

ARCA biopharma, Inc.  
Form 424B4  
August 18, 2014

**Prospectus Supplement No. 22**

**Filed pursuant to Rule 424 (b)(4)**

**(to Prospectus dated May 30, 2013)**

**Registration No. 333-187508**

**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 ), and by that certain Prospectus Supplement No. 21 dated August 13, 2014 ( Supplement No. 21 ), 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, and Supplement No. 20, 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 August 18, 2014 (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 August 18, 2014, the last reported sale price of our common stock was \$1.39 per share.

**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 20 of our quarterly report on Form 10-Q for the period ended June 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 August 18, 2014**

**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): August 18, 2014 (August 18, 2014)**

**ARCA biopharma, Inc.**

**(Exact Name of Registrant as Specified in Charter)**

**Delaware**  
**(State or Other Jurisdiction**

**000-22873**  
**(Commission**

**36-3855489**  
**(I.R.S. Employer**

**of Incorporation)**

**File Number)**

**Identification No.)**

**11080 CirclePoint Road, Suite 140, Westminster, CO 80020**

**(Address of Principal Executive Offices) (Zip Code)**

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**(720) 940-2200**

**(Registrant's telephone number, including area code)**

**Not Applicable**

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

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))

**Section 8 Other Events**

**Item 8.01. Other Events.**

On August 18, 2014, ARCA biopharma, Inc. ( ARCA ) announced that the Company's Clinical Trial Application for Gencaro a pharmacologically unique beta-blocker and mild vasodilator being developed for atrial fibrillation, has been accepted by Health Canada. ARCA anticipates that clinical trial sites in Canada will be active in the fourth quarter of 2014. 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.

| <b>Exhibit Number</b> | <b>Description</b>   |
|-----------------------|--|
| 99.1                  | Press Release titled ARCA biopharma Announces Health Canada Acceptance of GENETIC-AF Clinical Trial Application dated August 18, 2014. |

**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: August 18, 2014

**ARCA biopharma, Inc.**

(Registrant)

By: /s/ Patrick M. Wheeler

Name: Patrick M. Wheeler

Title: Chief Financial Officer

**INDEX TO EXHIBITS**

| <b>Exhibit Number</b> | <b>Description</b>   |
|-----------------------|--|
| 99.1                  | Press Release titled ARCA biopharma Announces Health Canada Acceptance of GENETIC-AF Clinical Trial Application dated August 18, 2014. |



**ARCA BIOPHARMA ANNOUNCES HEALTH CANADA ACCEPTANCE OF GENETIC-AF CLINICAL TRIAL APPLICATION**

**Canadian Site Activation for Phase 2B/3 Clinical Trial to Begin in 2014**

**Gencaro Potentially the First Genetically-Targeted Cardiovascular Treatment**

*Westminster, CO, August 18, 2014* ARCA biopharma, Inc. (Nasdaq: ABIO), a biopharmaceutical company developing genetically-targeted therapies for cardiovascular diseases, today announced that the Company's Clinical Trial Application (CTA) for the GENETIC-AF clinical trial evaluating Gencaro™ as a potential treatment for atrial fibrillation (AF) has been accepted by Health Canada. ARCA anticipates that clinical trial sites in Canada will be active in the fourth quarter of 2014.

ARCA is evaluating Gencaro, a pharmacologically unique beta-blocker and mild vasodilator, as a potential treatment for AF in the Phase 2B/3 GENETIC-AF clinical trial, which is currently enrolling patients in the United States. ARCA has identified common genetic variations that it believes predict individual patient response to Gencaro, giving it potential to be the first genetically-targeted therapy for the prevention of atrial fibrillation.

Dr. Michael R. Bristow, Founder and CEO of ARCA, commented, "At ARCA, we believe 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. If the GENETIC-AF trial successfully confirms the atrial fibrillation data analysis from a prior Phase 3 clinical trial, Gencaro has the potential to be the first genetically targeted treatment for the prevention of this important cardiovascular disorder and provide a much needed treatment option for patients in an area of high unmet medical need."

**About 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 2014 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. 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 of 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. We believe 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.

### **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 for prevention of symptomatic AF/atrial flutter in HFREF patients. ARCA plans to enroll only patients with the genetic variant of the beta-1 cardiac receptor which the Company believes responds most favorably to Gencaro. GENETIC-AF has an adaptive design, under which the Company initiated the trial as a Phase 2B trial in 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 our pre-trial statistical assumptions, whether the trial should proceed to Phase 3 and seek to enroll an additional 420 patients.

The AF indication for Gencaro was chosen based on clinical data from the previously conducted Phase 3 heart failure trial of 2,708 patients (the BEST trial). The Company believes data from the BEST trial indicate that Gencaro may have a genetically regulated effect in reducing or preventing AF, whereas the Company believes the therapeutic benefit of Toprol-XL does not appear to be enhanced in patients with this genotype. A retrospective analysis of data from the BEST trial shows that the entire cohort of patients in the BEST trial treated with Gencaro had a 41% reduction in the risk of new onset AF (time-to-event) compared to placebo ( $p = 0.0004$ ). In the BEST DNA substudy, patients with the beta-1 389 arginine homozygous genotype experienced a 74% ( $p = 0.0003$ ) reduction in risk of AF when receiving Gencaro, based on the same analysis.

### **About ARCA biopharma**

ARCA biopharma is dedicated to developing genetically-targeted therapies for cardiovascular diseases. The Company's lead product candidate, Gencar<sup>TM</sup> (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, 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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