Please read the discussion of recent accounting pronouncements for the expected impact of this new accounting guidance.

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

Research and Development—Costs and expenses that can be clearly identified as research and development are charged to expense as incurred in accordance with FASB ASC 730-10. Included in research and development costs are operating costs, facilities, supplies, external services, clinical trial and manufacturing costs, overhead directly related to the Company’s research and development operations, and costs to acquire technology licenses.

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Earnings (Loss) per Share—Basic earnings (loss) per share is computed using the weighted-average number of common shares outstanding during the period. Diluted earnings (loss) per share are computed using the weighted-average number of common shares and dilutive potential common shares outstanding during the period. Dilutive potential common shares primarily consist of stock options and restricted stock units issued to employees and warrants to purchase Common Stock of the Company. All outstanding stock options, restricted stock units and warrants for the years ended September 30, 2018, 2017 and 2016 have been excluded from the calculation of Diluted earnings (loss) per share due to their anti-dilutive effect.

Stock-Based Compensation—The Company accounts for share-based compensation arrangements in accordance with FASB ASC 718, which requires the measurement and recognition of compensation expense for all share-based payment awards to be based on estimated fair values. The Company uses the Black-Scholes option valuation model to estimate the fair value of its stock options at the date of grant. The Black-Scholes option valuation model requires the input of subjective assumptions to calculate the value of stock options. For restricted stock units, the value of the award is based on the Company's stock price at the grant date. For performance-based restricted stock unit awards, the value of the award is based on the Company's stock price at the grant date, with consideration given to the probability of the performance condition being achieved. The Company uses historical data and other information to estimate the expected price volatility for stock option awards and the expected forfeiture rate for all awards. Expense is recognized over the vesting period for all awards and commences at the grant date for time-based awards and upon the Company's determination that the achievement of such performance conditions is probable for performance-based awards. This determination requires significant judgment by management.

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

#### Recent Accounting Pronouncements

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

2018. Any future option, milestone or royalty payments received will be accounted for under the sales-based royalty exception provided for under this new revenue recognition guidance. Additionally, there will be no impact to cash from or used in operating, financing or investing activities on the Company's Consolidated Statement of Cash Flows as a result of the adoption of the new standard.

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

In May 2017, the FASB issued ASU No. 2017-09, which is an update to Topic 718, Compensation - Stock Compensation. The update provides guidance on determining which changes to the terms and conditions of share-based payment awards, including stock options, require an entity to apply modification accounting under Topic 718. ASU 2017-09 becomes effective for the Company in the first quarter of fiscal 2019. The Company does not expect that ASU 2017-09 will have a material impact on the Company's results of operations and consolidated financial statements.

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

## NOTE 2. COLLABORATION AND LICENSE AGREEMENTS

### Amgen Inc.

On September 28, 2016, the Company entered into two Collaboration and License agreements, and a Common Stock Purchase Agreement with Amgen Inc., a Delaware corporation (“Amgen”). Under one of the license agreements (the “Second Collaboration and License Agreement” or “AMG 890 (ARO-LPA) Agreement”), Amgen has received a worldwide, exclusive license to Arrowhead’s novel, RNAi ARO-LPA program. These RNAi molecules are designed to reduce elevated lipoprotein(a), which is a genetically validated, independent risk factor for atherosclerotic cardiovascular disease. Under the other license agreement (the “First Collaboration and License Agreement” or “ARO-AMG1 Agreement”), Amgen received an option to a worldwide, exclusive license for ARO-AMG1, an RNAi therapy for an undisclosed genetically validated cardiovascular target. In both agreements, Amgen is wholly responsible for clinical development and commercialization.

Under the Common Stock Purchase Agreement, the Company has sold 3,002,793 shares of Common Stock to Amgen at a price of \$7.16 per share. Subject to Amgen’s exercise of the Option, as defined in the ARO-AMG1 Agreement, Amgen has agreed to purchase, and the Company has agreed to sell, an additional \$5 million worth of shares of Common Stock based on a 30 trading day formula surrounding the date of the Option exercise.

Under the terms of the agreements taken together, the Company has received \$35 million in upfront payments, \$21.5 million in the form of an equity investment by Amgen in the Company’s Common Stock and could receive up to \$617 million in option payments, and development, regulatory and sales milestone payments. The Company is further eligible to receive single-digit royalties for sales of products under the ARO-AMG1 Agreement and up to low double-digit royalties for sales of products under the AMG 890 (ARO-LPA) Agreement.

Under the terms of the AMG 890 (ARO-LPA) Agreement, the Company has granted a worldwide, exclusive license to AMG 890 (ARO-LPA). The Company is also responsible for assisting Amgen in the oversight of certain development and manufacturing activities (the “AMG 890 (ARO-LPA) R&D Services”), most of which are to be covered at Amgen’s cost. The Company has determined that the significant deliverables under the AMG 890 (ARO-LPA) Agreement include the license and the AMG 890 (ARO-LPA) R&D Services. The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and the AMG 890 (ARO-LPA) R&D Services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. Therefore, the deliverables are not separable and, accordingly, the license and the AMG 890 (ARO-LPA) R&D Services are being treated as a single unit of accounting. The Company recognized revenue on a straight-line basis from November 18, 2016 (the Hart-Scott-Rodino clearance date), through October 31, 2017, which was the date where the AMG 890 (ARO-LPA) R&D Services were substantially completed. The Company received the upfront payment of \$30 million due under the AMG 890 (ARO-LPA) Agreement in November 2016. The upfront \$30 million payment was initially recorded as Deferred Revenue. During the years ended September 30, 2018 and 2017, \$2.7 million and \$27.3 million of this upfront payment were recognized into Revenue, respectively. This upfront payment has been recognized as Revenue in its entirety as of September 30, 2018.

On August 1, 2018, the Company announced that it had earned a \$10 million milestone payment from Amgen following the administration of the first dose of AMG 890 (ARO-LPA) in a phase 1 clinical study. The Company has recognized this payment as Revenue in its entirety during the year ended September 30, 2018 as the performance

obligations had already been substantially completed.

Under the new revenue recognition guidance there would be no change to our historical accounting for the AMG 890 (ARO-LPA) Agreement as the performance obligations have been substantially completed as of September 30, 2018. Additionally, any future milestone or royalty payments due under the AMG-890 (ARO-LPA) Agreement will be recognized in the period the milestone is achieved under the sales-based royalty exception allowed under accounting rules. Finally, the costs to obtain this agreement were immaterial.

Under the terms of the ARO-AMG1 Agreement, the Company has granted an option to a worldwide, exclusive license to ARO-AMG1, an undisclosed genetically validated cardiovascular target. The Company is also responsible for developing, optimizing and manufacturing the candidate through certain preclinical efficacy and toxicology studies to determine whether the candidate the Company has developed meets the required criteria as defined in the agreement (the “Arrowhead Deliverable”). The Company delivered the candidate in August 2018 and Amgen currently has the option to an exclusive license for the intellectual property generated through the Company’s development efforts. If Amgen exercises its option, it would likely assume all development,

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regulatory and commercialization efforts for the candidate. The Company determined that the significant deliverables under the ARO-AMG1 Agreement include the option to license and the development and manufacturing activities toward achieving the Arrowhead Deliverable (the “ARO-AMG1 R&D Services”). The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the option to license and ARO-AMG1 R&D Services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. Therefore, the deliverables are not separable and, accordingly, the option to license and ARO-AMG1 R&D Services are being treated as a single unit of accounting. The Company has recognized revenue on a straight-line basis from October 1, 2016, through September 30, 2018, as the Company completed the Arrowhead Deliverable during the three months ended September 30, 2018. The Company received an upfront payment of \$5 million due under this agreement in September 2016. The upfront \$5 million payment was initially recorded as Deferred Revenue. During the years ended September 30, 2018 and 2017, \$2.5 million and \$2.5 million of this upfront payment were recognized into Revenue, respectively. This upfront payment has been recognized as Revenue in its entirety as of September 30, 2018.

Under the new revenue recognition guidance there would be no change to our historical accounting for the ARO-AMG1 Agreement as the Arrowhead Deliverable was completed during the three months ended September 30, 2018. Additionally, any future option, milestone or royalty payments due under the ARO-AMG1 Agreement will be recognized in the period the milestone is achieved under the sales-based royalty exception allowed under accounting rules. Finally, the costs to obtain this agreement were immaterial.

The Company also entered into a separate services agreement and separate statements of work with Amgen to provide certain services related to process development, manufacturing, materials supply, discovery studies, and other consulting services related to AMG 890 (ARO-LPA) and ARO-AMG1. During the years ended September 30, 2018, 2017, 2016, these work orders generated approximately \$1.0 million, \$1.5 million and \$0 of Revenue, respectively.

Janssen Pharmaceuticals, Inc.

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



The Company has evaluated these agreements in accordance with the new revenue recognition requirements that became effective for the Company on October 1, 2018.

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

The Company determined the transaction price totaled approximately \$197.8 million which includes the upfront payment, the premium paid by JJDC for its equity investment in the Company, and estimated payments for ARO-HBV drug materials on hand and additional material to be manufactured. The Company has allocated the total \$197.8 million initial transaction price to its one distinct performance obligation for the ARO-HBV license and the associated Janssen R&D Services. This revenue will be recognized using a proportional performance method (based on actual labor hours versus estimated total labor hours) beginning in October 2018 and ending as the Company's efforts in overseeing the ongoing phase 1 / 2 clinical trial are completed.

### NOTE 3. PROPERTY AND EQUIPMENT

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

|   | September<br>30,<br>2018 | September<br>30, 2017 |
|---|--------------------------|-----------------------|
| Computers, office equipment and furniture       | \$ 600,334               | \$ 600,334            |
| Research equipment                              | 10,751,627               | 9,660,960             |
| Software  | 152,676                  | 132,078               |
| Leasehold improvements                          | 12,236,150               | 12,208,380            |
| Total gross fixed assets                        | 23,740,787               | 22,601,752            |
| Less: Accumulated depreciation and amortization | (9,805,362 )             | (7,088,733 )          |
| Property and equipment, net                     | \$ 13,935,425            | \$ 15,513,019         |

Depreciation and amortization expense for Property and Equipment the for the years ended September 30, 2018, 2017 and 2016 was \$2,998,846, \$2,990,010, and \$1,545,733, respectively.

### NOTE 4. INVESTMENTS

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The Company invests a portion of its excess cash balances in short-term debt securities and may, from time to time, also invest in long-term debt securities. Investments at September 30, 2018 consisted of corporate bonds with maturities remaining of less than 12 months. The Company may also invest excess cash balances in certificates of deposits, money market accounts, government-sponsored enterprise securities, corporate bonds and/or commercial paper. The Company accounts for its investments in accordance with FASB ASC 320, Investments – Debt and Equity Securities. At September 30, 2018, all investments were classified as held-to-maturity securities.

The following tables summarize the Company’s short-term and long-term investments as of September 30, 2018, and September 30, 2017.

| As of September 30, 2018               |                     |                              |                               |                     |
|--|---------------------|------------------------------|-------------------------------|---------------------|
|  | Amortized<br>Cost   | Gross<br>Unrealized<br>Gains | Gross<br>Unrealized<br>Losses | Fair Value          |
| Commercial notes (due within one year) | \$46,400,176        | —                            | \$ (429,050 )                 | \$45,971,126        |
| <b>Total</b>                           | <b>\$46,400,176</b> | <b>\$</b>                    | <b>— \$ (429,050 )</b>        | <b>\$45,971,126</b> |

| As of September 30, 2017               |                     |                              |                               |                     |
|--|---------------------|------------------------------|-------------------------------|---------------------|
|  | Amortized<br>Cost   | Gross<br>Unrealized<br>Gains | Gross<br>Unrealized<br>Losses | Fair Value          |
| Commercial notes (due within one year) | \$40,769,539        | \$                           | — \$ (334,755 )               | \$40,434,784        |
| <b>Total</b>                           | <b>\$40,769,539</b> | <b>\$</b>                    | <b>— \$ (334,755 )</b>        | <b>\$40,434,784</b> |



## NOTE 5. INTANGIBLE ASSETS

Intangible assets subject to amortization include patents and a license agreement capitalized as part of the Novartis RNAi asset acquisition in March 2015. The license agreement associated with the Novartis RNAi asset acquisition is being amortized over the estimated life remaining at the time of acquisition, which was 21 years, and the accumulated amortization of the asset is approximately \$531,786. The patents associated with the Novartis RNAi asset acquisition are being amortized over the estimated life remaining at the time of acquisition, which was 14 years, and the accumulated amortization of the assets is approximately \$5,561,419. Amortization expense for the years ended September 30, 2018, 2017 and 2016 was \$1,700,429, \$1,700,429 and \$1,714,313, respectively. Amortization expense is expected to be approximately \$1,700,429 in 2019, \$1,700,429 in 2020, \$1,700,429 in 2021, \$1,700,429 in 2022, \$1,700,429 in 2023, and \$10,261,865 thereafter.

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

|                               | Intangible assets<br>subject to<br>amortization |
|-------------------------------|---|
| Balance at September 30, 2017 | \$ 20,464,439                                   |
| Impairment                    | -   |
| Amortization                  | (1,700,429 )                                    |
| Balance at September 30, 2018 | \$ 18,764,010                                   |

## NOTE 6. STOCKHOLDERS' EQUITY

At September 30, 2018, the Company had a total of 150,000,000 shares of capital stock authorized for issuance, consisting of 145,000,000 shares of Common Stock, par value \$0.001 per share, and 5,000,000 shares of Preferred Stock, par value \$0.001 per share.

At September 30, 2018, 88,505,302 shares of Common Stock were outstanding. At September 30, 2018, 8,732,569 shares of Common Stock were reserved for issuance upon exercise of options and vesting of restricted stock units granted or available for grant under Arrowhead's 2004 Equity Incentive Plan and 2013 Incentive Plan, as well as for inducement grants made to new employees.

On January 22, 2018, the Company sold 11,500,000 shares of Common Stock in a fully underwritten public offering, at a public offering price of \$5.25 per share. Net proceeds to the Company were approximately \$56.6 million after deducting underwriting commissions and discounts and other offering expenses payable by the Company.

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

## NOTE 7. COMMITMENTS AND CONTINGENCIES

Leases

The Company leases approximately 8,500 square feet of office space for its corporate headquarters in Pasadena, California. The lease will expire in September 2019. Monthly rental payments are approximately \$28,100 per month, increasing approximately 3% annually.

The Company also leases approximately 60,000 square feet of office and laboratory space for its research facility in Madison, Wisconsin. The lease will expire in September 2026. As part of this lease, the Company was provided a primary tenant improvement allowance of \$2.1 million which is accounted for as Deferred Rent and a secondary tenant improvement allowance of \$2.7 million which is accounted for as a Note Payable on the Company's Consolidated Balance Sheet. Monthly rental payments, including payments of principal and interest on the Note Payable are approximately \$186,300 per month. The monthly rental payments (excluding principal and interest on the Note Payable), will increase approximately 2.5% annually.

Facility rent expense for the years ended September 30, 2018, 2017 and 2016 was \$1,288,000, \$1,441,000 and \$839,000, respectively.

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As of September 30, 2018, future minimum lease payments due in fiscal years under operating leases are as follows:

|                     |             |
|---------------------|-------------|
| 2019                | \$1,435,409 |
| 2020                | 1,044,431   |
| 2021                | 1,070,496   |
| 2022                | 1,097,168   |
| 2023                | 1,124,445   |
| 2024 and thereafter | 3,544,882   |
| Total               | \$9,316,831 |

#### Note Payable

As part of the Company's lease for its research facility in Madison, Wisconsin discussed above, the Company entered into a \$2.7 million promissory note payable with its landlord to finance certain tenant improvements made to the new facility. The note will be amortized over the 10-year term of the lease, commencing on October 1, 2016. The note bears interest at a rate of 7.1% and is payable in equal monthly installments of principal and interest.

As of September 30, 2018, future principal payments due in fiscal years under the note payable are as follows:

|                     |             |
|---------------------|-------------|
| 2019                | \$223,820   |
| 2020                | 240,258     |
| 2021                | 257,903     |
| 2022                | 276,845     |
| 2023                | 297,177     |
| 2024 and thereafter | 1,029,015   |
| Total               | \$2,325,018 |

In October 2018, the Company repaid the entire balance due for the Note Payable associated with its Madison research and development facility lease discussed above.

#### Litigation –

The Company and certain of its officers and directors were named as defendants in a putative consolidated class action in the United States District Court for the Central District of California regarding certain public statements in connection with the Company's hepatitis B drug research. The consolidated class action, initially filed as Wang v. Arrowhead Research Corp., et al., No. 2:14-cv-07890 (C.D. Cal., filed Oct. 10, 2014), and Eskinazi v. Arrowhead Research Corp., et al., No. 2:14-cv-07911 (C.D. Cal., filed Oct. 13, 2014), asserted claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and sought damages in an unspecified amount. Additionally, three putative stockholder derivative actions captioned Weisman v. Anzalone et al., No. 2:14-cv-08982 (C.D. Cal., filed Nov. 20, 2014), Bernstein (Backus) v. Anzalone, et al., No. 2:14-cv-09247 (C.D. Cal., filed Dec. 2, 2014); and Johnson v. Anzalone, et al., No. 2:15-cv-00446 (C.D. Cal., filed Jan. 22, 2015), were filed in the United States District Court for the Central District of California, alleging breach of fiduciary duty by the Company's Board of Directors in connection with the alleged facts underlying the securities claims. An additional consolidated derivative action asserting similar claims was filed in Los Angeles County Superior Court, initially filed as Bacchus v. Anzalone, et al., (L.A. Super., filed Mar. 5, 2015); and Jackson v. Anzalone, et al. (L.A. Super., filed Mar. 16, 2015). Each of these suits seeks damages in unspecified amounts and some seek various forms of injunctive relief. On October 7, 2016, the federal district court dismissed the consolidated class action with prejudice. Following the dismissal of the

consolidated class action, the parties for the Weisman and Johnson actions jointly stipulated to dismiss the actions, with the parties bearing their own fees and costs. The parties to the Bernstein and consolidated derivative action agreed to stay the matters pending the resolution of the Ninth Circuit appeal of the dismissal of the consolidated class action. On February 15, 2018, the Ninth Circuit issued a memorandum affirming the district court's dismissal of all claims. Plaintiffs in the consolidated derivative action voluntarily dismissed their case. The parties to the Bernstein action filed a stipulation to continue the stay of the action pending resolution of the Ninth Circuit appeal in Meller v. Arrowhead Pharmaceuticals, Inc., Case No. 2:16-cv-08505 (C.D. Cal.). The Company believes it has meritorious defenses and intends to vigorously defend itself in each of these matters. The Company makes provisions for liabilities when it is both probable that a liability has been incurred and the amount can be reasonably estimated. No such liability has been recorded related to these matters. The Company does not expect these matters to have a material effect on its Consolidated Financial Statements.

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The Company and certain executive officers were named as defendants in a putative consolidated class action in the United States District Court for the Central District of California regarding certain public statements in connection with the Company's drug research programs. The consolidated class action, initially filed as *Meller v. Arrowhead Pharmaceuticals, Inc., et al.*, No. 2:16-cv-08505 (C.D. Cal., filed Nov. 15, 2016), *Siegel v. Arrowhead Pharmaceuticals, Inc., et al.*, No. 2:16-cv-8954 (C.D. Cal., filed Dec. 2, 2016), and *Unz v. Arrowhead Pharmaceuticals, Inc., et al.*, No. 2:17-cv-00310 (C.D. Cal., filed Jan. 13, 2017) asserts claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 regarding certain public statements in connection with the Company's drug research programs and seek damages in an unspecified amount. Additionally, a putative stockholder derivative action captioned *Johnson v. Anzalone, et al.*, (Los Angeles County Superior Court, filed January 19, 2017) asserting substantially similar claims is pending in Los Angeles County Superior Court and is stayed pending the related consolidated class action. Two additional putative stockholder derivative actions, captioned *Lucas v. Anzalone, et al.*, No. 2:17-cv-03207 (C.D. Cal., filed April 28, 2017), and *Singh v. Anzalone, et al.*, No. 2:17-cv-03160 (C.D. Cal., filed April 27, 2017), alleging breach of fiduciary duty by the Company's Board of Directors in connection with the alleged facts underlying the securities claims, are pending in the United States District Court for the Central District of California. The Lucas and Singh actions have been consolidated. On December 21, 2017, the federal district court dismissed the consolidated class action with prejudice. On December 27, 2017 the plaintiffs appealed the dismissal to the United States Court of Appeals for the Ninth Circuit. The Lucas and Singh actions are stayed pending resolution of the Ninth Circuit appeal. The Company believes it has meritorious defenses and intends to vigorously defend itself in these matters. The Company makes provisions for liabilities when it is both probable that a liability has been incurred and the amount can be reasonably estimated. No such liability has been recorded related to these matters. The Company cannot predict the ultimate outcome of this matter and cannot accurately estimate any potential liability the Company may incur or the impact of the results of this matter on the Company.

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

#### Purchase Commitments

In the normal course of business, we enter into various purchase commitments for the manufacture of drug components, for toxicology studies, and for clinical studies. As of September 30, 2018, these future commitments were estimated at approximately \$27.5 million, of which approximately \$20.1 million is expected to be incurred in fiscal 2019, and \$7.4 is expected to be incurred beyond fiscal 2019.

#### Technology License Commitments

The Company has licensed from third parties the rights to use certain technologies for its research and development activities, as well as in any products the Company may develop using these licensed technologies. These agreements and other similar agreements often require milestone and royalty payments. Milestone payments, for example, may be required as the research and development process progresses through various stages of development, such as when clinical candidates enter or progress through clinical trials, upon NDA and upon certain sales level milestones. These milestone payments could amount to the mid to upper double-digit millions of dollars. During the years ended September 30, 2018, 2017 and 2016, the Company reached milestones amounting to \$0, \$0 and \$3.0 million, respectively, based on progress achieved on the Company's previous clinical candidates. In certain agreements, the Company may be required to make mid to high single-digit percentage royalty payments based on a percentage of the sales of the relevant products.

NOTE 8. STOCK-BASED COMPENSATION

Arrowhead has two plans that provide for equity-based compensation. Under the 2004 Equity Incentive Plan and 2013 Incentive Plan, as of September 30, 2018, 1,783,568 and 6,262,690 shares, respectively, of Arrowhead's Common Stock are reserved for the grant of stock options, stock appreciation rights, restricted stock awards and performance unit/share awards to employees, consultants and others. No further grants may be made under the 2004 Equity Incentive Plan. As of September 30, 2018, there were options granted and outstanding to purchase 1,783,568 and 3,057,022 shares of Common Stock under the 2004 Equity Incentive Plan and the 2013 Incentive Plan, respectively, and there were 2,965,999 restricted stock units granted and outstanding under the 2013 Incentive Plan. Also, as of September 30, 2018, there were 683,809 shares reserved for options and 2,500 restricted stock units issued as inducement grants to new employees outside of equity compensation plans. During the year ended September 30, 2018, no options or restricted stock units were granted under the 2004 Equity Incentive Plan, 467,000 options and 1,243,000 restricted stock units were granted under the 2013 Incentive Plan, and 355,000 options and 2,500 restricted stock units were granted as inducement awards to new employees outside of equity incentive plans.

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The following table summarizes information about stock options:

|                                   | Number of<br>Options<br>Outstanding | Weighted-<br>Average<br>Exercise<br>Price<br>Per Share | Weighted-<br>Average<br>Remaining<br>Contractual<br>Term | Aggregate<br>Intrinsic<br>Value |
|-----------------------------------|-------------------------------------|--|--|---------------------------------|
| Balance At September 30, 2017     | 5,549,543                           | \$ 6.00  |  |                                 |
| Granted                           | 822,000                             | 5.97   |  |                                 |
| Cancelled                         | (242,533)                           | 6.83   |  |                                 |
| Exercised                         | (604,611)                           | 4.39   |  |                                 |
| Balance At September 30, 2018     | 5,524,399                           | \$ 6.14  | 6.0 years  | \$72,152,284                    |
| Exercisable At September 30, 2018 | 3,998,427                           | \$ 6.62  | 5.1 years  | \$50,361,428                    |

Stock-based compensation expense related to stock options for the years ended September 30, 2018, 2017 and 2016 was \$3,265,348, \$4,524,833 and \$6,361,396, respectively. The Company does not recognize an income tax benefit as the Company is currently operating at a loss and an actual income tax benefit may not be realized. For non-qualified stock options, the expense creates a timing difference, resulting in a deferred tax asset, which is fully reserved by a valuation allowance.

The grant date fair value of the options granted by the Company for the years ended September 30, 2018, 2017 and 2016 was \$4,141,318, \$849,816 and \$6,426,707, respectively.

The intrinsic value of the options exercised during the years ended September 30, 2018, 2017 and 2016 was \$5,805,317, \$35,512 and \$142,690, respectively.

As of September 30, 2018, the pre-tax compensation expense for all outstanding unvested stock options in the amount of approximately \$5,117,079 will be recognized in the Company's results of operations over a weighted average period of 2.7 years.

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

The assumptions used to value stock options are as follows:

|                          | Years ended September 30, |              |              |
|--------------------------|---------------------------|--------------|--------------|
|                          | 2018                      | 2017         | 2016         |
| Dividend yield           | —                         | —            | —            |
| Risk-free interest rate  | 2.05 – 2.99%              | 1.34 – 2.31% | 1.05 – 1.89% |
| Volatility               | 110%                      | 79%          | 89%          |
| Expected life (in years) | 6.25                      | 5.85         | 6.25         |

|   |        |        |        |
|---|--------|--------|--------|
| Weighted average grant date fair value per share of options granted | \$5.04 | \$1.33 | \$4.58 |
|---|--------|--------|--------|

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

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

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

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## Restricted Stock Units

Restricted stock units (RSUs), including time-based and performance-based awards, were granted under the Company's 2013 Incentive Plan and as inducement grants granted outside of the Plan. During the year ended September 30, 2018, the Company issued 1,243,000 RSUs under the 2013 Incentive Plan and 2,500 RSUs as an inducement award to a new employee outside of the equity incentive plans. At vesting, each outstanding RSU will be exchanged for one share of the Company's Common Stock. RSU recipients may elect to net share settle upon vesting, in which case the Company pays the employee's income taxes due upon vesting and withholds a number of shares of Common Stock of equal value. RSU awards generally vest subject to the satisfaction of service requirements or the satisfaction of both service requirements and achievement of certain performance targets.

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

|                                | Number of<br>RSUs | Weighted-<br>Average<br>Grant<br>Date<br>Fair Value |
|--------------------------------|-------------------|---|
| Unvested at September 30, 2017 | 3,108,000         | \$ 2.45   |
| Granted                        | 1,245,500         | 3.68  |
| Vested                         | (1,335,000)       | 2.43  |
| Forfeited                      | (50,000 )         | 1.55  |
| Unvested at September 30, 2018 | 2,968,500         | \$ 2.99   |

During the years ended September 30, 2018, 2017 and 2016, the Company recorded \$5,189,259, \$3,366,762 and \$5,234,420 of expense related to RSUs, respectively. Such expense is included in stock-based compensation expense in the Company's Consolidated Statement of Operations and Comprehensive Loss. The Company does not recognize an income tax benefit as the Company is currently operating at a loss and an actual income tax benefit may not be realized. For RSUs, the expense creates a timing difference, resulting in a deferred tax asset, which is fully reserved by a valuation allowance.

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

As of September 30, 2018, the pre-tax compensation expense for all unvested RSUs in the amount of approximately \$2,451,889 will be recognized in the Company's results of operations over a weighted average period of 2.6 years.

## NOTE 9. FAIR VALUE MEASUREMENTS

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

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

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

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

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The following table summarizes fair value measurements at September 30, 2018 and September 30, 2017 for assets and liabilities measured at fair value on a recurring basis:

September 30, 2018:

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

September 30, 2017:

|                           | Level 1      | Level 2 | Level 3 | Total        |
|---------------------------|--------------|---------|---------|--------------|
| Cash and cash equivalents | \$24,838,567 | \$—     | \$—     | \$24,838,567 |
| Short-term investments    | 40,434,784   | —       | —       | 40,434,784   |
| Derivative liabilities    | —            | —       | 695,114 | 695,114      |
| Contingent Consideration  | \$—          | \$—     | \$—     | \$—          |

As part of a financing in January 2013, Arrowhead issued warrants to purchase up to 833,530 shares of Common Stock (the “2013 Warrants”) of which 0 warrants were outstanding at September 30, 2018. Further, as part of a financing in December 2012, Arrowhead issued warrants to purchase up to 912,543 shares of Common Stock (the “2012 Warrants”) of which warrants to exercise 143,811 shares remained unexercised and were cancelled at their expiration during the three months ended December 31, 2017. Each of the Warrants contained a mechanism to adjust the strike price upon the issuance of certain dilutive equity securities. If during the terms of the Warrants, the Company issued Common Stock at a price lower than the exercise price for the Warrants, the exercise price would be reduced to the amount equal to the issuance price of the Common Stock. As a result of these features, the Warrants were subject to derivative accounting as prescribed under ASC 815. Accordingly, the fair value of the Warrants on the date of issuance was estimated using an option pricing model and recorded on the Company’s Consolidated Balance Sheet as a derivative liability. The fair value of the Warrants was estimated at the end of each reporting period and the change in the fair value of the Warrants was recorded as a non-operating gain or loss as change in value of derivatives in the Company’s Consolidated Statement of Operations and Comprehensive Loss. During the years ended September 30, 2018, 2017 and 2016, the Company recorded a non-cash gain/(loss) from the change in fair value of the derivative liability of \$432,141, \$870,760 and \$(293,072), respectively.

The following is a reconciliation of the derivative liability related to these Warrants:

|                             |           |
|-----------------------------|-----------|
| Value at September 30, 2017 | \$695,114 |
| Issuance of instruments     | —         |
| Change in value             | (432,141) |
| Net settlements             | (262,973) |
| Value at September 30, 2018 | \$—       |

The derivative assets/liabilities were estimated using option pricing models that are based on the individual characteristics of the warrants or instruments on the valuation date, as well as assumptions for expected volatility, expected life and risk-free interest rate. Changes in the assumptions used could have a material impact on the resulting fair value. The primary input affecting the value of the Company's derivatives liabilities was the Company's stock price. Other inputs have a comparatively insignificant effect.

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As of September 30, 2015, the Company had a liability for contingent consideration related to its acquisition of the Roche RNAi business completed in 2011. The fair value measurement of the contingent consideration obligations is determined using Level 3 inputs. The fair value of contingent consideration obligations is based on a discounted cash flow model using a probability-weighted income approach. The measurement is based upon unobservable inputs supported by little or no market activity based on the Company's assumptions and experience. Estimating timing to complete the development and obtain approval of products is difficult, and there are inherent uncertainties in developing a product candidate, such as obtaining U.S. Food and Drug Administration (FDA) and other regulatory approvals. In determining the probability of regulatory approval and commercial success, the Company utilizes data regarding similar milestone events from several sources, including industry studies and its own experience. These fair value measurements represent Level 3 measurements as they are based on significant inputs not observable in the market. Significant judgment is employed in determining the appropriateness of these assumptions as of the acquisition date and for each subsequent period. Accordingly, changes in assumptions could have a material impact on the amount of contingent consideration expense the Company records in any given period. In November 2016, the Company announced the discontinuation of its clinical trial efforts for ARC-520, ARC-AAT and ARC-521. Given this development, the Company assessed the fair value of its contingent consideration obligation to be \$0 at September 30, 2018 and September 30, 2017.

#### NOTE 10. - INCOME TAXES

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

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

Components of the net deferred tax asset (liability) at September 30, 2018 and 2017 are as follows:

|                                      | 2018         | 2017         |
|--------------------------------------|--------------|--------------|
| Deferred tax assets:                 |              |              |
| Accrued compensation                 | \$ 1,085,908 | \$ 1,337,619 |
| Stock compensation                   | 4,188,368    | 5,670,468    |
| Capitalized research and development | 1,227,137    | 2,196,542    |
| Fixed Assets                         | 404,836      | 203,477      |
| Net operating losses                 | 114,142,741  | 132,119,837  |
| Intangible Assets                    | 3,854,752    | 5,358,700    |
| Deferred Revenue                     | —            | 1,068,206    |
| Deferred Rent                        | 566,535      | 865,675      |
| Capital Loss                         | 709,779      | 1,020,162    |

|                                       |               |               |
|---------------------------------------|---------------|---------------|
| Total deferred tax assets             | 126,180,056   | 149,840,686   |
| Valuation allowance                   | (116,875,075) | (136,625,436) |
| Deferred tax liabilities:             |               |               |
| State taxes                           | (9,304,981 )  | (13,215,250 ) |
| Total deferred tax liability          | (9,304,981 )  | (13,215,250 ) |
| Net deferred tax assets (liabilities) | \$—           | \$—           |

The Company has concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company may not realize the benefit of all of its deferred tax assets. Accordingly, management has provided a 100% valuation allowance against its deferred tax assets until such time as management believes that its projections of future profits as well as expected future tax rates make the realization of these deferred tax assets more-likely-than-not. Significant judgment is required in the evaluation of deferred tax benefits and differences in future results from our estimates could result in material differences in the realization of these assets. The Company has recorded a full valuation allowance related to all of its deferred tax assets. The Company has performed an assessment of positive and negative evidence regarding the realization of the net deferred tax asset in accordance with FASB ASC 740-10, "Accounting for Income Taxes." This assessment included the evaluation of scheduled reversals of deferred tax liabilities, the availability of carry forwards and estimates of projected future taxable income.

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As of September 30, 2017, the Company had available gross federal net operating loss (NOL) carry forwards of \$284.8 million and gross state NOL carry forwards of \$196.6 million. Gross federal NOL carry forwards for 2018 are estimated at \$62.8 million, and gross state NOL carry forwards for 2018 are estimated at \$62.8 million. The NOLs expire at various dates through 2038.

The provisions for income taxes for the years ended September 30, 2018 and 2017 are as follows:

|                             | 2018    | 2017  |
|-----------------------------|---------|-------|
| <b>Federal:</b>             |         |       |
| Current                     | —       | —     |
| Deferred                    | —       | —     |
| Total Federal               | —       | —     |
| <b>State:</b>               |         |       |
| Current                     | \$2,400 | 2,400 |
| Deferred                    | —       | —     |
| Total State                 | \$2,400 | 2,400 |
| Provision from income taxes | \$2,400 | 2,400 |

The Company's effective income tax rate differs from the statutory federal income tax rate as follows for the years ended September 30, 2018 and 2017:

|                                    | 2018   | 2017    |
|------------------------------------|--------|---------|
| At U.S. federal statutory rate     | 21.0 % | 34.0 %  |
| State taxes, net of federal effect | 7.9    | 4.9     |
| Stock compensation                 | 2.6    | (5.8 )  |
| Mark-to-market adjustments         | 0.2    | 0.9     |
| Valuation allowance                | 36.2   | (23.1 ) |
| True-up on deferred taxes          | —      | (3.0 )  |
| State blended rate change          | —      | (5.7 )  |
| Federal tax rate change in 2018    | (67.9) | —       |
| Other                              | —      | (2.2 )  |
| Effective income tax rate          | 0.0 %  | 0.0 %   |

In December 2017, the President of the United States signed into law the Tax Cuts and Jobs Act, or TCJA, tax reform legislation. The TCJA makes significant changes in U.S. tax law including a reduction in the corporate tax rates, changes to net operating loss carryforwards and carrybacks, and a repeal of the corporate alternative minimum tax. The TCJA reduced the U.S. corporate tax rate from the current rate of 35 percent down to 21 percent starting on January 1, 2018. As a result of the TCJA, we were required to revalue deferred tax assets and liabilities at 21 percent. This revaluation resulted in a provision of \$37.0 million to income tax expense in continuing operations and a corresponding reduction in the valuation allowance. As a result, there was no impact to our Consolidated Statements of Comprehensive Loss as a result of the reduction in tax rates. The other provisions of the TCJA did not have a material impact on our Consolidated Financial Statements.

The Company has adopted guidance issued by the FASB that clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements and prescribes a recognition threshold of more likely than not and a measurement process for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. In making this assessment, a company must determine whether it is more likely than not that a

tax position will be sustained upon examination, based solely on the technical merits of the position and must assume that the tax position will be examined by taxing authorities. The Company's policy is to include interest and penalties related to unrecognized tax benefits in income tax expense. The Company has not recognized any unrecognized tax benefits and does not have any interest or penalties related to uncertain tax positions as of September 30, 2018 and 2017.

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



## NOTE 11. EMPLOYEE BENEFIT PLANS

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

For the years ended September 30, 2018, 2017, and 2016, we recorded expenses under this plan of \$451,623, \$426,470 and \$476,835, respectively.

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

## NOTE 12. UNAUDITED QUARTERLY FINANCIAL DATA

The following table presents selected unaudited quarterly financial data for each full quarterly period of the years ended September 30, 2018 and 2017:

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

| Year ended September 30, 2017      | First<br>Quarter | Second<br>Quarter | Third<br>Quarter | Fourth<br>Quarter |
|------------------------------------|------------------|-------------------|------------------|-------------------|
| Revenues                           | \$4,365,496      | \$8,985,930       | \$9,342,498      | \$8,713,785       |
| Operating Losses                   | \$(14,901,887)   | \$(6,129,642)     | \$(5,714,164)    | \$(10,250,216)    |
| Net Loss                           | \$(12,086,108)   | \$(6,042,557)     | \$(5,519,741)    | \$(10,731,889)    |
| Loss per share (Basic and Diluted) | \$(0.17)         | \$(0.08)          | \$(0.07)         | \$(0.14)          |

## NOTE 13. SUBSEQUENT EVENTS

On October 3, 2018, the Company entered into a License Agreement (“Janssen License Agreement”) and a Research Collaboration and Option Agreement (“Janssen Collaboration Agreement” with Janssen Pharmaceuticals, Inc. (“Janssen”)

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

In October 2018, the Company repaid the entire balance due for the Note Payable associated with its Madison research and development facility lease discussed in Note 7 – Commitments and Contingencies above.