ARCA biopharma, Inc.
Form 424B4
July 20, 2015
Table of Contents

Filed Pursuant to Rule 424(b)(4)
Registration No. 333-205533

PROSPECTUS

42,021,579 Shares of Common Stock

16,808,632 Shares of Common Stock Issuable Upon Exercise of the Warrants

This prospectus relates to the disposition from time to time of up to 58,830,211 shares of our common stock, which includes 16,808,632 shares of our common stock issuable upon the exercise of warrants held by the selling stockholders named in this prospectus. The selling stockholders acquired the common stock and the warrants to purchase common stock from us in a private placement that closed in June 2015, and that is more fully described in the section entitled Prospectus Summary. We are not selling any common stock under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholders. We will, however, receive net proceeds of any warrants exercised for cash.

The selling stockholders may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholders may sell their shares of common stock in the section entitled Plan of Distribution on page 10. The selling stockholders will bear all commissions and discounts, if any, attributable to the sale or disposition of the shares, or interests therein. We will bear all costs, expenses and fees in connection with the registration of the shares. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is listed on The NASDAQ Capital Market under the symbol ABIO. On July 17, 2015, the last reported sale price of our common stock on The NASDAQ Capital Market was $1.32 per share.

AN INVESTMENT IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY REVIEW THE RISKS AND UNCERTAINTIES REFERRED TO UNDER THE HEADING RISK FACTORS BEGINNING ON PAGE 5 OF THIS PROSPECTUS AND UNDER ANY SIMILAR HEADINGS IN ANY AMENDMENT OR SUPPLEMENT TO THIS PROSPECTUS OR IN ANY FILING WITH THE SECURITIES AND EXCHANGE COMMISSION THAT IS INCORPORATED BY

REFERENCE HEREIN.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this Prospectus is July 20, 2015

Table of Contents

Table of Contents

ABOUT THIS PROSPECTUS

You should rely only on the information contained or incorporated by reference in this prospectus and any related prospectus supplement. We have not, and the selling stockholders have not, authorized anyone to provide you with different information. No one is making offers to sell or seeking offers to buy these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus and any prospectus supplement is accurate only as of the date on the front of this prospectus or the prospectus supplement, as applicable, and that any information incorporated by reference in this prospectus or any prospectus supplement is accurate only as of the date given in the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled Where You Can Find More Information.

This prospectus and the information incorporated herein by reference includes trademarks, service marks and trade names owned by us or others. All trademarks, service marks and trade names included or incorporated by reference into this prospectus or any applicable prospectus supplement are the property of their respective owners.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus. This summary does not contain all the information you should consider before investing in our common stock. You should read and consider carefully the more detailed information in this prospectus, including the factors described under the heading Risk Factors in this prospectus beginning on page 5, any prospectus supplement and the documents incorporated by reference herein, before making an investment decision.

Unless we have indicated otherwise, or the context otherwise requires, references in this to ARCA, the Company, we, us and our refer to ARCA biopharma, Inc.

Overview

We are a biopharmaceutical company principally focused on developing genetically-targeted therapies for cardiovascular diseases. Our lead product candidate, Gencaro (bucindolol hydrochloride), is a pharmacologically unique beta-blocker and mild vasodilator that we are evaluating in a clinical trial for the treatment of atrial fibrillation, or AF, in patients with heart failure and left ventricular systolic dysfunction, or HFREF. We have identified common genetic variations in receptors in the cardiovascular system that we believe interact with Gencaro s pharmacology and may predict patient response to the drug.

We are testing this hypothesis in a Phase 2B/3 clinical trial of Gencaro, known as GENETIC-AF. We are pursuing this indication for Gencaro because data from a prior Phase 3 HF trial of Gencaro in 2,708 heart failure, or HF, patients, or the BEST trial, which suggested that Gencaro may be successful in reducing or preventing AF.

In April 2015, the U.S. Food and Drug Administration, or FDA, designated as a Fast Track development program the investigation of Gencaro for the prevention of atrial fibrillation/atrial flutter in a genetically targeted heart failure population (heart failure patients with reduced left ventricular ejection fraction).

Fast Track drug development designation was included in the FDA Modernization Act of 1997, or FDAMA, as a formal process to enhance interactions with the FDA during drug development. A drug development program with Fast Track designation is eligible for consideration for some or all of the following programs for expediting development and review: scheduled meetings to seek FDA input into development plans, priority review of the New Drug Application, or NDA, the option of submitting portions of an NDA for review prior to submission of the complete application and potential accelerated approval.

AF is a disorder in which the normally regular and coordinated contraction pattern of the heart s two small upper chambers, or 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 is considered an epidemic cardiovascular disease. 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 United States in 2010 ranged from 2.7 million to 6.1 million people. AF increases the risk of stroke and may also contribute to worsening heart failure. The approved therapies for the treatment or prevention AF have certain disadvantages in HFREF patients, such as 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 is a Phase 2B/3 multi-center, randomized, double-blind clinical trial comparing the safety and efficacy of Gencaro to an active comparator, the beta-blocker Toprol XL (metoprolol succinate), in HFREF patients with a current or recent history of paroxysmal (AF episodes lasting 7 days or less) or persistent AF who have a beta-1 389 arginine homozygous genotype, the genotype we believe responds most favorably to Gencaro. The primary endpoint of GENETIC-AF, time to recurrent symptomatic AF/atrial flutter, or AFL, or all-cause mortality, will be measured over a twenty-four week period after a patient has established a normal heart rhythm.

We believe data from the BEST trial indicate that Gencaro may have a genetically regulated effect in reducing or preventing AF, whereas we believe 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. The beta-1 389 arginine homozygous genotype was present in about 47% of the patients in the BEST pharmacogenetic substudy, and we estimate it is present in about 50% of the U.S. general population.

Table of Contents

We have created an adaptive design for GENETIC-AF and are seeking to enroll approximately 200 HFREF patients in the Phase 2B portion of the study who have recently experienced at least one episode of paroxysmal or persistent AF and who have the beta-1 389 arginine homozygous genotype that we believe responds most favorably to Gencaro. In addition to measuring the primary endpoint of recurrent symptomatic AF/AFL or all-cause mortality, an additional efficacy measure in the Phase 2B portion of GENETIC-AF will be AF burden, defined as a patient s percentage of time in AF per day, regardless of symptoms. At least 150 patients in the Phase 2B portion of the trial will have either a newly or previously implanted Medtronic device that measures and records AF burden. The GENETIC-AF Data Safety Monitoring Board, or 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 DSMB will make their recommendation based on analysis of certain trial data after 200 patients have completed 24 weeks of follow-up, the period for measuring the primary end-point of the trial. The DSMB interim analysis will focus on available data regarding the primary end point, AF/AFL event rates, AF burden, and safety. Should the DSMB interim analysis conclude that the interim data is consistent with pre-trial statistical assumptions and indicates potential for achieving statistical significance for the Phase 3 endpoint, the DSMB may recommend that the study proceed to Phase 3. The DSMB may also recommend changes to the study design before the trial proceeds to Phase 3, or it may recommend that the study not proceed to Phase 3. Based on the DSMB recommendation, and other factors, including input from the trial s Steering Committee, the Company will make the final determination on the trial s development steps. The full Phase 2B/3 trial is designed for 90 percent power at a p-value of less than 0.01 significance level to detect a 25 percent reduction in the risk of AF recurrence or death in patients in the Gencaro arm compared to patients in the Toprol XL arm.

In consultation with the GENETIC-AF Steering Committee, we implemented amendments to the trial protocol in March 2015 which we believe may expand the eligible target population, increase the patient screening and enrollment rate, and simplify trial procedures. We have undertaken these protocol amendments because patient enrollment in the trial has not met our original projections. 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, or paroxysmal AF. Previously, these patients were not eligible to be enrolled in the trial. We believe this expanded target population has the potential to improve trial screening and enrollment rates and could 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, we now project that the enrollment of 200 patients for the Phase 2B portion of the trial may be completed by the end of 2016, with the DSMB interim analysis finishing in the first half of 2017. We do not yet know how these protocol changes will impact enrollment or if our new enrollment projections will prove to be accurate. We met with the FDA, prior to implementation, to confirm the acceptability of the amendments to the protocol and received no objections.

Our GENETIC-AF clinical trial of Gencaro requires a companion diagnostic test to identify the patient s receptor genotype. We have an agreement with Laboratory Corporation of America, or LabCorp, to provide the companion diagnostic test and services to support our GENETIC-AF trial. LabCorp has developed the genetic test and obtained an Investigational Device Exemption, or IDE, from the United States Food and Drug Administration, or the FDA, for the companion diagnostic test which is being used in our GENETIC-AF clinical trial.

Medtronic, Inc., or Medtronic, a leader in medical technologies to improve the treatment of chronic diseases, including cardiac rhythm disorders, is collaborating with us on the GENETIC-AF trial. Under the collaboration with Medtronic, ARCA is conducting a substudy that includes continuous monitoring of the cardiac rhythms of at least 150 patients enrolled during the Phase 2B portion of the trial. The collaboration is administered by a joint ARCA-Medtronic committee. Medtronic uses its proprietary CareLink System to collect and analyze the cardiac rhythm data from the implanted Medtronic devices and the data will be used by the DSMB as part of the interim

analysis. Medtronic will support the reimbursement process for U.S. patients enrolled in the Phase 2B portion, and will provide financial support of unreimbursed costs for a certain number of U.S. patients in the Phase 2B portion up to a certain maximum amount per patient. If GENETIC-AF proceeds to Phase 3, we will seek to enroll an additional 100 patients, with Medtronic devices for monitoring and recording AF burden, in the substudy. Medtronic will provide the agreed upon CareLink System cardiac rhythm data collection and analysis for the Phase 3 portion of the substudy and support the reimbursement process.

We have been granted patents in the United States, Europe, and other jurisdictions for methods of treating AF and HF patients with Gencaro based on genetic testing, which, if we are granted patent term extension, may provide market exclusivity for these uses of Gencaro into approximately 2030 in the United States and Europe.

To support the continued development of Gencaro, in June 2015, we completed a private placement that raised approximately $34 million of net proceeds as additional funds for the Phase 2B portion of the GENETIC-AF trial and to support our ongoing operations. We are seeking to enroll approximately 200 HFREF patients in the Phase 2B portion of the GENETIC-AF trial, and we anticipate that our current cash and cash equivalents will be sufficient to fund our operations, at our projected cost structure, through the end of 2017. However, in light of the significant uncertainties regarding clinical development timelines and costs for developing drugs such as

Table of Contents

Gencaro, we may need to raise a significant amount of additional capital due to changing circumstances that may cause us to consume capital significantly faster or slower than we currently anticipate. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate. If GENETIC-AF proceeds to Phase 3, we will be required to raise additional funds prior to completion of the Phase 3 portion.

Corporate Information

On January 27, 2009, we completed a business combination, or the Merger, with Nuvelo, Inc. Immediately following the Merger, we changed our name from Nuvelo, Inc. to ARCA biopharma, Inc. Our principal offices are located in Westminster, Colorado, and our telephone number is (720) 940-2200. Our website address is www.arcabiopharma.com. We do not incorporate the information on our website into this prospectus, and you should not consider it part of this prospectus. For further information regarding us and our financial information, you should refer to our recent filings with the Securities and Exchange Commission, or the SEC. See Where You Can Find More Information and Incorporation of Certain Documents by Reference.

Each of ARCA, ARCA biopharma, Gencaro and Gencaro Test is a registered trademark of ARCA biopharma, Inc. Each of the other trademarks, trade names or service marks appearing in this prospectus belongs to its respective holder.

Table of Contents

THE OFFERING

Common stock offered by selling stockholders	58,830,211 (1)
Use of proceeds	We will not receive any proceeds from the sale of the shares of common stock covered by this prospectus. A portion of the shares covered by this prospectus are issuable upon exercise of warrants to purchase our common stock. Upon exercise of any of the warrants for cash, the applicable selling stockholder would pay us the exercise price set forth in the warrants. We expect to use any such proceeds for general working capital purposes.
NASDAQ Capital Market trading symbol for common stock	ABIO

(1) Includes 16,808,632 shares of common stock that may be issued upon the exercise of warrants held by the selling stockholders.

The selling stockholders named in this prospectus may offer and sell up to 58,830,211 shares of our common stock, including 16,808,632 shares of our common stock issuable upon exercise of warrants. Throughout this prospectus, when we refer to the share of our common stock being registered on behalf of the selling stockholders, we are referring to the shares of common stock that have been issued pursuant to the securities purchase agreement in the private placement described below, or that may be issuable upon the exercise of the warrants issued in such private placement. When we refer to the selling stockholders in this prospectus, we are referring to the investors in the private placement who are named in this prospectus as the selling stockholders and, as applicable, any donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from the selling stockholders as a gift, pledge or other non-sale transfer.

The Private Placement

On June 10, 2015, we entered into a securities purchase agreement with certain investors named in the table in the section entitled Selling Stockholders, pursuant to which we sold 42,021,579 units, with each unit consisting of one share of our common stock and a warrant to purchase 0.4 shares of our common stock. The warrants have an exercise price of $0.8716, will become exercisable on December 13, 2015 and expire seven years after their date of issuance, unless earlier terminated. In connection with the closing of the private placement, on June 16, 2015, we agreed to file this registration statement with the Securities Exchange Commission, or SEC, to register for resale the shares issued in the private placement and the shares issuable upon exercise of the warrants issued in the private placement. We received gross proceeds of approximately $37.0 million before deduction of offering expenses.

The issuance of shares of common stock and warrants sold in this private placement was exempt from registration under the Securities Act of 1933, as amended, or the Securities Act, pursuant to the exemption for transactions by an issuer not involving a public offering under Section 4(a)(2) of the Securities Act and Regulation D promulgated under the Securities Act.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. Prior to making a decision about investing in our common stock, you should consider carefully the specific risk factors discussed in the sections entitled Risk Factors contained in our most recent Annual Report on Form 10-K for the fiscal year ending December 31, 2014 and subsequent Quarterly Report on Form 10-Q for the quarter ending March 31, 2015, each as filed with the SEC, and which are incorporated in this prospectus by reference in their entirety, as well as any amendment or updates to our risk factors reflected in subsequent filings with the SEC, including any prospectus supplement hereto. These risks and uncertainties are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us, or that we currently view as immaterial, may also impair our business. If any of the risks or uncertainties described in our SEC filings or any additional risks and uncertainties actually occur, our business, financial condition, results of operations and cash flow could be materially and adversely affected. In that case, the trading price of our common stock could decline and you might lose all or part of your investment.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents that we have filed with the SEC that are incorporated by reference in this prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or the safe harbor created by those sections. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, estimate, predict, project, potential, c negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. Discussions containing these forward-looking statements may be found, among other places, in Business and Management s Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference from our most recent Annual Report on Form 10-K for the fiscal year ending December 31, 2014 and our Quarterly Reports on Form 10-Q for the quarter ending March 31, 2015, as well as any amendments thereto reflected in subsequent filings with the SEC. These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus or documents incorporated by reference will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this prospectus. You should read this prospectus, any accompanying prospectus supplement and the documents incorporated by reference completely and with the understanding that our actual future results may be materially different from what we expect.

Examples of these statements include, but are not limited to, statements regarding the following: the timing and results of any clinical trials, including GENETIC-AF, any potential future GENETIC-AF trials, the ongoing Gencaro trial for the prevention of atrial fibrillation, 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, the potential for rNAPc2 to be developed for, or to effectively treat hemorrhagic fever viruses, including the Ebola virus, our ability to obtain additional funding or enter into a strategic or other transaction, the extent to which our issued and pending patents may protect our products and technology, the potential of such product candidates to lead to the development of safe or effective therapies, our ability to enter into collaborations, our ability to maintain listing of our common stock on a national exchange, our future operating expenses, our future losses, our future expenditures, and the sufficiency of our cash resources to maintain operations. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and the SEC filings incorporate herein by reference, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain.

We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and our website.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of shares of our common stock by the selling stockholders pursuant to this prospectus. A portion of the shares covered by this prospectus are issuable upon exercise of warrants to purchase our common stock. Upon exercise of any of the warrants for cash, the applicable selling stockholder would pay us the exercise price set forth in the warrants. The cash exercise price of the warrants is $0.8716 per share. We intend to use the net proceeds generated by warrant cash exercises, if any, to fund the ongoing Phase 2B/3 trial for the prevention of atrial fibrillation, working capital and general corporate purposes. We cannot estimate how many, if any, of the warrants will be exercised as a result of this offering. We will bear all costs, expenses and fees in connection with the registration of shares of our common stock to be sold by the selling stockholders. The selling stockholders will bear all legal fees, commissions and discounts, if any attributable to their respective sales of shares.

It is possible that the warrants may expire and may never be exercised. The warrants contain a net exercise provision therefore the warrant holder may elect to utilize this feature and in this case we would not receive any proceeds from their exercise. Pending their use as described above, we intend to invest the net proceeds in high quality, short-term, interest-bearing securities.

Table of Contents

SELLING STOCKHOLDERS

On June 16, 2015, we issued to the selling stockholders named below an aggregate of 42,021,579 shares of common stock and warrants to purchase an additional 16,808,632 shares of common stock in a private placement. The shares of common stock being offered by the selling stockholders are those issued to the selling stockholders and those issuable to the selling stockholders upon exercise of the warrants. For additional information regarding the issuance of the common stock and the warrants, see Prospectus Summary Private Placement above. We are registering the shares of common stock in order to permit the selling stockholders to offer the shares for resale from time to time. The selling stockholders include entities affiliated with Venrock Healthcare Capital Partners, entities affiliated with New Enterprise Associates, funds managed by Franklin Advisers, Inc., entities affiliated with RA Capital Management, Tekla Life Sciences Investors, Capital Ventures International and entities affiliated with DAFNA LifeScience, L.P..

The table below, including the footnotes thereto, lists the selling stockholders and other information regarding the beneficial ownership (as determined under Section 13(d) of the Exchange Act of 1934 and the rules and regulations thereunder) of the shares of common stock held by each of the selling stockholders based in part on information provided to us by the selling stockholders. The second column lists the number of shares of common stock beneficially owned by the selling stockholders, based on their respective ownership of shares of common stock and warrants, as of June 30, 2015, assuming exercise of the warrants held by each such selling stockholder on that date without taking account of any limitations on exercise set forth therein.

The third column lists the shares of common stock being offered by this prospectus by the selling stockholders and does not take into account any limitations on exercise of the warrants set forth therein.

In accordance with the terms of a registration rights agreement with the holders of the common stock and the warrants, this prospectus generally covers the resale of the sum of (i) the shares of common stock issued to the selling stockholders and (ii) the maximum number of shares of common stock issuable upon exercise of the warrants determined as if the outstanding warrants were exercised in full (without regard to any limitations on exercise contained therein) as of the trading day immediately preceding the date this registration statement was initially filed with the SEC. Because the exercise price of the warrants may be adjusted, the number of shares that will actually be issued may be more or less than the number of shares being offered by this prospectus.

The fourth column assumes the sale of all of the shares offered by the selling stockholders pursuant to this prospectus. However, because the selling stockholders may sell all or some of their shares under this prospectus from time to time, or in another permitted manner, we cannot assure you as to the actual number of shares that will be sold by the selling stockholders. The percentage of shares owned after the offering is based on 63,219,990 shares of our common stock outstanding as of June 30, 2015, which includes the outstanding shares of common stock offered by this prospectus, plus the number of shares of our common stock issuable within 60 days of June 30, 2015 upon the exercise of any warrants, or other convertible securities, held by the selling stockholders.

Under the terms of the warrants, a selling stockholder may not exercise the warrants to the extent (but only to the extent) such selling stockholder and any of its affiliates would beneficially own a number of shares of our common stock which would exceed 9.9% of our outstanding common stock, provided, however, that if the outstanding shares of common stock held by such selling stockholder and its affiliates, together, without giving effect to such selling stockholder s warrants, exceeds 9.9% of our outstanding common stock, prior to the exercise of any warrants, then such selling stockholder may not exercise the warrants to the extent (but only to the extent) such selling stockholder and any of its affiliates would beneficially own a number of shares of our common stock that would exceed 19.9% of our outstanding common stock. RA Capital Healthcare Fund, L.P., RA Capital Management, LLC, Blackwell Partners LLC Series A, and Peter Kolchinsky are considered one entity for the purposes of calculating the 9.9% maximum

percentage described in the preceding sentence. The number of shares in the second column does not reflect these limitations. The selling stockholders may sell all, some or none of their shares in this offering. See Plan of Distribution.

Table of Contents

Selling Stockholder	Common Stock Beneficially Owned Before the Offering (1)(2)	Number of Shares of Common Stock to be Offered (2)	Stock Beneficially Owned After the Offering (3)	Percentage Ownership After Offering
Venrock Healthcare Capital Partners II, L.P. (4)	7,523,072	7,523,072		* %
VHCP Co-Investment Holdings II, LLC (4)	3,050,466	3,050,466		*
Venrock Healthcare Capital Partners, L.P. (4)	3,830,943	3,830,943		*
VHCP Co-Investment Holdings, LLC (4)	700,573	700,573		*
Growth Equity Opportunities Fund IV, LLC (5)	14,310,051	14,310,051		*
Franklin Templeton Investment Funds Franklin Biotechnology Discovery Fund (6)	7,239,877	7,239,877		*
Franklin Strategic Series Franklin Biotechnology Discovery Fund (6)	4,685,166	4,685,166		*
RA Capital Healthcare Fund, L.P. (7)	6,542,873	6,542,873		*
Blackwell Partners LLC Series A (7)	1,407,155	1,407,155		*
Tekla Life Sciences Investors (8)	7,950,029	7,950,029		*
Capital Ventures International (9)	795,003	795,003		*
DAFNA LifeScience, L.P. (10)	453,152	453,152		*
DAFNA LifeScience Market Neutral, L.P. (10)	31,800	31,800		*
DAFNA LifeScience Select, L.P. (10)	310,051	310,051		*

* Less than 1%.

(1) Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Shares of common stock that can be acquired under options or warrants that are currently exercisable, or which will become exercisable no later than 60 days after June 30, 2015, are deemed outstanding for the purposes of computing the percentage of the person holding such options or warrants, but not deemed outstanding for the purposes of computing the percentage of any other person. Except as indicated by footnote and subject to community property laws where applicable, the persons named in the table have sole voting and investment power with respect to all shares of common stock shown beneficially owned by them.

(2) Includes all shares issuable upon the exercise of warrants without regard to restrictions on exercise.

(3) Assumes sale of all shares available for sale under this prospectus and no further acquisitions of shares by the selling stockholders.

(4) VHCP Management, LLC (VHCP Management) is the general partner of Venrock Healthcare Capital Partners, L.P. (VHCP) and the manager of VHCP Co-Investment Holdings, LLC (Co-Invest) and may be deemed to beneficially own the shares held by either VHCP or Co-Invest. VHCP Management II, LLC (VHCP Management II) is the general partner of Venrock Healthcare Capital Partners II, L.P. (VHCP II) and the manager of VHCP Co-Investment Holdings II, LLC (Co-Invest II) and may be deemed to beneficially own the shares held by either VHCP II or Co-Invest II. Drs. Anders D. Hove and Bong Y. Koh are the managing members of VHCP Management and VHCP Management II and may be deemed to beneficially own the shares beneficially owned by either VHCP Management or VHCP Management II. VHCP Management and VHCP Management II disclaim beneficial ownership over all shares held by VHCP and Co-Invest and VHCP II and Co-Invest II, respectively, except to the extent of their respective pecuniary interests therein. The address for VHCP, VHCP II, Co-Invest and Co-Invest II is 3340 Hillview Avenue, Palo Alto, CA 94304.

(5)

The shares are directly held by Growth Equity Opportunities Fund IV, LLC (GEO IV) and indirectly held by New Enterprise Associates 15, L.P. (NEA 15), the sole member of GEO IV, NEA Partners 15, L.P. (NEA Partners 15), the sole general partner of NEA 15, NEA 15 GP, LLC (NEA 15 GP), the sole general partner of NEA Partners 15, and the individual managers of NEA 15 GP (NEA 15, NEA Partners 15, NEA 15 GP and the individual managers of NEA 15 GP, together, the Indirect Reporting Persons). The individual managers of NEA 15 GP are Peter J. Barris, Forest Baskett, Anthony A. Florence, Jr., Krishna Kittu Kolluri, Josh Makower, David M. Mott, Jon Sakoda, Scott D. Sandell, Peter W. Sonsini, Ravi Viswanathan and Harry R. Weller. The address for GEO IV is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093.

(6) Franklin Advisers, Inc. (FAV), an indirectly wholly owned subsidiary of a public traded company, Franklin Resources, Inc. (FRI), is the beneficial owner of these securities for purposes of Rule 13d-3 under the Exchange Act in its capacity as the investment adviser to Franklin Strategic Series Franklin Biotechnology Discovery Fund and Franklin Templeton Investment

Table of Contents

Funds Franklin Biotechnology Discovery Fund. When an investment management contract (including a sub-advisory agreement) delegates to FAV investment discretion or voting power over the securities held in the investment advisory accounts that are subject to that agreement, FRI treats FAV as having sole investment discretion or voting authority, as the case may be, unless the agreement specifies otherwise. Accordingly, FAV reports for purposes of Section 13(d) of the Exchange Act that it has sole investment discretion and voting authority over the securities covered by any such investment management agreement, unless otherwise specifically noted. The address for FAV is One Franklin Parkway, San Mateo, CA 94403.

(7) Peter Kolchinsky, as Manager of RA Capital Management, LLC, which is the general partner of RA Capital Healthcare Fund, L.P. and the investment advisor of Blackwell Partners, LLC Series A, has voting and investment power over the shares held by Blackwell Partners, LLC Series A and RA Capital Healthcare Fund, L.P. The notice address for Blackwell Partners, LLC Series A and RA Capital Healthcare Fund, L.P. is 20 Park Plaza, Suite 1200, Boston, MA 02116.

(8) Tekla Capital Management, or TCM, maintains investment management responsibility for Tekla Life Sciences Investors. Daniel Omstead is the managing member of TCM and has investment responsibility for TCM. TCM and Daniel Omstead disclaim beneficial ownership of such securities except to the extent of any pecuniary interest therein.

(9) Heights Capital Management, Inc., the authorized agent of Capital Ventures International (CVI), has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed have investment discretion and voting power over the shares held by CVI. The address for CVI; c/o Heights Capital Management, Inc., its authorized agent is 101 California Street, Suite 3250, San Francisco, CA 94111.

(10) DAFNA Capital Management, LLC is the investment advisor of DAFNA Life Science LP, DAFNA Life Science Market Neutral LP and DAFNA Life Science Select LP (the DAFNA Funds). Nathan Fischel is the Chief Executive Officer and Fariba Ghodsian is the Chief Investment Officer of DAFNA Capital Management, LLC and they may be deemed to have shared voting and investment power with respect to the securities held by the DAFNA Funds. The address for DAFNA Lifescience LP, DAFNA Lifescience Market Neutral LP and DAFNA Lifescience Select LP is 10990 Wilshire Boulevard, Suite 1400, Los Angeles, CA 90024.

Table of Contents

PLAN OF DISTRIBUTION

We are registering the shares of common stock issued to the selling stockholders and the shares of common stock issuable upon exercise of the warrants to permit the resale of these shares of common stock by the selling stockholders from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. We will bear all fees and expenses incident to our obligation to register the shares of common stock.

The selling stockholders may sell all or a portion of the shares of common stock held by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agent s commissions. The shares of common stock may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions, pursuant to one or more of the following methods:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing or settlement of options, whether such options are listed on an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;

short sales made after the date this registration statement is declared effective by the SEC;

broker-dealers may agree with a selling securityholder to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares of common stock under Rule 144 promulgated under the Securities Act, if available, rather than under this prospectus. In addition, the selling stockholders may transfer the shares of common stock by other means not described in this prospectus. If the selling stockholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved).

In connection with sales of the shares of common stock or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling stockholders may also sell shares of common stock short and deliver shares of common stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares.

The selling stockholders may pledge or grant a security interest in some or all of the warrants or shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

Table of Contents

To the extent required by the Securities Act and the rules and regulations thereunder, the selling stockholders and any broker-dealer participating in the distribution of the shares of common stock may be deemed to be underwriters within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of common stock is made, a prospectus supplement, if required, will be distributed, which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling stockholders and any discounts, commissions or concessions allowed or re-allowed or paid to broker-dealers.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any selling stockholder will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus forms a part.

The selling stockholders and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholders and any other participating person. To the extent applicable, Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the stock purchase agreement, estimated to be $330,000 in total, including, without limitation, SEC filing fees and expenses of compliance with state securities or blue sky laws; provided, however, a selling stockholder will pay all underwriting discounts and selling commissions, if any. We will indemnify the selling stockholders against liabilities, including some liabilities under the Securities Act in accordance with the securities purchase agreements or the selling stockholders will be entitled to contribution. We may be indemnified by the selling stockholders against civil liabilities, including liabilities under the Securities Act that may arise from any written information furnished to us by the selling stockholder specifically for use in this prospectus, in accordance with the related securities purchase agreements or we may be entitled to contribution.

Once sold under the registration statement, of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

Table of Contents

LEGAL MATTERS

The validity of our common stock being offered hereby has been passed upon for us by Cooley LLP, Broomfield, Colorado.

EXPERTS

The financial statements of ARCA biopharma, Inc. (the Company) as of December 31, 2014 and 2013, and for each of the years in the two year period ended December 31, 2014, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The audit report covering the December 31, 2014 financial statements contains an explanatory paragraph that states that the Company s recurring losses from operations and its dependence upon raising additional funds from strategic transactions, sales of equity, and/or issuance of debt raise substantial doubt about the entity s ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of that uncertainty.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We are a reporting company and file our annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and obtain copies of our reports, proxy statements and other information we file with the SEC, at the SEC s public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available at the SEC s web site at http://www.sec.gov.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No.000-22873):

- our annual report on Form 10-K for the year ended December 31, 2014, filed with the SEC on March 19, 2015;
- our quarterly report on Form 10-Q for the quarterly period ended March 31, 2015, filed with the SEC on May 12, 2015;
- our current reports on Form 8-K and Form 8-K/A filed with the SEC on February 4, 2015, February 17, 2015, February 23, 2015, March 16, 2015, April 13, 2015, June 5, 2015, June 11, 2015, June 23, 2015 and July 16, 2015; and

the description of our securities contained in our Form S-1 filed with the SEC on March 25, 2013.

We also incorporate by reference into this prospectus all documents (other than Current Reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are subsequently filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of the offering of the securities made by this prospectus (including documents filed after the date of the initial registration statement and prior to the effectiveness of the registration statement). These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded to the extent that a statement contained in this prospectus or any subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to Brian L. Selby, Vice President, Finance, ARCA biopharma, Inc., 11080 CirclePoint Road, Suite 140, Westminster, Colorado 80020; telephone: (720) 940-2200. In addition, all of the documents incorporated by reference into this prospectus may be accessed via the Internet at our website: http://www.arcabiopharma.com.