ARCA biopharma, Inc.
Form 10-K
February 27, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission File Number: 000-22873

ARCA BIOPHARMA, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	36-3855489
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

11080 CirclePoint Road, Suite 140, Westminster, CO 80020

(Address of Principal Executive Offices) (Zip Code)

(720) 940-2200

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock $0.001 par value	The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Exchange Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 and Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
	Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes No

The aggregate market value of the common stock held by non-affiliates of the Registrant on June 29, 2018, the last business day of the most recently completed second fiscal quarter, was $7,650,869 based on the last sale price of the common stock as reported on that day by the The Nasdaq Capital Market.

As of February 22, 2019, the Registrant had 18,355,111 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

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PART I

Item 1. Business

Some of the statements under "Business," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report constitute forward-looking statements. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "int "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these ter comparable terminology, although not all forward-looking statements contain these words. Examples of these statements include, but are not limited to, statements regarding the following: potential future development plans for Gencaro, including the likelihood that any Phase 3 clinical trial results for Gencaro to satisfy the requirements of our Special Protocol Assessment agreement, the expected features and characteristics of Gencaro, including the potential for genetic variations to predict individual patient response to Gencaro or AB171, Gencaro's potential to treat atrial fibrillation, or AF, future treatment options for patients with AF, the potential for Gencaro to be the first genetically-targeted AF prevention treatment, statements regarding potential Phase 3 development plans for Gencaro, including the timing and results thereof, the expected features and characteristics of AB171 as a potential genetically-targeted treatment for peripheral arterial disease and for heart failure, or HF, the potential timeline for development of AB171, including any Investigational New Drug, or IND, application submission related thereto, and the ability of ARCA's financial resources to support its operations through the third quarter of 2019, the sufficiency of our current capital to reach certain of our corporate objectives, our ability to obtain additional funding when needed or enter into a strategic or other transaction, including our ability to raise sufficient capital to fund any Phase 3 clinical trials for Gencaro and our other operations, 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 Annual Report, 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.

In addition, you should refer to the "Risk Factors" section of this Annual Report for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report 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.

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

The terms "ARCA," "the Company," "we," "us," "our" and similar terms refer to ARCA biopharma, Inc.

Overview

We are a biopharmaceutical company applying a precision medicine approach to developing genetically-targeted therapies for cardiovascular diseases. Precision medicine refers to the tailoring of medical treatment to the individual characteristics of each patient through the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment. Our lead product candidate, Gencaro™ (bucindolol hydrochloride), is an investigational, pharmacologically unique beta-blocker and mild vasodilator that we are developing to treat atrial fibrillation, or AF, in certain patients who also have heart failure, or HF.

Gencaro has a mechanism of action that we believe is unique in the beta-blocker drug class and is modulated by a specific genotype. We estimate this genotype is present in about 50% of North American and European general populations. We believe that Gencaro's potential efficacy is enhanced in treating patients who have this genotype and, if Gencaro is approved by the U.S. Food and Drug Administration, or the FDA, Gencaro could potentially be a safe and effective therapy for treating AF in patients who have HF. We also believe that Gencaro, if approved, will have market exclusivity based on patents and new chemical entity status, if approved in the United States, Europe or other markets.

In February 2018, we reported the results of our Phase 2B clinical trial, known as GENETIC-AF, in which we evaluated Gencaro for the prevention of AF recurrence in patients with HF and a left ventricular ejection fraction, or LVEF, < 0.50. This population included 267 patients that had HF with reduced LVEF < 0.40, or HFrEF, or HF with mid-range LVEF ≥ 0.40 and < 0.50, or HFmrEF. GENETIC-AF compared Gencaro to TOPROL-XL (metoprolol succinate), a drug approved for treating HFrEF that is also prescribed, but not approved, for treating AF in patients with HFrEF. There are no approved or guideline recommended drug therapies for prevention of AF in HFmrEF patients, which constituted approximately one-half of the GENETIC-AF patients.

In GENETIC-AF, Gencaro was observed to have a similar treatment effect to TOPROL-XL (metoprolol succinate) in the overall population for prevention of AF recurrence. However, additional analyses prespecified in the statistical analysis plan showed statistically significant treatment effects in favor of Gencaro in the majority of the Phase 2B population (N=196; HR=0.54; p = 0.011). Gencaro also showed statistically significant treatment effects compared to TOPROL-XL for the prevention of AF recurrence in a subset of these patients with HFmrEF (N=91; HR=0.42; p = 0.017). We plan to conduct a pivotal Phase 3 trial, known as PRECISION-AF, evaluating Gencaro in HFmrEF patients because of Gencaro's observed potential treatment effect in these patients in GENETIC AF.

The prevalence of AF is higher in HFmrEF patients as compared with HF generally; it is estimated that 30%-60% of HFmrEF patients also have AF. For patients with HF, AF can contribute to the disease processes that lead to the progression of heart failure and worsening clinical outcomes including hospitalizations and death. This increased risk of illness and death when AF is present with heart failure is true across the spectrum of HF, including HFmrEF. Given these risks and the absence of HF or AF therapies specifically indicated for the HFmrEF population, we believe there is an unmet medical need for drug therapy with greater efficacy to prevent or delay the development of AF in these patients.

In February 2019, we received a Special Protocol Assessment agreement, or SPA, from the FDA for our planned Phase 3 clinical program. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of certain clinical trials that are intended to form the primary basis for determining a drug product's efficacy and safety. Upon specific request by a clinical trial sponsor, the FDA evaluates the protocol and responds to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate for the indication studied. An SPA agreement can potentially reduce the regulatory risk of bringing a drug to market.

Our SPA details a single adequate and well-controlled Phase 3 clinical trial (PRECISION-AF) designed as a double-blind, active-controlled, multicenter, international, study comparing Gencaro with TOPROL-XL (metoprolol succinate) for the prevention of recurrent AF or all-cause mortality, or ACM, in HFmrEF patients. Eligible patients will have HFmrEF, a recent AF event and the genotype which we believe responds most favorably to Gencaro. The primary endpoint of the submitted trial will be time to first event of atrial fibrillation/atrial flutter or ACM during a 26-week follow-up period. Subject to securing significant additional financing, we anticipate initiating PRECISION-AF in the fourth quarter of 2019.

We believe that Gencaro, if approved, could potentially be a safe and more effective therapy than currently available therapeutics for treating heart failure patients with AF. We believe Gencaro has the potential to be unique in several aspects, including:

- The first genetically-targeted cardiovascular therapy;
- The only drug therapy indicated for AF in patients with HFmrEF; and
- The only therapy for AF approved against an active comparator.

The genotype that we believe enhances Gencaro's efficacy can be detected by a genetic test that can be performed by a centralized laboratory or potentially at the point of care during the patient visit. We also believe that Gencaro, if

approved, will have market exclusivity based on patents and new chemical entity status in the United States, Europe or other markets in which it may be approved.

The Proposed Gencaro Phase 3 Clinical Trial

Based on our GENETIC-AF trial results, as well as results of previous Phase 3 pharmacogenetic substudy data from the Phase 3 heart failure clinical trial of bucindolol, known as the BEST trial, we submitted an SPA to the FDA detailing our proposed Phase 3 clinical trial and potential approval path for Gencaro. In February 2019, we received an SPA agreement for PRECISION-AF, a Phase 3 pivotal study comparing Gencaro against TOPROL-XL for the treatment of AF in HFmrEF patients with the beta-1 389 arginine homozygous genotype.

The PRECISION-AF Phase 3 clinical trial is designed as a double-blind, active-controlled, multicenter, international, adaptive study comparing Gencaro with TOPROL-XL for the prevention of recurrent AF/atrial flutter, or AF/AFL, or all-cause mortality, or ACM, in HFmrEF patients. The study will enroll approximately 400 patients at investigative sites in the United States, Europe and Australia. Eligible patients will have HFmrEF (LVEF 40 and < 50%), a recent AF event and the beta-1 389 arginine homozygous genotype which we believe responds most favorably to Gencaro. The planned trial will use standard significance criteria ($p < 0.01$ with adjustment for interim analysis) for the primary endpoint and will include an interim analysis after a portion of total patients have been enrolled. The interim analysis is designed to assess safety, validate initial study assumptions and maintain adequate statistical power for the primary endpoint. Subject to securing additional financing, we anticipate initiating PRECISION-AF in the fourth quarter of 2019. Any future development of Gencaro, including initiating any Phase 3 clinical trial, is dependent on obtaining significant additional financing, even if we enter into a strategic collaboration around the development of Gencaro.

GENETIC-AF and BEST Trial DNA Substudy

Our planned Phase 3 development program of Gencaro is based on the results from GENETIC-AF and a prospectively designed DNA substudy of adrenergic receptor polymorphisms in the BEST trial, a previous Phase 3 study of bucindolol in 2,708 HF patients. Based on data from the BEST trial, Gencaro showed potential evidence of enhanced efficacy in treating AF and in reducing mortality and hospitalizations in HF patients with the beta 1 389 arginine homozygous genotype.

GENETIC-AF enrolled 267 patients from the United States, Canada and Europe. The primary analysis was conducted to evaluate the evidence of safety and superior efficacy of Gencaro versus an active comparator, TOPROL-XL. The primary endpoint of the trial was time to recurrent AF/AFL or ACM. Eligible patients had LVEF < 50%, a history of paroxysmal AF (episodes lasting 7 days or less) or persistent AF (episodes lasting more than 7 days and less than 1 year) in the past 6 months, and the beta-1 389 arginine homozygous genotype that we believe responds most favorably to Gencaro. A subgroup of patients underwent continuous (24/7) heart rhythm monitoring via implanted loop recorders or other implanted therapeutic devices of Medtronic, Inc., or Medtronic, a global healthcare solutions company, to evaluate daily AF burden, or AFB. A prespecified time-to-first event analysis was conducted using a total AFB of at least 6 hours per day to define an event of AF recurrence.

Overall, Gencaro demonstrated a similar treatment benefit compared to the active comparator, TOPROL-XL (hazard ratio of 1.01 [95% confidence interval: 0.71, 1.42]). In the U.S. patient cohort of 127 patients (approximately 50% of all patients and events), a trend for benefit in favor of Gencaro over TOPROL-XL was observed (hazard ratio of 0.70, [95% confidence interval: 0.41, 1.19]). The GENETIC-AF results in the United States were consistent with what had been observed in the pharmacogenetic substudy of the BEST heart failure trial, taking into account that BEST was placebo controlled and GENETIC-AF was Gencaro versus an active comparator. However, our analysis also showed significant treatment effects in favor of Gencaro in a majority of patients in the trial, based on factors pre-specified in the statistical analysis plan.

We believe that the inclusion of a small number of patients in the trial (13.9% of overall population) with long-standing and heavily pretreated HF and AF led to attenuation of the treatment effect estimates for the primary endpoint of GENETIC-AF. Therefore, in accordance with procedures outlined in the Statistical Analysis Plan, post-hoc analyses were performed that excluded 37 patients with extraordinarily long durations of HF and AF (subjects who had been diagnosed with HF and/or AF for more than 12 years). In these analyses, we observed a trend for benefit in favor of Gencaro over TOPROL-XL by intermittent, clinic-based heart rhythm monitoring for the entire cohort (230 patients [N=115 for each treatment arm], hazard ratio of 0.68, [95% confidence interval: 0.45, 1.02]) and for the HFmrEF cohort (113 patients, hazard ratio of 0.61, [95% confidence interval: 0.34, 1.10]). The onset of AF relative to the development of HF was also identified in our post-hoc analyses to have a relationship to treatment effect. In these analyses, there was an attenuation of the treatment effect estimates for the primary endpoint in patients

who had long-standing AF (i.e., more than 2 years) prior to developing HF. We believe this is due to differences in the underlying pathophysiology for AF patients who eventually develop HF compared to HF patients who subsequently develop AF. Therefore, a post-hoc analysis was performed in the above patient population (N=230) that excluded patients who had developed AF for more than 2 years prior to developing HF. In these analyses, a significant reduction in the GENETIC-AF primary endpoint was observed in the overall population (N=196; HR=0.54; 95% CI: 0.33, 0.87; p = 0.011) and in the HFmrEF cohort (N=91; HR=0.42; 95% CI: 0.21, 0.86; p = 0.017). Based upon our analysis of the GENETIC-AF data, we believe further clinical development of Gencaro can be successful using entry criteria to identify HFmrEF patients with the characteristics for disease duration and onset described above and outlined in the following table:

GENETIC-AF Subgroup Analysis: Time to First AF/AFL/ACM Event

Population	Time to AF/AFL/ACM		
Subpopulation	N	HR (95% CI)	P-value
All Patients	267	1.01 (0.71, 1.42)	0.961
HF and AF for less than 12 years	230	0.68 (0.45, 1.02)	0.064
AF not more than 2 years prior to HF	196	0.54 (0.33, 0.87)	0.011
HFmrEF	91	0.42 (0.21, 0.86)	0.017

Stratified Cox proportional hazards model with adjustment for: 1) HF etiology, 2) LVEF, 3) rhythm at randomization, 4) device type, 5) previous Class 3 AA use (subpopulations only).

Gencaro was generally safe and well-tolerated, with 84% of patients attaining their target dose compared to 72% of patients receiving TOPROL-XL. The most frequently reported adverse events were similar in both groups and consistent with the known safety profile of the beta-blocker class of drugs. Adverse events assessed as related to study drug by the investigator occurred in 23.8% of patients in the Gencaro group and in 30.1% of patients in the TOPROL-XL group. Of note, adverse events of bradycardia were less frequently reported in the Gencaro group (3.7%) compared to patients receiving TOPROL-XL (12.0%). During the 24-week efficacy follow-up period there were three deaths (ACM) in the TOPROL-XL group and none in the Gencaro group. Three patients died in the long-term treatment extension period after receiving Gencaro for more than a year.

We believe data from the BEST trial indicate that Gencaro may have a genetically regulated effect in reducing or preventing AF in HFrEF patients. A retrospective analysis of data from the BEST trial shows that all patients in the trial treated with Gencaro had a 41% reduction in the risk of new onset AF (time-to-event) compared to placebo (p = 0.0004). In a substudy in the trial, which considered only patients with the genotype believed to enhance Gencaro's efficacy (known as the beta-1 389 arginine homozygous genotype), patients treated with Gencaro experienced a 74% (p = 0.0003) reduction in risk of AF, based on the same analysis. In addition, the BEST study, the beta-1 389 arginine homozygous genotype Gencaro demonstrated enhanced efficacy in reducing mortality, hospitalizations, and ventricular tachycardia /ventricular fibrillation, or VT/VF. Furthermore, patients with a beta 1 389 arginine homozygous genotype who entered the trial in AF had statistically significant reductions in major cardiovascular or HF mortality/hospitalization composite endpoints, which we believe is the first and thus far only demonstration of effectiveness of a beta-blocker in reducing major HF events in HFrEF patients with permanent AF. The beta-1 389 arginine homozygous genotype was present in about 50% of the patients screened and all enrolled patients in the GENETIC-AF trial and 47% of the patients in the BEST pharmacogenetic substudy, and we estimate it is present in about 50% of the North American and European general populations.

Our GENETIC-AF clinical trial of Gencaro required a companion diagnostic test to identify the patient's receptor genotype. Laboratory Corporation of America, or LabCorp, developed the genetic test, obtained an Investigational Device Exemption, or IDE, from the FDA and provided the companion diagnostic test and services to support our GENETIC AF trial. We retain all rights to the genetic test. Future clinical trials of Gencaro, if any, are expected to use a similar diagnostic test to identify the patient's receptor genotype.

Medtronic collaborated with us on the GENETIC-AF trial in supporting our AFB substudy. The collaboration was administered by a joint ARCA-Medtronic committee. Medtronic used its proprietary CareLink System to collect and analyze the cardiac rhythm data from the implanted Medtronic devices. In April 2018, Medtronic and ARCA agreed to extend the current U.S., Canadian and European Clinical Trial Collaboration Agreement for an additional year.

We have been granted patents in the United States, Europe, and other jurisdictions for methods of treating AF and HF patients with Gencaro based on genetic testing. If Gencaro is approved, we believe our patent portfolio and new chemical entity exclusivity may provide market exclusivity for the indications of Gencaro that we may develop for up to 10 years after approval in the United States, Europe and other markets, depending on when the drug is approved.

AB171

AB171 is a thiol-containing derivative of isosorbide mononitrate. Pre-clinical data from human endothelial cells indicate that compared to nitrates in clinical use, AB171 has a genotype specific enhancement of nitric oxide, or NO, release and produces less peroxynitrite, a biologically harmful product of nitrate action. AB171 also has potent anti-oxidant properties, and these effects may contribute to its favorable differentiation from other nitrates for prevention of myocardial remodeling, anti-atherosclerotic effects and the loss of effectiveness when used as a sustained therapy. We believe the unique pharmacology of AB171, coupled with targeting to genetically-identified enhanced response subpopulations, has the potential to translate to better long-term responses than currently

available treatments. We have identified what we believe to be a pharmacogenetic target for AB171 we believe may enable genetically-targeted cardiovascular development programs in two cardiovascular indications: HF and peripheral arterial disease. The European Patent Office has issued to us a patent on methods of treating cardiovascular disease and conditions with a thiol-substituted isosorbide mononitrate based on genetic targeting. The European patent has been validated in ten countries: Denmark, France, Germany, Ireland, Italy, Netherlands, Spain, Sweden, Switzerland and the United Kingdom. We also have related patent applications pending in the United States Patent Office and Canadian Intellectual Property Office.

We are currently designing the preclinical development plan for AB171 and initiated Investigational New Drug, or IND, enabling activities during 2018; subject to availability of capital, this work would be followed by nonclinical studies with AB171 to support future submission of an IND application, as a potential genetically-targeted treatment for peripheral arterial disease and for HF.

Financial Resources

To support the continued development of Gencaro, including the planned PRECISION-AF clinical trial, we will need additional financing to fund the Phase 3 trial and our general and administrative costs through its projected completion. Considering the substantial time and costs associated with the development of Gencaro and the risk that we may be unable to raise a significant amount of capital on acceptable terms, we may also pursue partnering and licensing opportunities, a strategic combination or other strategic transactions. If we are delayed in obtaining financing or are unable to complete a strategic transaction, we may discontinue our development activities on Gencaro or discontinue our operations.

We believe our cash and cash equivalents balance as of December 31, 2018, together with the $2.4 million of net proceeds raised in 2019 from sales of our common stock, will be sufficient to fund our operations, at our current cost structure, through the third quarter of 2019. However, 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.

In 2017, we entered into a sales agreement, as amended, with an agent to sell, from time to time, our common stock having an aggregate offering price of up to $10.2 million, in an “at the market offering.” In January 2019, we amended the amended sales agreement to increase the maximum aggregate value of shares which we may issue and sell from time to time under this sales agreement by approximately $2.5 million, from $10.2 million to $12.7 million. As of February 22, 2019, we have sold an aggregate of 9,242,406 shares of our common stock pursuant to the terms of such sales agreement, as amended, for aggregate gross proceeds of approximately $12.6 million. Net proceeds received in the period were approximately $11.9 million, after deducting initial expenses for executing the “at the market offering” and commissions paid to the placement agent. We have sold all shares available under the current prospectus.

On October 18, 2018, we held a special meeting of our stockholders to approve a series of certificates of amendment to the Company’s restated certificate of incorporation, as amended, to effect a reverse split of the Company’s outstanding common stock, at a ratio of between 1-for-3 and 1-for-20, inclusive, and to authorize the Company’s board of directors to, for a period of up to one-year, select and file such a certificate of amendment to effect such a reverse split of the Company’s outstanding common stock, if, in the our board’s judgment, it is deemed necessary. Our board of directors has not selected a ratio for the reverse split.

Our Strategy

Our mission is to become a leading biopharmaceutical company developing cardiovascular therapies, using genetic targeting, where possible, to enhance therapeutic response. To achieve this goal, we are pursuing the following strategies:

- Advance the development of Gencaro. We intend to advance Phase 3 clinical development of Gencaro as a therapy for HF patients with AF. In PRECISION-AF, we plan to evaluate Gencaro as a therapy for patients with HFmrEF, for whom no approved drug therapy currently exists. We received an SPA agreement for PRECISION AF that, if successful, could qualify as a single, pivotal trial and support the submission of an NDA for Gencaro. However, our execution of PRECISION-AF and other future Gencaro development is dependent upon our ability to finance those efforts through raising capital or a strategic partnership, or a combination thereof.
- Raise additional funding or complete a strategic transaction. To support our continued operations, we expect to seek additional funding through the sale of public or private equity or debt securities, the completion of a strategic transaction, or a combination thereof.
- Product lifecycle and indication expansion of Gencaro. We believe the treatment of AF in HFmrEF patients is an unmet medical need with a near-term and straightforward regulatory pathway. We believe there are product indication expansion opportunities for Gencaro for the entire spectrum of heart failure, including HFrEF and HFpEF patients with AF, other cardiac arrhythmias, and new formulation development. We are seeking the support of strategic partners to develop these opportunities.

- Advance the development of AB171. During 2018, we initiated IND-enabling development activities with AB171, a thiol-substituted isosorbide mononitrate, as a potential genetically-targeted treatment for HR and peripheral arterial disease. Further development of AB171 is dependent on additional financing.
- Build a cardiovascular pipeline. Our management and employees, including our chief executive officer, are experienced in cardiovascular research, molecular genetics and clinical development of cardiovascular therapies. We are seeking to leverage this expertise to identify, acquire and develop other cardiovascular products or candidates, particularly those with potential for pharmacogenetic based development, such as AB171.

Our strategies are dependent upon our ability to obtain additional funding through the sale of public or private equity or debt securities, the completion of a strategic transaction, or a combination thereof. If we are unable to secure additional funding or complete a strategic transaction, we may not be able to continue development of Gencaro, notwithstanding our receipt of an SPA agreement from the FDA.

Atrial Fibrillation in Heart Failure Market Background and Opportunity

Heart failure is a chronic condition in which the heart is unable to pump enough blood to meet the body's demands for oxygen. Heart failure has numerous serious consequences, including severe impacts on quality of life, increased hospitalizations, lost wages and productivity, and premature death. Heart failure is the leading cause of death in the developed world. According to the 2019 American Heart Association, or AHA, Heart Disease and Stroke Statistics, there were an estimated 6.2 million Americans aged 20 years or more with HF (based on data between 2013 and 2016). The spectrum of heart failure includes HF in which LVEF is 50% or more and is considered preserved ejection fraction, known as HFpEF, and heart failure in which the LVEF is less than 40%, considered reduced ejection fraction, or HFrEF and LVEF of at least 40%, but less than 50%, considered mid-range ejection fraction, known as HFmrEF. Together, HFrEF and HFmrEF comprise an estimated 64% of all HF patients in the United States. In 2012, the economic cost of HF in the United States was estimated to be nearly $31 billion, of which two-thirds, or over $20 billion, was attributable to direct medical costs.

HFmrEF is a subgroup of HF patients with reduced LVEF for whom there are no approved AF drug therapies. The prevalence of AF is higher in HFmrEF patients as compared with HF generally; it is estimated that 30%-60% of HFmrEF patients also have AF. Approximately one-half of the trial population in GENETIC-AF Phase 2B study were HFmrEF patients. In patients with heart failure, atrial fibrillation contributes to the disease processes that lead to the progression of heart failure and worsening clinical outcomes including hospitalizations and death. This increased risk of illness and death when AF is present with heart failure is true across the spectrum of HF, including HFmrEF.

AF, the most common sustained cardiac arrhythmia, is a potentially serious disorder in which the normally regular and coordinated contraction pattern of the heart's two small upper chambers, or the atria, becomes irregular, rapid and uncoordinated. AF can have significant quality of life impacts and potentially serious medical consequences, including increasing the risk of stroke and other cardiovascular problems. In individuals with heart failure, AF contributes to the disease processes that lead to the progression of heart failure and worsening clinical outcomes. AF is considered an epidemic cardiovascular disease and a major public health burden. The estimated number of individuals with AF globally in 2015 was 33.3 million. According to AHA Heart Disease and Stroke Statistics Reports from 2017 - 2019, the prevalence of AF in the United States was estimated to be 5.2 million people in 2015. In the European Union, the prevalence of AF was estimated to be 8.8 million (age 55 and over) in 2010. It is estimated that AF costs the U.S. economy about $6.0 billion annually.

AF and HF share many of the same risk factors and about 40% of people having either AF or HF will develop the other condition. Both AF and HF are related to dysfunction and remodeling of the myocardium, and as such share many pathophysiologic features including chamber dilatation, increased interstitial fibrosis and cardiac myocyte apoptosis. However, longstanding AF that eventually leads to left ventricular dysfunction and HF has a different pathophysiology compared to HF with AF developing secondarily. In longstanding AF, fibrosis and hypertrophy develop in both the atrium and ventricles, whereas in HF that precedes AF there is predominantly eccentric hypertrophy and contractile dysfunction in the ventricle and to a lesser extent in the atrium, with only minimal fibrosis

in most cases.

Although AF increases stroke risk above an already increased risk in HF, this risk can be mitigated by administration of oral anticoagulants. Although stroke is the most feared complication of AF, it is the increased risk of mortality and hospitalization conferred by new onset AF in HF that is of major concern. AF in patients with HF may predispose to progression of the disease, including worsening of left ventricular dysfunction, increased hospitalization burden, and increased risk of death. This increased risk of morbidity and mortality with AF appears to be true across the spectrum of HF, including HFmrEF.

Relationship of AF to Clinical Outcomes

AF is an important cardiovascular, or CV, endpoint and it has an even greater impact in patients with HF. An important clinical consequence of AF in HF is an increase in the risk of embolic events including stroke, and for this reason alone it is preferable for a HF patient to be in sinus rhythm, or SR. In patients with established HF it is clear that new onset AF, including new AF events after conversion of persistent AF to SR, is associated with increased mortality and worsening HF risks. Framingham Heart Study data indicate there is a potential interrelationship between the development of AF and HF, with each condition developing as HF progresses and often (21% of the time) both presenting contemporaneously. In the Framingham study, when AF developed after HF there was a 1.6-fold (95% CI: 1.2, 2.1) increase in mortality after adjusting for potential modifiers, and when HF developed after AF the hazard ratio was 2.7 (95% CI: 1.9, 3.7).

Additional supporting data is from the Women's Health Study, which is based on 1011 AF cases developed over a 15.4 year span. In this study, new onset AF was associated with a 2.1-fold (95% CI: 1.6, 2.8) increase in ACM and a 4.2-fold (95% CI: 2.7, 6.5) increase in CV mortality. Moreover, in women with new onset AF, the risk of developing HF increased by 14.7-fold (95% CI: 11.2, 19.2). New onset AF also worsens the prognosis in patients with established HF, a finding that was observed in the BEST trial as well.

Treatment of Atrial Fibrillation in Heart Failure

Effective medical therapy for HF patients with AF must address both disease conditions. Patients with both HF and AF have a significantly worse prognosis, and therefore we believe effective therapies for these patients should be of paramount importance. However, the current drug therapy options for patients with both heart failure and atrial fibrillation are limited. Treatments that have been approved and are effective for HF or AF in isolation are now understood to have efficacy and/or safety limitations if used in patients in whom both conditions are present. Importantly, none of the beta blockers approved for heart failure, or other indications, have been studied exclusively in or approved for patients with HFmrEF, a substantial segment of the total HF population.

In treating heart failure, several drugs classes have been shown to improve outcomes and ameliorate symptoms and are now considered standard of care, including in patients with co-morbid AF. Three drugs in the beta-blocker class are approved in the United States for the treatment of heart failure (metoprolol, carvedilol, and bisoprolol). These drugs have the highest level of recommendation in the United States and European Union heart failure guidelines and are prescribed for most patients with HFrEF who also have AF. They continue to be viewed as foundational therapy for these patients in part for their efficacy in controlling the high heart rate that is typically found with AF, rate control, and is believed to contribute to the pathological effects of AF in HF patients. However, the beta blockers approved for HF are only mildly effective at maintaining normal cardiac rhythm, or rhythm control, a characteristic recognized as increasingly important in treating AF. Furthermore, recent evidence indicates that the efficacy of these beta blockers is uncertain when AF is present and becomes permanent. Additionally, none of these beta blockers have been exclusively studied in patients with HFmrEF, thus there is limited evidence of efficacy in patients with HFmrEF, a substantial subgroup of the HF population and about one half of the study population in GENETIC-AF. Therefore, we believe there is a significant unmet medical need for a beta-blocker with greater efficacy in controlling AF and in providing better symptom relief and outcome benefits for these patients, including patients with HFmrEF.

The goals of current medical therapy for AF are to maintain sinus rhythm or to control ventricular rate in patients who cannot maintain sinus rhythm in order to minimize patient symptoms and avoid the risk of further complications and disease progression. Addressing the rhythm and rate abnormalities of AF is believed to be particularly important in HF patients because of the relationship between the presence of AF and worsening heart failure. However, the current treatment options for controlling AF in HF patients have significant limitations. Anti-arrhythmic drugs are a drug class that is often prescribed to control the irregular heartbeat of AF, and these drugs are frequently used in addition to

beta-blockers in patients with both heart failure and atrial fibrillation to treat the AF arrhythmia. However, most anti-arrhythmic agents with AF indications are either contraindicated or have significant label warnings for use in HF patients due to an increased risk of mortality.

In the United States, anti-arrhythmic drug therapy is confined to the Class 3 anti-arrhythmic agents, amiodarone and dofetilide, and amiodarone is not approved for the treatment of AF. In addition, amiodarone has multiple toxicities, is pro-arrhythmic, and likely increases mortality in HFrEF. Although the pro-arrhythmia of dofetilide can be reduced by in-hospital monitoring on institution of therapy, this requirement of dofetilide use does not preclude the potential occurrence of drug induced arrhythmias that can result in death. Considering these safety concerns, physicians treating heart failure patients seek to limit the use of anti-arrhythmic drugs.

Surgical techniques, such as ablation, are also used in some patients with heart failure to control the arrhythmia of atrial fibrillation. However, surgical methods are invasive and have other drawbacks, and are not a substitute for drug therapy to provide heart failure benefits, such as with beta-blockade, but rather are generally used in heart failure patients as an additive therapy. Anticoagulants are effective against the risk of stroke in AF patients and are widely prescribed, but these drugs do not address the pathological effects of the irregular and rapid heartbeat that is the hallmark of AF.

Consequently, we believe there is an unmet medical need for new therapeutics that may provide better treatment for patients with HF and AF, which can safely treat the rhythm and rate disorders in these patients with greater efficacy, while improving their clinical outcomes and prognoses.

Gencaro

Gencaro (bucindolol hydrochloride) is a nonselective beta-adrenergic receptor blocking agent with mild vasodilator properties. Gencaro is considered part of the beta-blocker class of compounds because of its property of blocking both beta-1 and beta-2, receptors in the heart. The blocking of these receptors prevents them from binding with other molecules, primarily the neurotransmitter norepinephrine, or NE, which activate these receptors. We believe Gencaro has two unique anti-adrenergic properties not possessed by other beta-blockers currently approved for the treatment of HF: (1) it is moderately sympatholytic, i.e., it lowers adrenergic drive to a level that can be detected on measurements of central or systemic venous norepinephrine levels, and, (2) through “inverse agonism” promotes inactivation of active-state human myocardial beta-1 receptors in a genotype specific manner. These properties, as described below, were observed to interact with receptor polymorphisms in such a way that we believe targeting specific genotypes of these variants could improve the therapeutic response of patients. We believe Gencaro’s efficacy is enhanced in patients with the beta 1 389 arginine homozygous genotype, which we estimate is present in about 50% of the North American and European general populations.

Gencaro was the subject of the BEST trial, a Phase 3 HF mortality trial in 2,708 patients, mostly in the United States. The BEST trial included a DNA bank of over 1,000 patients, which was used to evaluate the effect of genetic variations in cardiac receptors on patients’ response to Gencaro. ARCA-affiliated scientists conducted genetic sub-studies with data from the BEST DNA bank that showed patients with certain variations in these receptors had substantially improved outcomes on primary and certain secondary clinical endpoints in the BEST trial, such as mortality, cardiovascular mortality, HF progression, hospitalization and prevention of arrhythmias, relative to the counterpart genotype groups and the general patient population of the trial. We believe that these genetically determined receptor variations, which are detectable using standard DNA testing technology, can serve as diagnostic markers for predicting enhanced therapeutic response to Gencaro, and potentially avoiding adverse events in individual patients. We have patented our methods for treating AF and HF patients with Gencaro in the United States, Europe and other markets based on genetic testing.

Pharmacology and Pharmacogenetics

Gencaro’s pharmacology appears to be different from other compounds in the beta-blocker class in several fundamental respects. First, under previous sponsors, studies in human myocardial preparations showed Gencaro, but not other tested beta-blockers approved to treat HF, predisposes to a shift in equilibrium of beta-1 389 arginine but not 389 glycine receptors from a constitutively active to an inactive state, a property known as inverse agonism. Second, other studies, including BEST, indicated that Gencaro lowers the systemic levels of the neurotransmitter norepinephrine, or NE, released by cardiac and other adrenergic nerves. The beta-1 389 arginine receptor, 100% of the receptor population in patients with a 389 arginine homozygous genotype, has much higher affinity for binding to NE compared to 389 glycine receptors, and published data indicate that NE lowering from Gencaro is beneficial in patients who have only beta-1 389 arginine receptors. In contrast, patients with lower NE affinity beta-1 389 glycine genotypes may have blunting of efficacy from greater amounts of NE lowering. We believe that Gencaro's inverse agonist property contributes to the enhanced lowering of heart failure and arrhythmia event rates in patients who are beta-1 389 arginine homozygous genotype relative to individuals who are beta-1 389 Gly carriers or to the general population. In addition, we believe the unique NE lowering properties of Gencaro have a selectively beneficial effect in patients who have only beta-1 389 arginine receptors, because of the high affinity of these receptors for NE. As a result, the GENETIC-AF trial was targeted at patients with the beta-1 389 arginine homozygous genotype, which was present in approximately 50% of screened patients. We believe that these properties and their pharmacogenetic implications for modulating effectiveness are unique to Gencaro, and if the drug is approved, will be described in in the prescribing information.

Gencaro Heart Failure Development and the DNA Substudy

Gencaro was the subject of a major heart failure study known as the BEST trial, a double-blind, placebo-controlled, multi-center study of bucindolol's effect on reduction of mortality and morbidity in an advanced chronic HF population (LVEF less than 35%). The primary endpoint of the BEST trial was ACM, and the pre-specified main secondary endpoint was progression of HF, defined as death from HF, cardiac transplant, HF hospitalization, or an emergency room visit for the treatment of worsening HF not requiring hospitalization. The trial was planned to run four and one-half years, and enroll 2,800 patients. The trial enrolled a total of 2,708 chronic, mostly U.S., HF patients. The trial was notable for including a major DNA bank, in which 1,040 of the BEST patients participated by providing blood for DNA analysis. The DNA bank provided the basis for the genetic substudies that discovered Gencaro's modulation by genetic variations of the beta-1 cardiac receptor.

The BEST trial was terminated early because, after positive mortality results from two other HF trials involving other beta-blockers had been reported, a substantial number of BEST trial investigators concluded that it was unethical to continue to give placebo to

BEST trial participants. It was initially reported the trial had failed to reach its primary endpoint of ACM, showing a 10% risk reduction in mortality with a p-value of 0.10. Our reanalysis of the BEST results in accordance with the FDA approved, pre-specified statistical analysis plans (which had not been performed by the sponsors of BEST) demonstrated a 13% risk reduction on the primary endpoint of ACM in the BEST trial with a p-value of 0.053.

The results of the genetic substudies that were conducted using the BEST DNA bank were not available until several years after the completion of the trial. Importantly, these substudies indicated a significant enhancement of response on the major heart failure clinical endpoints from the BEST trial in patients with the beta-1 389 arginine homozygous genotype. The risk reduction on HF clinical efficacy endpoints such as mortality and hospitalization ranged from 34% to 48% in this genotype. In addition, in arrhythmia endpoints of atrial fibrillation, or VT/VF, tracked by adverse events, or AEs, and surveillance electrocardiograms, or ECGs, the risk reduction by bucindolol in the beta 1 389 arginine homozygous genotype appeared to be even greater, with risk reductions of 74% for both endpoints.

Shown below are certain of the primary and secondary endpoint data from the BEST HF DNA substudy results, by genotype:

BEST Trial Clinical Responses† by Genotype Groups

Endpoint (entire BEST DNA substudy, n = 1040 patients)	{beta-1 389 Arg/ Arg + any alpha-2C} "Very Favorable" Patient Type (47%)	{beta-1 389 Gly carrier+ alpha-2C Ins/Ins} "Favorable" Patient Type (40%)	{beta-1 389 Gly carrier + alpha-2C Del carrier} "Unfavorable" Patient Type (13%)
All Cause Mortality (ACM), TTE	38%*	25%	4%
Cardiovascular Mortality (CVM), TTE	48%*	40%*	11%
ACM + transplantation	43%*	24%	4%
HF (HF) Progression	34%**	20%	1%
HF Hosp days/patient	48%**	17%	19%
AF prevention (from AE and ECG db) ‡	74%**	6%	33%
VT/VF prevention (from AE db)	74%**	49%*	24%
Entered DNA substudy in AF, n = 111	beta-1 Arg/Arg, any alpha-2C	beta-1 389 Gly C, any alpha-2C	
ACM/HF Hosp, TTE	77%*	52%	
Cardiovascular (CV) mortality/CV Hosp	72%*	7%	

†Covariate adjusted, transplant censored analysis with 1 – hazard ratio estimates presented ‡n 925 patients who entered in SR
*p<0.05; **p ≤ 0.007; TTE: Time To Event
Analysis of BEST trial for AF

The BEST study data were further analyzed focusing on AF prevention, rate control in patients with established AF, and on clinical outcomes of patients with AF. Although there was no pre-determined AF endpoint, including reduction in risk of AF, in the BEST trial, according to our analysis of adverse events and surveillance ECG's during the trial, 7.9% of patients developed new onset AF, with a greater incidence observed in the placebo group (9.7%) compared to the bucindolol group (6.2%). This corresponded to a 36% reduction in the incidence of new onset AF (based on crude

event rates) for patients receiving bucindolol ($p = 0.002$). In a time to event analysis, the risk of new onset AF was reduced by 41% ($p = 0.0004$) with bucindolol treatment. Patients in the BEST study with the beta-1 389 Arg/Arg genotype who received Gencaro had a 74% reduction in the risk of developing new onset AF ($p = 0.0003$).

Further published analyses of the data from BEST suggest that Gencaro may also have potential efficacy for other clinical endpoints and outcomes related to AF. A published analysis of the BEST data revealed that of the 303 patients in the BEST trial with established AF, 67% of those who received Gencaro achieved ventricular response rate control, defined as a resting heart rate of less than or equal to 80 beats per minute without symptomatic bradycardia ($p < 0.005$). In AF patients who achieved ventricular response rate control, Gencaro produced a 39% reduction ($p = 0.025$) in cardiovascular mortality/cardiovascular hospitalizations. In addition, Gencaro also improved cardiovascular clinical endpoints for those AF patients possessing the beta-1 389 arginine genotype that ARCA believes is most favorable for Gencaro response. In a substudy of 1,040 patients in BEST in which patient genotypes were analyzed, Gencaro was associated with a 72% decrease ($p = 0.039$) in cardiovascular mortality/cardiovascular hospitalizations in those 52 AF patients in the substudy with the beta-1 389 arginine homozygous genotype.

Analysis of the BEST Study data also shows that Gencaro has potential efficacy against the serious arrhythmias of VT/VF, which also appears to be genetically regulated. A published report demonstrated that patients in the BEST Trial who received Gencaro experienced a 58% reduction in the incidence of VT/VF ($p = 0.00006$), adjusted for the competing risk of mortality. In addition, the authors of this report determined that Gencaro reduced the incidence of VT/VF by 74% ($p = 0.00005$) in patients with the beta-1 389 arginine homozygous genotype.

Clinical and Regulatory Strategy

The regulatory strategy for Gencaro is to obtain an initial approval to treat atrial fibrillation in a genotype specific population with HFmrEF. We enrolled patients with the beta-1 389 arginine homozygous genotype in our GENETIC-AF Phase 2B clinical trial because our analysis of the BEST DNA substudy demonstrated a 74% reduction in AF events, in addition to reducing event rates for major clinical endpoints such as mortality and HF hospitalizations.

In February 2018, we reported the results of GENETIC-AF, our Phase 2B clinical superiority trial, in which we evaluated Gencaro for the treatment and prevention of recurrent AF in patients with HF (LVEF less than 0.50). GENETIC AF compared Gencaro to TOPROL-XL (metoprolol succinate), a drug approved for treating HFrEF that is considered a standard of care for treating AF in patients with HFrEF. The GENETIC-AF trial only enrolled patients with the beta 1 389 arginine homozygous genotype, the specific genotype that we believe enhances Gencaro's potential therapeutic effects. Overall, Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate. However, additional analyses prespecified in the statistical analysis plan also showed clinically meaningful treatment effects in favor of Gencaro in a large majority of the Phase 2 population. Gencaro also showed a significant treatment effect compared to Toprol XL in reducing AF recurrence in a subgroup of HF patients with HFmrEF. About one-half of the GENETIC-AF population were HFmrEF patients, a HF population for which there are no approved or guideline-recommended therapies. We plan to conduct a Phase 3 pivotal superiority trial, known as PRECISION-AF, evaluating Gencaro in this population because of Gencaro's observed potential treatment effect in these patients in the GENETIC AF trial, the unmet medical need for approved or guideline recommended drug therapies for prevention of AF in HFmrEF patients, and what we believe to be a near-term path to potential regulatory approval with this indication.

Based on our GENETIC-AF trial results, as well as results of previous Phase 3 pharmacogenetic substudy data from the Phase 3 heart failure clinical trial of bucindolol, known as the BEST trial, we submitted an SPA to the FDA detailing our proposed Phase 3 clinical trial and potential approval path for Gencaro. In February 2019, we received an SPA agreement for PRECISION-AF, a Phase 3 pivotal study comparing Gencaro against TOPROL-XL for the treatment of AF in HFmrEF patients with the beta-1 389 arginine homozygous genotype. FDA also provided guidance on the possible development of Gencaro in HFrEF and HFpEF patients, which we feel are potential product life cycle opportunities for Gencaro.

The PRECISION-AF Phase 3 clinical trial is designed as a double-blind, active-controlled, multicenter, international, adaptive study comparing Gencaro with TOPROL-XL for the prevention of recurrent AF/AFL or ACM, in HFmrEF patients. The study will enroll approximately 400 patients at investigative sites in the United States, Europe and Australia. Eligible patients will have HFmrEF, a recent AF event and the genotype which responds most favorably to Gencaro. A substudy planned to include a smaller group of patients within the trial would utilize AFB as one method to determine AF recurrence, as measured by an implanted cardiac electronic device. The planned trial will use standard significance criteria ($p < 0.01$with adjustment for interim analysis) for the primary endpoint and will include an interim analysis after a portion of total patients have been enrolled. The interim analysis is designed to assess safety, validate initial study assumptions and maintain adequate statistical power for the primary endpoint. Subject to

securing significant additional financing, we anticipate initiating PRECISION-AF in the fourth quarter of 2019. Any future development of Gencaro, including initiating the Phase 3 clinical trial, is dependent on obtaining additional financing, even if we enter into a strategic collaboration around the development of Gencaro.

In 2015, the FDA designated the investigation of Gencaro for the prevention of atrial fibrillation/atrial flutter in a genetically targeted heart failure population (heart failure patients with reduced LVEF) as a Fast Track development program.

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

The Gencaro Test

If approved, we believe that Gencaro will be the first cardiovascular drug to be integrated with a companion diagnostic to predict enhanced efficacy. We believe the drug label we will propose for Gencaro would identify the patient receptor genotype studied in the trial that can expect enhanced efficacy and, and that the label would recommend receptor genotype testing prior to initiation of therapy. Therefore, the commercialization of Gencaro may require that an FDA approved diagnostic test for this genotype be available. Such a test, or the Gencaro Test, could be performed by a variety of laboratory processes or platforms. We used one such platform for the GENETIC-AF trial, and retain all rights to it. We believe the Genaro Test could be developed and commercialized through a preferred diagnostic provider, by the company marketing Gencaro, or a combination of approaches. We also believe that point of care genetic tests, which could be performed during the patient's visit to the physician, may be feasible as part of the commercialization strategy.

Our GENETIC-AF clinical trial of Gencaro required a companion diagnostic test to identify the patient's receptor genotype. Laboratory Corporation of America, or LabCorp, developed the genetic test, obtained an IDE from the FDA and provided the companion diagnostic test and services to support our GENETIC-AF trial. We retain all rights to the genetic test. Future clinical trials of Gencaro, if any, are expected to use a similar diagnostic test to identify the patient's receptor genotype.

Licensing and Royalty Obligations

We have licensed worldwide rights to all preclinical and clinical data from development of bucindolol through the BEST trial from Cardiovascular Pharmacology and Engineering Consultants, LLC, or CPEC, who has licensed rights to this data from BMS. In addition, we have sublicensed CPEC's rights from Bristol Meyers Squibb, or BMS. CPEC is a licensing entity which holds the rights of the biotechnology companies that were the commercial sponsors of the BEST trial. If the FDA grants marketing approval for Gencaro, the license agreements state that we are required to make a milestone payment of $8.0 million within six months after FDA approval. The license agreements also state that we are required to make milestone payments of up to $5.0 million in the aggregate upon regulatory marketing approval in Europe and Japan. The licenses state that our royalty obligations range from 12.5% to 25% of revenue from the related product based on achievement of specified product sales levels including a 5% royalty that CPEC is obligated to pay BMS. The agreements state that we have the right to buy down the royalties to a range of 12.5% to 17% by making a payment to CPEC within six months of regulatory approval. In October 2017, we entered into an agreement with CPEC's minority owner, Aeolus Pharmaceuticals, Inc., or Aeolus, pursuant to which we acquired Aeolus' minority membership interest in CPEC. The transaction effectively buys-out Aeolus' royalty interest thereby reducing or eliminating the stated milestone and royalty obligations by 35% that could be payable by us, if Gencaro receives regulatory approval and is commercialized. In the transaction, we also acquired all of CPEC's rights to milestones and royalties for Europe and certain other territories outside of the United States.

All of the patents that were the subject of the CPEC and BMS licenses have expired. Based on this and the terms of these licenses, we believe that the financial obligations stated in these agreements will be reduced or eliminated, if and when they become payable under their stated terms.

We also have licensed worldwide rights to intellectual property covering the pharmacogenetic response of Gencaro based on the cardiac receptor polymorphisms, which is owned by the University of Colorado. We have no material future financial obligations under this license. We also have licensed exclusive, worldwide rights to develop and commercialize diagnostics for these receptor polymorphisms, for the purpose of prescribing Gencaro.

Development Pipeline

Our development activities are substantially focused on our lead product candidate, Gencaro, for the potential treatment of HF patients with AF. The primary endpoint of the GENETIC-AF trial was the prevention of AF in these

patients. We believe the treatment of AF in HFmrEF patients is an unmet medical need with a near term and straightforward regulatory pathway. We believe there are product indication expansion opportunities for Gencaro for the entire spectrum of heart failure, including HFrEF and HFpEF patients with AF, other cardiac arrhythmias, and new formulation development. We are seeking the support of strategic partners to develop these opportunities. Finally, we have developed and patented an isomer version of bucindolol, which appears to be substantially more potent than the current formulation.

We do not expect to pursue development of Gencaro for HFmrEF patients with AF or other disease indications without obtaining additional funding or entering into a strategic partnership or collaboration. We believe Gencaro has potential to address these additional indications, and that the clinical response of patients with these diseases may be genetically influenced, based on the same genetic markers we have identified for our proposed treatment of AF with Gencaro.

AB171 is a thiol-containing derivative of isosorbide mononitrate. Pre-clinical data indicate that AB171 may have anti-oxidant properties and may be favorably differentiated from other nitrates for prevention of myocardial remodeling, anti-atherosclerotic effects and the loss of effectiveness when used as a sustained therapy. We believe the unique pharmacology of AB171, coupled with targeting to genetically-identified enhanced response subpopulations, has the potential to translate to better long-term responses than currently available treatments. We have identified what we believe to be a pharmacogenetic target for AB171 that is the basis for our patents and which we believe may enable genetically-targeted cardiovascular development programs in two cardiovascular indications: HF

and peripheral arterial disease. The European Patent Office has issued to us a patent on methods of treating cardiovascular disease and conditions with a thiol-substituted isosorbide mononitrate based on genetic targeting. The European patent has been validated in ten countries: Denmark, France, Germany, Ireland, Italy, Netherlands, Spain, Sweden, Switzerland and the United Kingdom. We also have related patent applications pending in the United States Patent Office and Canadian Intellectual Property Office.

We are currently designing the preclinical development plan for AB171 and initiated IND enabling activities during 2018, and subject to availability of capital, to be followed by nonclinical studies with AB171 to support future submission of an IND application, as a potential genetically-targeted treatment for HF and peripheral arterial disease.

We also have exclusive pharmacogenetic and other patent rights to drug candidates that have potential indications in cardiovascular disease, oncology and other therapeutic areas. We may seek partners to assist us in the development of these candidates or who may license them. We may also seek funds to advance the development of the compounds on our own.

Competition

Current HF treatments include three beta-blockers approved for heart failure in the Unites States. However, their efficacy in providing control of the arrhythmia caused by AF, or rhythm control, is only mild. It is also now acknowledged that evidence is lacking that the approved beta-blockers provide outcome benefits for patients who develop permanent AF. Furthermore, these drugs have not demonstrated efficacy for patients with HFmrEF, a population included in the Gencaro development program. Current AF treatments include pharmaceutical, procedural or device intervention. There are several antiarrhythmic drugs approved by the FDA for the treatment and/or prevention of recurrent AF. However, these drugs have safety and/or administration concerns and all but one have contraindications or label warnings regarding their prescription in patients with heart failure.

Drugs that are currently approved or used for the treatment or prevention of AF in HF, including HFmrEF, either have not demonstrated efficacy in these patients, or have notable risks due to adverse side effects or lack sufficient efficacy. Therefore, in HF, and specifically in HFmrEF patients, we believe there is a substantial unmet medical need for AF therapies that are more effective and have fewer side effects than those currently available. We believe that Gencaro's treatment of AF in HF patients could provide a more effective and safer pharmacotherapy than treatments currently used in these patients.

The pharmaceutical industry is highly competitive. We face significant competition from pharmaceutical companies and biotechnology companies that are researching and selling products designed to treat cardiovascular conditions. Most of these companies have significantly greater financial, product development, manufacturing, and commercial resources than we have.

If approved, the drugs which Gencaro would potentially compete with are largely generic in the United States. Gencaro would be priced at a premium compared to these therapies. In addition, our proposed prescribing information for Gencaro includes a recommendation for genetic testing, which will add additional procedures to the process of prescribing Gencaro, which, together with its premium price, could make it more difficult for us to compete against existing or future therapies.

Manufacturing and Product Supply

Gencaro is a small molecule drug with an established manufacturing history. Multiple manufacturers of both the active pharmaceutical ingredients, or API, and drug product have successfully produced Gencaro for use in clinical trials over the course of its clinical development. We outsource all manufacturing and analytical testing of the Gencaro API and drug product. We have selected third party contract manufacturing organizations on the basis of their technical and regulatory expertise. Our approach with our contract manufacturing partners has been to replicate

the manufacturing processes that were used to support the prior pivotal clinical trial with Gencaro, and to minimize any changes from these baseline processes, thereby reducing technical and regulatory risk. We contracted with Groupe Novasep to complete the drug substance registration batches required for the Gencaro NDA. These batches were successful, and the resulting drug substance was used to supply the drug product registration campaign. Remaining inventory was placed in current Good Manufacturing Practice, or cGMP, storage to provide a backup supply for the GENETIC-AF trial, and for use as an initial source of drug substance to support eventual product launch, if approved.

For drug product production, we have contracted with Patheon, Inc. to manufacture the Gencaro tablets. Gencaro is produced in a tablet form, utilizing standard solid oral dosage processing techniques. Six separate dosage strengths were manufactured, with the maximum recommended dose of 50mg twice daily for patients weighing 75kg or less and 100mg twice daily for patients weighing more than 75kg. Registration batches were successfully completed by Patheon, Inc. and tablets from these runs were placed in cGMP storage to supply the GENETIC-AF trial. In addition, we contracted with a separate service provider for packaging and distribution of our clinical trial materials.

Research and Development Expenses

Our research and development expenses were $4.2 million for the year ended December 31, 2018 as compared to $14.1 million for 2017, a decrease of approximately $9.8 million. Subject to securing significant additional financing, we anticipate initiating our PRECISION AF clinical trial in the fourth quarter of 2019. R&D expense in 2019 is expected to be higher than 2018, if we initiate our PRECISION AF clinical trial. If we are unable to initiate our PRECISION AF clinical trial, then R&D expense is expected to be lower than 2018.

Government Regulation

Governmental authorities in the United States at the federal, state, and local levels and foreign countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, marketing, distribution, sampling, and import and export of pharmaceutical and medical device products. In the United States, the FDA regulates these activities at the federal level pursuant to the Federal Food Drug and Cosmetic Act, or the FDCA, and the regulations promulgated thereunder. In Canada, Health Canada regulates these activities. In Europe, the Competent Authorities and Ethics Committees of the respective countries regulate these activities. We anticipate that all of our product candidates will require regulatory approval by governmental agencies prior to commercialization. The process of obtaining approval and the subsequent process of maintaining compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. In addition, these statutes, rules, regulations and policies may change and our products may be subject to new legislation or regulations. Both before and after approval or clearance, failure to comply with the requirements of the FDA and other state and federal statutes can lead to significant penalties or could disrupt our ability to manufacture and sell these products. In addition, the FDA could refuse to provide certificates needed to export our products if the agency determines that we are not in compliance.

Premarket Approval of Drugs

FDA approval is required for marketing of any new drug, dosage form, indication, or strength. The steps required before new human therapeutic drug products are marketed in the United States and foreign countries include rigorous preclinical and clinical testing and other approval requirements by regulatory agencies, such as the FDA and comparable agencies in foreign countries. There is no guarantee that products will be approved in a specific timeframe or at all.

Preclinical Phase. Preclinical studies are generally conducted in the laboratory to identify potential drug candidates and to evaluate their potential efficacy and safety. These studies include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate short and long-term toxicity in animals. Preclinical studies are governed by numerous regulations, including but not limited to FDA’s Good Laboratory Practices.

Clinical Phase. Before human clinical trials can commence, an Investigational New Drug, or IND, application, submitted to FDA must become effective. For an IND to become effective, the applicant must submit, among other things, information on design of the proposed investigation, reports necessary to assess the safety of the drug for use in clinical investigation, and information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies. The clinical phase of development involves the performance of human studies, including adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication. Typically, clinical evaluation involves three sequential phases, which may overlap. During Phase 1, clinical trials are conducted with a relatively small number of subjects or patients to determine the early safety profile of a product candidate, as well as dose tolerance, absorption, and the pattern of drug distribution and drug metabolism. Phase 2 trials are conducted with groups of patients afflicted by a specific target disease to determine preliminary efficacy, optimal dosages and dosage tolerance and to identify possible adverse effects and safety risks. In Phase 3, larger-scale, multi- center trials are conducted with patients afflicted with a specific target disease over a longer term to confirm Phase 2 results and provide reliable and

conclusive data supporting efficacy and safety of a drug as required by regulatory agencies for drug approval. The conduct of clinical trials is subject to extensive regulation. FDA may delay or suspend clinical trials through clinical holds.

NDA Submission. In the United States, the results of preclinical and clinical testing along with chemistry, manufacturing and controls information, are submitted to the FDA in the form of an NDA. Under the current Prescription Drug User Fee Act, or PDUFA, after submission of an NDA and payment, or waiver, of the required fee, the FDA's goal is to review most standard NDAs within 10 months from the time that a sponsor's application is accepted as filed by the FDA, which can occur within a 60-day window following the initial submission of the application. At the end of the 10 months, the FDA's goal is to issue a "complete response," or approve the NDA. While FDA's goal is to issue a complete response within 10 months, the process may take longer than 10 months, particularly if multiple review cycles are required. Gencaro has been granted Fast Track Designation which allows for a rolling review of a marketing application. A rolling review allows FDA to consider reviewing portions of an NDA before the sponsor submits the complete application.

In responding to an NDA, the FDA may grant marketing approval or deny the application if the FDA determines that the application does not satisfy the statutory and regulatory approval criteria. A denial may include a request for additional information, including additional clinical data and/or an additional Phase 3 clinical trial. Data from clinical trials are not always conclusive and FDA may interpret data differently than we interpret data. Under the Food and Drug Modernization Act of 1997, the FDA is authorized to approve a drug based on a single adequate and well-controlled study if such study and other confirmatory data are sufficient to establish the drug's effectiveness. However, it has long been the FDA's general position that the standard of proof of a drug's effectiveness generally requires at least two well-controlled and adequate Phase 3 clinical studies demonstrating statistically significant results as compared to a placebo or active control (with p-values of less than 0.05) with respect to the primary endpoint or endpoints of the trial.

In addition, in accordance with current FDA law and regulations, the FDA may refer a drug to an advisory committee for review prior to approval. Most new compounds are referred to an FDA advisory committee, which could add additional time to the review process. There is no guarantee that the advisory committee will recommend approval of a drug candidate. In some cases, FDA may require completion, within a specified time period, of additional clinical studies after approval, referred to as Phase 4 clinical studies, to monitor the effect of a new product and may prevent or limit future marketing of the product based on the results of these post-marketing programs. Furthermore, prior to granting approval, the FDA generally conducts an inspection of the facilities, including outsourced facilities that will be involved in the manufacture, production, packaging, testing and control of the drug substance and finished drug product for compliance with current Good Manufacturing Practice, or cGMP, requirements.

If the FDA approves the NDA, the sponsor is authorized to begin commercialization of the drug in accordance with the approval. Even if the FDA approves the NDA, the FDA may decide later to suspend or withdraw product approval if compliance with regulatory standards is not maintained or if safety problems are recognized after the product reaches the market. In addition, the FDA requires surveillance programs to monitor approved products that have been commercialized, and the agency has the power to require additional clinical studies, to require changes in labeling or to prevent further marketing of a product based on the results of these post-marketing programs. The FDA also has authority to request implementation of a risk evaluation and mitigation strategy, or REMS, that could restrict distribution of Gencaro or require us to provide additional risk information to prescribers. Whether or not FDA approval has been obtained, approval of a product candidate by comparable foreign regulatory authorities is necessary prior to the commencement of marketing of a product candidate in those countries. The approval procedures vary among countries and can involve additional testing. The time required to obtain approval may differ from that required for FDA approval.

Post-approval Compliance. If regulatory approval for a drug or medical device is obtained, the product and the facilities manufacturing the product are subject to periodic inspection and continued regulation by regulatory authorities, including compliance with cGMP, as well as labeling, advertising, promotion, recordkeeping, and reporting requirements, including the reporting of adverse events. In addition, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for labeling, promotion to health care professionals, direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Companies are responsible for compliance with such requirements and would be responsible to ensure that all contract manufacturing organizations who perform work for them also comply with such requirements. Similarly, if a drug manufacturer hires contract sales representatives or consultants to promote its products, such organizations or individuals must comply with all of the same requirements applicable to the drug manufacturer. The FDA regularly inspects companies to determine compliance with cGMPs and other post-market requirements. Failure to comply with statutory requirements and the FDA's regulations can result in a variety of administrative or enforcement actions, including but not limited to an FDA Form 483 (which is issued by the FDA at the conclusions of an inspection when an investigator has observed any conditions that may constitute violations), a public warning letter, suspension or withdrawal of regulatory approvals, product recalls, product detentions, refusal to provide export certificates, seizure of products and criminal prosecution.

Drug Price Competition and Patent Term Restoration Act of 1984. Under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, Congress created an abbreviated FDA review process for generic versions of pioneer (brand name) drug products. The Hatch-Waxman Act also provides for patent term restoration and the award, in certain circumstances, of non-patent marketing exclusivities.

Generic Drug Approval. The Hatch-Waxman Act established an abbreviated FDA review process for drugs that are shown to be equivalent to approved pioneer drugs. Approval for a generic drug is obtained by filing an abbreviated NDA, or ANDA. Generic drug applications are "abbreviated" because they generally do not include clinical data to demonstrate safety and effectiveness. Instead, an ANDA applicant must establish that its product is bioequivalent to an approved drug and that it is the same as the approved drug with respect to active ingredient(s), route of administration, dosage form, strength and recommended conditions of use (labeling). The FDA will approve the generic as suitable for an ANDA if it finds that the generic does not raise questions of safety and effectiveness as compared to the pioneer drug. A drug is not eligible for ANDA approval if the FDA determines that it is not equivalent to the pioneer drug or if it is intended for a different use. Any applicant who files an ANDA seeking approval of a generic version of an approved drug listed in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book, must certify to the FDA that (i) no patent information on the drug has been listed in the Orange Book; (ii) that each patent listed in the Orange Book for that approved drug has expired; (iii) FDA should approve the product on the date on which a listed patent expires; or (iv) that such patent is invalid, unenforceable or will not be infringed by the manufacture, use or sale of the generic drug. If the ANDA applicant makes a certification pursuant to (iv) above, or a Paragraph IV certification, and the NDA holder files an infringement suit against the ANDA applicant within 45 days of receiving the Paragraph IV notification, the NDA owner is entitled to an automatic 30-month stay of FDA's ability to approve the ANDA. This 30-month stay will end early upon any decision by a court that the patent is invalid, unenforceable or not infringed by the generic drug.

Patent Term Extension. While the term of a U.S. patent is generally 20 years from the earliest priority date of a patent application (excluding a provisional patent application), a U.S. patent that covers subject matter requiring regulatory approval to market is eligible for an extension of that patent term. The Hatch-Waxman Act provides for the restoration of a portion of the patent term lost during product development and FDA review of an application. Patent Term Extension, or PTE, extends the term of an issued patent for generally (i) the length of the FDA approval process, i.e., the complete period of NDA review, and (ii) half of the time spent in clinical trials, i.e., the IND period. However, the maximum period of restoration cannot exceed five years, or restore the total remaining term of the patent to greater than 14 years from the date of FDA approval of the product.

Under 35 U.S.C. § 156(a), a patent covering a method of using a product is eligible for PTE if the following conditions are met:

1) the patent has not yet expired;
2) the patent was not previously extended;
3) the patent owner submits an application for PTE that includes all necessary supporting information within 60 days of FDA approval;
4) the product was subject to regulatory review before its commercial marketing or use; and
5) the drug application is for the first permitted commercial marketing of the product.

We have obtained four U.S. patents (U.S. Patent Nos. 7,678,824; 8,080,578; 8,093,286; 8,946,284). We believe that, if Gencaro is approved by the FDA, any one of the U.S. patents may be eligible for PTE, which could provide approximately 5 years of additional patent life based on our current clinical trial plans.

A Supplementary Protection Certificate, or SPC, is a form of patent term extension that is available for pharmaceutical products approved for marketing in the European Union, or EU. We obtained a patent in Europe on methods for using Gencaro that is similar to US Patent 7,678,824 (EP 1802775); this EU patent is in force in certain countries in Europe, including the United Kingdom, France, Germany, Italy and Spain. We believe that this patent may be eligible for an SPC, if Gencaro is approved for marketing in any European country in which the patent is in force, which could provide up to five years of additional patent life. We believe that our patents in other jurisdictions may also be eligible for similar term extensions.

Non-Patent Marketing Exclusivities. Separate and apart from patent protection, the Hatch-Waxman Act entitles approved drugs to various periods of non-patent statutory protection, known as marketing exclusivity. The

Hatch-Waxman Act provides five years of “new chemical entity” marketing exclusivity to the first applicant to gain approval of an NDA for a product that contains an active moiety not found in any other approved product. This exclusivity means that another manufacturer cannot submit an ANDA or 505(b)(2) NDA until the marketing exclusivity period ends. This exclusivity protects the entire new chemical entity franchise, including all products containing the active ingredient for any use and in any strength or dosage form, but will not prevent the submission or approval of stand-alone NDAs where the applicants have conducted their own clinical studies to demonstrate safety and effectiveness. There is an exception, however, for a competitor that seeks to challenge a patent with a Paragraph IV certification. Four years into the five-year exclusivity period, a manufacturer who alleges that one or more of the patents listed with the NDA is invalid, unenforceable or not infringed may submit an ANDA or 505(b)(2) NDA for a generic or modified version of the product.

The Hatch-Waxman Act also provides three years of "new use" marketing exclusivity for the approval of NDAs, and supplements, where those applications contain the results of new clinical investigations (other than bioavailability studies) essential to the FDA's approval of the applications. Such applications may be submitted for new indications, dosage forms, strengths, or new conditions of use of approved products. So long as the studies are essential to the FDA's approval or were conducted by or for the applicant, this three-year exclusivity prohibits the final approval of ANDAs or 505(b)(2) NDAs for products with the specific changes associated with those studies. It does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for other products containing the same active ingredient, without those changes.

Similar non-patent market exclusivity is provided for in the EU and other international jurisdictions. We believe that, if approved in the EU, Gencaro may be eligible for ten years of market exclusivity in the EU, measured from the date of approval there.

FDA Premarket Review of Medical Devices

Unless an exemption applies, each medical device that a company wishes to market in the United States requires either approval of a premarket approval application, or PMA, or clearance of a premarket notification, commonly known as a "510(k)" from the FDA. The FDA classifies medical devices into one of three classes. Devices deemed to pose lower risks are placed in either class I or II, which may require the manufacturer to submit to the FDA a 510(k) requesting permission to commercially distribute the device. Clearance of a 510(k) usually requires between three months and one year from the time of submission of the 510(k), although the process may take longer. The FDA's 510(k) clearance procedure is less rigorous than the PMA approval procedure, but is available only to companies who can establish that their device is substantially equivalent to a legally-marketed "predicate" device that was (i) on the market prior to the enactment of the Medical Device Amendments of 1976, (ii) reclassified from Class III to Class II, or (iii) has been cleared through the 510(k) procedure. 510(k)s must typically be supported by performance data, including preclinical data, bench testing, and in some cases, clinical data. Some low risk devices are exempted from this requirement. Devices deemed by the FDA to pose the greatest risks, or for which there is no predicate, are placed in class III, and require a PMA.

PMA Pathway. Generally, a PMA must be supported by extensive data and valid scientific evidence, including, but not limited to, technical, preclinical, clinical trials, manufacturing and labeling to demonstrate to the FDA's satisfaction a reasonable assurance of the safety and effectiveness of the device for its intended use. After a PMA is sufficiently complete, the FDA will accept the application and begin an in-depth review of the submitted information and will generally conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with FDA's Quality System Regulations, or QSR. By statute, the FDA has 180 days to review the "accepted application", although, generally, review of the application can take between one and three years, and it may take significantly longer. The PMA application process can be expensive, and there is a substantial "user fee" that must be paid to FDA in connection with the submission of a PMA application. If the FDA's evaluation of the PMA application or the manufacturing facility is not favorable, the FDA may deny approval of the PMA application or issue a "not approvable" letter. The FDA may also require additional clinical trials, which can delay the PMA approval process by several years. In addition, if FDA discovers that an applicant has submitted false or misleading information, FDA may refuse to review submissions until certain requirements are met pursuant to its Application Integrity Policy, or AIP. If the FDA approves the PMA, it may place restrictions on the device. After the PMA is approved, if significant changes are made to a device, its manufacturing or labeling, a PMA supplement containing additional information must be filed for prior FDA approval. PMA supplements often must be approved by the FDA before the modification to the device, the labeling, or the manufacturing process may be implemented. Delays in receipt of or failure to receive such clearances or approvals, the loss of previously received clearances or approvals, or the failure to comply with existing or future regulatory requirements could have a material adverse effect on our business, financial condition and results of operations.

Clinical Trials. Clinical trials are generally required to support a PMA application and are sometimes required for 510(k) clearance. These trials generally require an Investigational Device Exemption, or IDE, application approved in advance by the FDA for a specified number of patients, unless the proposed study is deemed a non-significant risk study, which is eligible for an exemption from the IDE requirements. The IDE application must be supported by appropriate data, such as animal and laboratory testing results. Clinical trials may begin if the IDE application is approved by the FDA and the appropriate institutional review boards, or IRBs, at the clinical trial sites. Submission of an IDE application does not give assurance that the FDA will issue the IDE. If the IDE application is approved, there can be no assurance the FDA will determine that the data derived from the trials support the safety and effectiveness of the device or warrant the continuation of clinical trials. An IDE supplement must be submitted to and approved by the FDA before a sponsor or investigator may make a change to the investigational plan in such a way that may affect its scientific soundness, study indication or the rights, safety or welfare of human subjects. The trial must also comply with the FDA's regulations, including the requirement that informed consent be obtained from each subject. Even if a trial is completed, the results of clinical testing may not adequately demonstrate the safety and efficacy of the device or may otherwise not be sufficient to obtain FDA clearance to market the product in the United States.

In Vitro Diagnostic Companion Diagnostic Devices. FDA has described IVD companion diagnostic devices as in vitro diagnostic devices that provide information that is essential for the safe and effective use of a corresponding therapeutic product. The use of an IVD companion diagnostic device with a particular therapeutic product is stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding therapeutic product, as well as in the labeling of any generic equivalents of the therapeutic

product. An IVD companion diagnostic device could be used to (i) identify patients who are most likely to benefit from a particular therapeutic product; (ii) identify patients likely to be at increased risk for serious adverse reactions as a result of treatment with a particular therapeutic product; or (iii) monitor response to treatment for the purpose of adjusting treatment (e.g., schedule, dose, discontinuation) to achieve improved safety or effectiveness. Although FDA's regulation of IVD companion diagnostic devices is evolving and implemented on a case-by-case basis, FDA's stated policy for a novel therapeutic product is that an IVD companion diagnostic device should be developed and approved or cleared contemporaneously to support the therapeutic product's safe and effective use. The clinical performance and clinical significance of the IVD companion diagnostic device is to be established using data from the clinical development program of the corresponding therapeutic product. FDA recognizes, however, that there may be cases where contemporaneous development may not be possible. With respect to the Gencaro Test, there is no assurance that we will be able to develop and obtain approval or clearance contemporaneously with Gencaro. Failure to develop the Gencaro Test or obtain clearance or approval could delay approval of Gencaro, if FDA regards the Gencaro Test as an IVD companion diagnostic test that is essential to the safe and effective use of Gencaro.

Continuing Regulation. After a device is placed on the market, numerous regulatory requirements apply to the manufacturer, or holder of a PMA approval. Unless subject to an exemption, medical devices distributed in the United States must be manufactured in compliance with the FDA's Quality System Regulations, or QSRs, and current good manufacturing practices. These regulations govern the manufacturing process, including design, manufacture, testing, release, packaging, distribution, documentation and purchasing, as well as complaint handling, corrective and preventative actions and internal auditing. In complying with the QSRs, manufacturers must expend significant time, money and effort. Companies are also subject to other post-market and general requirements, including but not limited to product listing and establishment registration, post-market surveillance requirements, limitations on promotion, and requirements for recordkeeping and reporting of certain adverse events, malfunctions, corrections and removals. As discussed above, FDA regularly inspects companies to assess compliance with the QSRs and other post-market requirements. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, and potential civil and criminal penalties. As part of such arrangement, we will seek to have the diagnostic company take responsibility for compliance with the FDA's device approval and on-going regulatory requirements.

International Marketing Approvals. International sales of medical devices are subject to foreign government regulations, which vary substantially from country to country and are subject to change. The time required to obtain approval by a foreign country may be longer or shorter than that required for FDA clearance or approval, and the requirements may differ.

Other Regulatory Requirements. We are also subject to various federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our work. The extent and character of governmental regulation that might result from future legislation or administrative action cannot be accurately predicted.

Medical Device Tax

In March 2010, the U.S. Congress adopted and President Obama signed into law comprehensive health care reform legislation. Among other initiatives, these laws impose significant new taxes on medical device makers in the form of a 2.3% excise tax on U.S. medical device sales, with certain exemptions, beginning on January 1, 2013. On January 22, 2018, legislation was enacted suspending the medical device tax in 2018 and 2019. It will be reinstated on January 1, 2020, unless a permanent repeal takes place before that date. The Gencaro Test is likely to be subject to this tax if this tax is reinstated in the future.

Intellectual Property

The future success of our business will partly depend on our ability to maintain market exclusivity for Gencaro, if approved, in the United States and important international markets, and for other products or product candidates that we may acquire or develop. We will rely on statutory protection, patent protection, trade secrets, know-how, and in-licensing of technology rights to maintain protection for our products.

We believe that both patent protection and data exclusivity statutes will give Gencaro, if approved, market exclusivity in the United States and in major international markets. If approved by the FDA or international regulatory agencies, Gencaro will qualify as a New Chemical Entity, or NCE, as it has never received regulatory approval in any jurisdiction. As an NCE, Gencaro, if approved, will enjoy market exclusivity in the United States and most international markets under data exclusivity statutes. These laws provide for an exclusivity period beginning from regulatory approval, during which any generic competitor is barred from submitting an application that relies on the data that has been submitted in connection with the approval of the NCE. In the United States, the Hatch-Waxman Act provides for an initial period of up to five years from approval of the NCE, during which a generic application attempting to rely on the data submitted for the NCE cannot be filed with the FDA. This period can be effectively extended to seven and one-half years from FDA approval because a provision of the Hatch-Waxman Act provides for an automatic 30-month extension of the exclusivity

period if we promptly pursue litigation against a company attempting to enter the market with a generic for a drug that is covered by a composition of matter or method of use patent.

Many international markets have data exclusivity statutes that are analogous to Hatch-Waxman and sometimes more protective. The analogous statute in the European Medicines Evaluation Agency will, in general, provide Gencaro with a minimum of ten years of protection from marketing approval before such a generic application may be approved. Protection under Hatch-Waxman and other data exclusivity statutes is sometimes considered superior to patent protection, as the generic cannot be marketed during the period of exclusivity, thus eliminating the need to initiate patent infringement litigation with its accompanying risks and costs.

In addition to protection under data exclusivity statutes, we believe that Gencaro's patent portfolio will also provide market exclusivity, if approved. We have been granted patents in the United States and Europe that claim the use of Gencaro in patients predicted to have a favorable response to the drug based on genetic polymorphisms in the genes encoding the beta-1 and/or alpha-2C receptors. We believe that this patent strategy may deter generic competition because of the threat of patent litigation or may exclude generic competition from the market until the patents expire if we are successful in litigation. Consequently, if our patent strategy is successful, we believe we may avoid generic competition with Gencaro in the United States or certain countries in Europe until at least the expiration of these patents, which would be no earlier than 2026 in the United States and into 2025 in Europe. In addition, we believe that if Gencaro is approved, any one of our U.S. patents may be entitled to an extension of its term and the European patent may be entitled to an extension through a supplemental protection certificate in one or more countries in Europe. The length of any such extension may vary by country. We cannot predict whether any such extensions will be granted, but if they are, they may provide market exclusivity for Gencaro into approximately 2031 in the United States and Europe. In addition, we were granted a patent on the S-isomer formulation of Gencaro, which we believe could be important in Gencaro's future development and could extend market exclusivity of the S-isomer form in the United States to approximately 2034, assuming it is the first approved formulation.

For AB171, the European Patent Office issued patent on methods of treating cardiovascular disease and conditions with a thiol-substituted isosorbide mononitrate based on genetic targeting. The European patent, entitled "Methods and Compositions for Cardiovascular Diseases and Conditions," provides protection for this novel approach to treating patients with cardiovascular disease and conditions. The European patent has been validated in ten countries: Denmark, France, Germany, Ireland, Italy, Netherlands, Spain, Sweden, Switzerland and the United Kingdom. We have related patent applications pending at the United States Patent Office and Canadian Intellectual Property Office.

We also have other patent rights in additional drug candidates having possible indications in cardiovascular disease, oncology, and other therapeutic areas; these are in both early and later stages of development. We may seek collaborators to assist us in the development of these candidates or we may seek to raise funds to advance the development of the compounds on our own.

Employees

As of December 31, 2018, we had 15 full-time employees. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Corporate Information

On January 27, 2009, we completed a business combination, or the Merger, between Nuvelo, Inc., or Nuvelo, a corporation originally incorporated in 1992, and its subsidiary, ARCA biopharma, Inc. Immediately following the Merger, we changed our name from Nuvelo, Inc. to ARCA biopharma, Inc. Our principal offices are located in Westminster, Colorado.

We file our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, electronically with the U.S. Securities and Exchange Commission, or the SEC. The public may read or copy any materials that have been filed with the SEC at the SEC's Public Reference Rooms at 100 F Street, N.E., Washington, D.C. 20549 on official business days during the hours of 10:00 a.m. and 3:00 p.m. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports on our website at http://www.arcabiopharma.com on the earliest practicable date following the filing with the SEC or by contacting the Investor Relations Department at our corporate office by calling (720) 940-2200. Information found on our website is not incorporated by reference into this report.

Item 1A. Risk Factors

An investment in our securities involves certain risks, including those set forth below and elsewhere in this report. In addition to the risks set forth below and elsewhere in this report, other risks and uncertainties not known to us, that are beyond its control or that we deem to be immaterial may also materially adversely affect our business operations. You should carefully consider the risks described below as well as other information and data included in this report.

Risks Related to Our Business and Financial Condition

We will need to raise substantial additional funds through public or private equity transactions and/or complete one or more strategic transactions, to continue development of Gencaro or any of our other product candidates. 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 and our other product candidates, including the costs associated with clinical trials related thereto, and the substantial cost of commercializing Gencaro, if it is approved, we will need to raise substantial additional funding through public or private equity or debt transactions or a strategic combination or partnership. If we are delayed in obtaining funding or are unable to complete a strategic transaction, we may discontinue our development activities on Gencaro and our other product candidates or discontinue our operations. Even if we are able to fund continued development and Gencaro or any of our other product candidates 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 or any other product candidate.

We believe our cash and cash equivalents balance as of December 31, 2018, together with the $2.4 million of net proceeds raised in 2019 from sales of our common stock, will be sufficient to fund our operations, at our projected cost structure, through the third quarter of 2019. In 2017, we entered into a sales agreement, as amended, with an agent to sell, from time to time, our common stock having an aggregate offering price of up to $10.2 million, in an “at the market offering.” In January 2019, we further amended our sales agreement to increase the maximum aggregate value of shares which we may issue and sell from time to time under this sales agreement by approximately $2.5 million, from $10.2 million to $12.7 million. As of February 22, 2019, we have sold an aggregate of 9,242,406 shares of our common stock pursuant to the terms of such sales agreement, as amended, for aggregate gross proceeds of approximately $12.6 million. Net proceeds received in the period were approximately $11.9 million, after deducting initial expenses for executing the “at the market offering” and commissions paid to the placement agent. We have sold all shares available under the current prospectus. Sales of our common stock dilute the ownership interest of our stockholders and may cause the price per share of our common stock to decrease. 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:

- the costs and timing for potential additional clinical trials in order to gain possible regulatory approval for Gencaro and our other product candidates;
- the market price of our stock and the availability and cost of additional equity capital from existing and potential new investors;
- 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;
- 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, 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.

Our management and our independent registered public accounting firm, in their report on our financial statements as of and for the fiscal year ended December 31, 2018, 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, 2018 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 accounting firm concluded as of December 31, 2018 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 for a period from one year after our financial statements have been issued. We believe our cash and cash equivalents balance as of December 31, 2018, together with the $2.4 million of net proceeds raised in 2019 from sales of our common stock, will be sufficient to fund our operations, at our projected cost structure, through the third quarter of 2019. We cannot be certain that we will be able to make any other sale of our common stock in any future offering to cover our future capital needs, or at all. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. If we are delayed in completing or are unable to complete additional funding and/or a strategic transaction, we may discontinue our development activities or operations, but there are no assurances that these reductions would be sufficient to allow us to continue to operate as a going concern. Therefore, even if we resolve this uncertainty, our independent registered public accountants and/or management could conclude that uncertainty as to our ability to continue as a going concern could exist at a future date.

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. We may be forced to 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 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. If we cannot raise sufficient funds, 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.

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. We began screening patients for our Phase 2B GENETIC-AF clinical trial in April 2014 and enrolled our first patient in June 2014. Enrollment was completed in August 2017 having randomized 267 HFrEF patients with AF. The Phase 2B trial completed the patient treatment phase in December 2017 and we reported top-line data in February 2018. We received guidance from the FDA following an End-of-Phase 2 meeting regarding the Phase 3 program for Gencaro as a potential genetically-targeted treatment for AF patients with HF with the beta 1 389 arginine homozygous genotype. In consultation with the FDA, we developed key elements of the Phase 3 clinical trial needed to support a potential NDA, details of which were confirmed via the FDA SPA process. Any future development of Gencaro, including initiating the Phase 3 clinical trial, is dependent on obtaining additional financing, even if we enter into a strategic collaboration.

Failure to demonstrate that a product candidate, including Gencaro, is safe and effective, or significant delays in demonstrating such safety and efficacy, would adversely affect our business. For instance, in February 2018, we announced the top-line results of our Phase 2B GENETIC-AF clinical trial in which Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate (TOPROL-XL). 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 or any of our other product candidates and, as a result, will need to complete a strategic transaction, or, alternatively, raise substantial additional funds to enable commercialization of Gencaro or any of our other product candidates, if approved. Failure to successfully provide for the commercialization of Gencaro or any other product candidate, if approved, would damage our business.

We have received an SPA agreement from the FDA relating to our planned Phase 3 program for Gencaro. This SPA agreement does not guarantee approval of Gencaro or any other particular outcome from regulatory review.

Following our End-of-Phase 2 meeting with the FDA, we requested agreement from the FDA under a SPA for our planned Phase 3 clinical trial of Gencaro, which we received in February 2019. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of certain clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to the effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding a SPA must be clearly documented in a SPA letter or the minutes of a meeting between the sponsor and the FDA.

However, a SPA agreement does not guarantee approval of a product candidate, even if the trial is conducted in accordance with the protocol. Moreover, the FDA may revoke or alter our SPA agreement in certain circumstances. In particular, a SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, we fail to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by us in our request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

Even though we obtained an agreement on our SPA, we cannot assure you that our planned Phase 3 clinical trial will succeed, will be deemed binding by the FDA under our SPA agreement, or will result in any FDA approval for Gencaro. Moreover, if the FDA revokes or alters its agreement under our SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may not deem the data sufficient to support an application for regulatory approval, which could materially adversely affect our business, financial condition and results of operations.

If we are not able to maintain the requirements for listing on the Nasdaq Capital Market, we could be delisted, which could have a material 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, (i) a minimum closing bid price of $1.00 per share, (ii) 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 (iii) either: (x) stockholders' equity of at least $2.5 million; or (y) a total market value of listed securities of at least $35 million.

We have received three potential delisting notices from Nasdaq since 2012. In 2012, 2015 and 2018, 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 business days. We subsequently regained compliance with Nasdaq's minimum closing bid price requirements related to the 2012 and 2015 notices, effecting a 1 for 6 reverse split of our common stock in March 2013 and a 1 for 7 reverse split of our common stock in September 2015. On April 11, 2018, we received notification from Nasdaq, or the Notice, 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 business days.

On October 9, 2018, we received a written notification from NASDAQ granting an additional 180 calendar day period, until April 8, 2019, to regain compliance with the minimum bid price requirement. The minimum bid price requirement will be met if our common stock has a closing bid of at least $1.00 per share for a minimum of 10 consecutive business days during the 180 day period. If our stock does not trade above these levels, we may seek to execute a reverse split of our common stock in order to regain compliance. This second 180 day period relates exclusively to the bid price deficiency and ARCA could be delisted during the 180 day period for failure to maintain compliance with any other listing requirements that occurs during the 180 day period. In October 2018, we held a special meeting of our stockholders, at which our stockholders approved a series of certificates of amendment to our restated certificate of incorporation, as amended, to effect a reverse split of our outstanding common stock, at a ratio of between 1 for 3 and 1-for-20, inclusive, and to authorize our board of directors to, for a period of up to one-year, to select and file such a certificate of amendment to effect such a reverse split of our outstanding common stock, if, in the judgment of our board of directors, it is deemed necessary. However, our board of directors has yet to approve any such stock split, and, even if effected, the effect of a reverse stock split on the market price of our common stock cannot be predicted with any certainty, and the history of similar stock split combinations for companies in like circumstances is varied. It is possible that the per share price of our common stock after the reverse stock split will not rise in proportion to the reduction in the number of shares of common stock outstanding resulting from the reverse stock split, effectively reducing our market capitalization, and there can be no assurance that the market price per post-reverse split share will either exceed or remain in excess of the $1.00 minimum bid price for a sustained period of time. We cannot provide any assurance when or if the closing bid price of our common stock will again be greater than $1.00. The market price of our common stock may vary based on other factors that are unrelated to the number of shares outstanding, including our future performance.

The delisting of our common stock from a national exchange could impair the liquidity and market price of the common stock. It could also materially, adversely affect our access to the 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.

In future periods, if we do not meet the minimum stockholders' equity, minimum closing bid price requirements, or any other listing requirements, we would be subject to delisting from the Nasdaq Capital Market.

As of February 22, 2019, the closing price of our common stock was $0.46 per share, rounded to the nearest penny, and the total market value of our listed securities was approximately $8.4 million. As of December 31, 2018, we had stockholders' equity of $6.0 million.

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

If we have difficulty enrolling a sufficient number of patients in any future clinical trial, we may need to delay or terminate our trial, which would have a negative impact on our business. Delays in enrolling patients in any future 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.

The GENETIC-AF clinical trial required that we identify and enroll a large number of patients with the condition under investigation and the trial enrolled only those patients having a specific genotype, and certain patients who have or are willing to have a Medtronic device implanted for monitoring and recording AFB data. Because of the rigorous enrollment criteria, our clinical trial timelines were delayed from our original projections. We anticipate that any future Phase 3 clinical trial of Gencaro may have similar enrollment criteria, and we cannot guarantee that we will not have similar issues in any future clinical trials.

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

We will receive regulatory approval for our product candidates only 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 current or future clinical trials for Gencaro or any other product candidate will demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products.

For example, GENETIC-AF was designed as an adaptive trial. The DSMB conducted a pre-specified interim analysis of study endpoints for efficacy, safety and futility. Based on the efficacy and safety data of the interim analysis, the DSMB recommended completing the Phase 2B trial with no changes to the trial design, rather than transition GENETIC-AF to a Phase 3 trial. In February 2018, we announced top-line results of the Phase 2B trial, which indicated that Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate (TOPROL-XL). We have not determined if these results of GENETIC-AF, and cannot predict if the results from a future Phase 3 clinical trial, even with a SPA agreement, would allow us to obtain regulatory approval for Gencaro.

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 3 clinical trial and have limited staff with the requisite experience to do so. We therefore rely on contract research organizations, or CROs, to conduct certain aspects of our clinical trial. While certain of our employees have experience in designing and administering clinical trials, these employees have no such experience as employees of ARCA.

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 will rely on contract research organizations to conduct substantial portions of our clinical trials, including any future clinical trial of Gencaro, and as a result, we will be unable to directly control the timing, conduct and expense of all aspects of our clinical trials.

We do not currently have sufficient staff with the requisite experience to conduct our clinical trials and therefore will rely on third parties to conduct certain aspects of any future clinical trials. We previously contracted with a CRO to conduct components of our GENETIC-AF trial and anticipate contracting with a CRO to conduct components of any future clinical trial for Gencaro or any future clinical trials for our other product candidates. As a result, we will have less control over many details and steps of any trial, the timing and completion of any trial, the required reporting of adverse events and the management of data developed through any trial 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, such as CROs, may have staffing difficulties, may undergo changes in priorities or may become financially distressed, adversely affecting their willingness or ability to conduct our trial. We may experience unexpected cost increases that are beyond our control. Problems with the timeliness or quality of the work of a CRO may lead us to seek to terminate the relationship and use an alternative service provider. However, making any change may be costly and may delay ongoing trials, if any, 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 though we anticipate relying on CROs in the future, we will likely have to devote substantial resources and rely on the expertise of our employees to manage the work being done by the CROs.

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 commencement and completion of clinical trials, particularly with respect to steps for commencing and continuing our 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 any 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 or any other product candidate, if it occurs, is expected to require years of additional clinical development, including the completion of genetic trials. There can be no assurance 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 expect to depend on existing and future collaborations with third parties for the development of some of our product candidates. If those collaborations are not successful, we may not be able to complete the development of these product candidates.

We had a collaboration agreement with Medtronic that supported our GENETIC-AF clinical trial. If our arrangement with Medtronic, as amended, is continued as part of our future development of Gencaro, we will have limited control over the amount and timing of resources that they dedicate to the development of Gencaro. This is also likely to be true in any future collaboration with third parties and we may seek additional third party collaborators for the development of Gencaro or other product candidates. Our ability to benefit from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaborators may elect to take over manufacturing rather than retain us as manufacturers and may encounter problems in starting up or gaining approval for their manufacturing facility and so be unable to continue development of product candidates;
- we may be required to undertake the expenditure of substantial operational, financial and management resources in connection with any collaboration;
- we may be required to issue equity securities to collaborators that would dilute our existing stockholders' percentage ownership;
- we may be required to assume substantial actual or contingent liabilities;
- collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products; and
- collaborators may experience financial difficulties.

We face a number of challenges in seeking additional collaborations. Collaborations are complex and any potential discussions may not result in a definitive agreement for many reasons. For example, whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors, such as the design or results of our clinical trials, the potential market for our product candidates, the costs and complexities of manufacturing and delivering our product candidates to patients, the potential of competing products, the existence of uncertainty with respect to ownership or the coverage of our intellectual property, and industry and market conditions generally. If we were to determine that additional collaborations for our Gencaro development is necessary and were unable to enter into such collaborations on acceptable terms, we might elect to delay or scale back the development or commercialization of Gencaro in order to preserve our financial resources or to allow us adequate time to develop the required physical resources and systems and expertise ourselves.

Collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner, or at all. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

Any future clinical trial for Gencaro will require the use of a third-party diagnostic services provider to administer a genetic test needed to identify the patient receptor genotypes of clinical trial participants, and as a result, we will be unable to directly control the timing, conduct and expense of the genetic test.

We anticipate that any future clinical trial of Gencaro, if any, will require a companion diagnostic test that identifies the patient's receptor genotype. The trial would only enroll those patients with the receptor that has the potential for enhanced efficacy, the beta-1 389 Arg receptor as detected by a beta-1 389 Arg/Arg genotype. Accordingly, we anticipate that any future clinical trial for Gencaro will require the use of a third-party diagnostic service to perform the genetic testing. There has been limited experience in our industry in prospective development of companion diagnostics required to perform the required molecular profiling. We entered into an agreement with LabCorp to provide the diagnostic services of the genetic test needed to support our GENETIC-AF trial. To provide those services, LabCorp obtained from the FDA an IDE for the companion diagnostic test being used in our GENETIC-AF clinical trial. We would expect a similar agreement and approval would be necessary for any companion diagnostic used in any future clinical trials for Gencaro.

The FDA and similar regulatory authorities outside the United States regulate companion diagnostics. Companion diagnostics require separate or coordinated regulatory approval prior to commercialization. Changes to regulatory advice could delay our development programs or delay or prevent eventual marketing approval for our product candidates that may otherwise be approvable. In July 2011, the FDA issued draft guidance that stated that if safe and effective use of a therapeutic depends on an in vitro diagnostic, the FDA generally will not approve the therapeutic unless the FDA approves or clears this "in vitro companion diagnostic device" at the same time that the FDA approves the therapeutic. The approval or clearance of the companion diagnostic would occur through the FDA's Center for Devices and Radiological Health. In 2014, the FDA issued guidance on in vitro companion diagnostic devices. The guidance allows for flexibility by the FDA in the case of therapeutic products to treat serious conditions for which no alternative treatment exists and the benefits of using the companion diagnostic outweigh the risk, but it is unclear how this discretion may be applied by the agency with respect to the companion diagnostic test related to any Gencaro clinical trials. The FDA's evolving position on the topic of companion diagnostics could affect our clinical development programs that utilize companion diagnostics. In particular, the FDA may limit our ability to use retrospective data, otherwise disagree with our approaches to trial design, biomarker qualification, clinical and analytical validity, and clinical utility, or make us repeat aspects of a trial or initiate new trials.

Given our limited experience in developing diagnostics, we expect to rely primarily on third parties for the design and manufacture of the companion diagnostics for our product candidates. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our product candidates that require such diagnostics, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not receive marketing approval and we may not realize the full commercial potential of any products that receive marketing approval. As a result, our business could be materially harmed.

We will need to establish a collaborative arrangement with a third-party diagnostics services provider to obtain marketing clearance or approval of the companion genetic test. There is no guarantee that the FDA will grant timely clearance or approval of the genetic 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 genetic test that is simple to administer and widely available will be critical to the successful commercialization of Gencaro. The genetic 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 one or more third-party diagnostic services providers are unable to obtain FDA approval of the genetic test at all or in parallel with the approval of Gencaro, or are 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, the commercial launch of Gencaro may be significantly and adversely affected.

Regulatory approval is required for the genetic test to be used in our Gencaro clinical trials and to support the commercialization of the test, if approved. Delays or failures in obtaining such regulatory approval, including any required validation analyses may prevent a third-party diagnostics provider from commercializing such genetic test and will adversely affect our business, operating results and prospects.

Before a genetic test can be used commercially, including in conjunction with Gencaro, if it is approved for marketing, the third-party diagnostics provider must obtain FDA Premarket Approval, or PMA, for such test. The FDA may require additional validation of the genetic test we used in GENETIC-AF prior to any approval of Gencaro or the genetic test or prior to the use of such test in any future clinical trials for Gencaro. We anticipate the genetic test will be required as a condition to prescribing Gencaro. There is no guarantee the FDA will approve the anticipated

PMA submission for the genetic test. Even if the genetic test is eventually approved, performing additional validation work necessary to support the PMA, if required, for current or future genetic test products, including one associated with Gencaro, would require additional time and expense and the outcome would be uncertain. Moreover, such delays or increased costs or failures could adversely affect our business, operating results and prospects for commercializing the genetic test.

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

Any diagnostic 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 genetic 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, if approved, to suffer and may prevent us from generating revenue or utilizing the genetic test further in any clinical trial. 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.

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

The genetic test is an important component of the commercial strategy for Gencaro in addition to being required for our clinical trials. We believe that the genetic 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 genetic 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 therapy in patients with HF. For instance, the top-line results of our Phase 2B GENETIC-AF clinical trial indicated that Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate (TOPROL-XL). If our future clinical trials in Gencaro do not show that Gencaro has a clear therapeutic benefit as compared to other drugs in the beta-blocker class currently on the market, then prescribers may be unlikely to prescribe Gencaro to patients, even if approved. Any one of these factors could affect prescriber behavior, which in turn may substantially impede market acceptance of the genetic test, which could cause significant harm to Gencaro's ability to compete, and in turn harm our business.

Our failure to raise substantial additional funding or enter into a strategic transaction may materially and adversely affect our business.

Unless we are able to raise substantial additional funding for the development of Gencaro through other means, we will need to complete a strategic transaction to continue the development of Gencaro through its next phase of clinical development, the regulatory submission process, the commercialization phase, and to continue our other operations. The strategic transactions that we may consider include a potential combination or partnership. Our board of directors and management team have and will continue to devote substantial time and resources to obtaining additional capital or 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 such a strategic transaction may materially and adversely affect our business.

We may be limited in our ability to access sufficient funding through a public or private equity offering 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 at a price per share less than (i) the closing price of our common stock on the Nasdaq Capital Market immediately preceding the signing of the binding agreement, or (ii) the average closing price of our common stock on the Nasdaq Capital Market for the five trading days immediately preceding the signing of the binding agreement requires stockholder approval unless the offering qualifies as a "public offering" for purposes of the Nasdaq rules. As of December 31, 2018, we had approximately 13.9 million shares of common stock outstanding, 20% of which is approximately 2.8 million shares. SEC rules impose restrictions on our ability to raise funds through the registered offering of our securities pursuant to a "shelf" registration statement on Form S-3. Under SEC rules, we are prohibited from selling securities under such a registration statement if the aggregate market value of the securities sold thereunder in any twelve-month period exceeds one-third of the market value of our outstanding common stock held by non-affiliates. In 2017, we entered into a sales agreement, as amended, with an agent to sell, from time to time, our common stock having an aggregate offering price of up to $10.2 million, in one or more "at the market offerings." In January 2019, we further amended our sales agreement to increase the maximum aggregate value of shares which we may issue and sell from time to time under this sales agreement by approximately $2.5 million, from $10.2 million to $12.7 million. As of February 22, 2019, we have sold an aggregate of 9,242,406 shares of our common stock pursuant to the terms of such sales agreement, as amended, for aggregate gross proceeds of approximately $12.6 million. Net proceeds received in the period were approximately $11.9 million, after deducting initial expenses for executing the "at the market offering" and commissions paid to the placement agent. We have sold all shares available under the current prospectus. Due to these sales, we may be limited in our ability to sell securities registered on Form S-3 over the next 12 months, which may substantially limit our ability to effect future financings. 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 January 2013, we entered into separate subscription agreements with certain institutional investors in connection with a private investment in public equity, 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, while the warrants issued in such financing 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. The restrictions imposed by the terms of our previous 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.

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

Our historical losses have had and will continue to have an adverse effect on our stockholders' equity and working capital, among other things. We are years away from commercializing a product and generating any product revenue. As a result, we expect to continue to incur significant operating losses for the foreseeable future. Even if we ultimately receive regulatory approval for Gencaro or our other product candidates, sales of such products may not generate sufficient revenue for it to achieve or maintain profitability. Because of the numerous risks and uncertainties associated with developing therapeutic drugs, we may experience larger than expected future losses and may never

reach profitability.

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 for such drug. 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 Complete Response Letter, or 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. We completed a Phase 2B clinical study of Gencaro in HFrEF patients to assess its efficacy in reducing or preventing AF. We enrolled 267 HFrEF patients with AF in the Phase 2B trial. We reported top-line Phase 2B data in February 2018. In the third quarter of 2018, we submitted a SPA to the FDA for a Phase 3 clinical trial. In February 2019, the FDA has approved our SPA request. Even though the FDA approved our SPA, this product candidate will require years of additional clinical development. Even if we conduct additional studies in accordance with our SPA agreement or 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 initiate 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 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 or, availability of clinical trial sites;

- other clinical trials seeking to enroll subjects with similar profile;

- failure of our clinical trials and clinical investigators to be in compliance with GCP;
- unforeseen safety issues, including negative results from ongoing preclinical studies;
- inability to monitor patients adequately during or after treatment;
- difficulty recruiting and monitoring multiple study sites;
- 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; and
- an insufficient number of patients who have, or are willing to have, a Medtronic device implanted for monitoring and recording AF burden data.

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 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 will 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 include 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.

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. Healthcare 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 United States 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;

- 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;

- seek an injunction;

- pursue criminal prosecutions;

- close the facilities of our contract manufacturers; or

- impose civil or criminal penalties.

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

Commercialization of Gencaro or any other product candidate, if approved, 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 United States. 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.

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 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.

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 the API for Gencaro. For drug production, we have contracted with Patheon, Inc. to manufacture the Gencaro tablets. In addition, we have contracted with a separate service provider for packaging and distribution of our clinical trial materials. 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, stability testing failures, 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 laws 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.

Transitioning from a clinical development 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 clinical development stage company.

We are a clinical 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 clinical development 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 clinical development stage company and continue our business.

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 accepted treatments for AF. In addition, our proposed prescribing information for Gencaro is expected to include a requirement for genetic testing of the patient to ascertain if they have the genotype that we believe responds most favorably to Gencaro. This additional step will add incremental cost and procedures to prescribing Gencaro, which could make it more difficult to compete against existing therapies.

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. For instance, the top-line results of our Phase 2B GENETIC-AF clinical trial indicated that Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate (TOPROL XL). If our future clinical trials in Gencaro do not show that Gencaro has a clear therapeutic benefit as compared to other drugs in the beta-blocker class currently on the market, then prescribers may be unlikely to prescribe Gencaro to patients, even if approved. 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 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. Each medical device manufacturer has 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 genetic test if it is approved for marketing. On January 22, 2018, legislation was enacted suspending the medical device tax in 2018 and 2019. It will be reinstated on January 1, 2020, unless a permanent repeal takes place before that date. 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.

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 we do. 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 2018, our research and development activities were dedicated to Gencaro and initiating IND-enabling development activities with AB171. We expect our research and development activities in 2019 will be focused on regulatory activities related to Gencaro, initiating the PRECISION AF clinical trial, subject to obtaining additional financing, and continuing IND-enabling development activities with AB171. 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 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.

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 principal executive officer and principal financial officer, does not expect that our internal control over financial reporting will prevent all error and all fraud. We continue to operate with a small staff for financial reporting. Though the process and design of our internal controls over financial reporting have not been altered, the small number of staff involved in financial reporting may limit 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.

Comprehensive tax reform bills could adversely affect our business and financial condition.

On December 22, 2017, and effective January 1, 2018, the U.S. government enacted H.R. 1, “An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018” (informally titled the Tax Cuts and Jobs Act) which includes significant changes to the taxation of business entities. The Tax Cuts and Jobs Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign

earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the Tax Cuts and Jobs Act remains subject to interpretation and further guidance from U.S. taxing authorities and as a result, the overall impact of this tax reform is uncertain and may change due to interpretation changes, and our business and financial condition could be adversely affected. The impact of the Tax Cuts and Jobs Act on holders of our common stock is also uncertain and could be adverse. We are unable to predict what tax reform may be proposed or enacted in the future or what effect such changes would have on our business, but such changes, to the extent they are brought into tax legislation, regulations, policies or practices, could affect our effective tax rates in the future in countries where we have operations and have an adverse effect on our overall tax rate in the future, along with increasing the complexity, burden and cost of tax compliance. We urge our stockholders to consult with their legal and tax advisors with respect to the Tax Cuts and Jobs Act and the potential tax consequences of investing in or holding our common stock.

Failure to comply with data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and our partners may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, as amended, or HIPAA. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

International data protection laws, including, without limitation, the European Union Directive 95/46/EC, or the Directive, and the European Union’s General Data Protection Regulation, or the GDPR, that became effective in May 2018, and member state data protection legislation, may also apply to health-related and other personal information obtained outside of the United States. These laws impose strict obligations on the ability to process health-related and other personal information of data subjects in the European Union, including in relation to use, collection, analysis, and transfer of such personal information. These laws include several requirements relating to the consent of the individuals to whom the personal data relates, limitations on data processing, establishing a legal basis for processing, notification of data processing obligations or security incidents to appropriate data protection authorities or data subjects, the security and confidentiality of the personal data and various rights that data subjects may exercise.

The Directive and the GDPR prohibits, without an appropriate legal basis, the transfer of personal data to countries outside of the European Economic Area, or EEA, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Although there are legal mechanisms to allow for the transfer of personal data from the EEA and Switzerland to the United States, uncertainty about compliance with European Union data protection laws remains. For example, ongoing legal challenges in Europe to the mechanisms allowing companies to transfer personal data from the EEA to the United States could result in further limitations on the ability to transfer personal data across borders, particularly if

governments are unable or unwilling to reach new or maintain existing agreements that support cross-border data transfers, such as the European Union-U.S. and Swiss-U.S. Privacy Shield framework. Additionally, other countries have passed or are considering passing laws requiring local data residency.

Under the GDPR, regulators may impose substantial fines and penalties for non-compliance. Companies that violate the GDPR can face fines of up to the greater of 20 million Euros or 4% of their worldwide annual turnover (revenue). The GDPR increases our responsibility and potential liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR and other EU and international data protection rules.

Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

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 to all preclinical and clinical data from development of bucindolol through the BEST trial from Bristol Meyers Squibb, or 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. In October 2017, we entered into an agreement with Aeolus pursuant to which we acquired Aeolus' minority membership interest in CPEC. The transaction effectively buys-out Aeolus' royalty interest thereby reducing or eliminating the stated milestone and royalty obligations that could be payable by us, if Gencaro receives regulatory approval and is commercialized.

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 genetic 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 United States 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, in opposition proceedings in a foreign patent office, or in a post-grant challenge proceeding such as an ex parte reexamination or inter partes review at the U.S. Patent and Trademark 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 alpha-2C receptors. We have obtained patents that claim methods involving Gencaro after a patient's receptor genotype has been determined. We anticipate that any NDA for Gencaro will request a label including 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.

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 United States.

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, inter partes review, or post-grant review) in the United States 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

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 genetic 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;

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

- progress of any future clinical trials for Gencaro or our other product candidate, including enrollment and any data that may become available;

- 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.

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 December 31, 2018, approximately 13.9 million shares of common stock were outstanding, and 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 December 31, 2018, approximately 2.7 million shares of our common stock were issuable upon the exercise of outstanding warrants. 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. For instance, in July 2015, we filed a registration statement on Form S-3 which registered for resale an aggregate of 2.4 million shares of our common stock issuable upon exercise of outstanding warrants. 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 December 31, 2018, there were approximately 604,000 shares of our common stock which may be issued upon the exercise of outstanding stock options, and we anticipate that we will continue to issue stock option and restricted stock unit awards to our employees and consultants in the fiscal year ended December 31, 2019 and thereafter. If and when these options are exercised and these restricted stock units are vested, such shares will be available for sale in the open market without further registration under the Securities Act. The existence of these outstanding options and restricted stock units may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms. The exercise of those options and vesting of the restricted stock units, and the prompt resale of shares of our common stock received, may also result in downward pressure on the price of our common stock.

In the absence of a significant strategic transaction, we will need to raise significant additional capital to finance the research, development and commercialization of Gencaro and our other product candidate. 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 approximately 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:

- 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.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our headquarters facility consists of approximately 5,300 square feet of office space in Westminster, Colorado, which is leased until November 2019. We believe that this facility is adequate to meet our current needs.

Item 3. Legal Proceedings

Not applicable.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

As of March 7, 2011, our common stock began trading on The Nasdaq Capital Market under the symbol "ABIO", and was previously traded under the same symbol on The Nasdaq Global Market. Prior to completion of the merger with Nuvelo, Nuvelo's common stock traded under the symbol "NUVO" on The Nasdaq Global Market from January 31, 2003 to January 27, 2009 (except for the period between June 19, 2003 and March 19, 2004, where it temporarily traded under the symbol "NUVOD"). Stockholders

As of February 22, 2019, we had approximately 47 stockholders of record of our common stock, and the last sale price reported on The Nasdaq Capital Market for our common stock as of such date was $0.46 per share, rounded to the nearest penny.

Dividend Policy

The holders of our 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 in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

Information relating to our equity compensation plans as of December 31, 2018, under which our equity securities were authorized for issuance, is included in Item 12 of Part III of this Annual Report.

Unregistered Sales of Equity Securities and Use of Proceeds

None.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

We have included or incorporated by reference into this Management's Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this Annual Report on Form 10-K, and from time to time our management may make, statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Forward-looking statements may be identified by words including "anticipate," "plan," "believe," "intend," "estimate," "expect," "should," "may," "potential" and similar expressions.

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

Overview

We are a biopharmaceutical company applying a precision medicine approach to developing genetically-targeted therapies for cardiovascular diseases. Precision medicine refers to the tailoring of medical treatment to the individual characteristics of each patient through the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment. Our lead product candidate, Gencaro™ (bucindolol hydrochloride), is an investigational, pharmacologically unique beta-blocker and mild vasodilator that we are developing to treat atrial fibrillation, or AF, in certain patients who also have heart failure, or HF.

Gencaro has a mechanism of action that we believe is unique in the beta-blocker drug class and is modulated by a specific genotype. We estimate this genotype is present in about 50% of North American and European general populations. We believe that Gencaro's potential efficacy is enhanced in treating patients who have this genotype and, if Gencaro is approved by the U.S. Food and Drug Administration, or the FDA, Gencaro could potentially be a safe and effective therapy for treating AF in patients who have HF. We also believe that Gencaro, if approved, will have market exclusivity based on patents and new chemical entity status, if approved in the United States, Europe or other markets.

In February 2018, we reported the results of our Phase 2B clinical trial, known as GENETIC-AF, in which we evaluated Gencaro for the prevention of AF recurrence in patients with HF and a left ventricular ejection fraction, or LVEF, < 0.50. This population included 267 patients that had HF with reduced LVEF < 0.40, or HFrEF, or HF with mid-range LVEF ≥ 0.40 and < 0.50, or HFmrEF. GENETIC-AF compared Gencaro to TOPROL-XL (metoprolol succinate), a drug approved for treating HFrEF that is also prescribed, but not approved, for treating AF in patients with HFrEF. There are no approved or guideline recommended drug therapies for prevention of AF in HFmrEF patients, which constituted approximately one-half of the GENETIC-AF patients.

In GENETIC-AF, Gencaro was observed to have a similar treatment effect to TOPROL-XL (metoprolol succinate) in the overall population for prevention of AF recurrence. However, additional analyses prespecified in the statistical analysis plan showed statistically significant treatment effects in favor of Gencaro in the majority of the Phase 2B population (N=196; HR=0.54; p = 0.011). Gencaro also showed statistically significant treatment effects compared to TOPROL-XL for the prevention of AF recurrence in a subset of these patients with HFmrEF (N=91; HR=0.42; p = 0.017). We plan to conduct a pivotal Phase 3 trial, known as PRECISION-AF, evaluating Gencaro in HFmrEF patients because of Gencaro's observed potential treatment effect in these patients in GENETIC AF.

In February 2019, we received a Special Protocol Assessment, or SPA, agreement with the FDA in support of our planned Phase 3 clinical program. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of certain clinical trials that are intended to form the primary basis for determining a drug product's efficacy and safety. Upon specific request by a clinical trial sponsor, the FDA evaluates the protocol and responds to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate for the indication studied. An SPA agreement can potentially reduce the regulatory risk of bringing a drug to market.

To support the continued development of Gencaro, including the planned PRECISION-AF clinical trial, we will need additional financing to fund the Phase 3 trial and our general and administrative costs through its projected completion. Considering the substantial time and costs associated with the development of Gencaro and the risk that we may be unable to raise a significant amount of capital on acceptable terms, we may also pursue partnering and licensing opportunities, a strategic combination or other strategic transactions. If we are delayed in obtaining financing or are unable to complete a strategic transaction, we may discontinue our development activities on Gencaro or discontinue our operations.

We believe our cash and cash equivalents balance as of December 31, 2018, together with the $2.4 million of net proceeds raised in 2019 from sales of our common stock, will be sufficient to fund our operations, at our current cost structure, through the third quarter of 2019. However, 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.

In 2017, we entered into a sales agreement, as amended, with an agent to sell, from time to time, our common stock having an aggregate offering price of up to $10.2 million, in an "at the market offering." In January 2019, we amended the amended sales agreement to increase the maximum aggregate value of shares which we may issue and sell from

time to time under this sales agreement by approximately $2.5 million, from $10.2 million to $12.7 million. As of February 22, 2019, we have sold an aggregate of 9,242,406 shares of our common stock pursuant to the terms of such sales agreement, as amended, for aggregate gross proceeds of approximately $12.6 million. Net proceeds received in the period were approximately $11.9 million, after deducting initial expenses for executing the “at the market offering” and commissions paid to the placement agent. We have sold all shares available under the current prospectus.

On October 18, 2018, we held a special meeting of our stockholders to approve a series of certificates of amendment to the Company's restated certificate of incorporation, as amended, to effect a reverse split of the Company's outstanding common stock, at a ratio of between 1-for-3 and 1-for-20, inclusive, and to authorize the Company's board of directors to, for a period of up to one-year, select and file such a certificate of amendment to effect such a reverse split of the Company's outstanding common stock, if, in the our board's judgment, it is deemed necessary. Our board of directors has not selected a ratio for the reverse split.

Results of Operations

Research and Development Expenses

Research and development, or R&D, expense is comprised primarily of clinical development, manufacturing process development, and regulatory activities and costs. Our R&D expense continues to be almost entirely generated by our activities relating to the development of Gencaro.

Our research and development expenses were $4.2 million for the year ended December 31, 2018 as compared to $14.1 million for 2017. The $9.8 million decrease in research and development expenses in 2018 as compared to 2017 was primarily related to our GENETIC-AF clinical trial that was completed in 2017.

Clinical expense decreased approximately $7.5 million for the year ended December 31, 2018. The decrease was related to our GENETIC-AF clinical trial that was completed in 2017.

Manufacturing process development costs decreased approximately $2.1 million for the year ended December 31, 2018 compared to 2017. The decrease was a result of decreased production of clinical trial materials used in our GENETIC-AF clinical trial that was completed in 2017.

Subject to securing significant additional financing, we anticipate initiating our PRECISION AF clinical trial in the fourth quarter of 2019. R&D expense in 2019 is expected to be higher than 2018, if we initiate our PRECISION AF clinical trial. If we are unable to initiate our PRECISION AF clinical trial, then R&D expense is expected to be lower than 2018.

General and Administrative Expenses

General and administrative, or G&A, expenses primarily consist of personnel costs, consulting and professional fees, insurance, facilities and depreciation expenses, and various other administrative costs.

G&A expenses were $3.9 million for the year ended December 31, 2018, compared to $4.6 million for 2017, a decrease of approximately $0.8 million. The decrease in expenses during 2018 was comprised primarily of decreased personnel costs, non-cash stock-based compensation expense, consulting costs, professional fees and travel costs in 2018, as compared to 2017.

G&A expenses in 2019 are expected to be consistent with those in 2018 as we maintain administrative activities to support our ongoing operations.

Interest and Other Income

Interest and other income was $162,000 for the year ended December 31, 2018 as compared to $167,000 for 2017, resulting in a decrease of $5,000. This decrease was due lower marketable securities balances as we funded our operations. We expect interest income to be lower in 2019 than in 2018, as we continue to use our cash and cash equivalents to fund our operations.

Interest Expense

Interest expense was $8,000 for the year ended December 31, 2018 as compared to $6,000 for 2017. The amounts were nominal to our overall operations. Based on our current capital structure, interest expense is expected to be negligible in 2019.

Income Tax Benefit

Income tax benefit was $31,000 for the year ended December 31, 2018 as compared to $61,000 for 2017, related to the Protecting Americans from Tax Hikes Act of 2015, or PATH Act, which allows qualified small businesses to monetize up to $250,000 of research and experimentation tax credits through payroll tax refunds.

Liquidity and Capital Resources

Cash, Cash Equivalents and Marketable Securities

	December 31,	
	2018	2017
	(in thousands)	
Cash and cash equivalents	$6,608	$8,702
Marketable securities, short-term	—	3,050
Cash, cash equivalents and marketable securities	$6,608	$11,752

As of December 31, 2018, we had total cash, cash equivalents and marketable securities of approximately $6.6 million, as compared to $11.8 million as of December 31, 2017. The net decrease of $5.1 million during the year primarily reflects the approximately $8.2 million of cash used to fund operating activities during year ended December 31, 2018, partially offset by $3.4 million of cash proceeds from sales of our common stock.

On April 11, 2018, 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. On October 9, 2018, we received a written notification from NASDAQ granting an additional 180 calendar day period, until April 8, 2019, to regain compliance with the minimum bid price requirement. The minimum bid price requirement will be met if our common stock has a closing bid of at least $1.00 per share for a minimum of 10 consecutive business days during the 180 day period. This second 180 day period relates exclusively to the bid price deficiency and we could be delisted during the 180 day period for failure to maintain compliance with any other listing requirements that occurs during the 180 day period. If we are not able to regain compliance with the closing bid requirement in such period, we may be subject to delisting from the Nasdaq Capital Market. If delisted it could substantially impact our access to the 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 acceptable terms, or at all.

On October 18, 2018, we held a special meeting of its stockholders, at which our stockholders approved a series of certificates of amendment to our restated certificate of incorporation, as amended, to effect a reverse split of our outstanding common stock, at a ratio of between 1-for-3 and 1-for-20, inclusive, and to authorize our board of directors to, for a period of up to one-year, to select and file such a certificate of amendment to effect such a reverse split of our outstanding common stock, if, in the judgment of our board of directors, it is deemed necessary. Our board of directors has not selected a ratio for the reverse split.

Cash Flows from Operating, Investing and Financing Activities

	Years Ended December 31,	
	2018	2017
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$(8,244)	$(17,472)

Investing activities	3,046	12,926
Financing activities	3,104	5,847
Net (decrease) increase in cash and cash equivalents	$(2,094)	$1,301

Net cash used in operating activities for the year ended December 31, 2018 decreased approximately $9.2 million compared with 2017. This was primarily due to a lower net loss in 2018, as discussed in more detail above, offset by changes in operating assets and liabilities.

Net cash provided by investing activities for the year ended December 31, 2018 was $3.0 million, consisting of $3.1 million of proceeds from the maturities of marketable securities, offset by $4,000 for the purchase of property and equipment. Net cash provided by investing activities for the year ended December 31, 2017 was $12.9 million, consisting of $18.4 million of proceeds from the maturities of marketable securities, offset by $5.5 million for the purchases of marketable securities and $3,000 for the purchase of property and equipment.

Net cash provided by financing activities was $3.1 million for the year ended December 31, 2018 representing $3.4 million of net proceeds from sales of our common stock pursuant to our sales agreement, less $0.3 million in payments on a vendor financing arrangement. Net cash provided by financing activities was $5.8 million for the year ended December 31, 2017 representing $6.1 million of net proceeds from sales of our common stock pursuant to our sales agreement, less $0.3 million in payments on a vendor financing arrangement.

Sources and Uses of Capital

Our primary sources of liquidity to date have been capital raised from issuances of shares of our preferred and common stock. The primary uses of our capital resources to date have been to fund operating activities, including research, clinical development and drug manufacturing expenses, license payments, and spending on capital items.

In 2017, we entered into a sales agreement, as amended, with an agent to sell, from time to time, our common stock having an aggregate offering price of up to $10.2 million, in an “at the market offering.” In January 2019, we amended the amended sales agreement to increase the maximum aggregate value of shares which we may issue and sell from time to time under this sales agreement by approximately $2.5 million, from $10.2 million to $12.7 million. As of February 22, 2019, we have sold an aggregate of 9,242,406 shares of our common stock pursuant to the terms of such sales agreement, as amended, for aggregate gross proceeds of approximately $12.6 million. Net proceeds received in the period were approximately $11.9 million, after deducting initial expenses for executing the “at the market offering” and commissions paid to the placement agent. We have sold all shares available under the current prospectus.

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:

- the costs and timing for the potential additional clinical trials, including PRECISION AF, in order to gain possible regulatory approval for Gencaro or any other product candidate;
- the market price of our stock and the availability and cost of additional equity capital from existing and potential new investors;
- our ability to retain the listing of our common stock on the Nasdaq Capital Market;
- our ability to control costs associated with its operations;
- general economic and industry conditions affecting the availability and cost of capital;
- 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.

We believe that our cash and cash equivalents as of December 31, 2018, together with the $2.4 million of net proceeds raised in 2019 from sales of our common stock, will be sufficient to fund our operations, at our projected cost structure, through the third quarter of 2019. However, our forecast of the period of time through which our financial resources will be adequate to support our current and forecasted operations could vary materially. We will need to raise additional capital to fund future operations and any additional development of Gencaro or any other product candidates. Such financing would likely result in dilution to our existing 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. The significant uncertainties surrounding the clinical development timelines and costs and the ability to raise a significant amount of capital raises substantial doubt about our ability to continue as a going concern from one year after the Company’s financial statements have been issued.

Critical Accounting Policies and Estimates

A critical accounting policy is one that is both important to the portrayal of our financial condition and results of operation and requires management’s most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. While our significant accounting policies are described in Note 1 of “Notes to Financial Statements” included within Item 8 in this report, we believe the following

critical accounting policy affected our most significant judgments, assumptions, and estimates used in the preparation of our financial statements and, therefore, is important in understanding our financial condition and results of operations.

Accrued Outsourcing Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued outsourcing expenses. This process involves identifying services that third parties have performed on our behalf and estimating the level of service performed and the associated cost incurred for these services as of the balance sheet date. Examples of estimated accrued outsourcing expenses include contract service fees, such as fees payable to contract manufacturers in connection with the production of materials related to our drug product, and service fees from clinical research organizations. We develop estimates of liabilities using our judgment based upon the facts and circumstances known at the time.

Off-Balance Sheet Arrangements

We have not participated in any transactions with unconsolidated entities, such as special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements.

Indemnifications

In the ordinary course of business, we enter into contractual arrangements under which we may agree to indemnify certain parties from any losses incurred relating to the services they perform on our behalf or for losses arising from certain events as defined within the particular contract. Such indemnification obligations may not be subject to maximum loss clauses. We have entered into indemnity agreements with each of our directors, officers and certain employees. Such indemnity agreements contain provisions, which are in some respects broader than the specific indemnification provisions contained in Delaware law. We also maintain an insurance policy for our directors and executive officers insuring against certain liabilities arising in their capacities as such.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Not applicable.

Item 8. Financial Statements and Supplementary Data

Report of Independent Registered Public Accounting Firm

The Stockholders and Board of Directors

ARCA biopharma, Inc.:

Opinion on the Financial Statements

We have audited the accompanying balance sheets of ARCA biopharma, Inc. (the Company) as of December 31, 2018 and 2017, the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in note 1 to the financial statements, the Company has incurred recurring losses from operations and needs to raise capital to fund its clinical development programs. The Company's ability to raise such capital is uncertain. As a result, there is substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2006.

Denver, Colorado

February 27, 2019

ARCA BIOPHARMA, INC.

BALANCE SHEETS

	As of December 31,	
	2018	2017
	(in thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$6,608	$8,702
Marketable securities	—	3,050
Other current assets	169	547
Total current assets	6,777	12,299
Property and equipment, net	24	42
Other assets	24	24
Total assets	$6,825	$12,365
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$230	$622
Accrued compensation and employee benefits	150	757
Accrued expenses and other liabilities	413	691
Total current liabilities	793	2,070
Deferred rent, net of current portion	—	20
Total liabilities	793	2,090
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5 million shares authorized; no shares issued or outstanding at December 31, 2018 and 2017	—	—
Common stock, $0.001 par value; 100 million shares authorized at December 31, 2018 and 2017; 13,924,058 and 11,775,062 shares issued and outstanding at December 31, 2018 and	14	12

2017, respectively		
Additional paid-in capital	144,952	141,266
Accumulated other comprehensive loss	—	(2)
Accumulated deficit	(138,934)	(131,001)
Total stockholders' equity	6,032	10,275
Total liabilities and stockholders' equity	$6,825	$12,365

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

	Years Ended December 31,	
	2018	2017
	(in thousands, except share and per share amounts)	
Costs and expenses:		
Research and development	$4,239	$14,076
General and administrative	3,879	4,636
Total costs and expenses	8,118	18,712
Loss from operations	(8,118)	(18,712)
Interest and other income	162	167
Interest expense	(8)	(6)
Loss before income taxes	(7,964)	(18,551)
Income tax benefit	31	61
Net loss	$(7,933)	$(18,490)
Change in unrealized loss on marketable securities	2	17
Comprehensive loss	$(7,931)	$(18,473)
Net loss per share:		
Basic and diluted	$(0.57)	$(1.77)
Weighted average shares outstanding:		
Basic and diluted	13,849,055	10,431,391

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

	Stockholders' Equity					
	Common stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	
	Shares	Amount	Capital	Loss	Deficit	Total
	(in thousands, except share and per share amounts)					
Balance, December 31, 2016	9,082,366	$ 9	$ 134,715	$ (19)	$ (112,511)	$ 22,194
Issuance of common stock for cash, net of offering costs	2,677,525	3	6,093	—	—	6,096
Issuance of common stock upon vesting of Restricted Stock Units	15,171	—	—	—	—	—
Share-based compensation	—	—	458	—	—	458
Change in unrealized loss on marketable securities	—	—	—	17	—	17
Net loss	—	—	—	—	(18,490)	(18,490)
Balance, December 31, 2017	11,775,062	12	141,266	(2)	(131,001)	10,275
Issuance of common stock for cash, net of offering costs	2,133,828	2	3,413	—	—	3,415
Issuance of common stock upon vesting of Restricted Stock Units	15,168	—	—	—	—	—
Share-based compensation	—	—	273	—	—	273
Change in unrealized loss on marketable securities	—	—	—	2	—	2
Net loss	—	—	—	—	(7,933)	(7,933)
Balance, December 31, 2018	13,924,058	$ 14	$ 144,952	$ —	$ (138,934)	$ 6,032

See accompanying Notes to Financial Statements

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ARCA BIOPHARMA, INC.

STATEMENTS OF CASH FLOWS

	Years Ended December 31,	
	2018	2017
	(in thousands)	
Cash flows from operating activities:		
Net loss	$(7,933)	$(18,490)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	22	27
Amortization of other assets	—	329
Amortization of premiums and discounts on marketable securities	2	119
Share-based compensation	273	458
Change in operating assets and liabilities:		
Other current assets	689	437
Accounts payable	(392)	(583)
Accrued compensation and employee benefits	(607)	38
Accrued expenses and other liabilities	(298)	193
Net cash used in operating activities	(8,244)	(17,472)
Cash flows from investing activities:		
Purchase of property and equipment	(4)	(3)
Purchases of marketable securities	—	(5,471)
Proceeds from maturities of marketable securities	3,050	18,400
Net cash provided by investing activities	3,046	12,926
Cash flows from financing activities:		
Proceeds from the issuance of common stock	3,532	6,551
Common stock offering costs	(117)	(448)
Repayment of principal on vendor finance agreement	(311)	(256)
Net cash provided by financing activities	3,104	5,847
Net (decrease) increase in cash and cash equivalents	(2,094)	1,301
Cash and cash equivalents, beginning of year	8,702	7,401
Cash and cash equivalents, end of year	$6,608	$8,702
Supplemental cash flow information:		
Interest paid	$8	$6
Income tax refund received	$54	$38
Supplemental disclosure of noncash investing and financing transactions:		
Common stock offering costs accrued but not yet paid	$—	$7
Change in unrealized loss on marketable securities	$2	$17

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

NOTES TO FINANCIAL STATEMENTS

(1) The Company and Summary of Significant Accounting Policies

Description of Business

ARCA biopharma, Inc. (the Company or ARCA), a Delaware corporation, is headquartered in Westminster, Colorado. The Company is a biopharmaceutical company applying a precision medicine approach to developing genetically-targeted therapies for cardiovascular diseases. The Company's lead product candidate, Gencaro™ (bucindolol hydrochloride), is an investigational, pharmacologically unique beta-blocker and mild vasodilator that ARCA is developing for the potential treatment of atrial fibrillation (AF) in certain patients who also have heart failure (HF).

In February 2018, the Company completed its Phase 2B clinical superiority trial, known as GENETIC-AF, in which the Company evaluated Gencaro for the treatment of AF in patients with heart failure with reduced left ventricular ejection fraction (HFrEF) and mid-range left ventricle ejection fraction (HFmrEF) against an active comparator, the beta-blocker TOPROL-XL (metoprolol succinate), a drug indicated for treating HFrEF that is also prescribed, but not approved, for treating AF in patients with HFrEF. Enrollment in GENETIC-AF was limited to patients that possess the specific genotype that the Company believes enhances Gencaro's potential therapeutic effects. The planned development program of Gencaro is, in part, based on the results of the Company's completed GENETIC-AF Phase 2B clinical trial and a prospectively designed DNA substudy of adrenergic receptor polymorphisms in the BEST trial, a previous Phase 3 study of HF patients.

GENETIC-AF was a Phase 2B, multi-center, randomized, double-blind, clinical superiority trial comparing the safety and efficacy of Gencaro against TOPROL-XL, that enrolled 267 patients. The Company reported top-line Phase 2B trial data in February 2018. Overall, Gencaro demonstrated a similar treatment benefit compared to the active comparator, metoprolol succinate; however, trends for benefit in favor of bucindolol were observed in multiple subpopulations of patients in the trial. Based on these data, the Company believes further clinical development of Gencaro is warranted. Based on review of the Phase 2 GENETIC-AF trial results, as well as its alignment with previous Phase 3 pharmacogenetic substudy data from the BEST trial, the FDA stated that data from a single pivotal Phase 3 clinical trial may be sufficient to support approval of Gencaro for the treatment of AF in patients with HF. The Company, in consultation with the FDA, developed key elements of the Phase 3 clinical trial needed to support a potential New Drug Application (NDA), details of which were submitted for evaluation and confirmed via the FDA's Special Protocol Assessment (SPA) process in February 2019.

During 2018, ARCA initiated Investigational New Drug enabling development activities with AB171, a thiol-substituted isosorbide mononitrate, as a potential genetically-targeted treatment for peripheral arterial disease and for HF.

The Company will need to raise additional capital to fund future operations and any additional development of Gencaro or AB171. If the Company is unable to obtain additional funding or is unable to complete a strategic transaction, it may have to discontinue development activities on Gencaro or discontinue its operations.

Liquidity and Going Concern

The Company devotes substantially all of its efforts towards obtaining regulatory approval and raising capital necessary to fund its operations and it is subject to a number of risks associated with clinical research and development, including dependence on key individuals, the development of and regulatory approval of commercially viable products, the need to raise adequate additional financing necessary to fund the development and commercialization of its products, and competition from larger companies. The Company has not generated revenue to date and has incurred substantial losses and negative cash flows from operations since its inception. The Company has historically funded its operations through issuances of common and preferred stock.

The Company believes that its cash and cash equivalents as of December 31, 2018, together with the $2.4 million of net proceeds raised in 2019 from sales of its common stock, as discussed in Note 11, will be sufficient to fund its operations, at its projected cost structure, through the end of the third quarter of 2019. In light of the significant uncertainties regarding clinical development timelines and costs for developing drugs such as Gencaro, the Company will need to raise additional capital to finance the Company's future operations and any additional development of Gencaro or any other product candidates. If the Company is delayed in completing or is unable to complete additional financing and/or a strategic transaction, the Company may discontinue its development activities or operations.

Due to the current status of the Gencaro development program, the current amount of cash and cash equivalents held, the anticipated costs to be incurred for existing operations as well as exploring other corporate strategic alternatives, and the uncertainty of the

Company's ability to raise a significant amount of capital, management has determined there is substantial doubt about the Company's ability to continue as a going concern from one year after the Company's financial statements have been issued. The Company could delay or cancel certain planned expenditures related to its drug development programs and/or implement cost reduction measures to conserve its cash balances; however, there is no assurance that those measures would be adequate to allow the Company to continue as a going concern for a period beyond one year from the issuance of these financial statements. These financial statements have been prepared with the assumption that the Company will continue as a going concern and will be able to realize its assets and discharge its liabilities 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 the inability of the Company to continue as a going concern. The Company may not be able to raise sufficient capital on acceptable terms, or at all, to continue development of Gencaro or to otherwise continue operations and may not be able to execute any strategic transaction.

The Company's liquidity, and its ability to raise additional capital or complete any strategic transaction, depends on a number of factors, including, but not limited to, the following:

- the costs and timing for the potential additional clinical trials in order to gain possible regulatory approval for Gencaro or any other product candidate;
- the market price of the Company's stock and the availability and cost of additional equity capital from existing and potential new investors;
- the Company's ability to retain the listing of its common stock on the Nasdaq Capital Market;
- general economic and industry conditions affecting the availability and cost of capital;
- the Company's ability to control costs associated with its operations;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the terms and conditions of the Company's existing collaborative and licensing agreements.

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

On April 11, 2018, the Company received notification from Nasdaq of potential delisting of its shares from the Nasdaq Capital Market because the closing bid price of its common stock had not met the minimum closing bid price of $1.00 per share during the preceding 30 days. On October 9, 2018, ARCA received a written notification from NASDAQ granting an additional 180 calendar day period, until April 8, 2019, to regain compliance with the minimum bid price requirement. The minimum bid price requirement will be met if the Common Stock has a closing bid of at least $1.00 per share for a minimum of 10 consecutive business days during the 180 day period. If the Company is not able to regain compliance with the closing bid requirement in such period, the Company may be subject to delisting from the Nasdaq Capital Market. If delisted, it could substantially impact the Company's access to the 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 the Company's ability to raise capital on acceptable terms, or at all.

On October 18, 2018, the Company held a special meeting of its stockholders, at which stockholders authorized the Company's board of directors to amend the Company's restated certificate of incorporation, as amended, to effect a reverse split of the Company's outstanding common stock, if, in the judgment of the Company's board of directors, it is

deemed necessary to maintain NASDAQ compliance or for other reasons. The Company's board of directors has not selected a ratio for the reverse split.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) and include all adjustments necessary for the fair presentation of our financial position, results of operations and cash flows for the periods presented. Management has performed an evaluation of the Company's activities through the date of filing of this Annual Report on Form 10-K, and the subsequent events are disclosed in Note 11.

Recent Accounting Pronouncements

In January 2016, Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities (ASU 2016-01). ASU 2016-01 requires equity investments to be measured at fair value with changes in fair value recognized in net income; simplifies the impairment assessment of equity investments without readily determinable fair values by requiring a qualitative assessment to identify impairment; eliminates the requirement for public business entities to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet; requires public business entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes; requires an entity to present separately in other comprehensive income the portion of the total change in the fair value of a liability resulting from a change in the instrument-specific credit risk when the entity has elected to measure the liability at fair value in accordance with the fair value option for financial instruments; requires separate presentation of financial assets and financial liabilities by measurement category and form of financial assets on the balance sheet or the accompanying notes to the financial statements and clarifies that an entity should evaluate the need for a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the entity's other deferred tax assets. ASU 2016-01 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The adoption of ASU 2016-01 as of January 1, 2018, had no impact to the Company's financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842) (ASU 2016-02), which requires lessees to recognize assets and liabilities for the rights and obligations created by most leases on their balance sheet. In July 2018, FASB issued ASU No. 2018 11, Topic 842 - Targeted Improvements. The update requires modified retrospective transition, with the option to initially apply the new standard at the adoption date and recognize a cumulative-effect adjustment and elect various practical expedients. The guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company plans to apply the practical expedients permitted within the guidance, which allows the Company to carryforward its historical lease classification, and to apply the transition option which does not require application of the guidance to comparative periods in the year of adoption. The Company has completed preliminary calculations of the impact that ASU 2016-02 will have on its financial statements and related disclosures and it is expected that the operating lease commitment discussed in Note 6 will be recognized as operating lease liability, at its present value, and the corresponding right-of-use asset will be recognized. The Company does not expect this guidance will have a material impact on the financial statements.

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement, which modifies the disclosure requirements on fair value measurements. The new guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Upon the effective date, certain provisions are to be applied prospectively, while others are to be applied retrospectively to all periods presented. An entity is permitted to early adopt any removed or modified disclosures upon issuance of this ASU and delay adoption of the additional disclosures until their effective date. The Company is currently evaluating the impact of the amendments on the financial statement disclosures. Since the amendments impact only disclosure requirements, the Company does not expect the amendments to have a material impact on the financial statements.

The Company reviewed all other recently issued accounting pronouncements and concluded that they were either not applicable or not expected to have a significant impact to the financial statements.

Accounting Estimates in the Preparation of Financial Statements

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. The Company bases estimates on various assumptions that are believed to be reasonable under the circumstances. The Company believes significant judgment was involved in estimating the clinical trial accruals, and in estimating other accrued liabilities, stock-based compensation, and income taxes. Management is continually evaluating and updating these estimates, and it is possible that these estimates will change in the future or that actual results may differ from these estimates.

Cash Equivalents

Cash equivalents generally consist of money market funds and debt securities with maturities of 90 days or less at the time of purchase. The Company invests its excess cash in securities with strong ratings and has established guidelines relative to diversification and maturity with the objective of maintaining safety of principal and liquidity.

Marketable Securities

The Company has designated its marketable securities as available-for-sale securities and accounted for them at their respective fair values. Marketable securities are classified as short-term or long-term based on the nature of the securities and their availability to meet current operating requirements. Marketable securities that are readily available for use in current operations are classified as short-term available-for-sale securities and are reported as current marketable securities in the accompanying balance sheets. Marketable securities that are not considered available for use in current operations are classified as long-term available-for-sale securities and are reported as a component of long-term assets in the accompanying balance sheets.

Securities that are classified as available-for-sale are measured at fair value, including accrued interest, with temporary unrealized gains and losses reported as a component of stockholders' equity until their disposition. The Company reviews all available-for-sale securities at each period end to determine if they remain available-for-sale based on the Company’s then current intent and ability to sell the security if it is required to do so.

All of the Company’s marketable securities are subject to a periodic impairment review. The Company recognizes an impairment charge when a decline in the fair value of its investments below the cost basis is judged to be other-than-temporary.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents and marketable securities. The Company has no off-balance-sheet concentrations of credit risk, such as foreign exchange contracts, option contracts, or foreign currency hedging arrangements. The Company maintains cash and cash equivalent balances in the form of bank demand deposits and money market fund accounts with financial institutions that management believes are creditworthy. Such balances may at times exceed the insured amount.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Cost includes expenditures for equipment, leasehold improvements, replacements, and renewals. Maintenance and repairs are charged to expense as incurred. When assets are sold, retired, or otherwise disposed of, the cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is reflected in operations. The cost of property and equipment is depreciated using the straight-line method over the estimated useful lives of the related assets. Leasehold improvements are amortized over the shorter of the life of the lease or the estimated useful life of the assets.

Accrued Outsourcing Expenses

As part of the process of preparing its financial statements, the Company is required to estimate accrued outsourcing expenses. This process involves identifying services that third parties have performed on the Company’s behalf and estimating the level of service performed and the associated cost incurred for these services as of the balance sheet date. Examples of estimated accrued outsourcing expenses include contract service fees, such as fees payable to contract manufacturers in connection with the production of materials related to the Company’s drug product, and service fees from clinical research organizations. The Company develops estimates of liabilities using its judgment based upon the facts and circumstances known at the time.

Segments

The Company operates in one segment. Management uses one measure of profitability and does not segment its business for internal reporting.

Research and Development

Research and development costs are expensed as incurred. These consist primarily of salaries, contract services, and supplies.

Costs related to clinical trial and drug manufacturing activities are based upon estimates of the services received and related expenses incurred by contract research organizations (CROs), clinical study sites, drug manufacturers, collaboration partners, laboratories, consultants, or otherwise. Related contracts vary significantly in length, and could be for a fixed amount, a variable amount based on actual costs incurred, capped at a certain limit, or for a combination of these elements. Activity levels are monitored through communications with the vendors, including detailed invoices and task completion review, analysis of expenses against budgeted amounts, and pre-approval of any changes in scope of the services to be performed. Certain significant vendors may also provide an estimate of costs incurred but not invoiced on a periodic basis. Expenses related to the CROs and clinical studies, as well as contract drug manufacturers, are primarily based on progress made against specified milestones or targets in each period.

In accordance with certain research and development agreements, we are obligated to make certain upfront payments upon execution of the agreement. We record these upfront payments as prepaid research and development expenses, which are included in Other

current assets or Other assets in the accompanying Balance Sheets. Such payments are recorded to research and development expense as services are performed. We evaluate on a quarterly basis whether events and circumstances have occurred that may indicate impairment of remaining prepaid research and development expenses.

Stock-Based Compensation

The Company's stock-based compensation cost recognized is based on the estimated grant date fair value. The Company recognizes compensation costs for its stock-based awards on a straight-line basis over the requisite service period for the entire award, as adjusted for expected forfeitures.

Income Taxes

The current benefit for income taxes represents actual or estimated amounts payable or refundable on tax returns filed or to be filed each year. Deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the period that includes the enactment date. The overall change in deferred tax assets and liabilities for the period measures the deferred tax expense or benefit for the period. The measurement of deferred tax assets may be reduced by a valuation allowance based on judgmental assessment of available evidence if deemed more likely than not that some or all of the deferred tax assets will not be realized. The Company has recorded a valuation allowance against all of its deferred tax assets, as management has concluded that it is more likely than not that the net deferred tax asset will not be realized through future taxable income, based primarily on the Company's history of operating losses. The Company has not performed an Internal Revenue Code Section 382 limitation study. Depending on the outcome of such a study, the gross amount of net operating losses recognizable in future tax periods could be limited.

(2) Net Loss Per Share

The Company calculates basic loss per share by dividing net loss by the weighted average common shares outstanding during the period. Diluted loss per share is computed by dividing net loss by the weighted average number of common shares outstanding during the period increased to include, if dilutive, the number of additional common shares that would have been outstanding if the potential common shares had been issued. The Company's potentially dilutive shares include stock options, restricted stock units and warrants for common stock.

Because the Company reported a net loss for the years ended December 31, 2018 and 2017, all potentially dilutive shares of common stock have been excluded from the computation of the dilutive net loss per share for all periods presented. Such potentially dilutive shares of common stock consist of the following:

	Years Ended December 31,	
	2018	2017
Potentially dilutive securities, excluded:		
Outstanding stock options	604,003	611,975

Unvested restricted stock units	—	15,168
Warrants to purchase common stock	2,669,855	3,633,008
	3,273,858	4,260,151

(3) Marketable Securities and Fair Value Disclosures

There were no marketable securities as of December 31, 2018. Marketable securities consisted of the following as of December 31, 2017 (in thousands):

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Short-term available-for-sale securities:				
Corporate bonds	$3,052	$ —	$ (2)	$3,050
Total	$3,052	$ —	$ (2)	$3,050

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date (exit price). Inputs used to measure fair value are classified into the following hierarchy:

- Level 1—Unadjusted quoted prices in active markets for identical assets or liabilities. The Company's Level 1 assets consist of money market investments. The Company does not have any Level 1 liabilities.
- Level 2—Unadjusted quoted prices in active markets for similar assets or liabilities; unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active; or inputs other than quoted prices that are observable for the asset or liability. The Company's Level 2 assets consist of corporate bonds and commercial paper securities. The Company does not have any Level 2 liabilities.
- Level 3—Unobservable inputs for the asset or liability. The Company does not have any Level 3 assets or liabilities.

The following table identifies the Company's assets that were measured at fair value on a recurring basis (in thousands):

	Balance	Level 1	Level 2	Level 3
December 31, 2018				
Money market	$6,529	$6,529	$—	$ —
Total	$6,529	$6,529	$—	$ —
December 31, 2017				
Money market	$8,189	$8,189	$—	$ —
Corporate bonds	3,725	—	3,725	—
Total	$11,914	$8,189	$3,725	$ —

As of December 31, 2018 and 2017, the Company had $6.5 million and $8.9 million, respectively, of cash equivalents consisting of money market funds, and corporate bonds in 2017, with original maturities of 90 days or less. The Company has the ability to liquidate these investments without restriction. The Company determines fair value for these money market funds and equity securities with Level 1 inputs through quoted market prices. There were no

transfers between any fair value hierarchy levels in 2018 or 2017.

Fair Value of Other Financial Instruments

The carrying amount of other financial instruments, including accounts payable, approximated fair value due to their short maturities. As of December 31, 2018 and 2017, the Company did not have any debt outstanding.

(4) Property and Equipment

Property and equipment consist of the following (in thousands):

	Estimated Life	December 31, 2018	December 31, 2017
Computer equipment	3 years	$ 65	$ 74
Lab equipment	5 years	142	142
Furniture and fixtures	5 years	62	83
Computer software	3 years	70	85
Leasehold improvements	Lesser of useful life or life of the lease	59	59
		398	443
Accumulated depreciation and amortization		(374)	(401)
Property and equipment, net		$ 24	$ 42

For the years ended December 31, 2018 and 2017, depreciation and amortization expense was $22,000 and $27,000, respectively.

(5) Related Party Arrangements

Transactions with the Company’s President and Chief Executive Officer

The Company has entered into unrestricted research grants with its President and Chief Executive Officer’s academic research laboratory at the University of Colorado. Funding of any unrestricted research grants is contingent upon the Company’s financial condition, and can be deferred or terminated at the Company’s discretion. Total expense under these arrangements for the years ended December 31, 2018 and 2017 was $325,000 and $418,000, respectively, of which $111,000 was unpaid and included in accrued expenses and other liabilities as of December 31, 2018.

(6) Commitments and Contingencies

The Company has or is subject to the following commitments and contingencies:

Employment Agreements

The Company maintains employment agreements with several key executive employees. The agreements may be terminated at any time by the Company with or without cause upon written notice to the employee, and entitle the employee to wages in lieu of notice for periods not exceeding one calendar year from date of termination without cause or by the employee for good reason. Certain of these agreements also provide for payments to be made under certain conditions related to a change in control of the Company.

Operating Lease

On August 1, 2013 the Company entered into a lease agreement for approximately 5,300 square feet of office facilities in Westminster, Colorado which has served as the Company's primary business office since October 1, 2013. Effective March 2, 2016, the lease was renewed for an additional 38 month term beginning October 1, 2016 and expiring on November 30, 2019.

Below is a summary of the future minimum lease payments committed for the Company's facility in Westminster, Colorado as of December 31, 2018 (in thousands):

2019	$83
Total future minimum lease payments	$83

Rent expense under these leases for the years ended December 31, 2018 and 2017 was $82,000 and $82,000, respectively.

Cardiovascular Pharmacology and Engineering Consultants, LLC

ARCA has licensed worldwide rights to all preclinical and clinical data from development of bucindolol through the BEST trial from Cardiovascular Pharmacology and Engineering Consultants, LLC (CPEC), who has licensed rights to this data from Bristol Myers Squib (BMS). CPEC is a licensing subsidiary of Indevus Pharmaceuticals Inc. (a wholly owned subsidiary of Endo Pharmaceuticals), holding ownership rights to certain clinical trial data of Gencaro. Under the terms of its license agreement with CPEC, the Company will incur milestone and royalty obligations upon the occurrence of certain events. If the FDA grants marketing approval for Gencaro,

the license agreement states that the Company will owe CPEC a milestone payment of $8.0 million within six months after FDA approval. The license agreement states that a milestone payment of up to $5.0 million in the aggregate shall be paid upon regulatory marketing approval in Europe and Japan. The license agreement also states that the Company's royalty obligation ranges from 12.5% to 25% of revenue from the related product based on achievement of specified product sales levels, including a 5% royalty that CPEC is obligated to pay under its original license agreement for Gencaro. The agreement states that the Company has the right to buy down the royalties to a range of 12.5% to 17% by making a payment to CPEC within six months of regulatory approval.

In October 2017, the Company entered into an agreement with CPEC's minority owner, Aeolus Pharmaceuticals, Inc. (Aeolus) pursuant to which the Company acquired Aeolus' minority membership interest in CPEC. The transaction effectively buys-out Aeolus' royalty interest thereby reducing or eliminating the stated milestone and royalty obligations that could be payable by the Company, if Gencaro receives regulatory approval and is commercialized. As a result of this transaction, the Company, together with Endo Pharmaceuticals, Inc., indirectly hold the remaining licensee rights of CPEC to certain Gencaro clinical data, as discussed above. The acquisition cost of this interest did not have a material impact on the Company's annual financial statements.

(7) Equity Financings and Warrants

2017 Equity Financing

On January 11, 2017, the Company entered into a Capital on Demand ™ Sales Agreement (the Sales Agreement) with JonesTrading Institutional Services LLC, as agent (JonesTrading), pursuant to which the Company may offer and sell, from time to time through JonesTrading, shares of the Company's common stock, par value $0.001 per share (the Common Stock), having an aggregate offering price of up to $7.3 million. On August 21, 2017 and January 25, 2019, the Company amended its Capital on Demand Sales Agreement. The amendments, among other things, increased the maximum aggregate offering value of shares of the Company's common stock which the Company may issue and sell from time to time under the Sales Agreement from $7.3 million to $12.7 million (the Shares).

Under the amended Sales Agreement, JonesTrading may sell the Shares by any method permitted by law and deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on or through The NASDAQ Capital Market, on any other existing trading market for the Common Stock or to or through a market maker. In addition, under the amended Sales Agreement, JonesTrading may sell the Shares by any other method permitted by law, including in negotiated transactions. The Company may instruct JonesTrading not to sell Shares if the sales cannot be effected at or above the price designated by the Company from time to time.

The Company is not obligated to make any sales of the Shares under the amended Sales Agreement. The offering of Shares pursuant to the amended Sales Agreement will terminate upon the earlier of (a) the sale of all of the Shares subject to the amended Sales Agreement or (b) the termination of the amended Sales Agreement by JonesTrading or the Company, as permitted therein.

The Company paid JonesTrading a commission rate equal to 3.0% of the aggregate gross proceeds from each sale of Shares and agreed to provide JonesTrading with customary indemnification and contribution rights. The Company will also reimburse JonesTrading for certain specified expenses in connection with entering into and amending the Sales Agreement.

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Under the amended Sales Agreement, the Company sold an aggregate of 2,133,828 and 2,677,525 shares of Common Stock pursuant to the terms of such Sales Agreement, as amended, for net proceeds of approximately $3.4 million and $6.1 million during the years ended December 31, 2018 and 2017, respectively, including initial expenses for executing the “at the market offering” and commissions to the placement agent.

See Note 11 for subsequent sales under the Sales Agreement.

Warrants

Warrants to purchase shares of common stock were granted as part of various financing and business agreements. All outstanding warrants were recorded in additional paid-in capital at their estimated fair market value at the date of grant using a Black-Scholes option-pricing model.

As of December 31, 2018, these warrants, by year of expiration, are summarized below:

Year of Expiration	Number of Warrants	Weighted Average Exercise Price
2019	224,323	$ 15.73
2020	44,299	15.96
2022	2,401,233	6.10
	2,669,855	$ 7.07

(8) Share-based Compensation

Stock Plans

The Company’s equity incentive plan, the 2013 Equity Incentive Plan (the Equity Plan), was approved by stockholders on September 17, 2013, and amended in June 2016 to increase the reserve for issuance under this Equity Plan by 1,000,000 shares. The maximum number of shares issuable under this plan is 1,321,428 shares.

The Equity Plan provides for the granting of stock options (including indexed options), restricted stock units, stock appreciation rights, restricted stock purchase rights, restricted stock bonuses, performance shares, performance units and deferred stock units. Under the Equity Plan, awards may be granted to employees, directors and consultants of ARCA, except for incentive stock options, which may be granted only to employees. As of December 31, 2018, options and awards for 597,342 shares were outstanding under the Equity Plan, and 615,976 shares were reserved for future awards.

In general, the Equity Plan authorizes the grant of stock options that vest at rates set by the Board of Directors or the Compensation Committee thereof. Generally, stock options granted by ARCA under the equity incentive plans become exercisable ratably for a period of three to four years from the date of grant and have a maximum term of ten years. The exercise prices of stock options under the equity incentive plan generally meet the following criteria: the exercise price of incentive stock options must be at least 100% of the fair market value on the grant date and exercise price of options granted to 10% (or greater) stockholders must be at least 110% of the fair market value on the grant

date.

In conjunction with the adoption of the Equity Plan, the Company discontinued grants under its previous plan, the Amended and Restated ARCA biopharma, Inc. 2004 Equity Incentive Plan (the 2004 Plan), effective September 17, 2013. The 2004 Plan expired in 2014; however, options outstanding under the 2004 plan will continue to vest according to the original terms of each grant. As of December 31, 2018, options to purchase 5,383 shares with a weighted average exercise price of $102.16 per share were outstanding under this plan. Other stock plans that were assumed by ARCA in the Merger still have options outstanding that will continue to vest according to the original terms of each grant, but no new options can be granted under these plans, as the plans have expired. As of December 31, 2018, options to purchase 1,278 shares with a weighted average exercise price of $233.94 were outstanding under these plans.

The Company granted options for 40,000 and 469,600 shares of common stock in the years ended December 31, 2018 and 2017, respectively. The fair values of employee stock options granted in the years ended December 31, 2018 and 2017 were estimated at the date of grant using the Black-Scholes model with the following assumptions and had the following estimated weighted average grant date fair value per share:

	Years Ended December 31,	
	2018	2017
Expected term	5.3 years	5.8 years
Expected volatility	90 %	73 %
Risk-free interest rate	2.59%	1.99%
Expected dividend yield	0 %	0 %
Weighted-average grant date fair value per share	$0.52	$1.60

A summary of ARCA's stock option activities for the years ended December 31, 2018 and 2017, and related information as of December 31, 2018, is as follows:

	Options Outstanding			
	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Options outstanding - December 31, 2016	629,629	$ 6.30		
Granted	469,600	2.54		
Exercised	—	—		
Forfeited and cancelled	(487,254)	3.05		

Options outstanding - December 31, 2017	611,975	$ 6.00	8.14	$ —
Granted	40,000	0.72		
Exercised	—	—		
Forfeited and cancelled	(47,972)	9.51		
Options outstanding - December 31, 2018	604,003	$ 5.37	7.29	$ —
Options exercisable - December 31, 2018	486,420	$ 6.04	7.13	$ —
Options vested and expected to vest -				
December 31, 2018	603,842	$ 5.38	7.29	$ —

The aggregate intrinsic value in the table above represents the total intrinsic value, based on our closing price as of December 31 of the respective year, which would have been received by the option holders had all the option holders with in-the-money options exercised as of that date. As of December 31, 2018, the unrecognized compensation expense related to unvested options, excluding estimated forfeitures, was $186,000 which is expected to be recognized over a weighted average period of 1.1 years. The Company recognizes compensation costs for its share-based awards on a straight-line basis over the requisite service period for the entire award, as adjusted for expected forfeitures.

Restricted Stock Units

The Company began granting restricted stock units (RSUs) to employees during 2013 in conjunction with the adoption of the Equity Plan. The fair value of RSU awards is the closing price of the Company’s common stock on the date of grant and was recognized as

compensation expense on a straight-line basis over the respective vesting period. The stock awards granted had a requisite service period between three and four years with annual vesting on the grant anniversary date.

A summary of RSU activity for the years ended December 31, 2018 and 2017 is presented below:

	Restricted Stock Units Outstanding	
	Number of Shares	Weighted Average Grant Date Fair Value
RSUs outstanding - December 31, 2016	30,739	$ 7.91
Granted	—	—
Vested and released	(15,171)	7.94
Forfeited and cancelled	(400)	6.03
RSUs outstanding - December 31, 2017	15,168	$ 7.94
Granted	—	—
Vested and released	(15,168)	7.94
Forfeited and cancelled	—	—
RSUs outstanding - December 31, 2018	—	$ —

As of December 31, 2018, all compensation cost related to stock awards was recognized.

Non-cash Stock-based Compensation

For the years ended December 31, 2018 and 2017, the Company recognized the following non-cash, share-based compensation expense (in thousands):

	Years Ended December 31,	
	2018	2017
Research and development	$117	$169
General and administrative	156	289
Total	$273	$458

Stock-based compensation expense related to non-employees was negligible in 2018 and 2017. ARCA did not recognize any tax benefit related to employee stock-based compensation cost as a result of the full valuation allowance on its net deferred tax assets.

(9) Employee Benefit Plans

The Company has a 401(k) plan and makes a matching contribution equal to 100% of the employee's first 3% of the employee's contributions and 50% of the employee's next 2% of contributions. The Company adopted the plan in 2006 and contributed $115,000 and $135,000 for the years ended December 31, 2018 and 2017, respectively.

(10) Income Taxes

Effective June 1, 2005, the Company changed from an S-Corporation to a C-Corporation. As an S-Corporation, the net operating loss carryforwards were distributed to the Company's stockholders; such amounts were not significant. As of December 31, 2018, the Company has net operating loss carryforwards of approximately $165.2 million, and approximately $1.8 million of research and development credits that may be used to offset future taxable income. The Company's net operating loss carryforwards through December 31, 2017 will expire beginning 2025 through 2037. The net operating loss carryforwards beginning in 2018, have no expiration, but are limited to 80% of taxable income. Utilization of net operating losses and tax credits, including those acquired as a result of the Merger, will be subject to an annual limitation due to ownership change limitations provided by Internal Revenue Code Section 382. The Company believes that an ownership change limitation as defined under Section 382 of the U.S. Internal Revenue Code occurred as a result of its various historical financing transactions, and its offering of common stock completed in June 2015. Future utilization of the federal net operating losses and tax credit carryforwards accumulated from June 2005 to the change in ownership date will be subject to annual limitations to offset future taxable income. The annual limitation may result in the expiration

of the net operating losses and credits before utilization. As such, a portion of the Company's net operating loss carryforwards may be limited.

In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the period in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income and tax planning strategies in making this assessment. Due primarily to the Company's history of operating losses, management is unable to conclude that it is more likely than not that the Company will realize the benefits of these deductible differences, and accordingly has provided a valuation allowance against the entire net deferred tax asset of approximately $43.5 million at December 31, 2018, reflecting an increase of approximately $1.9 million from December 31, 2017. During 2017, deferred tax assets decreased $20.1million related to the remeasurement of the deferred tax assets from 34% to the new 2018 U.S. Federal corporate income tax rate of 21%. The deferred tax assets are primarily comprised of net operating loss carryforwards and research and experimentation credit carryforwards. As of December 31, 2018, the Company has not performed an Internal Revenue Code Section 382 limitation study. Depending on the outcome of such a study, the gross amount of net operating losses recognizable in future tax periods could be limited. A limitation in the carryforwards would decrease the carrying amount of the gross amount of the net operating loss carryforwards, with a corresponding decrease in the valuation allowance recorded against these gross deferred tax assets.

Income tax benefit for the years ended December 31, 2018 and 2017 were related to a federal research and experimentation income tax credits related to the Protecting Americans from Tax Hikes Act of 2015, or PATH Act, which allows qualified small businesses to monetize up to $250,000 of research and experimentation tax credits through payroll tax refunds. Income tax benefit attributable to our loss from operations before income taxes differs from the amounts computed by applying the U.S. federal statutory income tax rate of 21% for 2018 and 34% for 2017, as a result of the following (in thousands):

	Years ended December 31,	
	2018	2017
U.S. federal income tax benefit at statutory rates	$(1,666)	$(6,286)
State income tax benefit, net of federal benefit	(290)	(565)
Research and experimentation credits	(144)	(303)
Change in tax rate	—	20,085
Deferred tax asset adjustment	34	37
Other	134	122
Change in valuation allowance	1,901	(13,151)
Income tax benefit	$(31)	$(61)

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes, as well as operating loss and tax credit carryforwards. The income tax effects of temporary differences and carryforwards that give rise to significant portions of the Company's net deferred tax assets consisted of the following (in thousands):

	As of December 31,	
	2018	2017
Net operating loss carryforwards	$40,742	$38,566
Charitable contribution carryforwards	433	455
Research and experimentation credits	1,796	1,682
Capitalized intangibles	409	608
Stock-based compensation	127	148
Depreciation and amortization	1	1
Accrued compensation	20	168
Other	1	—
Total deferred tax assets	43,529	41,628
Valuation allowance	(43,529)	(41,628)
Net deferred tax assets	$—	$—

Since the Company is in a loss carryforward position, the Company is generally subject to U.S. federal and state income tax examinations by tax authorities for all years for which a loss carryforward is available. Thus, the Company's open tax years extend back to 2009. The Company believes that its tax filing positions and deductions related to tax periods subject to examination will be sustained upon audit and does not anticipate any adjustment will result in a material adverse effect on the Company's financial condition, result of operations, or cash flow. For the years ended December 31, 2018 and 2017, the Company has no reserve for uncertain tax positions. The Company does not expect that the total amounts of unrecognized tax benefits will significantly increase or decrease within the subsequent twelve months. In the event the Company concludes it is subject to interest or penalties arising from uncertain tax positions, the Company will record interest and penalties as a component of other income and expense. No interest or penalties were recognized in the financial statements for the years ended December 31, 2018 and 2017.

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(11) Subsequent Event

In January 2019, the Company amended the Sales Agreement to increase the maximum aggregate value of shares which it may issue and sell from time to time under the Sales Agreement by approximately $2.5 million, from $10.2 million to $12.7 million. Subsequent to December 31, 2018, the Company sold an aggregate of 4,431,053 shares of its Common Stock pursuant to the terms of the Sales Agreement, as amended, for aggregate gross proceeds of approximately $2.5 million. Net proceeds received in the period were approximately $2.4 million, after deducting initial expenses for executing the "at the market offering" and commissions paid to the placement agent. As of February 22, 2019, the Company has sold all shares available under its current prospectus to the Company's registration statement on Form S-3 (No. 333-217450).

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Under the supervision and with the participation of management, including our Principal Executive Officer and our Principal Financial Officer, we have evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e) and 15d-15(e). Based on this evaluation, our Principal Executive Officer and Principal Financial Officer have concluded that our disclosure controls and procedures were effective as of the end of the period covered by this annual report.

Management’s Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act). Our internal control system is designed to provide reasonable assurance to management and our board of directors regarding the preparation and fair presentation of published financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect all misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of management, including our Principal Executive Officer and Principal Financial Officer, we have assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making our assessment of internal control over financial reporting, we used the criteria issued in the report Internal Control-Integrated Framework (2013) by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). We have concluded that our internal control over financial reporting was effective as of December 31, 2018 based on these criteria.

This annual report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Management’s report was not subject to attestation by our independent registered public accounting firm pursuant to the exemption from Section 404(b) of the Sarbanes-Oxley Act for non-accelerated filers provided by the Dodd-Frank Wall Street Reform and Consumer Protection Act.

Changes in Internal Control over Financial Reporting

During the fourth quarter of 2018, there were no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Limitations on the Effectiveness of Controls

Our management, including our Principal Executive Officer and Principal Financial Officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. 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, if any, within our company have been detected.

Item 9B. Other Information

None

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Our directors, executive officers and key employees as of February 22, 2019 are as follows:

Name	Age	Position
Dr. Michael R. Bristow	74	President and Chief Executive Officer and Director
Thomas A. Keuer	60	Chief Operating Officer
Christopher D. Ozeroff	60	Secretary, Senior Vice President and General Counsel
Brian L. Selby	57	Vice President, Finance and Chief Accounting Officer
Dr. Linda Grais (1) (2)*	62	Director
Dr. Raymond L. Woosley (2) (3)*	76	Director
Mr. Robert E. Conway (1)* (2)	65	Director
Mr. Dan J. Mitchell (1) (3)	61	Director
Dr. Anders Hove (3)	53	Director

* Committee Chairperson

(1) Member of the Audit Committee

(2) Member of the Compensation Committee

(3) Member of the Nominating and Corporate Governance Committee

Michael R. Bristow, M.D., Ph.D. Dr. Bristow was one of the founders of ARCA in September 2004, and has served as a Director since that time. Dr. Bristow has also served as the Company's President and Chief Executive Officer since July 2009. Previously, Dr. Bristow served as the President and Chief Executive Officer of the Company from September 2004 to November 2006, and as the Company's Chief Science and Medical Officer from November 2006 to July 2009. Dr. Bristow is a Professor of Medicine and the former Head of Cardiology at the University of Colorado Health Sciences Center, where he has been since October 1991. Dr. Bristow was one of the founders of Myogen, Inc. and served as Myogen's Chief Science and Medical Officer from October 1996 to February 2006 and as a Scientific Advisor to Myogen from February 2006 until the acquisition of Myogen by Gilead Sciences, Inc. in November 2006. We believe Dr. Bristow is an appropriate member of the Company's Board of Directors given his extensive experience and expertise as a cardiologist, medical researcher and drug developer in the field of cardiovascular medicine, and heart failure specifically, and his experience as a founder and manager of cardiovascular-focused, public pharmaceutical company. Dr. Bristow also has extensive experience with, and knowledge of, ARCA's business, as the founder and former Chief Science and Medical Officer of the Company, and the current President and Chief Executive Officer of ARCA, and as a member of the Board of Directors of ARCA since the founding of the Company. Dr. Bristow holds a M.D. and Ph.D. from the University of Illinois.

Thomas A. Keuer. Mr. Keuer has served as the Company's Chief Operating Officer since December 2014. Mr. Keuer served as the Company's Executive Vice President, Pharmaceutical Operations from 2006 to 2014. Prior to joining the Company, Mr. Keuer served as the SVP of Operations for Insmed, Inc. from 2004 to 2006. Prior to Insmed, Mr. Keuer served as the VP of Engineering for Baxter Healthcare from 1998 to 2004. Prior to Baxter, Mr. Keuer served as the VP of Operations for Somatogen, Inc. Mr. Keuer received his M.S. in Biochemical Engineering from Rice

University and received his B.S. in Chemical Engineering from the University of Texas, Austin.

Christopher D. Ozeroff. Mr. Ozeroff is a co-founder of ARCA. Mr. Ozeroff has served as the Company's Senior Vice President, General Counsel and Secretary since 2009, has served as the Company's General Counsel and Secretary since the Company's founding, and has also served as Executive Vice President, Business Development from 2004 to 2009. Prior to joining the Company, Mr. Ozeroff was a partner with the law firm of Hogan & Hartson L.L.P., where he practiced in such areas as finance, acquisitions, public offerings, and licensing. Mr. Ozeroff completed his undergraduate degree at Stanford University and his law degree at the University of Chicago Law School.

Brian L. Selby. Mr. Selby has served as the Company's Vice President, Finance and Chief Accounting Officer since December 2014. Previously, Mr. Selby served as the Company's Controller from 2007 to 2014. Prior to joining the Company, Mr. Selby served as the Controller for Myogen, Inc., a publicly traded pharmaceutical company subsequently acquired by Gilead, from 2004 to 2007. Prior to Myogen, Mr. Selby served as the Controller for several private and publicly traded companies and earlier in his career was an audit professional with Deloitte. Mr. Selby received his M.S. in Accounting from the University of Colorado and received his B.S., in Business Administration and Finance from Colorado State University, and is a certified public accountant.

Linda Grais, M.D. Dr. Grais has served as a member of the Board of Directors since May 2007. Dr. Grais has been a director of Ocera Therapeutics, Inc., a public biopharmaceutical company, since January 2008 and became President and Chief Executive Officer of Ocera in June 2012, and served in that role until Ocera's acquisition by Mallinckrodt Pharmaceuticals in December 2017. Dr. Grais served as a Managing Member at InterWest Partners, a venture capital firm from May 2005 until February 2011. From July 1998 to July 2003, Dr. Grais was a founder and executive vice president of SGX Pharmaceuticals Inc., a drug discovery company. Prior to that, she was a corporate attorney at Wilson Sonsini Goodrich & Rosati, where she practiced in such areas as venture financings, public offerings and strategic partnerships. Before practicing law, Dr. Grais worked as an assistant clinical professor of Internal Medicine and Critical Care at the University of California, San Francisco. Dr. Grais received a B.A. from Yale University, magna cum laude, and Phi Beta Kappa, an M.D. from Yale Medical School and a J.D. from Stanford Law School. Since September 2015, Dr. Grais has served on the board of PRA Health Sciences, a public contract research organization. Dr. Grais also joined the boards of Corvus Pharmaceuticals and Zosano Pharma Corp., both publicly traded pharmaceutical companies, in January 2019. We believe Dr. Grais is an appropriate member of the Board of Directors because of her diverse training and experience as both a medical doctor and a lawyer, her experience as a founder and senior executive of a pharmaceutical company, and her experience as an investor in new life sciences companies. She also has extensive experience with and knowledge of the Company's business from her service on the Board of Directors of the Company since 2007.

Raymond L. Woosley, M.D., Ph.D. Dr. Woosley was appointed to the Board of Directors in July 2013. Since 2012, Dr. Woosley is the Director of the Arizona Center for Education and Research on Therapeutics (AzCERT), an independent, nonprofit research and education organization. Dr. Woosley is currently the President Emeritus of the Critical Path Institute (C-Path), a non-profit, public-private partnership with the Federal Food and Drug Administration, of which he was a founder in November 2004, and where he served as President, Chief Executive Officer and Chairman of the board of directors from 2005 to 2011. Since 2012, Dr. Woosley has also been the Director of AzCERT, an independent, nonprofit research and education organization. Since 2001, Dr. Woosley has also been a Professor of Medicine and Pharmacology at The University of Arizona Health Sciences Center (UAHSC), and, since 2012, Professor Emeritus, where he was also Vice President for Health Sciences from 2001 to 2005, and Dean of the College of Medicine from 2001 to 2002. Since 2015, he has been Professor of Medicine in the University of Arizona, College of Medicine-Phoenix. From 1988 to 2001, Dr. Woosley was a professor of medicine at the Georgetown University School of Medicine, where he was also Director of the Institute of Cardiovascular Sciences from 1994 to 2000, and Division Chief, Clinical Pharmacology, in the Department of Medicine from 1988 to 1994. Dr. Woosley earned his Ph.D. in Pharmacology from the University of Louisville and his M.D. from the University of Miami. Dr. Woosley's research has been published in over 312 peer-reviewed publications and 50 book chapters. We believe Dr. Woosley is an appropriate member of the Board of Directors, given his expertise and experience in cardiovascular clinical pharmacology, anti-arrhythmic therapeutics, pharmacogenetic drug development and therapeutic regulatory approval.

Robert E. Conway Mr. Conway was appointed to the Board of Directors in September 2013, and has served as the Chairman of our Board of Directors since 2014. Mr. Conway served as the Chief Executive Officer and member of the board of directors of Array Biopharma, a publicly traded pharmaceutical company, from 1999 to 2012. Prior to joining Array, Mr. Conway was the Chief Operating Officer and Executive Vice President of Hill Top Research, Inc., from 1996 to 1999. From 1979 until 1996, Mr. Conway held various executive positions for Corning Inc. including Corporate Vice President and General Manager of Corning Hazleton, Inc., a contract research organization. From 2004 to 2013, he served on the board of directors of PRA International, Inc., which was a public company for a portion of his tenure there, from 2012 to the present, he has served on the board of directors of eResearch Technology, Inc., a private company, and from 2015 to July 2017, he has served on the board of directors of Nivalis Therapeutics, Inc. a public, clinical stage pharmaceutical company. In July 2017, Nivalis Therapeutics, Inc. combined with Alpine Immune Sciences, Inc., a public, clinical stage pharmaceutical company, and Mr. Conway continues to serve on the board of directors following such combination. In addition, Mr. Conway is a member of the Strategic Advisory

Committee of Genstar Capital, LLC and is a member of the board of directors of CRF Bracket, Inc. and ClinOne, Inc. Mr. Conway received a B.S. in accounting from Marquette University in 1976. We believe Mr. Conway is an appropriate member of the Board of Directors given his experience and expertise in the pharmaceutical industry, in pharmaceutical development and clinical trials, and in corporate finance, governance, accounting and public company compliance.

Dan J. Mitchell Mr. Mitchell was appointed to the Board of Directors in February 2014. He founded, and is a manager of Sequel Venture Partners, L.L.C., a venture capital firm formed in January 1997. Prior to founding Sequel Venture Partners, Mr. Mitchell was a founder of Capital Health Venture Partners, a health care focused venture capital firm, where he was a General Partner from October 1986 until 2006, and he was in the Venture Capital Division of the Trust Department of the First National Bank of Chicago from 1983 to 1985. He currently serves on the board of directors of several private companies. Mr. Mitchell holds a B.S. from the University of Illinois and an M.B.A. from the University of California at Berkeley. We believe Mr. Mitchell is an appropriate member of the Board of Directors given his expertise and experience in the pharmaceutical industry, pharmaceutical development, and in corporate finance and governance.

Anders Hove, M.D. Dr. Hove has served as a member of the Board of Directors since February 2017. Dr. Hove owns Acorn Capital Advisors and is a partner at Amzak Health, a partnership focusing on long-term investments in biotech, specialty pharma and medical device companies. Dr. Hove was most recently a general partner of Venrock Associates, a venture capital firm, which he joined in January 2004 and remained at through December 2016. In 2008, Dr. Hove was a founder of Venrock Healthcare Capital Partners, Venrock's public funds focused on small capitalization biotech companies and late-stage private companies. From 1996 to 2004, Dr. Hove was a fund manager at BB Biotech Fund, an investment firm, and from 2002 to 2003 he also served as Chief Executive Officer of Bellevue Asset Management, LLC, an investment company. Dr. Hove previously held senior level positions in the medical, clinical and business operations of the pharmaceuticals division of Ciba-Geigy and Novartis. Mr. Hove was a member of the boards of directors of Anacor Pharmaceuticals, a publicly traded pharmaceutical company, from 2005 until its acquisition by Pfizer in June 2016, and Edge Therapeutics, a publicly traded biotechnology company, from 2015 to 2016. In addition, Dr. Hove is a member of the board of directors of MC2 Therapeutics. He received a M.Sc. in Biotechnology Engineering from the Technical University of Denmark, an M.D. from the University of Copenhagen and an M.B.A. from the Institut Européen d'Administration des Affaires (INSEAD). We believe Dr. Hove is an appropriate member of the Company's Board of Directors, given his extensive training and experience as a medical doctor and masters of business administration, an executive in the pharmaceutical industry, and as an investor in biotechnology companies.

ADDITIONAL INFORMATION REGARDING THE BOARD OF DIRECTORS AND CORPORATE GOVERNANCE

Election of Board of Directors

Directors are elected by a plurality of the votes of the holders of shares present in person or represented by proxy and entitled to vote on the election of directors at our annual stockholders' meetings. The Company's Amended and Restated Certificate of Incorporation, as amended, provides that the Board of Directors is divided into three classes to provide for staggered terms and that each director will serve for a term of three years or less, depending on the class to which the Board of Directors has assigned a director not previously elected by the stockholders. There are currently two Class I directors whose terms expire at the annual stockholders' meeting in 2019, two Class II directors whose terms expire at the annual meeting in 2020 and two Class III directors whose terms expire at the annual stockholders' meeting in 2021. The two Class I directors, Dr. Linda Grais and Dr. Anders Hove, are currently scheduled for re-election to the Board of Directors at the 2019 annual stockholders' meeting, for a three-year term ending on the date of the annual meeting in 2022 or until their successors are duly elected and qualified or appointed.

Our executive officers are appointed by and serve at the discretion of our Board. There are no family relationships between our directors and executive officers.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16 of the Exchange Act requires the Company's directors and executive officers, and persons who own more than 10% of its common stock, to file with the SEC initial reports of ownership and reports of changes in ownership of common stock of the Company. Such persons are required by SEC regulation to furnish us with copies of all Section 16(a) forms that they file.

To the Company's knowledge, based solely upon its review of the copies of such reports furnished to it and written representations that no other reports were required, during the fiscal year ended December 31, 2018, all Section 16(a) filing requirements applicable to its officers, directors and ten percent beneficial owners were complied with.

Code of Ethics

The Company has adopted the ARCA biopharma, Inc. Code of Business Conduct and Ethics that applies to all officers, directors and employees. The Code of Business Conduct and Ethics is available on the Company's website at www.arcabiopharma.com. If the Company makes any substantive amendments to the Code of Business Conduct and Ethics or grants any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, the Company will promptly disclose the nature of the amendment or waiver on its website and file any current report on Form 8-K required by applicable law or NASDAQ listing standards.

Audit Committee

The Audit Committee was established by the Board of Directors in accordance with Section 3(a)(58)(A) of the Exchange Act, to oversee the Company's corporate accounting and financial reporting processes and audits of its financial statements. For this purpose, the Audit Committee performs several functions. The Audit Committee evaluates the performance of and assesses the qualifications of the independent registered public accounting firm; determines and approves the engagement of the independent registered public accounting firm; determines whether to retain or terminate the existing independent registered public accounting firm or to appoint and engage a new independent registered public accounting firm; reviews and approves the retention of the independent registered public accounting firm to perform any proposed permissible non-audit services; monitors the rotation of partners of the

independent registered public accounting firm on the Company's audit engagement team as required by law; reviews and approves or rejects transactions between the company and any related persons; confers with management and the independent registered public accounting firm regarding the effectiveness of internal controls over financial reporting; establishes procedures, as required under applicable law, for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and the confidential and anonymous submission by employees of concerns regarding questionable accounting or auditing matters; and meets to review the Company's annual audited financial statements and quarterly financial statements with management and the independent registered public accounting firm, including a review of the Company's disclosures under the "Management's Discussion and Analysis of Financial Condition and Results of Operations" discussion in its Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q. As of December 31, 2018, the Audit Committee was composed of three directors: Mr. Conway (chair), Mr. Mitchell and Dr. Grais. The Audit Committee met four times during the fiscal year. The Board of Directors has adopted a written charter of the Audit Committee that is available to stockholders on the Company's website at www.arcabio.com.

The Board of Directors reviews the Nasdaq listing standards definition of independence for audit committee members on an annual basis and has determined that all members of the Audit Committee are independent (as independence is currently defined in Rule 5605(c)(2)(A)(i) and (ii) of the Nasdaq listing standards). The Board of Directors has also determined that Mr. Conway qualifies as an "audit committee financial expert," as defined in applicable SEC rules. The Board of Directors made a qualitative assessment of Mr. Conway's level of knowledge and experience based on several factors, including his prior experience, business acumen and independence.

Report of the Audit Committee of the Board of Directors[1]

The Audit Committee has reviewed and discussed the audited financial statements for the fiscal year ended December 31, 2018, with management of the Company. The Audit Committee has discussed with the independent registered public accounting firm the matters required to be discussed by Public Company Accounting Oversight Board ("PCAOB") Auditing Standard No. 1301, Communications with Audit Committees. The Audit Committee has also received the written disclosures and the letter from the independent registered public accounting firm required by applicable requirements of the PCAOB regarding the independent registered public accounting firm's communications with the Audit Committee concerning independence, and has discussed with the independent registered public accounting firm the accounting firm's independence. Based on the foregoing, the Audit Committee has recommended to the Board of Directors that the audited financial statements be included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018.

Mr. Robert Conway

Mr. Dan Mitchell

Dr. Linda Grais

Compensation Committee

The Compensation Committee is currently composed of three directors: Mr. Conway, Dr. Grais (chair) and Dr. Woosley. All members of the Compensation Committee are independent, as independence is currently defined in Rule 5605(a)(2) of the Nasdaq listing standards. The Compensation Committee met one time during the fiscal year. The Compensation Committee has adopted a written charter that is available to stockholders on the Company's website at www.arcabio.com.

The Compensation Committee of the Board of Directors acts on behalf of the Board of Directors to review, adopt and oversee the Company's compensation strategy, policies, plans and programs, including:

- overseeing succession planning for senior management of the Company, including a review of the performance and advancement potential of current and future senior management and succession plans for each and recommending, as appropriate, the retention of potential succession candidates;

- assessing the overall compensation structure of the Company and evaluating and recommending changes to the Company's compensation philosophies and strategies;

- reviewing and approving performance-based compensation plans or programs, including establishing goals and targets, applicable to the Chief Executive Officer and other members of the management team;

[1] The material in this report is not "soliciting material," is not deemed "filed" with the Commission and is not to be incorporated by reference in any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

administering, reviewing, and approving all executive compensation programs or plans, and all of the Company's incentive compensation and stock plans and awards thereunder of the Company, including amendments to the programs, plans or awards made thereunder; and

preparing and approving the Report of the Compensation Committee to be included as part of the Company's annual meeting proxy statement, to the extent required.

Compensation Committee Processes and Procedures

Typically, the Compensation Committee meets on a regular basis as it deems appropriate. The agenda for each meeting is usually developed by the Chair of the Compensation Committee. The Compensation Committee meets regularly in executive session. However, from time to time, various members of management and other employees as well as outside advisors or consultants may be invited by the Compensation Committee to make presentations, to provide financial or other background information or advice or to otherwise participate in Compensation Committee meetings. The Chief Executive Officer may not participate in, or be present during, any deliberations or determinations of the Compensation Committee regarding his compensation or individual performance objectives. The Compensation Committee has the sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation, including the authority to approve the consultant's reasonable fees and other retention terms.

In June 2013, the Company's Compensation Committee reviewed the Company's executive compensation considering general market conditions in the life science industry. As part of this review process, the Compensation Committee identified a peer group of biotechnology companies that it viewed as having a similar profile to ARCA at that time.

In setting 2018 base salary and cash bonus award amounts for the Company's named executive officers, the Compensation Committee considered peer group data and factors specific to the Company, and targeted cash compensation to be consistent with these metrics. The Compensation Committee recommended, and the Board of Directors approved, a base salary of $295,359 for Dr. Bristow, the Company's President and Chief Executive Officer, a base salary of $294,170 for Mr. Keuer, the Company's Chief Operating Officer, and a base salary of $288,683 for Mr. Ozeroff, the Company's Senior Vice President and General Counsel, for the fiscal year ended December 31, 2016. In early 2017, the Compensation Committee recommended, and the Board of Directors approved cash bonuses based on previous performance for the Named Executive Officers (as defined below), and also approved increases to Named Executive Officer salaries for the fiscal year 2017 as described in below under "Executive Compensation." There were no changes to the Named Executive Officers' salaries for 2018 and the Compensation Committee has yet to review or approve salaries for our Named Executive Officers in 2019.

Historically, the Compensation Committee has made most of the significant adjustments to annual compensation, determined bonus and equity awards and established new performance objectives at one or more meetings held during the first quarter of the year. However, the Compensation Committee also considers matters related to individual compensation, such as compensation for new executive hires, as well as high-level strategic issues, such as the efficacy of the Company's compensation strategy, potential modifications to that strategy and new trends, plans or approaches to compensation, at various meetings throughout the year. Generally, the Compensation Committee's process comprises two related elements: the determination of compensation levels and the establishment of performance objectives for the current year.

The Compensation Committee reviews and approves the compensation of the Chief Executive Officer and the other executive officers of the Company, including annual base salaries, annual and long-term incentive or bonus awards, employment agreements, and severance and change in control agreements/provisions, in each case as, when and if appropriate, and any special or supplemental benefits. For executives other than the Chief Executive Officer, the Compensation Committee solicits and considers evaluations and recommendations submitted to the Compensation Committee by the Chief Executive Officer. The Compensation Committee evaluates the performance of the Chief Executive Officer in light of Company and individual goals and objectives, and makes appropriate recommendations for improving performance. In performing the evaluation, the Chair of the Compensation Committee may solicit comments from the other non-employee members of the Board of Directors and lead the Board of Directors in an overall review of the Chief Executive Officer's performance in an executive session of non-employee members of the Board of Directors. If the compensation for the Chief Executive Officer or any other executive officer is governed by an employment agreement, the Compensation Committee approves such employment agreement and any amendments thereto.

For all executives as part of its deliberations, the Compensation Committee may review and consider, as appropriate, materials such as financial reports and projections, operational data, tax and accounting information, tally sheets that set forth the total compensation that may become payable to executives in various hypothetical scenarios, executive and director stock

ownership information, company stock performance data, analyses of historical executive compensation levels and current Company-wide compensation levels.

The Compensation Committee also considers the results of any "say-on-pay" vote of the Company's stockholders with regard to the compensation of the Company's executive officers when making compensation decisions. At the 2016 annual meeting of stockholders, the Company's stockholders approved, on an advisory basis, the compensation of the Company's named executive officers as described in the proxy statement for such annual meeting. The Compensation Committee believes that this advisory vote supports that the Company's current compensation practices are aligned with the best interests of stockholders and anticipates taking into account any subsequent advisory vote when making compensation decisions in the future.

Nominating and Corporate Governance Committee

The Nominating and Corporate Governance Committee is responsible for identifying, reviewing and evaluating candidates to serve as directors of the Company (consistent with criteria approved by the Board of Directors), reviewing and evaluating incumbent directors, recommending to the Board of Directors candidates for election to the Board of Directors, making recommendations to the Board of Directors regarding compensation for service on the Board of Directors and the committees thereof, making recommendations to the Board of Directors regarding the membership of the committees of the Board of Directors, assessing the performance of the Board of Directors and developing a set of corporate governance principles for the Company. As of December 31, 2018, the Nominating and Corporate Governance Committee was composed of three directors: Dr. Hove, Mr. Mitchell and Dr. Woosley (chair). All members of the Nominating and Corporate Governance Committee in 2018 were independent (as independence is currently defined in Rule 5605(a)(2) of the Nasdaq listing standards). The Nominating and Corporate Governance Committee met three times during the 2018 fiscal year. The Nominating and Corporate Governance Committee has adopted a written charter that is available to stockholders on the Company's website at www.arcabio.com.

The Nominating and Corporate Governance Committee periodically reviews the compensation of non-employee Directors for service on the Board of Directors and committees thereof. In 2015, the Nominating and Corporate Governance Committee began a review of its Director compensation levels considering general market conditions in the life science industry, and in comparison to other clinical stage biopharmaceutical companies, and in early 2016, the Committee recommended, and the Board of Directors approved, revised compensation for non-employee Directors, discussed in "Director Compensation" below.

The Board of Directors has adopted a process for identifying and evaluating director nominees, including stockholder nominees. Before recommending an individual to the Board of Directors for membership on the Board of Directors, the Nominating and Corporate Governance Committee canvasses its members and the Company's management team for potential candidates for the Board of Directors. The Nominating and Corporate Governance Committee also uses its network of contacts to identify potential candidates and, if it deems appropriate, may also engage a professional search firm. The Nominating and Corporate Governance Committee will consider stockholders' recommendations for nominees to serve as director if notice is timely received by the Secretary of the Company. Candidates nominated by stockholders will be evaluated in the same manner as other candidates. The Nominating and Corporate Governance Committee keeps the Board of Directors apprised of its discussions with potential nominees, and the names of potential nominees received from its current directors, management, and stockholders, if the stockholder notice of nomination is timely made.

Although the Board of Directors has not adopted a fixed set of minimum qualifications for candidates for membership on the Board of Directors, the Nominating and Corporate Governance Committee generally considers several factors in its evaluation of a potential member, such as the candidate's education, professional background and field of expertise including industry or academic experience in the pharmaceutical and biotechnology fields, experience in

corporate governance and management, the reasonable availability of the potential member to devote time to the affairs of the Company, as well as any other criteria deemed relevant by the Board of Directors or the Nominating and Corporate Governance Committee. However, the Nominating and Corporate Governance Committee retains the right to modify these qualifications from time to time. Candidates for director nominees are reviewed in the context of the current composition of the Board of Directors, the operating requirements of the Company and the long-term interests of stockholders. In conducting this assessment, the Nominating and Corporate Governance Committee typically considers diversity, age, skills and such other factors as it deems appropriate given the current needs of the Board of Directors and the Company, to maintain a balance of knowledge, experience and capability. The Nominating and Corporate Governance Committee believes it is essential that Board of Directors members come from a variety of backgrounds and experiences.

In the case of incumbent directors whose terms of office are set to expire, the Nominating and Corporate Governance Committee reviews these directors' overall contributions to the Company and the Board of Directors during their terms, including level of attendance, level of participation, quality of performance and contribution to the Board of Directors' responsibilities and actions, and any relationships and transactions that might impair the directors' independence. In the case of new director candidates, the Nominating and Corporate Governance Committee also determines whether the nominee is independent for Nasdaq and SEC purposes, which determination is based upon applicable Nasdaq listing standards, applicable SEC rules and regulations and the advice

of counsel, if necessary. The Nominating and Corporate Governance Committee conducts any appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the Board of Directors. The Nominating and Corporate Governance Committee meets to discuss and consider the candidates' qualifications and then determines whether to recommend a nominee to the Board of Directors by majority vote.

Stockholders who wish to recommend individuals for consideration by the Nominating and Corporate Governance Committee to become nominees for election to the Board of Directors may do so by delivering a written recommendation to the Nominating and Corporate Governance Committee addressed to the Corporate Secretary, between 60 and 90 days before the one year anniversary date of ARCA's last annual meeting of stockholders. Recommendations must include the full name of the proposed nominee, a description of the proposed nominee's business experience for at least the previous five years, complete biographical information, a description of the proposed nominee's qualifications as a director, and a representation that the recommending stockholder is a beneficial or record owner of ARCA's stock. Any such submission must be accompanied by the written consent of the proposed nominee to be named as a nominee and to serve as a director if elected. To date, the Nominating and Corporate Governance Committee has not rejected a timely director nominee from a stockholder.

In 2018, the Nominating and Corporate Governance Committee did not pay any fees to assist in the process of identifying or evaluating director candidates.

Stockholder Communications with the Board of Directors

Stockholders who wish to communicate with the Board of Directors may do so by e-mail by using the following email address: directors@arcabio.com; or by mail by following the directions as set forth on ARCA's website at www.arcabio.com, under the section titled "Corporate Governance" and the subsection titled "Governance Documents".

Item 11. Executive Compensation

Executive Compensation

The following table shows for the fiscal years ended December 31, 2018 and December 31, 2017, compensation awarded to, paid to, or earned by the Company's principal executive officer and its two most highly compensated executive officers as of December 31, 2018, collectively, the Named Executive Officers:

Summary Compensation Table for Fiscal 2018 and 2017

Name and Principal Position	Year	Salary ($)(1)	Option Awards ($)(2)	Non-Equity Incentive Plan Awards ($)(3)	All Other Compensation ($)	Total ($)
Michael R. Bristow	2018	304,219	—	—	16,271	320,490

President and Chief Executive Officer						
	2017	302,856	137,281	91,300	16,256	547,693
Thomas A. Keuer	2018	303,000	—	—	23,786	326,786
Chief Operating Officer						
	2017	301,642	80,428	54,500	20,597	457,167
Christopher D. Ozeroff	2018	297,343	—	—	12,914	310,257
Secretary, Senior Vice President and General Counsel						
	2017	296,011	76,654	53,500	12,110	438,275

(1) The amounts reported under “Salary” in the above table represent the actual amounts paid during the calendar year. Because the Company’s actual pay dates do not always coincide with the first and last days of the year, these amounts may differ from the base salary amounts authorized by the Company’s Board of Directors and described in the narrative that follows.

(2) The amounts reported under "Option Awards" in the above table reflect the grant date fair value of these awards as determined in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation – Stock Compensation, excluding the effects of estimated forfeitures. The vesting schedule for options included in the above table are included in the table of "Outstanding Equity Awards at Fiscal Year End" below. The value of stock option awards was estimated using the Black-Scholes option-pricing model. The valuation

assumptions used in the valuation of option grants may be found in Note 8 to the Company's financial statements included in this annual report on Form 10-K for the year ended December 31, 2018.

(3) Represents cash bonuses earned under the 2017 Bonus Plan. Cash bonuses earned and reported above in 2017 were paid in 2018. No 2018 cash bonus plan was adopted for the 2018 fiscal year and, accordingly, the Company does not anticipate paying any bonuses for 2018 performance in 2019. See "Executive Compensation" for descriptions of the 2017 Bonus Plan.

Narrative Disclosure to Summary Compensation Table

Employment Agreements or Arrangements

Michael R. Bristow, M.D., Ph.D. Dr. Bristow serves as the Company's President and Chief Executive Officer under an Employment and Retention Agreement dated as of June 4, 2008, as amended. Pursuant to such employment agreement, Dr. Bristow is permitted to continue his academic work for the University of Colorado Health Sciences Center and for the Cardiovascular Institute, so long as it does not interfere with his duties as President and Chief Executive Officer of ARCA.

On February 16, 2017, the Board of Directors approved a 2017 base salary of $304,219 for Dr. Bristow.

On March 1, 2018, the Board of Directors approved a cash bonus of $91,300 for Dr. Bristow. The cash bonus was earned under the 2017 Bonus Plan for services rendered in 2017. See "Non-Equity Incentive Plan Compensation" below for descriptions of the 2017 Bonus Plan. There were no changes to the Named Executive Officers' salaries for 2018 and the Compensation Committee has yet to review or approve salaries for our Named Executive Officers in 2019.

If the Company terminates Dr. Bristow's employment without "cause," or if Dr. Bristow terminates his employment with "good reason" (as these terms are defined in his employment agreement), the Company has agreed to pay Dr. Bristow a severance payment equivalent to (i) (a) 12 months of his base salary, if such termination occurs on the same day as or within 13 months after a change of control of the Company, or (b) six months of his base salary if such termination does not occur on the same day as or within 13 months after a change of control of the Company, (ii) a pro rata portion of any bonus compensation under any employee bonus plan that has been approved by the Board of Directors payable to him for the fiscal year in which his employment terminated to be paid at the same time that such incentive bonus would have been paid had the termination not occurred, and (iii) reimbursement to cover out-of-pocket costs to continue group health insurance benefits under COBRA for 6 months, whether he elects or is eligible to receive COBRA (provided, that even if he does not elect or is not eligible to receive COBRA, he will receive the equivalent of such out-of-pocket expenses paid by him not to exceed the costs that the benefits would equal under COBRA if he were so eligible). In addition, ARCA may elect in its sole discretion, to pay additional severance equal to up to 6

months of base salary, which additional payment would extend the covenants and obligations under Dr. Bristow's Employee Intellectual Property, Confidentiality and Non-Compete Agreement for such additional period. The severance payment is conditioned on the execution by Dr. Bristow of a legal release in a form acceptable to the Company. A termination for "cause" includes Dr. Bristow's willful misconduct, gross negligence, theft, fraud, or other illegal or dishonest conduct, any of which are considered to be materially harmful to the Company; refusal, unwillingness, failure, or inability to perform his material job duties or habitual absenteeism; or violation of fiduciary duty, violation of any duty of loyalty, or material breach of any material term of his employment agreement or his Employee Intellectual Property, Confidentiality and Non-Compete Agreement, or any other agreement, with the Company. "Good reason" includes a relocation by us of Dr. Bristow's normal work location greater than 30 miles; a decrease in current base salary by more than 15%, with certain exceptions; and the Company's unilateral decision to significantly and detrimentally reduce Dr. Bristow's job responsibilities.

Thomas A. Keuer. Mr. Keuer serves as the Company's Chief Operating Officer under an Amended and Restated Employment Agreement that was effective as of January 1, 2015.

Under his employment agreement, Mr. Keuer is entitled to receive an annual base salary of $280,000, subject to annual increases if approved by the Company's Board of Directors or Compensation Committee and is eligible to receive an annual bonus as determined by the Board of Directors or Compensation Committee in its sole discretion.

On February 16, 2017, the Board of Directors approved a 2017 base salary of $303,000 for Mr. Keuer.

On March 1, 2018, the Board of Directors approved a cash bonus of $54,500 for Mr. Keuer. The cash bonus was earned under the 2017 Bonus Plan for services rendered in 2017. See "Non-Equity Incentive Plan Compensation" below for descriptions of the 2017 Bonus Plan. There were no changes to the Named Executive Officers' salaries for 2018 and the Compensation Committee has yet to review or approve salaries for our Named Executive Officers in 2019.

If the Company terminates Mr. Keuer's employment without "cause," or if Mr. Keuer terminates his employment with "good reason" (as these terms are defined in his employment agreement), the Company has agreed to pay Mr. Keuer a severance payment equivalent to (i) (a) 12 months of his base salary, if such termination occurs on the same day as or within 13 months after a change of control of the Company, or (b) six months of his base salary if such termination does not occur on the same day as or within 13 months after a change of control of the Company, (ii) a pro rata portion of any bonus compensation under any employee bonus plan that has been approved by the Board of Directors payable to him for the fiscal year in which his employment terminated to be paid at the same time that such incentive bonus would have been paid had the termination not occurred, and (iii) reimbursement to cover out-of-pocket costs to continue group health insurance benefits under COBRA for (x) 12 months, if such termination occurs on the same day as or within 13 months after a change of control of the Company, or (y) six months if such termination does not occur on the same day as or within 13 months after a change of control of the Company, whether he elects or is eligible to receive COBRA (provided, in either event, that even if he does not elect or is not eligible to receive COBRA, he will receive the equivalent of such out-of-pocket expenses paid by him not to exceed the costs that the benefits would equal under COBRA if he were so eligible). In addition, ARCA may elect in its sole discretion, to pay additional severance equal to up to 12 months of base salary, which additional payment would extend the covenants and obligations under Mr. Keuer's Employee Intellectual Property, Confidentiality and Non-Compete Agreement for such additional period. The severance payment is conditioned on the execution by Mr. Keuer of a legal release in a form acceptable to the Company. A termination for "cause" includes Mr. Keuer's willful misconduct, gross negligence, theft, fraud, or other illegal or dishonest conduct, any of which are considered to be materially harmful to the Company; refusal, unwillingness, failure, or inability to perform his material job duties or habitual absenteeism; or violation of fiduciary duty, violation of any duty of loyalty, or material breach of any material term of his employment agreement or his Employee Intellectual Property, Confidentiality and Non-Compete Agreement, or any other agreement, with the Company. "Good reason" includes a relocation by us of Mr. Keuer's normal work location greater than 30 miles; a decrease in current base salary by more than 15%, with certain exceptions; and the Company's unilateral decision to significantly and detrimentally reduce Mr. Keuer's job responsibilities.

Christopher D. Ozeroff. Mr. Ozeroff serves as the Company's Senior Vice President and General Counsel under an Employment and Retention Agreement dated as of June 12, 2008, as amended.

Under his employment agreement, Mr. Ozeroff is entitled to receive an annual base salary of $259,000, subject to annual increases if approved by the Company's Board of Directors or Compensation Committee and is eligible to receive an annual bonus as determined by the Board of Directors or Compensation Committee in its sole discretion.

On February 16, 2017, the Board of Directors approved a 2017 base salary of $297,343 for Mr. Ozeroff.

On March 1, 2018, the Board of Directors approved a cash bonus of $53,500 for Mr. Ozeroff. The cash bonus was earned under the 2017 Bonus Plan for services rendered in 2017. See "Non-Equity Incentive Plan Compensation" below for descriptions of the 2017 Bonus Plan. There were no changes to the Named Executive Officers' salaries for 2018 and the Compensation Committee has yet to review or approve salaries for our Named Executive Officers in 2019.

If the Company terminates Mr. Ozeroff's employment without "cause," or if Mr. Ozeroff terminates his employment with "good reason" (as these terms are defined in his employment agreement), the Company has agreed to pay Mr. Ozeroff a severance payment equivalent to (i) (a) 12 months of his base salary, if such termination occurs on the same day as or within 13 months after a change of control of the Company, or (b) six months of his base salary if such termination does not occur on the same day as or within 13 months after a change of control of the Company, (ii) a pro rata portion of any bonus compensation under any employee bonus plan that has been approved by the Board of Directors payable to him for the fiscal year in which his employment terminated to be paid at the same time that such incentive bonus would have been paid had the termination not occurred, and (iii) reimbursement to cover

out-of-pocket costs to continue group health insurance benefits under COBRA for 6 months, whether he elects or is eligible to receive COBRA (provided, that even if he does not elect or is not eligible to receive COBRA, he will receive the equivalent of such out-of-pocket expenses paid by him not to exceed the costs that the benefits would equal under COBRA if he were so eligible). In addition, ARCA may elect in its sole discretion, to pay additional severance equal to up to 6 months of base salary, which additional payment would extend the covenants and obligations under Mr. Ozeroff's Employee Intellectual Property, Confidentiality and Non-Compete Agreement for such additional period. The severance payment is conditioned on the execution by Mr. Ozeroff of a legal release in a form acceptable to the Company. A termination for "cause" includes Mr. Ozeroff's willful misconduct, gross negligence, theft, fraud, or other illegal or dishonest conduct, any of which are considered to be materially harmful to the Company; refusal, unwillingness, failure, or inability to perform his material job duties or habitual absenteeism; or violation of fiduciary duty, violation of any duty of loyalty, or material breach of any material term of his employment agreement or his Employee Intellectual Property, Confidentiality and Non-Compete Agreement, or any other agreement, with the Company. "Good reason" includes a relocation by us of Mr. Ozeroff's normal work location greater than 30 miles; a decrease in current base salary by more than 15%, with certain exceptions; and the Company's unilateral decision to significantly and detrimentally reduce Mr. Ozeroff's job responsibilities.

Non-Equity Incentive Plan Compensation

In February 2007, the Compensation Committee and the Board of Directors of ARCA established a bonus structure for its entire executive team. The philosophy employed was to create incentives for the executive officers to achieve key corporate goals. The Compensation Committee retained discretion to change the bonus structure and the bonus payment amounts as it considered appropriate.

2017 Cash Bonus Plan

The Board of Directors has set corporate goals for 2017, or the 2017 Goals, which may be updated at the Board of Directors' discretion during 2017. Attainment of the 2017 Goals is a prerequisite to the payment of any awards to employees under the Company's 2017 Cash Bonus Plan, including executive officers.

The amount payable to each employee is set as a target percentage of each employee's annual salary, or the target bonus percentage, or TBP, but employees, including executive officers, may receive more or less than 100% of their TBP, based upon corporate goal achievement, individual performance and the discretion of the Board of Directors.

To receive a cash bonus (if any), each individual employee must be actively employed by the Company, and in good standing, on December 31, 2017. Employees hired after January 1, 2017, will have their cash bonus (if any) prorated based on the percentage of time the employee worked at ARCA in 2017. The 2017 Goals are based on (1) the GENETIC-AF Data and Safety Monitoring Board analysis and enrollment of GENETIC-AF; (2) financing goals; and (3) corporate transaction objectives.

2018 Cash Bonus Plan

The Compensation Committee and Board of Directors did not approve a bonus structure or goals for 2018. As such, the Company does not anticipate paying any cash bonuses to its Named Executive Officers in 2019 for performance in the 2018 fiscal year.

Other Elements of Executive Compensation Program

The remaining elements of the Company's executive compensation program, like its broader employee compensation programs, are intended to make the Company's overall compensation program competitive with those of its peer companies, keeping in mind the constraints imposed by the Company's reliance on capital markets as a primary source of cash. The remaining elements of the Company's executive compensation program, (401(k) Plan, Medical, Dental, and Vision Plans, Life and Disability Insurance) are available to all Company employees.

Outstanding Equity Awards at Fiscal year end

The following table shows for the fiscal year ended December 31, 2018, certain information regarding outstanding equity awards at fiscal year end for the Named Executive Officers.

A description of the equity incentive plans we maintain is set forth in Note 8 to the Company's financial statements included in this annual report on Form 10-K.

	Option Awards			
	Number of Securities Underlying Unexercised Options	Number of Securities Underlying Unexercised Options	Option Exercise Price	Option Expiration
Name	(#) Exercisable	(#)Unexercisable	($)	Date
Michael R. Bristow, President and Chief Executive Officer	596	—	233.94	1/23/2019
	380	—	124.74	2/18/2020
	714	—	94.08	5/20/2021
	28,142	—	9.66	9/16/2023
	12,260	—	9.66	9/16/2023
	7,357	—	13.65	2/26/2024
	3,700	—	4.69	2/11/2025
	22,667	4,533(1)(3)	3.30	6/8/2026
	25,667	16,333(2)(3)	2.50	2/15/2027
Thomas A. Keuer, Chief Operating Officer	584	—	121.80	6/25/2019
	190	—	124.74	2/18/2020
	476	—	94.08	5/20/2021
	4,775	—	9.66	9/16/2023
	1,428	—	10.85	10/14/2023
	1,500	—	13.65	2/26/2024
	1,950	—	4.69	2/11/2025
	13,000	2,600 (1)(3)	3.30	6/8/2026
	15,400	9,800 (2)(3)	2.50	2/15/2027
Christopher Ozeroff, Secretary, Senior Vice President and General Counsel	152	—	124.74	2/18/2020
	476	—	94.08	5/20/2021
	6,091	—	9.66	9/16/2023
	1,500	—	13.65	2/26/2024
	1,850	—	4.69	2/11/2025
	12,334	2,466 (1)(3)	3.30	6/8/2026
	14,667	9,333 (2)(3)	2.50	2/15/2027

(1) Options vest in 36 monthly installments measured from June 9, 2016.

(2) Options vest in 36 monthly installments measured from February 16, 2017.

(3) In the event of a change in control of the Company, 50% of the unvested shares subject to this award shall become fully and immediately vested upon the closing date of such change in control, provided, however, that on the earlier of (i) the one-year anniversary of the closing date or (ii) involuntary termination, any options that remain unvested on

such earlier date shall become fully and immediately vested.

Option Exercises And Stock Vested

The following table sets forth certain information regarding option exercises and restricted stock units that vested during the year ended December 31, 2018, with respect to the Named Executive Officers:

	Option Awards		Stock Awards	
Name	Number of Shares Acquired on Exercise (#)	Value Realized on Exercise ($)(1)	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting ($)(2)
Michael R. Bristow	—	—	4,316	2,477
Thomas A. Keuer	—	—	2,429	1,403
Christopher Ozeroff	—	—	2,367	1,371

(1) The value realized on exercise of the options equals the difference between the market price of the underlying stock at exercise and the exercise or base price of the options, multiplied by the number of shares acquired on exercise.

(2) The value realized on vesting of restricted stock units equals the market value of the Company's Common Stock on the vesting date, multiplied by the number of shares that vested.

Director Compensation

The following table shows for the fiscal year ended December 31, 2018, certain information with respect to the compensation of all non-employee directors of the Company:

Director Compensation for Fiscal 2018 (1)

	Fees Earned or Paid in Cash ($)	Option Awards ($)(2)	Nonqualified Deferred Compensation Earnings ($)	All Other Compensation ($)	Total ($)
Linda Grais, M.D. (3)	52,500	4,640		—	57,140
Raymond L. Woosley, M.D. (4)	50,000	4,640		—	54,640
Robert E. Conway (5)	80,000	4,640		—	84,640
Dan J. Mitchell (6)	47,500	4,640		—	52,140
Anders Hove (7)	40,000	4,640		—	44,640

(1) Dr. Bristow, our President and Chief Executive Officer, was also a director during the year ended December 31, 2018, but did not receive any additional compensation for his service as a director. Dr. Bristow's compensation as an executive officer is set forth above under "Executive Compensation—Summary Compensation Table."

(2) The amounts reported under "Option Awards" in the above table reflect the aggregate grant date fair value of these awards as determined in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation – Stock Compensation, excluding the effects of estimated forfeitures. The value of stock option awards was estimated using the Black-Scholes option-pricing model. The valuation assumptions used in the valuation of option awards may be found in Note 8 to the Company's financial statements included in this annual report on Form 10-K for the year ended December 31, 2018.

(3) The aggregate number of shares issuable upon exercise of option awards outstanding at December 31, 2018, for Dr. Grais was 30,138, of which all shares were fully vested.

(4) The aggregate number of shares issuable upon exercise of option awards outstanding at December 31, 2018, for Dr. Woosley was 29,063, of which all shares were fully vested.

(5) The aggregate number of shares issuable upon exercise of option awards outstanding at December 31, 2018, for Mr. Conway was 28,941, of which all shares were fully vested.

(6) The aggregate number of shares issuable upon exercise of option awards outstanding at December 31, 2018, for Mr. Mitchell was 28,438, of which all shares were fully vested.

(7) The aggregate number of shares issuable upon exercise of option awards outstanding at December 31, 2018, for Dr. Hove was 18,000, of which all shares were fully vested.

In 2016, the Company revised its compensation plan for non-employee directors to provide that non-employee directors will be compensated for their service on the Board of Directors, as follows:

- Each non-employee director will receive an annual retainer fee of $35,000;
- As additional compensation for their services, each non-employee director will receive (i), upon joining the Board of Directors, an initial option grant to purchase 10,000 shares of the Company's Common Stock under the Amended and Restated ARCA 2013 Equity Incentive Plan, as amended, or the Amended 2013 Plan and (ii), on an annual basis, an annual option grant to purchase 8,000 shares of the Company's Common Stock under the Amended 2013 Plan;
- The Chairman of the Board of Directors will receive an additional annual retainer fee of $25,000;
- The Audit Committee chair will receive an additional annual retainer fee of $15,000;
- The chairs of the Compensation Committee and the Nominating and Corporate Governance Committee will each receive an additional annual retainer fee of $10,000;
- Each non-chair member of the Audit Committee will receive an additional annual retainer fee of $7,500; and
- Each non-chair member of the Compensation Committee and the Nominating and Corporate Governance Committees will receive an additional annual retainer fee of $5,000.

At the March 1, 2018, meeting of the Board of Directors, the Board of Directors awarded annual stock option grants to the Company's non-employee directors. Mr. Mitchell, Dr. Grais, Dr. Woosley, Mr. Conway and Dr. Hove each were granted options to purchase 8,000 shares of Common Stock under the Amended 2013 Plan vesting over one year. The purchase price for the options issued on March 1, 2018, was $0.72 per share, which was equal to the closing price of the Company's Common Stock on Nasdaq on the date of the grant. If the non-employee director's service terminates in connection with or at any time following a change in control, then any unexpired options that remain unvested shall become fully vested.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Equity Compensation Plan Information

The following table sets forth information as of December 31, 2018, for all of our equity compensation plans:

	No. of Securities to be Issued Upon Exercise of Outstanding Options Units	Weighted Average Exercise Price of Outstanding Options ($)	No. of Securities Remaining Available for Future Issuance Under Equity Compensation Plans Excluding Securities Reflected in Column(a)
	(a)	(b)	(c)
Equity compensation plans approved by security holders	604,003	5.37	615,976
Equity compensation plans not approved by security holders	—	—	—
Total	604,003	5.37	615,976

On September 17, 2013, our stockholders approved the ARCA biopharma, Inc. 2013 Equity Incentive Plan, or the 2013 Plan, at the Company's 2013 annual meeting of stockholders. The 2013 Plan is the successor to the Amended and Restated ARCA biopharma, Inc. 2004 Equity Incentive Plan, or the 2004 Plan. On June 9, 2016, our stockholders approved the Amended 2013 Plan. A description of the 2013 Plan and the Amended 2013 Plan is set forth in Note 8 to the Company's financial statements included in this annual report on Form 10-K.

Compensation Risks

We believe our approach to goal setting, setting of targets with payouts at multiple levels of performance, and evaluation of performance results assist in mitigating excessive risk-taking that could harm the value or reward poor judgment by our executives. We believe several features of our programs reflect sound risk management practices. We believe we have allocated compensation among base salary and short and long-term compensation target opportunities in such a way as to not encourage excessive risk-taking. The multi-year vesting of equity awards properly accounts for the time horizon of risk. Furthermore, the Compensation Committee assesses and monitors

whether any of our compensation policies and programs has the potential to encourage excessive risk-taking on an annual basis.

Security Ownership of Certain Beneficial Owners

The following table sets forth certain information regarding the ownership of the Company's Common Stock as of February 22, 2019, by: (i) each director and nominee for director, (ii) each of our named executive officers, (iii) all executive officers and directors of the Company as a group, and (iv) all those known by the Company to be beneficial owners of more than five percent of its Common Stock. Unless otherwise noted below, the address of each beneficial owner listed on the table is c/o ARCA biopharma, Inc., 11080 CirclePoint Road, Suite 140, Westminster, Colorado, 80020.

We have determined beneficial ownership in accordance with the rules of the SEC. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons and entities named in the table below have sole voting and investment power with respect to all shares of Common Stock that they beneficially own, subject to applicable community property laws. The table is based upon information supplied by officers, directors and principal stockholders and Schedules 13G or 13D, Form 4s or other ownership reports filed with the SEC. For purposes of this table, certain of our outstanding warrants that may be exercisable for fractional shares have been rounded down to the nearest whole number.

In computing the number of shares of Common Stock beneficially owned by a person and the percentage ownership of that person, we deemed outstanding shares of Common Stock subject to options, restricted stock units, or warrants held by that person that are currently exercisable or exercisable within 60 days of February 22, 2019. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

The percentages below are based on 18,335,111 shares of our Common Stock outstanding as of February 22, 2019.

Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned
Directors and Named Executive Officers		
Michael R. Bristow, M.D., Ph.D. (1)	212,997	1.15%
Thomas A. Keuer (2)	56,990	*
Christopher D. Ozeroff (3)	58,898	*
Linda Grais, M.D. (4)	30,138	*
Robert E. Conway (5)	63,941	*
Raymond L. Woosley (6)	29,063	*
Dan J. Mitchell (7)	39,438	*
Anders Hove, M.D. (8)	18,000	*
All current directors and executive officers as a group (9 persons) (9)	548,400	2.93%
5% Stockholders		
Tekla Life Sciences Investors (10)	1,135,718	6.08%
Renaissance Technologies LLC (11)	818,533	4.46%

*Represents beneficial ownership of less than 1% of our Common Stock.

(1) Includes the following owned by (i) Investocor Trust: 19,986 shares, Dr. Bristow is the sole trustee of Investocor Trust; (ii) NFS as Custodian for Michael Bristow's IRA: (a) 25,459 shares and (b) 17,821 shares issuable upon the exercise of warrants, which warrants are immediately exercisable; and (iii) options to purchase 108,576 shares that are exercisable within 60 days of February 22, 2019.
(2) Includes options to purchase 43,837 shares that are exercisable within 60 days of February 22, 2019.
(3) Includes options to purchase 41,381 shares that are exercisable within 60 days of February 22, 2019.
(4) Includes options to purchase 30,138 shares that are exercisable within 60 days of February 22, 2019.
(5) Includes options to purchase 28,941 shares that are exercisable within 60 days of February 22, 2019.
(6) Includes options to purchase 29,063 shares that are exercisable within 60 days of February 22, 2019.
(7) Includes options to purchase 28,438 shares that are exercisable within 60 days of February 22, 2019.
(8) Includes options to purchase 18,000 shares that are exercisable within 60 days of February 22, 2019.
(9) See Notes (1) through (8) above. Also, includes additional options to purchase 38,934 shares that are exercisable within 60 days of February 22, 2019 beneficially owned by our executive officers not listed by name in the table above.
(10) Based on a Schedule 13G/A filed with the SEC on February 12, 2019. Includes 324,491 shares issuable upon exercise of warrants, which warrants are immediately exercisable. Tekla Capital Management LLC ("TCM"), as an investment adviser to Tekla Life Sciences Investors ("HQL"), shares beneficial ownership over the shares held by HQL. Each of TCM and Daniel R. Omstead, through his control of TCM, has sole power to dispose of the shares

beneficially owned by HQL. Neither TCM nor Daniel R. Omstead has the sole power to vote or direct the vote of the shares beneficially owned by HQL, which power resides in the fund's Board of Trustees. TCM carries the voting of shares under written guidelines established by the funders Board of Trustees. The address for Tekla Life Sciences Investors is 100 Federal Street, 19th Floor, Boston, MA 02110.

(11) Based upon a Schedule 13G filed with the SEC on February 12, 2019. Renaissance Technologies Holdings Corporation is deemed to beneficially own the shares owned by Renaissance Technologies LLC, because of Renaissance Technologies Holdings Corporation's majority ownership of Renaissance Technologies LLC. The address for Renaissance Technologies Holdings Corporation and Renaissance Technologies LLC is 800 Third Avenue, New York, NY 10022.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Independence of the Board of Directors

As required under the Nasdaq listing standards, a majority of the members of a listed company's board of directors must qualify as "independent," as affirmatively determined by the board of directors. Our Board of Directors consults with the Company's counsel to ensure that the Board of Directors' determinations are consistent with relevant securities and other laws and regulations regarding the definition of "independent," including those set forth in pertinent listing standards of the Nasdaq, as in effect from time to time.

Consistent with these considerations, after review of all relevant identified transactions or relationships between each director, or any of his or her family members, and the Company, its senior management and its independent registered public accounting firm, the Board of Directors has affirmatively determined that the following five directors are independent directors within the meaning of the applicable Nasdaq listing standards: Mr. Conway, Dr. Grais, Mr. Mitchell, Dr. Hove and Dr. Woosley. In making this determination, the Board of Directors found that none of the directors or nominees for director had a material or other disqualifying relationship with the Company. Dr. Bristow, the Company's President and Chief Executive Officer is not an independent director by virtue of his employment relationship with the Company.

Certain Transactions With or Involving Related Persons

The following is a summary of transactions since January 1, 2017, to which we have been a party in which the amount involved exceeded the lesser of $120,000 or one percent of the average of our total assets at fiscal year end for 2017 and 2018, and in which any of our executive officers, directors or holders of more than 5% of our capital stock, or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest, other than compensation arrangements disclosed in "Item 11. Executive Compensation" of this Form 10-K.

Transactions With the Company's President and Chief Executive Officer

The Company has entered into unrestricted research grants with the academic research laboratory of Dr. Bristow, the Company's President and Chief Executive Officer, at the University of Colorado. Funding of any unrestricted research grants is contingent upon the Company's financial condition, and can be deferred or terminated at the Company's discretion. Total expense under these arrangements for the years ended December 31, 2018 and 2017 was approximately $325,000 and $418,000, respectively, of which $111,000 was unpaid and included in Accrued expenses and other liabilities as of December 31, 2018.

Policies and Procedures for Related Party Transactions

Our Audit Committee reviews and approves all related party transactions. This review covers any material transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, and a related party had or will have a direct or indirect material interest, including, purchases of goods or services by or from the related party or entities in which the related party has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related party.

Item 14. Principal Accountant Fees and Services

The following table represents aggregate fees billed, or expected to be billed, to us for the fiscal years ended December 31, 2018 and December 31, 2017, by KPMG LLP, our independent registered public accounting firm.

	Fiscal Year Ended 2018	Fiscal Year Ended 2017
Audit Fees (1)	$154,500	$193,500
Audit-related Fees	—	—
Tax Fees	—	—
All Other Fees	—	—
All Other Fees		-
Total Fees	$154,500	$193,500

(1) Audit Fees include fees for the (i) audit of the financial statements included in our Form 10-K for our fiscal years ended December 31, 2018, and December 31, 2017, (ii) review of interim financial statements included on Forms 10-Q and (iii) attest, consent and review services normally provided by the accountant in connection with SEC filings.

All fees described above were approved by the Audit Committee.

Pre-Approval Policies and Procedures

The above services performed by the independent registered public accounting firm were pre-approved in accordance with the pre-approval policy and procedures adopted by the Audit Committee. This policy describes the permitted audit, audit-related, tax, and other services that our independent registered public accounting firm may perform. The policy also requires that our independent registered public accounting firm provide in writing:

- an annual description of all relationships between the independent registered public accounting firm and the client that may reasonably be thought to bear on independence;

- confirm that, in the independent registered public accounting firm's professional judgment, the independent registered public accounting firm is independent of the client under SEC requirements;
- discuss with the Audit Committee the independent registered public accounting firm's independence and the potential effects on its independence of performing any non-audit related services.

The services expected to be performed by our independent registered public accounting firm during the subsequent fiscal year are presented to the Audit Committee for pre-approval. Any pre-approval must describe, in writing, the particular service or category of services.

Requests for audit, audit-related, tax, and other services not contemplated by those pre-approved services must be submitted to the Audit Committee for specific pre-approval. Generally, pre-approval is considered at the Audit Committee's regularly scheduled meetings. However, the authority to grant specific pre-approval between meetings, as necessary, has been delegated to the chairman of the Audit Committee. If the chairman is not available, the other two Audit Committee members together have the authority to grant specific pre-approval between meetings. The chairman or the other members must update the Audit Committee at the next regularly scheduled meeting of any services that were granted specific pre-approval.

The Audit Committee pre-approved all audit related services rendered in 2018 and did not rely on the waiver of pre-approval requirement provided by paragraph (c)(7)(i)(C) of Rule 2-01 of Regulation S-X promulgated under the Exchange Act.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Report:

1. Financial statements filed as part of this Report are listed under Part II, Item 8, page 49 of this Annual Report on Form 10 K.
2. No schedules are required because either the required information is not present or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements or the notes thereto.

(b) Exhibits

A list of exhibits filed with this report or incorporated herein by reference is found in the Exhibit Index.

EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference Form	Filing Date	Number	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended.	10-K	3/27/2009	3.1	
3.1(a)	Certificate of Amendment to Restated Certificate of Incorporation.	8-K	3/5/2013	5.1	
3.1(b)	Certificate of Amendment to Restated Certificate of Incorporation.	8-K	9/3/2015	3.1	
3.2	Second Amended and Restated Bylaws of the Registrant, as amended.	10-Q	11/16/2009	3.2	
4.1	Form of Common Stock Certificate.	8-K	1/28/2009	4.1	
4.2	Form of Warrants to Purchase Shares of Common Stock.	8-K	1/23/2013	4.1	
4.3	Form of Warrant to Purchase shares of Common Stock.	8-K	6/11/2015	4.1	
4.4	Form of Warrant to Purchase shares of Common Stock.	8-K	6/11/2015	4.2	
4.5	Reference is made to Exhibits 3.1, 3.1(a), 3.1(b) and 3.2				
10.1§	License and Sublicense Agreement, dated October 28, 2003, by and between ARCA Discovery, Inc. and CPEC, L.L.C.	10-Q	5/15/2009	10.1	
10.2	Amendment to License and Sublicense Agreement, dated February 22, 2006, by and between ARCA Discovery, Inc. and CPEC L.L.C.	10-Q	5/15/2009	10.2	
		8-K	1/28/2009	10.1	

10.3†	ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.2
10.4†	Amendment No. 1 to the ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.3
10.5†	Amendment No. 2 to the ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.4
10.6†	Amendment No. 3 to the ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.5
10.7†	Amendment No. 4 to the ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.6
10.8†	Amendment No. 5 to the ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.7
10.9†	Amendment No. 6 to the ARCA Discovery, Inc. 2004 Stock Incentive Plan.	8-K	1/28/2009	10.8
10.10†	ARCA biopharma, Inc. 2004 Stock Incentive Plan, Form of Executive Incentive Stock Option Agreement.	8-K	1/28/2009	10.9
10.11†	ARCA biopharma, Inc. 2004 Stock Incentive Plan, Form of Non-Executive Incentive Stock Option Agreement.			

Exhibit No.	Description	Incorporated by Reference Form	Filing Date	Number	Filed Herewith
		8-K	1/28/2009	10.10	
10.12†	ARCA biopharma, Inc. 2004 Stock Incentive Plan, Form of Nonqualified Stock Option Agreement.				
		10-K	3/27/2009	10.34	
10.13†	ARCA biopharma, Inc. 2004 Equity Incentive Plan (f/k/a Nuvelo, Inc. 2004 Equity Incentive Plan), Form of Partial Acceleration Stock Option Agreement.				
		10-K	3/27/2009	10.35	
10.14†	ARCA biopharma, Inc. 2004 Equity Incentive Plan (f/k/a Nuvelo, Inc. 2004 Equity Incentive Plan), Form of No Acceleration Stock Option Agreement.				
		10-K	3/27/2009	10.36	
10.15†	ARCA biopharma, Inc. 2004 Equity Incentive Plan (f/k/a Nuvelo, Inc. 2004 Equity Incentive Plan), Form of Director Stock Option Agreement.				
		10-K	3/27/2009	10.37	
10.16†	ARCA biopharma, Inc. 2004 Equity Incentive Plan (f/k/a Nuvelo, Inc. 2004 Equity Incentive Plan), Form of Notice of Grant of Stock Option.				
		10-K	3/27/2009	10.38	
10.17†	ARCA biopharma, Inc. 2004 Equity Incentive Plan (f/k/a Nuvelo, Inc. 2004 Equity Incentive Plan), Form of Notice of Director Grant of Stock Option.				
		10-K	3/27/2009	10.43	
10.18†	Amended and Restated Employment and Retention Agreement, dated June 4, 2008, by and between ARCA biopharma, Inc. and Michael R. Bristow.				
		10-K	3/27/2009	10.46	
10.19	Assignment and Assumption Agreement, dated January 26, 2009, by and between ARCA biopharma, Inc. and ARCA biopharma Colorado, Inc.				
		10-K	3/27/2009	10.45	
10.20†	Amended and Restated Employment Agreement, dated June 12, 2008, by and between ARCA biopharma, Inc. and Christopher D. Ozeroff.				
		10-K	3/27/2009	10.48	

10.21	Assignment and Assumption Agreement, dated January 26, 2009, by and between ARCA biopharma, Inc. and ARCA biopharma Colorado, Inc.	10-Q/A	8/21/2009	10.1
10.22†	Amended and Restated ARCA biopharma, Inc. 2004 Equity Incentive Plan.	10-Q	8/10/2009	10.5
10.23†	Form of Option Amendment pursuant to ARCA biopharma, Inc. 2004 Equity Incentive Plan and ARCA biopharma, Inc. 2004 Stock Option Plan (change of control).	10-Q	8/10/2009	10.6
10.24†	Form of Option Agreement and Grant Notice pursuant to ARCA biopharma, Inc. 2004 Equity Incentive Plan (NDA/change of control acceleration).	10-K	3/27/2009	10.52
10.25	Form of Indemnification Agreement between ARCA biopharma, Inc. and its directors and officers.	8-K	4/18/2011	10.1
10.26	Form of Subscription Agreement.	8-K	1/11/2017	10.1
10.27	Capital on Demand™ Sales Agreement, dated January 11, 2017, by and between ARCA biopharma, Inc. and JonesTrading Institutional Services LLC.			

Exhibit No.	Description	Incorporated by Reference Form	Filing Date	Number	Filed Herewith
10.28	Amendment No. 1 to Capital on Demand™ Sales Agreement, dated August 21, 2017, by and between ARCA biopharma, Inc. and JonesTrading Institutional Services LLC.	8-K	8/21/2017	10.1	
10.29	Amendment No. 2 to Capital on Demand™ Sales Agreement, dated January 25, 2019, by and between ARCA biopharma, Inc. and JonesTrading Institutional Services LLC.	8-K	1/25/2019	10.1	
10.30§	Amended and Restated Exclusive License Agreement, dated August 12, 2011, by and between the Regents of the University of Colorado and ARCA biopharma, Inc.	10-Q	8/15/2011	10.5	
10.31	Form of Subscription Agreement.	8-K	12/22/2011	10.1	
10.32	Form of Registration Rights Agreement.	8-K	12/22/2011	10.2	
10.33	Form of Subscription Agreement.	8-K	8/3/2012	10.1	
10.34	Form of Subscription Agreement by and among the Company and the purchasers identified therein, dated October 22, 2012.	8-K	10/23/2012	10.1	
10.35	Form of Registration Rights Agreement.	8-K	10/23/2012	10.2	
10.36	Form of Subscription Agreement by and among the Company and the purchasers identified therein, dated December 18, 2012.	8-K	12/19/2012	10.1	
10.37	Form of Registration Rights Agreement.	8-K	12/19/2012	10.2	
10.38	Form of Amendment to the Registration Rights Agreement, dated December 18, 2012.	8-K	12/19/2012	10.3	
10.39	Form of Subscription Agreement by and among the Company and the purchasers identified therein, dated January 22, 2013.	8-K	1/23/2013	10.1	

10.40	Form of Registration Rights Agreement.	8-K	1/23/2013	10.2
10.41	Subscription Agreement.	8-K	2/1/2013	10.1
10.42	Placement Agency Agreement by and between ARCA biopharma, Inc. and Dawson James Securities, Inc., dated January 21, 2014.	8-K	2/4/2014	1.1
10.42(a)	Amendment No. 1 Placement Agency Agreement by and between ARCA biopharma, Inc. and Dawson James Securities, Inc., dated January 31, 2014.	8-K	2/4/2014	1.2
10.43	Securities Purchase Agreement by and among the Company and the purchasers identified therein, dated June 10, 2015.	8-K	6/11/2015	10.1
10.44	Office Lease Agreement by and between ARCA biopharma, Inc. and Circle Point Properties, LLC, effective August 1, 2013.	8-K	8/6/2013	10.1

Exhibit No.	Description	Incorporated by Reference Form	Filing Date	Number	Filed Herewith
10.45	Amendment to Office Lease Agreement by and between ARCA biopharma, Inc. and Circle Point Properties, LLC, effective March 2, 2016.	8-K	3/7/2016	10.1	
10.46†	Amendment Agreement by and between ARCA biopharma, Inc. and Michael R. Bristow, effective as of June 13, 2013.	10-Q	8/13/2013	10.6	
10.47†	Amendment Agreement by and between ARCA biopharma, Inc. and Christopher Ozeroff, effective as of June 13, 2013.	10-Q	8/13/2013	10.8	
10.48†	ARCA biopharma, Inc. 2013 Equity Incentive Plan.	8-K	9/23/2013	10.1	
10.49†	Form of Stock Option Agreement and Option Grant Notice under 2013 Equity Incentive Plan (Standard).	8-K	9/23/2013	10.2	
10.50†	Form of Stock Option Agreement and Option Grant Notice under 2013 Equity Incentive Plan (Officer).	8-K	9/23/2013	10.3	
10.51†	Form of Stock Option Agreement and Option Grant Notice under 2013 Equity Incentive Plan (Director).	8-K	9/23/2013	10.4	
10.52†	Form of Restricted Stock Unit Award Agreement and Notice of Grant Award under 2013 Equity Incentive Plan (Standard).	8-K	9/23/2013	10.5	
10.53†	Form of Restricted Stock Unit Award Agreement and Notice of Grant Award under 2013 Equity Incentive Plan (Officer).	8-K	9/23/2013	10.6	
10.54†	Employment Agreement, dated December 29, 2014, by and between ARCA biopharma, Inc. and Brian Selby.	8-K/A	12/30/2014	10.1	
10.55†	Amended and Restated Employment Agreement, dated December 29, 2014, by and between ARCA biopharma, Inc. and Thomas A. Keuer.	8-K/A	12/30/2014	10.2	

23.1	Consent of KPMG LLP, Independent Registered Public Accounting Firm.	X
24.1	Power of Attorney (included in the signature page hereto).	X
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. sec. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	XBRL Instance Document (filed electronically herewith)	X
101.SCH	XBRL Taxonomy Extension Schema Document (filed electronically herewith)	X

Exhibit No.	Description	Incorporated by Reference Form	Filing Date	Number	Filed Herewith
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document (filed electronically herewith)				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document (filed electronically herewith)				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document (filed electronically herewith)				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document (filed electronically herewith)				X

† Indicates management contract or compensatory plan or arrangement required to be filed as an exhibit pursuant to Item 15(b) of Form 10-K.

§ Confidential treatment has been requested for portions of this document, which are omitted and filed separately with the SEC. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ARCA biopharma, Inc.

By: /S/ BRIAN L. SELBY
Brian L. Selby

Vice President, Finance

(Principal Financial Officer and Principal Accounting Officer)

Date: February 27, 2019

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Michael R. Bristow and Brian L. Selby, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution for him, and in his name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of ARCA biopharma, Inc., in the capacities and on the dates indicated.

Signature	Title	Date
/S/ Michael R. Bristow Michael R. Bristow	President and Chief Executive Officer and Director (Principal Executive Officer)	February 27, 2019
/S/ Brian L. Selby Brian L. Selby	Vice President, Finance (Principal Financial Officer and Principal Accounting Officer)	February 27, 2019
/S/ Linda Grais	Director	February 27, 2019

Linda Grais

/s/ Raymond Woosley Raymond Woosley	Director	February 27, 2019
/s/ Robert Conway Robert Conway	Director	February 27, 2019
/s/ Daniel Mitchell Daniel Mitchell	Director	February 27, 2019
/s/ Anders Hove Anders Hove	Director	February 27, 2019