

# BIOCARDIA, INC.

To our fellow shareholders,

Another year is completed and I remain optimistic about the strength of our therapeutic programs and the progress we are making. There is intense effort being put forth by the entire BioCardia team, and our clinical partners are getting closer to the rate of patient recruitment required to complete the Phase III CardiAMP™ Heart Failure Trial.

I wanted to take a moment to lay out our progress across our product pipeline in recent months and share some thoughts about our efforts to build long-term financial health for the company.

## *The Big Picture*

Our primary objective today is to deliver positive CardiAMP Cell Therapy trial data that enables the therapy to be approved by the FDA as a treatment for heart failure. This requires not only full enrollment of the trial, but also persuasive outcomes. The CardiAMP Heart Failure trial was designed based on positive outcomes from the Phase II trial to have greater than 95% power, or a very high probability of meeting the primary endpoint. To be successful, we must also deliver the safety profile we have seen in our trials to date. CardiAMP cell therapy is the primary focus of the company because of its potential to meaningfully improve lives and do so cost-effectively. Our innovative approach to rapidly processing a patient's own cells at the point of care, rather than sending them out for expensive and time consuming lab manipulation, is intended to make the therapy dramatically less expensive for patients and the healthcare system as a whole, and make it more accessible to more patients when compared to other cell therapies.

## *CardiAMP Early Phase III Pivotal Trial Results are Promising*

Compelling data from the 10-patient roll-in cohort were presented at last November's American Heart Association Scientific Sessions, showing meaningful improvements in the primary endpoint of exercise capacity, with eight of the 10 patients experiencing exercise improvement. This improvement is more than triple the average improvement over baseline reported in the CardiAMP Phase II trial, and greater than the average improvement seen in a number of pivotal trials for implantable cardiac resynchronization therapy (CRT) to treat heart failure. It's notable that these CRT therapies were approved by the FDA with substantially the same clinical endpoint. Moreover, the early CardiAMP data showed that there were no treatment emergent major adverse cardiac events at 30 days, and all patients were alive and out of the hospital at one year.

Patients in this cohort also showed improvement in a key measure of heart function and in quality of life. In earlier clinical trials, CardiAMP showed the potential to not simply slow or stop disease progression, but actually improve heart function, and it is very encouraging that the early Phase III

results suggest the same. If the data continues in this fashion, CardiAMP cell therapy could be the first therapy developed in the last 20 years to improve intrinsic heart muscle function in chronic heart failure, resulting in improved quality of life and exercise performance in patients suffering from this life-threatening disease. This goal drives us as BioCardians daily as we continue the development of this potentially first-in-class therapeutic option for patients.

#### *CardiAMP Enrollment is Full Speed Ahead*

Thirty-five patients have been treated in the CardiAMP HF Trial to date. We are pleased to see a continuation of the strong safety profile in addition to positive initial improvements in patients' functional capacity achieved in the roll-in cohort. While enrollment has been slower than originally anticipated, it is now accelerating, and we expect this trend to continue.

There are several reasons for the slow start, and we have addressed many of them:

- Our cell potency assay is one of the unique elements of CardiAMP therapy and the best data in the field suggests that identifying patients with high quality bone marrow will maximize the probability of the trial's success. This means that we intentionally exclude a group of patients in screening, although that number is currently somewhat higher than we anticipate it will ultimately be.
- Implementation of our Medicare reimbursement within each center has been new for many clinical research groups and has required a learning curve. Additionally, the coverage excludes patients who are ineligible for Medicare and whose insurers do not follow Medicare's reimbursement guidelines for investigational therapies, thereby affecting enrollment. However, it's important to note that obtaining Medicare reimbursement for the trial was a very positive achievement and greatly reduces our expense of running the trial.
- Until the end of 2018, we were competing with two other trials for the same patient population and for the attention of several leading centers. Those studies are now completed and these centers are now joining our trial.

We are grateful to our strong clinical partners for working with us to resolve these issues.

Whereas we began 2018 with 7 centers participating, we now have 21 active world-class centers in the CardiAMP Heart Failure Trial and continue to add other sites. We thank those centers that are delivering on their enrollment commitments and are working closely with others as they aim to do better.

#### *CardiALLO™ Gets to the FDA*

While CardiAMP remains our primary focus, we feel it is important to offer an alternative for patients who do not qualify for the rigorous requirements of the autologous cell therapy. With that

in mind, we recently filed an IND with the FDA for our second cell therapy candidate – CardiALLO – which, once accepted, will enable us to begin an investigational study when we believe the time is right for the business. The CardiALLO trial is specifically designed for patients with low bone marrow cell potency, as determined by our proprietary CardiAMP assay.

CardiALLO is a culture-expanded “off the shelf” mesenchymal cell therapy for the treatment of ischemic heart failure using allogenic cells, or those from a separate donor. The therapy uses NK1R+ mesenchymal stem cells, which are believed to be activated by Substance P, a chemical that has been shown to facilitate healing and minimize damage within the body. We are excited about the potential of CardiALLO to give us two complementary therapies to help heart failure patients who do not have good options today.

Additionally, we see an opportunity to leverage our work with this proprietary cell population for other clinical indications, in order to generate greater value for both patients and shareholders without significant additional expense to BioCardia. For example, there is interesting clinical data in the literature that has been generated in stroke, diabetes, rheumatoid arthritis and Crohn’s disease, and my sense is that our CardiALLO cells have the potential to offer superiority to other therapies currently in development.

#### *Enabling Products Enhance Our Therapeutic Mission*

Part of our success to date with CardiAMP is the enabling technologies that enhance successful delivery of the therapy. While they don’t get as much attention, they are important tools in our arsenal and are being leveraged beyond our own needs. Our Helix™ Biotherapeutic Delivery System has been chosen for use in a total of 12 cell therapy trials to date (including our own ongoing CardiAMP Heart Failure Trial, approved CardiAMP Chronic Myocardial Ischemia Trial, and recently submitted CardiALLO Heart Failure Trial). In September 2018, the presentation of the clinical safety experience encompassing 300 procedures in these trials showed that the Helix system presents the lowest risk to patients for cell and gene delivery to the heart, when compared to all other delivery systems in the scientific literature for which data is available. This builds on previous data from 2017 which showed that the system is also the most efficient for our lead cell therapy program. Each delivery procedure utilizing the Helix system relies on our Morph™ steerable guide catheter technology, which has been used in more than 10,000 patients aged two months to 96 years to help treat a broad variety of serious vascular diseases.

Continuous improvement in our enabling technologies enhances our therapeutic programs and those of our partners, and underlies our potential for revenue growth even while we conduct our therapeutic trials. Enhancements to the Helix system have been made or are underway to further de-risk the cell therapy clinical programs. One of these is being made to significantly upgrade our Morph steerable guide platform with what we call “DNA” technology, which we have shown is able

to eliminate “whip” when navigating curved anatomy, provides for bidirectional control, is more durable, and should be less expensive to manufacture in volume than our current Morph device.

By making this slight reconfiguration of the Morph platform we have opened up a new product opportunity for the technology. In the fourth quarter of 2018, we submitted a 510(k) to the FDA for the AVANCE™ steerable introducer, based on this Morph “DNA” technology. AVANCE is intended to address the large and growing market for transseptal access, which enables entry via the left side of the heart through the interatrial septum. The global transseptal access systems market is currently estimated at \$550 million and is extremely competitive. The physicians we train to perform the CardiAMP cell therapy procedures are among those who may use AVANCE in their normal practice and they have provided extensive input in its development. We intend to submit a 510(k) for another Morph steerable guide product which also incorporates “DNA” technology by the end of this year.

### *Building Long-Term Financial Health*

We are building BioCardia for long-term success and are taking financial actions now that will enable the company to thrive over time. As you may know from our SEC filings, the Board and a majority of shareholders recently voted to move forward with a reverse stock split. When companies make this move, it can sometimes be perceived negatively. However, I want to outline for you why this move is a positive development, based on our careful consideration.

The split should not be taken on its own. It is one piece of a larger strategy. It is a step we must take as part of qualifying to uplist to a major exchange – either NASDAQ or NYSE. To qualify for an uplist, we must bring the share price above \$3 per share for at least 30 days, which, for us, requires the split. We anticipate that uplisting will make our stock more accessible to investment funds and analyst coverage, which has the potential to attract new investors, increasing liquidity, access to capital and shareholder value over time. Over the long term, we believe an uplisting will open up opportunities for us as a company and for you, our fellow shareholders.

### *The Path Ahead*

We believe the steps we are taking should also help to secure the financing necessary to complete the CardiAMP Heart Failure Trial. Completion of the trial and analysis of the 12-month results will enable us to file for FDA approval, assuming the results are as positive as we anticipate. Additional financing is expected to also allow us to make progress on other initiatives, including further development of CardiALLO and the Helix system, and commercial availability of AVANCE and Morph “DNA” products. Having multiple platform products where we can succeed de-risks the Company and increases its attractiveness to investors and partners. But make no mistake, CardiAMP is still at the heart of our efforts.

I thank you for your continued support and ask that you remain with us on this journey to bring better options to patients, their families and physicians dealing with cardiovascular disease.

Sincerely,



Peter Altman, PhD  
Chief Executive Officer  
BioCardia, Inc.  
April 22, 2019

### **Forward-Looking Statements**

Certain statements in this shareholder letter are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as “may,” “might,” “would,” “should,” “could,” “project,” “estimate,” “pro-forma,” “predict,” “potential,” “strategy,” “anticipate,” “attempt,” “develop,” “plan,” “help,” “believe,” “continue,” “intend,” “expect,” “future” or other similar terms or expressions that concern BioCardia’s expectations, strategy, plans or intentions (including the negative of any of the foregoing). These forward-looking statements are based on BioCardia’s current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, our need for additional financing; our ability to continue as a going concern; clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results; our clinical trials may be suspended or discontinued due to unexpected side effects or other safety risks that could preclude approval of our cell therapy systems; our ability to, or the time periods by which we expect to, obtain regulatory approval for our cell therapy systems; market acceptance of our cell therapy systems; 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; developments relating to our competitors and the healthcare industry; and the impact of general economic, industry or political conditions in the United States or internationally. Additional risks and uncertainties relating to BioCardia and its business can be found under the heading “Risk Factors” in BioCardia’s most recent quarterly and annual reports filed with the SEC.

While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and BioCardia does not undertake any obligation to update or revise any such statements to reflect subsequent events or circumstances, except as required by law.