



BIOCARDIA[®]

Developing cellular and cell-derived therapeutics for the treatment of cardiovascular and pulmonary diseases

Corporate Presentation
BioCardia, Inc. (NASDAQ: BCDA)

Peter Altman, PhD
President and CEO
paltman@biocardia.com

www.biocardia.com

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Problem: Heart failure, a disease with enormous unmet need

- 56.2 million people worldwide have HF. ¹
- In the United States, HF costs are projected to increase to \$70 billion in 2030, half related to hospitalization. ¹
- In Japan, one million patients have heart failure with 31 to 47% having ischemic etiology ² and it is considered a national priority.
- Despite guideline directed medical therapy:
 - High mortality: 50% mortality at five years ³
 - Frequent hospitalizations
 - Significant quality of life impairment
- No therapies directly address myocardial microvascular dysfunction and its impact on adverse remodeling.

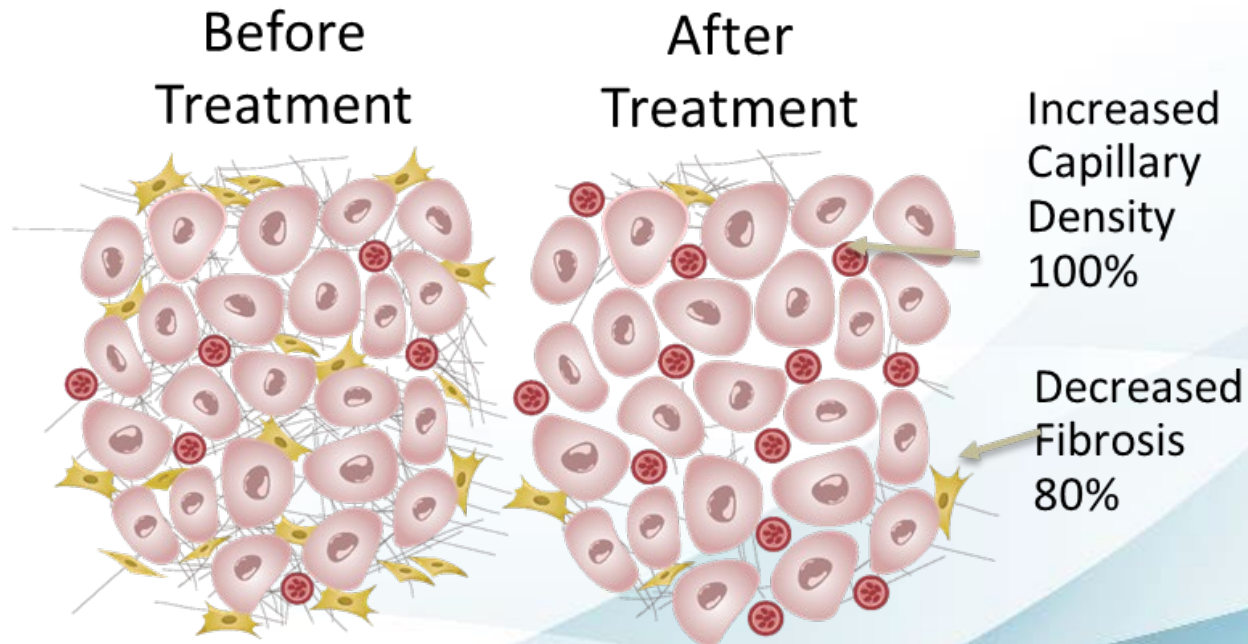


Sources of data:

1. Martin et al 2024 Heart disease and statistics from the American Heart Association
2. Heart failure epidemiology and novel treatments in Japan: facts and numbers Masaaki Konishi, European Heart Journal 2016.,
3. EMPOROR -Reduced Trial, NEJM, 2020.

Potential Solution: Enhancing Microvascular Function

- New mechanism of action:
 - improve microvascular capillary density
 - reduce fibrosis
 - prevent adverse remodeling
- Mechanism driven primarily by cell mediated paracrine signaling
- Not intended to regenerate new myocardium



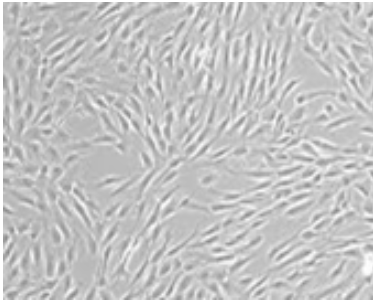
Silva et al. Tex Heart Inst J (2011);38(3):219-24.

Takahashi, M. et al. (2006) Am J Physiol Heart Circ 291:H886-H893.

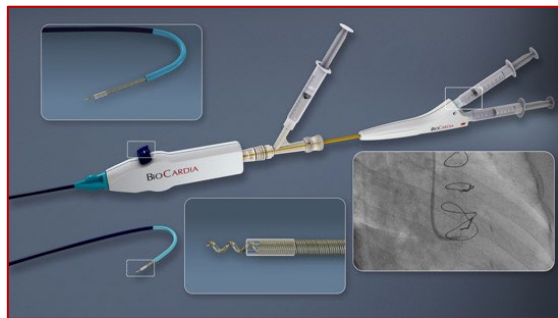
Proprietary Regenerative Medicine Platform Overview



- CardiAMP® Autologous Mononuclear Cells (lead program, utilizes delivery)



- CardiALLO™ Allogeneic Mesenchymal Cells (earlier stage, also utilizes delivery)



- Proprietary Delivery Systems
Transendocardial catheter-based local delivery technology

CardiAMP® Cell Therapy: Lead Program

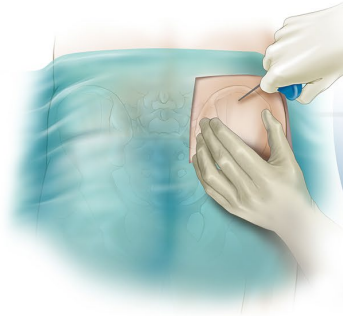
FDA Breakthrough Designation / Has CMS Reimbursement

Autologous Cell Therapy For ischemic HFrEF

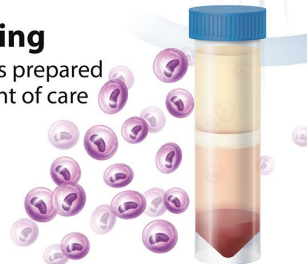
Pre-procedure Screening

Small amount of bone marrow collected from hipbone and sent to lab for testing

- 1 Cell Collection**
Small amount of bone marrow obtained from hipbone
~ 20 minutes



- 2 Cell Processing**
Bone marrow cells prepared for transfer at point of care
~ 25 minutes



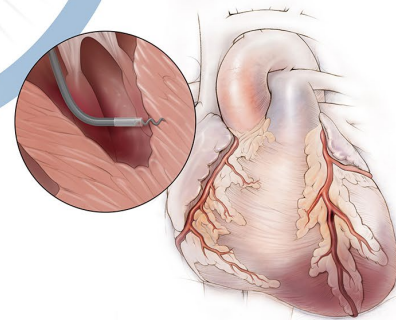
CardiAMP™ Therapy



Post-procedure

Patient leaves hospital the next day

- 3 Cell Delivery**
Bone marrow cells injected into damaged heart tissue through a catheter-based procedure
~30 to 45 minutes



04142-C (MKT)

CardiAMP System Development Status

198 Procedures and Counting



FDA Breakthrough Device Designation granted based on results from Phase I and II trials.



CMS Reimbursement Code C9782 for CardiAMP Cell Therapy for both treated and control patients at \$20,000 (\$35,000 for a treatment and a control)

**TABMMI Ph I
Cell Therapy Trial**

Open label clinical trial on 20 patients (NCT00507468) ¹

- Safety, Early Efficacy

**TAC-HFT Ph II
Cell Therapy Trial**

Double-blind controlled clinical trial in 33 patients (NCT00768066) ^{2,3}

- Safety and Efficacy signals

**CardiAMP HF Ph III
Cell Therapy Trial**

Double-blind controlled clinical trial in 125 patients (NCT02438306) ^{4,5}

- Efficacy in patients having elevated biomarkers of heart stress (NTproBNP)

Japan's Pharmaceutical and Medical Device Agency has indicated that this clinical data is likely sufficient for regulatory approval.



**CardiAMP HF 2 Ph III
Cell Therapy Trial**

Actively enrolling in USA at four centers.

1. De la Fuente, Eurointervention 2011,
2. Wong Po Foo WCRM 2015,
3. Heldman JAMA 2014.
4. Raval ACC 2025.
5. Raval THT 2026.

CardiAMP Key clinical insights

- **Benefit seen across patients in three trials***

- Reduced mortality and non-fatal major adverse cardiac events
- Improved heart function
- Improved quality of life

- **Heart failure patients are heterogeneous**

Analysis suggests greater benefit in patients with both high concentrations of important cell types and evidence of active heart stress.

- Proprietary patient Cell Population Analysis (CPA) may be used to define dosages
- Biomarkers for heart stress (NTproBNP) identify responder population

- **Strategic direction**

- Focus on precision-defined patient populations
- Once approved, Japan support to be top priority

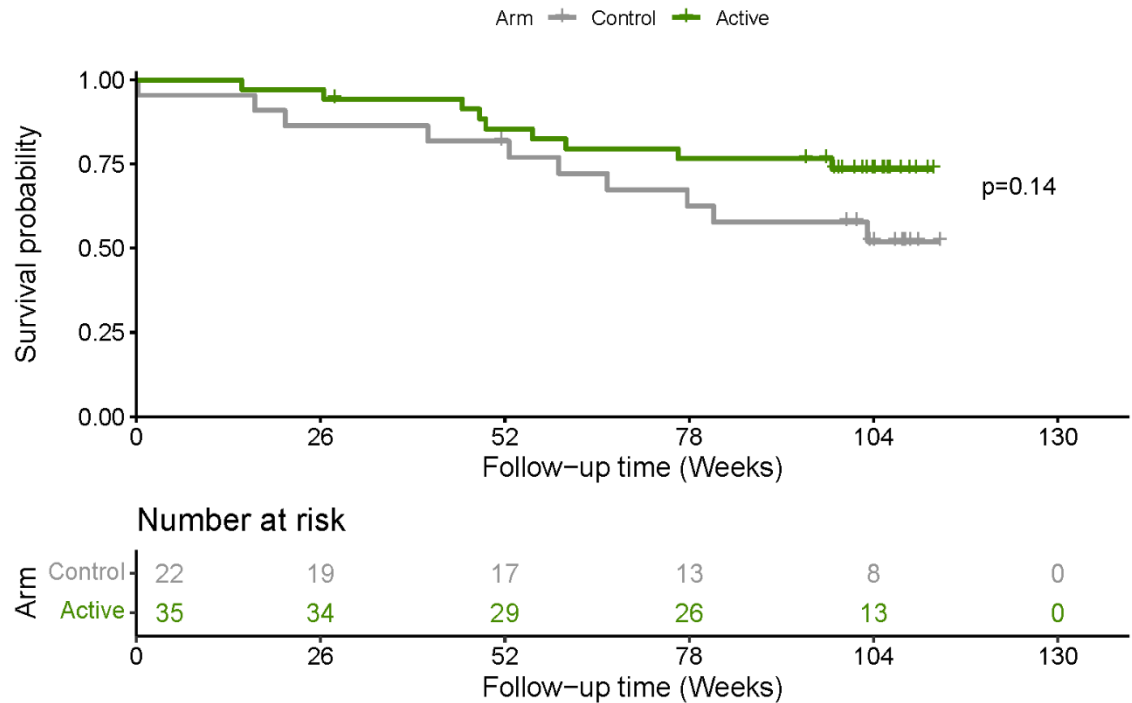
* Details on clinical trial results provided on website and manuscripts available on request.

CardiAMP HF Phase III Results in Patients with NTproBNP/BNP >500 pg/ml

Composite outcome of three tiers – all benefit treatment



MACE Free Survival: NTproBNP/BNP >500 pg/ml Subgroup

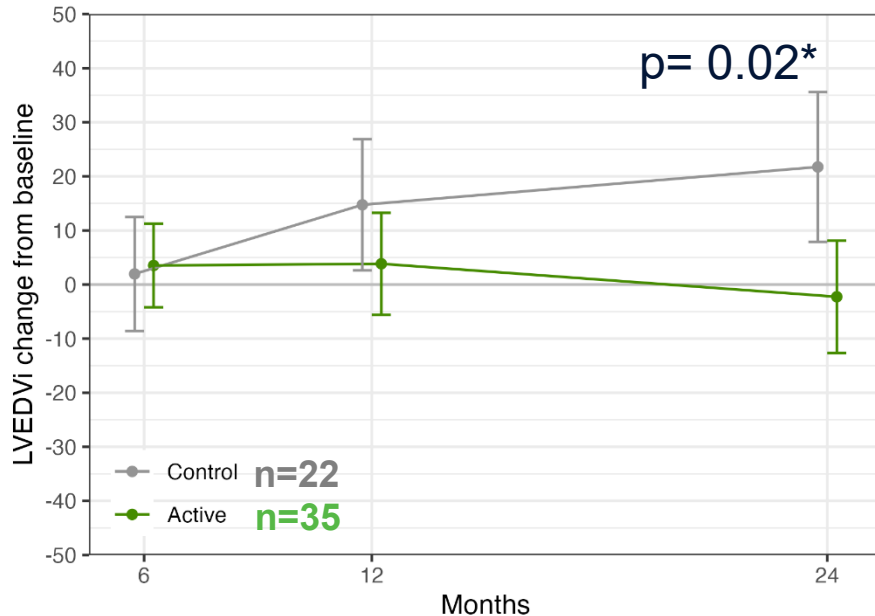


HTx = Heart Transplant; LVAD = Left ventricular Assist Device; MACE = Major Adverse Cardiac Event; 6MWD = six minute walk distance ; MLHFQ = Minnesota Living with Heart Failure Quality of Life; WR = Win Ratio ; CI = Confidence Interval; NTproBNP = Biomarker of heart stress

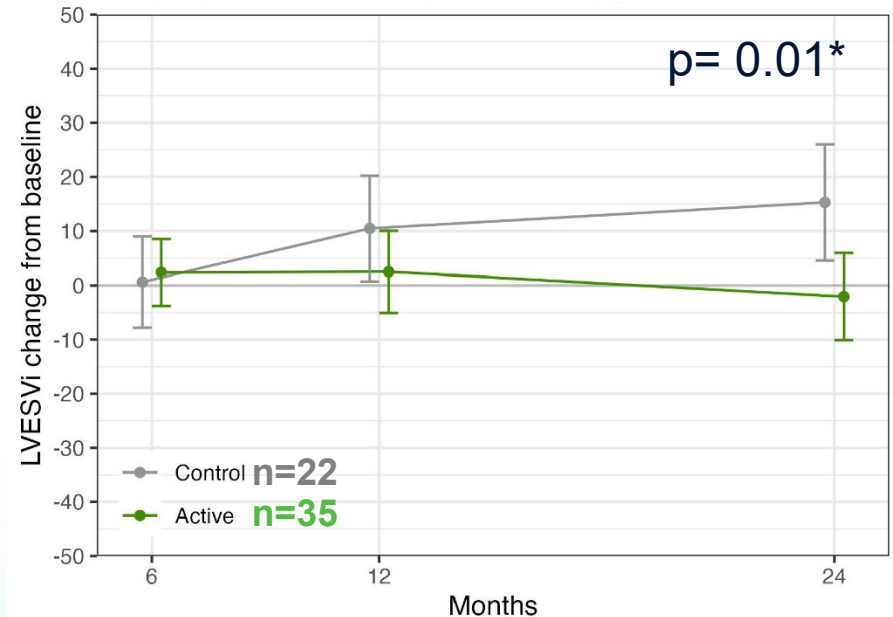
A = Active treatment group
C = control placebo procedure group

CardiAMP HF Phase III Results in Patients with NTproBNP/BNP >500 pg/ml
Left Ventricular End Diastolic Volume Index (LVEDVi) and Left Ventricular End Diastolic Volume Index (LVESVi) show prevention of negative heart enlargement. This has long been known to align with positive outcomes.**

LVEDVi



LVESVi



** Kramer DG et al Quantitative Evaluation of Drug or Device Effects on Ventricular Remodeling as Predictors of Therapeutic Effects on Mortality in Patients With Heart Failure and Reduced Ejection Fraction: a Meta-analytic Approach JACC 2010

CardiAMP HF Pathways to Approval and Reimbursement

JAPAN



- **Japan Pharmaceutical and Medical Devices Agency (PMDA) has said they are likely to accept existing evidence of safety and efficacy as sufficient for market release.**
 - Initial indication identical to CardiAMP HF Trial with elevated NTproBNP.
 - PMDA Submission ~ 6 months.
 - Approval ~12 months after submission.
 - Initial CardiAMP indication ~20,000 patients / year; previous cardiac cell therapy in Japan reimbursed at \$124,000
 - Post marketing study with CV societies (with reimbursement)



**Japan
Heart Failure
Society**



**Cardiovascular
Interventional
Therapeutics
(CVIT)**

BIOCARDIA®

CardiAMP HF Pathways to Approval and Reimbursement

JAPAN



■ Target initial population for CardiAMP cell therapy

- In Japan, total ischemic HFrEF patients are ~ 300,000 and anticipate ~20,000 initial reachable patients with unmet need as discussed with PMDA. Previously Heartsheet, a cardiac cell therapy was reimbursed at \$124,000.
- In Japan, there is potential to exceed ramp of transcatheter aortic valve replacement (TAVR) cases which rose from 925 to 7,778 in 5 years, exceeding the growth rate of TAVR in the USA over the same period. The number of hospitals performing TAVR increased drastically from 15 to 170 in the same period. TAVR competed with surgical valve replacement. CardiAMP addresses unmet clinical need.

Tentative timelines with Post Marketing Surveillance Studies (PMSS)

	2026	2027	2028	2029
Japan	Submission	Approval	Commercial/PMS	Commercial/PMSS

1. Kaneko T, et al. Practice Patterns and Outcomes of Transcatheter Aortic Valve Replacement in the United States and Japan: A Report From Joint Data Harmonization Initiative of STS/ACC TVT and J-TVT. J Am Heart Assoc. 2022 Mar 15;11(6):e023848.

CardiAMP HF Pathways to Approval and Reimbursement USA

- Target initial population for CardiAMP cell therapy
 - Patients with ischemic heart failure, on guideline directed medical therapy but still having biomarker evidence of active heart stress ~ 1 million patients in USA ^{1, 2}
 - Reimbursement in USA is currently \$20,000 per treated patient, while investigational.
- FDA Breakthrough Designation
- FDA supportive that CardiAMP HF II Trial could be sufficient for a successful Premarket Application (PMA) submission.
- FDA supportive of endpoint.
- Discussions ongoing.

1. Martin et al 2024 Heart disease and statistics from the American Heart Association
2. Vedin 2017 Significance of Ischemic Heart Disease in Patients With Heart Failure and Preserved, Midrange, and Reduced Ejection Fraction

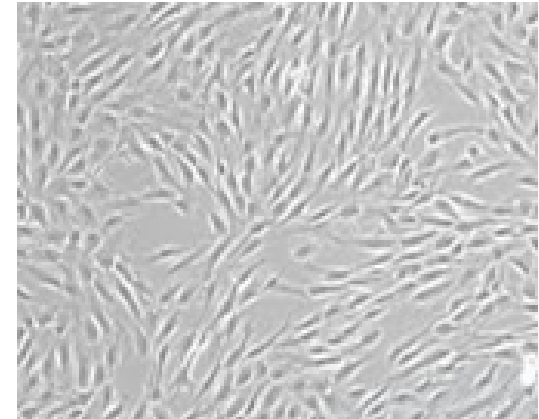
Ongoing Confirmatory CardiAMP HF II Clinical Trial

- Double Blind Procedure Placebo Controlled Randomized (1:1) Trial (NCT06258447)
 - NYHA Class II and III, EF < 40%, Ischemic etiology, with elevated NTproBNP
 - Patients on stable Guideline Directed Medical Therapy
 - One month screening to baseline delay to address Hawthorne Effect
 - Finkelstein Schoenfeld composite endpoint including: Mortality, Major adverse cardiac events, Quality of life measures
 - Power of 80% with 160 patients
 - Up to 250 patients at up to 40 centers
 - 4 World Class centers activated and enrolling



CardiALLO Allogeneic Cell Therapy Strategic Optionality

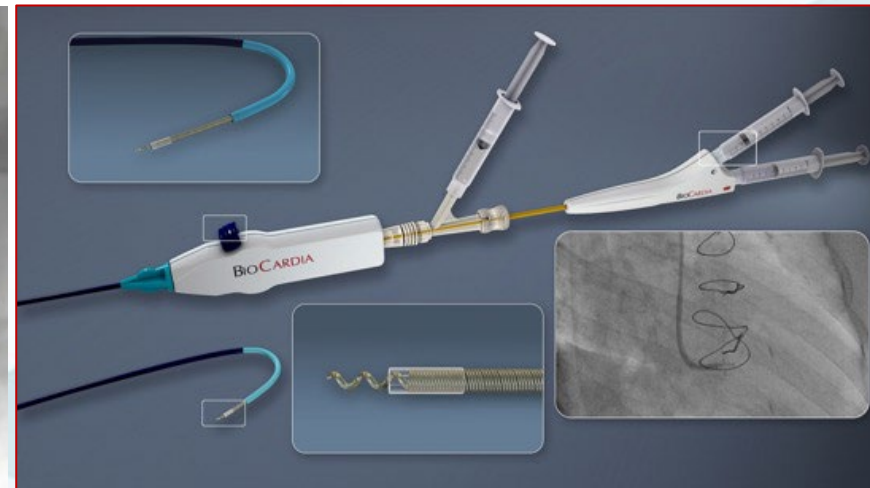
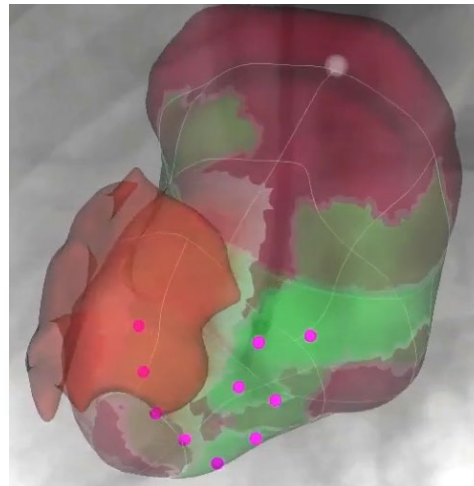
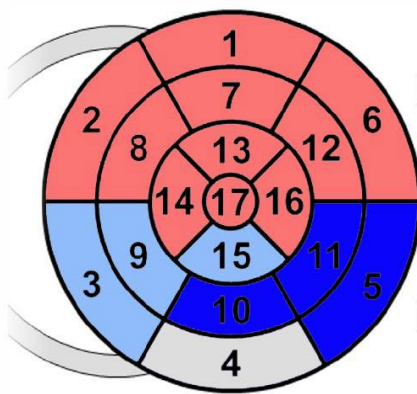
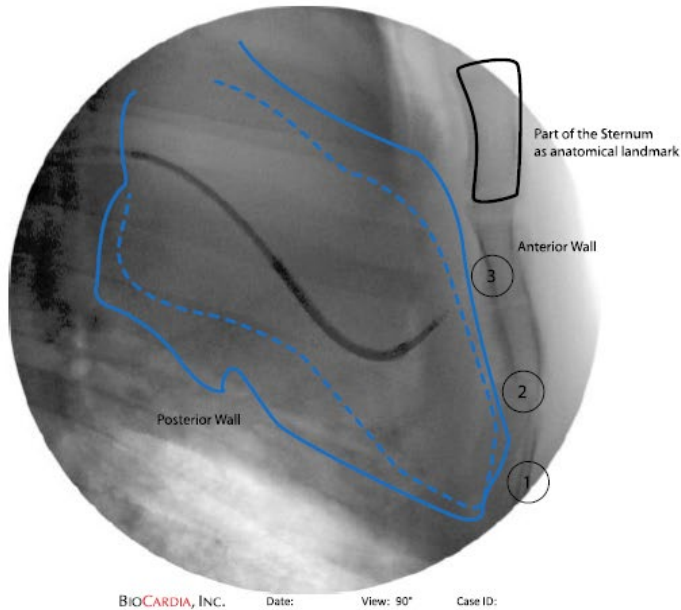
- Donor derived mesenchymal cells manufactured and cryopreserved for therapy
 - Potential advantages
 - Off the shelf availability – reduces clinical procedural logistics
 - No need for performing a tissue collection on treatment day
 - Limits patient to patient variation of therapy
 - Single donor creates a cell bank for multiple patients.
 - Clinical development focused on safety and biological activity
 - 48 Patients treated in three trials to date – all with positive results



Delivery as a Differentiator

Precision Transendocardial Delivery

- Proprietary catheter-based delivery systems
- Designed for targeted myocardial injection
- Delivery quality recognized as a key variable in cardiac cell therapy outcomes
- DeNovo Approval Pathway Possible based on May 2026 FDA PreSub.



Intellectual Property Overview

- Exclusive rights to over 60 patents and patent applications in USA, Europe, China, India, and Japan with goal to protect the company's platform and therapeutic initiatives.

US090931719982

(12) **United States Patent**
(10) **Patent No.:** US 9,517,199 B2
(45) **Date of Patent:** *Dec. 13, 2016

(54) **TREATMENT FOR CHRONIC MYOCARDIAL INFARCT**

(71) Applicant: **BioCardia, Inc.**, San Carlos, CA (US)

(72) Inventors: **Luis M. de la Fuente**, Buenos Aires (AR); **Shirley R. Sharkey**, Santa Fe, NM (US); **Judith Argenteffer**, Buenos Aires (AR); **Edmundo Ponzio**, Buenos Aires (AR); **Peter A. Altman**, Menlo Park, CA (US)

(73) Assignee: **BioCardia, Inc.**, San Carlos, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 73 days. This patent is subject to a terminal disclaimer.

(21) Appl. No. **14403045**

(22) Filed: **Feb. 24, 2015**

(65) **Prior Publication Data**
US 2015/0164786 A1 Jun. 18, 2015

Related U.S. Application Data

(63) Continuation of application No. 139535061, filed on Jul. 30, 2013, which is a continuation of application No. 117753869, filed on Apr. 16, 2007, now Pat. No. 6,449,925.

(51) **Int. Cl.**
A61N 8/08 (2006.01)
A61N 8/06 (2006.01)
A61K 35/28 (2015.01)
A61K 35/54 (2015.01)
A61K 35/52 (2015.01)
A61K 35/53 (2015.01)

(52) **U.S. Cl.**
CPC: **A61N 8/0829** (2013.01); **A61K 35/54** (2013.01); **A61K 35/28** (2013.01); **A61K 35/52** (2013.01); **A61K 35/53** (2013.01)

(58) **Field of Classification Search**
See application file for complete search history.

(56) **References Cited**
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7,080,815 B2 2/2010 Ferguson
7,299,349 B2 9/2010 Uno et al.
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2009/0144411 A1 5/2009 Kowalski et al.
2009/0144411 A1 5/2009 De La Fuente et al.
2013/0032122 A1 12/2013 De La Fuente et al.

(57) **ABSTRACT**
A method of treating chronic post-myocardial infarction including helical needle transendocardial delivery of autologous bone marrow (ABM) mononuclear cells around regions of hypoxia or ischemia in chronic post-myocardial infarction (MI) patients. The treatment is safe and improves oxygenation and function (EF).

40 Claims, 3 Drawing Sheets

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau
WIPO | PCT

(43) International Publication Date: 02 April 2020 (02.04.2020)

(40) International Publication Number: WO 2020/069215 A1

(51) **International Patent Classification:**
A61K 35/28 (2015.01); **A61K 35/52** (2015.01); **A61K 35/53** (2015.01); **A61K 35/54** (2015.01); **C12N 2/00** (2010.01)

(52) **International Classification:**
PCT/US2019/05273

(53) **International Filing Date:** 26 September 2019 (26.09.2019)

(54) **Publication Language:** English

(56) **Priority Date:** 27 September 2018 (27.09.2018) US 62,737,627

(71) **Applicant:** **BIOCARDIA, INC.**, 125 Shoreway, Suite B, San Carlos, California 94070 (US)

(72) **Inventors:** **MCNICE, Ian**, 125 Shoreway, Suite B, San Carlos, California 94070 (US); **ALTMAN, Peter**, 125 Shoreway, Suite B, San Carlos, California 94070 (US); **GRANT, Evie**, Wilson Sorenson Goodrich & Rosati, 609 Page Mill Road, Palo Alto, California 94304 (US)

(74) **Agent:** **GRANT, Evie**, Wilson Sorenson Goodrich & Rosati, 609 Page Mill Road, Palo Alto, California 94304 (US)

(84) **Designated States (unless otherwise indicated, for every kind of national protection available):** AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BR, BS, BN, BW, BY, BZ, CA, CC, CD, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, IL, IN, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LI, LR, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TD, TH, TN, TR, TT, TZ, UG, UJ, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States (unless otherwise indicated, for every kind of regional protection available):** ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IL, IT, LI, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG)

(84) **Designated States (unless otherwise indicated, for every kind of national protection available):** AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BR, BS, BN, BW, BY, BZ, CA, CC, CD, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, IL, IN, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LI, LR, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TD, TH, TN, TR, TT, TZ, UG, UJ, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States (unless otherwise indicated, for every kind of regional protection available):** ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IL, IT, LI, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG)

(54) **Title:** **BONE MARROW DERIVED NEUROKININ-1 RECEPTOR POSITIVE (NK1R+) PRECURSOR CELLS FOR THERAPEUTIC APPLICATIONS**

(57) **Abstract:** The present disclosure provides use of neucanin 1 receptor (NK1R) as a marker for identifying and/or isolating mononuclear cells. The present disclosure provides cell populations enriched by methods of the present disclosure and therapeutic use of these cells and agents derived from these cells.

Figure 1

US 2020039802 A1

(15) **United States**
(12) **Patent Application Publication**
(10) **Pub. No.:** US 2020/039802 A1
(45) **Pub. Date:** Dec. 24, 2020

(54) **RADIAL AND TRANS-ENDOCARDIAL DELIVERY CATHETER**

(71) Applicant: **BioCardia, Inc.**, San Carlos, CA (US)

(72) Inventors: **Wai Hoosh**, Newark, CA (US); **Ofra Jay**, Palmdale, San Carlos, CA (US); **Scott Camba**, Menlo Park, CA (US); **James B. Rees**, Livermore, CA (US); **Ken Yoon**, San Jose, CA (US); **Judith Argenteffer**, Buenos Aires (AR); **Peter Altman**, Menlo Park, CA (US)

(73) Assignee: **BioCardia, Inc.**, San Carlos, CA (US)

(21) Appl. No. **17018403**

(22) Filed: **Sep. 2, 2020**

Related U.S. Application Data

(60) Continuation of application No. 160595480, filed on Aug. 5, 2016, now Pat. No. 10,700,265, which is a division of application No. 14,901,035, filed on Sep. 30, 2014, now Pat. No. 10,071,225.

(60) Provisional application No. 61/884,834, filed on Sep. 30, 2013.

Publication Classification

(51) **Int. Cl.**
A61M 25/00 (2006.01)
A61M 25/09 (2006.01)
A61M 25/01 (2006.01)
CPC: **A61M 25/0046** (2013.01); **A61M 25/0047** (2013.01); **A61M 25/0048** (2013.01); **A61M 25/0049** (2013.01)

(52) **U.S. Cl.**
A61M 25/0046 (2013.01); **A61M 25/0047** (2013.01); **A61M 25/0048** (2013.01); **A61M 25/0049** (2013.01)

(57) **ABSTRACT**
A catheter-injection catheter includes a catheter body having a distal end, a proximal end, a stiff proximal portion, a flexible distal portion, and a delivery lumen extending therebetween. In a first embodiment, a straight injection needle extends distally from a distal tip of the flexible portion of the catheter body and a plurality of penetration limiting elements positioned circumferentially about a base of the straight injection needle and configured to hold radially inwardly against a shaft of the needle, which is contained in a tubular lumen and to extend radially outwardly when retracted. In a second embodiment, a helical needle extends from the distal tip of the flexible portion of the catheter body. The helical needle has at least one helical delivery lumen connected to receive an injectable substance from the delivery lumen of the catheter body.






U.S. Patent Oct. 12, 2021 Sheet 1 of 4 US 11,141,568 B2

Fig. 1

Fig. 2

Fig. 3

Executive Management Team

				
Peter Altman	David McClung	Debby Holmes-Higgin	Edward Gillis	Farhan Shahib
CEO	CFO	VP Clinical	SVP Devices	VP of Quality



Board of Directors:

- Andrew Blank, Chairman of the Board, CEO Archive America, Board Member Neumentum
- Jay Moyes, Chairman Audit Committee, Board Member Puma Biotechnology, Inc.
- Simon Stertz, M.D., Professor of Medicine Cardiology Emeritus, Stanford
- Martin Slosman, CEO, InspireMD
- Bill Facteau, CEO Earlens, Board member Aerin Medical
- Jim Allen, CEO United Toll Systems, LLC.

Financial Data and Significant Anticipated Catalysts

	Year Ended 2023 (\$ mm)	Year Ended 2024 (\$mm)	Year Ended 2025 (\$mm)
Net Loss	\$11.6	\$7.9	\$8.2
Cash used in operations	\$10.0	\$8.0	\$7.4
Cash & Equivalents	\$1.1	\$2.4	\$2.5
Debt	N/A	N/A	N/A

11.0 M shares of common stock issued and outstanding.

7.9 M Warrants outstanding at weighted average of \$1.88 strike price.

CardiAMP Cell Therapy

Q2 '26 Data Readout EuroPCR in 2nd Indication
 Q3 '26 Peer Reviewed Manuscript
 Q4 '26 Japan PMDA Submission for Approval
 Q4 '27 Japan Approval
 Q3 '28 HF II completes enrollment
 Q3 '29 HF II Topline Data

Helix Delivery

Q2 '26 FDA Pre-Sub Amendment

Heart3D Fusion Imaging

Q4'26 First in Man

No milestones on CardiALLO platform or Morph DNA platform are being detailed at this time.

NASDAQ: BCDA

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