ARCA biopharma, Inc.
Form 10-Q
November 14, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

QUARTERLY REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2018

OR

TRANSITION REPORT UNDER 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 (State or Other Jurisdiction of Incorporation or Organization)	36-3855489 (I.R.S. Employer Identification Number)
11080 CirclePoint Road, Suite 140, Westminster, CO (Address of Principal Executive Offices)	80020 (Zip Code)

(720) 940-2200

(Registrant's Telephone Number, including Area Code)

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 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 whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an 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	Small 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 Exchange Act). Yes No

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Class	Number of Shares Outstanding
Common Stock $0.001 par value	On November 12, 2018: 13,924,058

ARCA BIOPHARMA, INC.

FORM 10-Q

FOR THE QUARTER ENDED SEPTEMBER 30, 2018

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

ARCA BIOPHARMA, INC.

BALANCE SHEETS

(Unaudited)

	September 30, 2018	December 31, 2017
	(in thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$8,056	$8,702
Marketable securities	—	3,050
Other current assets	336	547
Total current assets	8,392	12,299
Property and equipment, net	29	42
Other assets	24	24
Total assets	$8,445	$12,365
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$217	$622
Accrued compensation and employee benefits	184	757
Accrued expenses and other liabilities	577	691
Total current liabilities	978	2,070
Deferred rent, net of current portion	4	20
Total liabilities	982	2,090
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value; 100 million shares authorized at September 30, 2018 and December 31, 2017; 13,923,825	14	12

and 11,775,062 shares issued and outstanding at September 30, 2018 and December 31, 2017, respectively		
Additional paid-in capital	144,894	141,266
Accumulated other comprehensive loss	—	(2)
Accumulated deficit	(137,445)	(131,001)
Total stockholders' equity	7,463	10,275
Total liabilities and stockholders' equity	$8,445	$12,365

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
	(in thousands, except share and per share amounts)			
Costs and expenses:				
Research and development	$740	$3,488	$3,614	$11,242
General and administrative	922	987	2,977	3,173
Total costs and expenses	1,662	4,475	6,591	14,415
Loss from operations	(1,662)	(4,475)	(6,591)	(14,415)
Interest and other income	40	44	124	128
Interest expense	(2)	(2)	(8)	(6)
Loss before income taxes	(1,624)	(4,433)	(6,475)	(14,293)
Benefit from income taxes	31	—	31	—
Net loss	$(1,593)	$(4,433)	$(6,444)	$(14,293)
Change in unrealized loss on marketable securities	—	2	2	16
Comprehensive loss	$(1,593)	$(4,431)	$(6,442)	$(14,277)
Net loss per share:				
Basic and diluted	$(0.11)	$(0.39)	$(0.47)	$(1.43)
Weighted average shares outstanding:				
Basic and diluted	13,923,825	11,502,654	13,823,793	9,982,739

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

(unaudited)

	Stockholders' Equity					
	Common stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Amount				
	(in thousands, except 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	85,068	—	69	—	—	69
Issuance of common stock upon vesting of Restricted Stock Units	5,434	—	—	—	—	—
Share-based compensation	—	—	101	—	—	101
Change in unrealized loss on marketable securities	—	—	—	10	—	10
Net loss	—	—	—	—	(4,338)	(4,338)
Balance, March 31, 2017	9,172,868	9	134,885	(9)	(116,849)	18,036
Issuance of common stock for cash, net of offering costs	934,214	1	2,109	—	—	2,110
Issuance of common stock upon vesting of Restricted Stock Units	9,504	—	—	—	—	—
Share-based compensation	—	—	119	—	—	119
Change in unrealized loss on marketable securities	—	—	—	4	—	4
Net loss	—	—	—	—	(5,522)	(5,522)
Balance, June 30, 2017	10,116,586	10	137,113	(5)	(122,371)	14,747
Issuance of common stock for cash, net of offering costs	1,634,158	2	3,915	—	—	3,917
Share-based compensation	—	—	119	—	—	119
Change in unrealized loss on marketable securities	—	—	—	2	—	2
Net loss	—	—	—	—	(4,433)	(4,433)
Balance, September 30, 2017	11,750,744	12	141,147	(3)	(126,804)	14,352

Issuance of common stock for cash, net of offering costs	24,085	—	—	—	—	—
Issuance of common stock upon vesting of Restricted Stock Units	233	—	—	—	—	—
Share-based compensation	—	—	119	—	—	119
Change in unrealized loss on marketable securities	—	—	—	1	—	1
Net loss	—	—	—	—	(4,197)	(4,197)
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	5,430	—	—	—	—	—
Share-based compensation	—	—	97	—	—	97
Change in unrealized loss on marketable securities	—	—	—	2	—	2
Net loss	—	—	—	—	(2,735)	(2,735)
Balance, March 31, 2018	13,914,320	14	144,776	—	(133,736)	11,054
Issuance of common stock upon vesting of Restricted Stock Units	9,505	—	—	—	—	—
Share-based compensation	—	—	60	—	—	60
Net loss	—	—	—	—	(2,116)	(2,116)
Balance, June 30, 2018	13,923,825	14	144,836	—	(135,852)	8,998
Share-based compensation	—	—	58	—	—	58
Net loss	—	—	—	—	(1,593)	(1,593)
Balance, September 30, 2018	13,923,825	$ 14	$ 144,894	$ —	$ (137,445)	$ 7,463

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

STATEMENTS OF CASH FLOWS

(unaudited)

	Nine Months Ended September 30,	
	2018	2017
	(in thousands)	
Cash flows from operating activities:		
Net loss	$(6,444)	$(14,293)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	17	21
Amortization of other assets	—	269
Amortization of premiums and discounts on marketable securities	2	109
Share-based compensation	215	339
Change in operating assets and liabilities:		
Other current assets	522	186
Accounts payable	(405)	29
Accrued compensation and employee benefits	(573)	(526)
Accrued expenses and other liabilities	(235)	590
Net cash used in operating activities	(6,901)	(13,276)
Cash flows from investing activities:		
Purchases of property and equipment	(4)	(2)
Purchases of marketable securities	—	(5,471)
Proceeds from maturities of marketable securities	3,050	13,650
Net cash provided by investing activities	3,046	8,177
Cash flows from financing activities:		
Proceeds from the issuance of common stock	3,532	6,515
Common stock offering costs	(117)	(419)
Repayment of principal on vendor finance agreement	(206)	(256)
Net cash provided by financing activities	3,209	5,840
Net (decrease) increase in cash and cash equivalents	(646)	741
Cash and cash equivalents, beginning of period	8,702	7,401
Cash and cash equivalents, end of period	$8,056	$8,142
Supplemental cash flow information:		
Interest paid	$6	$6
Income tax refund received	$31	$—
Supplemental disclosure of noncash investing and financing		

transactions:		
Vendor finance agreement	$105	$—
Change in unrealized loss on marketable securities	$2	$16

See accompanying Notes to Financial Statements

ARCA BIOPHARMA, INC.

NOTES TO FINANCIAL STATEMENTS

(unaudited)

(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 heart failure (HF) patients at risk for atrial fibrillation (AF).

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 our 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. In July 2018, the Company received guidance from the U.S. Food and Drug Administration (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 a specific genotype. 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 confirmation via the FDA's Special Protocol Assessment (SPA) process. In late October 2018, the Company received a No Agreement letter from the FDA on its SPA. After further correspondence and following provision of information regarding the SPA, the FDA has agreed to reconsider the SPA request. To facilitate this process, the Company has requested a meeting with the FDA, which, if granted, is expected to occur in December 2018. At this time, the Company does not know when the FDA will provide a further decision on its SPA request.

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 current cash and cash equivalents will be sufficient to fund its operations, at its projected cost structure, through the end of the first 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 unaudited financial statements of the Company were prepared in accordance with generally accepted accounting principles for interim financial information and instructions to Form 10-Q and pursuant to Regulation S-X. Accordingly, these financial statements do not include all of the information and footnotes required by accounting principles generally accepted in the United States of America (GAAP) for complete financial statements. In the opinion of management, these financial statements include all normal and recurring adjustments considered necessary for a fair presentation of these interim financial statements. The results of operations for the nine months ended September 30, 2018 are not necessarily indicative of results expected for the full year ending December 31, 2018. The Company has generated no revenue to date and its activities have consisted of seeking regulatory approval, research and development, exploring strategic alternatives for further developing and commercializing Gencaro, and raising capital. These unaudited financial statements should be read in conjunction with the audited financial statements and footnotes thereto for the year ended December 31, 2017 included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission. Amounts presented are rounded to the nearest thousand, where indicated, except per share data and par values.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. 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.

Accrued Expenses

As part of the process of preparing its financial statements, the Company is required to estimate accrued 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 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 professional service fees, such as attorneys, consultants, and clinical research organizations. The Company develops estimates of liabilities using its judgment based upon the facts and circumstances known at the time.

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 our 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. Early application is permitted. ASU 2016-02 requires modified retrospective adoption for all leases existing at, or entered into after, the date of initial application, with an option to use certain transition relief. While the Company is currently evaluating the transition methods and the impact that ASU 2016-02 will have on its financial statements and related disclosures, it is expected that the operating lease commitment discussed in Note 6 will be recognized as operating lease liability and right-of-use asset.

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 thefinancial statements.

In August 2018, the SEC adopted the final rule under SEC Release No. 33-10532, Disclosure Update and Simplification, amending certain disclosure requirements that were redundant, duplicative, overlapping, outdated or superseded. In addition, the amendments expanded the disclosure requirements under Regulation S-K and Regulation S-X under the Securities Exchange Act of 1934, as amended, on the analysis of stockholders' equity for interim financial statements. Under the amendments, an analysis of changes in each caption of stockholders' equity presented in the balance sheet must be provided in a note or separate statement. The analysis should present a reconciliation of the beginning balance to the ending balance of each period for which a statement of comprehensive income is required to be filed. The updated disclosures were included in this Quarterly Report on Form 10-Q.

(2) Net Loss Per Share

The Company calculates basic earnings per share by dividing net loss by the weighted average common shares outstanding during the period. Diluted earnings 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 three and nine months ended September 30, 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:

	September 30,	
	2018	2017
Potentially dilutive securities, excluded:		
Outstanding stock options	604,265	820,587
Unvested restricted stock units	233	15,401
Warrants to purchase common stock	2,669,855	3,656,978
	3,274,353	4,492,966

(3) Marketable Securities and Fair Value Disclosures

There were no marketable securities as of September 30, 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
September 30, 2018				
Money market	$8,078	$8,078	$—	$ —
Total	$8,078	$8,078	$—	$ —
December 31, 2017				
Money market	$8,189	$8,189	$—	$ —
Corporate bonds	3,725	—	3,725	—
Total	$11,914	$8,189	$3,725	$ —

As of September 30, 2018 and December 31, 2017, the Company had $8.1 million and $8.9 million, respectively, of cash equivalents consisting of money market funds and commercial paper 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 of assets between fair value hierarchy levels during the nine-month period ended September 30, 2018.

Fair Value of Other Financial Instruments

The carrying amount of other financial instruments, including accounts payable and notes payable approximated fair value due to their short maturities.

(4) Property and Equipment

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

	Estimated Life	September 30, 2018	December 31, 2017
Computer equipment	3 years	$ 65	$ 74
Lab equipment	5 years	142	142
Furniture and fixtures	5 years	83	83
Computer software	3 years	83	85
Leasehold improvements	Lesser of useful life or life of the lease	59	59
		432	443
Accumulated depreciation and amortization		(403)	(401)
Property and equipment, net		$ 29	$ 42

For the nine months ended September 30, 2018 and 2017, depreciation and amortization expense was $17,000 and $21,000, 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 nine months ended September 30, 2018 and 2017 was $274,000 and $301,000 respectively.

(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 the 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 September 30, 2018 (in thousands):

Remainder of 2018	$22
2019	83
Total future minimum lease payments	$105

Rent expense for the nine months ended September 30, 2018 and 2017 was $62,000 and $62,000, 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 bought 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, discussed above. The acquisition cost of this interest did not have a material impact on the Company's financial statements.

(7) Equity Financings and Warrants

At the Market 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, the Company amended its Capital on Demand Sales Agreement. The amendment, 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 $10.2 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.

Under this Sales Agreement, the Company sold an aggregate of 4,811,353 shares of Common Stock pursuant to the terms of such Sales Agreement, as amended, for aggregate gross proceeds of approximately $10.1 million and net proceeds received were approximately $9.5 million, including initial expenses for executing the “at the market offering” and commissions to the placement agent. As of September 30, 2018, the Company had sold all shares available for this offering under its prospectus to the Company’s registration statement on Form S-3 (No. 333-217459).

Warrants

Warrants to purchase shares of common stock were previously 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 September 30, 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

For the three and nine month periods ended September 30, 2018 and 2017, the Company recognized the following non-cash, share-based compensation expense in the statements of operations (in thousands):

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2018	2017	2018	2017
Research and development	$26	$44	$92	$124
General and administrative	32	75	123	215
Total	$58	$119	$215	$339

Stock option transactions for the nine month period ended September 30, 2018 under the Company’s stock incentive plans were as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual

			Term (in years)
Options outstanding at December 31, 2017	611,975	$ 6.00	8.14
Granted	40,000	0.72	
Exercised	—	—	
Forfeited and cancelled	(47,710)	8.37	
Options outstanding at September 30, 2018	604,265	$ 5.47	7.54
Options exercisable at September 30, 2018	447,317	$ 6.50	7.29
Options vested and expected to vest	604,014	$ 5.47	7.54

Stock award transactions related to restricted stock units for the nine month period ended September 30, 2018 under the Company’s stock incentive plans were as follows:

	Number of Shares	Weighted Average Grant Date Fair Value
Restricted stock units outstanding at December 31, 2017	15,168	$ 7.94
Granted	—	—
Vested and released	(14,935)	7.98
Forfeited and cancelled	—	—
Restricted stock units outstanding at September 30, 2018	233	$ 5.23

(9) Income Taxes

In accordance with GAAP, a valuation allowance should be provided if it is more likely than not that some or all of the Company's deferred tax assets will not be realized. The Company's ability to realize the benefit of its deferred tax assets will depend on the generation of future taxable income. Due to the uncertainty of future profitable operations and taxable income, the Company has recorded a full valuation allowance against its net deferred tax assets. The Company believes its tax filing positions and deductions related to tax periods subject to examination will be sustained upon audit and, therefore, has no reserve for uncertain tax positions.

Income tax benefit of $31,000 for the nine months ended September 30, 2018 was related to a federal research and experimentation income tax credit related to the Protecting Americans from Tax Hikes Act of 2015 (PATH Act) which allows qualified small businesses to monetize up to $250,000 of research and experimentation tax credits through payroll tax refunds. The PATH Act refunds were not effective until 2017.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Management's Discussion and Analysis of Financial Condition and Results of Operations contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the Private Securities Litigation Reform Act of 1995. Examples of these statements include, but are not limited to, statements regarding the following: potential future development plans for Gencaro™ (bucindolol hydrochloride), our lead product candidate, the potential approval of any Special Protocol Assessment, or SPA, application we submitted to the U.S. Food and Drug Administration, or the FDA, potential future development plans for Gencaro, including any plans regarding a Phase 3 clinical trial related thereto, the expected features and characteristics of Gencaro, including the potential for genetic variations to predict individual patient response to Gencaro or AB171, a thiol-substituted isosorbide mononitrate, 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, the expected features and characteristics of AB171 as a potential genetically-targeted treatment for peripheral arterial disease, or PAD, 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, 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, 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. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed herein and elsewhere. These and other factors are identified and described in more detail in ARCA's filings with the U.S. Securities and Exchange Commission, or the SEC, including without limitation the Company's annual report on Form 10-K for the year ended December 31, 2017, and subsequent filings. Forward-looking statements may be identified by words including "will," "plan," "anticipate," "believe," "intend," "estimates," "expect," "should," "may," "potential" and similar expressions. The Company disclaims any i or obligation to update these forward-looking statements.

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 for the potential treatment of patients with chronic heart failure with reduced left ventricular ejection fraction, or HFrEF, or mid-range ejection fraction, or HFmrEF, who also have atrial fibrillation, or AF, or at risk of developing AF.

In February 2018, we reported the results of our Phase 2B clinical superiority trial, known as GENETIC-AF, in which we evaluated Gencaro for the treatment and prevention of AF in patients with HFrEF (LVEF <0.40) or HFmrEF (LVEF >=0.40 and <0.50). 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. The GENETIC-AF trial only enrolled patients with the beta 1 389 arginine homozygous genotype, the specific genotype that the we believe enhances Gencaro's potential therapeutic effects. In our trial, HFrEF was defined as a left

ventricular ejection fraction, or LVEF, of less than 50%. 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.

In July 2018, we received guidance from the U.S. Food and Drug Administration, or the FDA, from an End-of-Phase 2 meeting regarding the Phase 3 program for Gencaro. 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 with the beta 1 389 arginine homozygous genotype. In consultation with the FDA, we developed key elements for a Phase 3 clinical trial needed to support a potential New Drug Application, or NDA, details of which were submitted to the FDA for evaluation and confirmation via the FDA Special Protocol Assessment, or SPA, process. In late October 2018, we received a No Agreement letter from the FDA on our SPA. After further correspondence and following provision of information regarding the SPA, the FDA has agreed to reconsider our SPA request. To facilitate this process, we have requested a meeting with the FDA, which, if granted, is expected to occur in December 2018. At this time, we do not know when the FDA will provide a further decision on our SPA request.

GENETIC-AF and BEST Trial DNA Substudy

Our planned Phase 3 development program of Gencaro is based on the results from our 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 bucindolol (Gencaro) 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, atrial flutter, or AFL, or ACM. Eligible patients had HFrEF or HFmrEF, 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 the Company believes 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, to evaluate daily 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.

In all patients, 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. The primary endpoint results described above were determined by intermittent, clinic-based heart rhythm monitoring. However, a subset of patients (N=69) also underwent continuous heart rhythm monitoring with Medtronic implanted therapeutic devices to determine AF recurrence based on AFB, a method that can identify AF with more certainty than intermittent clinic-based monitoring. In this substudy, Gencaro demonstrated trends for benefit compared to TOPROL-XL in the overall substudy population (hazard ratio of 0.74, [95% confidence interval: 0.38, 1.45]) for the endpoint of time to AF recurrence.

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/or 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 or 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 (230 patients [N=115 for each treatment arm], hazard ratio of 0.68, [95% confidence interval: 0.45, 1.02]) and by continuous heart rhythm monitoring with Medtronic implanted therapeutic devices (60 patients, hazard ratio of 0.61, [95% confidence interval: 0.25, 1.44]). Based upon our analysis of the GENETIC-AF data, we believe further clinical development of Gencaro is justified using entry criteria to identify patients who do not have long-standing HF and/or AF that we believe is likely recalcitrant to treatment with beta-blocker therapy.

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.

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. 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, provided the companion diagnostic test and services to support our GENETIC-AF trial. LabCorp has developed the genetic test and obtained an Investigational Device Exemption, or IDE, from the FDA for the companion diagnostic test used in our GENETIC AF clinical 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, a global healthcare solutions company, 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.

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 commonly occurs together with HFrEF and HFmrEF, with AF being both a cause and a result of HFrEF and HFmrEF. By increasing heart rate and producing irregular cycle lengths, AF may contribute to the disease processes that leads 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 the 2017 American Heart Association report on Cardiovascular Disease, approximately 5.2 million people in the United States had AF in 2015. Hospitalization rates for AF increased by 23% among U.S. adults from 2000 to 2010 and hospitalizations account for the majority of the economic cost burden associated with AF. In a global registry of AF patients, the rates of heart failure (of all types) ranged from 33% in patients with paroxysmal (episodes lasting 7 days or less) to 56% in patients with permanent AF.

We believe there is a significant need for drug therapies that are safe and effective for HFrEF patients with AF or at risk of developing it, as the existing drug therapies for the treatment or prevention AF have certain safety disadvantages in HFrEF patients, such as toxic or cardiovascular adverse effects. Most of the approved drugs for AF are contra indicated or have warnings in their prescribing information for such patients. Consequently, in the treatment and prevention of AF in HFrEF patients, we believe there is an unmet medical need for new treatments that have fewer side effects and are more effective than currently available therapies.

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. We believe our patent portfolio and new chemical entity exclusivity may provide market exclusivity for the indications of Gencaro that we may develop, into approximately 2030 or 2031 in the United States, Europe and other markets.

AB171

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 Investigational New Drug, or IND, enabling activities during 2018, to be followed, subject to availability of capital, 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.

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.

R&D expense for the three months ended September 30, 2018 was $0.7 million compared to $3.5 million for the corresponding period of 2017, a decrease of approximately $2.7 million. R&D expense for the nine months ended September 30, 2018 was $3.6 million compared to $11.2 million for the corresponding period of 2017, a decrease of approximately $7.6 million.

Clinical expense decreased approximately $2.0 million for the three months and $5.6 million for the nine months ended September 30, 2018, as compared to the corresponding periods of 2017. The decrease in costs were related to our GENETIC-AF clinical trial, being completed in 2017, so these costs did not recur in 2018.

Manufacturing process development costs decreased approximately $0.6 million for the three months and $1.8 million for the nine months ended September 30, 2018, as compared to the corresponding periods of 2017. The decreases were a result of decreased of production of clinical trial materials used in our GENETIC-AF clinical trial, being completed in 2017, so these costs did not recur in 2018.

We expect R&D expense in 2018 to be lower than 2017 as our GENETIC-AF clinical trial has been completed.

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 for the three months ended September 30, 2018 were relatively unchanged at $0.9 million compared to $1.0 million for the corresponding period of 2017. G&A expenses for the nine months ended September 30, 2018 were $3.0 million compared to $3.2 million for the corresponding periods of 2017. The $65,000 decrease for the three-month period and $196,000 decrease for the nine-month period were comprised primarily of decreased non-cash stock-based compensation expense, consulting costs, professional fees and travel costs in 2018, as compared to the corresponding period in 2017.

G&A expenses in 2018 are expected to be consistent with those in 2017 as we maintain administrative activities to support our ongoing operations.

Interest and Other Income

Interest and other income was $40,000 and $44,000 in the three months ended September 30, 2018 and 2017, respectively. Interest and other income was $124,000 and $128,000 in the nine months ended September 30, 2018 and 2017, respectively. We expect interest income to be lower in 2018 than in 2017, as we continue to use our cash and cash equivalents to fund our operations.

Interest Expense

Interest expense was $2,000 in the three months ended September 30, 2018 and 2017. Interest expense was $8,000 and $6,000 in the nine months ended September 30, 2018 and 2017, respectively. Based on our current capital structure, interest expense for the remainder of 2018 is expected to be negligible.

Income Tax Benefit

Income tax benefit was $31,000 for the three and nine months ended September 30, 2018, 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. We had no income tax benefit received during the three and nine months ended September 30, 2017.

Liquidity and Capital Resources

Cash, Cash Equivalents and Marketable Securities

	September 30, 2018	December 31, 2017
	(in thousands)	
Cash and cash equivalents	$8,056	$ 8,702
Marketable securities, short-term	—	3,050
Cash, cash equivalents and marketable securities	$8,056	$ 11,752

As of September 30, 2018, we had total cash, cash equivalents and marketable securities of $8.1 million, as compared to $11.8 million as of December 31, 2017. The net decrease of $3.7 million during the nine-month period primarily reflects the net proceeds of $3.4 million from the issuance of common stock, offset by $6.9 million of cash used to fund operating activities during the nine months ended September 30, 2018.

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

	Nine Months Ended September 30,	
	2018	2017
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$(6,901)	$(13,276)
Investing activities	3,046	8,177
Financing activities	3,209	5,840
Net (decrease) increase in cash and cash equivalents	$(646)	$741

Net cash used in operating activities for the nine months ended September 30, 2018 decreased $6.4 million compared with the same period in 2017. This was primarily due to lower outflows related 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 nine months ended September 30, 2018 was $3.0 million, consisting of $3.1 million of proceeds from the maturities of marketable securities, partially offset by $4,000 used for the purchase of property and equipment. Net cash provided by investing activities for the nine months ended September 30, 2017 was $8.2 million, consisting of $13.7 million of proceeds from the maturities of marketable securities, offset by $5.5 million for the purchases of marketable securities and $2,000 for the purchase of property and equipment.

Net cash provided by financing activities was $3.2 million for the nine months ended September 30, 2018 representing net proceeds from our “at the market” equity offering executed in January 2017, less approximately $0.2 million of payments on a vendor financing arrangement. Net cash provided by financing activities was $5.8 million for the nine months ended September 30, 2017 representing $6.1 million of net proceeds from our “at the market” equity offering executed in January 2017, less approximately $0.3 million of payments on a vendor financing arrangement. As of September 30, 2018, we have sold all shares available for this offering under our prospectus to our registration statement on Form S-3 (No. 333-217459).

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, shares of our common stock having an aggregate offering price of up to $10.2 million, in one or more “at the market offerings.” Pursuant to the terms of such sales agreement, as amended, we have sold an aggregate of 4,811,353 shares of our common stock for aggregate gross proceeds of approximately $10.1 million. Net proceeds received pursuant to the sales agreement were approximately $9.5 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 for this offering under the prospectus to our registration statement on Form S-3 (No. 333-217459).

Our ability to execute our Gencaro development program in accordance with our projected time line depends on a number of factors, including, but not limited to, the following:

- our ability to control costs associated with the clinical trial and our operations;
- our ability to retain the listing of our common stock on the Nasdaq Capital Market;
- the market price of our stock and the availability and cost of additional equity capital from existing and potential new investors;
- 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 current cash and cash equivalents will be sufficient to fund our operations, at our projected cost structure, through the end of the first 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 our 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. Our significant accounting policies are described in Note 1 of "Notes to Financial Statements" included within our 2017 Annual Report on Form 10-K filed with the SEC. Following is a discussion of the accounting policies that we believe involve the most difficult, subjective or complex judgments and estimates.

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate accrued 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 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 professional service fees, such as attorneys, consultants, and 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 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosures. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) of the Securities Exchange Act of 1934, an evaluation was carried out under the supervision and with the participation of management, including our principal executive officer and principal financial officer, of the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) as of the end of the quarter covered by this report. Based on the foregoing, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at a reasonable level of assurance.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that would materially affect or is reasonably likely to materially affect, our internal control over financial reporting.

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PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

None

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 our 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 September 30, 2018 will be sufficient to fund our operations, at our projected cost structure, through the end of the first quarter of 2019. 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, as of September 30, 2018 and December 31, 2017, and our independent registered public accounting firm, in their report on our financial statements as of and for the fiscal year ended December 31, 2017, 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 financial statements for the nine months ended September 30, 2018 and our audited financial statements for the fiscal year ended December 31, 2017 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. As of September 30, 2018, our management 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 for a period from one year after our quarterly financial statements have been issued. As of December 31, 2017, our management and our independent registered public accounting firm concluded that, due to our need for additional capital and the uncertainties surrounding our ability to raise such funding, substantial doubt existed as to our ability to continue as a going concern for a period from one year after our annual financial statements had been issued. We believe our cash and cash equivalents balance as of September 30, 2018 will be sufficient to fund our operations, at our projected cost structure, through the end of the first quarter of 2019. We cannot be certain that we will be able to make any sales 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 may be confirmed via the FDA SPA process, but we cannot guarantee that the FDA will agree to any SPA we submit. For instance, in late October 2018, we received a No Agreement letter from the FDA on our SPA. After further correspondence and following provision of information regarding the SPA, the FDA has agreed to reconsider our SPA request. To facilitate this process, we have requested a meeting with the FDA, which, if granted, is expected to occur in December 2018. At this time, we do not know when the FDA will provide a further decision on our SPA request. Any future development of Gencaro, including initiating the Phase 3 clinical trial, is dependent on obtaining additional financing or entering 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 requested a SPA from the FDA relating to our planned Phase 3 program for Gencaro, and we cannot guarantee that the FDA will issue an agreement on the SPA. Even if we do obtain the FDA's agreement, a SPA would 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. In late October 2018, we received a No Agreement letter from the FDA on our SPA. After further correspondence and following provision of information regarding the SPA, the FDA has agreed to reconsider our SPA request. To facilitate this process, we have requested a meeting with the FDA, which, if granted, is expected to occur in December 2018. At this time, we do not know when the FDA will provide a further decision on our SPA request. 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, even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its 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, the sponsor fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a 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.

There is no assurance that the FDA will ultimately agree with the design and size of any Phase 3 clinical program for which we request a SPA. Even if we do obtain agreement on a SPA, we cannot assure you that our planned Phase 3 clinical trial will succeed, will be deemed binding by the FDA under a SPA, if granted, or will result in any FDA approval for Gencaro. Moreover, if the FDA revokes or alters its agreement under an 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 April 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 November 12, 2018, the closing price of our common stock was approximately $0.71 per share, and the total market value of our listed securities was approximately $9.9 million. As of September 30, 2018, we had stockholders' equity of $7.5 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, 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. It is difficult to predict how FDA will implement the guidance. For example, 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 will be applied by the agency. 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 or convertible debt offering.

Nasdaq rules impose restrictions on our ability to raise funds through a private offering of our common stock, convertible debt or similar instruments without obtaining stockholder approval. Under Nasdaq rules, an offering of more than 20% of our total shares outstanding for less than the greater of book or market value requires stockholder approval unless the offering qualifies as a "public offering" for purposes of the Nasdaq rules. As of September 30, 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." Pursuant to the terms of such sales agreement, as amended, we have sold an aggregate of 4,811,353 shares of our common stock for aggregate gross proceeds of approximately $10.1 million. Net proceeds received in the period were approximately $9.5 million, after deducting initial expenses for executing the "at the market offering" and commissions paid to the placement agent. 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 the fourth quarter, we received a No Agreement letter from the FDA on our SPA. After further correspondence and following provision of information regarding the SPA, the FDA has agreed to reconsider our SPA request. To facilitate this process, we have requested a meeting with the FDA, which, if granted, is expected to occur in December 2018. At this time, we do not know when the FDA will provide a further decision on our SPA request. Even if the FDA ultimately agrees to our SPA, this product candidate will require years of additional clinical development. Even if we conduct additional studies in accordance with further FDA guidance and submit or file a new or amended NDA, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

In the event that we or our collaborators conduct preclinical studies that do not comply with Good Laboratory Practices, or GLP, or incorrectly design or carry out human clinical trials in accordance with Good Clinical Practices, or GCP, or those clinical trials fail to demonstrate clinical significance, it is unlikely that we will be able to obtain FDA approval for product development candidates. Our inability to successfully 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 2017, our research and development activities were dedicated to Gencaro. To date, our research and development activities in 2018 have been, and we expect they will continue to be for the remainder of 2018, focused on regulatory activities related to Gencaro and initiating 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. In addition, it is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act. 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 HIPAA, as amended. 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.

EU General Data Protection Regulation which was officially adopted in April 2016 and was applicable in May 2018, and member state implementing legislation, may also apply to health-related and other personal information obtained outside of the United States. The EU General Data Protection Regulation, which introduced new data protection requirements in the EU, as well as substantial fines for breaches of the data protection rules. The EU General Data Protection Regulation will increase our responsibility and 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 new EU data protection rules.

Uncertainty about compliance with EU data protection laws remains and data protection authorities from the different EU Member States may interpret the EU Data Protection Regulation and national laws differently, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data in the EU.

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;