

ARCA biopharma, Inc.  
Form 424B4  
March 16, 2015

Prospectus Supplement No. 31      Filed pursuant to Rule 424(b)(4)  
Registration No. 333-187508  
(to Prospectus dated May 30, 2013)

125,000 Shares of Series A Convertible Preferred Stock

12,500,000 Shares of Common Stock Underlying the Preferred Stock

Warrants to Purchase up to 6,250,000 Shares of Common Stock and

6,250,000 Shares of Common Stock Underlying the Warrants

ARCA biopharma, Inc.

This prospectus supplement supplements the prospectus dated May 30, 2013 (the “Prospectus”), as supplemented by that certain Prospectus Supplement No. 1 dated July 17, 2013 (“Supplement No. 1”), by that certain Prospectus Supplement No. 2 dated July 19, 2013 (“Supplement No. 2”), by that certain Prospectus Supplement No. 3 dated July 24, 2013 (“Supplement No. 3”), by that certain Prospectus Supplement No. 4 dated July 30, 2013 (“Supplement No. 4”), by that certain Prospectus Supplement No. 5 dated August 6, 2013 (“Supplement No. 5”), by that certain Prospectus Supplement No. 6 dated September 4, 2013 (“Supplement No. 6”), by that certain Prospectus Supplement No. 7 dated September 23, 2013 (“Supplement No. 7”), by that certain Prospectus Supplement No. 8 dated October 29, 2013 (“Supplement No. 8”), by that certain Prospectus Supplement No. 9 dated November 6, 2013 (“Supplement No. 9”), by that certain Prospectus Supplement No. 10 dated November 13, 2013 (“Supplement No. 10”), by that certain Prospectus Supplement No. 11 dated November 21, 2013 (“Supplement No. 11”), by that certain Prospectus Supplement No. 12 dated December 5, 2013 (“Supplement No. 12”), by that certain Prospectus Supplement No. 13 dated January 8, 2014 (“Supplement No. 13”), by that certain Prospectus Supplement No. 14 dated February 10, 2014 (“Supplement No. 14”), by that certain Prospectus Supplement No. 15 dated February 12, 2014 (“Supplement No. 15”), by that certain Prospectus Supplement No. 16 dated February 18, 2014 (“Supplement No. 16”), by that certain Prospectus Supplement No. 17 dated March 3, 2014 (“Supplement No. 17”), by that certain Prospectus Supplement No. 18 dated March 20, 2014 (“Supplement No. 18”), by that certain Prospectus Supplement No. 19 dated May 13, 2014 (“Supplement No. 19”), by that certain Prospectus Supplement No. 20 dated June 9, 2014 (“Supplement No. 20”), by that certain Prospectus Supplement No. 21 dated August 13, 2014 (“Supplement No. 21”), by that certain Prospectus Supplement No. 22 dated August 18, 2014 (“Supplement No. 22”), by that certain Prospectus Supplement No. 23 dated November 12, 2014 (“Supplement No. 23”), by that certain Prospectus Supplement No. 24 dated December 1, 2014 (“Supplement No. 24”), by

that certain Prospectus Supplement No. 25 dated December 10, 2014 (“Supplement No. 25”), by that certain Prospectus Supplement No. 26 dated December 11, 2014 (“Supplement No. 26”), by that certain Prospectus Supplement No. 27 dated December 30, 2014 (“Supplement No. 27”), by that certain Prospectus Supplement No. 28 dated February 4, 2015 (“Supplement No. 28”), by that certain Prospectus Supplement No. 29 dated February 17, 2015 (“Supplement No. 29”), and by that certain Prospectus Supplement No. 30 dated February 23, 2015 (“Supplement No. 30”, and together with Supplement No. 1, Supplement No. 2, Supplement No. 3, Supplement No. 4, Supplement No. 5, Supplement No. 6, Supplement No. 7, Supplement No. 8, Supplement No. 9, Supplement No. 10, Supplement No. 11, Supplement No. 12, Supplement No. 13, Supplement No. 14, Supplement No. 15, Supplement No. 16, Supplement No. 17, Supplement No. 18, Supplement No. 19, Supplement No. 20, Supplement No. 21, Supplement No. 22, Supplement No. 23, Supplement No. 24, Supplement No. 25, Supplement No. 26, Supplement No. 27, Supplement No. 28, and Supplement No. 29, the “Supplements”), which form a part of our Registration Statement on Form S-1 (Registration No. 333-187508). This prospectus supplement is being filed to update and supplement the information in the Prospectus and the Supplements with the information contained in our current report on Form 8-K, filed with the Securities and Exchange Commission (the “Commission”) on March 16, 2015 (the “Current Report”). Accordingly, we have attached the Current Report to this prospectus supplement..

The Prospectus, the Supplements and this prospectus supplement relate to the offer and sale of up to 125,000 shares of Series A Convertible Preferred Stock (“Preferred Stock”) which are convertible into 12,500,000 shares of Common Stock, warrants to purchase up to 6,250,000 shares of our Common Stock and 6,250,000 shares of Common Stock underlying the warrants.

This prospectus supplement should be read in conjunction with the Prospectus and the Supplements. This prospectus supplement updates and supplements the information in the Prospectus and the Supplements. If there is any inconsistency between the information in the Prospectus, the Supplements and this prospectus supplement, you should rely on the information in this prospectus supplement.

Our common stock is traded on the Nasdaq Global Market under the trading symbol “ABIO.” On March 16, 2015, the last reported sale price of our common stock was \$0.81 per share.

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Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “Risk Factors” beginning on page 5 of the Prospectus and beginning on page 22 of our quarterly report on Form 10-Q for the period ended September 30, 2014 before you decide whether to invest in shares of our common stock.

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

The date of this prospectus supplement is March 16, 2015

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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the  
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 16, 2015 (March 16, 2015)

ARCA biopharma, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware                                              000-22873                                              36-3855489  
(State or Other Jurisdiction (Commission File Number) (I.R.S. Employer

of Incorporation)                                                                                              Identification No.)

11080 CirclePoint Road, Suite 140, Westminster, CO 80020

(Address of Principal Executive Offices) (Zip Code)

(720) 940-2200

(Registrant's telephone number, including area code)

Not Applicable

(Former Name or Former Address, if Changed Since Last Report)

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

£ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

£ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

£ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

£ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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Section 8 — Other Events

Item 8.01. Other Events.

On March 16, 2015, ARCA biopharma, Inc. (“ARCA”) provided a GENETIC-AF clinical trial update. The press release is furnished as Exhibit 99.1 hereto, the contents of which are incorporated herein by reference.

Section 9 — Financial Statements and Exhibits

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

| Exhibit<br>Number | Description                                                                                           |
|-------------------|-------------------------------------------------------------------------------------------------------|
| 99.1              | Press Release titled “ARCA biopharma Provides GENETIC-AF Clinical Trial Update” dated March 16, 2015. |

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: March 16, 2015

ARCA biopharma, Inc.  
(Registrant)

By: /s/ Brian L. Selby  
Name: Brian L. Selby  
Title: VP, Finance and Chief Accounting Officer

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INDEX TO EXHIBITS

| Exhibit<br>Number | Description                                                                                           |
|-------------------|-------------------------------------------------------------------------------------------------------|
| 99.1              | Press Release titled “ARCA biopharma Provides GENETIC-AF Clinical Trial Update” dated March 16, 2015. |







Exhibit 99.1

ARCA Biopharma provides genetic-af clinical trial update

GENETIC-AF Trial Evaluating Gencaro™ as Potential Treatment for Atrial Fibrillation

Protocol Amended to Broaden Trial Population and Increase Enrollment Rate

Phase 2B of GENETIC-AF Anticipated to Complete Enrollment by Year-End 2016

Westminster, CO, March 16, 2015 – ARCA biopharma, Inc. (Nasdaq: ABIO), a biopharmaceutical company developing genetically-targeted therapies for cardiovascular diseases, today provided an update on GENETIC-AF, the Company's Phase 2B/3 clinical trial evaluating Gencaro (bucindolol hydrochloride) as a potential treatment for atrial fibrillation (AF).

ARCA was founded on the belief that a personalized medicine approach to drug development, tailoring medical treatment to the individual genetic characteristics of each patient, can enable more effective therapies, improve patient outcomes and reduce healthcare costs. ARCA's lead development program is intended to be a direct implementation of those ideas. Gencaro is being developed as a potential treatment for AF. ARCA has identified common genetic variations that it believes may predict individual patient response to Gencaro, giving it the potential to be the first genetically-targeted AF prevention treatment. AF is considered an epidemic cardiovascular disease with an estimated prevalence of at least 2.7 million Americans in 2010.

#### GENETIC-AF Clinical Trial

GENETIC-AF is a Phase 2B/3, multi-center, randomized, double-blind clinical trial comparing the safety and efficacy of Gencaro to Toprol-XL (metoprolol succinate) for the treatment of AF in patients with heart failure and left ventricular systolic dysfunction (HFREF patients). The primary endpoint of GENETIC-AF is time to symptomatic AF/atrial flutter (AFL). ARCA is enrolling only HFREF patients with the genetic variant of the cardiac beta-1 adrenergic receptor, which the Company believes responds most favorably to Gencaro, the 389 arginine homozygous genotype (ADRB1 Arg389Arg). GENETIC-AF has an adaptive design, under which the Company initiated the trial as a Phase 2B trial seeking to enroll approximately 200 patients. The GENETIC-AF Data Safety Monitoring Board (DSMB) will analyze certain data from the Phase 2B portion of the trial and recommend, based on a comparison to the pre-trial statistical assumptions, whether the trial should proceed to Phase 3 and seek to enroll an additional 420 patients.

There are currently 38 active clinical trial sites in the United States and Canada. The Company anticipates that approximately 65 sites will be activated for the Phase 2B portion of GENETIC-AF. Trial enrollment, the number of patients randomized into one of the study's two treatment arms, has not met the Company's original projections, with the trial having screened 37 patients who met the general clinical inclusion criteria and signed informed consent for genotyping, resulting in 12 patients who were randomized into the trial. The percentage of screened patients who have the targeted genotype is consistent with pre-trial assumptions of approximately 50%. The Company believes the original trial eligibility criteria overly restricted the potential pool of appropriate patients for the trial and contributed to the number of screened patients who subsequently became ineligible for randomization. To address these issues,

the Company, in consultation with the GENETIC-AF Steering Committee comprised of experts in the fields of electrophysiology, heart failure and clinical trial

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methodology, has implemented amendments to the trial protocol that the Company believes may expand the eligible target population, increase the patient screening and enrollment rate, and simplify trial procedures.

Under the revised protocol, patients in sinus rhythm who have experienced symptomatic AF in the past 120 days are now eligible for inclusion in the trial, as are patients with AF episodes lasting 7 days or less (i.e., paroxysmal AF). Previously, these patients were not eligible to be enrolled in the trial. The Company believes this expanded target population, which is substantially larger than the original target population, has the potential to improve trial screening and enrollment rates and broaden the potential commercial market for Gencaro should it achieve regulatory approval in the future. The amendments to the protocol do not fundamentally alter or impact the original endpoints of the clinical trial. Based on the projected impact of the expanded patient population and the current enrollment rate, the Company anticipates that the enrollment of 200 patients for the Phase 2B portion of the trial may be completed by the end of 2016.

The Company has met with the U.S. Food and Drug Administration to confirm the acceptability of the amendments to the protocol and received no objections.

The revised clinical trial protocol has been distributed to participating clinical trial sites for review by their respective institutional review boards (IRB), or similar committee. IRBs review and approve clinical trial protocols for trials in which their organizations participate, a process with timelines that vary significantly from IRB to IRB and is out of the Company's control. The Company does not anticipate a significant change to the current enrollment rate until the revised protocol is adopted by clinical trial sites. The Company anticipates the first trial sites to be approved, trained and operating under the revised protocol in June 2015.

“We greatly appreciate the tremendous support and feedback from the clinical investigator community participating in GENETIC-AF,” said Dr. Michael R. Bristow, President and Chief Executive Officer of ARCA. “The adaptive nature of the clinical trial design for GENETIC-AF is an important feature that allows us to adapt certain aspects of the trial without compromising basic assumptions and the central goal, which is to test the hypothesis that Gencaro is safe and effective in preventing recurrent AF in a genetically defined HFREF population. We believe we have a significant opportunity to improve the treatment options for patients living with atrial fibrillation and look forward to providing future updates on the progress of GENETIC-AF.”

#### GENETIC-AF Trial Phase 2B Projected Timeline

|                                                                     |            |
|---------------------------------------------------------------------|------------|
| -Revised protocol distributed to participating clinical trial sites | March 2015 |
| -GENETIC-AF Trial Investigators meeting and training                | May 2015   |
| -First trial sites operating under revised protocol                 | June 2015  |
| -Approximately 65 clinical trial sites active in U.S. & Canada      | Q4 2015    |
| -Trial Enrollment Completion                                        | YE 2016    |
| -DSMB Interim Analysis Decision                                     | 1H 2017    |

The Company's forecast of the time periods to achieve these milestones is a forward-looking statement and involves risks and uncertainties, and actual results are likely to vary as a result of a number of factors, including the factors discussed in “Risk Factors” in the Company's periodic SEC filings.

#### Atrial Fibrillation (AF)

Atrial fibrillation, the most common sustained cardiac arrhythmia, is considered an epidemic cardiovascular disease and a major public health burden. The estimated number of individuals with AF globally in 2010 was 33.5 million.

According to the 2015 American Heart Association report on Heart Disease and Stroke Statistics, the estimated number of individuals with AF in the U.S. in 2010 ranged from 2.7 million to 6.1 million people.

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Hospitalization rates for AF increased by 23% among US adults from 2000 to 2010 and hospitalizations account for the majority of the economic cost burden associated with AF.

AF is a disorder in which the normally regular and coordinated contraction pattern of the heart's two small upper chambers (the atria) becomes irregular and uncoordinated. The irregular contraction pattern associated with AF causes blood to pool in the atria, predisposing the formation of clots potentially resulting in stroke. AF increases the risk of mortality and morbidity due to stroke, congestive heart failure and impaired quality of life. The approved therapies for the treatment or prevention AF have certain disadvantages in patients with heart failure and/or reduced left ventricular ejection fraction (HFREF) patients. These include toxic or cardiovascular adverse effects, and most of the approved drugs for AF are contra indicated or have warnings in their prescribing information for such patients. The Company believes there is an unmet medical need for new AF treatments that have fewer side effects than currently available therapies and are more effective, particularly in HFREF patients.

#### About ARCA biopharma

ARCA biopharma is dedicated to developing genetically-targeted therapies for cardiovascular diseases. The Company's lead product candidate, Gencaro™ (bucindolol hydrochloride), is an investigational, pharmacologically unique beta-blocker and mild vasodilator being developed for atrial fibrillation. ARCA has identified common genetic variations that it believes predict individual patient response to Gencaro, giving it the potential to be the first genetically-targeted atrial fibrillation prevention treatment. ARCA has a collaboration with Medtronic, Inc. for support of the GENETIC-AF trial. For more information please visit [www.arcabiopharma.com](http://www.arcabiopharma.com).

#### Safe Harbor Statement

This press release contains "forward-looking statements" for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements regarding, potential timing for patient enrollment in the GENETIC-AF trial, potential timeline for GENETIC-AF trial activities, the sufficiency of the Company's capital to support its operations, the potential for genetic variations to predict individual patient response to Gencaro, Gencaro's potential to treat atrial fibrillation, future treatment options for patients with atrial fibrillation, and the potential for Gencaro to be the first genetically-targeted atrial fibrillation prevention treatment. Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation, the risks and uncertainties associated with: the Company's financial resources and whether they will be sufficient to meet the Company's business objectives and operational requirements; results of earlier clinical trials may not be confirmed in future trials, the protection and market exclusivity provided by the Company's intellectual property; risks related to the drug discovery and the regulatory approval process; and, the impact of competitive products and technological changes. These and other factors are identified and described in more detail in ARCA's filings with the SEC, including without limitation the Company's annual report on Form 10-K for the year ended December 31, 2013, and subsequent filings. The Company disclaims any intent or obligation to update these forward-looking statements.

#### Investor & Media Contact:

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