

ARROWHEAD RESEARCH CORP

Form 424B5

February 19, 2014

Table of Contents

Filed pursuant to Rule 424(b)(5)

Registration Statement No. 333-193748

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus do not constitute an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED FEBRUARY 18, 2014

PROSPECTUS SUPPLEMENT

(To Prospectus dated February 12, 2014)

Shares

Common Stock

We are offering _____ shares of our common stock. Our common stock is currently listed on the Nasdaq Capital Market under the symbol ARWR. On February 14, 2014, the last reported sale price per share of our common stock on the Nasdaq Capital Market was \$18.99 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 SHARE	TOTAL
Public offering price	\$	\$

Edgar Filing: ARROWHEAD RESEARCH CORP - Form 424B5

Underwriting discounts and commissions	\$	\$
Proceeds to Arrowhead Research Corporation, before expenses	\$	\$

Delivery of the shares of common stock is expected to be made on or about February , 2014. We have granted the underwriters an option for a period of 30 days to purchase up to an 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 \$ million and the total proceeds to us, before expenses, will be \$ million.

Jefferies

Barclays

Deutsche Bank

Prospectus Supplement dated February , 2014.

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>CAPITALIZATION</u>	S-8
<u>DILUTION</u>	S-9
<u>UNDERWRITING</u>	S-10
<u>LEGAL MATTERS</u>	S-17
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-17

PROSPECTUS

	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>SECURITIES WE MAY OFFER</u>	3
<u>PLAN OF DISTRIBUTION</u>	4
<u>EXPERTS</u>	6
<u>LEGAL MATTERS</u>	6
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	6
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	6

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 section of the accompanying prospectus entitled Where You Can Find More Information.

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 Research Corporation and its subsidiaries, unless the context indicates otherwise. References to our common stock refer to the common stock of Arrowhead Research Corporation.

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 DPCs and homing peptides, 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 Additional Information* 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 targeted RNA interference (RNAi) therapeutics. We are leveraging our proprietary drug delivery technologies to develop drugs based on the RNA interference mechanism that efficiently silences disease-causing genes. These platforms have yielded several drug candidates under internal and partnered development. Our technologies also enable partners to create peptide-drug conjugates that specifically home to cell types of interest while sparing off-target tissues. Our pipeline includes clinical programs in chronic hepatitis B virus and partner-based programs in obesity and oncology.

Lead Product Candidate

ARC-520 is an RNAi-based therapeutic designed to treat chronic hepatitis B virus (HBV) infection. It is the first drug candidate from our Dynamic Polyconjugate® siRNA delivery platform. It is designed to treat chronic HBV infection by reducing the expression and release of new viral particles and key viral proteins with the goal of achieving a functional cure. We completed enrollment in a Phase 1 clinical trial in 2013 and expect to begin a Phase 2a trial in the first half of 2014 and a Phase 2b trial in the second half of 2014.

Platform Technologies

The Dynamic Polyconjugate (DPC®) platform is a small RNA delivery system that may be targeted to address multiple organ systems and cell types. It is a modular system that may be optimized on a target-by-target basis and has been demonstrated to promote multi-log gene knockdown, induce efficient endosomal escape, and has a favorable safety profile using a variety of siRNA molecules.

Our Homing Peptides platform is a vast, proprietary library of short peptides that have demonstrated rapid and specific internalization into a wide variety of cell types. This library is being mined for the potential targeting of RNAi therapeutics using the DPC delivery system as well as to enable partners to target traditional small molecule or peptide drugs.

Pipeline Development Strategy

Our internal drug pipeline is intended to drive value directly through the clinical development of novel therapeutics and to provide proof of concept for our platform technologies. Our core areas of focus for expanding our internal pipeline of RNAi therapeutics are: (1) develop intravenous (IV), administered liver-targeted candidates; (2) develop

subcutaneously administered liver-targeted candidates; and (3) explore extra-hepatic targets, including oncology.

We actively seek collaboration and licensing agreements with leading biopharmaceutical companies to augment their pipelines through the application of our technologies and to advance the development and commercialization of our own technology platforms and drug candidates. Partnerships are intended to provide access to external expertise and capital to complement our internal development and create commercialization opportunities in areas outside of our core focus.

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

S-3

Table of Contents

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 on page 6 of the accompanying prospectus and Incorporation of Certain Information by Reference on page S-17 of this prospectus supplement.

S-4

Table of Contents

THE OFFERING

Common stock we are offering	shares
Common stock to be outstanding immediately after this offering	shares
Option to purchase additional shares	We have granted the underwriter an option for a period of 30 days from the date of this prospectus supplement to purchase up to 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.
Nasdaq Capital Market Symbol	ARWR
The number of shares of common stock shown above to be outstanding after this offering is based on the 39,002,152 shares outstanding as of December 31, 2013 and excludes:	

10,741,086 shares of our common stock that are potentially issuable upon conversion of our outstanding non-voting preferred stock as of December 31, 2013;

1,377,779 shares of our common stock subject to options outstanding as of December 31, 2013 having a weighted average exercise price of \$7.25 per share;

3,553,551 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of December 31, 2013, having a weighted average exercise price of approximately \$5.51 per share; and

151,829 shares issuable or potentially issuable pursuant to other outstanding commitments.

If the underwriters' option to purchase additional shares is exercised in full, we will issue and sell an additional shares of our common stock and will have 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 sections captioned Risk Factors contained in our Annual Report on Form 10-K for the year ended September 30, 2013 and our subsequent Quarterly Report on Form 10-Q, which are incorporated by reference in their 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 occurs, 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.

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 \$ per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share. See Dilution on page S-9.

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.

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 \$ million, or approximately \$ million if the underwriters exercise in full their option to purchase up to additional shares of common stock, based on the public offering price of \$ 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.

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**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and our consolidated capitalization as of December 31, 2013:

on an actual basis; and

on an adjusted basis to give effect to the sale of _____ shares of our common stock we are offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of December 31, 2013	
	Actual (unaudited)	As Adjusted (unaudited)
Cash, cash equivalents and short-term investments	\$ 59,713,424	\$
Debt:		
Note payable	\$ 1,050,000	\$ 1,050,000
Total debt	1,050,000	1,050,000
Equity:		
Preferred stock, \$0.001 par value per share; 5,000,000 shares authorized, actual and as adjusted; 51,291 shares issued and outstanding, actual and as adjusted:	51	51
Common stock, \$0.001 par value per share; 145,000,000 shares authorized; 39,002,152 shares issued and outstanding, actual; _____ shares issued and outstanding, as adjusted	131,372	
Additional paid-in capital	259,369,442	
Accumulated deficit during the development stage	(176,769,281)	(176,769,281)
Total Arrowhead Research Corporation stockholders equity	82,731,584	
Non-controlling interest	(1,821,297)	(1,821,297)
Total stockholders equity	80,910,287	
Total capitalization	\$ 81,960,287	\$

The table above should be read in conjunction with our consolidated financial statements and related notes incorporated by reference in this prospectus supplement. The actual and as adjusted number of shares of our common stock issued and outstanding as set forth in the table above excludes:

10,741,086 shares of our common stock that are potentially issuable upon conversion of our outstanding non-voting preferred stock as of December 31, 2013;

1,377,779 shares of our common stock subject to options outstanding as of December 31, 2013 having a weighted average exercise price of \$7.25 per share;

3,553,551 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of December 31, 2013, having a weighted average exercise price of approximately \$5.51 per share; and

151,829 shares issuable or potentially issuable pursuant to other outstanding commitments.

Table of Contents**DILUTION**

Our net tangible book value as of December 31, 2013 was approximately \$77.7 million, or \$1.99 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 December 31, 2013. Dilution 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 _____ shares of our common stock in this offering at the public offering price of \$ _____ 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 December 31, 2013 would have been approximately \$ _____ million, or \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution of \$ _____ 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	\$
Net tangible book value per share as of December 31, 2013	\$ 1.99
Increase per share attributable to this offering	
As adjusted net tangible book value per share after this offering	
Dilution per share to new investors	\$

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

The table and figures above are based on the 39,002,152 shares of our common stock outstanding as of December 31, 2013 and exclude:

10,741,086 shares of our common stock that are potentially issuable upon conversion of our outstanding non-voting preferred stock as of December 31, 2013;

1,377,779 shares of our common stock subject to options outstanding as of December 31, 2013 having a weighted average exercise price of \$7.25 per share;

3,553,551 shares of our common stock that have been reserved for issuance upon exercise of outstanding warrants as of December 31, 2013, having a weighted average exercise price of approximately \$5.51 per share; and

151,829 shares issuable or potentially issuable pursuant to other outstanding commitments.

To the extent that outstanding options or warrants are exercised or our preferred stock is converted into common stock, 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.

Table of Contents**UNDERWRITING**

Subject to the terms and conditions set forth in the underwriting agreement, dated February , 2014, among us and Jefferies LLC, Barclays Capital Inc. and Deutsche Bank Securities Inc., 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	
Barclays Capital Inc.	
Deutsche Bank Securities Inc.	

Total:

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, other than the shares of our common stock that are the subject of the option referred to below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters or their controlling persons 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. The underwriters are not obligated to do so and 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 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.

Commissions 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 \$ 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.

S-10

Table of Contents

	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	\$	\$	\$	\$
Underwriting discounts and commissions paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with the offering, other than the underwriting discounts and commissions referred to above, will be approximately \$200,000.

Listing

Our common stock is currently listed on the Nasdaq Capital 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 _____ 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 engage in the following transactions without the prior written consent of the representatives:

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

otherwise dispose of any shares of our common stock, options or warrants to acquire shares of our 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.

These restrictions terminate after the close of trading of the shares of our common stock on and including the 90th day after the date of this prospectus supplement. However, subject to certain exceptions, in the event that either:

during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

then, in each case, the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of the earnings release or the occurrence of the material news or event, as applicable, unless the representatives waive, in writing, such extension.

The representatives may, in their sole discretion and at any time or from time to time before the termination of the lock-up 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.

S-11

Table of Contents

Stabilization

The underwriters have advised us that, 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 our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

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 Capital 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

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of 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.

S-12

Table of Contents

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

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 shares which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any shares 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 legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives for any such offer; or

- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of the shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any shares under, the offers contemplated in this prospectus will be deemed to have represented, warranted and agreed to and with each underwriter and us that:

- (a) it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and

S-13

Table of Contents

- (b) in the case of any shares acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (i) the shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State, other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the representatives has been given to the offer or resale; or (ii) where shares have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those shares to it is not treated under the Prospectus Directive as having been made to such persons.

For the purposes of this provision, the expression an offer to the public in relation to any shares 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 any shares to be offered so as to enable an investor to decide to purchase any shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Each underwriter has represented, warranted and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or the FSMA) to persons who are investment professionals falling within Article 19(5) of the FSMA (Financial Promotion) Order 2005 or in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied with and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

Notice to Investors in the United Kingdom

Deutsche Bank Securities Inc. has represented and agreed that (a) it has only communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or the FSMA, received by it in connection with the issue or sale of the shares (i) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (ii) to high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) and (d) of the Order, with all such persons together being referred to as relevant persons, and (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom. This prospectus supplement and its 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.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being

a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares 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 in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

S-14

Table of Contents

Notice to Prospective Investors in Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons 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 pursuant to Section 275(1), or any person pursuant to Section 275(1A), 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, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in 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

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor (for corporations, 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 S\$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;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

Notice to Prospective Investors in Japan

The shares of common stock have not been and will not be registered under the Financial Instruments and Exchange Law, as amended (the FIEL). Deutsche Bank Securities Inc. has represented and agreed that the shares which it purchases will be purchased by it as principal and that, in connection with the offering, it will not, directly or indirectly, offer or sell any shares in Japan or to, or for the benefit of, any resident of Japan (which term as used herein

means any person resident in Japan, including any corporation or entity organized under the laws of Japan) or to others for reoffer or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements under the FIEL and otherwise in compliance with such law and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to Prospective Investors in Switzerland

The prospectus does not constitute an issue prospectus pursuant to Article 652a or Article 1156 of the Swiss Code of Obligations, and the shares will not be listed on the SIX Swiss Exchange. Therefore, the prospectus may not comply with the disclosure standards of the Swiss Code of Obligations and/or the listing rules (including any prospectus schemes) of the SIX Swiss Exchange. Accordingly, the shares may not be offered to the public in or from Switzerland, but only to a selected and limited circle of investors, which do not subscribe to the shares with a view to distribution.

Table of Contents

Notice to Prospective Investors in Qatar

The shares described in this prospectus supplement have not been, and will not be, offered, sold or delivered, at any time, directly or indirectly in the State of Qatar in a manner that would constitute a public offering. This prospectus supplement has not been, and will not be, registered with or approved by the Qatar Financial Markets Authority or Qatar Central Bank and may not be publicly distributed. This prospectus supplement is intended for the original recipient only and must not be provided to any other person. It is not for general circulation in the State of Qatar and may not be reproduced or used for any other purpose.

Notice to Prospective Investors in Saudi Arabia

No offering, whether directly or indirectly, will be made to an investor in the Kingdom of Saudi Arabia unless such offering is in accordance with the applicable laws of the Kingdom of Saudi Arabia and the rules and regulations of the Capital Market Authority, including the Capital Market Law of the Kingdom of Saudi Arabia. The shares will not be marketed or sold in the Kingdom of Saudi Arabia by us or the underwriter.

This prospectus supplement may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Office of Securities Regulation issued by the Capital Market Authority. The Saudi Arabian Capital Market Authority does not make any representation as to the accuracy or completeness of this prospectus supplement and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this prospectus supplement. Prospective purchasers of the shares offered hereby should conduct their own due diligence on the accuracy of the information relating to the shares. If you do not understand the contents of this prospectus supplement, you should consult an authorized financial advisor.

Notice to Prospective Investors in the United Arab Emirates

This offering has not been approved or licensed by the Central Bank of the United Arab Emirates (UAE), Securities and Commodities Authority of the UAE and/or any other relevant licensing authority in the UAE including any licensing authority incorporated under the laws and regulations of any of the free zones established and operating in the territory of the UAE, in particular the Dubai Financial Services Authority (DFSA), a regulatory authority of the Dubai International Financial Centre (DIFC). The offering does not constitute a public offer of securities in the UAE, DIFC and/or any other free zone in accordance with the Commercial Companies Law, Federal Law No 8 of 1984 (as amended), DFSA Offered Securities Rules and NASDAQ Dubai Listing Rules, accordingly, or otherwise. The shares may not be offered to the public in the UAE and/or any of the free zones.

The shares may be offered and issued only to a limited number of investors in the UAE or any of its free zones who qualify as sophisticated investors under the relevant laws and regulations of the UAE or the free zone concerned.

Table of Contents

LEGAL MATTERS

Ropes & Gray 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 them. 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, the accompanying prospectus 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 Securities and Exchange Commission under Section 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, until the completion or termination of the offering of the securities covered by this prospectus supplement.

our annual report on Form 10-K for the fiscal year ended September 30, 2013, filed on December 18, 2013;

our quarterly report on Form 10-Q for the quarter ended December 31, 2013, filed on February 4, 2014;

our current reports on Form 8-K filed on October 10, 2013, February 7, 2014 and February 12, 2014;

the portions of our proxy statement on Schedule 14A, filed on December 20, 2013, incorporated by reference into the annual report referred to above; and

the description of our common stock contained in its registration statement on Form 8-A/A (Registration No. 000-21898), filed on November 1, 2010, 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 Street, Suite 1050, Pasadena, CA 91101 or may be made telephonically at (626) 304-3400.

Nothing in this prospectus supplement will be deemed to incorporate by reference information that is furnished to, but not filed with, the SEC pursuant to Items 2.02, 7.01 or 9.01 of Form 8-K.

Table of Contents

Prospectus

\$200,000,000

Arrowhead Research Corporation

Common Stock

Preferred Stock

Warrants

This prospectus will allow us to issue, from time to time in one or more offerings,

shares of our common stock,

shares of our preferred stock, and

warrants.

The common stock, preferred stock and warrants may be offered and sold separately or together in one or more series of issuances, for an aggregate dollar amount not to exceed \$200,000,000. We will provide specific terms of the securities in supplements to this prospectus.

In this prospectus, we refer to the common stock, preferred stock and the warrants collectively as the securities.

This prospectus provides a general description of the securities we may offer. We may sell the securities to or through underwriters, directly to investors or through agents, or through a combination of these methods. Each time we sell securities we will provide a prospectus supplement that will contain specific information about the terms of that sale, including the names of any underwriters or agents, and may add, update or change the information contained in this prospectus. You should read this prospectus and any prospectus supplement, and the information incorporated by reference herein and therein, carefully before you invest in our securities. This prospectus may not be used to consummate a sale of securities unless accompanied by a prospectus supplement for those securities.

Our common stock is listed on the Nasdaq Capital Market under the symbol ARWR. On February 10, 2014, the last reported sale price of our common stock on the Nasdaq Capital Market was \$17.99.

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 12, 2014

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>SECURITIES WE MAY OFFER</u>	3
<u>PLAN OF DISTRIBUTION</u>	4
<u>EXPERTS</u>	6
<u>LEGAL MATTERS</u>	6
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	6
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	6

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a shelf registration process. Under this shelf registration process, we may offer from time to time any combination of the securities described in this prospectus for a total dollar amount not to exceed \$200,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described under the heading **Where You Can Find More Information**.

We have not authorized any dealer, salesperson or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or any accompanying prospectus supplement as if we had authorized it. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus and any accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is correct on any date after their respective dates, even though this prospectus or any prospectus supplement is delivered or securities are sold on a later date.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of the federal securities laws. You can identify forward-looking statements by the use of the words believe, expect, anticipate, intend, estimate, project, should, may, plan, intend, assume and other expressions which predict or indicate future events and trends and which do not relate to historical matters. You should not rely on forward-looking statements, because they involve known and unknown risks, uncertainties and other factors, some of which are beyond the control of the Company. These risks, uncertainties and other factors may cause the actual results, performance or achievements of the Company to be materially different from the anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Factors that might cause these differences include the following:

the integration of multiple technologies and programs;

the ability to successfully complete development and commercialization of products and the Company's expectations regarding market growth;

the cost, timing, scope and results of ongoing safety and efficacy trials of preclinical and clinical testing;

the ability to successfully complete product research and further development;

the volume and profitability of product sales of future products;

changes in existing and potential relationships with corporate collaborators and partners;

the availability, cost, delivery and quality of materials supplied by contract manufacturers;

the timing, cost and uncertainty of obtaining regulatory approvals of our products;

the ability to obtain substantial additional funding;

the ability to develop and commercialize products before competitors that are superior to the alternatives developed by competitors;

the ability to retain certain members of management;

the Company's expectations regarding research and development expenses and general and administrative expenses;

the Company's expectations regarding cash balances, capital requirements, anticipated revenue and expenses, including infrastructure expenses;

Table of Contents

our belief regarding the validity of our patents and potential litigation; and

other factors detailed from time to time in filings with the Securities and Exchange Commission.

In addition, the 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, and elsewhere in the documents incorporated by reference in this prospectus, 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, 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.

ABOUT THE COMPANY

*Unless otherwise noted, (1) the term **Arrowhead** refers to Arrowhead Research Corporation, a Delaware corporation, (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 the company, (3) the term **Common Stock** refers to Arrowhead's Common Stock and (4) the term **stockholder(s)** refers to the holders of Common Stock or securities exercisable for Common Stock.*

Arrowhead Research Corporation is a biopharmaceutical company developing targeted RNAi therapeutics. The Company is leveraging its proprietary drug delivery technologies to develop targeted drugs based on the RNA interference (RNAi) mechanism that efficiently and specifically silence target genes. Arrowhead technologies also enable partners to create peptide-drug conjugates (PDCs) that specifically home to cell types of interest while sparing off-target tissues. Arrowhead's pipeline includes clinical programs in chronic hepatitis B virus and partner-based programs in obesity and oncology. Arrowhead is leveraging its in-house R&D expertise and capabilities, as well as a broad intellectual property portfolio for RNAi therapeutics, and RNAi and peptide delivery vehicles and targeting methods to seek development partnerships with other pharmaceutical and biotech companies committed to bringing RNAi therapeutics to market, as well as continuing the preclinical and clinical development of its own clinical candidates.

Our common stock is listed on the Nasdaq Capital Market under the symbol **ARWR**.

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 6.

Table of Contents

RISK FACTORS

We are a development-stage company and we have not yet generated significant revenues. 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 the applicable prospectus supplement. Our business, financial condition or results of operations 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 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 elsewhere in this prospectus.

USE OF PROCEEDS

Unless we provide otherwise in a supplement to this prospectus, 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; 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.

SECURITIES WE MAY OFFER

We may offer shares of our common stock, preferred stock and/or warrants to purchase common stock or preferred stock with a total value of up to \$200,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities.

Common Stock

The following summary of the terms of our common stock is subject to and qualified in its entirety by reference to our charter and by-laws, copies of which are on file with the SEC as exhibits to previous SEC filings. Please refer to "Where You Can Find More Information" below for directions on obtaining these documents.

We are authorized to issue 145,000,000 shares of common stock, par value \$0.001 per share, of which 39,741,199 shares were issued and outstanding as of January 31, 2014.

We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote per share on all matters that require stockholder approval. There are no cumulative voting rights. Our common stock does not carry any redemption rights or any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock.

Our common stock is listed on the NASDAQ Capital Market under the symbol ARWR . The transfer agent and registrar for the common stock is Computershare Trust Company. Its address is 350 Indiana St., Suite 800, Golden, CO 80401.

Table of Contents

Preferred Stock

We may issue shares of our preferred stock from time to time, in one or more series. 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 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 the 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.

As of January 31, 2014, 51,291 shares of preferred stock were issued and outstanding.

Warrants

We may issue warrants for the purchase of common stock and/or preferred stock in one or more series, from time to time. We may issue warrants independently or together with common stock and/or preferred stock, and the warrants may be attached to or separate from those securities.

If we issue warrants, they will be evidenced by warrant agreements or warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. We urge you to read the prospectus supplement related to any series of warrants we may offer, as well as the complete warrant agreement and warrant certificate that contain the terms of the warrants. If we issue warrants, forms of warrant agreements and warrant certificates relating to warrants for the purchase of common stock, preferred stock and debt securities will be incorporated by reference into the registration statement of which this prospectus is a part from reports we would subsequently file with the SEC.

PLAN OF DISTRIBUTION

We may sell our securities from time to time in any manner permitted by the Securities Act, including any one or more of the following ways:

directly to investors;

to investors through agents;

to dealers; and/or

through one or more underwriters or dealers.

Any underwritten offering may be on a best efforts or a firm commitment basis. 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. Under agreements into which we may enter, underwriters, dealers and agents who participate in the distribution of the securities may be entitled to indemnification by us against some liabilities, including liabilities under the Securities Act, or contribution from us for payments which the underwriters, dealers or agents may be required to make. Underwriters, dealers and agents may engage in transactions with us or perform services for us from time to time in the ordinary course of business.

The distribution of the securities may be effected from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

Table of Contents

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 seek authorization for listing and trading on the Nasdaq Capital Market for the shares of common stock sold pursuant to the registration statement of which this prospectus is a part and may seek to have any warrants we sell pursuant to this prospectus listed for trading on the Nasdaq Capital Market or another exchange. 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 of 1933, 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.

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.

If underwriters are utilized in the sale of the securities, the securities may be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at fixed public offering prices or at varying prices determined by the underwriters at the time of the sale. We may offer the securities to the public either through underwriting syndicates represented by managing underwriters or directly by the managing underwriters. If any underwriters are utilized in the sale of the securities, unless otherwise stated in the applicable prospectus supplement, the underwriting agreement will provide that the obligations of the underwriters are subject to specified conditions precedent and that the underwriters with respect to a sale of the securities will be obligated to purchase all of the securities offered if any are purchased.

Until the distribution of the securities is completed, rules of the Securities and Exchange Commission may limit the ability of any underwriters and selling group members to bid for and purchase the securities. As an exception to these rules, underwriters are permitted to engage in some transactions that stabilize the price of the securities, such as over

allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Over allotment involves sales in excess of the offering size which create a short position for the underwriter. Stabilizing transactions consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of the securities. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. The underwriters may also impose a penalty bid, under which selling concessions allowed to syndicate members or other broker-dealers for securities sold in the offering for their account may be reclaimed by the syndicate if the securities are repurchased by the syndicate in stabilizing or covering transactions. In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. The imposition of a penalty bid might also have an effect on the price of a security to the extent that it were to discourage resales of the security before the distribution is completed.

We do not make any representation or prediction as to the direction or magnitude of any effect that the transactions described above might have on the price of the securities. In addition, we do not make any representation that underwriters will engage in such transactions or that such transactions, once commenced, will not be discontinued without notice.

Table of Contents

Underwriters, dealers and agents may engage in transactions with us or perform services for us in the ordinary course of business.

If indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by particular institutions to purchase securities from us at the public offering price set forth in such prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in such prospectus supplement. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the applicable prospectus supplement.

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.

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, 2013, 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 Ropes & Gray LLP, San Francisco, California.

WHERE YOU CAN FIND MORE INFORMATION

We must comply with the informational requirements of the Securities Exchange Act of 1934, as amended, and we are required to file reports and proxy statements and other information with the Securities and Exchange Commission. You may read and copy these reports, proxy statements and other information at the Public Reference Room maintained by the Securities and Exchange Commission 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 Securities and Exchange Commission at 1-800-SEC-0330 for further information about the public reference room. The Securities and Exchange Commission also maintains a website that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the Securities and Exchange Commission. You may access the Securities and Exchange Commission's web site at <http://www.sec.gov>.

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 Securities and Exchange Commission allows us to incorporate by reference in this prospectus the information that we file with them. 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

Securities and Exchange Commission 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 Securities and Exchange Commission under Section 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, including those filed after the date of the initial registration statement and prior to the effectiveness of the registration statement, until all of the shares of common stock, preferred stock and warrant shares covered by this prospectus are sold:

The Company's annual report on Form 10-K for the fiscal year ended September 30, 2013, filed on December 18, 2013;

The Company's Quarterly Reports on Form 10-Q for the quarter ended December 31, 2013, filed on February 4, 2014;

The Company's Current Reports on Form 8-K filed on October 10, 2013 and February 7, 2014; and

Table of Contents

The description of the Company's Common Stock contained in its registration statement on Form 8-A/A (Registration No. 000-21898), filed on November 1, 2010, 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 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 Street, 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.

Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02 or 7.01 of Form 8-K.

Table of Contents

Shares

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

Barclays

Deutsche Bank

February , 2014