

ARROWHEAD PHARMACEUTICALS, INC.

Form 424B5

January 19, 2018

Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-214315

PROSPECTUS SUPPLEMENT

(To Prospectus dated February 3, 2017)

10,000,000 Shares

Common Stock

We are offering 10,000,000 shares of our common stock. Our common stock is currently listed on the Nasdaq Global Select Market under the symbol ARWR. On January 17, 2018, the last reported sale price per share of our common stock on the Nasdaq Global Select Market was \$5.72 per share.

Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER	TOTAL
	SHARE	
Public offering price	\$ 5.25	\$ 52,500,000
Underwriting discounts and commissions (1)	\$ 0.315	\$ 3,150,000
Proceeds to Arrowhead Pharmaceuticals, Inc., before expenses	\$ 4.935	\$ 49,350,000

- (1) We refer you to Underwriting beginning on page S-9 of this prospectus supplement for additional information regarding underwriting compensation.

Delivery of the shares of common stock is expected to be made on or about January 22, 2018. We have granted the underwriters an option for a period of 30 days to purchase up to 1,500,000 additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$3.6 million and the net proceeds to us, before expenses, will be \$56.8 million.

Joint Bookrunners

Jefferies

Barclays
Co-Managers

Joint Passive Bookrunner

Cantor

Chardan Capital Markets, LLC

B. Riley FBR, Inc.

Prospectus Supplement dated January 18, 2018.

Table of Contents**TABLE OF CONTENTS****PROSPECTUS SUPPLEMENT**

	Page
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-1
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-2
<u>PROSPECTUS SUMMARY</u>	S-3
<u>THE OFFERING</u>	S-5
<u>RISK FACTORS</u>	S-6
<u>USE OF PROCEEDS</u>	S-7
<u>DILUTION</u>	S-8
<u>UNDERWRITING</u>	S-9
<u>LEGAL MATTERS</u>	S-15
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-15

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	1
<u>ABOUT THE COMPANY</u>	2
<u>RISK FACTORS</u>	3
<u>USE OF PROCEEDS</u>	3
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	3
<u>DESCRIPTION OF SECURITIES</u>	4
<u>PLAN OF DISTRIBUTION</u>	12
<u>EXPERTS</u>	14
<u>LEGAL MATTERS</u>	14
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	14
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	14

You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the section of the prospectus supplement entitled Incorporation of Certain Information by Reference and in the sections of the accompanying prospectus entitled Where You Can Find More Information and Incorporation of Certain Information by Reference.

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents dated prior to the date of this prospectus supplement and incorporated by reference herein or therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein.

In this prospectus supplement, Arrowhead, the Company, we, us, and our and similar terms refer to Arrowhead Pharmaceuticals, Inc. and its subsidiaries, unless the context indicates otherwise. References to our common stock refer to the common stock of Arrowhead Pharmaceuticals, Inc.

All references in this prospectus supplement to our financial statements include, unless the context indicates otherwise, the related notes.

The industry and market data and other statistical information contained in this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference are based on management's own estimates, independent publications, government publications, reports by market research firms or other published independent sources, and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus contain or incorporate by reference forward-looking statements, and readers are cautioned that our actual results may differ materially from those discussed in the forward-looking statements. These forward-looking statements include, without limitation, statements regarding the progress and timing of clinical trials, the safety and efficacy of our product candidates, the goals of our development activities, estimates of the potential markets for our product candidates, projected cash needs and our expected future revenues, operations and expenditures. You can identify forward-looking statements by the use of the words believe, expect, anticipate, intend, estimate, project, will, should, may, plan, intend, assume and other words that predict or indicate future events and trends and which do not relate solely to historical matters. These statements relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These risks and uncertainties include, among others:

risks relating to the cost, timing, scope and results of ongoing safety and efficacy trials of our drug candidates;

risks inherent in attempting to commercialize new drugs;

risks relating to the development of drugs with a short development history, such as our compounds based on our TRiM™ platform, and related uncertainty as to safety and efficacy of these drug candidates;

risks relating to our ability to enter into revenue-generating collaborations or to achieve commercial acceptance of our drug candidates, if approved;

risks relating to our financial condition and our future capital requirements to complete development of our existing drug candidates and to develop other drug candidates;

risks relating to the validity and enforceability of our patents and potential litigation relating to intellectual property rights;

risks relating to our reliance on third parties;

risks relating to the volatility of our stock price; and

other factors detailed from time to time in filings with the SEC.

In addition, the factors described under the section captioned "Risk Factors" in this prospectus supplement, as may be updated from time to time by our future filings under the Securities Exchange Act, and elsewhere in the documents

incorporated by reference in this prospectus supplement, may result in these differences. You should carefully review all of these factors. These forward-looking statements were based on information, plans and estimates at the date of this prospectus supplement or the other document containing the forward-looking statement, and we assume no obligation to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events or other changes, except as may be required by law.

S-2

Table of Contents

PROSPECTUS SUMMARY

*The following summary of our business highlights certain of the information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference, which are described under *Incorporation of Certain Information by Reference* of this prospectus supplement and *Where You Can Find More Information* and *Incorporation of Certain Information by Reference* in the accompanying prospectus. You should also carefully consider the matters discussed in the section in this prospectus supplement titled *Risk Factors* and in the accompanying prospectus and in other periodic reports incorporated herein by reference.*

Our Company

We are a biopharmaceutical company developing medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, our therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. 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.

In fiscal 2017, we refocused our resources on therapeutics that exclusively utilize our Targeted RNAi Molecule (TRiM™) platform technology. Therapeutic candidates built on the TRiM™ platform have demonstrated high levels of pharmacologic activity in multiple animal models spanning several therapeutic areas. TRiM™ enabled therapeutic candidates 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; 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.

Pipeline Overview

We are 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 address conditions in virtually any therapeutic area and pursue disease targets that are not otherwise addressable by small molecules and biologics. The timing of our planned and already filed clinical trial applications (CTA) discussed below are based on calendar quarters, not fiscal quarters.

ARO-AAT is an RNAi therapeutic candidate for the treatment of liver disease associated with alpha-1 antitrypsin deficiency. ARO-AAT is designed to knock down the Alpha-1 antitrypsin (AAT) gene transcript and reduce the hepatic production of the mutant AAT protein. ARO-AAT is a next-generation subcutaneously administered compound that follows a previous generation AAT compound ARC-AAT. A CTA was filed in the fourth quarter of 2017.

ARO-HBV is an RNAi therapeutic candidate for the treatment of chronic hepatitis B infection with the goal of achieving a functional cure. ARO-HBV is a next-generation subcutaneously administered compound that

follows previous generation HBV compounds ARC-520 and ARC-521. A CTA was filed in the fourth quarter of 2017.

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 quarter of 2018.

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 is planned for the fourth quarter of 2018.

S-3

Table of Contents

ARO-LUNG1 is Arrowhead's first therapeutic candidate to utilize the TRiM™ platform to target an undisclosed disease of the lung. A CTA is planned for the fourth quarter of 2018.

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. It is the first drug candidate to utilize the TRiM™ platform to target tumors. A CTA is planned for 2019.

ARO-LPA (AMG 890) 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, Inc. acquired a worldwide, exclusive license in September 2016 to develop and commercialize ARO-LPA (AMG 890).

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

Our common stock is listed on the Nasdaq Global Select Market under the symbol ARWR.

Corporate Information

Our executive offices are located at 225 South Lake Avenue, Suite 1050, Pasadena CA 91101, and our telephone number is (626) 304-3400. Additional information regarding our company, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus. See

Where You Can Find More Information and Incorporation of Certain Information by Reference on page 14 of the accompanying prospectus and Incorporation of Certain Information by Reference on page S-15 of this prospectus supplement.

Table of Contents

THE OFFERING

Common stock we are offering	10,000,000 shares
Common stock to be outstanding immediately after this offering	84,785,426 shares
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to 1,500,000 additional shares.
Use of proceeds	We intend to use the net proceeds of this offering for general corporate purposes, including working capital, capital expenditures, research and development expenditures and clinical trial expenditures. A portion of the net proceeds may also be used for the acquisition of businesses, products and technologies that are complementary to ours, or for other strategic purposes. See Use of Proceeds.
Risk Factors	See Risk Factors beginning on page S-6 of this prospectus supplement for a discussion of factors you should read and consider carefully before investing in our common stock.

NASDAQ Global Select Market symbol ARWR

The number of shares of common stock shown above to be outstanding after this offering is based on the 74,785,426 shares outstanding as of September 30, 2017 and excludes:

5,549,543 shares of our common stock subject to options outstanding as of September 30, 2017 having a weighted average exercise price of \$6.00 per share; and

432,284 shares of our common stock that have been reserved for issuance exercise of outstanding warrants as of September 30, 2017, having a weighted average exercise price of approximately \$2.86 per share.

If the underwriters' option to purchase additional shares is exercised in full, we will issue and sell an additional 1,500,000 shares of our common stock and will have 86,285,426 shares outstanding immediately after the offering.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase additional shares.

Table of Contents

RISK FACTORS

*An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the section captioned **Risk Factors** contained in our Annual Report on Form 10-K for the year ended September 30, 2017, which is incorporated by reference in its entirety, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, and any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occur, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Additionally, we note that we are a development stage company and we have accrued net losses annually since inception. We urge you to consider our likelihood of success and prospects in light of the risks, expenses and difficulties frequently encountered by entities at similar stages of development*

This prospectus supplement, the accompanying prospectus and the incorporated documents also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned below. Forward-looking statements included in this prospectus supplement are based on information available to us on the date hereof, and all forward-looking statements in documents incorporated by reference are based on information available to us as of the date of such documents. We disclaim any intent to update any forward-looking statements.

Risks Relating to this Offering

We will have discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Although we intend to use the proceeds from this offering principally to support our ongoing and planned clinical development activities, we will retain discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which we choose to allocate and spend the net proceeds. Moreover, we may use the net proceeds for corporate purposes that may not increase our profitability or our market value.

You will experience immediate dilution.

Because the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution with respect to the common stock you purchase in this offering. Based on the public offering price of \$5.25 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$3.96 per share. See **Dilution** on page S-8.

Because we do not expect to pay dividends in the foreseeable future, you must rely on stock appreciation for any return on your investment.

We have paid no cash dividends on our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Accordingly, the success of your investment in our common stock will likely depend entirely upon any future

appreciation. There is no guarantee that our common stock will appreciate in value or even maintain the price at which you purchased your shares, and you may not realize a return on your investment in our common stock.

S-6

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the shares of common stock that we are offering will be approximately \$49.3 million or approximately \$56.7 million if the underwriters exercise in full their option to purchase up to 1,500,000 additional shares of common stock, based on the public offering price of \$5.25 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds of this offering for general corporate purposes, including working capital, capital expenditures, research and development expenditures and clinical trial expenditures. A portion of the net proceeds may also be used for the acquisition of businesses, products and technologies that are complementary to ours, or for other strategic purposes. Although we have no specific agreements, commitments or understandings with respect to any acquisition, we evaluate acquisition opportunities and engage in related discussions with other companies from time to time. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the application of these proceeds.

Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

S-7

Table of Contents**DILUTION**

Our net tangible book value as of September 30, 2017 was approximately \$60.4 million, or \$0.81 per share. Net tangible book value per share is determined by subtracting our total liabilities from our total tangible assets and dividing the result by the number of shares of our common stock outstanding as of September 30, 2017. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 10,000,000 shares of our common stock in this offering at the public offering price of \$5.25 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2017 would have been approximately \$109.7 million, or \$1.29 per share. This represents an immediate increase in net tangible book value of \$0.49 per share to existing stockholders and immediate dilution in net tangible book value of \$3.96 per share to new investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$ 5.25
Net tangible book value per share as of September 30, 2017	\$ 0.81
Increase per share attributable to this offering	\$ 0.49
As adjusted net tangible book value per share as of September 30, 2017 after this offering	\$ 1.29
Dilution per share to new investors purchasing our common stock in this offering	\$ 3.96

If the underwriters exercise in full their option to purchase up to 1,500,000 additional shares of common stock, the as adjusted net tangible book value after this offering would be \$1.36 per share, representing an increase in net tangible book value of \$0.55 per share to existing stockholders and immediate dilution of \$3.89 per share to new investors purchasing our common stock in this offering.

The table and figures above are based on the 74,785,426 shares of our common stock outstanding as of September 30, 2017 and exclude:

5,549,543 shares of our common stock subject to options outstanding as of September 30, 2017 having a weighted average exercise price of \$6.00 per share; and

432,284 shares of our common stock that have been reserved for issuance exercise of outstanding warrants as of September 30, 2017, having a weighted average exercise price of approximately \$2.86 per share.

To the extent that outstanding options or warrants are exercised or our common stock is issued pursuant to other outstanding commitments, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised

through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our existing stockholders.

S-8

Table of Contents**UNDERWRITING**

Jefferies LLC and Barclays Capital Inc. are acting as active joint bookrunners of this offering, and Cantor Fitzgerald & Co. is acting as passive bookrunner of this offering. Subject to the terms and conditions set forth in the underwriting agreement, dated January 18, 2018, by and among us and Jefferies LLC, Barclays Capital Inc. and Cantor Fitzgerald & Co., as the representatives of the underwriters named below we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name in the table below.

UNDERWRITER	NUMBER OF SHARES
Jefferies LLC	4,500,000
Barclays Capital Inc.	2,000,000
Cantor Fitzgerald & Co.	1,700,000
Chardan Capital Markets, LLC	900,000
B. Riley FBR, Inc.	900,000
Total:	10,000,000

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock, if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in our common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for our common stock, that you will be able to sell any of our common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of our common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of our common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$0.189 per share of our common stock. After the offering, the public offering price and concession to dealers may be reduced by the representatives. No such reduction shall change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without Exercise of Option to Purchase Additional Shares	With Full Exercise of Option to Purchase Additional Shares	Without Exercise of Option to Purchase Additional Shares	With Full Exercise of Option to Purchase Additional Shares
Public offering price	\$ 5.25	\$ 5.25	\$ 52,500,000	\$ 60,375,000
Underwriting discounts and commissions paid by us	\$ 0.315	\$ 0.315	\$ 3,150,000	\$ 3,622,500
Proceeds to us, before expenses	\$ 4.935	\$ 4.935	\$ 49,350,000	\$ 56,752,500

S-9

Table of Contents

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$50,000. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to \$20,000.

Right of First Refusal

We have also granted Jefferies LLC a right of first refusal for two years, subject to certain limitations, to act as joint bookrunning manager in our next equity financing.

Listing

Our common stock is currently listed on the Nasdaq Global Select Market under the symbol ARWR.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of 1,500,000 shares of our common stock at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We and our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or

otherwise transfer or dispose of any shares of common stock, options or warrants or other rights to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus supplement. Jefferies LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-day period referred to above release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our executive officers and directors who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of our common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

Table of Contents

A stabilizing bid is a bid for the purchase of shares of our common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of our common stock. A syndicate covering transaction is the bid for or the purchase of shares of our common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if shares of our common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities, and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

This prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by the underwriters or their respective affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they may routinely hedge their credit

exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

Australia

This prospectus supplement is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement in Australia:

S-11

Table of Contents

A. You confirm and warrant that you are either:

sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;

a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act, any offer made to you under this prospectus supplement is void and incapable of acceptance.

B. You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus supplement for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of any common stock which are the subject of the offering contemplated by this prospectus supplement and the accompanying prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of common stock shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an offer common stock to the public in relation to the common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the common stock to be offered so as to enable an investor to decide to purchase or subscribe to the common stock, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Canada

The shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities

Table of Contents

Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus supplement has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person

S-13

Table of Contents

pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA. Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a) a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:
 - i. to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;
 - ii. where no consideration is given for the transfer; or
 - iii. where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement and the accompanying prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement and the accompanying prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus supplement and the accompanying prospectus are only being distributed to, and are only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a relevant person).

This prospectus supplement and the accompanying prospectus and their contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

S-14

Table of Contents

LEGAL MATTERS

Gibson, Dunn & Crutcher LLP of San Francisco, California will issue an opinion with respect to the validity of the issuance of the securities being offered hereby. Latham & Watkins LLP of San Diego, California is counsel to the underwriters in connection with this offering.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement the information that we file with it. Incorporation by reference means that we can disclose important information to you by referring you to other documents that are legally considered to be part of this prospectus. Later information that we file with the SEC will automatically update and supersede the information in this prospectus supplement, any supplement and the documents listed below. Our SEC file number is 0-21898. We incorporate by reference the specific documents listed below and any future filings made with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Exchange Act, as amended, until all of the shares of common stock covered by this prospectus supplement are sold:

the Company's Annual Reports on Form 10-K for the fiscal years ended September 30, 2017, filed on December 12, 2017;

the Company's Definitive Proxy Statement on Schedule 14A, filed on February 1, 2017;

the Company's Current Reports on Form 8-K filed on December 12, 2017 and December 27, 2017; and

the description of the Company's Common Stock contained in its registration statement on Form 8-A/A (Registration No. 000-21898), filed on April 7, 2016, including any amendments or reports filed for the purpose of updating such description.

We will furnish without charge to each person, including any beneficial owner, to whom this prospectus supplement is delivered, upon written or oral request, a copy of any document incorporated by reference. Requests should be addressed to Corporate Secretary, 225 South Lake Avenue, Suite 1050, Pasadena, CA 91101 or may be made telephonically at (626) 304-3400.

* * *

S-15

Table of Contents

Prospectus

Arrowhead Pharmaceuticals, Inc.

Common Stock

Preferred Stock

Debt Securities

Warrants

From time to time we may offer common stock, preferred stock, debt securities and warrants consisting of a combination of any of these securities at an aggregate initial offering price not to exceed \$200,000,000. The debt securities that we may offer may consist of senior debt securities or subordinated debt securities, in each case consisting of notes or other evidence of indebtedness in one or more series. The warrants that we may offer will consist of warrants to purchase any of the other securities that may be sold under this prospectus. The securities offered under this prospectus may be offered separately, together or in series separate, and in amounts, at prices and on terms to be determined at the time of sale. A prospectus supplement that will set forth the terms of the offering of any securities will accompany this prospectus.

We may offer these securities through agents, underwriters or dealers or directly to investors. See Plan of Distribution in this prospectus. Each prospectus supplement will provide the amount, price and terms of the plan of distribution relating to the securities to be sold pursuant to such prospectus supplement. We will set forth the names of any underwriters or agents in the accompanying prospectus supplement, as well as the net proceeds we expect to receive from such sale.

You should read this prospectus, the prospectus supplement and the documents incorporated by reference in this prospectus and any prospectus supplement carefully before you invest. This prospectus may not be used to offer or sell any of the common stock, preferred stock, warrants or debt securities unless accompanied by a prospectus supplement.

Our common stock is traded on The Nasdaq Global Select Market under the symbol ARWR. On November 22, 2016, the closing sale price of our common stock on The Nasdaq Global Select Market was \$4.44 per share. Our principal executive offices are located at 225 South Lake Avenue, Suite 1050, Pasadena, California 91101, and our telephone number is (626) 304-3400.

Investing in our securities involves a high degree of risk. You should carefully consider the Risk Factors beginning on page 3 before you invest in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is February 3, 2017

Table of Contents

Table of Contents

<u>ABOUT THIS PROSPECTUS</u>	1
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	1
<u>ABOUT THE COMPANY</u>	2
<u>RISK FACTORS</u>	3
<u>USE OF PROCEEDS</u>	3
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	3
<u>DESCRIPTION OF SECURITIES</u>	4
<u>PLAN OF DISTRIBUTION</u>	12
<u>EXPERTS</u>	14
<u>LEGAL MATTERS</u>	14
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	14
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	14

You should rely only on the information contained or incorporated by reference into this prospectus and any prospectus supplement or any free writing prospectus that we may provide to you. We have not authorized anyone to provide you with different information. You must not rely upon any unauthorized information or representation. You should not assume that the information contained in this prospectus or any applicable prospectus supplement is accurate as of any date other than the date on the front cover of the prospectus or the prospectus supplement or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference. Our business, financial condition, results of operations and prospects may have changed since those dates. We are not making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the SEC), using a shelf registration process. Under this shelf registration process, we may offer common stock, preferred stock, debt securities or warrants over time in one or more offerings at prices and on terms to be determined by market conditions at the time of the offering, up to a total dollar amount of \$200,000,000. This prospectus only provides you with a general description of the securities we may offer. Each time we sell any common stock, preferred stock, debt securities or warrants under this prospectus, we will provide a prospectus supplement that will contain more specific information about the securities being offered and the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. Each prospectus supplement and any relating free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus. If there is any inconsistency between the information in this prospectus and any accompanying prospectus supplement or related free writing prospectus, you should rely on the information in the prospectus supplement or any related free writing prospectus we may authorize to be provided to you. This prospectus may not be used to sell any common stock, preferred stock, debt securities or warrants unless accompanied by a prospectus supplement. You should carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the additional information incorporated herein by reference as described under the headings *Where You Can Find More Information* and *Incorporation of Certain Information by Reference* in this prospectus, before you invest in any of the securities being offered hereby.

We have not authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document (unless the information specifically indicates that another date applies) and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading *Where You Can Find More Information*.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains certain forward-looking statements as that term is defined under the Private Securities Litigation Reform Act of 1995, and we intend that such forward-looking statements be subject to the safe harbors created thereby. For this purpose, any statements contained in this prospectus 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 our most recent Annual Report on Form 10-K, factors described under the section captioned "Risk Factors" in this prospectus, as may be updated from time to time by our future filings under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and elsewhere in the documents incorporated by reference in this prospectus. Readers should carefully review these risks, as well as the additional risks described in other documents we file from time to time with the SEC. In light of the significant risks and uncertainties inherent in the forward-looking information included herein, the inclusion of such information should not be regarded as a representation by us or any other person that such results will be achieved, and readers are cautioned not to place undue reliance on such forward-looking information. 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.

Table of Contents

ABOUT THE COMPANY

*Unless otherwise noted: (1) the term **Arrowhead** refers to Arrowhead Pharmaceuticals, Inc., a Delaware corporation, formerly known as Arrowhead Research Corporation and InterActive Group, Inc., (2) the terms **the Company**, **we**, **us** and **our** refer to the ongoing business operations of Arrowhead and its subsidiaries, whether conducted through Arrowhead or a subsidiary of Arrowhead, and (3) the term **Common Stock** refers to shares of Arrowhead's Common Stock and the term **stockholder(s)** refers to the holders of Common Stock or securities exercisable for Common Stock.*

Arrowhead develops novel drugs to 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 (RNAi) is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing. The Company's pipeline includes ARC-520 and ARC-521 for chronic hepatitis B virus, ARC-AAT for liver disease associated with alpha-1 antitrypsin deficiency, ARC-F12 for hereditary angioedema and thromboembolic disorders, ARC-LPA for cardiovascular disease and ARC-HIF2 for renal cell carcinoma.

Our executive offices are located at 225 South Lake Avenue, Suite 1050, Pasadena CA 91101 and our telephone number is (626) 304-3400. Additional information regarding our company, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus. See **Where You Can Find More Information** on page 14 and **Incorporation of Certain Information by Reference** on page 14.

Recent Developments

On November 15, 2016 the Company and certain executive officers were named as defendants in a putative securities class action filed in the Central District of California and captioned *Meller v. Arrowhead Pharmaceuticals, Inc., et al.*, No. 2:16-cv-08505. The plaintiff brings 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. The Company believes it has meritorious defenses and intends to vigorously defend itself in this matter. 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 this matter. The Company does not expect this to have a material effect on its Consolidated Financial Statements. With regard to legal fees, such as attorney fees related to this matter or any other legal matters, the Company's recognizes such costs as incurred.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described in the sections entitled "Risk Factors" in our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q, as filed with the SEC, which are incorporated herein by reference in their entirety, as well as any amendment or updates to our risk factors reflected in subsequent filings with the SEC, including any applicable prospectus supplement. Our business, financial condition, results of operations or prospects could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned elsewhere in this prospectus. For more information, see the section entitled "Where You Can Find More Information."

USE OF PROCEEDS

Unless otherwise stated in the applicable prospectus supplement, we intend to use the net proceeds from the sale of our securities and from the exercise of the warrants issued pursuant hereto, if any, for general corporate purposes, which may include one or more of the following:

working capital;

research and clinical development activities;

potential future acquisitions of companies and/or technologies;

repayment of debt; and

capital expenditures.

Our management will have broad discretion in the allocation of the net proceeds of any offering. Pending such uses, we intend to invest the net proceeds in short-term, investment grade, interest-bearing securities.

RATIO OF EARNINGS TO FIXED CHARGES

If we offer debt securities and/or preference equity securities under this prospectus, then we will, if required at that time, provide a ratio of earnings to fixed charges and/or ratio of combined fixed charges and preference dividends to earnings, respectively, in the applicable prospectus supplement for such offering.

Table of Contents

DESCRIPTION OF SECURITIES

Description of Capital Stock

The following is a description of our common stock and a summary of our preferred stock. You should refer to our Amended and Restated Certificate of Incorporation (the "Certificate of Incorporation") and our Amended and Restated Bylaws (the "Bylaws"), copies of which are filed as Exhibits 3.1 and 3.2 hereto, respectively, for the actual terms of our capital stock. Copies of our Certificate of Incorporation and Bylaws may be obtained as described under the heading "Where You Can Find More Information" in this prospectus.

We are authorized to issue up to 145,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share. As of November 22, 2016, 71,492,495 shares of common stock and 15,652 shares of preferred stock were issued and outstanding.

Common Stock

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

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

Preferred Stock

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

If we issue preferred stock, we will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designations relating to that series. If we issue preferred stock, we will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designations that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplement related to any series of preferred stock we may offer, as well as the complete certificate of designations that contains the terms of the applicable series of preferred stock.

Delaware Anti-Takeover Law

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

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Table of Contents

Section 203 of the DGCL defines a business combination to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

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

Description of Debt Securities

We may issue debt securities under an indenture to be entered into between us and a trustee chosen by us, qualified to act as such under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act") and appointed under an indenture. The indenture will be governed by the Trust Indenture Act.

The following is a summary of the indenture. It does not restate the indenture entirely. We urge you to read the indenture. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and we will file the indenture we enter into and the supplemental indentures or authorizing resolutions with respect to particular series of debt securities as exhibits to current or other reports we file with the SEC. See "Where You Can Find More Information" for information on how to obtain copies of the indentures and the supplemental indentures or authorizing resolutions. You may also inspect copies of the documents for the particular series at the office of the trustee. References below to an "indenture" are references to the applicable indenture, as supplemented, under which a particular series of debt securities is issued.

Terms of the Debt Securities

Our debt securities will be general obligations of Arrowhead. We may issue them in one or more series. Authorizing resolutions or a supplemental indenture will set forth the specific terms of each series of debt securities. We will provide a prospectus supplement for each series of debt securities that will describe:

the title of the debt securities and whether the debt securities are senior, senior subordinated, or subordinated debt securities;

the aggregate principal amount of the debt securities and any limit upon the aggregate principal amount of the series of debt securities, and, if the series is to be issued at a discount from its face amount, the method of computing the accretion of such discount;

the percentage of the principal amount at which debt securities will be issued and, if other than the full principal amount thereof, the percentage of the principal amount of the debt securities that is payable if maturity of the debt securities is accelerated because of a default;

the date or dates on which principal of the debt securities will be payable and the amount of principal that will be payable;

the rate or rates (which may be fixed or variable) at which the debt securities will bear interest, if any, or the method of calculation of such rate or rates, as well as the dates from which interest will accrue, the dates on which interest will be payable and the record date for the interest payable on any payment date;

any collateral securing the performance of our obligations under the debt securities;

the currency or currencies (including any composite currency) in which principal, premium, if any, and interest, if any, will be payable, and if such payments may be made in a currency other than that in which the debt securities are denominated, the manner for determining such payments, including the time and manner of determining the exchange rate between the currency in which such securities are denominated and the currency in which such securities or any of them may be paid, and any additions to, modifications of or deletions from the terms of the debt securities to provide for or to facilitate the issuance of debt securities denominated or payable in a currency other than U.S. dollars;

Table of Contents

the place or places where principal, premium, if any, and interest, if any, on the debt securities will be payable and where debt securities that are in registered form can be presented for registration of transfer or exchange;

the denominations in which the debt securities will be issuable, if different from \$2,000 and multiples of \$1,000 in excess thereof;

any provisions regarding our right to redeem or purchase debt securities or the right of holders to require us to redeem or purchase debt securities;

the right, if any, of holders of the debt securities to convert or exchange them into our common stock or other securities of any kind of us or another obligor, including any provisions intended to prevent dilution of the conversion rights and, if so, the terms and conditions upon which such securities will be so convertible or exchangeable, including the initial conversion or exchange price or rate or the method of calculation, how and when the conversion price or exchange ratio may be adjusted, whether conversion or exchange is mandatory, at the option of the holder or at our option, the conversion or exchange period, and any other provision in relation thereto;

any provisions requiring or permitting us to make payments to a sinking fund to be used to redeem debt securities or a purchase fund to be used to purchase debt securities;

the terms, if any, upon which debt securities may be senior or subordinated to our other indebtedness;

any additions to, modifications of or deletions from the terms of the debt securities with respect to events of default or covenants or other provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates;

whether and upon what terms the debt securities of such series may be defeased or discharged, if different from the provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates;

whether the debt securities will be issued in registered or bearer form and the terms of these forms;

whether the debt securities will be issued in whole or in part in the form of a global security and, if applicable, the identity of the depositary for such global security;

any provision for electronic issuance of the debt securities or issuance of the debt securities in uncertificated form; and

any other material terms of the debt securities, which may be different from the terms set forth in this prospectus.

The applicable prospectus supplement will also describe any material covenants to which a series of debt securities will be subject and the applicability of those covenants to any of our subsidiaries to be restricted thereby, which are referred to herein as restricted subsidiaries. The applicable prospectus supplement will also describe provisions for restricted subsidiaries to cease to be restricted by those covenants.

Events of Default and Remedies

Unless otherwise described in the applicable prospectus supplement, an event of default with respect to any series of debt securities will be defined in the indenture or applicable supplemental indenture or authorizing resolution as being:

our failure to pay interest on any debt security of such series when the same becomes due and payable and the continuance of any such failure for a period of 30 days;

our failure to pay the principal or premium of any debt security of such series when the same becomes due and payable at maturity, upon acceleration, redemption or otherwise;

our failure or the failure of any restricted subsidiary to comply with any of its agreements or covenants in, or provisions of, the debt securities of such series or the indenture (as they relate thereto) and such failure continues for a period of 60 days after our receipt of notice of the default from the trustee or from the holders of at least 25% in aggregate principal amount of the then outstanding debt securities of that series (except in the case of a default with respect to the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of the assets of us (or any other provision specified in the applicable supplemental indenture or authorizing resolution), which will constitute an event of default with notice but without passage of time);

default under any mortgage, indenture or instrument under which there may be issued or by which there may be secured or evidenced any indebtedness (other than non-recourse indebtedness, as defined in the indenture) for money borrowed by us or any of our restricted subsidiaries (or the payment of which is guaranteed by us or any of our restricted subsidiaries), whether such indebtedness or guarantee now exists or is created after the date we issue debt securities, if that default:

- (a) is caused by a failure to pay at final stated maturity the principal amount of such indebtedness prior to the expiration of the grace period provided in such indebtedness on the date of such default (a Payment Default); or
- (b) results in the acceleration of such indebtedness prior to its express maturity without such indebtedness having been discharged or such acceleration having been cured, waived, rescinded or annulled for the period and after the notice had been provided,

Table of Contents

and, in each case, the principal amount of any such indebtedness, together with the principal amount of any other such indebtedness under which there has been a Payment Default or the maturity of which has been so accelerated, aggregates \$50 million or more; or

certain events of bankruptcy, insolvency or reorganization occur with respect to us or any restricted subsidiary that is a significant subsidiary (as defined in the indenture).

The indenture will provide that the trustee may withhold notice to the holders of any series of debt securities of any default, except a default in payment of principal or interest, if any, with respect to such series of debt securities, if the trustee considers it in the interest of the holders of such series of debt securities to do so.

The indenture will provide that if any event of default has occurred and is continuing with respect to any series of debt securities, the trustee or the holders of not less than 25% in principal amount of such series of debt securities then outstanding may declare the principal of all the debt securities of such series to be due and payable immediately. However, the holders of a majority in principal amount of the debt securities of such series then outstanding by notice to the trustee may waive any existing default and its consequences with respect to such series of debt securities, other than any event of default in payment of principal or interest. Holders of a majority in principal amount of the then outstanding debt securities of any series may rescind an acceleration with respect to such series and its consequences, except an acceleration due to nonpayment of principal or interest on such series, if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to such series have been cured or waived.

The holders of a majority of the outstanding principal amount of the debt securities of any series will have the right to direct the time, method and place of conducting any proceedings for any remedy available to the trustee with respect to such series, subject to limitations specified in the indenture.

Defeasance

The indenture will permit us to terminate all our respective obligations under the indenture as they relate to any particular series of debt securities, other than the obligation to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal of and interest, if any, on the debt securities of such series to their maturity or redemption; and

complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

The indenture will also permit us to terminate all of our respective obligations under the indenture as they relate to any particular series of debt securities, including the obligations to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal and interest, if any, on the debt securities of such series to their maturity or redemption; and

complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that (A) we have received from, or there has been published by, the Internal Revenue Service a ruling, or (B) since the date such series of debt securities were originally issued, there has been a change in the applicable federal income tax law, in either case to the effect that, and based thereon such opinion of counsel shall state that, holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

Table of Contents

In addition, the indenture will permit us to terminate substantially all our respective obligations under the indenture as they relate to a particular series of debt securities by depositing with the trustee money or government obligations sufficient to pay all principal and interest on such series at its maturity or redemption date if the debt securities of such series will become due and payable at maturity within one year or are to be called for redemption within one year of the deposit.

Transfer and Exchange

A holder will be able to transfer or exchange debt securities only in accordance with the indenture. The registrar may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture.

Amendment, Supplement and Waiver

Without notice to or the consent of any holder, we and the trustee may amend or supplement the indenture or the debt securities of a series to:

cure any ambiguity, omission, defect or inconsistency;

comply with the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets;

provide that specific provisions of the indenture shall not apply to a series of debt securities not previously issued or to make a change to specific provisions of the indenture that only applies to any series of debt securities not previously issued or to additional debt securities of a series not previously issued;

create a series and establish its terms;

provide for uncertificated debt securities in addition to or in place of certificated debt securities;

add a guarantor subsidiary in respect of any series of debt securities;

secure any series of debt securities;

comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act;

make any change that does not adversely affect the rights of any holder; or

conform the provisions of the indenture to the final offering document in respect of any series of debt securities.

With the exceptions discussed below, we and the trustee may amend or supplement the indenture or the debt securities of a particular series with the written consent of the holders of at least a majority in principal amount of the debt securities of such series then outstanding. In addition, the holders of a majority in principal amount of the debt securities of such series then outstanding may waive any existing default under, or compliance with, any provision of the debt securities of a particular series or of the indenture relating to a particular series of debt securities, other than any event of default in payment of interest or principal. These consents and waivers may be obtained in connection with a purchase of, or tender offer or exchange offer for, debt securities.

Without the consent of each holder affected, we and the trustee may not:

reduce the amount of debt securities of such series whose holders must consent to an amendment, supplement or waiver;

reduce the rate of or extend the time for payment of interest, including defaulted interest;

reduce the principal of or extend the fixed maturity of any debt security or alter the provisions with respect to redemptions or mandatory offers to repurchase debt securities;

make any change that adversely affects any right of a holder to convert or exchange any debt security into or for shares of our common stock or other securities, cash or other property in accordance with the terms of such security;

modify the ranking or priority of the debt securities;

make any change to any provision of the indenture relating to the waiver of existing defaults, the rights of holders to receive payment of principal and interest on the debt securities, or to the provisions regarding amending or supplementing the indenture or the debt securities of a particular series with the written consent of the holders of such series;

waive a continuing default or event of default in the payment of principal of or interest on the debt securities;
or

make any debt security payable at a place or in money other than that stated in the debt security, or impair the right of any holder of a debt security to bring suit as permitted by the indenture.

Table of Contents

The right of any holder to participate in any consent required or sought pursuant to any provision of the indenture, and our obligation to obtain any such consent otherwise required from such holder, may be subject to the requirement that such holder shall have been the holder of record of debt securities with respect to which such consent is required or sought as of a record date fixed by us in accordance with the indenture.

Concerning the Trustee

The indenture will contain limitations on the rights of the trustee, should it become our creditor, to obtain payment of claims in specified cases or to realize on property received in respect of any such claim as security or otherwise. The indenture will permit the trustee to engage in other transactions; however, if it acquires any conflicting interest, it must eliminate such conflict or resign.

The indenture will provide that in case an event of default occurs and is not cured, the trustee will be required, in the exercise of its power, to use the degree of care of a prudent person in similar circumstances in the conduct of such person's own affairs. The trustee shall be under no obligation to exercise any of the rights or powers vested in it by the indenture at the request or direction of any of the holders pursuant to the Indenture, unless such holders shall have offered to the trustee security or indemnity satisfactory to the trustee against the costs, expenses and liabilities which might be incurred by it in compliance with such request or direction.

No Recourse against Others

The indenture will provide that a director, officer, employee or stockholder, as such, of the Company shall not have any liability for any obligations of the Company under the debt securities or the indenture or for any claim based on, in respect of or by reason of, such obligations or their creation.

Governing Law

The laws of the State of New York will govern the indenture and the debt securities.

Description of Warrants

General Description of Warrants

We may issue warrants for the purchase of debt securities, common stock, preferred stock or any combination of these securities. Warrants may be issued independently or together with other securities and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between a warrant agent and us. The warrant agent will act solely as our agent in connection with the warrants and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. The following outlines some of the general terms and provisions of the warrants that we may issue from time to time. Additional terms of the warrants and the applicable warrant agreement will be set forth in the applicable prospectus supplement. The following description, and any description of the warrants included in a prospectus supplement, may not be complete and is subject to and qualified in its entirety by reference to the terms and provisions of the applicable warrant agreement, which we will file with the SEC in connection with any offering of warrants.

Debt Warrants

The prospectus supplement relating to a particular issue of warrants exercisable for debt securities will describe the terms of those warrants, including the following:

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of the warrants;

the designation and terms of the debt securities purchasable upon exercise of the warrants;

Table of Contents

if applicable, the designation and terms of the securities that the warrants are issued with and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the principal amount and price of debt securities that may be purchased upon exercise of a warrant;

the dates on which the right to exercise the warrants commences and expires;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

whether the warrants represented by the warrant certificates or debt securities that may be issued upon exercise of the warrants will be issued in registered or bearer form;

information relating to book-entry procedures, if any;

if applicable, a discussion of material U.S. federal income tax considerations;

anti-dilution provisions of the warrants, if any;

redemption or call provisions, if any, applicable to the warrants; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Stock Warrants

The prospectus supplement relating to a particular issue of warrants exercisable for common stock or preferred stock will describe the terms of the common stock warrants and preferred stock warrants, including the following:

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of the warrants;

the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the securities that the warrants are issued with and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the number of shares and price of common stock or preferred stock that may be purchased upon exercise of a warrant;

the dates on which the right to exercise the warrants commences and expires;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

if applicable, a discussion of material U.S. federal income tax considerations;

anti-dilution provisions of the warrants, if any;

redemption or call provisions, if any, applicable to the warrants; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Exercise of Warrants

Each warrant will entitle the holder of the warrant to purchase at the exercise price set forth in the applicable prospectus supplement the principal amount of debt securities or shares of common stock or preferred stock being offered. Holders may exercise warrants at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will be void. Holders may exercise warrants as set forth in the prospectus supplement relating to the warrants being offered.

Table of Contents

Until a holder exercises the warrants to purchase any securities underlying the warrants, the holder will not have any rights as a holder of the underlying securities by virtue of ownership of warrants.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus from time to time in any manner permitted under the Securities Act. Registration of the securities covered by this prospectus does not mean, however, that those securities will necessarily be offered or sold.

We may sell the securities separately or together:

through one or more underwriters or dealers in a public offering and sale by them;

directly to investors;

to dealers; or

through agents.

We may also make direct sales through subscription rights distributed to our stockholders on a pro rata basis, which may or may not be transferable. In any distribution of subscription rights to stockholders, if all of the underlying securities are not subscribed for, we may then sell the unsubscribed securities directly to third parties or may engage the services of one or more underwriters, dealers or agents, including standby underwriters, to sell the unsubscribed securities to third parties.

We may sell the securities from time to time:

in one or more transactions at a fixed price or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

Any of the prices may represent a discount from prevailing market prices. We will describe the method of distribution of the securities and the terms of the offering in the prospectus supplement. Any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more of the transactions described above. Any underwritten offering may be on a best efforts or firm commitment basis. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the

underwriters' obligations to purchase the securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the securities if they purchase any of the securities. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

In any sale of the securities, underwriters or agents may receive compensation from us or from purchasers of the securities, for whom they may act as agents, in the form of discounts, concessions or commissions. Underwriters may sell the securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of the securities may be deemed to be underwriters under the Securities Act, and any discounts or commissions they receive from us and any profit on the resale of securities they realize may be deemed to be underwriting discounts and commissions under the Securities Act. Any initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

Each time we sell securities, we will describe the method of distribution of the securities in the prospectus supplement relating to such transaction. The applicable prospectus supplement will, where applicable:

identify any such underwriter or agent;

describe any compensation in the form of discounts, concessions, commissions or otherwise received from us by each such underwriter or agent and in the aggregate to all underwriters and agents;

identify the amounts underwritten or to be sold through the agent; and

identify the nature of the underwriter's or agent's obligation to take the securities.

Table of Contents

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement or in a post-effective amendment.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution.

Unless otherwise specified in the related prospectus supplement, all securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. Any common stock sold pursuant to a prospectus supplement will be listed for trading on The Nasdaq Global Select Market or other principal market for our common stock. We may apply to list any series of debt securities, preferred stock or warrants on an exchange, but we are not obligated to do so. Therefore, there may not be liquidity or a trading market for any series of securities.

Any underwriter may engage in over-allotment transactions, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. We make no representation or prediction as to the direction or magnitude of any effect that such transactions may have on the price of the securities. For a description of these activities, see the information under the heading **Underwriting** or **Plan of Distribution** in the applicable prospectus supplement.

Underwriters, broker-dealers or agents who may become involved in the sale of the common stock may engage in transactions with and perform other services for us in the ordinary course of their business for which they receive compensation.

To comply with applicable state securities laws, the securities offered by this prospectus will be sold, if necessary, in such jurisdictions only through registered or licensed brokers or dealers. In addition, securities may not be sold in

some states unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Table of Contents

EXPERTS

The financial statements of the Company incorporated in this prospectus by reference from the Company's Annual Report on Form 10-K for the year ended September 30, 2015 have been audited by Rose, Snyder & Jacobs, LLP as stated in their report incorporated by reference, and given upon the authority of said firm as experts in auditing and accounting.

LEGAL MATTERS

Certain legal matters, including the validity of the securities offered pursuant to this registration statement, will be passed upon for us by Gibson, Dunn & Crutcher LLP, San Francisco, California.

WHERE YOU CAN FIND MORE INFORMATION

We must comply with the informational requirements of the Exchange Act, and we are required to file reports and proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies at the prescribed rates from the Public Reference Section of the Securities and Exchange Commission at its principal office in Washington, D.C. You may call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC. You may access the SEC's web site at <http://www.sec.gov>. We maintain a website at www.arrowheadpharma.com. The information contained in, or that can be accessed through, our website is not incorporated by reference herein and is not part of this prospectus.

Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus the information that we file with it. Incorporation by reference means that we can disclose important information to you by referring you to other documents that are legally considered to be part of this prospectus. Later information that we file with the SEC will automatically update and supersede the information in this prospectus, any supplement and the documents listed below. Our SEC file number is 0-21898. We incorporate by reference the specific documents listed below and any future filings made with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Exchange Act, as amended, until all of the shares of common stock covered by this prospectus are sold:

The Company's Annual Report on Form 10-K for the fiscal year ended September 30, 2015, filed on December 14, 2015;

The Company's Quarterly Reports on Form 10-Q for the fiscal quarters ended December 31, 2015, March 31, 2016 and June 30, 2016, filed on February 9, 2016, May 10, 2016 and August 9, 2016, respectively;

The Company's Definitive Proxy Statement on Schedule 14A, filed on January 19, 2016;

The Company's Current Reports on Form 8-K filed on January 14, 2016, March 10, 2016, April 6, 2016, August 10, 2016, September 29, 2016 (Items 1.01, 3.02 and 9.01) and November 10, 2016;

The description of the Company's Common Stock contained in its registration statement on Form 8-A/A (Registration No. 000-21898), filed on April 7, 2016, including any amendments or reports filed for the purpose of updating such description; and

All documents filed by the Company pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, after the date of the original Registration Statement and prior to effectiveness of the registration statement of which this prospectus is a part, provided that all documents furnished by the Company to the SEC and not filed are not deemed incorporated by reference herein.

We will furnish without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any document incorporated by reference. Requests should be addressed to Corporate Secretary, 225 South Lake Avenue, Suite 1050, Pasadena, CA 91101 or may be made telephonically at (626) 304-3400.

Table of Contents

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. You should not assume that the information contained in this prospectus or the accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

Table of Contents

10,000,000 Shares

Common Stock

PROSPECTUS SUPPLEMENT

January 18, 2018

Joint Bookrunners

Jefferies

**Barclays
*Co-Managers***

Joint Passive Bookrunner

Cantor

Chardan Capital Markets, LLC

B. Riley FBR, Inc.