Bio-Leonhardt

Heart Regeneration Technology Platform

EXECUTIVE SUMMARY

2022

Company Overview

BioLeonhardt is developing a total heart regeneration system for failing hearts. The company's technology platform combines an implantable programmed bioelectric stimulator and an implantable, programmable, and refillable infusion pump that delivers a proprietary biologics mixed composition of stem cells and support factors specific to heart regeneration. The technology incorporates hundreds of patent claims and pending claims for controlling the precise regenerative protein expressions in specific bioelectric signaling sequences required for heart regeneration.

Background

Cardiovascular diseases (CVD) are the leading cause of death worldwide, accounting for nearly one-third (~18 million) of all global deaths annually[1]. More than half of all CVD-related deaths are attributed to ischemic heart disease (IHD), resulting in a loss of cardiomyocytes (CMs) – the cells responsible for generating the contractile force in the heart – leading to ventricular dysfunction and heart failure (HF).

Over 60 million people worldwide suffer from HF, with over 6.5 million people experiencing HF in the US alone[1]. One major study estimates that 960,000 new HF cases are diagnosed annually, contributing to 36% of cardiovascular disease deaths. Hospitalization for heart failure is a significant burden on the healthcare system; it is the number one cause of hospitalization in the US Medicare population. The global economic burden of HF is estimated to be more than $346 Billion.

Numerous surgical techniques, implantable devices, and pharmacological interventions developed in the last 50 years have dramatically improved patient outcomes and quality of life for patients with HF.[3, 4] **However, mortality rates have plateaued in the previous two decades, primarily because current interventions slow disease progression but do not reverse heart disease.**[1] This is likely due to the minimal regenerative capacity of the adult mammalian heart, the relative inability of CMs within the adult heart to reenter the cell cycle, and a lack of naturally occurring stem cells that can reproduce all cell types within the heart following injury.[5]

In a population-based retrospective cohort study of more than 7,800 patients discharged from the hospital with HF, the average lifespan was 5.5 years (STD +/− 10.0), ranging from 19.5 years for

low-risk women under 50 years old to 2.9 years for high-risk 80-year-old males.[6] In patients with three or more concomitant comorbidities, average lifespans were lower by approximately one year. BioLeonhardt is dedicated to developing technology to repair and regenerate diseased hearts, allowing people to keep their own hearts to live longer, healthier lives.

Company History

In 1987, Howard Leonhardt, the Founder, Executive Chairman, and CEO of BioLeonhardt, began a research collaboration with Dr. Robert O. Becker, the late author of the pioneering book *The Body Electric*, utilizing precise bioelectric signaling stimulation to heal wounds and improve circulation in the legs. Leonhardt Ventures LLC, the parent company of BioLeonhardt, completed its first heart regeneration animal case in 1988 with Dr. Race Kao and Dr. George Magovern in Pittsburgh, published in *The Physiologist* in 1989. Dr. Doris Taylor, the co-Chair of the Scientific Advisory Board of BioLeonhardt and former Board Director, published a landmark paper in *Nature Medicine* in 1998 on the use of myoblasts or muscle stem cells to regenerate damaged muscle.

In 1999, the team working with Dr. Shinichi Kanno published their first paper on bioelectric stimulation-controlled regeneration in *Circulation*, a Journal of The American Heart Association. Dr. William Abraham, a Co-Chair of the BioLeonhardt Scientific Advisory Board, was the lead author of the landmark 2002 MIRACLE clinical trial for cardiac resynchronization therapy for heart failure patients. In that same year, Howard Leonhardt, the Founder, Executive Chairman, and CEO of BioLeonhardt, filed his first patent describing the combination of bioelectric stimulation and stem cell biologics for heart and other organ regeneration and healing. The patent covered unique new signals for stem cell homing, myogenesis (muscle regeneration), and angiogenesis (formation of new blood vessels). In May 2001, working with Dr. Patrick Serruys, Dr. Doris Taylor, Dr. Warren Sherman, Dr. Pieter Smits, and Dr. Kumar Ravi in The Netherlands, the team completed the historic first-ever non-surgical repair of a human heart. This case became part of a complete pilot study published in the *Journal of American College of Cardiology* in 2003. The team raised over $100 million and completed more than ten animal studies. Additionally,

they published Pilot, Phase I, Phase II, and Phase II/III double-blinded, randomized, placebo-controlled clinical studies in peer-reviewed journals utilizing one-time end-ventricular delivery of muscle stem cells alone into damaged failing hearts.

In 2008, the Leonhardt regeneration product development team split into two groups. The first group, located in Florida, focused on adipose-derived cells and cosmetic, knee, veterinary, and vision procedures. The second group, located in California, called MyoStim Pacers, Inc. and MyoStim Peripheral, has since been re-named BioLeonhardt and VascuStim, respectively. They focus on bioelectric stimulation-controlled regenerative protein expressions and multi-component mixed stem cell-based biologic compositions for total heart regeneration and limb salvage. Howard Leonhardt joined BioLeonhardt and VascuStim full-time and launched an innovation accelerator to explore how what was learned in decades of heart and limb regeneration research could be applied to the regeneration of other organs.

Our Solution:

The company is developing what we believe is the first implantable combination bioelectric stimulator and refillable infusion pump coupled with a proprietary, mixed stem cell-based biologics composition for total heart regeneration.

The bioelectric stimulator is programmed with patented signals for:

Stem cell homing, proliferation, and controlled differentiation

- SDF1 and PDGF

Improving circulation/growing a new network of large diameter blood vessels

- VEGF, SDF1, PDGF, HIF1a, CXCL5, HGF, EGF, and eNOS

Regenerating muscle and growing new muscle

- Klotho, Follistatin, IGF1, S100a, SDF1, PDGF, and LIM muscle

Regenerating nerves

- Sonic hedgehog, IGF1, LIM.

Modulating inflammation

- A customized program releases anti-inflammatory cytokines at specific times

The proprietary BL-15 heart regeneration mixed composition includes:

- Selected muscle stem cells (MSCs) derived from skeletal muscle
- Patented Klotho-expressing M.S.C.s derived from the fat of bone marrow tissue
- Selected exosomes
- Micro RNA gel
- Secretome from amniotic sourcing
- Bioelectric pre-treated platelet-rich fibrin
- Heart matrix
- Selected alkaloids such as tetrahydroharmine
- Wharton's jelly
- Nutrient hydrogel w/ Klotho, SDF1, Follistatin, and other regenerative promoting proteins
- A stromal fraction from adipose tissue

Milestones

- **1Q 2022** Stimulator, pump, and biologics components suppliers chosen for upcoming studies - completed
- **April 2022** Complete sheep animal study with nearly all components
- **June 2022** Complete GLP-like sheep animal study for FDA filing
- **Sept. 2022** File Early Feasibility Study application with FDA.
- **Nov. 2022** OUS pilot study of 10 patients
- **2Q 2023** US EFS Study
- **3Q 2023** Phase II pivotal study of 150 patients
- **1Q 2024** CE Mark Europe and other foreign markets and sales launch OUS
- **2Q 2024** US FDA, PMA, and BLA approvals
- **3Q 2024** US product launch

Regulatory Status

- FDA IND approved for muscle stem cells and heart failure - Phase II pivotal study.
- FDA IND approved for muscle stem cells plus SDF1 combination cell and therapy Phase I study.
- Primary central component myoblasts/muscle stem cells have been studied in multiple studies under FDA supervision.
- FDA IND for adding nutrients and bioelectric support to muscle stem cells requires an amendment filing supported by pending data.
- The infusion pump is FDA-approved for other indications of use.
- The implantable stimulator is FDA-approved for other indications of use.

Funding

- $8 million has been invested in developing platform technology by founder Howard J. Leonhardt since 1999.
- $100 million+ was raised between 1999 and 2015 for the first-generation core technology (using immature myoblasts in a one-time delivery system), including
    - Four investments from Boston Scientific Guidant
    - Investments from Tyco Ventures, Ascent, Advent Morro, Presidential Capital, New World Angels, Astri Capital
    - Two investments from Abbott St. Jude Medical of $1 million each and $900,000 for the MyoCath patent license fee

Current Raise

- $15 million at $3 per share
- 20,000,000 shares authorized
- 13,300,631 shares are issued
- Current pre-money valuation - $39.9 million

Current Ownership - 40 shareholders

- Leonhardt Ventures LLC 75.3% with dilution floor at 50.1%
- Cal-X Stars Business Accelerator, Inc. 13.5% with dilution floor at 9%
- Dr. Leslie Miller 5%
- Leonhardt's Launchpads Utah, Inc. 4.5% with dilution floor at 4.5%
- Steve Smith 1%
- All others under 1%

Budget

2022

- Pre-Clinical Studies - $400,000
- Full development of implantable micro stimulator - $1,500,000 to $3,000,000
- First in Human OUS clinical study - $500,000 to $1,000,000
- FDA Regulatory Filing Assistance - $450,000

2023

- FDA Early Feasibility Study - $1,000,000
- Phase II Pivotal Study - $10,000,000
- Europe and USA Sales Launch - $3,000,000 to $5,000,000

Potential Profit Analysis

Costs

- Stimulator $800
- Infusion pump $800
- Biologics mixture $3000 - $6000
- **Total Cost** $4600 - $6600

Expected Retail Sale Price

- Stimulator $27,000
- Infusion pump $17,000
- Mixed biologics, per week $15,000

Reimbursement

- Stimulator $58,000 to hospital
- Infusion pump TBD
- Mixed biologics TBD

Leading Competitors

- Stimulator: Berlin Heels, NeuroTronik
- Infusion Pump: Medtronic, Flowonix, Boston Scientific
- Composition: Mesoblast, BioCardia

Intellectual Property

- Over 700 patent claims
- Patent issued for the bioelectric stimulator
- Patent issued for the bioelectric stimulator, pump, and composition combination
- Patent issued for myogenesis
- Patent issued for inflammation management
- Patent issued for Follistatin
- Patent issued for Sonic hedgehog
- Patent-pending for Klotho.
- Patent-pending for S100a.
- Stimulator and pump suppliers do not have any enforceable IP of their own.
- Leonhardt Ventures owns all related IP.

Management Team - Board of Directors

- **Howard Leonhardt - Founder, Executive Chairman, CEO, Lead Inventor**
  30+ years of sector experience. Previously developed and sold leading stent graft and heart valve systems.

- **Leslie Miller, M.D. – Chief Medical Officer and Board Director**
  40+ years of sector experience. Leader 100 clinical trials. Over 250 publications. Author and editor of leading textbooks on heart failure and regenerative medicine. Past President International Heart, Lung, and Blood Transplantation Society. 10-year Chairman of the Cardiovascular Medicine University of Minnesota.

- **Stuart Williams, Ph.D. – V.P., Research and Director, and Board Director**
  35+ years of sector experience. 300 published papers. Twenty-eight issued patents. Director of Cardiovascular Innovation Institute Regenerative Medicine, founder of Biomedical Engineering School at the University of Arizona, and the original inventor of adipose-derived cell therapies in the early 1990s.

- **Suresh Gurunathan –Chief Advisor, Implantable Stimulators**
  Co-founder NanoStim, developer of the first leadless pacemaker, sold to St. Jude Medical for $200 million developers of the first leadless pacemaker.

- **Robert Kellar, Ph.D. – Chief Bioengineering and Biologics Therapies Advisor and Board Director**
  30 + years of sector experience. Former research leader at Advance Tissue Sciences and WL Gore

- **Jorge Genovese, MD, Ph.D. – VP, Bioelectric Regeneration Research and R&D Lab Leader Irvine, CA**
  Former research leader at McGowan Regenerative Medicine Institute Pittsburgh, Director Cardiac Regeneration Lab and Program, University of Utah

- **Tim Henry, MD – Chief Advisor, Heart Stem Cell Therapies and Special Advisor, Board of Directors**
  Chief of Cardiology, Christ Hospital Cincinnati, President of Society Cardiovascular Angiography and Interventions (SCAI.) Experienced leader of numerous stem cell cardiovascular clinical studies.

- **Jeff Donofrio - VP Sales and Marketing Development, Physician Relations, Board Director**
  30+ years of industry experience. Formerly with WL Gore, Edwards, Cardiac Assist, current President of Second Heart Assist, Inc. Launched Cardiac Assist heart failure product in the US.

- **Jeremy Koff, MBA - VP Strategic Development Advisor and Board Director**
  30+ years of industry experience, many are serving Alfred Mann Companies.

- **Patrick Griffith, MD, FACS, MBA - VP Cardiovascular, Chief Cardiac Surgeon Advisor, Board Director**
  Executive Medical Director, Adventist Health Heart & Vascular Institute, Cardiothoracic Surgeon with 25+ years of surgical experience and more than 4,000 operations

- **Nic Chronos, MD - Chief Interventional Cardiology Advisor** - Former Director American Cardiovascular Research Institute Atlanta

- **Kristin Gentry - Chief Strategic Business Advisor**
  President, Gentry Ventures, 20+ years of investment industry experience

- **Dipti Itchhaporia, MD - Chief Cardiology Advisor, Special Board of Directors Advisor**
  Cardiologist, President of the American College of Cardiology

- **Karen Koch - Chief Advisor Business Development, Special Board of Directors Advisor.**
  20+ years of industry experience.

- **Doris Taylor, MD - Chief Advisor Heart Regeneration, former Board Director, Co-Chair Scientific Advisory Board**
  30+ years of experience. Former head of cardiac regeneration research at Duke University, University of Minnesota, and Texas Heart Institute

- **William Abraham, MD - Co-Chair Scientific Advisory Board**
  Former Chief of Heart Failure and Chair of Cardiovascular Medicine Ohio State University. Author of over 900 peer-reviewed publications

- **Hans Dohmann, M.D. - Chief Cardiologist Advisor**
  30+ years of cardiology experience. Former Ministry of Health, Rio De Janeiro, Brazil

[1] Roth et al., 2017
[2] Heart Failure Society of America, 2022
[3] Benjamin et al., 2017;
[4] Jones et al., 2019
[5] Sadak and Olsen, 2020
[6] Alder et al., 2012

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BioLeonhardt has shared access to the R&D lab at University Lab Partners via Leonhardt's Launchpads at 5270 California Ave, Irvine, CA 92617

Pre-Clinical Testing is held at California Medical Innovations Institute in San Diego, California at 11107 Roselle St, San Diego, CA 92121

www.leonhardtventures.com

https://bioleonhardt.com/