

Prospectus

Arrowhead Pharmaceuticals, Inc.

7,627,119 shares of Common Stock

This prospectus covers the sale of an aggregate of 7,627,119 shares of our Common Stock, \$0.001 par value per share (the "Shares"), by the selling security holders identified in this prospectus (collectively with any donees, pledgees, transferees or other successors-in-interest selling shares of Common Stock or interests in shares of Common Stock received after the date of this prospectus from such selling security holders as a gift, pledge, partnership distribution or other transfer, the "selling stockholders"). The Shares covered by this prospectus were issued to the selling stockholders on August 11, 2016 pursuant to that certain Securities Purchase Agreement, dated August 8, 2016 (the "Securities Purchase Agreement"), by and between the Company and the selling stockholders.

The Company will not receive any proceeds from the sale by the selling stockholders of the Shares. We are paying the cost of registering the Shares covered by this prospectus as well as various related expenses. The selling stockholders are responsible for all selling commissions, transfer taxes and other costs related to the offer and sale of their shares.

Sales of the Shares by the selling stockholders may occur at fixed prices, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. The selling stockholders may sell shares to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling stockholders, the purchasers of the Shares, or both. If required, the number of shares to be sold, the public offering price of those shares, the names of any underwriters, broker-dealers or agents and any applicable commission or discount will be included in a supplement to this prospectus, called a prospectus supplement.

The Company's Common Stock is traded on The Nasdaq Global Select Market under the symbol "ARWR." On September 27, 2016, the closing sale price of our Common Stock on The Nasdaq Global Select Market was \$7.13 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 2 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 September 29, 2016

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ABOUT THIS PROSPECTUS

You should read this prospectus, any applicable prospectus supplement and the information incorporated by reference in this prospectus before making an investment in the securities of Arrowhead Pharmaceuticals, Inc. See “Where You Can Find Additional Information” for more information, page 6. You should rely only on the information contained in or incorporated by reference in this prospectus or a prospectus supplement. We have not authorized anyone to provide you with different information. This prospectus may be used only in jurisdictions where offers and sales of these securities are permitted. You should assume that information contained in this prospectus, or in any document incorporated by reference, is accurate only as of any date on the front cover of the applicable document. Our business, financial condition, results of operations and prospects may have changed since that date.

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 Securities and Exchange Commission (the “SEC”). In light of the significant risks and uncertainties inherent in the forward-looking information included herein, the inclusion of such information should not be regarded as a representation by us or any other person that such results will be achieved, and readers are cautioned not to place undue reliance on such forward-looking information. 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.

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.

On September 29, 2016, we announced that we had entered into two Collaboration and License Agreements and a Common Stock Purchase Agreement with Amgen, Inc. Additional information regarding these agreements can be found in our Current Report on Form 8-K filed September 29, 2016, which is incorporated herein by reference.

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 6 and “Incorporation of Certain Information by Reference” on page 7.

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 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

The proceeds from the resale of the Shares under this prospectus are solely for the account of the selling stockholders. We will not receive any proceeds from the sale of Shares under this prospectus.

SELLING STOCKHOLDERS

The Company has included in this prospectus 7,627,119 shares of Common Stock, which were originally issued to the selling stockholders on August 11, 2016 pursuant to the Securities Purchase Agreement. In connection with the consummation of the transactions contemplated by the Securities Purchase Agreement, we agreed to file a registration statement with the SEC covering the resale of the Shares.

The following table sets forth certain information regarding the selling stockholders and the shares of Common Stock beneficially owned by each of them, which is based on information that is available to us as of September 1, 2016. Each of the selling stockholders may offer shares of Common Stock under this prospectus from time to time and may elect to sell none, some or all of the shares of Common Stock set forth next to its name. As a result, we cannot estimate the number of shares of Common Stock each of the selling stockholders will beneficially own after termination of sales under this prospectus. In addition, each of the selling stockholders may have sold, transferred or otherwise disposed of all or a portion of such holder's shares of Common Stock since the date on which it provided information for this table. We have not made independent inquiries about this.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our Common Stock.

We are relying on written commitments from each of the selling stockholders to notify us of any changes in its beneficial ownership after the date it originally provided the information below. See "Plan of Distribution" beginning on page 5.

Selling Security Holder(1)	# of Shares held before Offering	# Shares Being Offered	# of Shares held after Offering(2)	Percentage of Shares After Offering(2)
OrbiMed Partners Master Fund Limited (3)	1,380,573	1,380,573	—	—
OrbiMed Partners II, LP (3)	1,161,800	1,161,800	—	—
RA Capital Healthcare Fund, L.P. (4)	1,241,695	1,241,695	—	—
Blackwell Partners LLC – Series A (5)	283,729	283,729	—	—
Perceptive Life Sciences Master Fund, Ltd. (6)	847,458	847,458	—	—
Gaoling Fund, L.P. (7)	623,729	623,729	—	—
YHG Investment, L.P. (7)	54,237	54,237	—	—
RTW Master Fund, Ltd.	662,779	662,779	—	—
RTW Innovation Master Fund, Ltd.	15,187	15,187	—	—
667, L.P.(8)	424,844	86,600	338,244(9)	*
Baker Brothers Life Sciences, L.P. (8)	4,103,113	760,858	3,342,255(10)	4.88%
QVT Fund IV LP (11)	87,108	87,108	—	—
QVT Fund V LP (11)	379,997	379,997	—	—
Quintessence Fund L.P. (11)	41,369	41,369	—	—

* Less than 1%.

- (1) If required, information about other selling security holders, except for any future transferees, pledgees, donees or successors of the selling security holders named in the table above, will be set forth in a prospectus supplement or amendment to the registration statement of which this prospectus is a part. Additionally, post-effective amendments to the registration statement will be filed to disclose any material changes to the plan of distribution from the description contained in the final prospectus.
- (2) Assumes all shares of Common Stock offered by the selling stockholders hereby are sold and that the selling stockholders buy or sell no additional shares of Common Stock prior to the completion of this offering.
- (3) Samuel D. Isaly, Sven H. Borho, Carl L. Gordon, Jonathan T. Silverstein, W. Carter Neild and Geoffrey C. Hsu hold investment and voting control with respect to the Shares owned by OrbiMed Partners Master Fund Limited and OrbiMed Partners II, LP.
- (4) Peter Kolchinsky, as the Managing Member of RA Capital Management, LLC, which is the General Partner of RA Capital Healthcare Fund, L.P., has voting and investment power over the Shares owned by RA Capital Healthcare Fund, L.P.
- (5) Peter Kolchinsky, as Managing Member of RA Capital Management, LLC, which is the Investment Adviser for Blackwell Partners LLC—Series A, has voting and investment power over the Shares owned by Blackwell Partners LLC – Series A.
- (6) Joseph E. Edelman as the General Partner of Perceptive Advisors which is the investment advisor of Perceptive Life Sciences Master Fund, Ltd. has voting and investment power over the Shares owned by Perceptive Life Sciences Master Fund, Ltd.
- (7) Hillhouse Capital Management, Ltd. (an Exempted Company incorporated in the Cayman Islands) acts as the sole management company of Gaoling Fund, L.P. and YHG Investments, L.P. (each an Exempted Limited Partnership registered in the Cayman Islands, the "Funds"). Mr. Lei Zhang may be deemed to have controlling power over Hillhouse Capital Management, Ltd. Mr. Lei Zhang disclaims beneficial ownership of all of the Shares held by the Funds, except to the extent of his pecuniary interest therein.

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- (8) Julian C. Baker and Felix J. Baker are the managing partners of the advisor Baker Bros. Advisors LP and hold investment and voting power over the Shares owned by 667, L.P. and Baker Brothers Life Sciences, L.P. Baker Bros. Advisors LP is the investment advisor of 667, LP and Baker Brothers Life Sciences, LP. Julian C. Baker and Felix J. Baker disclaim beneficial ownership of the Shares held by 667, LP and Baker Brothers Life Sciences LP except to the extent of their indirect pecuniary interest.
- (9) Includes 304,778 shares issuable upon the conversion of the Company's Series C Preferred Stock.
- (10) Includes 2,366,212 shares issuable upon the conversion of the Company's Series C Preferred Stock.
- (11) Management of Quintessence Fund L.P., QVT Fund IV LP and QVT Fund V LP is vested in their general partner, QVT Associates GP LLC, which may be deemed to beneficially own the Shares held by Quintessence Fund L.P., QVT Fund IV LP and QVT Fund V LP. QVT Financial LP is the investment manager of Quintessence Fund L.P., QVT Fund IV LP and QVT Fund V LP and shares voting and investment control over the Shares held by Quintessence Fund L.P., QVT Fund IV LP and QVT Fund V LP. QVT Financial GP LLC is the general partner of QVT Financial LP and as such has complete discretion in the management and control of the business affairs of QVT Financial LP. The managing members of QVT Financial GP LLC are Daniel Gold, Nicholas Brumm, Arthur Chu and Tracy Fu. Each of Daniel Gold, Nicholas Brumm, Arthur Chu and Tracy Fu disclaims beneficial ownership of the Shares owned by Quintessence Fund, L.P., QVT Fund IV LP and QVT Fund V LP. Each of QVT Financial LP, QVT Associates GP LLC and QVT Financial GP LLC disclaims beneficial ownership of such Shares except to the extent of its pecuniary interest therein.

PLAN OF DISTRIBUTION

The selling stockholders may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of Common Stock or interests in shares of Common Stock on any stock exchange, market or trading facility on which the Common Stock is traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its own account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- through agreements between broker-dealers and the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of Common Stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of Common Stock in other circumstances, in which case the pledgees, transferees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our Common Stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Common Stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our Common Stock short and deliver these securities to close out their short positions, or loan or pledge the Common Stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into options or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to each such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the Common Stock offered by them will be the purchase price of the Common Stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of Common Stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders also may resell all or a portion of the shares of Common Stock in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the Common Stock or interests therein may be "underwriters" within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are "underwriters" within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

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To the extent required, the shares of our Common Stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealers or underwriters, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Common Stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Common Stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares of Common Stock against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (1) such time as all of the shares of Common Stock covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement or (2) the date on which all of the shares of Common Stock may be sold without restriction pursuant to Rule 144 of the Securities Act.

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:

- ⁿ The Company's Annual Report on Form 10-K for the fiscal year ended September 30, 2015, filed on December 14, 2015;
- ⁿ 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;
- ⁿ The Company's Definitive Proxy Statement on Schedule 14A, filed on January 19, 2016;
- ⁿ The Company's Current Reports on Form 8-K filed on January 14, 2016, March 10, 2016, April 6, 2016, August 10, 2016, and September 29, 2016;
- ⁿ 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
- ⁿ 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.

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.