

SCHEDULE 13G

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

Under the Securities Exchange Act of 1934  
(Amendment No. 2)\*

**Arrowhead Research Corporation**

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(Name of Issuer)

**Common Stock, par value \$0.001 per share**

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(Title of Class of Securities)

**042797209**

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(CUSIP Number)

**December 31, 2015**

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(Date of Event which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

Rule 13d-1(b)

Rule 13d-1(c)

Rule 13d-1(d)

\*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 (the "Act") or otherwise subject to the liabilities of that section of the Act, but shall be subject to all other provisions of the Act (however, see the Notes).

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors LP	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 3,680,499
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 3,680,499
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 3,680,499	
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 5.9% (1)	
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IA, PN	

(1) Based on 59,554,677 shares of common stock outstanding as of December 11, 2015, as reported in the Issuer's Form 10-K filed with the SEC on December 14, 2015.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors (GP) LLC	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 3,680,499
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 3,680,499
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 3,680,499	
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 5.9% (1)	
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> HC, OO	

(1) Based on 59,554,677 shares of common stock outstanding as of December 11, 2015, as reported in the Issuer's Form 10-K filed with the SEC on December 14, 2015.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b>  Felix J. Baker	
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	<b>SEC USE ONLY</b>	
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b>  United States	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b>  3,680,499
	<b>6</b>	<b>SHARED VOTING POWER</b>  -0-
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b>  3,680,499
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b>  -0-
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b>  3,680,499	
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b>  5.9% (1)	
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC	

(1) Based on 59,554,677 shares of common stock outstanding as of December 11, 2015, as reported in the Issuer's Form 10-K filed with the SEC on December 14, 2015.

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b>  Julian C. Baker		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b>  United States		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b>  3,680,499	
	<b>6</b>	<b>SHARED VOTING POWER</b>  -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b>  3,680,499	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b>  -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b>  3,680,499		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b>  5.9% (1)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b>  IN, HC		

(1) Based on 59,554,677 shares of common stock outstanding as of December 11, 2015, as reported in the Issuer's Form 10-K filed with the SEC on December 14, 2015.

**Amendment No. 2 to Schedule 13G**

This Amendment No. 2 to Schedule 13G amends and supplements the previously filed Schedules 13G filed by Baker Bros. Advisors LP (the “Adviser”). Baker Bros. Advisors (GP) LLC (the “Adviser GP”), Julian C. Baker and Felix J. Baker. Except as supplemented herein, such statements, as heretofore amended and supplemented, remain in full force and effect.

**Item 1(a) Name of Issuer:**

Arrowhead Research Corporation (the “Issuer”)

**Item 1(b) Address of Issuer’s Principal Executive Offices:**

225 S. Lake Avenue, Suite 1050

Pasadena, California 91101

**Item 2(a) Name of Person Filing:**

This Schedule 13G is being filed jointly by the Adviser, the Adviser GP, Felix J. Baker and Julian C. Baker (collectively, the “Reporting Persons”).

**Item 2(b) Address of Principal Business Office or, if None, Residence:**

The business address of each of the Reporting Persons is:

c/o Baker Bros. Advisors LP

667 Madison Avenue, 21<sup>st</sup> Floor

New York, NY 10065

(212) 339-5690

**Item 2(c) Citizenship:**

The Adviser is a limited partnership organized under the laws of the State of Delaware. The Adviser GP is a limited liability company organized under the laws of the State of Delaware. The citizenship of each of Julian C. Baker and Felix J. Baker is the United States of America.

**Item 2(d) Title of Class of Securities:**

Common Stock, par value \$0.001 per share (“Common Stock”)

**Item 2(e) CUSIP Number:**

042797209

**Item 3. If this statement is filed pursuant to §§240.13d-1(b) or (c), check whether the person filing is a:**

- (a)  Broker or dealer registered under Section 15 of the Exchange Act.
- (b)  Bank as defined in section 3(a)(6) of the Exchange Act.
- (c)  Insurance company as defined in section 3(a)(19) of the Exchange Act.
- (d)  Investment company registered under section 8 of the Investment Company Act of 1940.
- (e)  An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E).
- (f)  An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F).
- (g)  A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G).
- (h)  A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.
- (i)  A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940.
- (j)  Group, in accordance with Rule 13d-1(b)(1)(ii)(J).

**Item 4. Ownership.:**

Items 5 through 9 and 11 of each of the cover pages to this Amendment No. 2 are incorporated herein reference. Set forth below is the aggregate number of shares of Common Stock of the Issuer as well as shares of Common Stock that may be acquired upon conversion of the Series C Convertible Preferred Stock (“Series C Preferred”) convertible into Common Stock of the Issuer at an initial conversion price of \$5.86 per share, directly held by each of Baker Brothers Life Sciences, L.P. (“Life Sciences”) and 667, L.P. (“667”, and together with Life Sciences, the “Funds”), subject to the limitation on conversion described below. The information set forth below is based upon 59,554,677 shares of Common Stock outstanding as of December 11, 2015, as reported on the Issuer’s Form 10-K filed with the SEC on December 14, 2015. Such percentage figures are calculated in accordance with Rule 13d-3 under the Securities Exchange Act of 1934, as amended.

Name	Number of Shares of Common Stock we own or have the right to acquire within 60 days	Percent of Class Outstanding
667, L.P.	338,244	0.5%
Baker Brothers Life Sciences, L.P.	3,342,255	5.4%
<b>Total</b>	<b>3,680,499</b>	<b>5.9%</b>

The Series C Preferred is only exercisable to the extent that the holders thereof together with their affiliates would beneficially own, for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended, no more than 9.99% of the outstanding shares of Common Stock of the Issuer after conversion (“Beneficial Ownership Limitation”). As a result of this restriction, the number of shares that may be issued upon conversion of the Series C Preferred by the above holders may change depending upon changes in the outstanding shares. The number of shares of Common Stock issuable upon conversion of the Series C Preferred held by any Reporting Person affiliate will also depend upon the extent to which the Series C Preferred held by other affiliates have theretofore been converted. By written notice to the Issuer, the Funds may from time to time increase or decrease the Beneficial Ownership Limitation applicable to that Fund to any other percentage not in excess of 19.99% specified in such notice. Any such increase will not be effective until the 65th day after such notice is delivered to the Issuer. The Series C Preferred are eligible to vote with the common stock of the Company on an as-converted basis, but only to the extent that the Series C Preferred are eligible for conversion without exceeding the Beneficial Ownership Limitation.

Pursuant to the amended and restated management agreements among the Adviser, the Funds and their respective general partners, the Adviser has complete and unlimited discretion and authority with respect to the Funds’ investments and voting power over investments.

The Adviser GP, Felix J. Baker and Julian C. Baker as principals of the Adviser GP, and the Adviser may be deemed to be beneficial owners of securities of the Issuer directly held by the Funds, and may be deemed to have the power to vote or direct the vote of and the power to dispose or direct the disposition of such securities.

The Reporting Persons disclaim beneficial ownership of the securities held by each of the Funds, and this Amendment No. 2 shall not be deemed an admission that the Reporting Persons are the beneficial owners of such securities for purposes of Section 13(d) or for any other purpose.

**Item 5. Ownership of Five Percent or Less of a Class.:**

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following . N/A

**Item 6. Ownership of More than Five Percent on Behalf of Another Person.:**

The information in Item 4 is incorporated herein by reference.



**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control Person.:**

The information in Item 4 is incorporated herein by reference.

**Item 8. Identification and Classification of Members of the Group.:**

N/A

**Item 9. Notice of Dissolution of Group.:**

N/A

**Item 10. Certification.:**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

**SIGNATURE**

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

February 16, 2016

**BAKER BROS. ADVISORS LP**

By: Baker Bros. Advisors (GP) LLC, its general partner

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

**BAKER BROS. ADVISORS (GP) LLC**

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

/s/ Julian C. Baker

Julian C. Baker

/s/ Felix J. Baker

Felix J. Baker