

ARCA biopharma, Inc.
Form 424B5
August 03, 2012
Table of Contents

Filed Pursuant to Rule 424(b)(5)

Registration No. 333-172686

PROSPECTUS SUPPLEMENT

(To Prospectus dated April 4, 2011)

ARCA BIOPHARMA, INC.

2,436,599 Shares of Common Stock

Warrants to Purchase 1,827,449 Shares of Common Stock

We are offering for sale up to 2,436,599 shares of our common stock and warrants to purchase up to 1,827,449 shares of our common stock (and the shares of common stock issuable from time to time upon exercise of the warrants). The common stock and warrants will be sold in combination, with a warrant to purchase 0.75 shares of common stock for each one share of common stock sold. The negotiated purchase price for each share and related warrant is \$0.391. The exercise price of the warrants will be \$0.46 per share of common stock. The shares of common stock and warrants are immediately separable and will be issued separately. The warrants will be exercisable on the date that is six months after the warrants are issued and will expire on the sixth anniversary of the date the warrants are first exercisable. The purchasers will make payments to an escrow agent, and at the closing the escrow agent will release these payments to us and we will issue and deliver the securities.

For a more detailed description of the warrants, see the section entitled "Description of the Securities We Are Offering" beginning on page S-26, and for a more detailed description of our common stock, see the section entitled "Description of Capital Stock - Common Stock" beginning on page 7 of the accompanying prospectus.

Our common stock is quoted on the NASDAQ Capital Market under the symbol "ABIO". On August 2, 2012, the last reported sale price of our common stock on the NASDAQ Capital Market was \$0.46 per share. There is no established public trading market for the warrants, and we do not expect a market to develop. We do not intend to apply to list the warrants on any securities exchange.

As of August 2, 2012, the aggregate market value of our outstanding common stock held by non-affiliates was approximately \$6,069,656.42, based on 10,482,999 shares of outstanding common stock held by non-affiliates and a per share price of \$0.579, which was the last sale price of our common stock on The NASDAQ Capital Market on July 19, 2012. Within the prior 12 calendar month period that ends on, and includes the date of this prospectus supplement, we have sold securities in the amount of \$0 pursuant to General Instruction I.B.6 of Form S-3. The value of the securities offered hereby is \$2,010,803.19.

	Per Share and Related Warrant	Total
Public offering price	\$ 0.391	\$ 952,710.22
Placement agent commission (1)	\$ 0.025	\$ 61,926.16
Proceeds, before expenses, to us	\$ 0.366	\$ 890,784.06

- (1) We have retained Ladenburg Thalmann & Co. Inc. to act as exclusive placement agent in connection with this offering. The placement agent has no obligation to buy any of the securities from us or to arrange for the purchase or sale of any specific number or dollar amount of securities. In addition to a 6.5% commission, we have also agreed to reimburse the placement agent for certain of its expenses. See Plan of Distribution beginning on page S-28 of this prospectus supplement for more information regarding these arrangements.

Investing in our securities involves a high degree of risk. See Risk Factors beginning on page S-4 of this prospectus supplement and Risk Factors beginning on page 5 of the accompanying prospectus.

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

Ladenburg Thalmann & Co. Inc. is acting as the exclusive placement agent in this offering. We estimate the total expenses of this offering, excluding the placement agency fees and cost reimbursement, will be approximately \$125,000. Because there is no minimum offering amount required in this offering, the actual offering amount, the placement agency fees and net proceeds to us, if any, in this offering may be substantially less than the total offering amounts set forth above. We are not required to sell any specific number or dollar amount of the securities offered in this offering, but the placement agent will use its reasonable efforts to arrange for the sale of all of the securities offered. We anticipate the closing of the sale of securities will take place on or before August 8, 2012.

Ladenburg Thalmann & Co. Inc.

The date of this prospectus supplement is August 3, 2012.

Table of Contents**TABLE OF CONTENTS**

	Page
Prospectus Supplement	
<u>About This Prospectus Supplement</u>	i
<u>Prospectus Supplement Summary</u>	S-1
<u>Risk Factors</u>	S-4
<u>Special Note Regarding Forward-Looking Statements</u>	S-23
<u>Use of Proceeds</u>	S-24
<u>Dilution</u>	S-25
<u>Description of the Securities We Are Offering</u>	S-26
<u>Plan of Distribution</u>	S-28
<u>Legal Matters</u>	S-30
<u>Experts</u>	S-30
<u>Where You Can Find More Information</u>	S-30
<u>Important Information Incorporated by Reference</u>	S-30
Prospectus	
<u>About This Prospectus</u>	i
<u>Overview</u>	1
<u>Risk Factors</u>	5
<u>Forward-Looking Information</u>	5
<u>Use of Proceeds</u>	6
<u>Description of Capital Stock</u>	7
<u>Description of Debt Securities</u>	10
<u>Description of Warrants</u>	16
<u>Description of Units</u>	18
<u>Legal Ownership of Securities</u>	19
<u>Plan of Distribution</u>	22
<u>Legal Matters</u>	24
<u>Experts</u>	24
<u>Where You Can Find More Information</u>	24
<u>Incorporation by Reference</u>	24

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is a supplement to the accompanying prospectus that is also a part of this document. This prospectus supplement and the accompanying prospectus, dated April 4, 2011, are part of a registration statement on Form S-3 (File No. 333-172686) that we filed with the Securities and Exchange Commission, or the SEC, utilizing a shelf registration process. Under this shelf registration process, we may offer and sell from time to time in one or more offerings the securities described in the accompanying prospectus.

This document is in two parts. The first part is this prospectus supplement, which describes the securities we are offering and the terms of the offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information, some of which may not apply to the securities offered by this prospectus supplement. Generally, when we refer to this prospectus, we are referring to both documents combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein, on the other hand, you should rely on the information in this prospectus supplement. We urge you to carefully read this prospectus supplement and the accompanying prospectus and any related free writing prospectus, together with the information incorporated herein and therein by reference as described under the heading Where You Can Find Additional Information, before buying any of the securities being offered.

Table of Contents

You should rely only on the information that we have provided or incorporated by reference in this prospectus supplement and the accompanying prospectus and any related free writing prospectus that we may authorize to be provided to you. We have not, and the placement agent has not, authorized anyone to provide you with different information. No other dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement and the accompanying prospectus or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus supplement is an offer to sell only the securities offered hereby, and only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus supplement and the accompanying prospectus or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any related free writing prospectus, or any sale of a security.

This prospectus supplement 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 supplement is a part, and you may obtain copies of those documents as described below under the heading **Where You Can Find More Information**.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary is not complete and does not contain all of the information that you should consider before investing in the securities offered by this prospectus. You should read this summary together with the entire prospectus supplement and accompanying prospectus, including our financial statements, the notes to those financial statements and the other documents that are incorporated by reference in this prospectus supplement, before making an investment decision. See the Risk Factors section of this prospectus supplement on page S-4 for a discussion of the risks involved in investing in our securities.

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

Overview

We are a biopharmaceutical company whose principal focus is developing genetically-targeted therapies for cardiovascular diseases. Our lead product candidate, Gencaro™ (bucindolol hydrochloride), a pharmacologically unique beta-blocker and mild vasodilator, is being developed for the treatment of atrial fibrillation, or AF, in patients with heart failure, or HF. We have identified common genetic variations in the cardiovascular system that we believe interact with Gencaro's pharmacology and may predict patient response to the drug.

We have been granted patents in the U.S., Europe, and other jurisdictions for methods of treating AF and HF patients with Gencaro based on genetic testing, which we believe will provide market exclusivity for these uses of Gencaro into at least 2026 in the U.S. and into 2025 in Europe. In addition, we believe that if Gencaro is approved, the Gencaro patents will be eligible for patent term extension based on our current clinical trial plans which, if granted in the U.S., may provide market exclusivity into 2029, and if granted in Europe may provide market exclusivity into 2030.

We are planning to initiate a Phase 3 clinical study of Gencaro in AF patients with HF and/or left ventricular dysfunction. We believe AF is an attractive potential indication for Gencaro because data from the previously conducted Phase 3 HF trial of Gencaro in 2,708 HF patients, or the BEST HF trial, suggest that Gencaro may have a potentially significant effect in reducing or preventing AF. Based on our analysis of data from the BEST HF trial, we believe that Gencaro's prevention of AF in HF patients is pharmacogenetically regulated. We plan to enroll approximately 200-400 patients with persistent AF who have the genotype that appears to respond most favorably to Gencaro. We anticipate that this trial could begin approximately 6 months after we obtain sufficient funding.

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. These clots may travel from the heart and become lodged in the arteries leading to the brain and other organs, thereby blocking necessary blood flow and potentially resulting in stroke. AF is considered an epidemic cardiovascular disease that affects approximately 2-3 million Americans, making it one of the most common heart rhythm disorders. The approved therapies for the treatment or prevention AF have certain disadvantages, such as toxic side effects. 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 patients with HF where most of the approved drugs are contra-indicated or have warnings in their prescribing information.

The planned AF clinical trial is designed to be a multi-center, randomized, double-blind clinical trial to assess the safety and efficacy of Gencaro in AF patients with HF and/or left ventricular dysfunction, with the primary endpoint being time to recurrent symptomatic AF after direct current cardioversion. This AF trial is designed to compare Gencaro to the beta-blocker metoprolol CR/XL in the patient genotype we believe responds most favorably to Gencaro. The therapeutic benefit of metoprolol CR/XL does not appear to be enhanced in patients with this genotype. We believe data from the BEST HF trial indicate that Gencaro may have a potentially significant effect in reducing or preventing AF, and this effect may be one that is genetically regulated. The entire cohort of patients in the BEST HF trial that were treated with Gencaro had a 41% reduction in the risk of new onset AF (time-to-event) compared to placebo ($p = 0.0004$), although because there was not a predetermined AF clinical endpoint in the BEST HF trial, the data is based on a subsequent analysis of adverse events and surveillance electrocardiograms (ECGs). In the DNA sub-study, patients with the most favorable genotype for Gencaro experienced a 74% ($p = 0.0003$) reduction in risk of AF, based on the same analysis. This most favorable genotype was present in about 47% of the patients in the sub-study, and we estimate it is present in about 50% of the U.S. general population. We believe the AF study would take approximately two and one half years from enrollment of the first patient through completion.

We have exclusive patent rights to other product candidates that have potential indications in cardiovascular disease, oncology and other therapeutic areas, some of which are in early stages of development and others of which are in later stages of development. We are seeking development partners to assist us in the development of these product candidates or who may license rights to them. For

S-1

Table of Contents

example, we hold exclusive rights to rNAPc2, a recombinant protein that is a potent, long acting tissue factor inhibitor with a unique mechanism of action. Previously, preclinical studies of rNAPc2 showed evidence of potential efficacy against lethal hemorrhagic fever viruses.

Other Information

We were originally incorporated as Hyseq, Inc. in Illinois in 1992 and reincorporated in Nevada in 1993. On January 31, 2003, we merged with Variagenics, Inc., a publicly traded Delaware corporation based in Massachusetts, and, in connection with the merger, changed our name to Nuvelo, Inc. On March 25, 2004, we reincorporated in Delaware. On January 27, 2009, our wholly owned subsidiary merged with ARCA biopharma, Inc., a privately held Delaware corporation based in Colorado, and, in connection with the merger, we changed our name to ARCA biopharma, Inc. Our principal offices are located at 8001 Arista Place, Suite 430, Broomfield, Colorado 80021. Our telephone number is (720) 940-2200. Our internet address is <http://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 (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 us	2,436,599 shares
Common stock to be outstanding after this offering (assuming no exercise of the warrants offered by us)	14,619,598 shares
Warrants offered by us	Warrants to purchase 1,827,449 shares of common stock. Each warrant may be exercised at any time on or after the date that is the six-month anniversary of the date the warrants are issued until the fifth anniversary of the initial exercise date of the warrants at an exercise price of \$0.46 per share of common stock, subject to adjustment. This prospectus also relates to the offering of the shares of common stock issuable upon exercise of the warrants.
Use of proceeds	We intend to use the net proceeds from this offering solely for general corporate purposes, including clinical trials, research and development expenses and general and administrative expenses See Use of Proceeds on page S-24.
Market for the common stock and warrants	Our common stock is quoted and traded on the NASDAQ Capital Market under the symbol ABIO. However, there is no established public trading market for the offered warrants, and we do not expect a market to develop. In addition, we do not intend to apply to list the warrants on any securities exchange. The warrants are immediately separable from the common shares.
Risk factors	You should read the Risk Factors section on page S-4 of this prospectus supplement, the Risk Factors section on page 5 of the accompanying prospectus, and the Risk Factors section in our Annual Report for the year ended December 31, 2011 on Form 10-K for a discussion of factors to consider before deciding to purchase our securities.
NASDAQ Capital Market trading symbol for common stock	ABIO
The number of shares of common stock to be outstanding after this offering as reflected in the table above is based on the actual number of shares outstanding as of August 2, 2012, which was 12,182,999, and does not include, as of that date:	

884,000 shares of common stock issuable upon the exercise of outstanding options, with a weighted average exercise price of \$3.08 per share;

2.8 million shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of \$2.65 per share; and

477,000 shares of common stock reserved for future issuance under our Amended and Restated 2004 Equity Incentive Plan. Unless otherwise stated, outstanding share information throughout this prospectus supplement excludes such outstanding options and warrants to purchase shares of common stock and shares available for issuance.

Table of Contents

RISK FACTORS

Before you make a decision to invest in our securities, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also significantly impair our business operations and could result in a complete loss of your investment.

Risks Related to Our Business and Financial Condition

Our management and our independent registered public accountant, in their report on our financial statements as of and for the year ended December 31, 2011, have concluded that due to our need for additional capital, and the uncertainties surrounding our ability to raise such funding, substantial doubt exists as to our ability to continue as a going concern.

Our audited financial statements for the fiscal year ended December 31, 2011 and our unaudited financial statements for the three months ended March 31, 2012, were prepared assuming that we will continue as a going concern. The going concern basis of presentation assumes that we will continue in operation for the foreseeable future and will be able to realize our assets and discharge our liabilities and commitments in the normal course of business and do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from our inability to continue as a going concern. Our management and our independent registered public accountant have concluded that due to our need for additional capital, and the uncertainties surrounding our ability to raise such funding, substantial doubt exists as to our ability to continue as a going concern. We may be forced to further reduce our operating expenses and raise additional funds to meet our working capital needs, principally through the additional sales of our securities or debt financings. However, we cannot guarantee that we will be able to obtain sufficient additional funds when needed or that such funds, if available, will be obtainable on terms satisfactory to us. If we are unable to raise sufficient additional capital or complete a strategic transaction, we may be unable to continue to fund our operations, develop Gencaro or our other product candidates, or realize value from our assets and discharge our liabilities in the normal course of business. These uncertainties raise substantial doubt about our ability to continue as a going concern. If we become unable to continue as a going concern, we may have to liquidate our assets, and might realize significantly less than the values at which they are carried on our financial statements, and stockholders may lose all or part of their investment in our common stock.

We will need to raise substantial additional funds through the public or private debt and equity securities, from government funding or complete one or more strategic transactions, to continue development of Gencaro. If we are unable to raise such financing or complete such a transaction, we may not be able to continue operations.

In light of the expected development timeline to potentially obtain FDA approval for Gencaro, if at all, the substantial additional costs associated with the development of Gencaro, including the costs associated with the planned AF clinical trial, the substantial cost of commercializing Gencaro, if it is approved, we will need to raise substantial additional funding through public or private debt or equity transactions or a strategic combination or partnership, or government funding. If we are delayed in obtaining funding or are unable to complete a strategic transaction, we may discontinue our development activities on Gencaro or discontinue our operations. Even if we are able to fund continued development and Gencaro is approved, we expect that we will need to complete a strategic transaction or raise substantial additional funding through public or private debt or equity securities to successfully commercialize Gencaro.

We currently believe our cash and cash equivalents balance as of June 30, 2012, will be sufficient to fund our operations, at our current cost structure through September 30, 2012. As a result of the significant additional required development of Gencaro, including the additional clinical trials, we may not be able to raise sufficient capital on acceptable terms, or at all, to continue development of Gencaro or to continue operation and may not be able to execute any strategic transaction. We are unable to assert that our current cash and cash equivalents are sufficient to fund operations beyond that date, and as a result, there is substantial doubt about our ability to continue as a going concern beyond September 30, 2012. Changing circumstances 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.

Our liquidity, and our ability to raise additional capital or complete any strategic transaction, depends on a number of factors, including, but not limited to, the following:

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

the costs and timing for additional clinical trials in order to gain possible FDA approval for Gencaro;

the market price of our stock and the availability and cost of additional equity capital from existing and potential new investors;

S-4

Table of Contents

our ability to retain the listing of our common stock on the Nasdaq Capital Market;

general economic and industry conditions affecting the availability and cost of capital;

potential receipt of government or third party funding to further develop Gencaro or rNAPc2;

our ability to control costs associated with our operations;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and

the terms and conditions of our existing collaborative and licensing agreements.

The sale of additional equity or convertible debt securities would likely result in substantial dilution to our stockholders. If we raise additional funds through the incurrence of indebtedness, the obligations related to such indebtedness would be senior to rights of holders of our capital stock and could contain covenants that would restrict our operations. We also cannot predict what consideration might be available, if any, to us or our stockholders, in connection with any strategic transaction. Should strategic alternatives or additional capital not be available to us in the near term, or not be available on acceptable terms, we may be unable to realize value from our assets and discharge our liabilities in the normal course of business which may, among other alternatives, cause us to further delay, substantially reduce or discontinue operational activities to conserve our cash resources.

If we are not able to maintain the requirements for listing on the Nasdaq Capital Market, we could be delisted, which could have a materially adverse effect on our ability to raise additional funds as well as the price and liquidity of our common stock.

Our common stock is currently listed on The NASDAQ Capital Market. To maintain the listing of our common stock on The NASDAQ Capital Market we are required to meet certain listing requirements, including, among others, either: (i) a minimum closing bid price of \$1.00 per share, a market value of publicly held shares (excluding shares held by our executive officers, directors and 10% or more stockholders) of at least \$1 million and stockholders' equity of at least \$2.5 million; or (ii) a minimum closing bid price of \$1.00 per share, a market value of publicly held shares (excluding shares held by our executive officers, directors and 10% or more stockholders) of at least \$1 million and a total market value of listed securities of at least \$35 million. On April 12, 2012 we received notification from NASDAQ of potential delisting of our shares from the NASDAQ Capital Market because the closing bid price of our common stock had not met the minimum closing bid price of \$1.00 per share during the preceding 30 days. NASDAQ rules provide us a 180 calendar day grace period from the date of the Notice to regain compliance by meeting the continued listing standard. The continued listing standard will be met if our common stock has a minimum closing bid price of at least \$1.00 per share for a minimum of 10 consecutive business days during the 180 calendar day grace period. If we do not regain compliance within the 180 calendar day grace period, we will be afforded an additional 180 calendar day compliance period, provided that on the 180th day of the first grace period we (i) meet the applicable market value of publicly held shares requirement for continued listing and all other applicable requirements for initial listing on The Nasdaq Capital Market (except for the bid price requirement) based on our most recent public filings and market information and (ii) notify NASDAQ of our intent to cure this deficiency. If we do not indicate our intent to cure the deficiency or if it does not appear to NASDAQ that it would be possible for us to cure the deficiency, we would not be eligible for the second 180 day compliance period, and our securities would then be subject to delisting from the NASDAQ Capital Market. If we are unable to regain compliance during the first 180 calendar day grace period or, if applicable, the second 180 day compliance period, and we receive a delisting determination from NASDAQ we may, at that time, request a hearing to remain on the NASDAQ Capital Market, which request will ordinarily suspend such delisting determination until a decision by NASDAQ subsequent to the hearing.

There can be no assurance that we will be successful in maintaining the listing of our Common Stock on The NASDAQ Capital Market. This could impair the liquidity and market price of the Common Stock. In addition, the delisting of the Common Stock from a national exchange could materially adversely affect our access to capital markets, and any limitation on market liquidity or reduction in the price of the Common Stock as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all.

As of August 2, 2012, the closing bid price of our common stock was \$0.46 the total market value of our publicly held shares of our common stock (excluding shares held by our executive officers, directors and 10% or more stockholders) was approximately \$4.8 million and the total market value of our listed securities was approximately \$5.6 million. As of March 31, 2012, we had stockholders' equity of \$4.4 million.

Our failure to enter into a strategic transaction may materially and adversely affect our business.

Unless we are able to raise substantial additional funding through other means, we will need to complete a strategic transaction to continue the development of Gencaro or our other operations. The strategic transactions that we may consider include a potential combination or partnership. Our board of directors and management team has and will continue to devote substantial time and resources to the consideration and implementation of any such strategic transaction. In addition, conditions in the financial markets may lead to an increased number of biotechnology companies that are also seeking to enter into strategic transactions, which may limit our ability to negotiate favorable terms for any such transaction. Further, our current employees do not have experience in the strategic transaction process, and our previous efforts to enter into a strategic transaction have not been successful. As a result of these and other factors, there is substantial risk that we may not be able to complete a strategic transaction on favorable terms, or at all. The failure to complete a strategic transaction may materially and adversely affect our business.

Table of Contents

We may be limited in our ability to access sufficient funding through a private equity or convertible debt offering.

NASDAQ rules impose restrictions on our ability to raise funds through a private offering of our common stock, convertible debt or similar instruments without obtaining stockholder approval. Under NASDAQ rules, an offering of more than 20% of our total shares outstanding for less than the greater of book or market value requires stockholder approval unless the offering qualifies as a public offering for purposes of the NASDAQ rules. As of June 30, 2012, we had 12,182,999 shares of common stock outstanding, 20% of which is 2,436,599.8 shares. To the extent we seek to raise funds through a private offering of stock, convertible debt or similar instruments, we are limited in how much funding we could raise privately without requiring a stockholder vote.

In addition, we are currently subject to certain contractual rights of investors arising from our public and private equity financing transactions that limit the nature and price of future public and private financing transactions that we may effect. For example, in April 2011, we entered into separate subscription agreements with certain institutional investors in connection with a registered direct public offering, pursuant to which we sold shares of our common stock and warrants to purchase shares of our common stock to the investors. In connection with this transaction, we agreed that, subject to certain exceptions, we would not, within the three year period following the closing of the offering, while the warrants are outstanding, effect or enter into an agreement to effect any issuance of common stock or securities convertible into, exercisable for or exchangeable for common stock in a variable rate transaction, which means a transaction in which we issue or sell any convertible securities either (A) at a conversion price, exercise price or exchange rate or other price that is based upon and/or varies with the trading prices of, or quotations for, the shares of common stock at any time after the initial issuance of such convertible securities, or (B) with a conversion, exercise or exchange price that is subject to being reset at some future date after the initial issuance of the convertible securities or upon the occurrence of the specified or contingent events directly or indirectly related to our business or the market for our common stock. In addition, we agreed that, subject to certain exceptions, if we issue securities within one year following the closing of the offering, each investor would have the right to purchase its pro rata share of a specified proportion of the securities in the future offering on the same terms, conditions and price provided for in the proposed issuance of securities. In connection with this transaction we were also restricted from issuing or selling shares of our common stock or securities convertible into our common stock for 90 days following the transaction.

Similarly, in December 2011, we entered into separate subscription agreements with various institutional investors in connection with a private placement of our common stock and warrants. We granted to these investors certain registration rights with respect to the shares of common stock (including common stock issuable upon exercise of the warrants). In connection with this transaction, we agreed that, subject to certain exceptions, we would not, within the three year period following the closing of the offering, enter into any variable rate transaction. In connection with this transaction we were also restricted from issuing or selling shares of our common stock or securities convertible into our common stock for 45 days following the transaction.

The restrictions imposed by the terms of these offerings, and that could be imposed in future offerings, may limit our access to capital on agreeable terms and delay or make impossible certain otherwise available equity financing opportunities and could severely restrict our access to the capital necessary to conduct our business.

If we are not able to successfully develop, obtain FDA approval for and provide for the commercialization of Gencaro in a timely manner, we may not be able to continue our business operations.

We currently have no products that have received regulatory approval for commercial sale. The process to develop, obtain regulatory approval for and commercialize potential product candidates is long, complex and costly. In 2008 we submitted and the FDA accepted our NDA filing for Gencaro for the treatment of chronic HF. In 2009 the FDA issued a CRL in which the FDA stated that it could not approve the Gencaro NDA in its current form, and specified actions required for approval of the NDA, including conducting an additional Phase 3 clinical trial of Gencaro in patients with HF. In 2010 we reached agreement with the FDA, through the SPA process, on the design of a clinical trial to assess the safety and efficacy of Gencaro in approximately 3,200 patients with chronic HF who have the genotype that appears to respond most favorably to Gencaro. We plan to conduct a clinical study of Gencaro in approximately 200-400 HF patients with AF. Clinical trials are typically lengthy, complex and expensive and we do not currently have the resources to fund such a trial.

Failure to demonstrate that a product candidate, particularly Gencaro, is safe and effective, or significant delays in demonstrating such safety and efficacy, would adversely affect our business. Failure to obtain marketing approval of Gencaro from appropriate regulatory authorities, or significant delays in obtaining such approval, would also adversely affect our business and could, among other things, preclude us from completing a strategic transaction or obtaining additional financing necessary to continue as a going concern.

Even if approved for sale, a product candidate must be successfully commercialized to generate value. We do not currently have the capital resources or management expertise to commercialize Gencaro and, as a result, will need to complete a strategic transaction, or, alternatively, raise substantial additional funds to enable commercialization of Gencaro, if it is approved. Failure to successfully provide for the commercialization of Gencaro, if it is approved, would damage our business.

Table of Contents

Our clinical trials for our product candidates may not yield results that will enable us to further develop our products and obtain the regulatory approvals necessary to sell them.

We will only receive regulatory approval for our product candidates if we can demonstrate in carefully designed and conducted clinical trials that the product candidate is safe and effective. We do not know whether any future clinical trials, including the planned AF clinical trial for Gencaro, will demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products. Clinical trials are lengthy, complex and expensive processes with uncertain results. We have spent, and expect to continue to spend, significant amounts of time and money in the clinical development of our product candidates. We have never conducted a Phase 2 or Phase 3 clinical trial and do not currently have sufficient staff with the requisite experience to do so, and we therefore expect that we will have to rely on contract research organizations to conduct certain of our clinical trials. While certain of our employees have experience in designing and administering clinical trials, these employees have no such experience since being with us.

The results we obtain in preclinical testing and early clinical trials may not be predictive of results that are obtained in later studies. We may suffer significant setbacks in advanced clinical trials, even after seeing promising results in earlier studies. Based on results at any stage of clinical trials, we may decide to repeat or redesign a trial or discontinue development of one or more of our product candidates. If we fail to adequately demonstrate the safety and efficacy of our products under development, we will not be able to obtain the required regulatory approvals to commercialize our product candidates, and our business, results of operations and financial condition would be materially adversely affected.

Administering our product candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our product candidates and could result in the FDA or other regulatory authorities denying approval of our product candidates for any or all targeted indications.

If clinical trials for a product candidate are unsuccessful, we will be unable to commercialize the product candidate. If one or more of our clinical trials are delayed, we will be unable to meet our anticipated development timelines. Either circumstance could cause the market price of our common stock to decline.

We expect to rely on contract research organizations to conduct clinical trials, and as a result, will be unable to directly control the timing, conduct and expense of clinical trials.

We expect that we, or any strategic partners, will rely primarily on third parties to conduct clinical trials, including the Gencaro AF clinical trial that we plan to conduct. As a result, we will have less control over the conduct of the clinical trials, the timing and completion of the trials, the required reporting of adverse events and the management of data developed through the trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct our trials. We may experience unexpected cost increases that are beyond our control. Problems with the timeliness or quality of the work of a contract research organization may lead us or any strategic partner to seek to terminate the relationship and use an alternative service provider. However, making this change may be costly and may delay ongoing trials, and contractual restrictions may make such a change difficult or impossible. Additionally, it may be impossible to find a replacement organization that can conduct clinical trials in an acceptable manner and at an acceptable cost.

Even if we do use a contract research organization to conduct clinical trials, we will have to devote substantial resources and rely on the expertise of our employees to manage the work being done by the contract research organization. We have never conducted a clinical trial and do not currently have sufficient staff with the requisite experience to do so. The inability of our current staff to adequately manage any contract research organization that we hire may exacerbate the risks associated with relying on a contract research organization.

If we encounter difficulties enrolling patients in our clinical trials, our trials could be delayed or otherwise adversely affected.

Clinical trials for our product candidates require that we identify and enroll a large number of patients with the disorder or condition under investigation. We may not be able to enroll a sufficient number of patients to complete our clinical trials in a timely manner.

Patient enrollment is affected by factors including:

design of the protocol;

the size of the patient population;

eligibility criteria for the study in question;

perceived risks and benefits of the drug under study;

availability of competing therapies, including the off-label use of therapies approved for related indications;

efforts to facilitate timely enrollment in clinical trials;

S-7

Table of Contents

the success of our personnel in making the arrangements with potential clinical trial sites necessary for those sites to begin enrolling patients;

patient referral practices of physicians;

availability of clinical trial sites; and

other clinical trials seeking to enroll subjects with similar profiles.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have a negative effect on our business. Delays in enrolling patients in our clinical trials would also adversely affect our ability to generate any product, milestone and royalty revenues under collaboration agreements, if any, and could impose significant additional costs on us or on any future collaborators.

Our planned AF clinical trial will require the use of a third-party diagnostic services provider to administer the genetic test needed to identify the patient receptor genotypes of clinical trial participants. We do not currently have a third-party diagnostic services provider identified to perform this work for our planned AF clinical trial. If we have difficulty getting an arrangement for administering the Gencaro Test, the launch of our planned AF clinical trial could be delayed.

The planned AF clinical trial we intend to conduct with Gencaro requires a companion test that identifies the patient's receptor genotype, or Gencaro Test, and the trial will only enroll those patients with the receptor that has the potential for enhanced efficacy, the $\beta 1$ 389 Arg/Arg receptor. Accordingly, the planned AF clinical trial will require use of a third-party diagnostic service to perform the Gencaro Test. Previously we entered into a collaboration arrangement with LabCorp to develop and commercialize the Gencaro Test for the treatment of patients with HF. Under the terms of that collaboration, we licensed to LabCorp certain rights to commercialize a receptor genotype diagnostic for the $\beta 1$ and $\alpha 2C$ polymorphisms. We currently intend to pursue a separate arrangement with LabCorp or another third party to provide the diagnostic services of the Gencaro Test needed to support our planned AF trial.

Obtaining an arrangement with a third party for developing or administering the Gencaro Test for the AF clinical trial could delay the launch of our planned study.

Unless we are able to generate sufficient product revenue, we will continue to incur losses from operations and may not achieve or maintain profitability. We are years away from commercializing a product and generating product revenue.

We set goals for, and make public statements regarding, the timing of certain accomplishments, such as commencement and completion of clinical trials, the disclosure of trial results, the obtainment of regulatory approval and the sale of drug product, which we sometimes refer to as milestones. These milestones may not be achieved, and the actual timing of these events can vary dramatically due to a number of factors such as delays or failures in our clinical trials, disagreements with current or future collaborative partners, the uncertainties inherent in the regulatory approval process and manufacturing scale-up and delays in achieving manufacturing or marketing arrangements sufficient to commercialize our products. FDA approval of Gencaro, if it occurs, is expected to require years of additional clinical development, including the completion of a new multi-year active comparator superiority trial involving approximately 200-400 patients in a genotype-defined HF population with AF and additional clinical trials. There can be no assurance that our clinical trials will be completed, or that we will make regulatory submissions or receive regulatory approvals as planned. If we fail to achieve one or more of these milestones as planned, our business will be materially adversely affected.

We may not achieve our projected development goals in the time frames we announce and expect.

We set goals for, and make public statements regarding, the timing of certain accomplishments, such as the submission of responses to the CRL, the commencement and completion of clinical trials, the disclosure of trial results, the obtainment of regulatory approval and the sale of drug product, which we sometimes refer to as milestones. These milestones may not be achieved, and the actual timing of these events can vary dramatically due to a number of factors such as delays or failures in our clinical trials, disagreements with current or future collaborative partners, the uncertainties inherent in the regulatory approval process and manufacturing scale-up and delays in achieving manufacturing or marketing arrangements sufficient to commercialize our products. FDA approval of Gencaro, if it occurs, is expected to require years of additional clinical development, including the completion of a new multi-year active comparator superiority trial involving approximately 3,200 patients in a genotype-defined heart failure population pursuant to the SPA agreed to by us and the FDA. There can be no assurance that our

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

clinical trials will be completed, or that we will make regulatory submissions or receive regulatory approvals as planned. If we fail to achieve one or more of these milestones as planned, our business will be materially adversely affected.

S-8

Table of Contents

Our product candidates are subject to extensive regulation, which can be costly and time-consuming, and unsuccessful or delayed regulatory approvals could increase our future development costs or impair our future revenue.

The preclinical and clinical development, testing, manufacture, safety, efficacy, labeling, storage, recordkeeping, and subsequent advertising, promotion, sale, marketing, and distribution, if approved, of our product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States and elsewhere. These regulations also vary in important, meaningful ways from country to country. We are not permitted to market a potential drug in the United States until we receive approval of an NDA from the FDA. We have not received an NDA approval from the FDA for Gencaro or any of our other product candidates. There can be no guarantees with respect to our product candidates that clinical studies will adequately support an NDA, that the products will receive necessary regulatory approvals, or that they will prove to be commercially successful.

To receive regulatory approval for the commercial sale of any product candidates, we must demonstrate safety and efficacy in humans to the satisfaction of regulatory authorities through preclinical studies and adequate and well-controlled clinical trials of the product candidates. This process is expensive and can take many years, and failure can occur at any stage of the testing. Our failure to adequately demonstrate the safety and efficacy of our product candidates will prevent regulatory approval and commercialization of such products. In 2008 we submitted and the FDA accepted our NDA filing for Gencaro for the treatment of chronic HF. In 2009 the FDA issued a CRL in which the FDA stated that it could not approve the Gencaro NDA in its current form, and specified actions required for approval of the NDA, including conducting an additional Phase 3 clinical trial of Gencaro in patients with HF. In 2010 we reached agreement with the FDA, through the SPA process, on the design of a clinical trial to assess the safety and efficacy of Gencaro in approximately 3,200 patients with chronic HF who have the genotype that appears to respond most favorably to Gencaro. We are planning to conduct a clinical study of Gencaro in approximately 200-400 HF patients with AF. This product candidate will require years of clinical development. Even if we conduct additional studies in accordance with further FDA guidance and submit or file a new or amended NDA, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

In the event that we or our collaborators conduct preclinical studies that do not comply with Good Laboratory Practices or GLP or incorrectly design or carry out human clinical trials in accordance with Good Clinical Practices or GCP or those clinical trials fail to demonstrate clinical significance, it is unlikely that we will be able to obtain FDA approval for product development candidates. Our inability to successfully and effectively complete clinical trials for any product candidate on schedule, or at all, will severely harm our business. Significant delays in clinical development could materially increase product development costs or allow our competitors to bring products to market before we do, impairing our ability to effectively commercialize any future product candidate. We do not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including:

delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;

delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidates for use in trials;

delays or failures in reaching agreement on acceptable terms with prospective study sites;

delays or failures in obtaining approval of our clinical trial protocol from an institutional review board, or IRB, to conduct a clinical trial at a prospective study site;

delays in recruiting patients to participate in a clinical trial, which may be due to the size of the patient population, eligibility criteria, protocol design, perceived risks and benefits of the drug, availability of other approved and standard of care therapies, availability of clinical trial sites;

other clinical trials seeking to enroll subjects with similar profile;

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

failure of our clinical trials and clinical investigators to be in compliance with the FDA's Good Clinical Practices;

unforeseen safety issues, including negative results from ongoing preclinical studies;

inability to monitor patients adequately during or after treatment;

difficulty monitoring multiple study sites; and

failure of our third-party contract research organizations, clinical site organizations and other clinical trial managers, to satisfy their contractual duties, comply with regulations or meet expected deadlines.

S-9

Table of Contents

In addition, any approvals we may obtain may not cover all of the clinical indications for which we seek approval or permit us to make claims of superiority over currently marketed competitive products. Also, an approval might contain significant limitations in the form of narrow indications, warnings, precautions or contraindications with respect to conditions of use. If the FDA determines that a risk evaluation and mitigation strategy, or REMS, is necessary to ensure that the benefits of the drug outweigh the risks, we may be required to include as part of the NDA a proposed REMS that may include a package insert directed to patients, a plan for communication with healthcare providers, restrictions on a drug's distribution, or a Medication Guide, to provide better information to consumers about the drug's risks and benefits. Finally, an approval could be conditioned on our commitment to conduct further clinical trials, which we may not have the resources to conduct or which may negatively impact our financial situation.

The manufacture and tableting of Gencaro is done by third party suppliers, who must also meet current Good Manufacturing Practices, or cGMP, requirements and pass a pre-approval inspection of their facilities before we can obtain marketing approval.

All of our product candidates are prone to the risks of failure inherent in drug development. The results from preclinical animal testing and early human clinical trials may not be predictive of results obtained in later human clinical trials. Further, although a new product may show promising results in preclinical or early human clinical trials, it may subsequently prove unfeasible or impossible to generate sufficient safety and efficacy data to obtain necessary regulatory approvals. The data obtained from preclinical and clinical studies are susceptible to varying interpretations that may delay, limit or prevent regulatory approval, and the FDA and other regulatory authorities in the United States and elsewhere exercise substantial discretion in the drug approval process. The numbers, size and design of preclinical studies and clinical trials that will be required for FDA or other regulatory approval will vary depending on the product candidate, the disease or condition for which the product candidate is intended to be used and the regulations and guidance documents applicable to any particular product candidate. The FDA or other regulators can delay, limit or deny approval of any product candidate for many reasons, including, but not limited to:

Side effects;

Safety and efficacy;

Defects in the design of clinical trials;

The fact that the FDA or other regulatory officials may not approve our or our third party manufacturer's processes or facilities; or

The fact that new regulations may be enacted by the FDA or other regulators may change their approval policies or adopt new regulations requiring new or different evidence of safety and efficacy for the intended use of a product candidate.

In light of widely publicized events concerning the safety of certain drug products, regulatory authorities, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of certain drug products, revisions to certain drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and approval. Data from clinical trials may receive greater scrutiny with respect to safety and the product's risk/benefit profile, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense, and a delay or failure in obtaining approval or approval for a more limited indication than originally sought. Aside from issues concerning the quality and sufficiency of submitted preclinical and clinical data, the FDA may be constrained by limited resources from reviewing and determining the approvability of the Gencaro NDA in a timely manner.

In pursuing clinical development of Gencaro for an AF indication, we would likely be required to amend the Gencaro HF NDA or prepare a new NDA. The FDA could approve Gencaro, but without including some or all of the prescribing information that we have requested. For instance, the FDA could approve Gencaro for AF in a more limited patient population or included additional warnings in the drug's label. This, in turn, could substantially and detrimentally impact our ability to successfully commercialize Gencaro and effectively protect our intellectual property rights in Gencaro.

If our product candidates receive regulatory approval, we would be subject to ongoing regulatory obligations and restrictions, which may result in significant expenses and limit our ability to develop and commercialize other potential products.

If a product candidate of ours is approved by the FDA or by another regulatory authority, we would be held to extensive regulatory requirements over product manufacturing, testing, distribution, labeling, packaging, adverse event reporting and other reporting to regulatory authorities, storage, advertising, marketing, promotion, distribution, and record keeping. Regulatory approvals may also be subject to significant limitations on the indicated uses or marketing of the product candidates. Potentially costly follow-up or post-marketing clinical studies may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority. Previously unknown problems with the product candidate, including adverse events of unanticipated severity or frequency, may result in additional regulatory controls or restrictions on the marketing or use of the product or the need for post marketing studies, and could include suspension or withdrawal of the products from the market.

S-10

Table of Contents

Furthermore, our third-party manufacturers and the manufacturing facilities that they use to make our product candidates are regulated by the FDA. Quality control and manufacturing procedures must continue to conform to cGMP after approval. Drug manufacturers and their subcontractors are required to register their facilities and products manufactured annually with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA, state and/or other foreign authorities. Any subsequent discovery of problems with a product, or a manufacturing or laboratory facility used by us or our collaborators, may result in restrictions on the product, or on the manufacturing or laboratory facility, including a withdrawal of the drug from the market or suspension of manufacturing. Any changes to an approved product, including the way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our third-party manufacturers will also be subject to ongoing FDA requirements for submission of safety and other post-market information.

The marketing and advertising of our drug products by our collaborators or us will be regulated by the FDA, certain state agencies or foreign regulatory authorities. Violations of these laws and regulations, including promotion of our products for unapproved uses or failing to disclose risk information, are punishable by criminal and civil sanctions and may result in the issuance of enforcement letters or other enforcement action by the FDA, U.S. Department of Justice, state agencies, or foreign regulatory authorities that could jeopardize our ability to market the product.

In addition to the FDA, state or foreign regulations, the marketing of our drug products by us or our collaborators will be regulated by federal, state or foreign laws pertaining to health care fraud and abuse, such as the federal anti-kickback law prohibiting bribes, kickbacks or other remuneration for the order or recommendation of items or services reimbursed by federal health care programs. Many states have similar laws applicable to items or services reimbursed by commercial insurers. Violations of these laws are punishable by criminal and civil sanctions, including, in some instances, imprisonment and exclusion from participation in federal and state health care programs, including the Medicare, Medicaid and Veterans Affairs healthcare programs. Because of the far-reaching nature of these laws, we may be required to discontinue one or more of our practices to be in compliance with these laws. Health care fraud and abuse regulations are complex, and even minor irregularities can potentially give rise to claims that a statute or prohibition has been violated. Any violations of these laws, or any action against us for violations of these laws, even if we successfully defend against it, could have a material adverse effect on our business, financial condition and results of operations.

We could also become subject to false claims litigation under federal statutes, which can lead to civil money penalties, restitution, criminal fines and imprisonment, and exclusion from participation in Medicare, Medicaid and other federal and state health care programs. These false claims statutes include the False Claims Act, which allows any person to bring a suit on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, under federal programs or contracts claims or other violations of the statute and to share in any amounts paid by the entity to the government in fines or settlement. These suits against pharmaceutical companies have increased significantly in volume and breadth in recent years. Some of these suits have been brought on the basis of certain sales practices promoting drug products for unapproved uses. This new growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay fines or restitution, or be excluded from the Medicare, Medicaid, Veterans Affairs and other federal and state healthcare programs as a result of an investigation arising out of such action. We may become subject to such litigation and, if we are not successful in defending against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations. We could also become subject to false claims litigation and consumer protection claims under state statutes, which also could lead to civil monetary penalties, restitution, criminal fines and imprisonment, and exclusion from participation in state health care programs.

Of note, over the past few years there has been an increased focus on the sales and marketing practices of the pharmaceutical industry at both the federal and state level. Additionally, the law or regulatory policies governing pharmaceuticals may change. New statutory requirements may be enacted or additional regulations may be adopted that could prevent or delay regulatory approval of our product candidates or limit our ability to commercialize our products. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the U.S. or elsewhere.

If we, our collaborators or our third-party manufacturers fail to comply with applicable continuing regulatory requirements, our business could be seriously harmed because a regulatory agency may:

issue untitled or warning letters;

suspend or withdraw our regulatory approval for approved products;

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

seize or detain products or recommend a product recall of a drug or medical device, or issue a mandatory recall of a medical device;

refuse to approve pending applications or supplements to approved applications filed by us;

suspend our ongoing clinical trials;

restrict our operations, including costly new manufacturing requirements, or restrict the sale, marketing and/or distribution of our products;

S-11

Table of Contents

seek an injunction;

pursue criminal prosecutions;

close the facilities of our contract manufacturers; or

impose civil or criminal penalties.

We will need to establish a collaborative arrangement with a third-party diagnostics services provider to obtain marketing clearance or approval of the companion Gencaro Test. There is no guarantee that the FDA will grant timely clearance or approval of the Gencaro Test, if at all, and failure to obtain such timely clearance or approval would adversely affect our ability to market Gencaro.

The drug label we intend to seek for Gencaro would identify the patient receptor genotype for which the drug is approved. Accordingly, we believe developing a Gencaro Test that is simple to administer and widely available will be critical to the successful commercialization of Gencaro and also to the ability to conduct our planned AF clinical trial.

The Gencaro Test will be subject to regulation by the FDA and by comparable agencies in various foreign countries. The process of complying with the requirements of the FDA and comparable agencies is costly, time consuming and burdensome.

Despite the time and expense expended, regulatory clearance or approval is never guaranteed. If regulatory clearance or approval is delayed, or if a third-party diagnostic services provider is unable to obtain FDA approval of the Gencaro Test at all or in parallel with the approval of Gencaro, or is unable to commercialize the test successfully and in a manner that effectively supports the commercial efforts for Gencaro, or if the information concerning the differential response to Gencaro resulting from certain genetic variation is not included in the approval label for Gencaro, our planned AF clinical trial and the commercial launch of Gencaro may be significantly and adversely affected.

Reliance on third parties to commercialize Gencaro could negatively impact our business. If we are required to establish a direct sales force in the U.S. and are unable to do so, our business may be harmed.

Commercialization of Gencaro, particularly the establishment of a sales organization, will require substantial additional capital resources. We currently intend to pursue a strategic partnership alternative for the commercialization of Gencaro, if it is approved, and we have suspended our efforts to build internal sales, marketing and distribution capabilities. If we elect to rely on third parties to sell Gencaro and any other products, then we may receive less revenue than if we sold such products directly. In addition, we may have little or no control over the sales efforts of those third parties.

If we are unable to complete a strategic transaction, we would be unable to commercialize Gencaro or any other product candidate without substantial additional capital. Even if such capital were secured, we would be required to build internal sales, marketing and distribution capabilities to market Gencaro in the U.S. None of our current employees have experience in establishing and managing a sales force.

In the event we are unable to sell Gencaro and other selected product candidates, either directly or through third parties via a strategic transaction, the commercialization of Gencaro, if it is approved, may be delayed indefinitely.

Future sales of Gencaro may suffer if its marketplace acceptance is negatively affected by the Gencaro Test.

The Gencaro Test is an important component of the commercial strategy for Gencaro in addition to being required to proceed with our planned AF trial. We believe that the Gencaro Test helps predict patient response to Gencaro, and that this aspect of the drug is important to its ability to compete effectively with current therapies. The Gencaro Test adds an additional step in the prescribing process, an additional cost for the patient and payors, the risk that the test results may not be rapidly available and the possibility that it may not be available at all to hospitals and medical centers. Although we anticipate that Gencaro, if approved in a timely manner, would be the first genetically-targeted cardiovascular drug, Gencaro will be one of a number of successful drugs in the beta-blocker class currently on the market. Prescribers may be more familiar with these other beta-blockers, and may be resistant to prescribing Gencaro as an AF or HF therapy. Any one of these factors could affect prescriber behavior, which in turn may substantially impede market acceptance of the Gencaro Test, which could cause significant harm to Gencaro's ability to compete, and in turn harm our business.

We are dependent on our key personnel.

The success of our business is highly dependent on the principal members of our board of directors and executive management, including our Chairman of the Board, Richard B. Brewer, and our President and Chief Executive Officer, Michael R. Bristow. The loss of the services of any such individual might seriously harm our product development, partnering and financing efforts. Recruiting and training personnel with the requisite skills is challenging and we compete for talent with companies that are larger and have more financial resources.

S-12

Table of Contents

Our workforce furlough in July, 2012 and any future workforce and expense reductions may have an adverse impact on our internal programs and may divert management attention.

In July, 2012, we placed five full time equivalent and two part time employees on furlough (out of a total of 11 full-time equivalent and 2 part-time employees we employed prior to the furlough) in order to preserve our capital resources and to manage our operating expenses. This reduction in force may limit our ability to complete all of our corporate objectives. We may be required to implement further workforce and expense reductions in the future. Further workforce and expense reductions could result in reduced progress on our internal programs. In addition, employees, whether or not directly affected by a reduction, may seek future employment with our business partners or competitors. Although our employees are required to sign a confidentiality agreement at the time of hire, the confidential nature of certain proprietary information may not be maintained in the course of any such future employment. In addition, the implementation of expense reduction programs may result in the diversion of efforts of our executive management team and other key employees, which could adversely affect our business.

We have no manufacturing capacity which puts us at risk of lengthy and costly delays of bringing our products to market.

We do not currently operate manufacturing facilities for clinical or commercial production of our product candidates, including their active pharmaceutical ingredients, or API. We have no experience in drug formulation or manufacturing, and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We do not intend to develop facilities for the manufacture of product candidates for clinical trials or commercial purposes in the foreseeable future.

We have contracted with Groupe Novasep to manufacture commercial quantities of the API for Gencaro. For drug production, we have contracted with Patheon, Inc. to manufacture the Gencaro tablets. These contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our products. In addition, these manufacturers may have staffing difficulties, may not be able to manufacture our products on a timely basis or may become financially distressed. In the event of errors in forecasting production quantities required to meet demand, natural disaster, equipment malfunctions or failures, technology malfunctions, strikes, lock-outs or work stoppages, regional power outages, product tampering, war or terrorist activities, actions of regulatory authorities, business failure, strike or other difficulty, we may be unable to find an alternative third-party manufacturer in a timely manner and the production of our product candidates would be interrupted, resulting in delays and additional costs, which could impact our ability to commercialize and sell our product candidates.

We or our contract manufacturers may also fail to achieve and maintain required manufacturing standards, which could result in patient injury or death, product recalls or withdrawals, an order by governmental authorities to halt production, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business. Contract manufacturers also often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. In addition, our contract manufacturers are subject to ongoing inspections and regulation by the FDA, the U.S. Drug Enforcement Agency and corresponding foreign and state agencies and they may fail to meet these agencies' acceptable standards of compliance. If our contract manufacturers fail to comply with applicable governmental regulations, such as quality control, quality assurance and the maintenance of records and documentation, we may not be able to continue production of the API or finished product. If the safety of any API or product supplied is compromised due to failure to adhere to applicable law or for other reasons, this may jeopardize our regulatory approval for Gencaro and other product candidates, and we may be held liable for any injuries sustained as a result.

Upon the occurrence of one of the aforementioned events, the ability to switch manufacturers may be difficult for a number of reasons, including:

the number of potential manufacturers is limited and we may not be able to negotiate agreements with alternative manufacturers on commercially reasonable terms, if at all;

long lead times are often needed to manufacture drugs;

the manufacturing process is complex and may require a significant learning curve; and

the FDA must approve any replacement prior to manufacturing, which requires new testing and compliance inspections.

If a third-party diagnostics provider responsible for the Gencaro Test or certain of its third-party suppliers fail to comply with ongoing FDA or other foreign regulatory authority requirements, or if there are unanticipated problems with the Gencaro Test, these products could be subject to restrictions or withdrawal from use in trial or from the market.

Any medical device for which a third-party diagnostics provider obtains clearance or approval, and the manufacturing processes, reporting requirements, post-approval clinical data and promotional activities for such product, will be subject to continued regulatory review, oversight and periodic inspections by the FDA and other domestic and foreign regulatory bodies. With respect to the Gencaro Test, to the extent applicable, any third-party diagnostics provider and certain of its suppliers will be required to comply with the FDA's Quality System Regulation, or QSR, and International Standards Organization, or ISO, requirements which cover the methods and documentation of the design, testing, production, control, quality assurance, labeling, packaging, storage and shipping of any product for which clearance or approval is obtained. Regulatory bodies, such as the FDA, enforce the QSR and other regulations through periodic inspections. The failure by a third-party diagnostics provider, or certain of its third-party manufacturers or suppliers, as the case may be, to comply with applicable statutes and regulations administered by the FDA and other regulatory bodies, or the failure to timely and adequately respond to any adverse inspectional observations or product safety issues, could result in, among other things, enforcement actions. If any of these actions were to occur, it could harm our reputation and cause product sales and profitability of Gencaro to suffer and may prevent us from generating revenue or utilizing the Gencaro Test further in any clinical trial.

Table of Contents

Even if regulatory clearance or approval is granted, such clearance or approval may be subject to limitations on the intended uses for which the product may be marketed and reduce our potential to successfully commercialize the product and generate revenue from the product.

A third-party diagnostics provider may need to conduct clinical trials to support current or future versions of the Gencaro Test. Delays or failures in any such clinical trials may prevent a third-party diagnostics provider from commercializing any modified or new versions of the Gencaro Test and will adversely affect our business, operating results and prospects.

Based on discussions with the FDA, we do not believe that additional clinical data are needed for the Gencaro Test submission. However, the FDA may require clinical data for the Gencaro Test submission and/or future products. Initiating and completing clinical trials necessary to support 510(k)s or PMAs, if required, for current or future products will be time consuming and expensive and the outcome uncertain. Moreover, the results of early clinical trials are not necessarily predictive of future results, and any product we or our third party suppliers advance into clinical trials may not have favorable results in later clinical trials.

Conducting successful clinical studies may require the enrollment of large numbers of patients, and suitable patients may be difficult to identify and recruit. Patient enrollment in clinical trials and completion of patient participation and follow-up depends on many factors, including: the size of the patient population; the number of patients to be enrolled; the nature of the trial protocol; the attractiveness of, or the discomforts and risks associated with, the treatments received by enrolled subjects; the availability of appropriate clinical trial investigators, support staff, and proximity of patients to clinical sites; and the patients' ability to meet the eligibility and exclusion criteria for participation in the clinical trial and patient compliance. For example, patients may be discouraged from enrolling in clinical trials if the trial protocol requires them to undergo extensive post-treatment procedures or follow-up to assess the safety and effectiveness of our products or if they determine that the treatments received under the trial protocol are not attractive or involve unacceptable risks or discomforts. In addition, patients participating in clinical trials may die before completion of the trial or suffer adverse medical events unrelated to investigational products.

Development of sufficient and appropriate clinical protocols to demonstrate safety and efficacy are required, and we or the third-party diagnostics provider may not adequately develop such protocols to support clearance and approval. The trials will require the submission and approval of an investigational device exemption, or IDE, from the FDA. There is no guarantee that the FDA will approve the third-party diagnostics provider's or our future IDE submissions. Further, the FDA may require them or us to submit data on a greater number of patients than originally anticipated and/or for a longer follow-up period or change the data collection requirements or data analysis applicable to our clinical trials. Delays in patient enrollment or failure of patients to continue to participate in a clinical trial may cause an increase in costs and delays in the approval and attempted commercialization of future products or result in the failure of the clinical trial. In addition, despite considerable time and expense invested in such clinical trials, the FDA may not consider the data to be adequate to demonstrate safety and efficacy. Such increased costs and delays or failures could adversely affect our or our third party suppliers' business, operating results and prospects.

Transitioning from a developmental stage company will require successful completion of a number of steps, many of which are outside of our control and, consequently, we can provide no assurance of our successful and timely transition from a developmental stage company.

We are a development stage biopharmaceutical company with a limited operating history. To date we have not generated any product revenue and have historically funded our operations through investment capital. Our future growth depends on our ability to emerge from the developmental stage and successfully commercialize or provide for the commercialization of Gencaro and our other product candidates, which in turn, will depend, among other things, on our ability to:

conduct an additional clinical trial and develop and obtain regulatory approval for Gencaro or other product candidates;

successfully partner a companion genetic test with the commercial launch of Gencaro;

enter into a strategic transaction enabling the continued development and commercialization of Gencaro, or alternatively, raise significant additional capital to enable these activities;

pursue additional indications for Gencaro and develop other product candidates, including other cardiovascular therapies; and

obtain commercial quantities of Gencaro or other product candidates at acceptable cost levels. Any one of these factors or other factors discussed in this report could affect our ability to successfully commercialize Gencaro and other product candidates, which could impact our ability to earn sufficient revenues to transition from a developmental stage company and continue our business.

S-14

Table of Contents

If approved by the FDA, Gencaro will be entering a competitive marketplace and may not succeed.

Gencaro is a new type of beta-blocker and vasodilator being developed for AF. While we anticipate that this drug, if approved, would be the first genetically-targeted cardiovascular drug, and potentially the only beta-blocker approved for AF, Gencaro will be one of a number of successful drugs in the beta-blocker class currently on the market. For example, currently, there are three branded beta-blockers indicated for chronic HF in New York Health Association, or NYHA, class II-IV patients: Toprol-XL (once-a-day formulation), Coreg and Coreg CR (once-a-day). Toprol-XL and Coreg have generic equivalents commercially available in the U.S. (metoprolol succinate and carvedilol, respectively). The price of the generic forms of these drugs will be less than the anticipated price of Gencaro, if approved. As a result, Gencaro may not be successful in competing against these existing drugs.

Our commercial opportunity may be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient or are less expensive than Gencaro. If products with any of these properties are developed, or any of the existing products are better marketed, then prescriptions of Gencaro by physicians and patient use of Gencaro could be significantly reduced or rendered obsolete and noncompetitive. Further, public announcements regarding the development of any such competing drugs could adversely affect the market price of our common stock and the value of our assets.

Future sales of our products may suffer if they are not accepted in the marketplace by physicians, patients and the medical community.

Gencaro or our other product candidates may not gain market acceptance among physicians, patients and the medical community. The degree of market acceptance of Gencaro or our other product candidates will depend on a number of factors, such as its effectiveness and tolerability, as compared with competitive drugs. Also, prevalence and severity of side-effects could negatively affect market acceptance of Gencaro or our other product candidates. Failure to achieve market acceptance of Gencaro would significantly harm our business.

If we are unable to obtain acceptable prices or adequate reimbursement from third-party payors for Gencaro, or any other product candidates that we may seek to commercialize, then our revenues and prospects for profitability will suffer.

Our or any strategic partner's ability to commercialize Gencaro, or any other product candidates that we may seek to commercialize, is highly dependent on the extent to which coverage and reimbursement for these product candidates will be available from:

governmental payors, such as Medicare and Medicaid;

private health insurers, including managed-care organizations; and

other third-party payors.

Many patients will not be capable of paying for our potential products themselves and will rely on third-party payors to pay for their medical needs. A primary current trend in the U.S. health care industry is toward cost containment. Large private payors, managed-care organizations, group purchasing organizations and similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products.

Cost-control initiatives could decrease the price we might establish for products, which could result in product revenues lower than anticipated. If the prices for our product candidates decrease, or if governmental and other third-party payors do not provide adequate coverage and reimbursement levels, then our revenue and prospects for profitability will suffer.

Health care reform measures could materially and adversely affect our business.

The business and financial condition of pharmaceutical and biotechnology companies are affected by the efforts of governmental and third-party payors to contain or reduce the costs of health care. The U.S. Congress has enacted legislation to reform the health care system. While we anticipate that this legislation may, over time, increase the number of patients who have insurance coverage for pharmaceutical products, it also imposes cost containment measures that may adversely affect the amount of reimbursement for pharmaceutical products. These measures include increasing the minimum rebates for products covered by Medicaid programs and extending such rebates to drugs dispensed to Medicaid

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

beneficiaries enrolled in Medicaid managed care organizations as well as expansion of the 340(B) Public Health Services drug discount program. In addition, such legislation contains a number of provisions designed to generate the revenues necessary to fund the coverage expansion, including new fees or taxes on certain health-related industries, including medical device manufacturers. Beginning in 2013, each medical device manufacturer will have to pay an excise tax (or sales tax) in an amount equal to 2.3% of the price for which such manufacturer sells its medical devices. Such excise taxes may impact any potential sales of the Gencaro Test if it is approved for marketing. In foreign jurisdictions there have been, and we expect that there will continue to be, a number of legislative and regulatory proposals aimed at changing the health care system. For example, in some countries other than the United States, pricing of prescription drugs is subject to government control and we expect to see continued efforts to reduce healthcare costs in international markets.

S-15

Table of Contents

Some states are also considering legislation that would control the prices of drugs, and state Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Managed care organizations continue to seek price discounts and, in some cases, to impose restrictions on the coverage of particular drugs. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding constraint on prices and reimbursement for drugs. It is likely that federal and state legislatures and health agencies will continue to focus on additional health care reform in the future although we are unable to predict what additional legislation or regulation, if any, relating to the health care industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation or regulation would have on our business. We or any strategic partner's ability to commercialize Gencaro, or any other product candidates that we may seek to commercialize, is highly dependent on the extent to which coverage and reimbursement for these product candidates will be available from government payors, such as Medicare and Medicaid, private health insurers, including managed care organizations, and other third-party payors, and any change in reimbursement levels could materially and adversely affect our business. Further, the pendency or approval of future proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to obtain strategic partnerships or licenses.

Our competitors may be better positioned in the marketplace and thereby may be more successful than us at developing, manufacturing and marketing approved products.

Many of our competitors currently have significantly greater financial resources and expertise in conducting clinical trials, obtaining regulatory approvals, managing manufacturing and marketing approved products than us. Other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. In addition, these third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring therapies and therapy licenses complementary to our programs or advantageous to our business. We expect that our ability to compete effectively will depend upon our ability to:

successfully and rapidly complete clinical trials for any product candidates and obtain all requisite regulatory approvals in a cost-effective manner;

build an adequate sales and marketing infrastructure, raise additional funding, or enter into strategic transactions enabling the commercialization of our products;

develop competitive formulations of our product candidates;

attract and retain key personnel; and

identify and obtain other product candidates on commercially reasonable terms.

If we fail to identify and license or acquire other products or product candidates, then we may be unable to expand our business, and the acquisition or licensing of other products or product candidates may put a strain on our operations and will likely require us to seek additional financing.

One of our strategies is to license or acquire clinical-stage products or product candidates and further develop them for commercialization. The market for licensing and acquiring products and product candidates is intensely competitive and many of our competitors may have greater resources than us. If we undertake any additional acquisitions, whether of product candidates or other biopharmaceutical companies, the process of integrating an acquired product candidate or complementary company into our business may put a strain on our operations, divert personnel, financial resources and management's attention. In 2012, we expect our research and development activities will be dedicated to Gencaro. If we are not able to substantially expand our research and development efforts, or identify, or license or acquire other products or product candidates or complete future acquisitions, then we will likely be unable to expand our pipeline of product candidates. In addition, any future acquisition would give rise to additional operating costs and will likely require us to seek additional financing. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating

results.

We would be subject to applicable regulatory approval requirements of the foreign countries in which we market our products, which are costly and may prevent or delay us from marketing our products in those countries.

In addition to regulatory requirements in the United States, we would be subject to the regulatory approval requirements in each foreign country where we market our products. In addition, we might be required to identify one or more collaborators in these foreign countries to develop, seek approval for and manufacture our products and any companion genetic test for Gencaro. If we decide to pursue regulatory approvals and commercialization of our product candidates internationally, we may not be able to obtain the required foreign regulatory approvals on a timely basis, if at all, and any failure to do so may cause us to incur additional costs or prevent us from marketing our products in foreign countries, which may have a material adverse effect on our business, financial condition and results of operations.

S-16

Table of Contents

If our internal control over financial reporting is not considered effective, our business and stock price could be adversely affected.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us to evaluate the effectiveness of our internal control over financial reporting as of the end of each fiscal year, and to include a management report assessing the effectiveness of our internal control over financial reporting in our annual report on Form 10-K for that fiscal year. Our management, including our chief executive officer and chief financial officer, does not expect that our internal control over financial reporting will prevent all error and all fraud. During the first quarter of 2011 there was a reduction in our workforce which included personnel involved in financial reporting and our internal control processes. Though the process and design of our internal controls over financial reporting have not been altered, the reduction in staff may have limited our ability to properly segregate internal control procedures which could result in deficiencies or material weaknesses in our internal controls in the future. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud involving a company have been, or will be, detected. The design of any system of controls is based in part on certain assumptions about the likelihood of future events, and we cannot assure you that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become ineffective because of changes in conditions or deterioration in the degree of compliance with policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected. We cannot assure you that we or our independent registered public accounting firm will not identify a material weakness in our internal control over financial reporting in the future. A material weakness in our internal control over financial reporting would require management to consider our internal control over financial reporting as ineffective. If our internal control over financial reporting is not considered effective, we may experience a loss of public confidence, which could have an adverse effect on our business and on the market price of our common stock.

Risks Related to Intellectual Property and Other Legal Matters

If product liability lawsuits are successfully brought against us, then we will incur substantial liabilities and may be required to limit commercialization of Gencaro or other product candidates.

We face product liability exposure related to the testing of our product candidates in human clinical trials, and may face exposure to claims by an even greater number of persons once we begin marketing and distributing our products commercially. If we cannot successfully defend against product liability claims, then we will incur substantial liabilities.

Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for our products and product candidates;

injury to our reputation;

withdrawal of clinical trial participants;

costs of related litigation;

substantial monetary awards to patients and others;

loss of revenues; and

the inability to commercialize our products and product candidates.

We have obtained limited product liability insurance coverage. Such coverage, however, may not be adequate or may not continue to be available to us in sufficient amounts or at an acceptable cost, or at all. We may not be able to obtain commercially reasonable product liability insurance for any product candidate.

Defending against claims relating to improper handling, storage or disposal of hazardous chemicals, radioactive or biological materials could be time consuming and expensive.

Our research and development of product candidates may involve the controlled use of hazardous materials, including chemicals, radioactive and biological materials. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from the materials. Various laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued or be required to pay fines for any injury or contamination that results from our use or the use by third parties of these materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

The loss of any rights to market key products would significantly impair our operating results.

We have licensed from CPEC, who has licensed rights in Gencaro from Bristol Meyers Squibb (BMS), the exclusive rights to Gencaro for all therapeutic and diagnostic uses in any country until the later of (i) 10 years from the first commercial sale of Gencaro in such country, or (ii) the termination of our commercial exclusivity in such country. This license includes a sublicense to us from BMS. We are obligated to use commercially reasonable efforts to develop and commercialize Gencaro, including obtaining regulatory approvals. Our ability to develop and commercialize Gencaro is dependent on numerous factors, including some factors that are outside of our control. CPEC has the right to terminate our license if we materially breach our obligations under the license agreement and fail to cure any such breach within the terms of the license.

Table of Contents

If our license agreement with CPEC is terminated for reasons related to non-payment of fees, or for any other breach, then we would have no further rights to develop and commercialize Gencaro for any indication. The termination of this license, or of any other agreement which enables us to market a key product or product candidate, could significantly and adversely affect our business.

Certain intellectual property licensed by us is the subject of additional licensing arrangements to which the party that has licensed rights to us is subject. If such parties were to breach the terms of such licenses or such licenses were otherwise to terminate, our and our partners' rights to use such technology and develop and commercialize their products such as the Gencaro Test may terminate and our business would be materially harmed.

Third parties may own or control patents or patent applications that we may be required to license to commercialize our product candidates or that could result in litigation that would be costly and time consuming.

Our or any strategic partner's ability to commercialize Gencaro and other product candidates depends upon our ability to develop, manufacture, market and sell these drugs without infringing the proprietary rights of third parties. A number of pharmaceutical and biotechnology companies, universities and research institutions have or may be granted patents that cover technologies similar to the technologies owned by or licensed to us. We may choose to seek, or be required to seek, licenses under third party patents, which would likely require the payment of license fees or royalties or both. We may also be unaware of existing patents that may be infringed by Gencaro, the genetic testing we intend to use in connection with Gencaro or our other product candidates. Because patent applications can take many years to issue, there may be other currently pending applications that may later result in issued patents that are infringed by Gencaro or our other product candidates. Moreover, a license may not be available to us on commercially reasonable terms, or at all.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we are infringing on its technology, then our business and results of operations could be harmed by a number of factors, including:

infringement and other intellectual property claims, even if without merit, are expensive and time-consuming to litigate and can divert management's attention from our core business;

monetary damage awards for past infringement can be substantial;

a court may prohibit us from selling or licensing product candidates unless the patent holder chooses to license the patent to us; and

if a license is available from a patent holder, we may have to pay substantial royalties.

We may also be forced to bring an infringement action if we believe that a competitor is infringing our protected intellectual property. Any such litigation will be costly, time-consuming and divert management's attention, and the outcome of any such litigation may not be favorable to us.

Our intellectual property rights may not preclude competitors from developing competing products and our business may suffer.

Our competitive success will depend, in part, on our ability to obtain and maintain patent protection for our inventions, technologies and discoveries, including intellectual property that we license. The patent positions of biotechnology companies involve complex legal and factual questions, and we cannot be certain that our patents and licenses will successfully preclude others from using our technology. Consequently, we cannot be certain that any of our patents will provide significant market protection or will not be circumvented or challenged and found to be unenforceable or invalid. In some cases, patent applications in the U.S. and certain other jurisdictions are maintained in secrecy until patents issue, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention or in opposition proceedings in a foreign patent office, any of which could result in substantial cost to us, even if the eventual outcome is favorable. There can be no assurance that a court of competent jurisdiction would hold any claims in any issued patent to be valid. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using such technology. Regardless of merit, the listing of patents in the FDA Orange Book for Gencaro may be challenged as being improperly listed. We may have to defend against such claims and possible associated

antitrust issues. We could also incur substantial costs in seeking to enforce our proprietary rights against infringement.

While the composition of matter patents on the compound that comprises Gencaro have expired, we hold the intellectual property concerning the interaction of Gencaro with the polymorphisms of the $\beta 1$ and 2C receptors. We have obtained patents that claim methods involving Gencaro after a patient's receptor genotype has been determined. Our NDA requested a label that will include a claim that efficacy varies based on receptor genotype and a recommendation in the prescribing information that prospective patients be tested for their receptor genotype. We believe that under applicable law, a generic bucindolol label would likely be required to include this recommendation as it pertains directly to the safe or efficacious use of the drug. Such a label may be considered as inducing infringement, carrying the same liability as direct infringement. If the label with the genotype information for Gencaro is not approved, or if generic labels are not required to copy the approved label, competitors could have an easier path to introduce competing products and our business may suffer. The approved label may not contain language covered by the patents, or we may be unsuccessful in enforcing them.

Table of Contents

We may not be able to effectively protect our intellectual property rights in some foreign countries, as our patents are limited by jurisdiction and many countries do not offer the same level of legal protection for intellectual property as the U.S.

We require our employees, consultants, business partners and members of our scientific advisory board to execute confidentiality agreements upon the commencement of employment, consulting or business relationships with us. These agreements provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions resulting from work performed for us, utilizing the property or relating to our business and conceived or completed by the individual during employment shall be our exclusive property to the extent permitted by applicable law.

Third parties may breach these and other agreements with us regarding our intellectual property and we may not have adequate remedies for the breach. Third parties could also fail to take necessary steps to protect our licensed intellectual property, which could seriously harm our intellectual property position.

If we are not able to protect our proprietary technology, trade secrets and know-how, then our competitors may develop competing products. Any issued patent may not be sufficient to prevent others from competing with us. Further, we have trade secrets relating to Gencaro, and such trade secrets may become known or independently discovered. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, opposed, invalidated or circumvented, which could allow competitors to market similar products or limit the patent protection term of our product candidates. All of these factors may affect our competitive position.

If the manufacture, use or sale of our products infringe on the intellectual property rights of others, we could face costly litigation, which could cause us to pay substantial damages or licensing fees and limit our ability to sell some or all of our products.

Extensive litigation regarding patents and other intellectual property rights has been common in the biopharmaceutical industry. Litigation may be necessary to assert infringement claims, enforce patent rights, protect trade secrets or know-how and determine the enforceability, scope and validity of certain proprietary rights. Litigation may even be necessary to defend disputes of inventorship or ownership of proprietary rights. The defense and prosecution of intellectual property lawsuits, U.S. Patent and Trademark Office interference proceedings, and related legal and administrative proceedings (e.g., a reexamination) in the U.S. and internationally involve complex legal and factual questions. As a result, such proceedings are costly and time-consuming to pursue, and their outcome is uncertain.

Regardless of merit or outcome, our involvement in any litigation, interference or other administrative proceedings could cause us to incur substantial expense and could significantly divert the efforts of our technical and management personnel. Any public announcements related to litigation or interference proceedings initiated or threatened against us could cause our stock price to decline. Adverse outcomes in patent litigation may potentially subject us to antitrust litigation which, regardless of the outcome, would adversely affect our business. An adverse determination may subject us to the loss of our proprietary position or to significant liabilities, or require us to seek licenses that may include substantial cost and ongoing royalties. Licenses may not be available from third parties, or may not be obtainable on satisfactory terms. An adverse determination or a failure to obtain necessary licenses may restrict or prevent us from manufacturing and selling our products, if any. These outcomes could materially harm our business, financial condition and results of operations.

Risks Related to Stock Price Volatility

Ownership of our common stock is highly concentrated, and it may prevent you and other stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause our stock price to decline.

Our executive officers, directors and their affiliates beneficially owned approximately 14% of our outstanding common stock as of December 31, 2011. Accordingly, these executive officers, directors and their affiliates, acting individually or as a group, have substantial influence over the outcome of a corporate action of ours requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. These stockholders may also delay or prevent a change in control of us, even if such change in control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the value of our common stock due to investors' perception that conflicts of interest may exist or arise.

Our stock price is expected to be volatile.

Our common stock could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

the regulatory status of Gencaro and the Gencaro Test, and whether and when they are approved for sale, if at all, and the labeling or other conditions of use imposed by the FDA;

S-19

Table of Contents

our ability to secure substantial additional funding or complete a strategic transaction or to complete development of and commercialize Gencaro;

potential receipt of government or third party funding to further develop Gencaro or rNAPc2;

the results of our future clinical trials and any future NDAs of our current and future product candidates;

the entry into, or termination of, key agreements, including key strategic alliance agreements;

the results and timing of regulatory reviews relating to our product candidates;

failure of any of our product candidates, if approved, to achieve commercial success;

general and industry-specific economic conditions that may affect our research and development expenditures;

the results of clinical trials conducted by others on drugs that would compete with our product candidates;

issues in manufacturing our product candidates or any approved products;

the initiation of or material developments in or the conclusion of litigation to enforce or defend any of our intellectual property rights;

the loss of key employees;

the introduction of technological innovations or new commercial products by our competitors;

changes in estimates or recommendations by securities analysts, if any, who cover our common stock;

future sales of our common stock;

changes in the structure of health care payment systems;

period-to-period fluctuations in our financial results; and

our ability to retain the listing of our common stock on the NASDAQ Capital Market.

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

Future sales or the possibility of future sales of our common stock may depress the market price of our common stock.

Sales in the public market of substantial amounts of our common stock could depress prevailing market prices of our common stock. As of June 30, 2012, 12,182,999 shares of common stock were outstanding. All of these shares are freely transferable without restriction or further registration under the Securities Act, except for shares held by our directors, officers and other affiliates and unregistered shares held by non-affiliates. The sale of these additional shares, or the perception that such sales may occur, could depress the market price of our common stock.

As of June 30, 2012, approximately 2.8 million shares of our common stock were issuable upon the exercise of outstanding warrants, all of which were exercisable as of that date. Once a warrant is exercised, if the shares of our common stock issued upon the exercise of any such warrant are not available for sale in the open market without further registration under the Securities Act, then the holder can arrange for the resale of shares either by invoking any applicable registration rights, causing the shares to be registered under the Securities Act and thus freely transferable, or by relying on an exemption to the Securities Act. If these registration rights, or similar registration rights that may apply to securities we may issue in the future, are exercised, it could result in additional sales of our common stock in the market, which may have an adverse effect on our stock price.

As of June 30, 2012 there were approximately 884,000 shares of our common stock which may be issued upon exercise of outstanding stock options. If and when these options are exercised, such shares will be available for sale in the open market without further registration under the Securities Act. The existence of these outstanding options may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms. The exercise of those options, and the prompt resale of shares of our common stock received, may also result in downward pressure on the price of our common stock.

Table of Contents

In the absence of a significant strategic transaction, we will need to raise significant additional capital to finance our capital requirements, including the research, development and commercialization of our drug products. If future securities offerings occur, they would dilute our current stockholders' equity interests and could reduce the market price of our common stock.

We do not expect to pay cash dividends, and accordingly, stockholders must rely on stock appreciation for any return on their investment.

We anticipate that we will retain our earnings, if any, for future growth and therefore do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock will provide a return to stockholders. Investors seeking cash dividends should not invest in our common stock.

We have implemented anti-takeover provisions that could discourage, prevent or delay a takeover, even if the acquisition would be beneficial to our stockholders.

Provisions of our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions:

establish a classified board of directors so that not all members of our board may be elected at one time;

authorize the issuance of up to 5 million additional shares of preferred stock that could be issued by our board of directors to increase the number of outstanding shares and hinder a takeover attempt;

limit who may call a special meeting of stockholders;

prohibit stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders; and

establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at a stockholder meeting.

Specifically, our certificate of incorporation provides that all stockholder action must be effected at a duly called meeting and not by a written consent. The bylaws provide, however, that our stockholders may call a special meeting of stockholders only upon a request of stockholders owning at least 50% of our outstanding common stock. These provisions of our certificate of incorporation and bylaws could discourage potential acquisition proposals and could delay or prevent a change in control. We designed these provisions to reduce our vulnerability to unsolicited acquisition proposals and to discourage certain tactics that may be used in proxy fights. These provisions, however, could also have the effect of discouraging others from making tender offers for our shares. As a consequence, they also may inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

We are permitted to issue shares of our preferred stock without stockholder approval upon such terms as our board of directors determines. Therefore, the rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of our preferred stock that may be issued in the future. In addition, the issuance of preferred stock could have a dilutive effect on the holdings of our current stockholders.

We are subject to the Delaware anti-takeover laws regulating corporate takeovers. These anti-takeover laws prevent a Delaware corporation from engaging in a merger or sale of more than 10% of its assets with any stockholder, including all affiliates and associates of the stockholder, who owns 15% or more of the corporation's outstanding voting stock, for three years following the date that the stockholder acquired 15% or more of the corporation's stock unless:

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

the board of directors approved the transaction where the stockholder acquired 15% or more of the corporation's stock;

after the transaction in which the stockholder acquired 15% or more of the corporation's stock, the stockholder owned at least 85% of the corporation's outstanding voting stock, excluding shares owned by directors, officers and employee stock plans in which employee participants do not have the right to determine confidentially whether shares held under the plan will be tendered in a tender or exchange offer; or

on or after this date, the merger or sale is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock that is not owned by the stockholder.

The provisions of our governing documents and current Delaware law may, collectively:

lengthen the time required for a person or entity to acquire control of us through a proxy contest for the election of a majority of our board of directors;

discourage bids for our common stock at a premium over market price; and

generally deter efforts to obtain control of us.

Additional Risks Related to This Offering

S-21

Table of Contents

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

We have not allocated specific amounts of the net proceeds from this offering for any specific purpose. Our management will have significant flexibility in applying the net proceeds of this offering. You will be relying on the judgment of our management with regard to the use of these net proceeds, and subject to any agreed upon contractual restrictions under the terms of the subscription agreement, you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the net proceeds will be invested in a way that does not yield a favorable, or any, return for us. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flow.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. After giving effect to the sale by us of 2,436,599 shares of common stock in this offering, and based on a public offering price of \$0.391 per share and related warrant in this offering and a pro forma net tangible book value per share of our common stock of \$0.358 as of March 31, 2012, without giving effect to the potential exercise of the warrants being offered by this prospectus supplement, if you purchase shares in this offering, you will suffer immediate and substantial dilution of \$0.042 per share in the net tangible book value of the common stock purchased. See Dilution on page S-25 for a more detailed discussion of the dilution you will incur in connection with this offering.

There is no public market for the warrants to purchase common stock in this offering.

There is no established public trading market for the warrants being sold in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the warrants on any securities exchange. Without an active market, the liquidity of the warrants will be limited.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, accompanying prospectus and the documents that we have filed with the SEC that are incorporated by reference in this prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, 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," "continue," "ongoing" or the 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 and our Quarterly Reports on Form 10-Q, 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. 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 the planned Gencaro trial for the prevention of atrial fibrillation 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 supplement, accompanying prospectus and the documents incorporated 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.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the securities we are offering will be approximately \$750,000, assuming that we sell all of the securities we are offering, after deducting the placement agent's fees and estimated offering expenses payable by us. This amount does not include the proceeds, if any, we may receive from the exercise of the warrants issued in this offering. Net proceeds is what we expect to receive after paying the placement agency fees and other expenses of this offering payable by us.

We agreed to use the net proceeds from this offering solely for general corporate purposes, including clinical trials, research and development expenses and general and administrative expenses.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering for general corporate purposes. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term interest bearing instruments.

Table of Contents**DILUTION**

Our net tangible book value on March 31, 2012 was approximately \$4.4 million, or approximately \$0.358 per share of common stock. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding.

After giving effect to the sale of 2,436,599 shares of common stock and warrants to purchase an additional 1,827,449 shares of common stock offered by us in this offering at a price of \$0.391 per share and related warrant (and excluding shares of common stock issued and any proceeds received upon exercise of the warrants), less the placement agency fees and other estimated expenses of this offering payable by us, our adjusted net tangible book value on March 31, 2012 would have been approximately \$5.1 million, or \$0.349 per share of common stock. Assuming the completion of the offering, this represents an immediate decrease in net tangible book value of \$0.009 per share to our existing stockholders and an immediate dilution of \$0.042 per share to anyone who purchases our common stock and warrants in the offering. The following table illustrates this calculation on a per share basis, assuming that we sell all of the shares we are offering:

Public offering price per share (and related warrant)	\$ 0.391
Net tangible book value per share as of August 1, 2012	\$ 0.358
Decrease per share attributable to the new investors	\$ 0.009
Adjusted net tangible book value per share as of August 1, 2012 after giving effect to the offering	\$ 0.349
Dilution per share to new investors	\$ 0.042

Investors that acquire additional shares of common stock through the exercise of the warrants offered hereby may experience additional dilution depending on our net tangible book value at the time of exercise.

The foregoing table is based on 12,182,999 common shares outstanding at August 2, 2012, which does not take into effect further dilution to new investors that could occur upon the exercise of outstanding options or warrants having a per share exercise price less than the public offering price.

In addition, the calculations in the foregoing table do not take into account, as of August 2, 2012:

884,000 shares of common stock issuable upon the exercise of outstanding options, with a weighted average exercise price of \$3.08 per share;

2.8 million shares of common stock issuable upon the exercise of outstanding warrants, with a weighted average exercise price of \$2.65 per share; and

477,000 shares of common stock reserved for future issuance under our Amended and Restated 2004 Equity Incentive Plan.

To the extent that any of our outstanding options or warrants are exercised, we grant additional options under our stock option plans or issue additional warrants, or we issue additional shares of common stock in the future, there may be further dilution to new investors.

Table of Contents

DESCRIPTION OF THE SECURITIES WE ARE OFFERING

In this offering, we are offering a maximum of 2,436,599 shares of our common stock and warrants to purchase an additional 1,827,449 shares of our common stock and the shares of common stock issuable upon exercise of such warrants. The common stock and warrants will be sold in combination, with a warrant to purchase 0.75 shares of common stock at an exercise price of \$0.46 per share of common stock for each share of common stock sold. The negotiated purchase price for each share and related warrant is \$0.391. The shares of common stock and warrants are immediately separable and will be issued separately.

Common Stock

A description of the common stock we are offering pursuant to this prospectus supplement is set forth under the heading Description of Capital Stock Common Stock, starting on page 7 of the accompanying prospectus. As of August 2, 2012, we had 12,182,999 shares of common stock outstanding, before giving effect to the sale of any shares in this offering.

Warrants

The material terms and provisions of the warrants being offered pursuant to this prospectus supplement and the accompanying prospectus are summarized below. The summary is subject to, and qualified in its entirety by, the form of warrant which will be provided to each purchaser in this offering and will be filed as an exhibit to a Current Report on Form 8-K with the SEC in connection with this offering.

Each purchaser of shares will receive, for each share purchased, a warrant representing the right to purchase 0.75 shares of common stock at an exercise price of \$0.46 per share of common stock. The warrants will be exercisable on the date that is six months after the warrants are issued and will terminate on the sixth anniversary of the date the warrants are first exercisable. The exercise price and the number of shares for which each warrant may be exercised is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price and number of warrants held by a purchaser (or such purchaser's direct or indirect transferee) are subject to appropriate adjustment in the event of cash dividends or other distributions to holders of shares of our common stock.

There is no established public trading market for the warrants, and we do not expect a market to develop. We do not intend to apply to list the warrants on any securities exchange. Without an active market, the liquidity of the warrants will be limited. In addition, in the event our common stock price does not exceed the per share exercise price of the warrants during the period when the warrants are exercisable, the warrants will not have any value.

Holder of the warrants may exercise their warrants to purchase shares of our common stock on or before the termination date by delivering an exercise notice, appropriately completed and duly signed. Payment of the exercise price for the number of shares for which the warrant is being exercised must be made within one trading day following such exercise. In the event that the registration statement relating to the warrant shares is not effective and another exemption from registration is not available, a holder of warrants may only exercise its warrants for a net number of warrant shares pursuant to the cashless exercise procedures specified in the warrants. Warrants may be exercised in whole or in part, and any portion of a warrant not exercised prior to the termination date shall be and become void and of no value. The absence of an effective registration statement or applicable exemption from registration does not alleviate our obligation to deliver common stock issuable upon exercise of a warrant.

Upon the holder's exercise of a warrant, we will issue the shares of common stock issuable upon exercise of the warrant within three trading days of our receipt of notice of exercise subject to payment of the aggregate exercise price therefor.

The shares of common stock issuable on exercise of the warrants will be, when issued in accordance with the warrants, duly and validly authorized, issued and fully paid and non-assessable. We will authorize and reserve at least that number of shares of common stock equal to the number of shares of common stock issuable upon exercise of all outstanding warrants.

If, at any time a warrant is outstanding, we consummate any fundamental transaction, as described in the warrants and generally including any consolidation or merger into another corporation, the consummation of a transaction whereby another entity acquires more than 50% of our outstanding common stock, or the sale of all or substantially all of our assets, or other transaction in which our common stock is converted into or exchanged for other securities or other consideration, the holder of any warrants will thereafter receive upon exercise of the warrants, the securities or other consideration to which a holder of the number of shares of common stock then deliverable upon the exercise or conversion of such warrants would have been entitled upon such consolidation or merger or other transaction.

Table of Contents

In the event of a fundamental transaction, each warrant holder will have the right to require us, or our successor, to repurchase its warrant for an amount equal to the Black-Scholes value of the remaining unexercised portion of the warrant with such payment to be made in the same form of consideration (whether securities, cash or property) as is received by the holders of Common Stock in the fundamental transaction.

The warrants are not exercisable by their holder to the extent (but only to the extent) that such holder or any of its affiliates would beneficially own in excess of 4.9% of our common stock.

Amendments and waivers of the terms of the warrants require the written consent of the holder of such warrant and us.

THE HOLDER OF A WARRANT WILL NOT POSSESS ANY RIGHTS AS A STOCKHOLDER UNDER THAT WARRANT UNTIL THE HOLDER EXERCISES THE WARRANT. THE WARRANTS MAY BE TRANSFERRED INDEPENDENT OF THE COMMON STOCK WITH WHICH THEY WERE ISSUED, SUBJECT TO APPLICABLE LAWS.

S-27

Table of Contents

PLAN OF DISTRIBUTION

Placement Agency Agreement and Subscription Agreement

Ladenburg Thalmann & Co. Inc., which we refer to as the placement agent, has agreed to act as the exclusive placement agent in connection with this offering subject to the terms and conditions of a placement agency agreement dated as of August 2, 2012. The placement agent is not purchasing or selling any shares or warrants offered by this prospectus supplement, nor is it required to arrange the purchase or sale of any specific number or dollar amount of the shares and related warrants, but has agreed to use reasonable efforts to arrange for the sale of all of the shares and related warrants offered hereby. Therefore, we will enter into a subscription agreement directly with each investor in connection with this offering and we may not sell the entire amount of shares and related warrants offered pursuant to this prospectus supplement. Either we or the placement agent may terminate the placement agency agreement upon ten days' written notice.

The placement agent proposes to arrange for the sale to one or more purchasers of the shares and related warrants offered pursuant to this prospectus supplement through separate subscription agreements between each purchaser and us. We will enter into subscription agreements with each of the purchasers pursuant to which we will sell to the purchasers an aggregate of 2,436,599 shares of our common stock, and warrants to purchase an additional 1,827,449 shares of our common stock, at a price of \$0.391 per share and related warrant. A warrant to purchase 0.75 shares of our common stock at an exercise price of \$0.46 will be issued with each share purchased. We negotiated the price for the shares and related warrants offered in this offering with the purchasers. The factors considered in determining the price included the recent market price of our common stock, the general condition of the securities market at the time of this offering, the history of, and the prospects, for the industry in which we compete, our past and present operations, and our prospects for future revenues.

The placement agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act of 1933, as amended, or the Securities Act, and any fees or commissions received by it and any profit realized on the resale of securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the placement agent would be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock and warrants by the placement agent. Under these rules and regulations, the placement agent:

may not engage in any stabilization activity in connection with our securities; and

may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until it has completed its participation in the distribution.

From time to time in the ordinary course of their respective businesses, the placement agent or its affiliates was in the past or may in the future engage in investment banking and/or other services with us and our affiliates for which it has or may in the future receive customary fees and expenses.

Under the subscription agreements, we have agreed to indemnify the purchasers against certain losses resulting from our breach of any of our representations, warranties, or covenants under agreements with the purchasers as well as under certain other circumstances described in the subscription agreements.

We have agreed, subject to certain exceptions, to indemnify the placement agent against liabilities under the Securities Act of 1933, as amended and certain other liabilities relating to its service as placement agent. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

Fees

The placement agent will be entitled to a cash fee of 6.5% of the gross proceeds paid to us for the shares and related warrants we sell in this offering (excluding any proceeds from exercise of the warrants). We will also reimburse the placement agent for all expenses that have been incurred by the placement agent in connection with the offering, subject to a maximum of the lesser of \$15,000 or total compensation to the placement agent, when combined with the cash fee, of 8% of the gross proceeds of the offering.

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

The following table shows the per share and total placement agency fees we will pay to the placement agent in connection with the sale of the shares and warrants offered pursuant to this prospectus supplement assuming the purchase of all of the shares of common stock and warrants offered hereby:

Placement agent fees and placement agent expenses per share (and related warrant)	\$ 0.03
Total placement agent fees and placement agent expenses payable by us	\$ 76,926

S-28

Table of Contents

Because there is no minimum offering amount in this offering, the actual total placement agency fees, if any, are not presently determinable and may be substantially less than the maximum amount set forth above. The maximum fees to be received by any member of the Financial Industry Regulatory Association, or FINRA, or independent broker-dealer may not be greater than 8% of the initial gross proceeds from the sale of any shares of common stock and warrants being offered hereby.

The sale of up to 2,436,599 shares of common stock and warrants to purchase up to 1,827,449 shares of common stock will be completed on or about August 8, 2012. We estimate the total offering expenses of this offering that will be payable by us, excluding the placement agency fees, will be approximately \$140,000, which include legal and printing costs, various other fees and reimbursement of the placement agents' expenses. At the closing, Computershare Trust Company N.A. will credit the shares of common stock to the respective accounts of the purchasers. We will mail warrants directly to the purchasers at their respective addresses set forth in the subscription agreements.

The foregoing does not purport to be a complete statement of the terms and conditions of the placement agency agreement and subscription agreements. Copies of the placement agency agreement and the subscription agreements will be included as exhibits to our current report on Form 8-K that will be filed with the SEC and incorporated by reference into the Registration Statement of which this prospectus supplement forms a part. See "Where You Can Find More Information" on page S-30.

Table of Contents

LEGAL MATTERS

Selected legal matters with respect to the validity of the securities offered by this prospectus supplement will be passed upon for us by Cooley LLP, Broomfield, Colorado, Ellenoff Grossman & Schole LLP, New York, NY, and Sichenzia Ross Friedman Ference LLP, New York, NY, are acting as counsel for the placement agent in connection with various matters relating to the securities offered hereby.

EXPERTS

The consolidated financial statements of ARCA biopharma, Inc. (a development stage enterprise) as of December 31, 2011 and 2010, and for each of the years in the two year period ended December 31, 2011, and for the period from inception (December 17, 2001) through December 31, 2011, have been incorporated by reference in this prospectus supplement and the accompanying prospectus and the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2011, consolidated 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 our ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of that uncertainty.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities we are offering under this prospectus supplement. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Statements contained in this prospectus supplement as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference. We also file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other material we file with the SEC, at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information on the Public Reference Room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including ARCA biopharma. The SEC's Internet site can be found at <http://www.sec.gov>.

Our Internet address is www.arcabiopharma.com. There we make available free of charge, on or through the investor relations section of our website, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The information found on our website is not part of this prospectus supplement or any other report we file with or furnish to the Securities and Exchange Commission.

IMPORTANT INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement the information we file with it, which means that we can disclose important information to you by referring you to those documents. Information incorporated by reference is part of this prospectus supplement. Later information filed with the SEC will update and supersede this information. The SEC's Internet site can be found at <http://www.sec.gov>.

We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until this offering is completed:

Our Current Reports on Form 8-K filed with the SEC on January 19, 2012, March 26, 2012, March 30, 2012, April 16, 2012, and May 30, 2012.

Our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2012 filed with the SEC on May 14, 2012.

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2011 filed with the SEC on March 27, 2012 (the 2011 Form 10-K).

Our definitive proxy statement on Schedule 14A, filed with the SEC on April 5, 2012.

The description of common stock contained in our registration statement on Form 8-A, dated July 23, 1997 including any subsequent amendment or report filed for updating such description.

S-30

Table of Contents

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to those documents. You should direct any requests for documents to ARCA biopharma, Inc., Attention: Corporate Secretary, 8001 Arista Place, Suite 200, Broomfield, Colorado 80021. Our phone number is (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>.

In accordance with Rule 412 under the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Information that we file with the SEC after the date of this prospectus supplement that is incorporated by reference will automatically update and supersede the information contained in this prospectus supplement.

S-31

Table of Contents

Prospectus

\$50,000,000

ARCA BIOPHARMA, INC.

\$50,000,000

COMMON STOCK

PREFERRED STOCK

DEBT SECURITIES

WARRANTS

UNITS

From time to time, we may sell common stock, preferred stock, debt securities and/or warrants, either individually or in units, with a total value of up to \$50,000,000. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock or common stock, preferred stock or debt securities upon the exercise of warrants. We will specify in any accompanying prospectus supplement the terms of any offering. The prospectus supplement may also update or change the information set forth in this prospectus. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the NASDAQ Capital Market or any securities exchange of the securities covered by the prospectus supplement. Our common stock is traded on the NASDAQ Capital Market under the trading symbol ABIO. On March 7, 2011, the last reported sales price for our common stock was \$3.01 per share.

You should read this prospectus and any prospectus supplement carefully before you invest.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. SEE THE SECTION ENTITLED RISK FACTORS BEGINNING ON PAGE 5 OF THIS PROSPECTUS.

THIS PROSPECTUS MAY NOT BE USED TO OFFER OR SELL ANY SECURITIES UNLESS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to investors, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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 April 4, 2011

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	i
<u>OVERVIEW</u>	1
<u>RISK FACTORS</u>	5
<u>FORWARD-LOOKING INFORMATION</u>	5
<u>USE OF PROCEEDS</u>	6
<u>DESCRIPTION OF CAPITAL STOCK</u>	7
<u>DESCRIPTION OF DEBT SECURITIES</u>	10
<u>DESCRIPTION OF WARRANTS</u>	16
<u>DESCRIPTION OF UNITS</u>	18
<u>LEGAL OWNERSHIP OF SECURITIES</u>	19
<u>PLAN OF DISTRIBUTION</u>	22
<u>LEGAL MATTERS</u>	24
<u>EXPERTS</u>	24
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	24
<u>INCORPORATION BY REFERENCE</u>	24

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using the SEC’s shelf registration process. Under this shelf registration process, we may sell common stock, preferred stock, debt securities and/or warrants, either individually or in units, in one or more offerings up to a total dollar amount of \$50,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell common stock, preferred stock, debt securities and/or warrants, either individually or in units, we will provide a prospectus supplement that will contain more specific information about the securities offered and the terms of the offering. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. This prospectus, together with applicable prospectus supplements, includes all material information relating to this offering. Please carefully read both this prospectus and any prospectus supplement together with the additional information described below under “Where You Can Find More Information” and “Incorporation By Reference.”

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

You should rely only on the information we have provided or incorporated by reference in this prospectus, any prospectus supplement or any free writing prospectus. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any prospectus supplement or any free writing prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement or any free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any prospectus supplement or any free writing prospectus or any sale of a security.

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 Additional Information.”

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

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

OVERVIEW

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus. This summary may not contain all the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, including the Risk Factors section contained in this prospectus 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. and our subsidiaries.

Overview

We are a biopharmaceutical company whose principal focus is developing genetically-targeted therapies for heart failure and other cardiovascular diseases. Our lead product candidate is Gencaro™ (bucindolol hydrochloride), a pharmacologically unique beta-blocker and mild vasodilator being developed for the treatment of chronic heart failure, or HF. We have collaborated with LabCorp to develop the Gencaro Test, a companion test for the genetic markers that may predict clinical response to Gencaro.

We have identified common genetic variations in the cardiovascular system that we believe interact with Gencaro's pharmacology and may predict patient response to Gencaro treatment. We currently hold worldwide rights to Gencaro and have been granted patents in the U.S. and Europe for methods of treating heart failure patients with bucindolol based on genetic testing, which we believe will provide market exclusivity for Gencaro into 2025 in those markets. In addition, we believe that if Gencaro is approved, the U.S. Gencaro patent, as well as the patent issued in Europe, will be eligible for patent term extension which, if granted in the U.S., could provide an additional period of market exclusivity in the U.S. of approximately three years, and if granted in Europe could provide an additional five years of market exclusivity.

Gencaro has been the subject of extensive clinical development, culminating in a Phase 3 heart failure study known as the BEST trial. In September 2008, the U.S. Food and Drug Administration, or FDA, formally accepted for filing our New Drug Application, or NDA, for Gencaro as a potential treatment for HF. In May 2009, the FDA notified us through a Complete Response Letter, or CRL, that our NDA for Gencaro was not approvable in its current form, and specified additional actions and information required for approval of the NDA including the need for an additional Phase 3 clinical trial as described below. In May 2010, we reached agreement with the FDA on a Special Protocol Assessment, or SPA, for the design of an additional Phase 3 clinical trial to assess the safety and efficacy of Gencaro in approximately 3,200 patients with chronic heart failure who have the genotype that appears to respond most favorably to Gencaro. The SPA signifies the FDA's agreement that this trial, if successful, could serve as the clinical effectiveness basis for the approval of Gencaro. The trial is designed as an international, multi-center, randomized, double-blind clinical trial. The trial is intended to be a superiority comparison of Gencaro to the beta-blocker metoprolol CR/XL, which is approved for heart failure and other indications. The primary endpoint of the trial is a composite of cardiovascular mortality and cardiovascular hospitalization. The trial protocol includes two interim data analyses at pre-specified numbers of primary endpoint events. If the results of either interim analysis meet the pre-specified criteria, we believe that a complete response to the CRL could be formally submitted at that time. The first interim data analysis is planned at 630 primary endpoint events (57% of the projected total number). The trial protocol estimates reaching the first interim analysis 24-30 months into the trial. Even with a positive outcome at either interim analysis, the planned trial is designed to proceed to conclusion, estimated to take 3.5 years (including the time to reach the interim analysis). In order not to influence the planned trial's subsequent completion, even if the results of an interim data analysis are adequate to support approval of Gencaro, Gencaro would not be commercially available until after the conclusion of the trial. We currently expect we could begin the trial approximately one year after obtaining sufficient funding.

The investigation of Gencaro for the reduction of cardiovascular mortality and cardiovascular hospitalizations in a genotype-defined HF population was designated by the FDA as a fast track development program. According to the FDA's Fast Track Guidance document, fast track programs are designed to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs.

Table of Contents

We also hold exclusive rights to rNAPc2, a single-chain, small recombinant protein, originally isolated from the saliva of the canine hookworm. rNAPc2 is a potent, long acting, and selective inhibitor of tissue factor, the protein responsible for initiating the extrinsic coagulation pathway, the primary coagulation mechanism in humans. rNAPc2 was originally developed as a cardiovascular therapy for thrombosis and other indications. As a result, it has been safely tested in over 700 human patients in nine Phase 1 and Phase 2 clinical trials. Previously, pilot studies of rNAPc2 conducted in non-human primates demonstrated potential efficacy against two of the most deadly strains of hemorrhagic fever virus, Ebola and Marburg. We are currently seeking government funding to further develop rNAPc2, as a potential treatment for viral hemorrhagic fevers. Considering the substantial cost associated with the development of rNAPc2 and our limited financial resources, further development of rNAPc2 will be dependent upon receipt of government funding, which may not be available.

Other Information

We were originally incorporated as Hyseq, Inc. in Illinois in 1992 and reincorporated in Nevada in 1993. On January 31, 2003, we merged with Variagenics, Inc., a publicly traded Delaware corporation based in Massachusetts, and, in connection with the merger, changed our name to Nuvelo, Inc. On March 25, 2004, we reincorporated in Delaware. On January 27, 2009, our wholly owned subsidiary merged with ARCA biopharma, Inc., a privately held Delaware corporation based in Colorado, and, in connection with the merger, we changed our name to ARCA biopharma, Inc. Our principal offices are located at 8001 Arista Place, Suite 200, Broomfield, Colorado 80021. Our telephone number is (720) 940-2200. Our internet address is <http://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 (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.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings up to a total dollar amount of \$50,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity, if applicable;

rates and times of payment of interest or dividends, if any;

redemption, conversion or sinking fund terms, if any;

voting or other rights, if any;

conversion prices, if any; and

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

important federal income tax considerations.

The prospectus supplement will describe the terms of a specific offering of our securities and also may add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement may offer a security that is not registered and described in this prospectus at the time of its effectiveness.

Table of Contents

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Table of Contents

We may sell the securities directly or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. Subject to any preferences of outstanding shares of preferred stock, holders of common stock are entitled to dividends when and if declared by our board of directors.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Debt Securities. We may offer debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other secured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the prospectus supplements related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures may be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC, and supplemental indentures and forms of debt securities containing the terms of debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. The warrants will be evidenced by warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. In this prospectus, we have summarized certain general features of the warrants. We will incorporate by reference into the registration statement of which this prospectus is a part the form of warrant agreement, including a form of warrant certificate, that describes the terms of the series of warrants we are offering before the issuance of the related series of warrants. We urge you to read the prospectus supplements related to the series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the applicable series of warrants.

Units. We may issue units consisting of common stock, preferred stock, debt securities and/or warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the prospectus supplements related to the series of units being offered, as well as the unit agreements that contain the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

We will enter into the unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

Table of Contents

RISK FACTORS

An investment in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the risks and uncertainties set forth under the heading "Risk Factors" in any applicable prospectus supplement or free writing prospectus and in our filings with the SEC incorporated by reference in this prospectus, together with all the other information contained in this prospectus, any applicable prospectus supplement or free writing prospectus, or incorporated by reference in this prospectus. 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 prospectus supplement or any additional risks and uncertainties actually occur, our business, financial condition and results of operations could be materially and adversely affected. In that case, the trading price of securities being offered by this prospectus and the applicable prospectus supplement could decline and you might lose all or part of your investment.

CAUTIONARY NOTE REGARDING FORWARD LOOKING INFORMATION

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 of 1933, amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, 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, continue, ongoing or the 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 and our Quarterly Reports on Form 10-Q, 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, any free writing prospectus 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 the planned additional trial regarding Gencaro required under the CRL, 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, 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.

Table of Contents

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 Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and our website.

USE OF PROCEEDS

The expected use of proceeds of any specific offering of securities will be set out in the prospectus supplement relating to such offering. If not specified in a prospectus supplement relating to a particular offering of securities, we will use the net proceeds from the offering of these securities for general corporate purposes, including clinical trials, research and development expenses and general and administrative expenses.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and certain provisions of our restated certificate of incorporation is a summary and is qualified in its entirety by the provisions of our amended and restated certificate of incorporation.

Our authorized capital stock consists of 100,000,000 shares of common stock, \$0.001 par value, and 5,000,000 shares of preferred stock, \$0.001 par value. As of December 31, 2010, there were 8,834,535 shares of common stock outstanding and no shares of preferred stock outstanding

Common Stock

Holders of our common stock are entitled to one vote per share for the election of directors and all other matters submitted for stockholder vote, except matters submitted to the vote of another class or series of shares. Holders of common stock are not entitled to cumulative voting rights. The approval of 66 2/3% of the voting rights of the common stock is required to make certain amendments to our certificate of incorporation, amend our by-laws, and to remove a director from our board of directors.

The holders of common stock are entitled to dividends in such amounts and at such times, if any, as may be declared by our board of directors out of legally available funds. We have not paid any dividends on our common stock and do not anticipate paying any cash dividends on our common stock in the foreseeable future. Upon liquidation, dissolution or winding up of us, the holders of our common stock are entitled to share ratably in all net assets available for distribution to stockholders after payments to creditors and holders of senior securities. The common stock is not redeemable and has no preemptive, conversion or sinking fund rights. The rights of the holders of our common stock are subject to the rights of the holders of any preferred stock which may, in the future, be issued. All outstanding shares of our common stock are, and any shares of common stock issued pursuant to this prospectus when issued will be, duly authorized, validly issued, fully paid and non-assessable.

Preferred Stock

Our restated certificate of incorporation provides that our board of directors has the authority, without further action by the stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions of this preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of a series, without further vote or action by the stockholders.

We will fix the rights, preferences, privileges and restrictions of the preferred stock of each series in the certificate of designation relating to that series. We will incorporate by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

Table of Contents

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights, if any, of the preferred stock;

preemptive rights, if any;

restrictions on transfer, sale or other assignment, if any;

a discussion of any material or special U.S. federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposed amendment to our restated certificate of incorporation that would cause certain, specified changes in the rights of the preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The issuance of preferred stock, whether pursuant to this offering or otherwise, could adversely affect the voting power or other rights of holders of our common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Law. We are subject to Section 203 of the Delaware General Corporation Law, which regulates acquisitions of some Delaware corporations. In general, Section 203 prohibits, with some exceptions, a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date of the transaction in which the person becomes an interested stockholder, unless:

our board of directors approved either the business combination or the transaction in which the person became an interested stockholder prior to the time such person became an interested stockholder;

upon consummation of the transaction that resulted in the person becoming an interested stockholder, the person owned at least 85% of our voting stock outstanding at the time the transaction commenced, excluding shares owned by persons who are directors and also officers of the corporation and shares issued under employee stock plans under which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

Table of Contents

on or subsequent to the date the person became an interested stockholder, our board of directors approved the business combination and the stockholders other than the interested stockholder authorized the transaction at an annual or special meeting of stockholders by the affirmative vote of at least 66 2/3% of our outstanding stock not owned by the interested stockholder.

Section 203 defines a business combination to include:

any merger or consolidation involving us and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of our assets involving the interested stockholder;

in general, any transaction that results in the issuance or transfer by us of any of our stock to the interested stockholder;

any transaction involving us that has the effect of increasing the proportionate share of our stock owned by the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through us.

In general, Section 203 defines an interested stockholder as any person who, together with the person's affiliates and associates, owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of a corporation's outstanding voting stock.

Section 203 of the Delaware General Corporation Law could depress our stock price and delay, discourage or prohibit transactions not approved in advance by our board of directors, such as takeover attempts that might otherwise involve the payment to our stockholders of a premium over the market price of our common stock.

Certificate of Incorporation and Bylaw Provisions. Our restated certificate of incorporation includes a number of provisions that may have the effect of deterring hostile takeovers or delaying or preventing changes in control or our management. First, our board of directors can issue up to 5,000,000 shares of preferred stock, with any rights or preferences, including the right to approve or not approve an acquisition or other change in control. Second, our bylaws provide that all stockholder actions must be effected at a duly called meeting of stockholders and not by written consent. Third, our bylaws provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide timely notice in writing. Our bylaws also specify requirements as to the form and content of a stockholder's notice. These provisions may delay or preclude stockholders from bringing matters before a meeting of stockholders or from making nominations for directors at a meeting of stockholders, which could delay or deter takeover attempts or changes in management. Fourth, our restated certificate of incorporation provides that, subject to the rights of the holders of any outstanding series of our preferred stock, all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum. In addition, our restated certificate of incorporation provides that our board of directors may fix the number of directors by resolution. Fifth, our restated certificate of incorporation does not provide for cumulative voting for our directors. The absence of cumulative voting may make it more difficult for stockholders owning less than a majority of our stock to elect any directors to our board of directors.

Transfer Agent and Registrar

Computershare Trust Company N.A. has been appointed as the transfer agent and registrar for our common stock.

Listing on the NASDAQ Capital Market

Our common stock is listed on the NASDAQ Capital Market under the symbol ABIO.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below.

We will issue the senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue the subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We may file the forms of these documents as exhibits to the registration statement that includes this prospectus or incorporate them by reference from a report that we file with the SEC. We use the term "indentures" in this prospectus to refer to both the senior indenture and the subordinated indenture.

The indentures will be qualified under the Trust Indenture Act of 1939. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements related to the debt securities that we sell under this prospectus, as well as the indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

the title;

the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

whether or not we will issue the series of debt securities in global form, the terms and who the depositary will be;

the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a U.S. person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, and the price at which, we may redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemptions provisions;

Table of Contents

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability and/or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

pay dividends and make distributions in respect of our capital stock and the capital stock of our subsidiaries;

redeem capital stock;

place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders and affiliates;

issue or sell stock of our subsidiaries; or

effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of any material or special U.S. federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Table of Contents

Consolidation, Merger or Sale

Any successor to or acquiror of the indentures must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended or deferred;

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable and the time for payment has not been extended or delayed;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the debenture trustee or holders of a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the debenture trustee or the holders of a majority in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the debenture trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the debenture trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture or would subject the debenture trustee in its sole discretion to personal liability; and

subject to its duties under the Trust Indenture Act of 1939, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

the holder has given written notice to the debenture trustee of a continuing event of default with respect to that series;

Table of Contents

the holders of a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and

the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the debenture trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

We and the debenture trustee may change an indenture without the consent of any holders with respect to specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under Consolidation, Merger or Sale;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act of 1939;

to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under General, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment by a successor trustee;

to provide for uncertificated debt securities in addition to or in place of certificated debt securities;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default, or surrender rights of power conferred on us; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, we and the debenture trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

extending the fixed maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Table of Contents

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the debenture trustee;

compensate and indemnify the debenture trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the debenture trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series. See [Legal Ownership of Securities](#) for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of less than all of the outstanding debt securities of the same series that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Table of Contents

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee as our paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

Subordination of Subordinated Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

Table of Contents

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report that we file with the SEC.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

any material or special U.S. federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Table of Contents

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5:00 P.M. Eastern Time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

Outstanding Warrants

As of March 8, 2011, there were outstanding warrants to purchase 323,701 shares of our common stock, having an exercise price ranging from \$3.82 to \$19.48, with a weighted average exercise price per share of \$7.64. Any of the outstanding warrants may be exercised by applying the value of a portion of the warrant, which is equal to the number of shares issuable under the warrant being exercised multiplied by the fair market value of the security receivable upon the exercise of the warrant, less the per share price, in lieu of payment of the exercise price per share.

The warrants will expire at various times between October 2013 and August 2018.

Table of Contents

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we sell under this prospectus, as well as the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units. The provisions described in this section, as well as those described under Description of Capital Stock, Description of Debt Securities and Description of Warrants will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Table of Contents

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depository or warrant agent maintain for this purpose as the **holders** of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names as **indirect holders** of those securities. As we discuss below, indirect holders are not legal holders and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depository or its participants. Consequently, for securities issued in global form, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in **street name**. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depository participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, a warrant agreement or a security we have previously issued to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture, the warrant agreement or the security we have previously issued or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Table of Contents

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under **Special Situations When a Global Security Will Be Terminated**. As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

Table of Contents

If securities are issued only in the form of a global security, an investor should be aware of the following:

An investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

The depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security. We, any indenture trustee and any warrant agent also do not supervise the depositary in any way;

The depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

Financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived. The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee or warrant agent, is responsible for deciding the names of the institutions that will be the initial direct holders.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell securities through underwriters or dealers, through agents or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

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

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

A prospectus supplement or supplements will describe the terms of the offering of the securities, including:

the name or names of any underwriters, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

Edgar Filing: ARCA biopharma, Inc. - Form 424B5

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

Table of Contents

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the NASDAQ Capital Market may engage in passive market making transactions in the securities on the NASDAQ Capital Market in accordance with Rule 103 of Regulation M during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum compensation to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon for us by Cooley LLP, Broomfield, Colorado.

EXPERTS

The consolidated financial statements of ARCA biopharma, Inc. (a development stage enterprise) as of December 31, 2010 and 2009, and for each of the years in the two-year period ended December 31, 2010, and for the period from December 17, 2001 (inception) to December 31, 2010, have been incorporated by reference herein and in the registration statement in reliance on 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, 2010, consolidated 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 consolidated financial statements do not include any adjustments that might result from the outcome of that uncertainty.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as 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 BY REFERENCE

The SEC allows us to incorporate by reference information that we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. We incorporate by reference the following information or documents that we have filed with the SEC (Commission File No. 000-22873):

Our Current Reports on Form 8-K filed with the SEC on January 18, 2011, January 26, 2011 and February 17, 2011; and

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2010 filed with the SEC on March 8, 2011 (the 2010 Form 10-K).

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 filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement or (ii) after the date of this prospectus and until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus. 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, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to those documents. You should direct any requests for documents to ARCA biopharma, Inc., Attention: Corporate Secretary, 8001 Arista Place, Suite 200, Broomfield, Colorado 80021. Our phone number is (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>.

Table of Contents

2,436,599 Shares of Common Stock
Warrants to Purchase 1,827,449 Shares of Common Stock

ARCA BIOPHARMA, INC.

PROSPECTUS SUPPLEMENT

Ladenburg Thalmann & Co. Inc.

August 3, 2012