

BioCardia, Inc.  
Form 10-K  
March 30, 2017

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**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

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**Form 10-K**

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**(Mark One)**

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT  
OF 1934**

**For the fiscal year ended December 31, 2016**

**OR**

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT  
OF 1934**

**For the transition period from \_\_\_\_\_ to \_\_\_\_\_**

**Commission File Number 0-21419**

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**BIOCARDIA, INC.**

(Exact Name of Registrant as Specified in its Charter)

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**Delaware** **23-2753988**  
(State or Other Jurisdiction of Incorporation or Organization) (I.R.S. Employer Identification Number)

**125 Shoreway Road, Suite B**

**San Carlos, California 94070**

(Address of Principal Executive Offices, Including Zip Code)

**(650) 226-0120**

(Registrant's Telephone Number, Including Area Code)

**Securities Registered Pursuant to Section 12(g) of the Act: Common Stock**

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during

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the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

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

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

Large accelerated filer

Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, computed by reference to the average bid and asked price of such common equity, on June 30, 2016 was approximately \$11,511,284. Shares of the registrant's common stock held by each executive officer, director and holder of 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

The number of shares of the registrant's Common Stock outstanding as of March 24, 2017 was 457,655,631.

## DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement relating to the 2017 Annual Meeting of Stockholders to be held on June 15, 2017, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's fiscal year ended December 31, 2016.

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## **SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Any and all statements contained in this Annual Report that are not statements of historical fact may be deemed forward-looking statements. Terms such as “may,” “might,” “would,” “should,” “could,” “project,” “estimate,” “pro-forma,” “potential,” “strategy,” “anticipate,” “attempt,” “develop,” “plan,” “help,” “believe,” “continue,” “intend,” “expect,” “future” and similar import (including the negative of any of the foregoing) may be intended to identify forward-looking statements. However, not all forward-looking statements may contain one or more of these identifying terms. Forward-looking statements in this Annual Report may include, without limitation, statements regarding (i) the plans and objectives of management for future operations, including plans or objectives relating to the development of our cell therapy systems, (ii) a projection of income (including income/loss), earnings (including earnings/loss) per share, capital expenditures, dividends, capital structure or other financial items, (iii) our future financial performance, including any such statement contained in a discussion and analysis of financial condition by management or in the results of operations included pursuant to the rules and regulations of the SEC and (iv) the assumptions underlying or relating to any statement described in points (i), (ii) or (iii) above.

The forward-looking statements are not meant to predict or guarantee actual results, performance, events or circumstances and may not be realized because they are based upon our current projections, plans, objectives, beliefs, expectations, estimates and assumptions and are subject to a number of risks and uncertainties and other influences, many of which we have no control over. Actual results and the timing of certain events and circumstances may differ materially from those described by the forward-looking statements as a result of these risks and uncertainties. Factors that may influence or contribute to the inaccuracy of the forward-looking statements or cause actual results to differ materially from expected or desired results may include, without limitation:

our ability to obtain regulatory approval for our cell therapy systems;

market acceptance of our cell therapy systems;

the benefits of our cell therapy systems versus other products;

our ability to successfully sell and market our cell therapy systems;

competition from existing technologies or products or new technologies and products that may emerge;

the implementation of our business model and strategic plans for our business and our cell therapy systems;

the scope of protection we are able to establish and maintain for intellectual property rights covering our cell therapy systems;

estimates of our future revenue, expenses, capital requirements and our need for additional financing;

our financial performance;

developments relating to our competitors and the healthcare industry; and

other risks and uncertainties, including those listed under the section titled “Risk Factors.”

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report to conform these statements to actual results or to changes in our expectations.

You should read this Annual Report on Form 10-K and the documents that we reference in this Annual Report on Form 10-K and have filed with the SEC as exhibits to this Annual Report on Form 10-K with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect. We qualify all forward-looking statements by these cautionary statements.

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## **PART I**

### **ITEM 1. BUSINESS**

#### **Our History**

We were incorporated as NAM Corporation in Delaware on January 12, 1994 and subsequently changed our name to clickNsettle.com, Inc., then Cardo Medical, Inc., then Tiger X Medical, Inc., and finally BioCardia, Inc. on October 26, 2016 in connection with the merger of our wholly-owned subsidiary, Icicle Acquisition Corp., with and into BioCardia Lifesciences, Inc. (which was named BioCardia, Inc. prior to the merger). We previously operated as an orthopedic medical device company specializing in designing, developing and marketing high performance reconstructive joint devices and spinal surgical devices. Prior to the merger with BioCardia Lifesciences, Inc., our board of directors determined to discontinue operations in this area and seek a new business opportunity. As a result of the merger, we acquired the business of BioCardia Lifesciences, Inc. as described below.

On October 24, 2016, pursuant to an Agreement and Plan of Merger dated August 22, 2016, or the Merger Agreement, by and among the Company, Icicle Acquisition Corp., a Delaware corporation, and BioCardia Lifesciences, Inc., a merger was consummated pursuant to which BioCardia Lifesciences, Inc. became our wholly owned subsidiary such merger referred to herein as the Merger. As of immediately following the Merger, we had aggregate cash of \$24.0 million with which to pursue the operations and business opportunity of BioCardia Lifesciences, Inc.

Pursuant to the Merger Agreement, each share of BioCardia Lifesciences, Inc. capital stock issued and outstanding immediately preceding the Merger, including shares of BioCardia Lifesciences, Inc. common stock underlying outstanding preferred stock and convertible notes, were converted into the right to receive 19.3678009 shares, or the Exchange Ratio, of the Company's common stock, par value \$0.001 per share. Additionally, pursuant to the Merger Agreement, upon consummation of the Merger, the Company assumed all of BioCardia Lifesciences, Inc. options outstanding immediately prior to the Merger at the same Exchange Ratio.

All references to share amounts in this Annual Report on Form 10-K have been retroactively adjusted to reflect the impact of the Exchange Ratio.

In connection with the Merger, BioCardia Lifesciences, Inc. was determined to be the accounting acquirer, and consequently, the assets and liabilities and the historical operations reflected in the financial statements prior to the

Merger are those of BioCardia Lifesciences, Inc. and are recorded at their historical cost basis. The financial statements after completion of the Merger include the assets and liabilities of the Company and its subsidiary from the effective time of the Merger. Please refer to Note 3 in the consolidated financial statements for the accounting treatment for the Merger.

Our principal executive offices are located at 125 Shoreway Road, Suite B, San Carlos, CA 94070. Our telephone number is (650) 226-0120. Our website address is [www.biocardia.com](http://www.biocardia.com). Information contained in our website is not incorporated by reference into this Annual Report, and should not be considered to be a part of this Annual Report.

## Company Overview

We are a clinical-stage regenerative medicine company developing novel therapeutics for cardiovascular diseases with large unmet medical needs. Our lead therapeutic candidate is the CardiAMP Cell Therapy System, or CardiAMP. CardiAMP provides an autologous cell therapy for the treatment of heart failure that develops after a heart attack. We are actively enrolling and treating patients at three clinical sites in our U.S. Food and Drug Administration, or FDA, approved Phase III pivotal Investigational Device Exemption, or IDE, trial for CardiAMP in ischemic systolic heart failure. The Department of Health & Human Services Centers for Medicare & Medicaid Services, or CMS, has also approved the CardiAMP IDE for purposes of Medicare coverage. We anticipate enrolling up to 260 patients at up to 40 clinical sites by the end of 2018 and obtaining top-line data with one year patient follow-up in 2019. If our Phase III pivotal trial is successful, we believe we will be the first company to reach the market with a cell-based therapy to treat heart failure. In parallel, in 2017 we expect to submit a second IDE to FDA for the CardiAMP cell therapy in a second related cardiac indication of post myocardial infarction.

Our second therapeutic candidate is the CardiALLO Cell Therapy System, or CardiALLO, an allogenic culture expanded cell therapy derived from bone marrow cells. We anticipate preparation of an Investigational New Drug, or IND, application for submission to the FDA for a Phase II trial for CardiALLO for the treatment of heart failure that develops after a heart attack. This IND is expected to have improved Chemistry Manufacturing Controls in the IND relative to our previous co-sponsored investigations.

We are committed to applying our expertise in the fields of autologous and allogeneic cell-based therapies to improve the lives of patients with cardiovascular conditions. Autologous cell therapies use autologous cells, which means the patient's own cells, while allogeneic cell therapies use allogeneic cells, which means cells from a third party donor.

## Market Overview

Heart failure is a clinical condition in which the output of blood from the heart is insufficient to meet the metabolic demands of the body. In 2015, the American Heart Association, or AHA, report on heart disease statistics estimated that there are 5.7 million Americans over the age of 20 that have heart failure. Heart failure is increasingly prevalent due to the aging population and the increase in major cardiovascular risk factors, including obesity and diabetes. The AHA also estimates that one in five adults will develop heart failure after the age of 40. During heart failure progression, the heart steadily loses its ability to respond to increased metabolic demand, and mild exercise soon exceeds the heart's ability to maintain adequate output. Towards the end stage of the disease, the heart cannot pump enough blood to meet the body's needs at rest. At this stage, fluids accumulate in the extremities or in the lungs making the patient bedridden and unable to perform the activities of daily living. The long-term prognosis associated with heart failure is approximately 50% mortality at five years following the initial diagnosis.

Hospitalizations for heart failure are expensive, and the risk of death increases with each recurrent heart failure-related hospitalization. In 2014, the Journal of the American College of Cardiology reported that the one- and six-month readmission rates after heart failure-related hospitalization are close to 25% and 50%, respectively. In 2010, the AHA estimated that the direct and indirect cost of heart failure in the United States was \$39 billion, half of which was related to repeated hospitalizations, and by 2030 the total cost of heart failure in the United States is projected to increase to \$70 billion. There is growing pressure on hospitals to reduce readmissions for heart failure.

Heart failure is classified in relation to the severity of the symptoms experienced by the patient. The most commonly used classification system, established by the New York Heart Association, or NYHA, is as follows:

***Class I (mild):*** patients experience no or very mild symptoms with ordinary physical activity;

***Class II (mild):*** patients experience fatigue and shortness of breath during moderate physical activity;

***Class III (moderate):*** patients experience shortness of breath during even light physical activity; and

***Class IV (severe):*** patients are exhausted even at rest.

Despite guideline-directed therapies employing a wide range of pharmacologic, device, and surgical options, many patients deteriorate over time and develop advanced heart failure symptoms that cannot be effectively managed by existing medical therapies. At the end stage of heart failure, current treatment options include heart transplant surgery or implantation of a left ventricular assist device, or LVAD, a battery operated mechanical circulatory device used to partially or completely replace the function of the left ventricle of the heart. LVADs are used for patients awaiting a heart transplant or as a destination therapy for patients with NYHA Class IV heart failure who may never receive a heart transplant. Both of these end-stage treatment options require invasive open-chest surgery and can cost in excess of \$150,000 per procedure, as reported by the Journal of Heart and Lung Transplantation.

There are approximately 2.9 million NYHA Class II and Class III heart failure patients, of which we estimate approximately 60% are patients with ischemic systolic heart failure. Of this subset of 1.7 million patients, we estimate that approximately 70%, or over 1.2 million patients, will have a cell potency score sufficient to qualify for treatment with CardiAMP.

Bone marrow derived cell-based therapy has been shown to have the potential to restore cardiac function. In the past decade, intramyocardial delivery of bone marrow derived cell-based therapies in preclinical and clinical studies of heart failure has predominantly resulted in benefits, such as improvement in ventricular function, reduction in infarct size and increase in myocardial perfusion. An infarct is an area of dead tissue resulting from failure of blood supply, and myocardial perfusion is blood flow to heart tissue.

Recent systematic review and meta-analysis of the scientific literature from 23 randomized controlled trials prior to 2013, covering more than 1,200 participants, was published by Fisher in *Circulation Research* in January 2015. The review found evidence that bone marrow cell treatment, including intramyocardial delivery of bone marrow cells, has improved left ventricle ejection fraction, or LVEF, and chronic ischemic heart disease. The authors of the review found evidence for a potential beneficial clinical effect in terms of mortality and performance status after at least one year post-treatment in people who suffer from chronic ischemic heart disease and heart failure. Results in heart failure trials indicate that bone marrow derived cell-based therapy leads to a reduction in deaths and readmission to hospital and improvements over standard treatment as measured by tests of heart function. This review concluded that further research is required to confirm the results.

Published scientific papers provide clinical support for efficacy from randomized controlled clinical trials of intramyocardial delivery of bone marrow derived cells in closely related clinical conditions of chronic myocardial ischemia, diastolic heart failure, and subacute myocardial infarction.

Bone marrow cell homing to the heart is part of the body's natural repair process. After a heart attack or an acute injury to the heart, cells from bone marrow are known to home to the heart. For example, a population of bone marrow cells with a cell surface marker of CD34+ has certain receptors, including CXC-4 and CXC-7 receptors, that home to the SDF-1 ligand, which is activated in injured heart tissue. In the event of heart failure, the heart is believed to have fewer of these homing signals and a decreased ability to stimulate or recreate this signaling process, leading to a lower likelihood of heart tissue repair. A number of other bone marrow derived cells with unique cell surface markers have also been shown to have beneficial effects in animal models of heart failure and are under clinical investigation today.

To date, the research community has proposed three main mechanisms of action to explain the regenerative potential of bone marrow derived cells:

endothelial cell and myocyte growth through cell transdifferentiation, which means that a bone marrow cell becomes another cell type in the heart;

stimulation of endogenous cardiac stem cells for niche reconstruction, which means that a bone marrow cell stimulates the production of stem cells in the heart, which subsequently become a specific cell type in the heart; and

paracrine effects through the release of cytokines and growth factors leading to anti-apoptotic effects and angiogenesis, which means that proteins produced by the bone marrow cells stimulate beneficial reparative effects in the heart such as reduced inflammation, cell survival and the formation of new vascular networks.

There is increasing belief in the research community that the efficacy of bone marrow derived cells may reside in synergistic effects of two or more mechanisms of action promoting cardiac regeneration.

## Product Overview

BioCardia is developing two comprehensive biotherapeutic candidates for cardiac regenerative medicine, with an initial focus on heart failure resulting from a heart attack:

***CardiAMP***—autologous minimally processed bone marrow cells from a patient's own cells, with an FDA accepted Phase III pivotal trial. As of December 31, 2016, 62 patients have been treated in our Phase I and Phase II trials in ischemic heart failure and post-acute infarction; and

***CardiALLO***—allogeneic culture expanded mesenchymal bone marrow cells from a universal donor for use in multiple unrelated patients, entering Phase II development. To date, 94 patients have been treated in CardiALLO related mesenchymal stem cell Phase I and Phase II trials.

The development stage for these programs is provided below.

## Cell-Based Therapy Product Pipeline

### ***CardiAMP Cell Therapy System***

CardiAMP is our lead therapeutic program. CardiAMP for the treatment of heart failure, is a comprehensive investigational therapeutic treatment that is expected to be comprised of (i) a cell potency screening test, (ii) a point of care cell processing platform, and (iii) a biotherapeutic delivery system. CardiAMP has the potential to be the first comprehensive therapeutic treatment utilizing a patient's own cells for the treatment of ischemic systolic heart failure, which is heart failure that develops after a heart attack. In the screening process with the anticipated companion diagnostic, the physician extracts a small sample of the patient's bone marrow in an outpatient procedure performed under local anesthesia. The clinic sends the sample to a centralized diagnostic lab, which tests for identified biomarkers from which we generate a potency assay score for the patient. During the treatment, a clinician harvests and then prepares the patient's own bone marrow mononuclear cells, or autologous cells, using our point of care cell processing platform, which a cardiologist then delivers into the heart using our proprietary biotherapeutic delivery system. We designed the entire procedure to be performed in approximately 60 to 90 minutes, which we believe is substantially faster than alternative cell-based therapies in development. The patient then leaves the hospital the same or next day.

CardiAMP is believed to be the first therapeutic candidate to enter a clinical program with a bone marrow derived cell-based therapy for ischemic systolic heart failure patients who are not actively ischemic. It is also potentially the first therapeutic candidate to use a companion diagnostic, the CardiAMP potency assay, to identify patients who are likely responders to treatment with autologous cells. We also believe it is the first therapeutic candidate to initiate a Phase III pivotal trial in the United States for heart failure using point of care cell processing to isolate the bone marrow mononuclear cells, the first pivotal cardiac cell therapy to be regulated under an IDE, and the first cell therapy IDE to have national reimbursement approval from CMS.

### ***CardiAMP Preclinical Experience***

Extensive preclinical data with bone marrow mononuclear cells and media in which they have been incubated in animal models of heart disease have shown compelling results. Rats treated with media from cells showed reduced fibrotic scar at 28 days, increased microvascular density in central infarct and border zones, and demonstrated enhanced cardiac function. Swine studies have shown that there is a dose response relationship, with higher doses of bone marrow mononuclear cells resulting in reduced fibrosis and increased microvascular change in infarcted myocardium 60 days after treatment. The highest dose tested in this series of 200 million cells, with >20 million cells per segment, resulted in the highest capillary density and the least fibrosis. This is the dosage delivered in the CardiAMP Phase II trial, and to be delivered in the Phase III pivotal trial.



***CardiAMP Phase I Study: Transendocardial Autologous Marrow Cells in Myocardial Infarction***

The CardiAMP Phase I Transendocardial Autologous Marrow Cells in Myocardial Infarction or TABMMI trial enrolled 20 patients with ischemic systolic heart failure in an open label safety trial of bone marrow cells delivered with the Helix biotherapeutic delivery system at a dosage of 100 million cells. Results showed improvement in cardiac function as measured by left ventricular ejection fraction, improved exercise tolerance, and superior survival as compared to historical controls. The Phase I TABMMI study was submitted to the Argentine Administración Nacional de Medicamentos, Alimentos y Tecnología Médica.

In our TABMMI Phase I trial of CardiAMP cells, we enrolled 20 patients with previous evidence of having had a heart attack and who presented with a low ejection fraction of less than or equal to 40% and greater than or equal to 20%. Baseline evaluations included informed consent, history and physical examination, electrocardiogram, 24-hour Holter monitoring, echocardiography, routine blood tests and exercise tolerance testing. Reduced regional heart wall motion was coincident with the diseased coronary vessel in each patient. A total of 20 patients with heart failure (NYHA Class I, II and III) each received three to ten transendocardial infusions of cells using our Helix biotherapeutic delivery system in an open-label dose-escalation two cohort trial. Dosage administration ranged from 30 million to 130 million autologous bone marrow derived mononuclear cells, with an average of 96 million cells.

Bone marrow cells delivered in TABMMI demonstrated an excellent safety profile in this heart failure population, with no treatment related toxicities observed. The 20 patients who received CardiAMP cells, demonstrated improvements from baseline to both six-month and 12-month follow-up across a number of parameters important in heart failure, including statistically and clinically significant improvements in left ventricular, or LV, function (ejection fraction).

The results of the study demonstrated statistically significant functional improvements in echocardiographic measured heart function at both six- and 12-months follow-up compared to baseline. A total of 12 adverse events were observed in six patients, although none were related to the investigational delivery or cell transplantation procedure. The complete results of the 20 patients at two-year follow-up have been published by in the journal Eurointervention in 2011.

***CardiAMP Phase II Trial: Transendocardial Autologous Cells in Heart Failure Trial (TAC-HFT)***

In our co-sponsored Phase II Transendocardial Autologous Cells in Heart Failure Trial, patients with ischemic systolic heart failure were randomized on a one to one basis into two double-blind, placebo-controlled trials: TACHFT-BMC and TACHFT-MS. The IND for the TACHFT trial was filed with the FDA Center for Biologics Evaluation and Research in 2008 by the University of Miami, the co-sponsor of the trial.

In the safety dose escalation roll-in cohort stage of the study, eight patients received treatment with either CardiAMP cells, or autologous bone marrow mesenchymal cells, or MSC, at dosages of 100 million or 200 million cells. In the randomized, placebo-controlled efficacy stage of the study, 29 patients received treatment with either CardiAMP cells or placebo and 30 patients received treatment with either MSCs or placebo. The mode of administration was 10 intramyocardial infusions per patient using our Helix biotherapeutic delivery system into the myocardium adjacent to and into the infarcted tissue. All subjects had ischemic systolic heart failure (NYHA Class I, II or III).

TACHFT-BMC found CardiAMP cells to be safe at both dosages (100 million and 200 million cells) and that treated patients had increased their functional capacity, improved quality of life, symptoms and key markers of cardiac function predictive of survival, such as end systolic volume, or ESV. The TACHFT-BMC trial included a single dose of CardiAMP cells with a follow up observation period of 12 months. The Phase II, randomized, placebo-controlled study met its primary safety endpoint and demonstrated statistically significant and clinically meaningful improvements in secondary efficacy endpoints of functional capacity, as measured by the six minute walk distance (6MW), and in quality of life, as measured by the Minnesota Living with Heart Failure Questionnaire score.

A summary of the findings is below:

- high-dose CardiAMP cells (200 million cells) met the primary TACHFT-BMC safety endpoint with 0% treatment emergent major adverse cardiac events at 30 days, and demonstrated an excellent safety profile at 12 months with fewer clinical events in the treated group;

patients treated with CardiAMP cells, when compared to placebo, showed statistically and clinically significant improvements in functional capacity as measured by the six minute walk test and in quality of life as measured by the MLHF Questionnaire;

- benefit in preventing clinical events such as hospitalizations was confirmed at one year following treatment, although not at the level of statistical significance; and

- benefit in clinical outcomes was supported by improvement in patients' cardiac function, although not at the level of statistical significance.

Results at one year follow-up of the placebo controlled TAC-HFT BMC trial were published by Wong Po Foo et al in 2015 following a pooled analysis by Heldman et al in JAMA in 2013.

Heldman AW, et al Transendocardial Mesenchymal Stem Cells and Mononuclear Bone Marrow Cells for Ischemic Cardiomyopathy The TAC-HFT Randomized Trial JAMA.2013.282909.

Wong Po Foo et al., The transendocardial autologous cells in ischemic heart failure trial bone marrow mononuclear cells (TAC-HFT-BMC) randomized placebo controlled blinded study, Regenerative Medicine 2015, 10(7s), S169.

### ***CardiAMP Phase III Pivotal IDE Trial***

We designed the current Phase III pivotal trial to confirm the results of our Phase II TACHFT-BMC trial which showed that a high dose (200 million) of bone marrow cells improved functional capacity and quality of life. The Phase III pivotal trial is anticipated to serve as the basis for potential regulatory approval in the United States. The Phase III trial design excludes NYHA Class I patients and will include our CardiAMP potency assay and CardiAMP point of care cell processing platform, all of which we believe are improvements over our Phase II trial that should enhance the probability of regulatory approval. The primary endpoint will be superiority with respect to functional capacity as measured by the six minute walk test at one-year post-procedure. The inclusion criteria will include:

ages 21-90;

NYHA Class II or Class III heart failure classification;

chronic ischemic left ventricular dysfunction;

ejection fraction greater than or equal to 20% but less than or equal to 40%; and

a cell potency score greater than or equal to three as measured by the CardiAMP potency assay.

The Phase III pivotal trial is approved by FDA to enroll up to 260 patients, including an optional 10 patient roll-in cohort, at up to 40 U.S. clinical sites, with a 3:2 randomization of 250 patients to either treatment or sham control. In the sham control procedure, the clinician performs the entire therapy other than delivery of the CardiAMP cells. Centers are actively enrolling patients and we anticipate obtaining top line data in 2019.

*CardiAMP Phase III randomized pivotal trial design accepted by FDA*

We believe the remaining clinical efficacy risk is modest in light of the Phase I and II data in hand, and broader literature which supports CardiAMP as a therapeutic candidate. CardiAMP has the potential to significantly benefit patients who have limited options, and provide a cost-effective therapy to help reduce the substantial heart failure hospitalization and care costs.

Previous IDE clinical trials that led to FDA approval of Cardiac Resynchronization Therapy (CRT) devices for the treatment of heart failure followed the same IDE regulatory pathway that CardiAMP will follow and had similar endpoints to the proposed CardiAMP Heart Failure IDE trial. CRT is intended for patients that are NYHA III and IV versus the CardiAMP trial of NYHA II and III. Results from 5 out of 6 randomized pivotal CRT trials showed both smaller improvements in functional capacity as measured by the six minute walk test and smaller improvement in quality of life than the CardiAMP Phase II results. Although the benefits with CRT were less than observed in CardiAMP placebo controlled Phase II trial, these results for the permanently implantable CRT devices were sufficient to obtain FDA approval.

Our FDA accepted Phase III pivotal trial is designed to provide the primary support for the safety and efficacy of CardiAMP. The primary endpoint is functional capacity, as measured by the six minute walk test. Based on the results achieved in the Phase II trial, our Phase III pivotal trial is designed to have more than 90% probability of achieving a positive result with statistical significance. Statistical significance denotes the mathematical likelihood that the results observed are real and not due to chance.

We are also exploring the continued development of CardiAMP for post-acute myocardial infarction and intend to submit an IDE for this indication to the FDA in 2017. In the future, BioCardia may explore the development of CardiAMP for additional indications such as chronic myocardial ischemia and heart failure with preserved ejection fraction, or cardiac function as measured by the outbound blood pumped out of the heart with each heartbeat.

### ***CardiALLO Cell Therapy System***

Our second therapeutic candidate is the CardiALLO Cell Therapy System, or CardiALLO. CardiALLO is an allogeneic “off the shelf” mesenchymal stem cell product candidate that may be an alternative for patients who are not optimal candidates for CardiAMP. We anticipate preparation of an Investigational New Drug, or IND, application for submission to the FDA for a Phase II trial for CardiALLO for the treatment of ischemic systolic heart failure.

CardiALLO uses culture expanded allogeneic bone marrow derived MSCs for the treatment of ischemic systolic heart failure. We believe this therapy presents the advantages of an “off the shelf” therapy that does not require tissue harvesting or cell processing.

### ***CardiALLO Preclinical Experience***

Preclinical work with expanded MSCs in swine has been performed with our collaborators at three universities. Early studies showed cells could be efficiently delivered and tracked in the heart using iron oxide incubation techniques with magnetic resonance imaging. Immunohistochemistry stains also detailed that cells could be identified in the hearts after delivery. Randomized swine studies demonstrated that bone marrow derived mesenchymal stem cells, could be safely injected by using our Helix biotherapeutic delivery system three days after myocardial infarction. Cellular transplantation resulted in long-term engraftment, reduction in scar formation and near-normalization of cardiac function. As an additional finding, transplanted cells derived from an allogeneic donor were not rejected by the recipient, a major practical advance for the potential widespread application of this therapy. Studies have also been performed evaluating a variety of delivery strategies. Together, these findings supported that the direct injection of cellular grafts into damaged myocardium is safe and effective in the peri-infarct period.

### ***CardiALLO related Phase I /II Studies: POSEIDON, TAC-HFT-MSC, and TRIDENT***

We have co-sponsored three clinical trials for MSCs for the treatment of ischemic systolic heart failure. In substantially similar trial designs, the POSEIDON Phase I/II trial compared autologous MSCs to allogeneic MSCs, the TACHFT-MSC Phase II trial compared autologous MSCs to placebo, and the TRIDENT Phase II compared allogeneic MSCs at different doses. The first two trials shared common arms of autologous MSCs, enabling a bridge to placebo, leading us to conclude that allogeneic MSC therapy is superior to placebo. The IND for the TACHFT trial was filed with the FDA Center for Biologics Evaluation and Research in 2008 by the University of Miami, our co-sponsor for the trial. The POSEIDON trial was submitted by amendment under the same IND filed for the TACHFT study, and was co-sponsored by the University of Miami, the National Institutes of Health and us. The results from both of these studies can be submitted to the FDA in support of an IND for CardiALLO. The TRIDENT trial was also submitted by amendment to the same IND and continues to follow patients.

POSEIDON Phase I/II, TACHFT-MSD Phase II, and TRIDENT Phase I/II trials, inform and support our clinical efforts for CardiALLO. We are developing an optimized formulation and dosage strategy of CardiALLO cells for a planned clinical trial which we intend to initiate after we complete enrollment in the CardiAMP Phase III pivotal trial.

Additional data on these programs is available as two of these clinical studies have been published by Hare et al in JAMA in 2012 and Heldman et al in JAMA in 2013.

Heldman AW, et al Transcatheter Mesenchymal Stem Cells and Mononuclear Bone Marrow Cells for Ischemic Cardiomyopathy The TAC-HFT Randomized Trial JAMA.2013.282909.

Hare JM, et al. Comparison of Allogeneic vs Autologous Bone Marrow-Derived Mesenchymal Stem Cells Delivered by Transcatheter Injection in Patients With Ischemic Cardiomyopathy, The POSEIDON Randomized Trial, JAMA. 2012;308(22).

### ***CardiALLO Development***

CardiALLO is being advanced with an anticipated improved cell production strategy to be detailed in the Chemistry Manufacturing and Controls (CMC) of the IND in development. We believe the new CMC will reduce the likelihood of immune response to transplanted allogeneic cells further, may enhance efficacy, and will enable commercial scale up and global distribution. CardiALLO will require more extensive clinical development than CardiAMP, beginning with a Phase II trial that follows previous work, to confirm the results with the modified cell culture and dosage strategy.



We anticipate performing our own CMC development work in BioCardia laboratories to accelerate the effort and secure additional intellectual property, and in parallel develop an agreement with an established academic institution to culture and supply the MSC cells for CardiALLO clinical development. We expect to confirm the safety and efficacy of MSCs in our target patient population in a Phase II randomized controlled study. We expect the CardiALLO Phase II trial to enroll patients with control, low dose and high dose groups using the Helix biotherapeutic delivery system and the same inclusion criteria as the CardiAMP Phase III pivotal trial. We intend to begin enrolling the CardiALLO trial after the CardiAMP trial completes enrollment. In the United States, CardiALLO is expected to be regulated by the FDA as a biologic combination product with our Helix biotherapeutic delivery system.

Both CardiAMP and CardiALLO therapeutic programs have safety and efficacy support from completed clinical studies. The two therapeutic candidates provide compelling and synergistic approaches to replicating the natural response of bone marrow cells to cardiac injury. CardiAMP harnesses the potential of autologous minimally processed bone marrow cells, using a companion diagnostic to identify patients most likely to benefit from the therapy. CardiALLO utilizes younger universal donor mesenchymal stem cells and may be appropriate for patients who are not optimal candidates for the CardiAMP therapy.

#### ***Cell Processing and Cell Delivery Product Platforms***

BioCardia has developed and secured exclusive rights to enabling cell processing and cell delivery products, which are used as part of our CardiAMP and CardiALLO therapies, and which we believe validate our approach and development expertise: (i) the CardiAMP cell processing platform, (ii) the Helix transendocardial biotherapeutic delivery system, and (iii) our Morph vascular access products.

***CardiAMP cell processing platform***—processes bone marrow aspirate at the point of care to concentrate mononuclear cells and prepare the dosage form. We expect the CardiAMP cell processing platform to be approved in the United States for ischemic systolic heart failure as part of CardiAMP. The platform is currently cleared for use in the United States and in European Union for the preparation of a cell concentrate from bone marrow and is under investigational use for the treatment of heart failure.

***Helix biotherapeutic delivery system***—delivers therapeutics into the heart muscle with a penetrating helical needle from within the heart. This is a leading delivery platform in the field, which has increased safety and performance. We expect Helix to be approved in the United States as part of CardiAMP. The system is CE marked for commercial use in Europe and is under investigational use in the United States as part of our CardiAMP and CardiALLO development programs. We believe the Helix biotherapeutic system is the world's safest and most efficient platform for cardiac therapeutic delivery and has been used in more than 280 clinical procedures. The Helix biotherapeutic delivery system is designed to be used in any catheterization laboratory in the world without the need for additional capital equipment.

We supply our Helix biotherapeutic delivery system to selected partners developing other cell gene and protein therapeutic programs. These programs provide additional data, intellectual property rights, and opportunities to participate in the development of combination products for the treatment of cardiac diseases.



***Morph vascular access products***— provides enhanced control for Helix in biotherapeutic delivery and for other common interventions. We have secured all necessary approvals in the United States and Europe. Currently there are six Morph product model numbers approved for commercial sale in the United States via a 510(k) clearance and three in Europe under CE mark. The Morph products are valued by physicians performing difficult vascular procedures worldwide and they have been used in more than 10,000 clinical procedures to date.

## **Business Strategy**

We are committed to applying our expertise in the fields of autologous and allogeneic cell-based therapies to improve the lives of patients with cardiovascular conditions. We are pursuing the following business strategies:

***Complete Phase III pivotal trial of CardiAMP for patients with ischemic systolic heart failure.*** We have initiated our 260 patient CardiAMP Phase III pivotal trial with optional 10 patient roll-in cohort. Based on the results of the Phase II trial, the Phase III pivotal trial will focus on patients with NYHA Class II or III ischemic systolic heart failure, and the primary endpoint will be functional capacity as measured by the six minute walk test. The trial will use the CardiAMP potency assay to target patients most likely to benefit from our treatment. This trial has begun treating patients and is expected to have top-line trial results in 2019.

***Obtain FDA approval and commercialize CardiAMP using a highly-targeted cardiology sales force in the United States.*** Heart failure patients are primarily treated at leading hospitals and medical centers of excellence by a select group of cardiologists and heart failure specialists. Once we obtain FDA approval, we plan to use a targeted sales force focused on these particular physicians. We believe cardiologists, heart failure specialists and interventional cardiologists are typically early adopters of innovative biotherapeutic products, devices and technologies. We believe that CardiAMP will be adopted first by leading cardiologists and heart failure specialists at high-volume U.S. hospitals and medical centers, and progressively by a broader segment of the market. We anticipate using strategic or distribution partners to serve other geographies.

***Advance our CardiALLO program for the treatment of ischemic systolic heart failure.*** CardiALLO has the potential to benefit patients for whom CardiAMP is not optimal due to the lower potency of their bone marrow cells. CardiALLO allogeneic culture-expanded bone marrow derived cells, or CardiALLO cells, have performed well in a head to head trial with autologous mesenchymal bone marrow cells. This therapy may present advantages for patients or physicians who wish to avoid bone marrow aspiration, and our development work builds on our clinical development capabilities established through our CardiAMP program. This program positions us to provide therapy to patients ineligible for CardiAMP.

***Expand CardiAMP and CardiALLO into additional cardiac indications.*** CardiAMP and CardiALLO have potential therapeutic benefits for multiple cardiovascular indications in addition to ischemic systolic heart failure. We and our clinical collaborators have been gathering data on the application of CardiAMP cells to post-acute myocardial infarction, and in the future we may investigate the use of CardiAMP and CardiALLO cells for additional indications such as chronic myocardial ischemia and heart failure with preserved ejection fraction. Compelling clinical results

have been published for the application of cell-based formulations similar to CardiAMP cells in each of these diseases.

***Continue to partner our Helix biotherapeutic delivery system for use with other biotherapeutics.*** We plan to continue to make our Helix biotherapeutic delivery system available for use by qualified partners seeking to advance their own biotherapeutic candidates for similar indications.

## **Manufacturing**

The CardiAMP cell processing platform is manufactured for us by our partner Biomet Biologics. We currently manufacture our Helix biotherapeutic delivery system and Morph vascular access products in our San Carlos, California facility using components we source from third party suppliers. The last FDA inspection of our facility in 2016 issued one observation under form 483s which has been addressed to the FDA's satisfaction. Our last inspection by our European notified body in February 2017 reported one major and four minor observations, which we are currently addressing.

## **Sales and Marketing**

Our sales and marketing strategy is to market CardiAMP and CardiALLO, if approved by the FDA, for potential heart failure indications using a dedicated direct sales model focused on selected cardiologists and heart failure specialists. These physicians are typically affiliated with leading hospitals and medical centers and we believe that they tend to have well-established referral networks of interventional cardiologists and cardiac catheterization laboratories. We believe they represent a concentrated customer base suitable to a specialist care sales model. We believe that CardiAMP and CardiALLO will be adopted first by leading cardiologists and heart failure specialists at high-volume U.S. hospitals and medical centers, and progressively by a broader segment of the market. Cardiologists, heart failure specialists, and interventional cardiologists, have a history of early adoption of innovative products and technologies, in part because the rate of innovation in this sector has been sustained, and in part because of the large unmet medical needs of heart failure patients.

## **Competition**

The biotechnology and pharmaceutical industries in which we operate are subject to rapid change and are characterized by intense competition to develop new technologies and proprietary products. We face potential competition from many different sources, including larger and better-funded companies. While we believe that CardiAMP's unique strategy provides us with competitive advantages, particularly given that CardiAMP is designed to be administered in a safe and short procedure, we have identified several companies which are active in the advancement of cell-based and gene-based therapy products in the heart failure arena. Not only must we compete with other companies that are focused on cell-based therapy treatments, any products that we may commercialize will have to compete with existing therapies and new therapies that may become available in the future.

Some of the companies currently developing cell-based and gene-based therapies for cardiac indications include CapriCor Therapeutics, Celyad, CellProthera, Juventas Therapeutics, Mesoblast, Vericel, Uniqure, some of which are in the clinical stages of development with their product candidates.

However, these competitors may require delivery platforms for their own therapeutic programs. Because the clinical need is so large and our biotherapeutic delivery products have potential to enable multiple biotherapeutics, we view these companies also as potential collaborators and partners. To date, we have entered into agreements to provide our biotherapeutic delivery system to four of these firms for various pre-clinical and clinical studies. One is active in the clinic today. None of these relationships are believed to be material to our business at this time.

## **Intellectual Property**

We strive to protect and enhance the proprietary technologies that we believe are important to our business, and seek to obtain and maintain patents for any patentable aspects of our therapeutic candidates or products, including our anticipated companion diagnostic, their methods of use and any other inventions that are important to the development of our business. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in the fields targeted by our therapeutic candidates.

We have a large patent portfolio of issued and pending claims covering methods of use for CardiAMP, CardiALLO, Helix and Morph as well as design and elements of our manufacturing processes. As of December 31, 2016, we had developed or secured rights to over 20 patent families that included rights to over 75 U.S. patents with issued or patent pending applications. We have sole ownership of the patents that we consider to be material, other than the patents that we license exclusively from Biomet Biologics, LLC. We have also pursued international protection for some of these U.S. patents where appropriate. Our issued U.S. patents expire between 2017 and 2031, without taking into consideration patent term extension. We maintain trade secrets covering a significant body of know-how and proprietary information related to our core therapeutic candidates, biotherapeutic delivery systems and technologies. As a result, we believe our intellectual property position provides us with substantial competitive advantages for the commercial development of novel therapeutics for cardiovascular diseases.

### ***U.S. Regulatory Protection for CardiAMP and CardiALLO***

In addition to patent and trade secret protection, we may receive a 12-year period of regulatory exclusivity from the FDA upon approval of CardiAMP and CardiALLO pursuant to the Biologics Price Competition and Innovation Act. The exclusivity period, if granted, will run from the time of FDA approval. This exclusivity period, if granted, will supplement the intellectual property protection discussed above, providing an additional barrier to entry for any competitor seeking approval for a bio-similar version of the CardiAMP or CardiALLO cell therapy systems.

In addition, it is possible to extend the patent term of one patent covering CardiAMP and CardiALLO following FDA approval. This patent term extension, or PTE, is intended to compensate a patent owner for the loss of patent term during the FDA approval process. If eligible, we may use a PTE to extend the term of one of the patents discussed above beyond the expected expiration date.

### ***Trademarks***

We have registered our name, logo and the trademarks “BioCardia,” “CardiAMP,” “CardiALLO,” and “Morph” in the United States. We have registered the trademarks “CardiAMP” and “CardiALLO” for use in connection with a biological product, namely, a cell-based therapy product composed of bone marrow derived cells for medical use. We also have rights to use the “Helix” trademark in the United States. We have registered Morph for use in connection with steerable vascular access technology. We intend to pursue additional registrations in markets outside the United States where we plan to sell our therapies and products.

### ***Patent Term***



The term of individual patents and patent applications will depend upon the legal term of the patents in the countries in which they are obtained. In most countries, the patent term is 20 years from the date of filing of the patent application (or parent application, if applicable). For example, if an international Patent Cooperation Treaty, or PCT, application is filed, any patent issuing from the PCT application in a specific country expires 20 years from the filing date of the PCT application. In the United States, however, if a patent was in force on June 8, 1995, or issued on an application that was filed before June 8, 1995, that patent will have a term that is the greater of 20 years from the filing date, or 17 years from the date of issue.

Under the Hatch-Waxman Act, the term of a patent that covers an FDA-approved drug, biological product may also be eligible for PTE. PTE permits restoration of a portion of the patent term of a U.S. patent as compensation for the patent term lost during product development and the FDA regulatory review process if approval of the application for the product is the first permitted commercial marketing of a drug or biological product containing the active ingredient. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. The Hatch-Waxman Act permits a PTE for only one patent applicable to an approved drug, and the maximum period of restoration is five years beyond the expiration of the patent. A PTE cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and a patent can only be extended once, and thus, even if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions may be available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a BLA, we expect to apply for PTEs for patents covering our therapeutic candidates and products and their methods of use. For additional information on PTE, see “Government Regulation.”

### ***Proprietary Rights and Processes***

We may rely, in some circumstances, on proprietary technology and processes (including trade secrets) to protect our technology. However, these can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with those who have access to our confidential information, including our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our proprietary technology and processes may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors, contractors, or any future collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For this and more comprehensive risks related to our proprietary technology and processes, please see “Risk Factors—Risks Related to our Intellectual Property.”

### ***License Agreement with Biomet Biologics, LLC***

In October 2012, we entered into a license and distribution agreement with Biomet Biologics, LLC under which we obtained an exclusive, nontransferable, worldwide distribution right, patent license and trademark license to a point of care cell processing platform. Under the terms of the agreement, we are obligated to pay a royalty based on the price of the disposables in the CardiAMP cell processing platform for the duration of the agreement. We expect the royalty payments to Biomet Biologics, LLC for the licensed product to amount to a low or mid-single digit percentage of the expected price that we will charge for CardiAMP. The agreement has a term of 10 years or the time the last patent pursuant to the agreement expires, whichever is later. The agreement may be terminated by Biomet Biologics, LLC for a failure by us to meet any milestone requirements, including minimum purchase requirements, as well as by either party upon 30 days prior written notice in the event of a breach of any material term by the other party. We have the right to terminate the agreement upon 90 days prior written notice in the event the safety, efficacy or comparative effectiveness of the product is insufficient to meet our commercial needs.

### ***Technology Access Program for Biotherapeutic Delivery Systems***

Our preclinical work with partners and collaborators generally takes place under arrangements where we secure access to data, reports, and a non-exclusive license to delivery technology improvement inventions.

### ***Clinical Research Agreements for Biotherapeutic Delivery Systems***

Our clinical work with partners generally takes place under arrangements where we secure access to data, reports, and a non-exclusive license to technology improvement inventions. Financial terms of each agreement are anticipated to cover our costs and provide milestone payments. We hope to generate sales if any of our partners are successful with commercializing their products with our delivery platform.

## **Regulation**

Biological products, including cell-based therapy products, and medical devices are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, purity, potency, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products. FDA acceptance must be obtained before clinical testing of an investigational biological and medical device begins, and each clinical trial protocol for a cell-based therapy product is submitted to and reviewed by the FDA. FDA approval must be obtained before marketing of biological and/or medical devices. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals on a timely basis, or at all. To date, the FDA has never approved for commercial sale a cell-based therapy product intended to treat the heart.

Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates cell-based therapy products. For products that use medical devices, including diagnostics, to deliver cell therapies, CBER works closely with the FDA's Center for Devices and Radiological Health, or CDRH.

***U.S. Biological Product Development Process***

Our CardiALLO therapeutic candidate will be regulated in the United States as a biological product. The process required by the FDA before a biological product may be tested and marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLP, regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial begins;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations, commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety, purity and potency of the proposed biological product for its intended use;
- Preparation of and submission to the FDA of a biologics license application, or BLA, for marketing approval, after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with GMP, to assure that the facilities, methods and controls are adequate to

preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices, or GTPs, for the use of human cellular and tissue products;

• potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA; and

• FDA review and approval, or licensure, of the BLA for particular indications for use in the United States, which must be updated annually when significant changes are made.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our therapeutic candidates or product candidates will be granted on a timely basis, if at all. Before testing any biological product candidate, including a cell-based therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trials.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Clinical trials also must be reviewed by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

**Phase I.** The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients with the disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses and, if possible, to gain early evidence on effectiveness.

**Phase II.** The biological product is evaluated in a limited patient population with a specified disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule. Multiple Phase II clinical

trials may be conducted to obtain information prior to beginning larger and more expensive Phase III clinical trials.

***Phase III.*** Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites, to provide statistically significant evidence of clinical efficacy and to further test for safety. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product approval and labeling.

Post-approval clinical trials, sometimes referred to as Phase IV clinical trials, may be required by the FDA or voluntarily conducted after initial marketing approval to gain more information about the product, including long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase I, Phase II and Phase III clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk, including risks inferred from other unrelated trials. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Human cell-based therapy products are a new category of therapeutics. Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of human cell-based therapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval.

Concurrently with clinical trials, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

### ***U.S. Review and Approval Processes***



After the successful completion of clinical trials of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. The FDA may grant deferrals for submission of data or full or partial waivers. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual product fee for biological products and an annual establishment fee on facilities used to manufacture prescription biological products. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with GMP to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve a BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure GMP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post-marketing clinical trials, sometimes referred to as Phase IV clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved therapies and products that have been commercialized.

The FDA has agreed to certain review goals under PDUFA, and aims to complete its review of 90% of standard BLAs within ten months from filing and 90% of priority BLAs within six months from filing. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests, or the BLA sponsor otherwise provides, additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

#### ***Fast Track Designation, Accelerated Approval, Priority Review and Breakthrough Therapy Programs***

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast

Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biological product may request the FDA to designate the drug or biological product as a Fast Track product at any time during the clinical development of the product. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Other types of FDA programs intended to expedite development and review, such as priority review, accelerated approval and Breakthrough Therapy designation, also exist. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

A product may also be eligible for receipt of a Breakthrough Therapy designation. The Breakthrough Therapy designation is intended to expedite the FDA's review of a potential new drug for serious or life-threatening diseases where "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development." The designation of a drug as a Breakthrough Therapy provides the same benefits as are available under the Fast Track program, as well as intensive FDA guidance on the product's development program. Where appropriate, we intend to utilize regulatory programs that can help expedite our product development and commercialization efforts. However, Fast Track designation, priority review, accelerated approval and Breakthrough Therapy designation do not change the standards for approval, but may expedite the development or approval process.

### ***Post-Approval Requirements***

Maintaining substantial compliance with applicable federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to GMP. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the GMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products include reporting of GMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. In addition, the FDA conducts laboratory research related to the

regulatory standards on the safety, purity, potency and effectiveness of biological products.

We also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMPs and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain GMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

### ***U.S. Premarket Clearance and Approval Requirements for Medical Devices***

Unless an exemption applies, each medical device we wish to distribute commercially in the United States will require either prior premarket notification, or 510(k) clearance, or prior approval of a PMA application from the FDA. The FDA classifies medical devices into one of three classes. Devices deemed to pose low to moderate risk are placed in either class I or II, which, absent an exemption, requires the manufacturer to file with the FDA a 510(k) submission requesting permission for commercial distribution. This process is known as 510(k) clearance. Some low-risk devices are exempt from this requirement. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or certain implantable devices, or devices deemed not substantially equivalent to a previously cleared 510(k) device, are placed in class III, requiring approval of a PMA application.

### ***Regulation of CardiAMP through the PMA Pathway***

Combination products are therapeutic and diagnostic products that combine drugs, devices, and/or biological products. Because combination products involve components that would normally be regulated under different types of regulatory authorities, and frequently by different centers of the FDA, they raise regulatory, policy, and review management challenges. Differences in regulatory pathways for each component of the product can impact the regulatory processes for all aspects of product development and management, including preclinical testing, clinical investigation, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, and post-approval modifications.

A combination product is assigned to an FDA Agency Center or alternative organizational component that will have primary jurisdiction for its premarket review and regulation. For cell-based therapy and related products, the FDA established the Office of Cellular, Tissue and Gene Therapies within CBER to consolidate the review of such products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In our case, CardiAMP involves minimal manipulation of cells within the procedure room, enabling it to be the first cardiac cell-based therapy we are aware of that CBER has indicated it will regulate through the PMA pathway. Because CardiAMP will be approved through the PMA pathway, it is expected to only require a single pivotal clinical trial as

opposed to two pivotal clinical trials generally required for approval of biologics.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the cell-based therapy. After a PMA application is deemed complete, the FDA will accept the application for filing and begin an in-depth review of the submitted information. During this review period, the FDA may request additional information or clarification of information already provided. Also during the review period, an advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. FDA review of an initial PMA application is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

The FDA may approve a PMA application with post-approval conditions intended to ensure the safety and effectiveness of the device including, among other things, restrictions on labeling, promotion, sale and distribution, collection of long-term follow-up data from patients in the clinical trial that supported approval, or new post-approval studies. Failure to comply with the conditions of approval can result in materially adverse enforcement action, including the loss or withdrawal of the approval. PMA supplements are required for modifications that could affect device safety or effectiveness, including, for example, certain types of modifications to the device's indication for use, manufacturing process, labeling and design. PMA supplements often require submission of the same type of information as an original PMA application, except that the supplement is limited to information needed to support any changes to the device covered by the original PMA application, and may not require as extensive clinical data or the convening of an advisory panel.

A clinical trial is almost always required to support a PMA application. We expect that CardiAMP will require a single pivotal trial for PMA approval. However, there is no guarantee that the FDA will grant us regulatory clearance or approval to market CardiAMP on the basis of a single pivotal trial. Two well-controlled pivotal studies could be necessary to provide the FDA assurance of safety or effectiveness. In the United States, absent certain limited exceptions, human clinical trials intended to support product clearance or approval require an Investigational Device Exemption application, or IDE, which the FDA reviews. Some types of trials deemed to present "non-significant risk" are deemed to have an approved IDE once certain requirements are addressed and IRB approval is obtained. If the device presents a "significant risk" to human health, as defined by FDA regulations, the sponsor must submit an IDE application to the FDA and obtain IDE approval prior to commencing the human clinical trials. The IDE application must be supported by appropriate data, such as animal and laboratory trial results, showing that it is safe to evaluate the device in humans and that the trial protocol is scientifically sound. The IDE application must be approved in advance by the FDA for a specified number of subjects, unless the product is deemed a non-significant risk device and eligible for more abbreviated IDE requirements. Clinical trials for a significant risk device may begin once the IDE application is approved by the FDA and the responsible institutional review boards at the clinical trial sites. There can be no assurance that submission of an IDE will result in the ability to commence clinical trials. Additionally, after a trial begins, the FDA may place it on hold or terminate it if, among other reasons, it concludes that the clinical subjects are exposed to unacceptable health risks that outweigh the benefits of participation in the trial. During a trial, we are required to comply with the FDA's IDE requirements for investigator selection, trial monitoring, reporting, record keeping and prohibitions on the promotion or commercialization of investigational devices or making safety or efficacy claims for them, among other things. We are also responsible for the appropriate labeling and distribution of investigational devices. Our clinical trials must be conducted in accordance with FDA regulations and federal and state regulations concerning human subject protection, including informed consent and healthcare privacy. The investigators must also obtain patient informed consent, rigorously follow the investigational plan and trial protocol, control the disposition of investigational devices and comply with all reporting and record keeping requirements, among other things. The FDA's grant of permission to proceed with clinical trials does not constitute a binding commitment that the FDA will consider the trial design adequate to support marketing clearance or approval. In addition, there can be no assurance that the data generated during a clinical trial will meet the chosen study endpoints or otherwise produce results that will lead the FDA to grant marketing clearance or approval. Similarly, in Europe, the clinical trial must be approved by the local ethics committee and in some cases, including trials of high-risk devices, by the Ministry of Health in the applicable country.





After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Failure by us or our suppliers to comply with applicable regulatory requirements can result in enforcement action by the FDA or other regulatory authorities, which may result in sanctions and related consequences including, but not limited to:

- adverse publicity, untitled letters or warning letters;
- fines, injunctions, consent decrees and civil penalties;
- recall, detention or seizure of our products;
- operating restrictions, partial suspension or total shutdown of production;
- refusal of or delay in granting our requests for 510(k) clearance or premarket approval of new products or modified products;
- withdrawing 510(k) clearance or premarket approvals that are already granted;
- refusal to grant export approval for our products;
- criminal prosecution; and
- unanticipated expenditures to address or defend such actions.

Because elements of the broader CardiAMP therapy are already approved or cleared and manufactured for commercial use, we believe regulatory approval risks are primarily those of clinical efficacy.

***Regulation of Companion Diagnostics***

Companion diagnostics are subject to regulation by the FDA, the EMA and other foreign regulatory authorities as medical devices and require separate regulatory clearance or approval prior to commercial use. We anticipate that the CardiAMP potency assay will require approval under a PMA submitted to the CDRH prior to commercialization. We and our third-party collaborators who may develop our companion diagnostics will work cooperatively to generate the data required for submission with the PMA application, and will remain in close contact with the CDRH to ensure that any changes in requirements are incorporated into the development plans. We further anticipate that regulatory approval of the CardiAMP potency assay will be a prerequisite to our ability to market CardiAMP. Representatives of CDRH have participated in our meetings with CBER regarding CardiAMP to discuss the potential use of the CardiAMP potency assay, and we anticipate that future meetings will include representatives from both CBER and CDRH to ensure that the PMA submissions (for CardiAMP and the CardiAMP potency assay) are coordinated and subject to parallel review by these respective FDA centers. Accordingly, our objective is to align the development programs such that the CardiAMP potency assay will be developed and approved contemporaneously with CardiAMP.

In the United States, companion diagnostic tests used in conjunction with drug or biological products are classified as medical devices under the FD&C Act. We anticipate that our CardiAMP potency assay we are developing in conjunction with our CardiAMP therapeutic candidate will be subject to the PMA approval process.

On July 14, 2011, the FDA issued for comment a draft guidance document addressing the development and approval process for “In Vitro Companion Diagnostic Devices.” According to the draft guidance, for novel products such as CardiAMP, the PMA for a companion diagnostic device should be developed and approved contemporaneously with the biological product. While this draft guidance is not yet finalized, we believe our programs for the development of the CardiAMP potency assay are consistent with the draft guidance as proposed.

### ***Coverage and Reimbursement***

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government healthcare programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our therapeutic candidates or a decision by a third-party payor to not cover our therapeutic candidates could reduce physician usage of our products once approved and have a material adverse effect on our sales, results of operations and financial condition.

### ***Affordable Care Act***

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act, was enacted, which includes measures that have or will significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the Affordable Care Act of greatest importance to the pharmaceutical industry are the following:

• The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer’s outpatient drugs furnished to Medicaid patients. Effective in 2010, the Affordable Care Act made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers’ rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic agents from 15.1% of average manufacturer price (AMP) to 23.1% of AMP and adding a new rebate calculation for “line extensions” (*i.e.*, new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The Affordable Care Act also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010. Per a ruling by the U.S. Supreme Court in 2012, states have the option to expand their Medicaid programs which in turn expands the population eligible for Medicaid drug benefits. The Centers for Medicare & Medicaid

Services, or CMS, has proposed to expand Medicaid rebate liability to the territories of the United States as well. In addition, the Affordable Care Act provides for the public availability of retail survey prices and certain weighted average AMPs under the Medicaid program. The implementation of this requirement by the CMS may also provide for the public availability of pharmacy acquisition of cost data, which could negatively impact our sales.

In order for a pharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. Effective in 2010, the Affordable Care Act expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs when used for the orphan indication. In July 2013, the Health Resources and Services Administration (HRSA) issued a final rule allowing the newly eligible entities to access discounted orphan drugs if used for non-orphan indications. While the final rule was vacated by a federal court ruling, HRSA has stated it will continue to allow discounts for orphan drugs when used for any indication other than for orphan indications. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

Effective in 2011, the Affordable Care Act imposed a requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (*i.e.*, “donut hole”).

Effective in 2011, the Affordable Care Act imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

The Affordable Care Act required pharmaceutical manufacturers to track certain financial arrangements with physicians and teaching hospitals, including any “transfer of value” made or distributed to such entities, as well as any ownership or investment interests held by physicians and their immediate family members. Manufacturers were required to begin tracking this information in 2013 and to report this information to CMS by March 2014.

As of 2010, a new Patient-Centered Outcomes Research Institute was established pursuant to the Affordable Care Act to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.

There have been judicial and Congressional challenges and amendments to certain aspects of the Affordable Care Act, and with recent legislative activity we expect there could be additional challenges, amendments and attempts to repeal the Affordable Care Act. New state and federal healthcare reform measures could limit the amounts that federal and state governments will pay for our product candidates if we obtain regulatory approval for them, and could have other impacts on consequences which cannot be reasonably predicted at this time.

#### ***Other Healthcare Laws and Compliance Requirements***

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sale, marketing and education programs. In addition, we may be subject to patient privacy regulations by both the federal government and the states in which we conduct our business. The laws may affect our ability to operate include:

the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals and ownership and investment interest held by such physicians and their immediate family members;

HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and

State law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our future business activities could be subject to challenge under one or more of such laws. In addition, the Affordable Care Act broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and certain criminal healthcare fraud statutes. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the false claims laws or the civil monetary penalties statute.

We are also subject to the Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business.

Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar state laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and results of operations.

If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operation.

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

### ***Government Regulation Outside the United States***

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Because



biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval or clearance for a product, we must obtain the requisite approvals or clearances from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the PMA or IND prior to the commencement of human clinical trials. In Europe, for example, a Clinical Trial Authorization, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational biological product under European regulatory systems, we must submit a marketing authorization application. The application used to file the PMAs for CardiAMP and BLA for CardiALLO in the United States are similar to that required in Europe, with the exception of, among other things, country-specific document requirements. Europe also provides opportunities for market exclusivity. For example, in Europe, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in Europe from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by Europe's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;

- the applicant consents to a second orphan medicinal product application; or

- the applicant cannot supply enough orphan medicinal product.

For other countries outside of Europe, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

In Europe, we expect both CardiAMP and CardiALLO to be regulated as advanced therapy medicinal products, or ATMPs. To provide for a common framework for the marketing of ATMPs, Regulation (EC) No 1394/2007 of the European Parliament and of the Council on advanced therapy medicinal products, or ATMP Regulation, was adopted

in 2007. The ATMP Regulation was designed to ensure a high level of human health protection as well as the free movement of ATMPs in Europe. The cornerstone of the ATMP Regulation is that a marketing authorization must be obtained prior to the marketing of ATMPs. In turn, the marketing authorization can only be granted if, after a scientific assessment of the quality, efficacy and safety profile, it is demonstrated that the benefits outweigh the risks. The application for a marketing authorization must be submitted to the EMA and the final decision is taken by the European Commission. This procedure ensures that these products are assessed by a specialized body (the Committee for Advanced Therapies, or CAT) and that the marketing authorization is valid in all the European Union Member States.

The ATMP Regulation empowered the EMA to make scientific recommendations as to whether a given product should be considered an ATMP (hereinafter “classifications”). Additionally, it provided for a new instrument, the so-called certification procedure, designed as an incentive for small and medium sized enterprises, or SMEs, that were involved in the first stages of the development of ATMPs but lacked the resources to conduct clinical trials. Specifically, the certification that the quality and preclinical aspects of the development are in conformity with the relevant regulatory requirements was expected to help SMEs attract capital and to facilitate the transfer of research activities to entities with the capacity to market medicinal products.

The ATMP Regulation builds on the procedures, concepts, and requirements designed for chemical-based medicinal products. However, ATMPs present very different characteristics. Additionally, in contrast to chemical-based medicinal products, research in advanced therapies is –for the most part- conducted by academia, non-for-profit organizations, and SMEs, which only have limited financial resources and often lack exposure to the regulatory system that governs medicines.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

The advertising and promotion of our products in the EEA is subject to the provisions of the Medical Devices Directive, Directive 2006/114/EC concerning misleading and comparative advertising, and Directive 2005/29/EC on unfair commercial practices, as well as other national legislation in the EEA countries governing the advertising and promotion of medical devices. The European Commission has submitted a Proposal for a Regulation of the European Parliament and the Council on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009, to replace, inter alia, Directive 93/42/EEC and to amend regulations regarding medical devices in the European Union, which could result in changes in the regulatory requirements for medical devices in Europe. In Germany, the advertising and promotion of our products can also be subject to restrictions provided by the German Act Against Unfair Competition (Gesetz gegen den unlauteren Wettbewerb) and the law on the advertising of medicines (Heilmittelwerbegesetz), criminal law, and some codes of conduct with regard to medical products and medical devices among others. These laws may limit or restrict the advertising and promotion of our products to the general public and may impose limitations on our promotional activities with healthcare professionals.

Sales of medical devices are subject to foreign government regulations, which vary substantially from country to country. In order to market our products outside the United States, we must obtain regulatory approvals or CE Certificates of Conformity and comply with extensive safety and quality regulations. The time required to obtain approval by a foreign country or to obtain a CE Certificate of Conformity may be longer or shorter than that required for FDA clearance or approval, and the requirements may differ. In the EEA, we are required to obtain Certificates of Conformity before drawing up an EC Declaration of Conformity and affixing the CE Mark of conformity to our medical devices. Many other countries accept CE Certificates of Conformity or FDA clearance or approval although others, such as Brazil, Canada and Japan require separate regulatory filings.

## **Employees**

As of December 31, 2016, we had 14 full-time employees, consisting of clinical development, product development, regulatory, manufacturing, quality, finance, administration, sales, and marketing. We also regularly use independent contractors across the organization to augment our regular staff. None of our employees are covered by collective bargaining agreements and we consider relations with our employees to be good. We believe that our future success will depend in part on our continued ability to attract, hire and retain qualified personnel.

## **Available Information**

Our website is [www.biocardia.com](http://www.biocardia.com). Information contained on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K, and you should not consider information on our website to be part of this report unless specifically incorporated herein by reference. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on our investor relations website as soon as reasonably practicable after we electronically file such material with, or furnish it to the Securities and Exchange Commission, or SEC. The SEC also maintains a website that contains our SEC filings. The address of the website is [www.sec.gov](http://www.sec.gov). Further, a copy of this Annual Report on Form 10-K is located at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0300.

## ITEM 1A. RISK FACTORS

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, including the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and related notes, before investing in our common stock. If any of the follows risks occur, our business, financial condition, results of operations and prospects could be materially harmed. In that event, the market price of our common stock could decline, and you could lose part or all of your investment.*

### **Risks Related to Our Business**

*We have incurred operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability.*

We are a clinical-stage regenerative medicine company and we have not yet generated a profit. We have incurred net losses during each of our fiscal years since our inception. Our net loss for the year ended December 31, 2016 was \$10.3 million and our accumulated deficit totaled \$60.1 million. We do not know whether or when we will become profitable, if ever. We currently expect operating losses and negative cash flows to continue for at least the next several years.

To date, our only approved or cleared products are our Morph universal deflectable guide catheters and Morph AccessPro sheaths, or Morph, in the United States and Europe and our Helix biotherapeutic delivery system, or Helix, in Europe. Our limited commercialization experience and number of approved products makes it difficult to evaluate our current business and predict our future prospects. Our short commercialization experience and limited number of approved products also makes it difficult for us to forecast our future financial performance and growth and such forecasts are limited and subject to a number of uncertainties, including our ability to successfully complete our Phase III pivotal trial and obtain FDA approval for, and then successfully commercialize, CardiAMP.

Our ability to generate sufficient revenue to achieve profitability depends on our ability, either alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize our therapeutic candidates. We do not anticipate generating revenues from sales of CardiAMP, CardiALLO or any other therapeutic candidates within the next few years, and we may never generate sales of these products.

We anticipate that our expenses will increase in the future as we continue to incur significant research and development and other expenses related to our ongoing operations, seek regulatory approvals for our therapeutic candidates, scale-up manufacturing capabilities and hire additional personnel to support the development of our therapeutic candidates and commercialization efforts. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To achieve and maintain profitability, we must successfully develop our therapeutic candidates, obtain regulatory approvals and manufacture, market and sell those products for which we obtain regulatory approvals. If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our therapeutic candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement from third-party payors and adequate market share for our therapeutic candidates in those markets. We may not succeed in these activities, and we may never generate revenue from product sales that is significant enough to achieve profitability. Our failure to become or remain profitable would depress our market value and could impair our ability to raise capital, expand our business, discover or develop other product candidates or continue our operations. A decline in the value of our company could cause you to lose part or all of your investment.

Based upon our current operating plan, we believe that the cash on hand as a result of the Merger, together with our existing cash and cash equivalents, will enable us to fund our operations for at least the next twelve-month period following the date of issuance of our 2016 financial statements.

***Our success depends in large part on our ability to obtain approval for, and successfully commercialize, CardiAMP.***

The long-term viability of our company is largely dependent on the successful development and commercialization of the CardiAMP Cell Therapy System, or CardiAMP. We are currently enrolling patients in a Phase III pivotal trial that will be used to support regulatory approval of CardiAMP, and we do not have significant long term data on CardiAMP's safety and efficacy. While we expect to successfully complete our Phase III pivotal trial of CardiAMP, there can be no guarantee that the study will be completed, that the primary endpoints will be achieved, or that we will receive regulatory approval for the sale and marketing of CardiAMP in the United States. A number of companies in similar fields have suffered significant setbacks during clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising preliminary results. Because we are depending heavily on sales of CardiAMP to achieve our revenue goals, failure to successfully complete the study and receive U.S. Food and Drug Administration, or FDA, approval, in a timely manner or at all, will harm our financial results and ability to become profitable. Even if we obtain regulatory approval, our ability to successfully market this product will be limited due to a number of factors, including regulatory restrictions in our labeling or requirements to obtain additional post-approval data, if any. In addition, there can be no guarantee that CardiAMP will be accepted by the medical community as a valid alternative to currently available products. If we cannot sell CardiAMP as planned, our financial results will be harmed.

Although we have obtained FDA acceptance of a Phase III pivotal trial of CardiAMP for the treatment of ischemic systolic heart failure, this does not guarantee any particular outcome from regulatory review. CardiAMP is the first cardiac cell-based therapy with an accepted pivotal trial that is to be regulated by the FDA Center for Biologics Evaluation and Research, or CBER, via the pre-market approval, or PMA, pathway requiring a single pivotal trial. All other cardiac cell-based therapies in clinical trials are regulated by the same agency, but as biologics which generally require two separate pivotal trials. There is no guarantee that the FDA will grant us regulatory clearance or approval to market CardiAMP on the basis of a single pivotal trial, or that the FDA will continue to allow us to develop CardiAMP via the PMA pathway. Two well-controlled pivotal studies could be necessary to provide FDA assurance of safety or effectiveness.

FDA acceptance of a Phase III pivotal trial is not a guarantee of an approval of a product candidate or any permissible claims about the product candidate. Failure to successfully complete our Phase III trial of CardiAMP would significantly impair our financial results. Such a failure could (i) delay or prevent CardiAMP from obtaining regulatory approval, (ii) require us to perform another clinical trial, which will be expensive, may not be successful and will significantly delay our ability to commercialize CardiAMP and (iii) impair our ability to convince hospitals and physicians of the benefits of our CardiAMP product. Furthermore, even if we are granted regulatory clearances or approvals, they may include significant limitations on the indicated uses for CardiAMP, which may limit the market for this product.

***Our CardiAMP and CardiALLO therapeutic candidates are based on novel technology, which makes it difficult to accurately and reliably predict the time and cost of product development and subsequently obtaining regulatory approval. At the moment, no cell-based therapies have been approved in the United States for a cardiac indication.***

The success of our business depends on our ability to develop and commercialize our therapeutic candidates, including CardiAMP. We have concentrated our product research and development efforts on our CardiAMP therapeutic candidate, a novel type of cell-based therapy. Our future success depends on the successful development of this therapeutic approach. There can be no assurance that any development problems we experience in the future related to our therapeutic candidates and products will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may be unable to maintain and further develop sustainable, reproducible and scalable manufacturing processes, or transfer these processes to collaborators, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical study requirements of the FDA, the European Medicines Agency, or EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, intended use and market of the potential product candidates. The regulatory approval process for novel product candidates such as our CardiAMP and CardiALLO Cell Therapy System, or CardiALLO, can be more expensive and take longer than other, better known or extensively studied pharmaceutical or other product candidates to develop. In addition, adverse developments in clinical trials of cell-based products or therapies conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our therapeutic candidates. At the moment, no other cell-based therapies have



been approved in the United States for a cardiac indication, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our therapeutic candidates in either the United States or elsewhere.

Regulatory requirements governing cell-based therapy products have changed frequently and may continue to change in the future. For example, the FDA established the Office of Cellular, Tissue and Gene Therapies within CBER to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. These regulatory authorities and advisory groups and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with the FDA and other regulatory authorities, and our products could be reviewed by the FDA's advisory committee. We also must comply with applicable requirements, and if we fail to do so, we may be required to delay or discontinue development of our product candidates.

***We will require substantial additional financing to achieve our goals, and our failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.***

Our operations have consumed substantial amounts of cash since inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future in connection with our planned research, development and product commercialization efforts, including our planned clinical trials for our CardiAMP and CardiALLO therapeutic candidates. In addition, we will require additional financing to achieve our goals and our failure to do so could adversely affect our commercialization efforts. We anticipate that our expenses will increase substantially if and as we:

- continue the research and clinical development of our CardiAMP and CardiALLO therapeutic candidates;

- initiate and advance our CardiAMP and CardiALLO therapeutic candidates into larger and more expensive clinical studies, including a Phase III pivotal trial for our CardiAMP therapeutic candidate;

- seek to identify, assess, acquire, and/or develop other product candidates and technologies;

- seek regulatory and marketing approvals in multiple jurisdictions for our therapeutic candidates that successfully complete clinical studies;

- build and maintain a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval, or otherwise establish collaborations with third parties for the development and commercialization of our therapeutic candidates;

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further develop and implement our manufacturing processes and expand our manufacturing capabilities and resources for commercial production;

• seek coverage and reimbursement from third-party payors, including government and private payors for future products;

• seek to maintain, protect and expand our intellectual property portfolio; and

• seek to attract and retain skilled personnel.

If we were to experience any delays or encounter issues with any of the above, including clinical holds, failed studies, inconclusive or complex results, safety or efficacy issues, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval, it could further increase the costs associated with the above. Further, the net operating losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

***We may encounter substantial delays in our clinical studies.***

We cannot guarantee that any preclinical testing or clinical trials will be conducted as planned or completed on schedule, if at all. As a result, we may not achieve the expected clinical milestones outlined in this Report. A failure can occur at any stage of testing. Events that may prevent successful or timely commencement, enrollment or completion of clinical development include:

- delays in raising, or inability to raise, sufficient capital to fund the planned trials;
- delays in reaching a consensus with regulatory agencies on trial design;
- changes in trial design;
- inability to identify, recruit and train suitable clinical investigators;
- inability to add new clinical trial sites;
- delays in reaching agreement on acceptable terms for the performance of the trials with prospective clinical research organizations, or CROs, and clinical trial sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- delays in recruiting suitable clinical sites and patients (*i.e.*, subjects) to participate in clinical trials;
- imposition of a clinical hold by regulatory agencies for any reason, including negative clinical results, safety concerns or as a result of an inspection of manufacturing or clinical operations or trial sites;
- failure by us, CROs or other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's current Good Clinical Practices, or GCP, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery to the clinical sites;

- delays caused by patients not completing participation in a trial or not returning for post-treatment follow-up;
- delays caused by clinical trial sites not completing a trial;
- failure to demonstrate adequate efficacy;
- occurrence of serious adverse events in clinical trials that are associated with the therapeutic candidates or products that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or
- disagreements between us and the FDA or other regulatory agencies interpreting the data from our clinical trials.

Delays, including those caused by the above factors, can be costly and could negatively affect our ability to complete clinical trials for our therapeutic candidates. If we are not able to successfully complete clinical trials or are not able to do so in a timely and cost-effective manner, we will not be able to obtain regulatory approval and/or will not be able to commercialize our therapeutic candidates or products, which would have an adverse effect on our business. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our therapeutic candidates or products or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our therapeutic candidates or products and may harm our business and results of operations.

***We may find it difficult to enroll patients in our clinical trials, which could delay or prevent development of our therapeutic candidates.***

Identifying and qualifying patients to participate in clinical trials of our therapeutic candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our therapeutic candidates as well as completion of required follow-up periods. In general, if patients are unwilling to participate in our cell-based therapy trials because of negative publicity from adverse events in the biotechnology or cell-based industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting trials and obtaining regulatory approval for our therapeutic candidates may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our therapeutic candidates or termination of the clinical trials altogether.

Patient enrollment and completion of clinical trials are affected by factors including:

- size of the patient population;
- severity of the disease under investigation;
- design of the trial protocol;
- eligibility criteria for the particular trial;
- perceived risks and benefits of the product candidate being tested;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and

the degree of treatment effect in event-driven trials.

Once enrolled, patients may choose to discontinue their participation at any time during the trial, for any reason. Participants also may be terminated from the study at the initiative of the investigator, for example if they experience serious adverse clinical events or do not follow the study directions. If we are unable to maintain an adequate number of patients in our clinical trials, we may be required to delay or terminate an ongoing clinical trial, which would have an adverse effect on our business.

***We depend on our license and distribution agreement with Biomet Biologics, LLC, and if we fail to comply with our obligations under this agreement, or if our rights under this agreement are otherwise reduced or terminated, we could lose intellectual property rights that are important to our business.***

In October 2012, we entered into a license and distribution agreement with Biomet Biologics, LLC under which we obtained an exclusive, nontransferable, worldwide distribution right, patent license and trademark license to Biomet Biologic, LLC's point of care cell processing platform. Under the terms of the agreement, we are obligated to pay Biomet Biologics, LLC a royalty based on the price of the disposables in the CardiAMP cell processing platform. A breach or termination of this agreement would materially adversely affect the clinical development or commercialization strategy of our CardiAMP therapeutic candidate as currently planned. A reduction or elimination of our rights under this agreement may result in our having to negotiate new or reinstated arrangements on less favorable terms, or our not having sufficient intellectual property rights to operate our business as currently planned. The occurrence of such events could materially harm our business and financial condition.

***We rely on third parties to conduct some or all aspects of our product manufacturing, diagnostic protocol development, research, and preclinical and clinical testing, and these third parties may not perform satisfactorily.***

We do not currently, and do not expect to in the future, independently conduct all aspects of our product manufacturing, anticipated companion diagnostic testing, protocol development, research and monitoring and management of our ongoing preclinical and clinical programs. We currently rely, and expect to continue to rely, on third parties with respect to these items, and control only certain aspects of their activities.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, our commercialization activities or our therapeutic candidate or companion diagnostic development activities may be delayed or suspended. Our reliance on these third parties for research and development activities, including the conduct of any IDE and IND-enabling studies, reduces our control over these activities but does not relieve us of our responsibility to ensure compliance with all required legal, regulatory and scientific standards and any applicable trial protocols. For example, for therapeutic candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IDE and IND-enabling studies and clinical trials are conducted in accordance with the trial plan and protocols.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we may be delayed in completing, or unable to complete, the preclinical studies and clinical trials required to support future IDE and IND submissions and approval of our therapeutic candidates.

Reliance on third-party manufacturers entails exposure to risks to which we would not be subject if we manufactured the therapeutic candidates or companion diagnostic ourselves, including:

- we may be unable to negotiate manufacturing agreements with third parties under commercially reasonable terms;

- reduced control over the manufacturing process for our therapeutic candidates and companion diagnostic as a result of using third-party manufacturers for many aspects of manufacturing activities;

- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may be costly or damaging to us or result in delays in the development or commercialization of our therapeutic candidates or companion diagnostic; and



disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to delays in the development of our therapeutic candidates, including delays in our clinical trials, or failure to obtain regulatory approval for our therapeutic candidates, or it could impact our ability to successfully commercialize our current therapeutic candidates, companion diagnostic or any future products. Some of these events could be the basis for FDA or other regulatory action, including injunction, recall, seizure or total or partial suspension of production.

***We rely on third parties to conduct, supervise and monitor our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.***

We rely on CROs and clinical trial sites to ensure our clinical trials are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the FDA's GCPs for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA, the Competent Authorities of the Member States of the EEA, and comparable foreign regulatory authorities, enforce these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA, the EMA, or other foreign regulatory authorities may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of our therapeutic candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our therapeutic candidates. If any such event were to occur, our financial results and the commercial prospects for our therapeutic candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Further, switching or adding additional CROs involves additional costs and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which could materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We may also rely on other third parties to store and distribute our products for the clinical trials that we conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our therapeutic candidates or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue.

***We depend on third party vendors to manufacture some of our components and sub-assemblies, which could make us vulnerable to supply shortages and price fluctuations that could harm our business.***

We currently manufacture some of our components and sub-assemblies internally and rely on third party vendors for other components and sub-assemblies used in our products and therapeutic candidates. Our reliance on third party vendors subjects us to a number of risks that could impact our ability to manufacture our products and therapeutic candidates and harm our business, including:

- interruption of supply resulting from modifications to, or discontinuation of, a supplier's operations;

- delays in product shipments resulting from uncorrected defects, reliability issues or a supplier's failure to consistently produce quality components;

- price fluctuations due to a lack of long-term supply arrangements with our suppliers for key components;
- inability to obtain adequate supply in a timely manner or on commercially reasonable terms;
- difficulty identifying and qualifying alternative suppliers for components in a timely manner;
- inability of the manufacturer or supplier to comply with Quality System Regulations, or QSRs, enforced by the FDA and state regulatory authorities;
- inability to control the quality of products manufactured by third parties;
- production delays related to the evaluation and testing of products from alternative suppliers and corresponding regulatory qualifications; and
- delays in delivery by our suppliers due to changes in demand from us or their other customers.

Any significant delay or interruption in the supply of components or sub-assemblies, or our inability to obtain substitute components, sub-assemblies or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand of our customers and harm our business.

***Our future commercial success depends upon attaining significant market acceptance of our therapeutic candidates, if approved, among physicians, patients and healthcare payors.***

Even when product development is successful and regulatory approval has been obtained, our ability to generate significant revenue depends on the acceptance of our products by physicians, payors and patients. Many potential market participants have limited knowledge of, or experience with, cell-based products and therapies, so gaining market acceptance and overcoming any safety or efficacy concerns may be more challenging than for more traditional therapies. Our efforts to educate the medical community and third-party payors on the benefits of our therapeutic candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by conventional therapies marketed by our competitors. We cannot assure you that our products will achieve the expected market acceptance and revenue if and when they obtain the requisite regulatory approvals. Alternatively, even if we obtain regulatory approval, that approval may be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. The market acceptance of each of our therapeutic

candidates will depend on a number of factors, including:

- the efficacy and safety of the therapeutic candidate, as demonstrated in clinical trials;
- the clinical indications for which the product is approved and the label approved by regulatory authorities for use with the product, including any warnings that may be required on the label;
- acceptance by physicians and patients of the product as a safe and effective treatment;
- the cost, safety and efficacy of treatment in relation to alternative treatments;
- the continued projected growth of markets for our various indications;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects; and
- the effectiveness of our sales and marketing efforts.

Market acceptance is critical to our ability to generate significant revenue. Any therapeutic candidate, if approved and commercialized, may be accepted in only limited capacities or not at all. If any approved products are not accepted by the market to the extent that we expect, we may not be able to generate significant revenue and our business would suffer.

***If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our therapeutic candidates, conduct our clinical trials and commercialize our therapeutic candidates.***

We are highly dependent on the members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. Any of our executive officers could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

***We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.***

As of December 31, 2016, we had 14 full-time employees. As we mature and expand our research and development and other pre-commercialization activities, we expect to expand our full-time employee base and to hire more consultants and contractors. In addition, we currently plan to commercialize CardiAMP, if approved, using an internal sales force to selected cardiologists, heart failure specialists and third-party payors in the United States. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

***We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.***

Our industry is highly competitive and subject to rapid change. The industry continues to expand and evolve as an increasing number of competitors and potential competitors enter the market. Some of the pharmaceutical, biotechnology and medical device companies we expect to potentially compete with include Athersys, Capricor, Celyad, Juventas Therapeutics, Uniqure, CellproThera, and Mesoblast among others. Many of our competitors, potentially including the aforementioned, have significantly greater development, financial, manufacturing, marketing, technical and human resources than we do. Large pharmaceutical and medical device companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical and medical device products. Recent and potential future merger and acquisition activity in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Established companies may also invest heavily to accelerate discovery and development of novel products that could make our therapeutic candidates obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA approval or discovering, developing and commercializing our therapeutic candidates or competitors to our therapeutic candidates before we do. Specialized, smaller or early-stage companies may also prove to be significant competitors, particularly those with a focus and expertise in the stem cell industry and/or those with collaboration arrangements and other third party payors. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and results of operations will suffer.

***Even if we obtain regulatory approval for a product candidate, including our CardiAMP and CardiALLO therapeutic candidates, these products or therapies, along with our other regulated products, will be subject to ongoing regulatory scrutiny.***

Even if we obtain regulatory approval or clearance in a jurisdiction, regulatory authorities may still impose significant restrictions on the indicated uses or marketing of our therapeutic candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, once a product receives regulatory approval or clearance for sale, we are obligated to monitor and report adverse events and any failure of a product to meet the specifications in the applicable regulatory approval or clearance. We must also submit new or supplemental applications and obtain FDA approval or clearance for certain changes to the approved or cleared product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with good manufacturing practices or QSRs and adherence to commitments made in the applicable regulatory approval. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our therapeutic candidates, a regulatory agency may impose the following:

- restrictions on the marketing or manufacturing of our products, withdrawal of our products from the market, or voluntary or mandatory product recalls;

- costly regulatory inspections;

- fines, warning letters, or holds on clinical trials;

- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our collaborators, or suspension or revocation of applicable regulatory approvals;



- product seizure or detention, or refusal to permit the import or export of products; and

• injunctions or the imposition of civil or criminal penalties by FDA or other regulatory bodies.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our therapeutic candidates and generate revenues.

***Our ability to compete is highly dependent on demonstrating the benefits of CardiAMP to physicians, hospitals and patients.***

In order to generate sales, we must be able to clearly demonstrate that CardiAMP is both a more effective treatment system and less costly than alternative products and treatments offered by our competitors. If we are unable to convince physicians that CardiAMP leads to significant improvement in functional capacity, improved quality of life and reduced hospitalization, our business will suffer.

***We may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory agencies.***

We have not obtained regulatory approval for either our CardiAMP or CardiALLO therapeutic candidates. We must conduct extensive testing of our therapeutic candidates to demonstrate their safety and efficacy, including human clinical trials and, if applicable, preclinical animal testing, before we can obtain regulatory approval to market and sell them. Conducting such testing is a lengthy, time-consuming, and expensive process and there is a high rate of failure. Our current and completed preclinical and clinical results for our therapeutic candidates are not necessarily predictive of the results of our ongoing or future clinical trials. Promising results in preclinical studies of a therapeutic candidate may not be predictive of similar results in humans during clinical trials, and successful results from early human clinical trials of a therapeutic candidate may not be replicated in later and larger human clinical trials or in clinical trials for different indications. If the results of our ongoing or future clinical trials are negative or inconclusive with respect to the efficacy of our therapeutic candidates or if we or they do not meet the clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our therapeutic candidates, we may be prevented or delayed in obtaining marketing approval for our therapeutic candidates.

***If we fail to obtain and maintain necessary regulatory clearances or approvals for our therapeutic candidates or products, or if clearances or approvals for our therapeutic candidates or products in additional indications are delayed or not issued, our commercial operations would be harmed.***

We are required to timely file various reports with the FDA, require that we report to the regulatory authorities if our therapeutic candidates or products may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if the malfunction were to recur. If these reports are not filed timely, regulators may impose sanctions and sales may suffer, and we may be subject to product liability or regulatory enforcement actions, all of which could harm our business.

If we initiate a correction or removal to reduce a risk to health posed, we would be required to submit a publically available Correction and Removal report to the FDA and in many cases, similar reports to other regulatory agencies. This report could be classified by the FDA as a product recall which could lead to increased scrutiny by the FDA, other international regulatory agencies and our customers regarding the quality and safety of our therapeutic candidates or products. Furthermore, the submission of these reports has been and could be used by competitors against us in competitive situations and cause customers to delay purchase decisions or cancel orders and would harm our reputation.

The FDA and the Federal Trade Commission, or FTC, also regulate the advertising and promotion of our therapeutic candidates or products to ensure that the claims we make are consistent with our regulatory approvals, that there are adequate and reasonable data to substantiate the claims and that our promotional labeling and advertising is neither false nor misleading in any respect. If the FDA or FTC determines that any of our advertising or promotional claims are misleading, not substantiated or not permissible, we may be subject to enforcement actions, including warning

letters, and we may be required to revise our promotional claims and make other corrections or restitutions.

FDA and state authorities have broad enforcement powers. Our failure to comply with applicable regulatory requirements could result in enforcement action by FDA or state agencies, which may include any of the following sanctions:

- adverse publicity, warning letters, fines, injunctions, consent decrees and civil penalties;
- repair, replacement, refunds, recall or seizure of our products;
- operating restrictions, partial suspension or total shutdown of production;
- refusing our requests for premarket approval of new products, new intended uses or modifications to existing products;
- withdrawing premarket approvals that have already been granted; and
- criminal prosecution.

If any of these events were to occur, our business and financial condition would be harmed.

***Serious adverse events or other safety risks could require us to abandon development and preclude, delay or limit approval of our therapeutic candidates or products, or limit the scope of any approved indication or market acceptance.***

Participants in clinical trials of our investigational cell-based therapies and products may experience adverse reactions or other undesirable side effects. While some of these can be anticipated, others may be unexpected. We cannot predict the frequency, duration, or severity of adverse reactions or undesirable side effects that may occur during clinical investigation. If any of our therapeutic candidates or products, prior to or after any approval for commercial sale, cause adverse events or are associated with other safety risks, a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend (*e.g.*, through a clinical hold) or terminate clinical trials;
- regulatory authorities may deny regulatory approval of our therapeutic candidates or products;
- regulatory authorities may restrict the indications or patient populations for which a therapeutic candidate or products is approved;
- regulatory authorities may require certain labeling statements, such as warnings or contraindications or limitations on the indications for use, and/or impose restrictions on distribution in the form of a Risk Evaluation and Mitigation Strategy, or REMS, in connection with approval, if any;
- regulatory authorities may withdraw their approval, require more onerous labeling statements or impose a more restrictive REMS than any therapeutic candidate or product that is approved;
- we may be required to change the way the therapy or therapeutic candidate or product is administered or conduct additional clinical trials;
- patient recruitment into our clinical trials may suffer;
- we could be required to provide compensation to subjects for their injuries, *e.g.*, if we are sued and found to be liable or if required by the laws of the relevant jurisdiction or by the policies of the clinical site; or

our reputation may suffer.

There can be no assurance that adverse events associated with our therapeutic candidates or products will not be observed, even where no prior adverse events have occurred. We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants or if preliminary data demonstrate that our therapeutic candidates or products are unlikely to receive regulatory approval or are unlikely to be successfully commercialized. Regulatory agencies, IRBs or data safety monitoring boards may at any time recommend the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. If we elect or are forced to suspend or terminate a clinical trial for any reason this would have an adverse effect on our business.

***Our therapeutic candidates are intended to treat patients who are extremely ill, and patient deaths that occur in our clinical trials could negatively impact our business even if they are not shown to be related to our therapeutic candidates.***

Generally, patients remain at high risk following their treatment with our CardiAMP and CardiALLO therapeutic candidates. As a result, it is likely that we will observe severe adverse outcomes during our clinical trials for these therapeutic candidates, including patient death. If a significant number of study subject deaths were to occur, regardless of whether such deaths are attributable to our therapeutic candidates, our ability to obtain regulatory approval for the applicable therapeutic candidate may be adversely impacted and our business could be materially harmed.

***If we or our suppliers fail to comply with the FDA's QSRs, our manufacturing operations could be delayed or shut down and product sales could suffer.***

Our manufacturing processes and those of our third party suppliers are required to comply with the FDA's QSRs, which covers the procedures and documentation of the design, testing, production, control, quality assurance, labeling, packaging, storage and shipping. We are also subject to similar state requirements and licenses. In addition, we must engage in extensive record keeping and reporting and must make available our manufacturing facilities and records for periodic unannounced inspections by governmental agencies, including the FDA, state authorities and comparable agencies in other countries. If we fail a Quality System inspection, our operations could be disrupted and our manufacturing interrupted. Failure to take adequate corrective action in response to an adverse Quality System inspection could result in, among other things, a shut-down of our manufacturing operations, significant fines, suspension of marketing clearances and approvals, seizures or recalls, operating restrictions and criminal prosecutions, any of which would cause our business to suffer. Furthermore, our key component suppliers may not currently be or may not continue to be in compliance with applicable regulatory requirements, which may result in manufacturing delays and cause our revenues to decline.

We have registered with the FDA as a medical device manufacturer and have obtained a manufacturing license from the California Department of Health Services, or CDHS. The FDA has broad post-market and regulatory enforcement powers. We are subject to unannounced inspections by the FDA and the Food and Drug Branch of CDHS to determine our compliance with the QSR and other regulations, and these inspections may include the manufacturing facilities of our suppliers. If the FDA or CDHS inspect our facility and discover compliance problems, we may have to shut down our facility and cease manufacturing until we can take the appropriate remedial steps to correct the audit findings. Taking corrective action may be expensive, time consuming and a distraction for management and if we experience a shutdown or delay at our manufacturing facility we may be unable to produce our products, which may have an adverse impact on our business.

***The requirements to obtain regulatory approval of the FDA and regulators in other jurisdictions can be costly, time-consuming, and unpredictable. If we are unable to obtain timely regulatory approval for our therapeutic candidates, our business may be substantially harmed.***

The regulatory approval process is expensive and the time and resources required to obtain approval from the FDA or other regulatory authorities in other jurisdictions to sell any therapeutic candidate or product is uncertain and approval may take years. Whether regulatory approval will be granted is unpredictable and depends upon numerous factors, including the discretion of the regulatory authorities. For example, governing legislation, approval policies, regulations, regulatory policies, or the type and amount of preclinical and clinical data necessary to gain approval may change during the course of a therapeutic candidate's clinical development and may vary among jurisdictions. It is possible that none of our existing or future therapeutic candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval.

Further, regulatory requirements governing cell-based therapy products in particular have changed frequently and may continue to change in the future. For example, in November 2014, Japan's parliament enacted new legislation to promote the safe and accelerated development of treatments using stem cells. The new Pharmaceuticals, Medical Devices and Other Therapeutic Products Act, or PMDA Act, establishes a framework for expedited approval in Japan for regenerative medical products. As this is a new regulation, it is not clear yet what impact it will have on the operation of our business. Any regulatory review committees and advisory groups and any contemplated new guidelines may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our therapeutic candidates or products or lead to significant post-approval limitations or restrictions. As we advance our therapeutic candidates or products, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our therapeutic candidates or products. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a therapeutic candidate or product to market could decrease our ability to generate sufficient revenue to maintain our business.

Our therapeutic candidates could fail to receive regulatory approval for many reasons, including the following:

- we may be unable to successfully complete our ongoing and future clinical trials of therapeutic candidates;
- we may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a therapeutic candidate is safe, pure, and potent for any or all of a therapeutic candidate's proposed indications;
- we may be unable to demonstrate that a therapeutic candidate's benefits outweigh the risk associated with the therapeutic candidate;
- the FDA or other regulatory authorities may disagree with the design or implementation of our clinical trials;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or other regulatory authorities for approval;
- the FDA or other regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- a decision by the FDA, other regulatory authorities or us to suspend or terminate a clinical trial at any time;
- the data collected from clinical trials of our therapeutic candidates may be inconclusive or may not be sufficient to obtain regulatory approval in the United States or elsewhere;
- the inability to obtain sufficient quantities of the therapeutic candidates for use in clinical trials;
- our third party manufacturers of supplies needed for manufacturing therapeutic candidates may fail to satisfy FDA or other regulatory requirements and may not pass inspections that may be required by FDA or other regulatory authorities;
- the failure to comply with applicable regulatory requirements following approval of any of our therapeutic candidates may result in the refusal by the FDA or similar foreign regulatory agency to approve a pending PMA or a biologics license application, or BLA, or supplement to a PMA or BLA submitted by us for other indications or new therapeutic candidates or products; and



the approval policies or regulations of the FDA or other regulatory authorities outside of the United States may significantly change in a manner rendering our clinical data insufficient for approval.

We may gain regulatory approval for any of our therapeutic candidates in some but not all of the territories available and any future approvals may be for some but not all of the target indications, limiting their commercial potential. Regulatory requirements and timing of product approvals vary from country to country and some jurisdictions may require additional testing beyond what is required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. In addition, regulatory approval does not specify pricing or reimbursement which may not match our expectations based on the results of our clinical data.

***Even if we obtain and maintain approval for our therapeutic candidates or products from the FDA, we may never obtain approval for our therapeutic candidates or products outside of the United States, which would limit our market opportunities and adversely affect our business.***

Approval in the United States by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our therapeutic candidates or products, if approved, outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval.

Even if the FDA grants marketing approval, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a therapeutic candidate or product must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge, if approved, is also subject to approval. While we may decide to submit a request to the EMA for approval of our therapeutic candidates, including CardiAMP, as Advanced Therapeutic Medicinal Products, or ATMPs, in Europe, obtaining such approval is a lengthy and expensive process and the EMA has its own procedures for approval. Even if a therapeutic candidate or product is approved, the FDA or the EMA, as the case may be, may limit the indications for which it may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of therapeutic candidates or products with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval may be withdrawn. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our therapeutic candidates or products will be harmed and our business will be adversely affected.

***We may face competition from biosimilars due to changes in the regulatory environment.***

We may face competition for CardiALLO from biosimilars due to the changing regulatory environment. In the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be “highly similar,” or biosimilar to, or “interchangeable” with an FDA-approved innovator (original) biological product. This new pathway could allow competitors to reference data from innovator biological products already approved after 12 years from the time of approval. In his proposed budget for fiscal years 2014 and 2015, President Obama proposed to cut-down this 12-year period of exclusivity to seven years. The President has also proposed to prohibit additional periods of exclusivity due to minor changes in product

formulations, a practice often referred to as “evergreening.” In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data from biological products already approved, but will not be able to get on the market until 10 years after the time of approval. This 10-year period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with CardiALLO, if approved. Additionally, the FDA may approve our competitors’ products through a PMA pathway, similar to CardiAMP. If competitors are able to obtain marketing approval for biosimilars referencing CardiALLO, if approved, it may become subject to competition from such biosimilars with the attendant competitive pressure and consequences.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations may also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. We do not currently carry biological or hazardous waste insurance coverage.

Although we maintain workers’ compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities.



***We are subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act.***

Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse will be applicable to our business. Healthcare fraud and abuse regulations are complex and can be subject to varying interpretations as to whether or not a statute has been violated. The laws that may affect our ability to operate include:

the federal Anti-Kickback Statute which prohibits, among other things, the knowing and willful payment of remuneration to induce or reward patient referrals or the generation of business involving any item or service which may be payable by the federal health care programs (*e.g.*, drugs, supplies, or health care services for Medicare or Medicaid patients);

- the federal False Claims Act which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment for government funds (*e.g.*, payment from Medicare or Medicaid) or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim for government funds;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HIPAA imposes civil and criminal liability for the wrongful access or disclosure of protected health information;

the federal Physician Payments Sunshine Act, created under Section 6002 of the Patient Protection and Affordable Care Act, as amended, the ACA, requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, those physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members;

- the federal Food, Drug and Cosmetic Act which prohibits, among other things, the adulteration or misbranding of drugs and devices;

the U.S. Foreign Corrupt Practices Act which prohibits corrupt payments, gifts or transfers of value to non-U.S. officials; and

non-U.S. and U.S. state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

The federal fraud and abuse laws have been interpreted to apply to arrangements between medical device and pharmaceutical manufacturers and a variety of health care professional. Although the federal Anti-Kickback Statute has several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, all elements of the potentially applicable exemption or safe harbor must be met in order for the arrangement to be protected, and prosecutors have interpreted the federal healthcare fraud statutes to attack a wide range of conduct by medical device and pharmaceutical companies. In addition, most states have statutes or regulations similar to the federal anti-kickback and federal false claims laws, which apply to items and services covered by Medicaid and other state programs, or, in several states, apply regardless of the payor. Administrative, civil and criminal sanctions may be imposed under these federal and state laws.

Further, the ACA, among other things, amended the intent standard under the Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA makes clear that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the federal False Claims Act. Any violations of these laws, or any action against us for violation of these laws, even if we successfully defend against it, could result in a material adverse effect on our reputation, business, results of operations and financial condition.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could harm our ability to operate our business and our results of operations. In addition, the clearance or approval and commercialization of any of our products outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

***A failure to adequately protect private health information could result in severe harm to our reputation and subject us to significant liabilities, each of which could have a material adverse effect on our business.***

Throughout the clinical trial process, we may obtain the private health information of our trial subjects. There are a number of state, federal and international laws protecting the privacy and security of health information and personal data. As part of the American Recovery and Reinvestment Act of 2009, or ARRA, Congress amended the privacy and security provisions of HIPAA. HIPAA imposes limitations on the use and disclosure of an individual's healthcare information by healthcare providers conducting certain electronic transactions, healthcare clearinghouses, and health insurance plans, collectively referred to as covered entities. The HIPAA amendments also impose compliance obligations and corresponding penalties for non-compliance on certain individuals and entities that provide services to or perform certain functions on behalf of healthcare providers and other covered entities involving the use or disclosure of individually identifiable health information, collectively referred to as business associates. ARRA also made significant increases in the penalties for improper use or disclosure of an individual's health information under HIPAA and extended enforcement authority to state attorneys general. The amendments also create notification requirements to federal regulators, and in some cases local and national media, for individuals whose health information has been inappropriately accessed or disclosed. Notification is not required under HIPAA if the health information that is improperly used or disclosed is deemed secured in accordance with certain encryption or other standards developed by the U.S. Department of Health and Human Services, or HHS. Most states have laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. Many state laws impose significant data security requirements, such as encryption or mandatory contractual terms to ensure ongoing protection of personal information. Activities outside of the United States implicate local and national data protection standards, impose

additional compliance requirements and generate additional risks of enforcement for noncompliance. The European Union's Data Protection Directive, Canada's Personal Information Protection and Electronic Documents Act and other data protection, privacy and similar national, state/provincial and local laws may also restrict the access, use and disclosure of patient health information abroad. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws, to protect against security breaches and hackers or to alleviate problems caused by such breaches.



***A recall of any of our commercialized products, or the discovery of serious safety issues, could have a significant negative impact on us.***

The FDA and other relevant regulatory agencies have the authority to require or request the recall in the event of material deficiencies or defects in design or manufacture or in the event an unacceptable risk to health. Manufacturers may, under their own initiative, also initiate a recall. A government-mandated or voluntary recall could occur as a result of an unacceptable risk to health, component failures, manufacturing errors, design or labeling defects or other deficiencies and issues. Recalls would divert managerial and financial resources and have an adverse effect on our reputation, financial condition and operating results.

Further, under the FDA's reporting regulations, we are required to report to the FDA any event that reasonably suggests that our products may have caused or contributed to a death or serious injury or in which our product malfunctioned and, if the malfunction of the same or similar product marketed by us were to recur, would likely cause or contribute to death or serious injury. The FDA also requires reporting of serious, life-threatening, unexpected and other adverse experiences and the submission of periodic safety reports and other information. Malfunctions or other adverse event reports may result in a voluntary or involuntary recall and other adverse actions, which could divert managerial and financial resources, impair our ability to manufacture in a cost-effective and timely manner and have an adverse effect on our reputation, financial condition and operating results. Similar reporting requirements exist in Europe and other jurisdictions.

Any adverse event involving our products could result in future voluntary corrective actions, such as recalls or customer notifications, or regulatory agency action, which could include inspection, mandatory recall or other enforcement action. Any corrective action, whether voluntary or involuntary, will require the dedication of our time and capital, distract management from operating our business and may harm our reputation and financial results. For example, in 2014 we notified the FDA that we were going to initiate a voluntary recall of our Morph AccessPro product, which has been completed to the FDA's satisfaction, and in 2017 we updated our instructions for use for the Helix and Morph catheter products. There can be no guarantee that we will not experience similar product recalls or changes in the future with these products or our other products or therapeutic candidates, if approved.

***Modifications to our products may require reclassifications, new regulatory approvals or clearances, or may require us to cease marketing or recall the modified products until new CE marking is obtained.***

Currently there are six Morph product family model numbers approved for commercial use in the United States via a 510(k) clearance and three in Europe under CE Mark. A modification to these products could lead to a reclassification and could result in further requirements (including additional clinical trials) to maintain the each respective clearance or approval. If we fail to comply with such further requirements we may be required to cease marketing or to recall the modified product until we obtain clearance or approval, and we may be subject to significant regulatory fines or penalties.

***The financial performance of our enabling and delivery products may be adversely affected by medical device tax provisions in the healthcare reform laws in the United States.***

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act, imposes, among other things, an annual excise tax of 2.3% on any entity that manufactures or imports medical devices offered for sale in the United States beginning with tax year 2013. Under these provisions, the Congressional Research Service predicts that the total cost to the medical device industry may be up to \$20 billion over the next decade. On December 18, 2015, President Obama signed into law the Consolidated Appropriations Act, 2016 (H.R. 2029), which includes a two-year moratorium on the medical device excise tax. It amends section 4191 of the Internal Revenue Code to exempt medical device sales during the period of January 1, 2016 to December 31, 2017. Absent further legislative action, the tax will be automatically reinstated for medical device sales starting on January 1, 2018. The financial impact this tax may have on our business is unclear and there can be no assurance that our business will not be materially adversely affected by it.

***We work with outside scientists and their institutions in developing therapeutic candidates and products. These scientists may have other commitments or conflicts of interest, which could limit our access to their expertise.***

We work with scientific advisors and collaborators at academic research institutions in connection with our development programs. These scientific advisors serve as our link to the specific pools of trial participants we are targeting in that these advisors may:

- identify individuals as potential candidates for study;
- obtain their consent to participate in our research;
- perform medical examinations and gather medical histories;
- conduct the initial analysis of suitability of the individuals to participate in our research based on the foregoing; and
- collect data and biological samples from trial participants periodically in accordance with our study protocols.

These scientists and collaborators are not our employees, rather they serve as either independent contractors or the primary investigators under research collaboration agreements that we have with their sponsoring academic or research institution. Such scientists and collaborators may have other commitments that would limit their availability to us. Although our scientific advisors generally agree not to do competing work, if an actual or potential conflict of interest between their work for us and their work for another entity arises, we may lose their services. It is also possible that some of our valuable proprietary knowledge may become publicly known through these scientific advisors if they breach their confidentiality agreements with us, which would cause competitive harm to our business.

***The use, misuse or off-label use of our products or therapies, if approved, may result in injuries that lead to product liability suits, which could be costly to our business.***

We are not permitted to make claims about the use of our marketed products and will not be permitted to make claims about the use of our therapeutic candidates, if approved, outside of their approved indications. Further, we are not and will not be able to proactively discuss or provide information on off-label uses of such products, with very specific and limited exceptions. However, we cannot prevent a physician from using our products or therapeutic candidates, if approved, for off-label applications. Off-label use of our products or therapies, if approved, is more likely to result in complications that have serious consequences. Product liability claims are especially prevalent in our industry and could harm our reputation, divert management's attention from our core business, be expensive to defend and may

result in sizable damage awards against us. Although we maintain product liability insurance, the amount or breadth of our coverage may not be adequate for the claims that may be made against us. In addition, failure to follow FDA rules and guidelines relating to promotion and advertising can result in, among other things, the FDA's refusal to approve a product or therapeutic candidate, the suspension or withdrawal of an approved product or therapy from the market, product recalls, fines, disgorgement of money, operating restrictions, injunctions or criminal prosecutions.

***Our employees, principal investigators, consultants and collaboration partners may engage in misconduct or other improper activities, including noncompliance with laws and regulatory standards and requirements and insider trading.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of activity relating to pricing, discounting, marketing and promotion, sales commissions, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation, or a breach of insider trading laws. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our therapeutic candidates, if approved, we may be unable to generate any revenues.***

We currently have a limited organization for the sales, marketing and distribution of products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, including CardiAMP and CardiALLO, we must build our sales, distribution, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We have limited prior experience in the marketing, sale or distribution of approved products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our therapeutic candidates.

Our strategy is to obtain FDA approval and market CardiAMP for potential heart failure indications using a dedicated direct sales model focused on selected cardiologists and heart failure specialists. We may in the future, choose to align ourselves with collaborators as part of our commercialization strategy, particularly outside of the United States, and our future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our therapeutic candidates or companion diagnostic or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our therapeutic candidates and

companion diagnostic to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our therapeutic candidates or companion diagnostic, our ability to generate revenues from product sales, including sales of CardiAMP and CardiALLO, will be adversely affected.

Building an internal sales force involves many challenges, including:

- recruiting and retaining talented people;
- training employees that we recruit;
- setting the appropriate system of incentives;
- managing additional headcount; and
- integrating a new business unit into an existing corporate architecture.

If we are unable to build our own sales force or negotiate a strategic partnership for the commercialization of CardiAMP or CardiALLO in the United States, we may be forced to delay the potential commercialization of CardiAMP or CardiALLO or reduce the scope of our sales and marketing activities for CardiAMP or CardiALLO. To fund commercialization activities we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring CardiAMP or CardiALLO to market or generate product revenue.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

In addition, there are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any launch. If the commercial launch of a therapeutic candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

***We have limited experience manufacturing our therapeutic candidates or products in commercial quantities, which could harm our business.***

Because we have only limited experience in manufacturing therapeutic candidates or products in commercial quantities, we may encounter production delays or shortfalls. Such production delays or shortfalls may be caused by many factors, including the following:

- we intend to significantly expand our manufacturing capacity, and our production processes may have to change to accommodate this growth;

- key components and sub-assemblies of our products and therapeutic candidates are currently provided by a single supplier or limited number of suppliers, and we do not maintain large inventory levels of these components and sub-assemblies; if we experience a shortage in any of these components or sub-assemblies, we would need to identify and qualify new supply sources, which could increase our expenses and result in manufacturing delays;

- we may experience a delay in completing validation and verification testing for new controlled-environment rooms at our manufacturing facilities;

- we have limited experience in complying with FDA's QSRs, which applies to the manufacture of our products and therapeutic candidates; and

- to increase our manufacturing output significantly, we will have to attract and retain qualified employees, who are in short supply, for our manufacturing operations.

If we are unable to keep up with demand for our products, our revenues could be impaired, market acceptance for our products could be harmed and our customers might instead purchase our competitors' products. Our inability to successfully manufacture our products would materially harm our business.

***If we fail to obtain and sustain an adequate level of reimbursement for our products by third-party payors, sales and profitability would be adversely affected.***

Our ability to commercialize any therapeutic candidates or products successfully will depend, in part, on the extent to which coverage and reimbursement for our therapeutic candidates or products and related treatments will be available from government healthcare programs, private health insurers, managed care plans, and other organizations. Additionally, even if there is a commercially viable market, if the level of third-party reimbursement is below our expectations, our revenue and profitability could be materially and adversely affected.



Third-party payors, such as government programs, including Medicare in the United States, or private healthcare insurers, carefully review and increasingly question the coverage of, and challenge the prices charged for medical products and services, and many third-party payors limit coverage of or reimbursement for newly approved therapies or products. Reimbursement rates and coverage from private health insurance companies vary depending on the company, the insurance plan and other factors. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our therapeutic candidates to each private health insurance company separately, with no assurance that adequate coverage and reimbursement will be obtained.

A current trend in the U.S. healthcare industry as well as in other countries around the world is toward cost containment, including a number of legislative and regulatory changes to the health care system that could impact our ability to sell our approved therapies or products profitably. In particular, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 revised the payment methodology for many products under Medicare in the United States, which has resulted in lower rates of reimbursement. In 2010, the Affordable Care Act was enacted. This expansion in the government's role in the U.S. healthcare industry may further lower rates of reimbursement.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare payment reductions went into effect. The ATRA also, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

In Europe, the European Commission has submitted a Proposal for a Regulation of the European Parliament and the Council on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009, to replace, inter alia, Directive 93/42/EEC and to amend regulations regarding medical devices in the European Union, which could result in changes in the regulatory requirements for medical devices in Europe.

Large public and 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. In particular, third-party payors may limit the covered indications. Cost-control initiatives could decrease the price we might establish, which could result in revenue and profitability being lower than anticipated.

There may be significant delays in obtaining coverage and reimbursement for newly approved therapies or products, and coverage may be more limited than the purposes for which the therapy or product is approved by the FDA or other regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a therapy or product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels, if applicable, may also be insufficient to cover our and any partner's costs and may not be made permanent. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved therapies or products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize therapies or products and our overall financial condition.

Furthermore, reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. In many countries, therapies or products cannot be commercially launched until reimbursement is approved and the negotiation process in some countries can exceed 12 months. In addition, pricing and reimbursement decisions in certain countries can be affected by decisions taken in other countries, which can lead to mandatory price reductions and/or additional reimbursement restrictions across a number of other countries, which may thereby adversely affect our sales and profitability. In the event that countries impose prices which are not sufficient to allow us to generate a profit, this would adversely affect sales and profitability.

***Price controls may be imposed in foreign markets, which may adversely affect our future profitability.***

In some countries, particularly European Union member states, Japan, Australia and Canada, the pricing of therapies and products is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapy or product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partners may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our therapies or products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, revenues or profitability could be adversely affected.

***If the market opportunities for our therapeutic candidates or products are smaller than we believe they are, our revenues may be adversely affected and our business may suffer.***

It is very difficult to estimate the future commercial potential of CardiAMP, CardiALLO and our commercialized products due to factors such as safety and efficacy compared to other available treatments, changing standards of care, third-party payor reimbursement standards, patient and physician preferences, and the availability of competitive alternatives that may emerge. We believe that approximately 70% of the NYHA Class II and Class III ischemic heart failure patients in the United States will be eligible for CardiAMP due to a sufficient CardiAMP potency assay score. However, if considerably less than approximately 70% of NYHA Class II and Class III ischemic heart failure patients are eligible for CardiAMP due to an insufficient CardiAMP potency assay score, it would significantly and negatively impact our business, financial condition and results of operations.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our therapeutic candidates or products.***

We face an inherent risk of product liability as a result of the human clinical use of our therapeutic candidates and products and will face an even greater risk if we continue to commercialize our therapeutic candidates and products. For example, we may be sued if any therapy or product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of inherent dangers, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to

limit commercialization. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand, even if such products or therapies are approved;

- injury to our reputation;

- withdrawal of clinical trial participants;

- costs to defend the related litigations;

- a diversion of management's time and our resources;

- substantial monetary awards to trial participants or patients;

- recalls, withdrawals, or labeling, marketing or promotional restrictions;
- increased cost of liability insurance;
- loss of revenue;
- the inability to receive regulatory approvals or commercialize our approved products or therapies; and
- a decline in our share price.

Although we maintain product liability insurance with coverage that we believe is consistent with industry norms for companies at our stage of development, the amount or breadth of our coverage may not be adequate for the claims that may be made against us. Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products or therapies we develop. Additionally, our insurance policies have various exclusions, and we may be subject to a product liability claim for which we have no coverage or reduced coverage. Any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

***Our business and operations would suffer in the event of system failures.***

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants and potential collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. For example, our systems have been impacted by computer viruses in the past, and while we have not experienced any material system failure, accident or security breach that has resulted in lasting impacts to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for manufacturing our therapeutic candidates and conducting clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our therapeutic candidates could be delayed.

***Interruptions in supply or inventory loss may adversely affect our operating results and financial condition.***

Our therapeutic candidates and products are manufactured and distributed using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes, as well as strict company and government standards for manufacture and storage, subjects us to production risks. While batches released for use in clinical trials or for commercialization undergo sample testing, some defects may only be identified following release. In addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and delays of new product or therapy launches. Any supply interruption or the loss thereof could hinder our ability to timely distribute our approved products and satisfy demand. Any unforeseen storage failure or loss in supply could delay our clinical trials and, if our therapeutic candidates are approved, result in a loss of our market share and negatively affect our revenues and operations.

***We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. A majority of our management operates in our principal executive offices located in San Carlos, California and we currently manufacture our Helix and Morph products at this facility and use it for storage of our clinical trial materials. If our San Carlos offices were affected by a natural or man-made disaster, particularly those that are characteristic of the region, such as wildfires and earthquakes, or other business interruption, our ability to manage our domestic and foreign operations could be impaired, which could materially and adversely affect our results of operations and financial condition. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. The ultimate impact of any such events on us, our significant suppliers and our general infrastructure is unknown.

### **Risks Related to our Intellectual Property**

***We may not be able to protect our proprietary technology in the marketplace.***

Our success will depend, in part, on our ability to obtain patents, protect our trade secrets and operate without infringing on the proprietary rights of others. We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property of our therapeutic candidates and products. Patents might not be issued or granted with respect to our patent applications that are currently pending, and issued or granted patents might later be found to be invalid or unenforceable, be interpreted in a manner that does not adequately protect our current therapeutic candidates or products or any future therapeutic candidates or products, or fail to otherwise provide us with any competitive advantage. As such, we do not know the degree of future protection that we will have on our therapeutic candidates or products and technology, if any, and a failure to obtain adequate intellectual property protection with respect to our therapeutic candidates or products could have a material adverse impact on our business.

Filing, prosecuting and defending patents throughout the world would be prohibitively expensive, so our policy is to patent technology in jurisdictions with significant or otherwise relevant commercial opportunities or activities. However, patent protection may not be available for some of the therapeutic candidates or products we are developing. If we must spend significant time and money protecting or enforcing our patents, designing around

patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business, results of operations and financial condition may be harmed.

***The patent protection of biotherapeutics is complex and uncertain.***

The scope and extent of patent protection for our therapeutic candidates and products are particularly uncertain. To date, our principal therapeutic candidates have been based on specific subpopulations of known and naturally occurring adult stem cells. We anticipate that the therapeutic candidates or products we develop in the future will continue to include or be based on the same or other naturally occurring stem cells or derivatives or products thereof. Although we have sought and expect to continue to seek patent protection for our therapeutic candidates and products, their methods of use, methods of manufacture, and methods of delivery, any or all of them may not be subject to effective patent protection. Publication of information related to our therapeutic candidates and products by us or others may prevent us from obtaining or enforcing patents relating to these products and therapeutic candidates. Furthermore, others may independently develop similar therapeutic candidates or products, may duplicate our therapeutic candidates or products, or may design around our patent rights. In addition, any of our issued patents may be declared invalid. If we fail to adequately protect our intellectual property, we may face competition from companies who attempt to create a generic therapeutic candidate or product to compete with our therapeutic candidates or products.



Filing, prosecuting and defending patents on therapeutic candidates or products in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own therapeutic candidates or products and further, may export otherwise infringing therapeutic candidates or products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These therapeutic candidates or products may compete with our current or future therapeutic candidates or products, if any, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing therapeutic candidates or products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.***

We maintain certain of our proprietary know-how and technological advances as trade secrets, especially where we do not believe patent protection is appropriate or obtainable, including, but not exclusively, with respect to certain aspects of the manufacturing of our therapeutic candidates or products. However, trade secrets are difficult to protect. We take a number of measures to protect our trade secrets including, limiting disclosure, physical security and confidentiality and non-disclosure agreements. We enter into confidentiality agreements with our employees, consultants, outside scientific collaborators, contract manufacturing partners, sponsored researchers and other advisors and third parties to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection, or failure to adequately protect our intellectual property could enable competitors to develop generic products or use our proprietary information to develop other therapeutic candidates or products that compete with our therapeutic candidates or products or cause additional, material adverse effects upon our business, results of operations and financial condition.

***We may be forced to litigate to enforce or defend our intellectual property rights, and/or the intellectual property rights of our licensors.***

We may be forced to litigate to enforce or defend our intellectual property rights against infringement by competitors, and to protect our trade secrets against unauthorized use. In so doing, we may place our intellectual property at risk of being invalidated, unenforceable, or limited or narrowed in scope and may no longer be used to prevent the manufacture and sale of competitive product. Further, an adverse result in any litigation or other proceedings before government agencies such as the United States Patent and Trademark Office, or the USPTO, may place pending applications at risk of non-issuance. Further, interference proceedings, derivation proceedings, entitlement proceedings, ex parte reexamination, inter partes reexamination, inter partes review, post-grant review, and opposition proceedings provoked by third parties or brought by the USPTO or any foreign patent authority may be used to challenge inventorship, ownership, claim scope, or validity of our patent applications. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential and proprietary information could be compromised by disclosure during this type of litigation.

***Intellectual property disputes could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and/or management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of litigation proceedings more effectively than we can because of their greater financial resources and personnel. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct our clinical trials, continue our internal research programs, in-license needed technology or enter into strategic collaborations that would help us bring our therapeutic candidates to market. As a result, uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

***Patent reform legislation and recent court decisions could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.***

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO has and continues to develop and implement regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act. The full effect of these changes are currently unclear as the USPTO has not yet adopted all pertinent final rules and regulations, the courts have yet to address these provisions and the applicability of the Leahy-Smith Act and new regulations on specific patents, including our patents discussed herein, have not been determined and would need to be reviewed. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. As a result, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, all of which could have a material adverse effect on our business and financial condition.

On June 13, 2013, the U.S. Supreme Court decision in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, held that isolated DNA sequences are not patentable because they constitute a product of nature. The Supreme Court did not address stem cells in particular, and as a result, it is not yet clear what, if any, impact this recent Supreme Court decision or future decisions will have on the operation of our business.

***If third parties claim that our therapeutic candidates or other products infringe upon their intellectual property, commercialization of our therapeutic candidates or products and our operating profits could be adversely affected.***

There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry. We may, from time to time, be notified of claims that we are infringing upon patents, trademarks, copyrights, or other intellectual property rights owned by third parties, and we cannot provide assurances that other companies will not, in the future, pursue such infringement claims against us or any third-party proprietary technologies we have licensed. Any such claims could also be expensive and time consuming to defend and divert management's attention and resources, and could delay or prevent us from commercializing our therapeutic candidates or products. Our competitive position could suffer as a result. Although we have reviewed certain third-party patents and patent filings that we believe may be relevant to our therapeutic candidates or products, we have not conducted a freedom-to-operate search or analysis for our therapeutic candidates or products, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our therapeutic candidates or products. Thus, we cannot guarantee that our therapeutic candidates or products, or our commercialization thereof, do not and will not infringe any third party's intellectual property.

From time to time, we have reviewed the claims of specific patents owned by third parties. While we have concluded that no claims of any of these patents would be infringed by our products, that all relevant claims would expire before our products would be commercialized, or both, we cannot guarantee that the patent owners would not disagree and conclude that our products would infringe these claims.

***If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity of our therapeutic candidates or products, our business may be materially harmed.***

Depending on the timing, duration and specifics of FDA marketing approval of our therapeutic candidates or products, if any, one of the U.S. patents covering each of such approved therapeutic candidate or product or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our therapeutic candidates, including by the EMA in the European Union or the Pharmaceutical and Medical Devices Agency in Japan. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. In addition, if a patent we wish to extend is owned by another party and licensed to us, we may need to obtain approval and cooperation from our licensor to request the extension.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our therapeutic candidates or products will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties for manufacturing, and because we collaborate with various organizations and academic institutions on the advancement of our clinical trials, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our

trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

## Risks Related to Our Common Stock

*There is not now, and there may never be, an active, liquid and orderly trading market for our Common Stock, which may make it difficult to sell shares of our Common Stock.*

Our Common Stock is quoted on the OTC Markets Group Inc.'s over-the-counter inter-dealer quotation system, known as OTC Markets, and there is not any significant trading activity in our Common Stock or a market for shares of our Common Stock, and an active trading market for our shares may never develop or be sustained. As a result, investors in our Common Stock must bear the economic risk of holding those shares for an indefinite period of time. We do not now, and may not in the future, meet the initial listing standards of any national securities exchange, and our Common Stock may be quoted on the OTC Market's or another over-the-counter quotation system for the foreseeable future. In these marketplaces, our stockholders may find it difficult to obtain accurate quotations as to the market value of their shares of our Common Stock, and may find few buyers to purchase their stock and few market makers to support its price. As a result of these and other factors, investors may be unable to resell shares of our Common Stock at or above the price for which they purchased them, at or near quoted bid prices, or at all. Further, an inactive market may also impair our ability to raise capital by selling additional equity in the future, and may impair our ability to enter into strategic partnerships or acquire companies or products by using shares of our Common Stock as consideration.

*The market price and trading volume of our Common Stock may be volatile and may be affected by economic conditions beyond our control.*

The market price of our Common Stock is likely to be volatile. Some specific factors that could negatively affect the price of our Common Stock or result in fluctuations in its price and trading volume include:

- results of clinical trials of our therapeutic candidates;
- results of clinical trials of our competitors' products;
- regulatory actions with respect to our therapeutic candidates or products or our competitors' products;
- actual or anticipated fluctuations in our quarterly operating results or those of our competitors;

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publication of research reports by securities analysts about us or our competitors in the industry;

our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;

issuances by us of debt or equity securities;

litigation involving our company, including: stockholder litigation; investigations or audits by regulators into the operations of our company; or proceedings initiated by our competitors or clients;

strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;

the passage of legislation or other regulatory developments affecting us or our industry; fluctuations in the valuation of companies perceived by investors to be comparable to us;

trading volume of our Common Stock;

sales or perceived potential sales of our Common Stock by us, our directors, senior management or our stockholders in the future;



- short selling or other market manipulation activities;
- announcement or expectation of additional financing efforts;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities;
- changes in market conditions for biopharmaceutical stocks; and
- conditions in the U.S. financial markets or changes in general economic conditions.

***Our Common Stock may be subject to the “penny stock” rules of the SEC, and the trading market in our Common Stock is limited, which makes transactions cumbersome and may reduce the value of an investment in the stock.***

Rule 15c-9 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, establishes the definition of a “penny stock,” for the purposes relevant to us, as any equity security that has a market price of less than \$5.00 per share or with an exercise price of less than \$5.00 per share, subject to certain exceptions. For any transaction involving a penny stock, unless exempt, the rules require: (i) that a broker or dealer approve a person’s account for transactions in penny stocks in accordance with the provisions of Rule 15c-9; and (ii) the broker or dealer receive from the investor a written agreement to the transaction, setting forth the identity and quantity of the penny stock to be purchased, provided that any such purchase shall not be effected less than two business days after the broker or dealer sends such written agreement to the investor.

In order to approve a person’s account for transactions in penny stocks, the broker or dealer must: (i) obtain financial information, investment experience and investment objectives of the person; and (ii) make a reasonable determination that the transactions in penny stocks are suitable for that person and the person has sufficient knowledge and experience in financial matters to be reasonably expected to be capable of evaluating the risks of transactions in penny stocks.

The broker or dealer must also deliver, prior to any transaction in a penny stock, a disclosure schedule prescribed by the SEC relating to the penny stock market, which: (i) sets forth the basis on which the broker or dealer made the suitability determination; and (ii) in highlight form, confirms that the broker or dealer received a signed, written agreement from the investor prior to the transaction. Generally, brokers may be less willing to execute transactions in securities subject to the “penny stock” rules. This may make it more difficult for investors to dispose of our Common Stock and cause a decline in the market value of our Common Stock.

Disclosure also has to be made about the risks of investing in penny stocks in both public offerings and in secondary trading, the commissions payable to both the broker or dealer and the registered representative, current quotations for the securities and the rights and remedies available to an investor in cases of fraud in penny stock transactions. Finally, monthly statements must be sent disclosing recent price information for the penny stock held in the account and information regarding the limited market in penny stocks. As a result, it may be more difficult to execute trades of our Common Stock which may have an adverse effect on the liquidity of our Common Stock.

***If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.***

The trading market for our Common Stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

***Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.***

Our executive officers, directors, 5% stockholders and their affiliates beneficially own approximately 58.4% of our voting stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our Common Stock that you may believe are in your best interest as one of our stockholders.

***We have identified a material weakness in our internal control over financial reporting. If our remediation of this material weakness is not effective, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our Common Stock.***

Prior to the Merger, BioCardia Lifesciences, the accounting acquirer, was a private company with limited accounting personnel and systems to adequately execute accounting processes and other supervisory resources with which to address internal control over financial reporting. As a result of the Merger, the accounting personnel and systems of BioCardia Lifesciences became our accounting personnel and systems. In connection with the audit of our financial statements as of and for the years ended December 31, 2016 and 2015, we identified a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. The material weakness related to an insufficient number of qualified personnel and inadequate processes within our accounting function impacting our ability to appropriately segregate duties and to perform timely and effective review over general ledger account reconciliations and non-routine transactions.

We are implementing measures designed to improve our internal control over financial reporting to remediate this material weakness, including the following:

- we are formalizing our processes and internal control documentation and strengthening supervisory reviews by our management; and

- we are in the process of adding additional qualified accounting personnel and segregating duties amongst accounting personnel.

We cannot provide assurance that the measures we have taken to date, and are continuing to implement, will be sufficient to remediate the material weakness we have identified or avoid potential future material weaknesses. If the steps we take do not correct the material weakness in a timely manner, we will be unable to conclude that we maintain effective internal control over financial reporting. Accordingly, there could continue to be a reasonable possibility that a material misstatement of our financial statements would not be prevented or detected on a timely basis.

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal controls. Section 404 of the Sarbanes-Oxley Act requires that we evaluate and determine the effectiveness of our internal control over financial reporting and provide a management report on internal control over financial reporting. The Sarbanes-Oxley Act also requires that our management report on internal control over financial reporting be attested to by our independent registered public accounting firm, to the extent we are no longer a “smaller reporting company,” as defined in the Exchange Act. We do not expect our independent registered public accounting firm to attest to our management report on internal control over financial reporting for so long as we are a smaller reporting company.

We are in the process of designing and implementing the internal control over financial reporting required to comply with this obligation. If we identify any additional material weaknesses in our internal control over financial reporting, if we are unable to comply with the requirements of Section 404 in a timely manner, if we are unable to assert that our internal control over financial reporting is effective, or when required in the future, if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our Common Stock could be adversely affected, and we could become subject to investigations by the stock exchange on which our securities are listed, the SEC, or other regulatory authorities, which could require additional financial and management resources.

***We may be exposed to additional risks as a result of our reverse merger transaction.***

We may be exposed to additional risks as a result of our “reverse merger” transaction and rules and regulations relating to shell companies or former shell companies. There has been increased focus in recent years by government agencies on transactions such as the reverse merger transaction, and we may be subject to increased scrutiny and/or restrictions by the SEC and other government agencies and holders of our securities as a result of the completion of that transaction. This may make it more difficult for us to obtain coverage from securities analysts of major brokerage firms. The occurrence of any such event could cause our business or stock price to suffer.

***Our annual and quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.***

We expect our operating results to be subject to annual and quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our therapeutic candidates, products or future development programs;

- if any of our therapeutic candidates receives regulatory approval, the level of underlying demand for these therapeutic candidates and wholesalers’ buying patterns;

- addition or termination of clinical trials or funding support;

- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;

any intellectual property infringement lawsuit in which we may become involved;

regulatory developments affecting our therapeutic candidates or products or those of our competitors;

the timing and cost of, and level of investment in, research and development activities relating to our therapeutic candidates, which may change from time to time;

our ability to attract, hire and retain qualified personnel;

expenditures that we will or may incur to acquire or develop additional therapeutic candidates and technologies;

future accounting pronouncements or changes in our accounting policies;

the timing and success or failure of clinical studies for our therapeutic candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;

the risk/benefit profile, cost and reimbursement policies with respect to our therapeutic candidates, if approved, and existing and potential future therapies or biologics that compete with our products or therapeutic candidates; and

the changing and volatile U.S., European and global economic environments.

If our annual or quarterly operating results fall below the expectations of investors or securities analysts, the price of our Common Stock could decline substantially. Furthermore, any annual or quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that annual and quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

***Raising additional funds through debt or equity financing could be dilutive and may cause the market price of our Common Stock to decline.***

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic collaborations or partnerships, or marketing, distribution or licensing arrangements with third parties, we may be required to limit valuable rights to our intellectual property, technologies, therapeutic candidates or future revenue streams, or grant licenses or other rights on terms that are not favorable to us. Furthermore, any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our therapeutic candidates.

*Sales of a substantial number of shares of our Common Stock in the public market could cause our stock price to fall.*

Sales of a substantial number of shares of our Common Stock in the public market or the perception that these sales might occur, could depress the market price of our Common Stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our Common Stock.

Stockholders holding 286,566,412 shares of our Common Stock entered into lock-up agreements in connection with the Merger that restrict the stockholders' ability to transfer shares of our Common Stock for twelve months from the effective date of the Merger, subject to certain exceptions. Subject to certain limitations, including sales volume limitations with respect to shares held by our affiliates, substantially all of our outstanding shares prior to the Merger will be eligible for sale upon expiration of the lock-up period. In addition, shares issued or issuable upon exercise of options vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by stockholders currently subject to lock-up agreements could have a material adverse effect on the trading price of our Common Stock.



***Future sales and issuances of our Common Stock or rights to purchase our Common Stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.***

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell our Common Stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell our Common Stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

***We are at risk of securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

***Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.***

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. The Merger, our prior equity offerings and other changes in our stock ownership may have resulted in ownership changes. We have not performed an analysis to assess whether an ownership change has occurred. If we have experienced an ownership change at any time since our formation, utilization of our net operating loss carryforwards would be subject to an annual limitation under Section 382 of the Code. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

*We do not intend to pay dividends on our Common Stock so any returns will be limited to the value of our stock.*

We have never declared or paid any cash dividends on our Common Stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

#### **ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

#### **ITEM 2. PROPERTIES**

Our principal executive office is located at 125 Shoreway Road, Suite B, San Carlos, CA 94070 in a facility we lease encompassing 13,718 square feet of office, lab, and manufacturing space. The lease for this facility was renewed in October 2016 and expires in 2021. We believe that our leased facilities are adequate to meet our current needs.

### **ITEM 3. LEGAL PROCEEDINGS**

The Company may be subject to various claims, complaints, and legal actions that arise from time to time in the normal course of business. Management does not believe that the Company is party to any currently pending legal proceedings. There can be no assurance that existing or future legal proceedings arising in the ordinary course of business or otherwise will not have a material adverse effect on the Company's business, financial position, results of operations, or cash flows.

### **ITEM 4. MINE SAFETY DISCLOSURES**

Not applicable.

**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES****Market Information**

Our common stock trades on the OTC Pink tier of OTC Markets Group, Inc. under the symbol "BCDA." The following table sets forth the quarterly high and low sales prices of our common stock for the fiscal years 2016 and 2015 and the 2017 first quarter through the date of the filing, as quoted on OTC Markets. This information represents prices between dealers and does not include retail mark-ups, markdowns or commissions and may not represent actual transactions.

<b><u>Fiscal Year 2017</u></b>	<b>High</b>	<b>Low</b>
First Quarter	\$1.24	\$0.40

<b><u>Fiscal Year 2016</u></b>	<b>High</b>	<b>Low</b>
First Quarter	\$0.11	\$0.07
Second Quarter	\$0.16	\$0.07
Third Quarter	\$0.18	\$0.11
Fourth Quarter	\$1.28	\$0.10

<b><u>Fiscal Year 2015</u></b>	<b>High</b>	<b>Low</b>
First Quarter	\$0.13	\$0.09
Second Quarter	\$0.11	\$0.09
Third Quarter	\$0.11	\$0.07
Fourth Quarter	\$0.08	\$0.05

As of March 24, 2017, there were approximately 302 holders of record of our common stock. Because many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

**Dividend Policy**

We have never declared or paid any cash dividend on our capital stock. We currently intend to retain any future earnings and do not expect to pay any dividends in the foreseeable future. Any determination to declare or pay dividends in the future will be at the discretion of our board of directors and will depend on a number of factors, including our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

#### **Sales of Unregistered Securities**

None.

## **Securities Authorized for Issuance Under Equity Compensation Plans**

The information required by this item is incorporated by reference to our Proxy Statement for our 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2016.

There were no repurchases of equity securities by us during the fourth quarter of 2016.

## **ITEM 6. SELECTED FINANCIAL DATA**

Not applicable.

## **ITEM 7. MANAGEMENT’S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains certain forward-looking statements that involve risk and uncertainties. Our actual results may differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those set forth under the Section entitled “Risk Factors” in Item 1A, and other documents we file with the Securities and Exchange Commission. Historical results are not necessarily indicative of future results.*

### **Special Note Regarding Smaller Reporting Company Status**

We are filing this Annual Report on Form 10-K as a “smaller reporting company” (as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended) based on our public float (the aggregate market value of our common equity held by non-affiliates of the Company) as of the last business day of our second fiscal quarter of 2016. As a result of being a smaller reporting company, we are allowed and have elected to omit certain information, including three years of year-to-year comparisons and tabular disclosure of contractual obligations, from this Management’s Discussion and Analysis of Financial Condition and Results of Operations; however, we have provided all information for the periods presented that we believe to be appropriate and necessary.



## Overview

We are a clinical-stage regenerative medicine company developing novel therapeutics for cardiovascular diseases with large unmet medical needs. Our lead therapeutic candidate is the CardiAMP Cell Therapy System, or CardiAMP. We have initiated our U.S. Food and Drug Administration, or FDA, accepted Phase III pivotal trial for CardiAMP in ischemic systolic heart failure, began treating patients in February 2017 and expect to obtain top-line data in 2019. If our Phase III pivotal trial is successful, we believe we will be the first company to reach the market with a cell-based therapy to treat heart failure. Our second therapeutic candidate is the CardiALLO Cell Therapy System, or CardiALLO. We anticipate preparation of an Investigational New Drug, or IND, application for submission to the FDA for a Phase II trial for CardiALLO for the treatment of ischemic systolic heart failure. This IND is expected to have improved Chemistry Manufacturing Controls, or CMC, in the IND relative to our previous co-sponsored investigations. We are committed to applying our expertise in the fields of autologous and allogeneic cell-based therapies to improve the lives of patients with cardiovascular conditions. Autologous cell therapies use autologous cells, which mean the patient's own cells, while allogeneic cell therapies use allogeneic cells, which means cells from a third party donor.

To date, we have devoted substantially all of our resources to research and development efforts relating to our therapeutic candidates and biotherapeutic delivery systems, including conducting clinical trials, developing manufacturing and sales capabilities, in-licensing related intellectual property, providing general and administrative support for these operations and protecting our intellectual property. We have also generated modest revenues from sales of our approved products. We have funded our operations primarily through the sales of equity and convertible debt securities, and certain government and private grants. All convertible debt securities were converted into shares of our Common Stock in connection with the Merger.

We have incurred net losses in each year since our inception. Our net losses were approximately \$10.3 million and \$6.7 million for the years ended December 31, 2016 and 2015, respectively. As of December 31, 2016, we had an accumulated deficit of approximately \$60.1 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs, clinical trials, intellectual property matters, building our manufacturing and sales capabilities, and from general and administrative costs associated with our operations.

We expect to continue to incur significant expenses and increasing losses for at least the next several years. Accordingly, we anticipate that we will need to raise additional capital prior to the commercialization of CardiAMP and CardiALLO. Until such time that we can generate meaningful revenue from product sales, if ever, we expect to finance our operating activities through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, our therapeutic candidates. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research and development programs or the commercialization of any approved therapies or products or be unable to expand our



operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations.

## **Recent Events**

On August 22, 2016, the Company, Icicle Acquisition Corp., a Delaware corporation and our direct wholly-owned subsidiary, and BioCardia Lifesciences, Inc. (at the time, named BioCardia, Inc.) entered into an Agreement and Plan of Merger, or the Merger Agreement. On October 24, 2016, pursuant to the Merger Agreement, Icicle Acquisition Corp. merged with and into BioCardia Lifesciences, with BioCardia Lifesciences continuing as the surviving company. BioCardia Lifesciences was determined to be the accounting acquirer, and following the completion of the Merger, we assumed the business and operations of BioCardia Lifesciences and changed our name to BioCardia, Inc.

Pursuant to the Merger Agreement, each of the shares of BioCardia Lifesciences common stock issued and outstanding prior to the Merger, including shares of common stock underlying outstanding preferred stock, convertible notes (which converted into common stock immediately prior to the Merger), and stock options were converted into the right to receive 19.3678009 shares of our common stock.

For financial reporting purposes, the Merger is accounted for as an asset acquisition rather than a business combination because the Company did not meet the definition of a business as defined by US GAAP in advance of the Merger. The fair value of the purchase consideration, consisting of Tiger X common stock, was determined based on the fair value of the cash acquired by BioCardia Lifesciences in the Merger of \$19 million, which is considered the best indicator for the fair value of the purchase consideration. No other assets or liabilities were acquired by BioCardia Lifesciences. Transaction costs of \$96,000 were recorded as a debit to additional paid in capital.

The Merger is considered a tax free reverse triangular merger for tax purposes pursuant to Internal Revenue Code Sections 368(a) and 368(a)(2)(E) in which the Company continues as the parent and BioCardia Lifesciences as the wholly owned subsidiary, and is therefore treated as an acquisition of stock of BioCardia Lifesciences by the Company. Despite the stock acquisition treatment, none of our pre-Merger tax attributes remain available after the Merger as a result of limitations under Internal Revenue Code Section 382 due to lack of business continuity.

## **Financial Overview**

### ***Revenue***

We currently have a portfolio of enabling and delivery products, from which we have generated modest revenue.

### ***Cost of Goods Sold***

Cost of goods sold includes the costs of raw materials and components, manufacturing personnel and facility costs and other indirect and overhead costs associated with manufacturing our enabling and delivery products.

### ***Research and Development Expenses***

Our research and development expenses consist primarily of:

- salaries and related overhead expenses, which include share-based compensation and benefits for personnel in research and development functions;

- fees paid to consultants and contract research organizations, or CROs, including in connection with our preclinical studies and clinical trials and other related clinical trial fees, such as for investigator grants, patient screening, laboratory work, clinical trial material management and statistical compilation and analysis;

- costs related to acquiring and manufacturing clinical trial materials;

- costs related to compliance with regulatory requirements; and

- payments related to licensed products and technologies.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and clinical sites. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and the services are performed.

We plan to increase our research and development expenses for the foreseeable future as we continue to develop CardiAMP, and subject to the availability of additional funding, further advance the development of CardiALLO and any other therapeutic candidates for additional indications. We typically use our employee and infrastructure resources across multiple research and development programs, and accordingly we have not historically allocated resources specifically to our individual programs.

The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our therapeutic candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our therapeutic candidates.



### ***Selling, General and Administrative Expenses***

Selling, general and administrative expenses consist primarily of salaries and related costs for employees in executive, finance and administration, sales, corporate development and administrative support functions, including share-based compensation expenses and benefits. Other significant selling, general and administrative expenses include sales commissions, rent, accounting and legal services, obtaining and maintaining patents, the cost of consultants, occupancy costs, insurance premiums and information systems costs.

We expect that our selling, general and administrative expenses will increase as we operate as a public company, conduct our Phase III pivotal trial for CardiAMP, and subject to the availability of additional funding, conduct our Phase II trial for CardiALLO and prepare for commercialization. We believe that these increases will likely include increased costs for director and officer liability insurance, costs related to the hiring of additional personnel to support product commercialization efforts and operations as a public company and increased fees for outside consultants, attorneys and accountants. We also expect to incur increased costs to comply with corporate governance, internal controls, investor relations and disclosures, and similar requirements applicable to public companies.

### ***Other Income (Expense)***

Other income and expense consists primarily of interest charges we incur in periods when we have convertible debt outstanding, interest income we earn on our cash and cash equivalents and changes in the fair value of our warrant and convertible shareholder note derivative liabilities. Subsequent to the Merger we have no interest charges related to the convertible debt and changes in the fair value of our warrant and convertible shareholder note derivative liabilities as such instruments were converted, cancelled or exchanged as part of the Merger. We expect our interest income to increase following the completion of the Merger as we invest our cash on hand pending its use in our operations.

### **Critical Accounting Policies and Estimates**

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, as well as the reported expenses during the periods presented. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We define our critical accounting policies as those that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. The following discussion addresses what we believe to be the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments.

### ***Revenue Recognition***

We recognize revenue when persuasive evidence of an arrangement exists, delivery has occurred, the price to the buyer is fixed or determinable and collection from the customer is reasonably assured.

***Net Product Revenue.*** We recognize revenues from product sales when title and risk of loss have passed to the customer, which typically occurs upon delivery. Product sale transactions are evidenced by customer purchase orders, customer contracts, invoices, and/or the related shipping documents. Revenue is recognized net of provisions made for discounts, expected sales returns and allowances. Estimated returns and allowances are based on historical experience and other relevant factors. We accept returns for unused, unopened and resellable product in its original packaging, subject to a 20% restocking fee.

**Collaboration Agreement Revenue.** Collaboration agreement revenue is income from agreements under which we provide biotherapeutic delivery systems and customer training and support for their use in clinical trials and studies. We evaluate activities under these agreements to determine if they represent a multiple element arrangement by identifying the deliverables included within the agreement. We account for these deliverables as separate units of accounting if the following two criteria are met:

- the delivered items have value to the customer on a stand-alone basis; and
- if there is a general right of return relative to the delivered items, delivery or performance of the undelivered items is considered probable and within our control.

Factors considered in this determination include, among other things, whether any other vendors sell the items separately and if the customer could use the delivered item for its intended purpose without receipt of the remaining deliverables. A change in these assumptions could impact our reported revenue, which could have a material impact to our financial statements.

If multiple deliverables included in an arrangement are separable into different units of accounting, we allocate the arrangement consideration to those units of accounting based on their relative selling prices and recognize the associated revenue when the appropriate recognition criteria are met for those deliverables. The amount of allocable arrangement consideration is limited to the amounts that are fixed and determinable.

#### ***Research and Development—Clinical Trial Accruals***

As part of the process of preparing our financial statements, we are required to estimate our expenses resulting from our obligations under contracts with vendors and consultants and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. Our clinical trial accrual is dependent upon the timely and accurate reporting of expenses of our CROs and other third-party vendors.

Our objective is to reflect the appropriate clinical trial expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. We determine accrual estimates through discussion with applicable personnel and outside service providers as to the progress or state of completion of clinical trials, or the services completed. During the course of a clinical trial, we adjust the rate of clinical trial expense recognition if actual results differ from the estimates. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known at that

time. Although we do not expect that our estimates will be materially different from amounts actually incurred, our understanding of status and timing of services performed relative to the actual status and timing of services performed may vary and may result in our reporting amounts that are too high or too low for any particular period. Through December 31, 2016, there had been no material adjustments to our prior period estimates of accrued expenses for clinical trials. However, due to the nature of estimates, we cannot provide assurance that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials.

### ***Share-Based Compensation***

BioCardia Lifesciences granted share-based compensation under its 2002 Stock Plan and 2016 Plan, which were assumed by the Company in connection with the Merger. The exercise price of options granted in 2016 was equivalent to the fair market value of BioCardia Lifesciences stock at the date of grant. The number of shares, terms, and vesting periods are determined by BioCardia's board of directors or a committee thereof on an option-by-option basis. Options generally vest ratably over service periods of four years and expire 10 years from the date of grant. Compensation cost for employee share-based awards is based on the grant-date fair value and will be recognized over the vesting period of the applicable award on a straight-line basis.



We measure and recognize share-based compensation expense for equity awards to employees, directors and consultants based on fair value at the grant date. The unearned portion of nonemployee awards are remeasured at each reporting date. We use the Black-Scholes-Merton option-pricing model, or BSM, to calculate fair value. Share-based compensation expense recognized in the statements of operations is based on options ultimately expected to vest, taking into consideration estimated forfeitures, and is recognized in the period the services are performed. Share-based compensation expense is revised in subsequent periods, if necessary, if actual forfeitures differ from these estimates. When estimating forfeitures, we consider historic voluntary termination behaviors as well as trends of actual option forfeitures. For options granted to nonemployees, we revalue the unearned portion of the share-based compensation and the resulting change in fair value is recognized in the statements of operations over the period the related services are rendered.

The BSM option-pricing model requires the input of subjective assumptions, including the risk-free interest rate, the expected volatility in the value of our Common Stock, and the expected term of the option. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our share-based compensation expense could be materially different in the future.

### ***Income Taxes***

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

As of December 31, 2016, our total deferred tax assets, less our total deferred tax liabilities, were \$21.6 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards.

Utilization of the net operating loss carryforwards may be subject to a substantial annual limitation due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, and similar state provisions. These ownership change limitations may limit the amount of net operating loss carryforwards and other tax attributes that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points (by value) of the outstanding stock of a company by certain stockholders. Since our formation, we have raised capital through the issuance of capital stock on several occasions and we consummated the Merger in

October 2016. These transactions, separately or combined with the purchasing stockholders' subsequent disposition of those shares, may have resulted in such ownership changes, or could result in ownership changes in the future.

We have not performed an analysis to assess whether an ownership change has occurred. If we have experienced an ownership change at any time since our formation, utilization of our net operating loss carryforwards would be subject to an annual limitation under Section 382 of the Code, which is determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then applying any additional adjustments that are required. Any limitation may result in expiration of a portion of the net operating loss carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Due to the existence of the valuation allowance, future changes in our unrecognized tax benefits will not impact our effective tax rate. Any carryforwards that will expire prior to utilization as a result of such limitations will be removed from deferred tax assets, with a corresponding reduction of the valuation allowance.

## Results of Operations

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015 (in thousands):

	<b>Years Ended December 31,</b>	
	<b>2016</b>	<b>2015</b>
Revenue:		
Net product revenue	\$517	\$860
Collaboration agreement revenue	59	44
Total revenue	576	904
Cost and expenses:		
Cost of goods sold	746	1,061
Research and development	3,330	1,518
Selling, general and administrative	4,108	3,734
Total cost and expenses	8,184	6,313
Operating loss	(7,608 )	(5,409)
Write-off of deferred financing costs	-	(1,634)
Interest expense	(1,736 )	(1,386)
Other income (expense)	(966 )	1,732
Net loss	\$(10,310)	\$(6,697)

**Revenue.** Revenue decreased by approximately \$328,000 in 2016 compared to 2015 primarily due to a reduction in sales volumes for Morph products subsequent to the reduction in the sales and production workforce in August 2015. We expect sales in 2017 to be generally consistent with 2016.

**Cost of Goods Sold.** Cost of goods sold decreased by approximately \$315,000 in 2016 compared to 2015 consistent with the reduction in revenue.

**Research and Development Expenses.** Research and development expenses increased by approximately \$1.9 million in 2016 compared to 2015 primarily due to expenses incurred in the planning and preparation for the CardiAMP Phase III pivotal trial. We expect research and development expenses to increase as we increase enrollment of the CardiAMP Phase III pivotal trial.

*Selling, General and Administrative Expenses.* Selling, general and administrative expenses increased by approximately \$312,000 in 2016 compared to 2015 primarily due to indirect costs associated with the Merger and expenses incurred to transition to public company operations, including legal costs, audit, accounting, tax, valuation service and financial printing. We expect selling, general and administrative expenses to increase due to expenses to be incurred as we build our infrastructure to support the CardiAMP Phase III pivotal trial and enhance public company operations.

*Write Off of Deferred Financing Costs.* The Company deferred costs incurred for a planned initial public offering by BioCardia Lifesciences, or the IPO, which included legal, accounting and other professional fees. The IPO was delayed and subsequently withdrawn, and as a result, the Company recorded a write-off of deferred offering costs of \$1.6 million during the year ended December 31, 2015.

*Interest Expense.* Interest expense for the year ended December 31, 2016 and 2015 consisted primarily of interest expense related to convertible notes. The increase is attributable to longer period of principle outstanding in 2016.

*Other Income (Expense).* Other income (expense) for the year ended December 31, 2016 and 2015 consisted primarily of the changes in value of the convertible preferred stock warrant liabilities and the change in value of the convertible shareholder note derivative liability.

## Liquidity and Capital Resources

We have incurred net losses each year since our inception and as of December 31, 2016, we had an accumulated deficit of approximately \$60.1 million. We anticipate that we will continue to incur net losses for at least the next several years.

On October 24, 2016, we issued convertible notes with net proceeds of \$4.4 million. The convertible notes converted to common stock immediately prior to the Merger close. Also, we acquired \$18.9 million in cash as a result of the Merger. Prior to that time, we have funded our operations principally through the sales of equity and convertible debt securities. As of December 31, 2016, we had cash and cash equivalents of approximately \$21.4 million.

The following table shows a summary of our cash flows for the periods indicated (in thousands):

	<b>Years Ended December 31, 2016      2015</b>	
Net cash provided by (used in):		
Operating activities	\$(5,522 )	\$(7,023 )
Investing activities	18,921	(125 )
Financing activities	4,396	7,521
Net increase in cash and cash equivalents	\$17,795	\$373

*Cash Flows from Operating Activities.* The decrease in overall spending for operating activities of approximately \$1.5 million in 2016 compared to 2015 relates primarily to the spending for the anticipated IPO in 2015 coupled with reductions in operating costs attributable to the reduction in workforce that occurred in August 2015.

*Cash Flows from Investing Activities.* Net cash provided by investing activities of \$18.9 million during the year ended December 31, 2016 primarily consists of \$19.0 million acquired from an accounting perspective as part of the Merger. We had no significant investing activities during the year ended December 31, and 2015.

*Cash Flows from Financing Activities.* Net cash provided by financing activities of \$4.3 million during the year ended December 31, 2016 primarily the result of proceeds from the issuance of convertible notes. Net cash provided by financing activities of \$7.5 million during the year ended December 31, 2015 was primarily the result of proceeds from the issuance of convertible notes.

### ***Future Funding Requirements***

To date, we have generated modest revenue from sales of our approved products. We do not know when, or if, we will generate any revenue from our development stage biotherapeutic programs. We do not expect to generate any revenue from sales of our CardiAMP or CardiALLO therapeutic candidates unless and until we obtain regulatory approval. At the same time, we expect our expenses to increase in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our therapeutic candidates. In addition, subject to obtaining regulatory approval for any of our therapeutic candidates and companion diagnostic, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We anticipate that we will need additional funding in connection with our continuing operations.

Based upon our current operating plan, we believe that the cash on hand will enable us to fund our operations for at least the next 12 months from the date of issuance of these financial statements. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our therapeutic candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of our therapeutic candidates.

Our future capital requirements will depend on many factors, including:

- the progress, costs, results and timing of our CardiAMP and CardiALLO clinical trials;
- FDA acceptance of our CardiAMP and CardiALLO therapies for heart failure and for other potential indications;
- the outcome, costs and timing of seeking and obtaining FDA and any other regulatory approvals;
- the costs associated with securing, establishing and maintaining commercialization and manufacturing capabilities;
- the number and characteristics of product candidates that we pursue, including our product candidates in preclinical development;
- the ability of our product candidates to progress through clinical development successfully;
- our need to expand our research and development activities;
- the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
  - the general and administrative expenses related to being a public company;
- our need and ability to hire additional management and scientific, medical and sales personnel;
- the effect of competing technological and market developments; and
  - our need to implement additional internal systems and infrastructure, including financial and reporting systems.

Until such time that we can generate meaningful revenue from the sales of approved therapies and products, if ever, we expect to finance our operating activities through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements, and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our Common Stock holders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our Common Stock holders. Debt financing, if available, may involve agreements that include conversion discounts or covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, or strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, products or therapeutic candidates or to grant licenses on terms that may not be favorable to us.



## **Off-Balance Sheet Arrangements**

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under the rules of the Securities and Exchange Commission.

## **Recent Accounting Pronouncements**

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606), which provides comprehensive guidance for revenue recognition. ASU 2014-09 affects any entity which either enters into contracts with customers to transfer goods or services or enters into contracts for the transfer of nonfinancial assets. The core principle of the guidance provides that a company should recognize revenue when promised goods or services are transferred to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. Additionally, qualitative and quantitative disclosures are required about customer contracts, significant judgments and changes in judgments, and assets recognized from the costs to obtain or fulfill a contract. The new standard can be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of the change recognized at the date of the initial application in retained earnings.

In August 2015, the FASB issued ASU 2015-14 Revenue from Contracts with Customers, which deferred the effective date for implementation of the standard. Public entities are to apply the new standard for annual and interim reporting periods beginning after December 15, 2017 and earlier application is permitted only as of annual reporting periods beginning after December 15, 2016, including interim reporting periods within that reporting period. The Company has not elected early adoption and has not concluded on an adoption method. The Company has formed a task force that is beginning to assess the Company's customer contracts and the potential impacts the standard may have on previously reported revenues and future revenues. Given the relatively small volume of revenue arrangements, the Company believes that the analysis will be completed in sufficient time to adopt the new standard when required.

In February 2016, the FASB issued ASU 2016-02 Leases (Topic 842), which supersedes existing guidance on accounting for leases in "Leases (Topic 840)" and generally requires all leases to be recognized in the consolidated balance sheet. ASU 2016-02 is effective for annual and interim reporting periods beginning after December 15, 2018; early adoption is permitted. The provisions of ASU 2016-02 are to be applied using a modified retrospective approach. We are currently assessing the future impact of this ASU on our consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The standard is intended to simplify several areas of accounting for

share-based compensation arrangements, including the income tax impact, classification in the statement of cash flows and forfeitures. ASU 2016-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016, and early adoption is permitted. We will adopt this guidance, when required. The adoption of this guidance is not expected to have a material impact on our financial position, results of operations or cash flows.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

Not applicable.

## ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

### INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders  
BioCardia, Inc.:

We have audited the accompanying consolidated balance sheets of BioCardia, Inc. and subsidiary as of December 31, 2016 and 2015, and the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years in the two-year period ended December 31, 2016. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall consolidated financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of BioCardia, Inc. and subsidiary as of December 31, 2016 and 2015, and the results of their operations and their cash flows for each of the years in the two-year period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

(signed) KPMG LLP

San Francisco, California

March 30, 2017

## BIOCARDIA, INC.

## Consolidated Balance Sheets

(In thousands, except share and per share data)

	<b>December 31,</b>	
	<b>2016</b>	<b>2015</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$21,352	3,557
Accounts receivable, net of allowance for doubtful accounts of \$2 and \$4 at December 31, 2016 and 2015, respectively	74	107
Inventory	135	759
Prepaid expenses and other current assets	356	246
Total current assets	21,917	4,669
Property and equipment, net	111	150
Other assets	54	43
Total assets	\$22,082	4,862
<b>Liabilities and Stockholders' Equity (Deficit)</b>		
Current liabilities:		
Accounts payable	\$525	542
Accrued liabilities	544	692
Deferred rent	—	30
Deferred revenue	71	39
Grant liability	304	—
Convertible preferred stock warrant liability	—	275
Maturity date preferred stock warrant liability	—	10
Convertible shareholder notes derivative liability	—	1,044
Convertible shareholder notes, net of debt discount of \$1,528 at December 31, 2015	—	5,672
Total current liabilities	1,444	8,304
Deferred rent	56	—
Total liabilities	1,500	8,304
Stockholders' equity (deficit):		
Convertible preferred stock, \$0.001 par value, 0 and 43,502,124 shares authorized at December 31, 2016 and 2015, respectively; 0 and 110,500,514 shares issued and outstanding at December 31, 2016 and 2015, respectively	—	46,030
Preferred stock, \$0.001 par value, 50,000,000 shares authorized, no shares issued and outstanding at December 31, 2016 and 2015	—	—
Common stock, \$0.001 par value, 750,000,000 and 60,000,000 shares authorized at December 31, 2016 and 2015, respectively; 457,575,631 shares and 18,947,536 shares issued and outstanding at December 31, 2016 and 2015, respectively	458	19
Additional paid-in capital	80,266	341
Accumulated deficit	(60,142)	(49,832)
Total stockholders' equity (deficit)	20,582	(3,442)
Total liabilities and stockholders' equity (deficit)	\$22,082	4,862

See accompanying notes to financial statements.

## BIOCARDIA, INC.

## Consolidated Statements of Operations

(In thousands, except share and per share amounts)

	<b>Years ended December 31,</b>	
	<b>2016</b>	<b>2015</b>
Revenue:		
Net product revenue	\$517	860
Collaboration agreement revenue	59	44
Total revenue	576	904
Costs and expenses:		
Cost of goods sold	746	1,061
Research and development	3,330	1,518
Selling, general and administrative	4,108	3,734
Total costs and expenses	8,184	6,313
Operating loss	(7,608)	(5,409)
Other income (expense):		
Interest expense, net	(1,736)	(1,386)
Write-off of deferred offering costs	—	(1,634)
Change in fair value of convertible preferred stock warrant liability	250	274
Change in fair value of maturity date preferred stock warrant liability	10	87
Change in fair value of convertible shareholder notes derivative liability	(1,224)	1,373
Other expense	(2)	(2)
Total other expense, net	(2,702)	(1,288)
Net loss	\$(10,310)	(6,697)
Net loss per share, basic and diluted	\$(0.10)	(0.36)
Weighted-average shares used in computing net loss per share, basic and diluted	100,419,402	18,723,511

See accompanying notes to financial statements.

## BIOCARDIA, INC.

## Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(In thousands, except share data)

	Convertible preferred		Convertible preferred		Common stock		Additional	Accumulated	
	stock	Cost	stock	Cost	Shares	Cost	paid in	deficit	Total
	Shares		Shares				capital		
Balance at December 31, 2014	98,354,541	\$ 38,213	—	\$ —	18,494,023	\$ 18	\$ —	\$ (43,135)	\$ (43,111)
Reclassification from temporary equity to permanent equity	(98,354,541)	(38,213)	98,354,541	38,213	—	—	—	—	38,213
Conversion of convertible notes into series F preferred shares	—	—	12,075,610	7,781	—	—	—	—	7,781
Exercise of convertible preferred stock warrants for series D preferred shares	—	—	67,884	34	—	—	—	—	34
Exercise of convertible preferred stock warrants for series F preferred shares	—	—	2,479	2	—	—	—	—	2
Exercise of stock options	—	—	—	—	453,513	1	58	—	59
Share-based compensation	—	—	—	—	—	—	283	—	283
Net loss	—	—	—	—	—	—	—	(6,697 )	(6,697 )
Balance at December 31, 2015	—	—	110,500,514	46,030	18,947,536	19	341	(49,832)	(3,442)



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Exchange of convertible preferred stock	—	—	—	—	129,683	—	25	—	25
warrants to common stock									
Reclassification of convertible shareholder notes derivative liability	—	—	—	—	—	—	2,268	—	2,268
Conversion of convertible notes into common stock	—	—	—	—	97,093,236	97	12,059	—	12,156
Conversion of preferred stock into common stock	—	—	(110,500,514)	(46,030)	110,500,514	111	45,919	—	—
Issuance of common stock upon reverse merger	—	—	—	—	230,743,141	231	18,690	—	18,921
Exercise of stock options	—	—	—	—	161,521	—	22	—	22
Share-based compensation	—	—	—	—	—	—	942	—	942
Net loss	—	—	—	—	—	—	—	(10,310)	(10,310)
Balance at December 31, 2016	—	\$ —	—	\$ —	457,575,631	\$ 458	\$ 80,266	\$ (60,142)	\$ 20,582

See accompanying notes to financial statements.

## BIOCARDIA, INC.

## Consolidated Statements of Cash Flows

(In thousands)

	<b>Years ended December 31,</b>	
	<b>2016</b>	<b>2015</b>
Operating activities:		
Net loss	\$(10,310)	(6,697)
Adjustments to reconcile net loss to net cash used in operating activities:		
Write-off of inventory	597	—
Depreciation and amortization	39	47
Change in fair value of convertible preferred stock warrant liability	(250 )	(274 )
Change in fair value of maturity date preferred stock warrant liability	(10 )	(87 )
Change in fair value of convertible shareholder notes derivative liability	1,224	(1,373)
Share-based compensation	942	283
Non-cash interest expense on convertible shareholder notes	1,736	1,387
Changes in operating assets and liabilities:		
Accounts receivable	33	65
Inventory	27	(82 )
Prepaid expenses and other current assets	(110 )	(129 )
Deferred financing costs	—	48
Other assets	(11 )	—
Accounts payable	(17 )	228
Accrued liabilities excluding accrued interest on convertible note	226	(416 )
Deferred revenue	32	—
Deferred rent	26	(23 )
Grant liability	304	—
Net cash used in operating activities	(5,522 )	(7,023)
Investing activities:		
Purchase of property and equipment	—	(125 )
Cash acquired in reverse merger	19,017	—
Payment of transaction costs of reverse merger	(96 )	—
Net cash provided by (used in) investing activities	18,921	(125 )
Financing activities:		
Proceeds from the exercise of convertible preferred stock warrants	—	27
Proceeds from issuance of convertible notes and warrants	4,374	7,435
Proceeds from the exercise of stock options	22	59
Net cash provided by financing activities	4,396	7,521
Net increase in cash and cash equivalents	17,795	373
Cash and cash equivalents at beginning of year	3,557	3,184
Cash and cash equivalents at end of year	\$21,352	3,557

Supplemental disclosure for noncash investing and financing activities:

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Exchange of convertible preferred stock warrants for common stock	\$25	—
Conversion of convertible shareholder notes and related interest payable	\$12,156	7,781
Reclassification of convertible shareholder notes derivative liability	\$2,268	—
Conversion of preferred stock	\$46,030	—

See accompanying notes to financial statements.

## **(1) Summary of Business**

### ***(a) Description of Business***

The Company is a clinical-stage regenerative medicine company developing novel therapeutics for cardiovascular diseases with large unmet medical needs. Its lead therapeutic candidate is the CardiAMP cell therapy system and its second therapeutic candidate is the CardiALLO cell therapy system. To date the Company has devoted substantially all of its resources to research and development efforts relating to its therapeutic candidates and biotherapeutic delivery systems including conducting clinical trials, developing manufacturing and sales capabilities, in-licensing related intellectual property, providing general and administrative support for these operations and protecting its intellectual property.

The Company has three enabling device product lines: the CardiAMP cell processing system, the Helix biotherapeutic delivery system (“Helix”); and the Morph vascular access (“Morph”) product line offers advanced catheter products for interventional medicine.

### ***(b) Reverse Merger***

On August 22, 2016, the Company, its wholly-owned subsidiary, Icicle Acquisition Corp, and BioCardia Lifesciences, Inc. (at the time, named BioCardia, Inc.) entered into the Merger Agreement. The Merger Agreement closed on October 24, 2016, pursuant to which Icicle Acquisition Corp. merged with and into BioCardia Lifesciences, with BioCardia Lifesciences continuing as the surviving company. BioCardia Lifesciences was determined to be the accounting acquirer in the Merger based upon the terms of the Merger and other factors, including: (i) former BioCardia Lifesciences security holders owned approximately 54% of the combined company (on a fully diluted basis) immediately following the closing of the Merger, (ii) former BioCardia Lifesciences directors hold the majority of the board seats in the combined company, and (iii) former BioCardia Lifesciences management holds all of the key positions in the management of the combined company. Following the completion of the Merger, the Company changed its name to BioCardia, Inc.

### ***Exchange Ratio***

Pursuant to the Merger Agreement, each of the shares of BioCardia Lifesciences common stock issued and outstanding prior to the Merger, including shares of common stock underlying outstanding preferred stock, convertible notes (which converted into common stock immediately prior to the Merger), and stock options were converted into the right to receive 19.3678009 shares of Company common stock. The accompanying consolidated financial statements and notes to the consolidated financial statements give retroactive effect to the capital structure as a result of the Merger.

***(c) Reverse Stock Split***

On July 2, 2015, BioCardia Lifesciences effected a 1-for-7.131 reverse stock split of its common stock and convertible preferred stock. Neither the par value nor the authorized number of shares was adjusted as a result of the reverse stock split. All issued and outstanding common stock, convertible preferred stock, warrants, stock options and per share amounts contained in the accompanying financial statements and notes to the financial statements have been retroactively adjusted to give effect to the reverse stock split for all periods presented.

**(2) Significant Accounting Policies**

***(a) Basis of Presentation and Consolidation***

These consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States (GAAP) and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All material intercompany accounts and transactions have been eliminated during the consolidation process. The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions.

***(b) Liquidity***

The Company has incurred significant net losses and negative cash flows from operations since its inception and had an accumulated deficit of \$60.1 million as of December 31, 2016. Management expects operating losses and negative cash flows to continue through at least the next several years.

Upon closing of the Merger Agreement, the combined company had approximately \$24.0 million in cash, including \$19 million of cash acquired as part of the Merger and \$4.4 million in net proceeds from the issuance of convertible notes in October 2016. Management believes cash as of December 31, 2016 is sufficient to fund the Company for at least the next twelve-month period following the date of issuance of these financial statements. The Company also plans to raise other additional capital, potentially including debt and equity arrangements, to finance its future operations. If adequate funds are not available, the Company may be required to reduce operating expenses, delay or reduce the scope of its product development programs, obtain funds through arrangements with others that may require the Company to relinquish rights to certain of its technologies or products that the Company would otherwise seek to develop or commercialize itself, or cease operations. While the Company believes in the viability of its strategy to raise additional funds, there can be no assurances to that effect.

***(c) Use of Estimates***

The preparation of the financial statements in accordance with GAAP requires Company management to make certain estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ materially from those estimates. Significant items subject to such estimates and assumptions include the useful lives of property and equipment; allowances for doubtful accounts and sales returns; inventory valuation and reserves; fair value of the convertible preferred stock warrant liability; fair value of the maturity date preferred stock warrant liability; fair value of the convertible shareholder notes derivative liability; and share-based compensation.

***(d) Cash Equivalents***

The Company classifies all highly liquid investments with original maturities of three months or less at the date of purchase as cash equivalents. The Company maintains its cash and cash equivalents with reputable financial institutions.

***(e) Concentration of Credit Risk***

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash. The Company maintains its cash at financial institutions, which at times, exceed federally insured limits. At December 31, 2016, the Company's cash was held by one financial institution and the amount on deposit was in excess of FDIC insurance limits. The Company has not recognized any losses from credit risks on such accounts since inception. The Company believes it is not exposed to significant credit risk on cash.

***(f)Accounts Receivable and Allowance for Doubtful Accounts***

Accounts receivable are recorded at the invoiced amount and do not bear interest. The Company considers the creditworthiness of its customers, but does not require collateral in advance of a sale. The Company evaluates collectability and maintains an allowance for doubtful accounts for estimated losses inherent in its accounts receivable portfolio when necessary. The estimate is based on the Company's historical write-off experience, customer creditworthiness, facts and circumstances specific to outstanding balances and payment terms. Account balances are charged off against the allowance after all means of collection have been exhausted and the potential for recovery is considered remote. The allowance for doubtful accounts was \$2,000 and \$4,000 as of December 31, 2016 and 2015, respectively.

***(g) Inventory***

Inventory is stated at the lower of cost or net realizable value. Cost is determined using the average-cost method. Net realizable value is the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal, and transportation. The Company analyzes its inventory levels quarterly and writes down inventory that has become obsolete or has a cost basis in excess of its expected net realizable value or inventory quantities in excess of expected requirements. Excess requirements are determined based on comparison of existing inventories to forecasted sales, with consideration given to inventory shelf life. Expired inventory is disposed of and the related costs are recognized in cost of goods sold.

***(h) Deferred Financing Costs***

Deferred financing costs represent direct costs associated with future issuances of our corporate securities. Direct costs include, but are not limited to the legal, accounting and printing costs. Indirect costs associated with future issuance of corporate securities are expensed as incurred. Upon the completion of the proposed issuances, the deferred financing costs will be offset against the proceeds from the security issuance. If the proposed issuances are not completed, the deferred financing costs will be charged to expense. The Company deferred costs incurred for an initial public offering of BioCardia Lifesciences common stock, or the IPO, totaling approximately \$1,586,000 in 2015. In 2015, the IPO was delayed and subsequently withdrawn. The deferred offering costs for that offering in the amount of \$1,634,000 were expensed in 2015.

***(i) Property and Equipment, Net***

Property and equipment, net are carried at cost less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the related assets, as described in the table below. Maintenance and repairs are expensed as incurred. When assets are retired or otherwise disposed of, the cost and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is reflected in the accompanying consolidated statements of operations.

<b>Asset</b>	<b>Estimated useful lives (in years)</b>
Computer equipment and software	3
Laboratory and manufacturing equipment	3
Furniture and fixtures	3
Leasehold improvements	5 years or lease term, if shorter



***(j) Long-Lived Assets***

The Company evaluates long-lived assets such as property and equipment whenever events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. An impairment loss is recognized when estimated future undiscounted cash flows expected to result from the use of the asset and its eventual disposition is less than the carrying amount. When undiscounted future cash flows are not expected to be sufficient to recover an asset's carrying amount, the asset is written down to its fair value. There have been no impairments of the Company's long-lived assets in any of the years presented.

***(k) Clinical Trial Accruals***

As part of the process of preparing its consolidated financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors and consultants and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiation and may result in payment flows that do not match the periods over which materials or services are provided by the vendor under the contracts. The Company's objective is to reflect the clinical trial expenses in its consolidated financial statements by matching those expenses with the period in which the services and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. The Company makes estimates of its accrued expenses as of each balance sheet date in its consolidated financial statements based on the facts and circumstances known at that time. Although, the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services relative to the actual status and timing of services performed may vary and may result in reported amounts that differ from the actual amounts incurred.

***(l) Derivatives***

Fair value accounting requires bifurcation of embedded derivative instruments such as conversion features in equity instruments and warrants granted, and measurement of their fair value. In determining the appropriate fair value, the Company uses Monte Carlo simulation to calculate potential payouts in each of three conversion scenarios. In cases where the payout includes newly created equity shares and warrants, the Black-Scholes based option pricing method is used to calculate the amounts due to investors. Derivative instruments are subsequently adjusted to reflect fair value at the end of each reporting period. Any increase or decrease in the fair value is recorded in results of operations as a change in the fair value of derivatives. Once a derivative liability ceases to exist any remaining fair value is reclassified to additional paid-in capital if redeemed or through earnings if forfeited or expired.

***(m) Deferred Rent***

The Company's lease for its facility provides for fixed increases in minimum annual rental payments. The total amount of rental payments due over the lease term is charged to rent expense ratably over the life of the lease. Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis.

***(n) Revenue Recognition***

The Company recognizes revenue when persuasive evidence of an arrangement exists, delivery has occurred, the price to the buyer is fixed or determinable, and collection from the customer is reasonably assured.

**Net product revenue** – The Company currently has a portfolio of enabling and delivery products. The Company recognizes revenue from product sales when title and risk of loss have passed to the customer, which typically occurs upon delivery. Product sale transactions are evidenced by customer purchase orders, customer contracts, invoices and/or related shipping documents.

Revenue is recognized net of provisions made for discounts, expected sales returns and allowances. Estimated returns and allowances are based on historical experience and other relevant factors. The Company accepts returns for unused, unopened and resellable product in its original packaging, subject to a restocking fee. The sales return reserve was approximately \$1,000 and \$3,000 as of December 31, 2016 and 2015, respectively.

Amounts received from customers in advance of revenue recognition are recorded as deferred revenue on the consolidated balance sheets.

**Collaboration agreement revenue** – Collaboration agreement revenue is income from agreements under partnering programs with corporate and academic institutions, wherein the Company provides biotherapeutic delivery systems and customer training and support for their use in clinical trials and studies. These programs provide additional clinical data, intellectual property rights and opportunities to participate in the development of combination products for the treatment of cardiac disease. The Company evaluates activities under these agreements to determine if they represent a multiple element arrangement by identifying the deliverables included within the agreements. The Company accounts for these deliverables as separate units of accounting if the following two criteria are met:

The delivered items have value to the customer on a stand-alone basis

If there is a general right of return relative to the delivered items, delivery or performance of the undelivered items is considered probable and within the Company's control

Factors considered in this determination include, among other things, whether any other vendors sell the items separately and if the customer could use the delivered item for its intended purpose without receipt of the remaining deliverables.

If an arrangement includes multiple deliverables that are separable into different units of accounting, the Company allocates the arrangement consideration to those units of accounting based on their relative selling prices and recognizes the associated revenue when the appropriate recognition criteria are met for those deliverables. The amount of allocable arrangement consideration is limited to the amounts that are fixed and determinable.

***(o) Shipping Costs***

Costs incurred for the shipping of products to customers totaled approximately \$7,000 and \$11,000 for the years ended December 31, 2016 and 2015, respectively, and are included in cost of goods sold in the accompanying consolidated statements of operations.

***(p) Product Warranties***

The Company provides a standard warranty of serviceability on all its products for the duration of the product's shelf life, which is two years for Helix and Morph products currently. Estimated future warranty costs, if any, are accrued and charged to costs of goods sold in the period that the related revenue is recognized. Historical data and trends of product reliability and costs of repairing or replacing defective products are considered. Due to the low historical warranty claims experience, a general warranty accrual has not been required or recorded as of December 31, 2016 and 2015.

***(q) Research and Development***

The Company's research and development costs are expensed as incurred. Research and development expense includes the costs of basic research activities as well as other research, engineering, and technical effort required to develop new products or services or make significant improvement to an existing product or manufacturing process. Research and development costs also include pre-approval regulatory and clinical trial expenses and support costs for collaborative partnering programs wherein the Company provides biotherapeutic delivery systems and customer training and support for their use in clinical trials and studies. The Company's research and development costs consist primarily of:

Salaries, benefits and other personnel-related expenses, including share-based compensation

Fees paid for services provided by clinical research organizations, research institutions, consultants and other outside service providers

Costs to acquire and manufacture materials used in research and development activities and clinical trials

Laboratory consumables and supplies

Facility-related expenses allocated to research and development activities

Fees to collaborators to license technology

Depreciation expense for equipment used for research and development and clinical purposes.

***(r) Share-Based Compensation***

The Company measures and recognizes share-based compensation expense for equity awards to employees, directors and consultants based on fair value at the grant date. The unearned portion of nonemployee awards are remeasured at each reporting date. The Company uses the Black-Scholes-Merton (“BSM”) option pricing model to calculate fair value. Share-based compensation expense recognized in the consolidated statements of operations is based on options ultimately expected to vest, taking into consideration estimated forfeitures, and is recognized in the period the services are performed. Share-based compensation expense is revised in subsequent periods, if necessary, if actual forfeitures differ from these estimates. When estimating forfeitures, the Company considers historic voluntary termination behaviors as well as trends of actual option forfeitures. For options granted to nonemployees, the Company revalues the unearned portion of the share-based compensation and the resulting change in fair value is recognized in the consolidated statements of operations over the period the related services are rendered.

The BSM option pricing model requires the input of highly subjective assumptions, including the risk-free interest rate, the expected volatility in the value of the Company’s common stock, and the expected term of the option. These estimates involve inherent uncertainties and the application of management’s judgment. If factors change and different assumptions are used, our share-based compensation expense could be materially different in the future. These assumptions are estimated as follows:

***Risk-free Interest Rate***

The risk free interest rate assumption is based on the zero-coupon U.S. Treasury instruments appropriate for the expected term of the stock option grants.

***Expected Volatility***

As the Company does not have a sufficient trading history for its common stock, the expected stock price volatility is estimated based on volatilities of a peer group of similar companies by taking the average historic volatility for these peers for a period equivalent to the expected term of the stock option grants. The peer group was developed based on companies in the biotechnology and medical device industries whose shares are publicly-traded.

***Expected Term***

The expected term represents the period of time that options are expected to be outstanding. As the Company does not have sufficient historical experience for determining the expected term of the stock options awards granted, the expected life is determined using the simplified method, which is an average of the contractual terms of the option and its ordinary vesting period.

#### *Common Stock Valuation*

Prior to the completion of the Merger, due to the absence of a public market for the BioCardia Lifesciences common stock, it was necessary to estimate the fair value of the common stock underlying the share-based awards when performing fair value calculations using the BSM option pricing model. The fair value of the common stock underlying the share-based awards was assessed on each grant date by the board of directors of BioCardia Lifesciences. All options to purchase shares of the Company's common stock have been granted with an exercise price per share no less than the fair value per share of the common stock underlying those options on the grant date. For stock options granted subsequent to the Merger, the fair value is based on the closing price of common stock as reported on the OTC Markets on the date of grant.

***(s) Income Taxes***

The Company accounts for income taxes based on the asset and liability method whereby deferred tax asset and liability account balances are determined based on differences between the financial reporting and tax bases of assets, liabilities, operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of the deferred tax assets will not be realized.

In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, forecasts of future taxable income, and ongoing tax planning. In the event the Company was to determine that it would be able to realize its deferred tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance, which would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period such determination is made.

The Company recognizes and measures benefits for uncertain tax positions using a two-step approach. The first step is to evaluate the tax position taken or expected to be taken in a tax return by determining if the weight of available evidence indicates that it is more likely than not that the tax position will be sustained upon audit, including resolution of any related appeals or litigation processes. For tax positions that are more likely than not to be sustained upon audit, the second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon settlement. Significant judgment is required to evaluate uncertain tax positions. The Company evaluates its uncertain tax positions quarterly. Evaluations are based upon a number of factors, including the technical merits of the tax position, changes in facts or circumstances, changes in tax law, interactions with tax authorities during the course of audits, and effective settlement of audit issues. The Company's policy is to recognize interest and penalties related to unrecognized tax benefits as a component of income tax expense in the consolidated statements of operations and accrued interest and penalties within accrued liabilities in the consolidated balance sheets. No such interest and penalties have been recorded to date.

***(t) Fair Value of Financial Instruments***

The Company applies fair value accounting for all financial assets and liabilities and nonfinancial assets and liabilities that are required to be recognized or disclosed at fair value in the consolidated financial statements. The Company defines fair value as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Where observable prices or inputs are not available, valuation models are applied. These valuation techniques involve some level of management estimation and judgment, the degree of which is dependent on the price transparency for the instruments or market and the instruments complexity.



The Company's financial assets and liabilities consist principally of cash and cash equivalents, accounts receivable, accounts payable, warrants for convertible preferred stock, convertible notes and the convertible shareholder notes derivative liability. The fair value of the Company's cash equivalents is determined based on quoted prices in active markets for identical assets. The recorded values of the Company's accounts receivable and accounts payable approximate their current fair values due to the relatively short-term nature of these accounts. The fair value of the Company's convertible preferred stock warrants is measured using the BSM option pricing model. Convertible notes are recorded at amortized cost. The fair value of the Company's convertible shareholder notes derivative liability is measured utilizing a Monte Carlo simulation model. Based on borrowing rates currently available for loans with similar terms, the carrying value of convertible notes approximates fair value.

*(u) Net Loss per Share*

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. Common stock equivalents are comprised of convertible preferred stock, notes convertible into preferred stock, warrants to purchase convertible preferred stock and options outstanding under our stock option plans. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding since the effects of potentially dilutive securities are antidilutive due to our net loss position.

***(v) Recently Adopted Accounting Pronouncements***

In August 2014, the Financial Accounting Standards Board (“FASB”) issued ASU No. 2014-15, Presentation of Financial Statements — Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern, which requires management to evaluate, in connection with preparing financial statements for each annual and interim reporting period, whether there are conditions or events, considered in the aggregate, that raise substantial doubt about an entity’s ability to continue as a going concern within one year after the date that the financial statements are issued and provide related disclosures. The Company adopted ASU 2014-15 effective December 31, 2016. The adoption of this ASU did not have any material impact on our financial position, results of operations or cash flows.

In July 2015, the FASB issued Accounting Standard Update (“ASU”) No. 2015-11, “Inventory: Simplifying the Measurement of Inventory”, that requires inventory not measured using either the last in, first out (LIFO) or the retail inventory method to be measured at the lower of cost or net realizable value. Net realizable value is the estimated selling prices in the ordinary course of business, less reasonably predictable cost of completion, disposal and transportation. The new standard will be effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years, and will be applied prospectively. Early adoption is permitted. The Company early adopted ASU 2015-11 effective October 1, 2016. The adoption of this ASU did not have any material impact on our financial position, results of operations or cash flows.

***(w) Recently Issued Accounting Pronouncements***

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606), which provides comprehensive guidance for revenue recognition. ASU 2014-09 affects any entity which either enters into contracts with customers to transfer goods or services or enters into contracts for the transfer of nonfinancial assets. The core principle of the guidance provides that a company should recognize revenue when promised goods or services are transferred to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. Additionally, qualitative and quantitative disclosures are required about customer contracts, significant judgments and changes in judgments, and assets recognized from the costs to obtain or fulfill a contract. The new standard can be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of the change recognized at the date of the initial application in retained earnings.

In August 2015, the FASB issued ASU 2015-14 Revenue from Contracts with Customers, which deferred the effective date for implementation of the standard. Public entities are to apply the new standard for annual and interim reporting periods beginning after December 15, 2017 and earlier application is permitted only as of annual reporting periods beginning after December 15, 2016, including interim reporting periods within that reporting period. The Company has not elected early adoption and has not concluded on an adoption method. The Company has formed a task force that is beginning to assess the Company’s customer contracts and the potential impacts the standard may have on previously reported revenues and future revenues. Given the relatively small volume of revenue

arrangements, the Company believes that the analysis will be completed in sufficient time to adopt the new standard when required.

In February 2016, the FASB issued ASU 2016-02 Leases (Topic 842), which supersedes existing guidance on accounting for leases in “Leases (Topic 840)” and generally requires all leases to be recognized in the consolidated balance sheet. ASU 2016-02 is effective for annual and interim reporting periods beginning after December 15, 2018; early adoption is permitted. The provisions of ASU 2016-02 are to be applied using a modified retrospective approach. The Company is currently assessing the future impact of this ASU on its consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The standard is intended to simplify several areas of accounting for share-based compensation arrangements, including the income tax impact, classification in the statement of cash flows and forfeitures. ASU 2016-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016, and early adoption is permitted. The Company will adopt the ASU, when required. The adoption of this guidance is not expected to have a material impact on our financial position, results of operations or cash flows.

Other recent accounting pronouncements issued by the FASB, including its Emerging Issues Task Force, and the American Institute of Certified Public Accountants did not or are not believed by management to have a material impact on the Company's financial statement presentation or disclosures.

### **(3) Reverse Merger**

On October 24, 2016, we completed the Merger as discussed in Note 1. For financial reporting purposes, the Merger is accounted for as an asset acquisition by BioCardia Lifesciences rather than a business combination because we did not meet the definition of a business as defined by US GAAP as of immediately prior to the Merger. The fair value of the purchase consideration, consisting of Company common stock, was determined based on the fair value of the cash acquired by BioCardia Lifesciences of \$19 million, which is considered the best indicator for the fair value of the purchase consideration. No other assets or liabilities were acquired by BioCardia Lifesciences. Transaction costs of \$96,000 were recorded as a debit to additional paid in capital. Additionally, pursuant to the Merger Agreement, upon consummation of the Merger, the Company assumed all of BioCardia Lifesciences, Inc. options outstanding immediately prior to the Merger at the same Exchange Ratio.

The Merger is considered a tax free reverse triangular merger for tax purposes pursuant to Internal Revenue Code Sections 368(a) and 368(a)(2)(E) in which the Company continues as the parent and BioCardia Lifesciences as the wholly owned subsidiary, and is therefore treated as an acquisition of stock of BioCardia Lifesciences by the Company. Despite the stock acquisition treatment, none of our pre-Merger tax attributes remain available after the Merger as a result of limitations under Internal Revenue Code Section 382 due to lack of business continuity.

### **(4) Fair Value Measurements**

The fair value of financial instruments reflects the amounts that the Company estimates to receive in connection with the sale of an asset or paid in connection with the transfer of a liability in an orderly transaction between market participants at the measurement date (exit price). The Company follows a fair value hierarchy that prioritizes the use of inputs used in valuation techniques into the following three levels:

Level 1 – quoted prices in active markets for identical assets and liabilities

Level 2 – observable inputs other than quoted prices in active markets for identical assets and liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities

Level 3 – unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The following table sets forth the fair value of our financial assets measured on a recurring basis as of December 31, 2016 and indicates the fair value hierarchy utilized to determine such fair value (in thousands).

	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>	<b>Total</b>
Assets:				
Cash and cash equivalents	\$21,352	\$ —	\$ —	\$21,352

The following table sets forth the fair value of our financial assets and liabilities measured on a recurring basis as of December 31, 2015 and indicates the fair value hierarchy utilized to determine such fair value(in thousands).

	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>	<b>Total</b>
Assets:				
Cash and cash equivalents	\$3,557	\$ —	\$—	\$3,557
Liabilities:				
Convertible preferred stock warrant liability	\$—	\$ —	\$275	\$275
Maturity date preferred stock warrant liability	\$—	\$ —	\$10	\$10
Convertible shareholder notes derivative liability	\$—	\$ —	\$1,044	\$1,044

As discussed more fully in Notes 11 and 12, the Company issued warrants to purchase preferred stock in connection with the note agreements to various shareholders. The warrant liabilities were recorded at the fair value on the date of issuance and were remeasured each subsequent balance sheet date and as of the warrant exercise date, with fair value changes recognized as income (decrease in fair value) or expense (increase in fair value) in other income (expense) in the consolidated statements of operations.



In May 2015, the Company entered into note agreements with various stockholders of the Company and other lenders for a total of \$7.2 million (the “2015 Notes”). As discussed more fully in Note 12, the 2015 Notes include embedded derivative features that were determined to be a compound embedded derivative requiring bifurcation and separate accounting at estimated fair value. The Company estimated the fair value of the compound embedded derivative utilizing a Monte Carlo simulation model from inception through June 30, 2016. The inputs used to determine the estimated fair value of the compound embedded derivative instrument include the probability of an underlying event triggering the redemption event and its timing prior to the maturity date of the 2015 Notes. The fair value measurement is based upon significant inputs not observable in the market. These assumptions are inherently subjective and involve significant management judgment. Upon the completion of the Merger, the valuation of the compound embedded derivative was determined based on the settlement value of the common stock exchanged for the notes on October 24, 2016.

The following tables set forth the fair value of our financial liabilities that the Company remeasured on a recurring basis (in thousands):

	<b>Convertible Preferred Stock Warrant Liability</b>	<b>Maturity Date Preferred Stock Warrant Liability</b>	<b>Convertible Shareholder Note Derivative Liability</b>
Fair value December 31, 2015	\$ 275	\$ 10	\$ 1,044
Change in fair value	(250 )	(10 )	1,224
Exchange of convertible preferred stock warrants	(25 )	—	—
Conversion of convertible notes	—	—	(2,268 )
Fair value December 31, 2016	\$ —	\$ —	\$ —

## **(5) Inventories**

Inventories are stated at the lower of cost or net realizable value using the average cost method. Inventories consist of the following (in thousands):

	<b>December 31, 2016 2015</b>	
Raw materials	\$59	194
Work in process	—	36
Finished goods	76	529
Total	\$135	759

Write downs for excess or expired inventory are based on management's estimates of forecasted usage of inventories and are included in cost of goods sold. A significant change in the timing or level of demand for certain products as compared to forecasted amounts may result in recording additional write downs for excess or expired inventory in the future. Charges to cost of goods sold for inventory write-downs, reserve adjustments, scrap, shrinkage and expired inventories totaled approximately \$52,000 and \$261,000 for the years ended December 31, 2016 and 2015, respectively. In addition, the Company determined that certain finished goods would be used in the Company's upcoming Phase III clinical study and as a result \$597,000 of finished goods inventory has been charged to research and development expense during the period.



**(6) Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consisted of the following (in thousands):

	<b>December 31,</b>	
	<b>2016</b>	<b>2015</b>
Prepaid expenses	\$356	146
Refund receivable of deferred financing costs	—	100
Total	\$356	246

**(7) Property and Equipment, Net**

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

	<b>December 31,</b>	
	<b>2016</b>	<b>2015</b>
Computer equipment and software	\$143	143
Laboratory and manufacturing equipment	366	366
Furniture and fixtures	48	48
Leasehold improvements	325	325
Property and equipment, gross	882	882
Less accumulated depreciation	(771)	(732)
Property and equipment, net	\$111	150

Depreciation expense totaled approximately \$39,000 and \$47,000 for the years ended December 31, 2016 and 2015, respectively.

**(8) Commitments**

In November 2016, the Company entered into an amendment to its lease with respect to its office and laboratory space. The extended term of this lease is 60 months and expected to commence on January 1, 2017 and expire on December 31, 2021. Rent expense is recognized on a straight-line basis over the life of the lease. Rental expense was approximately \$321,000 and \$266,000 for the years ended December 31, 2016 and 2015, respectively. Future minimum lease payments under the lease as of December 31, 2016 are as follows (in thousands):

Years ending December 31:

2017	\$576
2018	594
2019	612
2020	631
2021 and thereafter	649
Total	\$3,062

#### **(9) Collaborative Agreements**

The Company has entered into various collaborations related to clinical development. These agreements allow partners to utilize the Company's enabling biotherapeutic delivery systems, including training and support during clinical and pre-clinical delivery of biotherapeutics. Under the terms of these agreements, the Company typically receives a use fee and payments for the systems and services provided. The Company gains access to certain data generated by its partners for use in its own product development efforts and also receives nonexclusive patent rights to any BioCardia technology improvement inventions.

**(10) Accrued Liabilities**

Accrued liabilities consisted of the following (in thousands):

	<b>December 31, 2016 2015</b>	
Accrued expenses	\$478	229
Accrued interest	—	374
Customer deposits	66	89
Total	\$544	692

**(11) Convertible Preferred Stock Warrant Liability**

The Company has historically issued warrants to purchase shares of the Company's preferred stock in connection with certain preferred stock offerings and note financings.

As of December 31, 2015, the outstanding Series D and Series F convertible preferred stock warrants are as follows (in thousands, except per share and share data):

<b>Share class</b>	<b>Exercise price per share</b>	<b>Value at grant date</b>	<b>Issue date</b>	<b>Expiration date</b>	<b>Shares December 31, 2015</b>	<b>Estimated Fair Value December 31, 2015</b>
Series D	\$ 0.37	\$ 0.30	January 2006	January 2016	325,861	\$ 2
Series D	\$ 0.37	\$ 0.30	July 2007	July 2017	203,691	20
Series D	\$ 0.37	\$ 0.30	August 2007	August 2017	203,691	20
Series D	\$ 0.37	\$ 0.30	September 2007	September 2017	203,691	20
Series F	\$ 0.64	\$ 0.27	April 2013	April 2016	888,176	94
Series F	\$ 0.64	\$ 0.28	April 2013	October 2017	482,699	115
Series F	\$ 0.64	\$ 0.28	April 2013	November 2017	11,620	3
Series F	\$ 0.64	\$ 0.27	May 2013	May 2016	13,169	1
					2,332,598	\$ 275

Upon the completion of the Merger, the Company exchanged 20% and 10% of outstanding Series D and Series F convertible preferred stock warrants for 81,460 and 48,223 shares of the Company's common stock, respectively, and cancelled the remaining convertible preferred stock warrants pursuant to the Merger Agreement. Upon the completion of the Merger, the valuation of the convertible preferred stock warrant liability was determined based on the settlement value of the common stock exchanged for the warrants, amounting to \$25,000, and the Company reclassified the balance of the convertible preferred stock warrant liability to additional paid-in capital.

The fair value of the warrants at December 31, 2015 included in current liabilities in the consolidated balance sheet and was determined using the BSM valuation model using the following assumptions:

	<b>December 31, 2015</b>		
Risk-free interest rate	0.14	—	0.86%
Volatility	98.5	—	116.25%
Dividend yield	None		
Contractual term (in years)	0.1	—	1.8

The contractual term of the warrants represents the period of time remaining before the warrant expires. Since prior to the Merger, the Company's shares were not publicly traded and its shares were rarely traded privately, expected volatility was estimated based on the average historical volatility of similar entities with publicly traded shares. The risk free rate was based on the U.S. Treasury yield curve with a maturity equal to the remaining contractual term of the warrant.

## (12) Convertible Notes

In May 2015, BioCardia Lifesciences entered into note agreements with various stockholders of BioCardia Lifesciences and other lenders for a total of \$7.2 million (the “2015 Notes”). The notes accrued 8% annual simple interest, matured 18 months from the issue date and were callable after the maturity date by written demand of a majority of the holders of the outstanding note principle. If BioCardia Lifesciences closed an effective registration statement filed under the Securities Act of 1933, as amended, covering the sale of BioCardia Lifesciences common stock (an IPO) prior to maturity, the outstanding principle and accrued interest would have automatically converted into shares of common stock at 80% of the price of the shares of common stock purchased in the IPO. If at any time prior to the maturity date, the Company closed a private placement of the Company’s preferred stock for aggregate sales proceeds of at least \$5.0 million excluding note conversions, at the note holder’s option (“Optional Conversion Right”), the outstanding principle and interest may have been converted into shares of the preferred stock at a conversion price equal to 80% of the price of the preferred shares plus preferred stock warrant coverage equal to 8% with an exercise price equal to the purchase price of the preferred stock shares. If the notes were held to maturity, subject to BioCardia Lifesciences authorizing sufficient shares of a new class of preferred stock (“Maturity Date Preferred Stock”), the holder would have had the option to convert the outstanding principle and interest to this new class of preferred stock at an exercise price of \$0.07 per share, plus 8% warrant coverage.

In August 2016, the Company and the holders of convertible notes amended the notes, pursuant to which the outstanding principal amount and all accrued interest through August 31, 2016 will automatically convert into shares of common stock at 80% of the conversion price of the convertible notes issued in October 2016, as described in the following paragraph. In addition, the amendment eliminated the payment of interest for the period subsequent to August 31, 2016, and through the date of the closing of the Merger. Upon the completion of the Merger, the 2015 Notes and related accrued interest converted into 67,443,988 shares of the Company’s common stock.

The 2015 Notes had redemption features that were determined to be a compound embedded derivative requiring bifurcation and separate accounting at estimated fair value. The changes in the estimated value are reflected in the change in fair value of convertible shareholder notes derivative liability in the consolidated statements of operations. We estimated the fair value of the compound embedded derivative utilizing a Monte Carlo simulation model. The inputs used to determine the estimated fair value of the compound embedded derivative instrument include the probability of an underlying event triggering the redemption event and its timing prior to the maturity date of the 2015 Notes. The fair value measurement is based upon significant inputs not observable in the market. These assumptions are inherently subjective and involve significant management judgment. Immediately prior to the closing of the Merger, the compound embedded derivative was remeasured based on the settlement value of the common stock exchanged for the notes, and we reclassified the balance of the convertible shareholder notes derivative liability to additional paid-in capital.

In October 2016, BioCardia Lifesciences issued convertible notes with an aggregate principle amount of approximately \$4.4 million, which accrued 8% annual simple interest. The principle and accrued and unpaid interest on the notes converted automatically into 29,649,248 shares of common stock upon the completion of the Merger.

The Company recognized interest expense, including amortization of the debt discount of approximately \$1.7 million and \$1.4 million for the years ended December 31, 2016 and 2015, respectively.

**(13) Convertible Preferred Stock**

At December 31, 2015, convertible preferred stock consisted of the following (in thousands, except share data):

	Shares		Liquidation	Carrying
	Authorized	Outstanding	amount	Value
Series A	7,703,785	20,923,195	\$ 3,082	\$ 3,082
Series B	2,567,390	6,972,887	2,567	2,567
Series C	3,256,601	8,606,455	1,806	1,806
Series D	11,773,243	31,004,350	11,415	11,425
Series E	2,212,960	6,010,107	3,319	3,319
Series F	15,988,145	36,983,520	23,830	23,831
Total convertible preferred stock	43,502,124	110,500,514	\$ 46,019	\$ 46,030

The conversion price of all convertible preferred stock outstanding at December 31, 2015 was \$1. Upon the completion of the Merger, convertible preferred stock converted into 110,500,514 shares of the Company's common stock.

**(14) Share-Based Compensation**

BioCardia Lifesciences adopted, and the BioCardia Lifesciences shareholders approved, the 2002 Stock Plan in 2002 (the "2002 Plan"), and the Company assumed the 2002 Plan in the Merger. We will not grant any additional awards under the 2002 Plan following the Merger. In 2016, BioCardia Lifesciences adopted, and the BioCardia Lifesciences shareholders approved, the 2016 Equity Incentive Plan (the "2016 Plan"), and the Company assumed the 2016 Plan in the Merger. We will grant awards, including incentive stock options and nonstatutory stock options, under the 2016 Plan following the Merger. Under the 2002 Plan and the 2016 Plan, the number of shares, terms, and vesting periods are determined by the Company's board of directors or a committee thereof on an option-by-option basis. Options generally vest ratably over service periods of four years and expire ten years from the date of grant. The per share exercise price shall be no less than the fair market value on the date of grant. Compensation cost for employee share-based awards is based on the grant-date fair value and is recognized over the vesting period of the applicable award on a straight-line basis.

The Company recognizes in the consolidated statements of operations the grant-date fair value of stock options and other equity-based compensation. Stock compensation attributable to manufacturing operations was not significant and was expensed directly to cost of goods sold in the consolidated statements of operations. Share-based compensation expense for the years ended December 31, 2016 and 2015 was recorded as follows (in thousands):

	<b>Years ended December 31, 2016 2015</b>	
Cost of goods sold	\$14	\$4
Research and development	127	29
Selling, general and administrative	801	250
Share-based compensation expense	\$942	\$283

As discussed in Note 3, the Company assumed all of the outstanding options to purchase shares of BioCardia Lifesciences, whether or not vested, under the 2002 and 2016 Plans, with such options henceforth representing the right to purchase a number of shares of the Company's common stock equal to approximately 19.3678009 multiplied by the number of shares of BioCardia Lifesciences common stock previously represented by such options.

As discussed in Note 3, for accounting purposes, however, BioCardia Lifesciences is considered to be the acquirer in the Merger; thus, BioCardia Lifesciences is deemed to have assumed in the Merger all of the outstanding options to purchase shares of the Company's common stock, which were fully vested prior to the Merger.

The exchange of options to purchase shares of BioCardia Lifesciences common stock for options to purchase shares of the Company, was accounted for as a modification of the awards because the legal exchange of the awards is considered a modification of BioCardia Lifesciences stock options. The modification of the stock options did not result in any incremental compensation expense as the modification did not increase the fair value of the stock options.



The following table summarizes activity under the Company's stock option plans, including the 2002 Plan and the 2016 Plan and related information (in thousands, except share and per share amounts and term):

	<b>Options outstanding</b>		<b>Weighted</b>	<b>Aggregate</b>
	<b>Number of</b>	<b>average</b>	<b>average</b>	<b>intrinsic</b>
	<b>shares</b>	<b>exercise</b>	<b>remaining</b>	<b>value</b>
		<b>price</b>	<b>contractual</b>	<b>(In</b>
			<b>term</b>	<b>thousands)</b>
			<b>(years)</b>	
Balance, December 31, 2015	13,788,475	0.15	6.6	
Options assumed in the Merger	80,000	0.22		
Stock options granted	32,177,804	0.15		
Stock options exercised	(161,521 )	0.14		
Stock options cancelled	(3,981,030 )	0.15		
Balance, December 31, 2016	41,903,728	0.15	8.7	\$ 39,046
Exercisable, December 31, 2016	9,306,443	0.14	5.7	\$ 8,731
Vested and expected to vest, December 31, 2016	40,273,850	0.15	8.6	\$ 37,530

The total intrinsic value of options exercised during the years ended December 31, 2016 and 2015 was approximately \$144,000 and \$137,000, respectively. The weighted average grant-date fair value of options granted in 2016 was \$0.11 per share.

#### *Employee Share-Based Compensation*

During the year ended December 31, 2016, BioCardia Lifesciences granted stock options to employees to purchase 26,287,617 shares of common stock. There were no grants to employees during the year ended December 31, 2015. The fair value of each option grant is estimated on the date of the grant using the BSM option pricing model with the weighted average assumptions in the table below.

	<b>2016</b>		
Risk-free interest rate	1.28	-	1.58%
Volatility		88%	
Dividend yield	None		
Expected term (in years)		6.25	

Unrecognized share-based compensation for employee options granted through December 31, 2016 is approximately \$2.8 million to be recognized over a remaining weighted average service period of 3.6 years.

The Company estimates forfeitures at the time of grant and revises those estimates in subsequent periods if actual forfeitures differ from those estimates. The Company uses historical data to estimate pre-vesting option forfeitures and records share-based compensation expense only for those awards that are expected to vest.

#### *Nonemployee Share-Based Compensation*

During the year ended December 31, 2016, BioCardia Lifesciences granted options to purchase 5,890,187 shares of common stock to consultants. These options were granted in exchange for consulting services to be rendered and vest over the term specified in the grant, which correlates to the period the services are rendered. No options to non-employees were granted during the year ended December 31, 2015. The Company recorded \$545,000 and \$10,000 for the years ended December 31, 2016 and 2015, respectively, as nonemployee share-based compensation expense.

The Company accounts for share-based compensation arrangements with nonemployees, using the BSM option pricing model, based on the fair value as these instruments vest. Accordingly, at each reporting date, the Company revalues the unearned portion of the share-based compensation and the resulting change in fair value is recognized in the consolidated statements of operations over the period the related services are rendered. The following assumptions were used to value the awards.

	<b>2016</b>			<b>2015</b>		
Risk-free interest rate	1.60	-	2.42%	1.26	-	2.30%
Volatility	89	-	91%	71	-	95%
Dividend yield	None			None		
Expected term (in years)	9.6	-	9.9	8.5	-	9.7

### **(15) Concentrations**

Most of the Company's customers are located in the United States. No single customer accounted for more than 10% of revenue in 2016 and one customer accounted for 29% of accounts receivable at December 31, 2016. No single customer accounted for more than 10% of revenue in 2015 and three customers accounted for 23% of accounts receivable at December 31, 2015.

### **(16) Net Loss per Share**

The following table sets forth the computation of the basic and diluted net loss per share for the years ended December 31, 2016 and 2015 (in thousands, except share and per share data):

	<b>Years Ended December 31,</b>	
	<b>2016</b>	<b>2015</b>
Numerator:		
Net loss	\$(10,310 )	\$(6,697 )
Denominator		
Weighted average shares used to compute net loss per share, basic and diluted	100,419,402	18,723,511
Net loss per share, basic and diluted	\$(0.10 )	\$(0.36 )

The following weighted-average outstanding common stock equivalents were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive:

	<b>December 31,</b>	
	<b>2016</b>	<b>2015</b>
Convertible preferred stock	—	110,500,514
Notes convertible into shares	—	104,779,880
Stock options to purchase common stock	41,903,728	13,788,475
Convertible preferred stock warrants	—	2,332,598
Total	41,903,728	231,401,467

**(17) Income Taxes**

The Company's provision for income taxes for the years ended December 31, 2016 and 2015 was \$0 for both years.

The provision for income taxes differs from the amount which would result by applying the federal statutory income tax rate to pre-tax income/(loss) for the years ended December 31, 2016 and 2015. The reconciliation of the provision computed at the federal statutory rate to the Company's provision (benefit) for income taxes is as follows (in thousands):

	<b>2016</b>	<b>2015</b>
Tax at federal statutory rate	\$(3,505)	\$(2,277)
State, net of federal benefit	(315 )	(335 )
Research and development credit	(89 )	(51 )
Stock-based compensation	136	89
Nondeductible interest	590	471
Warrant and derivative revaluation	328	(589 )
Merger cost	90	-
Other	4	5
Increase in valuation allowance	2,761	2,687
Total provision for income taxes	<b>\$-</b>	<b>\$-</b>

Deferred income taxes reflect the net tax effects of temporary differences between carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes as well as net operating loss and tax credit carryforwards, net of any adjustment for unrecognized tax benefits. The components of the net deferred income tax assets as of December 31, 2016 and 2015 are as follows (in thousands):

	<b>2016</b>	<b>2015</b>
Accrued compensation	\$154	\$69
Inventory adjustments	708	279
Deferred rent	22	12
Deferred revenue	23	15
Deferred financing costs	-	643
Depreciation and amortization - noncurrent	252	293
Share-based compensation	273	57
Net operating loss and tax credit carryforwards - noncurrent	20,196	17,529
Section 481A Adjustment	-	(32 )
Other	2	5
Gross deferred tax asset	21,630	18,870
Valuation allowance	(21,630)	(18,870)
Net deferred tax asset	<b>\$-</b>	<b>\$-</b>

The Company has approximately \$48.0 million and \$40.8 million of federal and state net operating loss carryforwards, respectively, as of December 31, 2016. For tax reporting purposes, operating loss carryforwards are available to offset future taxable income; such carryforwards expire in varying amounts beginning in 2022 and 2017 for federal and state purposes, respectively. Under current federal and California law, the amounts of and benefits from net operating losses carried forward may be impaired or limited in certain circumstances. Events which may

cause limitations in the amount of net operating losses that the Company may utilize in any one year include, but are not limited to, a cumulative ownership change of more than 50% over a three-year period. The Company's deferred tax asset and related valuation allowance would be reduced as a result. An analysis to determine the limitation of the net operating loss carryforwards has not been performed.

At December 31, 2016, the Company has federal and state research and development credits of approximately \$1.3 million and \$1.1 million available to offset future federal and state income taxes, respectively. The federal tax credit carryforward expires beginning in 2028. The state credit carryforward has no expiration.

The Company does not believe that these assets are realizable on a more-likely-than-not basis; therefore, the net deferred tax assets have been fully offset by a valuation allowance. The Company did not have any deferred tax liabilities as of December 31, 2016 or 2015. The net increase in the total valuation allowance for the years ending December 31, 2016 and 2015 were approximately \$2.8 million and 2.7 million, respectively, primarily from the net operating losses generated.

No liability related to uncertain tax positions is reported in the consolidated financial statements.

The aggregate changes in the balance of gross unrecognized tax benefits were as follows (in thousands):

	<b>2016</b>	<b>2015</b>
Balance, beginning of year	\$531	\$486
Additions based on tax positions related to the current year	77	45
Additions for tax positions related to prior years	-	-
Reductions for tax positions related to prior years	-	-
Balance, end of year	\$608	\$531

Recognition of approximately \$398,000 and \$344,000 of unrecognized tax benefits would not impact the effective tax rate at December 31, 2016 and 2015, respectively, if recognized.

The Company is subject to U.S. federal, California, Colorado, Georgia, Michigan, and New Jersey income taxes. Tax regulations within each jurisdiction are subject to the interpretation of the related tax laws and regulations and require significant judgment to apply. The Company was incorporated in 2002 and is subject to U.S. federal, state and local tax examinations by tax authorities for all prior years.

## **(18) Contingencies**

The Company may be subject to various claims, complaints, and legal actions that arise from time to time in the normal course of business. Management does not believe that any current legal or administrative proceedings are likely to have a material effect on our business, financial position, results of operations, or cash flows.

### **(19) Grant Funding**

In June 2016, the Company entered into a grant agreement with Maryland Technology Development Corporation (“TEDCO”). TEDCO was created by the Maryland State Legislature in 1998 to facilitate the transfer and commercialization of technology from Maryland’s research universities and federal labs into the marketplace. TEDCO administers the Maryland Stem Cell Research Fund to promote State funded stem cell research and cures through financial assistance to public and private entities operating within the State. Under the agreement, TEDCO has agreed to provide the Company an amount not to exceed \$750,000 to be used solely to finance the costs to conduct the research project entitled “Heart Failure Trial” over a period of three years.

The Company received approximately \$312,000 under the grant which will be accounted for as a reduction to research and development expenses as the related qualifying costs are incurred. Approximately \$8,000 of the qualifying costs had been incurred as of December 31, 2016. The remaining \$304,000 is recorded as grant liability on the consolidated balance sheet at December 31, 2016. The amount is recorded as a liability as the amounts are refundable, should a default by the Company, as defined in the agreement, occur prior to incurring the qualifying costs.

### **(20) Related Party Transactions**

In August 2016, the Company granted an option to purchase 5,027,726 shares of common stock, with 4-year vesting period and the exercise price of \$0.15 per share, to OPKO Health, Inc. (“OPKO”) as consideration for consulting services to be provided by OPKO in accordance with the consulting agreement entered into between the Company and OPKO. The Company recorded \$466,000 as expense related to the OPKO stock option during the year ended December 31, 2016. The estimated grant-date fair value of the option is \$5.3 million. The term of the consulting agreement is 4 years and will be automatically renewed for successive one year periods. The chairman and chief executive officer of OPKO is a beneficial owner of more than 5% of the outstanding shares of the Company’s common stock and OPKO itself is also a beneficial owner of more than 5% of the outstanding shares of the Company’s common stock.



## **ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

## **ITEM 9A. CONTROLS AND PROCEDURES**

### **Disclosure Controls and Procedures**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the Company's reports under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including our Chief Executive Officer and Vice President of Finance, as appropriate, to allow timely decisions regarding required disclosure. 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, as the Company's controls are designed to do, and management necessarily was required to apply its judgment in evaluating the risk related to controls and procedures.

In connection with the preparation of this Annual Report on Form 10-K, as of December 31, 2016, an evaluation was performed under the supervision and with the participation of our management, including the Chief Executive Officer and Vice President of Finance, of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act). Due to the material weakness in internal control over financial reporting noted below, our Chief Executive Officer and Vice President of Finance concluded that our disclosure controls and procedures were not effective as of December 31, 2016. These conclusions were communicated to the Audit Committee. Notwithstanding the existence of the material weakness described below, management has concluded that the consolidated financial statements in this Form 10-K fairly present, in all material respects, the Company's financial position, results of operations and cash flows for all periods and dates presented.

***Management's Report on Internal Control over Financial Reporting***

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to recent consummation of the Merger in accordance with SEC Regulation S-K Compliance and Disclosure Interpretations, Section 215.02. Management's assessment of internal control over financial reporting will be required for our 2017 Form 10-K.

***Previously Identified Material Weaknesses in Internal Control Over Financial Reporting***

We previously identified a material weakness in internal control over financial reporting during the audit of our 2015 financial statements that remains unremediated. The material weakness resulted from an insufficient number of qualified personnel and inadequate processes within our accounting function which has impacted our ability to appropriately segregate duties and to perform timely and effective reviews over general ledger account reconciliations and non-routine transactions.

We are implementing measures designed to improve our internal control over financial reporting to remediate this material weakness, including the following:

- we are formalizing our processes and internal control documentation and strengthening supervisory reviews by our management; and
- we are in the process of adding additional qualified accounting personnel and improving the segregation of duties within the company.

**Changes in Internal Control over Financial Reporting**

There were no changes to our internal control over financial reporting identified in connection with the evaluation required by rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2016 other than those noted above that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

None.

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## **PART III**

### **ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this item is incorporated by reference to our Proxy Statement for our 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2016.

We have adopted a Code of Business Conduct and Ethics that applies to all of our (1) officers, (2) employees (including our principal executive officer, principal financial officer, principal accounting officer or controller and other employees who perform financial or accounting functions), and (3) agents and representatives, including our independent directors and consultants, who are not employees of ours, with regard to their BioCardia-related activities. Our code of business conduct and ethics is available on our website at [www.biocardia.com](http://www.biocardia.com) under the heading “Corporate Governance” under the section titled “Investors”. We will post on this section of our website any amendment to our code of business conduct and ethics, as well as any waivers of our code of business conduct and ethics, that are required to be disclosed by the rules of the SEC.

### **ITEM 11. EXECUTIVE COMPENSATION**

The information required by this item is incorporated by reference to our Proxy Statement for our 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2016.

### **ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The information required by this item is incorporated by reference to our Proxy Statement for our 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2016.

### **ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE**

The information required by this item is incorporated by reference to our Proxy Statement for our 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2016.

#### **ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

The information required by this item is incorporated by reference to our Proxy Statement for our 2017 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year ended December 31, 2016.

## **PART IV**

### **ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

Documents filed as part of this report are as follows:

#### **1. Consolidated Financial Statements:**

Our Consolidated Financial Statements are listed in the “Index to Financial Statements” of BioCardia, Inc. in Part II, Item 8 of this Annual Report on Form 10-K.

#### **2. Financial Statement Schedules**

All financial statement schedules have been omitted because they are not required, not applicable, or the required information is included in the financial statements or notes thereto included in this Annual Report on Form 10-K.

#### **3. Exhibits**

The documents listed in the Exhibit Index of this Annual Report on Form 10-K are incorporated by reference or are filed with this report, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

## SIGNATURES

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

BIOCARDIA INC.

By: */s/ Peter Altman*  
*Peter Altman*  
*President and Chief Executive*  
*Officer*

Date: March 30, 2017

## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Peter Altman and David McClung, and each of them, his true and lawful attorneys-in-fact, each with full power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

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

Signature	Title	Date
<i>/s/ Peter Altman</i> (Peter Altman)	President and Chief Executive Officer and Director ( <i>Principal Executive Officer</i> )	March 30, 2017
<i>/s/ David McClung</i>	Vice President of Finance	March 30, 2017

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(David McClung)	<i>(Principal Financial and Accounting Officer)</i>	
/s/ Simon H. Stertz (Simon H. Stertz)	Chairman of the Board	March 30, 2017
/s/ Fernando L. Fernandez (Fernando L. Fernandez)	Director	March 30, 2017
/s/ Richard Krasno (Richard Krasno)	Director	March 30, 2017
/s/ Jay M. Moyes (Jay M. Moyes)	Director	March 30, 2017
/s/ Richard P. Pfenniger, Jr. (Richard P. Pfenniger, Jr.)	Director	March 30, 2017
/s/ Thomas Quertermous (Thomas Quertermous)	Director	March 30, 2017
/s/ Allan R. Tessler (Allan R. Tessler)	Director	March 30, 2017



## EXHIBIT INDEX

Exhibit Number	Description
2.1(1)	Asset Purchase Agreement, dated January 24, 2011, by and among Cardio Medical, Inc. (nka Tiger X Medical, Inc.), Cardio Medical, LLC (nka Tiger X Medical, LLC) and Arthrex, Inc.
2.2(2)	First Amendment to Asset Purchase Agreement, effective March 18, 2011, by and among Cardio Medical, Inc. (nka Tiger X Medical, Inc.), Cardio Medical, LLC (nka Tiger X Medical, LLC) and Arthrex, Inc.
2.3(3)	Asset Purchase Agreement, dated April 4, 2011, by and among Cardio Medical, Inc. (nka Tiger X Medical, Inc.), Cardio Medical, LLC (nka Tiger X Medical, LLC) and Altus Partners, LLC.
2.4(4)	Agreement and Plan of Merger dated August 22, 2016
2.5(5)	First Amendment to Agreement and Plan of Merger dated October 21, 2016
3.1(6)	Amended and Restated Certificate of Incorporation.
3.2(7)	Certificate of Amendment of Amended and Restated Certificate of Incorporation.
3.3(8)	Certificate of Amendment of Amended and Restated Certificate of Incorporation.
3.4(9)	Certificate of Amendment of Amended and Restated Certificate of Incorporation.
3.5(10)	Amended and Restated Bylaws
4.1(11)	Specimen common stock certificate
4.2(12)#	BioCardia 2002 Stock Plan, as amended
4.3(13)#	Form of Stock Option Agreement under BioCardia 2002 Stock Plan
4.4(14)#	Cardio Medical (nka BioCardia, Inc.) 2010 Equity Incentive Plan
4.5(15)#	Form of Stock Award Agreement under Cardio Medical 2010 Equity Incentive Plan
4.6(16)#	BioCardia 2016 Equity Incentive Plan
4.7(17)#	Form of Stock Option Agreement under BioCardia 2016 Equity Incentive Plan
4.8(18)#	Form of Restricted Stock Unit Agreement under BioCardia 2016 Equity Incentive Plan
10.1(19)#	Form of Indemnification Agreement for directors and executive officers
10.2*#	Form of Change of Control and Severance Agreement with each executive officer.
10.3(20)	Lease Agreement, dated September 29, 2008, by and between the Company and ARE-San Francisco No. 29, LLC.
10.4(21)	First Amendment to Lease, dated May 31, 2010, by and between the Company and ARE-San Francisco No. 29, LLC.
10.5(22)	Second Amendment to Lease, dated May 29, 2013 by and between the Company and ARE-San Francisco No. 29, LLC.
10.6*	Third Amendment to Lease, dated November 4, 2016, by and between the Company and ARE-San Francisco No. 29, LLC.
10.7(23) †	License and Distribution Agreement, dated October 30, 2012, by and between the Company and Biomet Biologics, LLC, as amended.
21.1*	Subsidiaries of BioCardia, Inc.
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1*	Power of Attorney (see page 77 of this Annual Report on Form 10-K).
31.1*	Certification of Principal Executive Officer.
31.2*	Certification of Principal Financial Officer.
32.1**	Certification of Principal Executive Officer Pursuant to Rule 13a-14(b) and Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Title 18, United States Code).

32.2\*\* Certification of Principal Financial Officer Pursuant to Rule 13a-14(b) and Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Title 18, United States Code).

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101.INS\* XBRL Instance Document.  
 101.SCH\* XBRL Taxonomy Extension Schema.  
 101.CAL\* XBRL Taxonomy Extension Calculation Linkbase.  
 101.DEF\* XBRL Taxonomy Extension Definition Linkbase.  
 101.LAB\* XBRL Taxonomy Extension Label Linkbase.  
 101.PRE\* XBRL Taxonomy Extension Presentation Linkbase.

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€Confidential treatment has been granted with respect to certain portions of this Exhibit.

#Indicates management contract or compensatory plan or arrangement.

\*Filed herewith.

\*\*Furnished herewith.

- (1) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on January 27, 2011.
- (2) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on March 24, 2011.
- (3) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on April 8, 2011.
- (4) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on August 25, 2016.
- (5) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (6) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on March 18, 2008.
- (7) Previously filed as an Annex to the Information Statement on Schedule 14C filed by us on September 30, 2008.
- (8) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on June 16, 2011.
- (9) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (10) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on February 1, 2008.
- (11) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (12) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (13) Previously filed as an exhibit to the registration statement on Form S-8 filed by us on February 8, 2017.
- (14) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on September 9, 2008.
- (15) Previously filed as an exhibit to the registration statement on Form S-8 filed by us on February 8, 2017.
- (16) Previously filed as an exhibit to the registration statement on Form S-8 filed by us on February 8, 2017.
- (17) Previously filed as an exhibit to the registration statement on Form S-8 filed by us on February 8, 2017.
- (18) Previously filed as an exhibit to the registration statement on Form S-8 filed by us on February 8, 2017.
- (19) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (20) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (21) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (22) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.
- (23) Previously filed as an exhibit to the Current Report on Form 8-K filed by us on October 27, 2016.