Business Plan

JAAN BIOTHERAPEUTICS L.L.C.

Business Plan Version Number 1.3

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1. Executive Summary

1.1 Mission

Jaan Biotherapeutics LLC (JBT) mission is to develop to develop "first in class" therapies that regenerate damaged heart muscle and to treat Ischemic heart disease (IHD), the largest single cause of death in the world and a major unmet medical need [1, 2]. It is a disease that does not discriminate by gender or race and is the No. 1 cause of death of women in the U.S.

1.2 Company

JBT was established in February 10th 2015 and is a **Woman Owned and Founded** Biotechnology small business. It is a Limited Liability Company with its principal offices located at 4445 Eastgate Mall, Suite 200, San Diego, CA 92121.

1.3 Business

JBT has exclusively licensed an option agreement for a first in class therapy (*METHODS FOR HEART REGENERATION. Notice of allowance received for U.S. Patent Application No. 14/052,538 on September 28th 2015*) from the Salk Institute [3]. The therapy inhibits four small pieces of ribonucleic acids (RNAs) or microRNAs (miR) known as miR-100, miR-99, Let-7a and Let-7c which in turn reactivates an endogenous cardiac muscle regeneration process that has been shut down in the adult human heart during evolution [4]. JBT is at the seed stage and preclinical stage of business, having just developed its first product, JBT-miR1, an adeno-associated virus (AAV) that delivers the four miR inhibitors to damaged cardiac muscle to reduce scarring. JBT's current focus is developing treatment for IHD after a heart attack, but the therapy could be applied to other cardiac diseases where cardiac muscle regeneration is required, such as viral myocarditis which effects children as well as adults. Actively collaborating with the Salk Institute in La Jolla and the University of California, San Diego (UCSD), JBT expects to develop at least two therapies to clinical trials in three years. This can be achieved because the funds that JBT expects to attain through seed funding, venture capital and government grant agencies will allow the conduct of preclinical dose range finding, efficacy and time course studies for virus and small molecule drug candidates that manipulate these miRs. JBT expects to file Investigational New Drug Applications (INDs) with the United States Food and Drug Administration (U.S. FDA) in Year 2 (2017) as well as identify a large non-rodent species required for preclinical development. Also in Year 2 JBT will aim to initiate the manufacture of clinical grade drug products, conduct non Good Laboratory Practice efficacy studies in selected large non-rodent species as well as validate pharmacokinetic (PK) and bioactivity assays. In Year 3 (2018) Good Laboratory Practice Safety (GLP) and Toxicology studies in our rodent and large non-rodent species will be conducted. This preclinical development plan should enable JBT to move these products through to Phase 1 clinical studies in Year 4 (2019) and Phase 2 clinical trials in Years 5 (2020) and 6 (2021). JBT will be continually reviewing the preclinical and clinical landscape for new therapies to treat heart failure. In parallel we will search for potential opportunities to license technology as well as developing our own proprietary new technology that could cure this debilitating disease.

1.4 Product or Service

JBT is developing new treatments to regenerate heart muscle. Scientists at the Salk Institute have demonstrated proof of concept data in a preclinical murine model of permanent cardiac ischemia, that AAV2/9 delivery of these four specific miRs inhibitors induces cardiac muscle cells to proliferate and reduce scar tissue after a single injection of two separate viruses [4]. Furthermore, heart function is increased up to 90 days. JBT has developed and refined a single AAV2/9 virus that can express all four human miR inhibitors, known as JBT-miR1. JBT-miR1 constitutes the next stepping stone in providing efficient and safe delivery of the regenerative therapy in the heart. The virus appears to reduce scarring and increase heart function in mice with a permanent heart attack and could potentially offer a treatment to the disease. In addition to the viral delivery approach, JBT is collaborating with a European manufacturer of two synthetic oligonucleotide antagomirs with the option to license these molecules if they are effective in in vivo studies which are planned to occur in year 1. JBT's efforts will set the stage to advance this treatment towards a testable and clinically relevant product that can be administered in conjunction with standard of care procedures for acute myocardial infarction (AMI) after perfusion has been restored to the heart.

1.5 The Market

The current global mortality rate from IHD is 13.2% of all deaths [1]. The potential target is 500,000 patients in the U.S. that experience an AMI and are admitted to an emergency room facility. Despite advances in reperfusion therapy

to treat Ischemia following an AMI, the annual direct and indirect costs of managing patients in the U.S. with IHD is expected to double from $11.5 billion within the next 15 years as the population ages [2]. Billions of cardiac muscle cells are lost in a single heart attack that results in a weaker heart. A significant factor in the increase in morbidity and mortality from this disease is the lack of available therapies to regenerate endogenous cardiac muscle cells following a heart attack to reduce muscle loss and scarring. With patients having a poor prognosis, there is a major unmet medical need for the development of new treatment approaches to replace lost heart muscle.

1.6 Competition

Despite a wide therapeutic arsenal, such as restoration of arterial perfusion with thrombolytic and antiplatelet therapy during percutaneous coronary intervention and coronary artery bypass grafting, recovery of cardiac function and prevention of the transition to heart failure (HF) is unsatisfactory. Current treatments do not replace lost heart muscle after a heart attack. JBT's main competitors are drugs and treatments that are in preclinical and early clinical development such as stem cell therapies. Autologous, cardiosphere-derived cardiac stem cells or myocytes derived from pluripotent stem cells and bone marrow derived cells are large competitors with approximately 59 clinical trials ongoing to investigate the clinical benefit of using stem cells to treat IHD. However, inconsistencies in benefits observed across completed clinical trials are attributed to differences in stem cell methodologies, technical challenges and complications such as tumorigenesis and arrhythmogenesis. JBTs technology removes the potential of rejection of exogenous cells by promoting the proliferation of endogenous functional cardiac myocytes. It offers a straightforward approach to therapy, simplifying production over stem cell strategies by producing cardiac progenitors without the need to collect, culture and transplant stem cells.

1.7 Risk/Opportunity

The greatest risks facing JBT are unknown safety and efficacy risks that may develop during preclinical and clinical development. Only one out of 100 preclinical candidates makes it to the market. This is a high risk and high reward business. Due to the time required to develop and commercialize our therapy the future landscape is uncertain. Nevertheless, through considered strategic planning and risk identification and mitigation by JBT's experienced management team, the uncertainty and potential problems can be managed. The opportunities are significant and there is a possibility to dominate a niche in the marketplace to become a major force in the industry and simultaneously have an impact on human health.

1.8 Management Team

JBT's strength is our extremely experienced drug development team. JBT currently consists of two women and five men who have a combined 215 years of experience in marketing and business development, finance, preclinical development, product development, clinical cardiology and clinical development, legal, and Chemistry Manufacturing Controls (CMC) and Quality.

- Bhawanjit Brar Ph.D. President and Founder of JBT has over 20 years in molecular cardiology research experience at outstanding academic institutions including University College London (UK), The Salk Institute (British Heart Foundation Fellow), and University of California, San Diego. She is a former Vice President of a biotechnology company that helped develop a novel therapy for the treatment of chronic heart failure (CHF) from Investigational New Drug (IND) Application to Phase 3 clinical trials in 7 years.
- Joseph Hansen J.D., C.P.A. is the Chief Financial Officer (CFO) who has over 25 years of experience serving as a CFO of both public and private companies including the biotechnology sector. He has also co-founded 3 companies.
- Professor Kirk Peterson M.D. is a current Director Emeritus of the Sulpizio Cardiovascular Center at UCSD Health Systems, the Director of the Seaweed Canyon Physiology Laboratory at UCSD School of Medicine and an outstanding translational scientist that specializes ischemic injury models and human cardiac catheterization. As our scientific advisor he has 40 years of experience.
- Professor Juan Carlos Izpisua-Belmonte Ph.D. is a current Professor at the Salk Institute, La Jolla in the Gene Expression Laboratory. He has over 30 years of experience and is our scientific advisor.
- Stanley A. Roberts, Ph.D., D.A.B.T is our toxicology consultant who has 40 years of expertise.
- CMC and Quality consultant is Ms. Shirley Cao has over 20 years of experience in manufacture of drug products.
- Our Business Development Executive is Mr. Louis Scotti (consultant) who is a former Arena pharmaceutical executive responsible for commercialization of an obesity drug. Mr. Scotti has over 30 years of experience.
- Our scientific consultant is Dr. Aitor Aguirre, Ph.D. who was the lead scientist on publication and patent and has 10 years of experience.

1.9 Capital Requirements

JBT's total funding needs are in the $5.75 million range assuming no funding is generated from the National Institutes of Health (NIH). This amount would satisfy all requirements through year 3. JBT has submitted and is planning on submitting grant applications totaling $5.35 million over the next three years. Grant applications are serial in nature. It is expected that due to preferences given to minority and women established entities, one or more of JBT's applications will be successful, however certainty is lacking thus necessitating the large capital funding request. Human clinical trials would begin in Year 4 and require a total of an additional estimated $15 million for Phase 1 and 2 clinical trials. A portion of this amount may also be raised through grant applications but there will likely be a need to achieve a liquidity event at this stage involving venture capital funding, an Initial Public Offering (IPO), or a license/partnership with a large pharmaceutical company. JBT is aware of the long lead times in attracting investments and is already actively seeking funding from a variety of sources. To assist in this, Mr. Louis Scotti has been made part of the team. He has previously been responsible for over twenty-five commercialization transactions. He will be assisted by Mr. Joseph Hansen, who has originated and closed over twenty merger and acquisition transactions.

1.10 Financial Plan

JBT's current plan is to seek early stage investors to assist in funding during its initial stages coupled and supplemented with government grants. We are applying for at least 2 grants of approximately $450,000 before 2016. In addition JBT is seeking investments from Seed Investors and Venture Capital firms or other private sources. If an investment is made it could greatly help deliver this revolutionary product to the people that need it sooner who are suffering from IHD.

1.12. Balance Sheet Summary and Valuation

Our valuation is in the $1.8 million range with our main asset being the option to license the patent, technology, people, and expertise. Our current liabilities are negligible and are under $10,000.

2.0 Mission

JBT intends to develop "first in class" therapies to treat Ischemic heart disease (IHD), the largest single cause of death in the Western World and an unmet medical need. It's licensed, proprietary technology manipulates microRNAs (miRs) to activate an endogenous cardiac muscle regeneration process which has been shut down in the adult human heart during evolution. The current focus is for the treatment of IHD after a heart attack, but the therapy may be applied to other cardiac diseases where cardiac muscle regeneration is required. The goal is to become a leading biopharmaceutical company developing treatments that regenerate heart muscle through in-licensing from academic institutions concurrent with JBTs proprietary technology development. JBT aspires to carry a reputation in the marketplace for developing and delivering products that cure heart failure by regenerating heart muscle and do not merely alleviate symptoms like current therapies. This can be achieved by cutting edge product development, streamlining and focusing preclinical and clinical development with a close understanding of market trends and needs. To accomplish this goal, JBT needs capital, management talent and larger and more efficient facilities. In pursuit of our goal, we resolve to treat stakeholders and customers who will be physicians and patients with the highest standards of ethical conduct and transparency providing them with safe and effective treatments.

3.0 The Company

JBT was founded in February 10th 2015 and with its sole purpose to develop treatments that regenerate heart muscle. The legal name of the business is Jaan Biotherapeutics LLC. It is a Limited Liability Company and small business. Its principal offices are located at 4445 Eastgate Mall, Suite 200, San Diego, CA 92121.

3.1 Facilities

JBT is leasing office space on an as needed basis at Sunroad Corporate Center, 4445 Eastgate Mall, Suite 200, San Diego, California, 92121. Sunroad Corporate business centre is an outstanding location at the heart of San Diego's growing biotechnology industry. The business center is just minutes from the University of California's San Diego (UCSD) campus, which has played a key role in promoting biosciences. Areas north of the city and within the 'Golden

Triangle', like University City and La Jolla, have seen a proliferation of hundreds of biotechnology and pharmaceutical companies.

Laboratory: Currently all laboratory work is conducted by JBT at the academic partners location and facilities. The UCSD Cardiovascular Core Physiology Laboratory ("Seaweed Canyon") is located in the BRFII Building, 9500 Gilman Drive, La Jolla, CA 92093.

Office: JBT currently has access to conference rooms, a computer server room, electronic key card documentation room and break rooms at Sunroad Corporate business centre. All offices have their own computer work stations that are part of a connected network. All computers are equipped with MS Office and other work relevant software. This facility is expected to be adequate for the next year (2016). After Year 1 (2017) new employees will be hired: Business Development Executive, Chemistry and Manufacturing and Controls Director, Toxicologist, Preclinical Development Director and a Chief Scientific Officer in addition to the CFO and President. At this stage JBT will lease larger space that will include a laboratory, animal vivarium, and common area space at the General Atomics Building 2, 3550 General Atomics Court San Diego CA 92121, less than 1 mile from the UCSD campus or a similar facility in the San Diego area. This facility should be adequate for the company's needs for at least 3 years after funding (2017-2020).

3.2 Regulations and permits

JBT operates in the Biopharmaceutical industry. JBT was incorporated in California, on February 10th 2015 (# 201504310246). JBT is registered as 079805635 in the U.S. federal government's System for Award Management (SAM), Grants.gov, eRA commons and Dun and Bradstreet and SBA. JBT is currently conducting animal experiments under UCSD's Institutional Animal Care and Use Committee (IACUC) which oversees the university's animal care and use program and is responsible for reviewing all animal use protocols, ensuring compliance with federal regulations, inspecting animal facilities and laboratories, and overseeing training and educational programs.

- The United States Department of Agriculture Registration Number: 93-R-0437
- Public Health Service. Grant Application NIH Animal Welfare Assurance Number: A3033-01
- The Association for Assessment and Accreditation of Laboratory Animal Care Institutional Number: 000505.

IACUC approved protocols for all animal work and procedures proposed for year 1 (2016) are already approved and in place at the Seaweed Canyon Laboratory. Seaweed Canyon conducts experiments on vertebrate animals under the protocol assigned to Professor Kirk Peterson as the Principal Investigator. Prior to award Seaweed Canyon will amend those protocols to include the number of animals needed for the work proposed here.

3.3 Strategic alliances

JBT has developed important strategic alliances with the academic institutions in San Diego, particularly the Salk Institute, where it has exclusively licensed an option agreement for the patent 'METHODS FOR HEART REGENERATION' [3] and has an important relationship with Professor Belmonte, the co-inventor of this technology. JBT has a significant, long standing relationship with Professor Kirk Peterson M.D., UCSD School of Medicine and Director Emeritus of the Sulpizio Cardiovascular Center UCSD Health Systems. Professor Kirk Peterson is an outstanding translational scientist that specializes in animal models of ischemic injury, cardiac gene delivery and human cardiac catheterization. In addition, JBT has a strong network of Key Opinion Leaders (KOLs) and clinical sites in the U.S., China, India and Europe and connections with cardiovascular group's at large pharmaceuticals including Merck, Astra Zeneca and Novartis. Most of these connection were originated by Bhawanjit Brar Ph.D., who is a former Vice President of a biotechnology company, Zensun USA, Inc. that led the development of a therapy to treat Chronic Heart Failure (CHF) from IND submission through to the design, management and completion of a successful multi-site U.S. Phase 2 clinical trial [5]. JBT consultants and employees are local to San Diego and are readily accessible.

4.0 The Business

Our business is based on the METHODS OF HEART REGENERATION patent [3]. JBT is a drug development entity with specific focus in developing first in class treatments that regenerate heart muscle after a heart attack using miR inhibitor technology. The company is at the seed stage of business, having just developed an optimized, single virus formulation, JBT-miR1 that simultaneously delivers and expresses the four miR inhibitors to the heart. Use of this AAV2, cross packaged into AAV9 capsids (AAV2/9) allows for time and temporal expression, cardiac tropism, and is non integrative, minimizing potential off-target side effects.

4.1 Product

IHD is the single largest cause of death worldwide [1, 2]. IHD includes stable and unstable angina, sudden coronary death, and more commonly is a result of myocardial infarction (MI). Most acute MI's (AMI) occur due to intra-arterial thrombus superimposed on an ulcerated or unstable atherosclerotic plaque. The plaque limits blood flow to the heart causing ischemia and irreversible death of ≈1 billion cardiac myocytes within hours. The size of the resulting infarction correlates with heart function deterioration, increased probability of a subsequent MI and mortality from CHF, the leading cause of death in the industrialized world [2]. Despite advances in reperfusion therapy, the annual direct and indirect costs of managing IHD in the U.S. is expected to double from $11.5 billion by 2030 as the population ages [2]. **A significant factor in the increase in morbidity and mortality from IHD is the lack of available therapies to regenerate endogenous cardiac muscle cells following an MI to reduce infarct size and scarring.**

4.1.1 Proliferation of adult cardiac myocytes in the ischemic heart:

Until the end of the last century, the human heart was believed to be a terminally differentiated post-mitotic organ, unable to be repaired after an injury. This dogma was challenged in 2001 by Beltrami et al. that demonstrated evidence of mitosis in cardiac myocytes after MI [6]. Studies by others confirmed that adult mammalian hearts can elicit a primitive regeneration response upon injury [4, 6, 7, 8, 9] with mature differentiated mononuclear mammalian cardiac myocytes re-entering the cell cycle upon application of chemical compounds targeting specific signaling pathways [10].

4.1.2 miR inhibition induces proliferation of cardiac myocytes:

A miR is a small non-coding RNA molecule conserved in plants, animals, and some viruses, which functions in RNA silencing and post-transcriptional regulation of gene expression [11-12]. Identified in 1993 [13], miRs are a vital and evolutionarily component of genetic regulation [14-20]. They function via base-pairing with complementary sequences within mRNA molecules, silencing the mRNA molecules, and modulating target protein expression and downstream signaling pathways [19-20]. Indeed, the human genome may encode over 1000 miRs [21] that target 60% of human genes [22-23]. By studying the mechanisms of heart regeneration in naturally occurring animals, such as zebrafish and neonatal mice, scientists have found that heart regeneration is a primarily cardiomyocyte-mediated process that occurs by dedifferentiation of mature cardiac myocytes followed by proliferation and further redifferentiation [24-25]. Epigenetic remodeling and cell cycle control are two key steps controlling this regenerative process [26-27]. A very important study [4] investigated the underlying mechanism of heart regeneration by concentrating on molecules of high therapeutic interest, and identified a series of miRs strongly involved in zebrafish heart regeneration. Focusing on those miRs presenting significant expression changes that were additionally conserved across vertebrates, both in sequence and 3' UTR binding sites, led to the identification of two miR families (miR-99/100, Let-7a/c) clustered in two well-defined genomic locations. This finding was supported by a common role for the miR-99a/Let-7c cluster in regulating vertebrate cardiomyogenesis [28]. MIRANDA-based miR-UTR binding predictions showed a strong interaction for miR-99/100 with zebrafish FNTβ (beta subunit of farnesyl-transferase) and SMARCA5 (SWI/SNF-related matrix associated actin-dependent regulator of chromatin subfamily a, member 5), linking the miR families to cell cycle and epigenetic control in cardiac myocytes. Interestingly miR-99/100 and Let-7a/c levels are low during early mammalian heart development and promote quick cardiac mass growth, but increase exponentially during late development, with a corresponding decrease FNTβ and SMARCA5 protein levels to block further cardiomyocyte proliferation. Postmortem analysis of injured human heart tissue, suggests that these miRs constitute a conserved roadblock to cardiac regeneration in adults [4].

4.1.3 Gene delivery of miR inhibitors to cardiac muscle

The application of RNAi technology can take many forms, but it is typically implemented within a cell in the form of a base-pair short hairpin (sh) RNA (shRNA), which is processed into an approximately 20 base pair small interfering RNA through the endogenous miR pathway [29]. Viral delivery of complementary sequences to miRs is a common approach [30-32]. AAV vectors are optimal in cardiovascular gene delivery since they a) contain no viral protein-coding sequences to stimulate an immune response, b) do not require active cell division for expression to occur and c) have a significant advantage over adenovirus vectors for stable, long-term expression of recombinant genes in cardiac myocytes in vivo [33-35]. To evaluate the potential therapeutic use of anti-miR-99/100 and anti-Let-7a/c to regenerate cardiac muscle in the murine heart, two viruses that express complementary inhibitor sequences to Let-7a/c and miR-99/100 were made by AAV2 Inverted Terminal Repeat (ITR) sequences cross packaged into AAV9 capsids (AAV2/9). The AAV2/9 serotype has clear cardiac tropism [35]. Intracardiac injection of active virus at a dose

of 1 x10^{11} viral genomes (vg) per mouse into the periphery of the infarcted area increased fractional shortening (FS), ejection fraction (EF) and ventricular wall thickness at 14 and 90 days post-MI compared with scrambled controls (**Fig 1A**). Importantly fibrotic scarring was significantly reduced 90 days post-MI (**Fig 1B**). Histological analyses revealed increased numbers of cardiac myocytes positive for the miR-99/100 target genes FNTβ and SMARCA5 18 days (**Fig 2A-B**) after injury in anti-miRs treated animals as well as dedifferentiated cardiac myocytes confirming proliferation (**Fig 2C**).

Figure 1 AAV2/9 Virus delivery of inhibitors of Let-7a/c and miR-99/100 increases Heart Function and reduces scarring in mice with LAD ligation

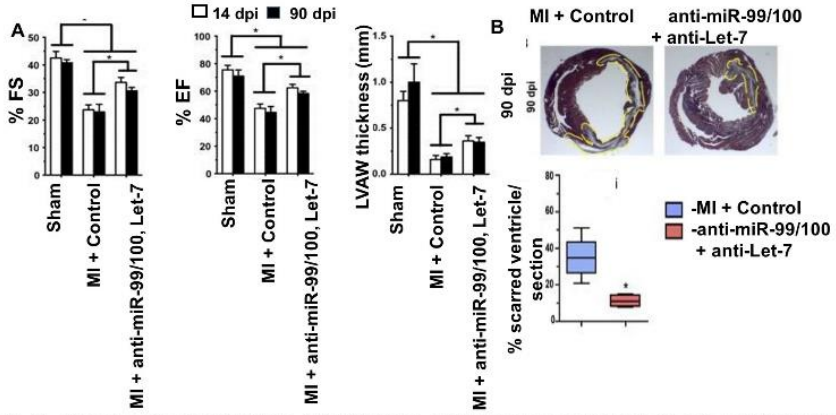
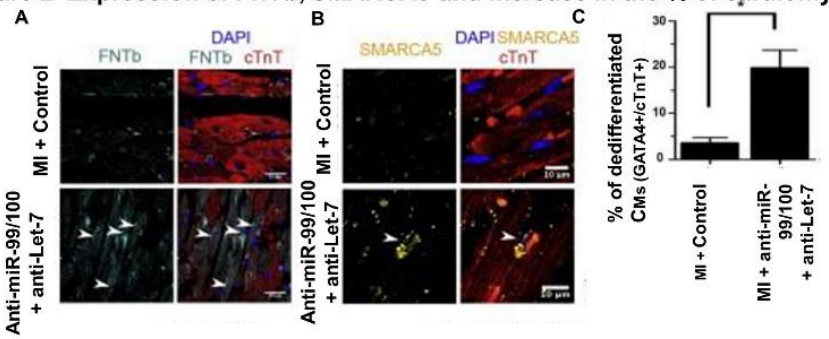


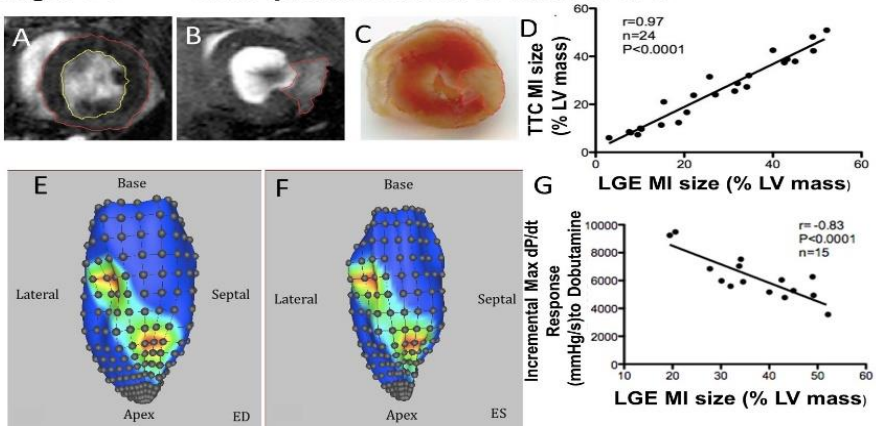
Figure 2 Expression of FNTb, SMARCA5 and increase in the % of cardiomyocytes



4.1.4 In vivo mouse models of ischemia

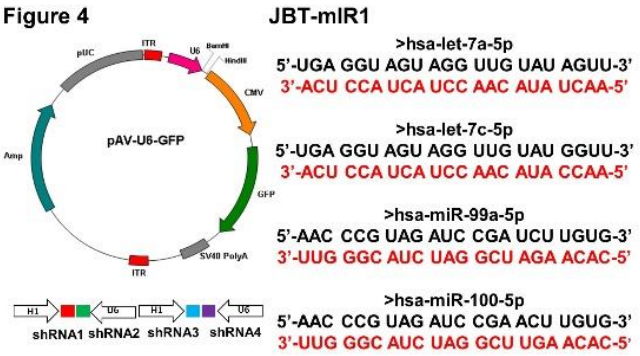
Most laboratories use 2D echocardiography (2D-Echo) to determine the degree of infarct in murine models of ischemia which is limited by planigraphic views that do not reflect the full extent of myocardial damage [4]. Professor Kirk Peterson and his laboratory are world-leaders in performing state-of-the-art animal models of ischemic injury [36-38, 41] and have developed a 3D reconstruction technique based on late gadolinium-enhanced (LGE) magnetic resonance cardiac imaging (MRI) (**Fig 3A-B, E-F**), with finite element analysis of endocardial area, providing a predictive, quantitative measure of the extent of myocardial loss and injury in a mouse model of MI. Notably, the measures of MI size with MRI correlate significantly with histologically stained 2,3,5-triphenyltetrazolium chloride (TTC) determination of infarct size (**Fig 3C-D**) and the contractile reserve of the left ventricle (LV) as assessed by inotropic stimulation using dobutamine in mice (**Fig 3G**). Combined with terminal hemodynamics this approach provides a more robust and accurate end-points for investigations aimed at studying the role of interventions, pharmacologic and genomic, that potentially limit the direct and reperfusion injury associated with acute MI and its longer-term prognosis.

Figure 3 MRI quantification of infarct size



4.1.5 Unique features or proprietary aspects of JBT Product

JBT has developed and refined an AAV construct that constitutes the next stepping stone in providing efficient and safe delivery of the RNAi regenerative therapy in the heart. Inserted into the pAV-U6-GFP vector are the four miR inhibitor sequences separated by a loop sequence. Each inhibitor is regulated by an alternate U6 or H1 promoter. Vector genomes with AAV2 ITR sequences are cross packaged into AAV9 capsids via transfection of AAV-293 cells. The virus is manufactured as a fee for service basis by a third party vendor [39-40] (**Fig 4**).



4.1.6 Preliminary Studies

Aguirre et al. [4] have shown that AAV2/9 inhibition of miR-99/100, Let-7a/c activates a cardiac regenerative response in mice with LAD ligation up to 90 days post-MI (**Fig 1-2**) and is proof-of-concept on the suitability of activating pro-regenerative responses for healing the diseased human heart. JBT has developed a single AAV2/9 construct that expresses the four microRNA inhibitor sequences, known as JBT-miR1. The 3D reconstruction technique based on late gadolinium-enhanced (LGE) magnetic resonance cardiac imaging (MRI) has finite element analysis of endocardial area, provides a predictive, quantitative measure of the extent of myocardial loss and injury in a mouse model of myocardial infarction. Similarly, JBT-miR1 injected (1 x10^{11} vg) into the LV of mice with LAD ligation reduced LGE myocardial infarction size (% LV Mass) to 12.61% (N=2) compared to 19.14% (N=2) in control treated mice as measured by MRI, 3 Weeks post-surgery. Therefore JBT-miR1 administration resulted in 34% more viable heart muscle compared to the control in this preliminary pilot study. The images in **Fig 5** are representative treated and control animals. Importantly our therapy can translate to human cardiac muscle cells. The miR sequences and their targets have been conserved through evolution from zebrafish to man. Human embryonic stem cell derived cardiac myocytes were incubated with lentivirus that could express inhibitors of miR-99/100, Let-7a/c for 1.5 weeks and induced a strong proliferative response as shown in **Fig 6**, suggesting that a similar response would be expected in the human heart.

Figure 5 MRI images of CD1 Mice Administered with Mock Virus Compared to JBT-miR1

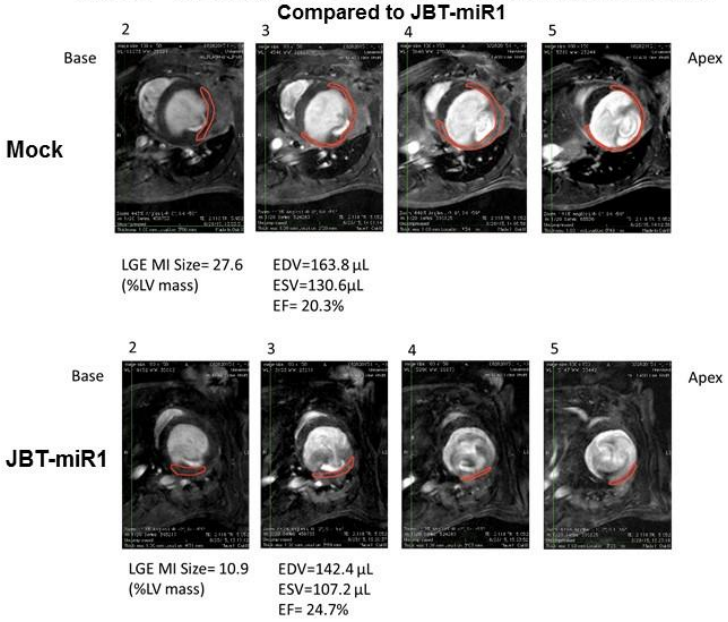
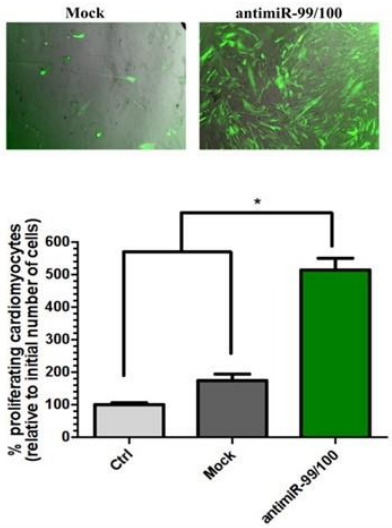


Figure 6. miR-99 / 100, Let-7a/c Inhibition Induces the Proliferation of Human Embryonic Stem Cell Derived Cardiac Myocytes



4.2 Research and Development

Our research and development is headed by Bhawanjit Brar Ph.D. in consultation with our scientific advisors. JBTs major objective is to develop JBT-miR1 through preclinical development and subsequently through to clinical trials. The therapy is based on the patent (METHODS FOR HEART REGENERATION [3]) and publication (In vivo activation of a conserved microRNA program induces mammalian heart regeneration, Aguirre A, et. al. [4]) that has been exclusively licensed by JBT in May 2015. JBT can extend the option agreement or exclusively license the patent(s)

by November 8th 2016. The publication received ample worldwide media coverage and is in the top 10 most influential articles ever published in Cell Stem Cell, and among the 5% most influential articles of all time, according to Altmetric statistics.

Between May 2015 and present our R&D yielded the following products and developments:

1. JBT-miR1 developed and tested in a small pilot study in CD1 mice.
2. Notice of Allowance Received for U.S. Patent Application No. 14/052,538 On September 28th 2015.
3. Agreement with Exiqon, Denmark to test two short (14mer and 15mer) in vivo inhibitors for these four microRNAs that are compatible and can be used together without problems of heteroduplex formation, which can be a common problem with oligonucleotides that are similar in sequence. These in vivo inhibitors have a half-life of 1- 2 weeks in vivo. If the preclinical experiments show efficacy, JBT has the option to enter into a Non Exclusive Manufacturing License Agreement for the two LNA antisense molecules to Let-7a/miR-100 and Let-7c/miR-99a if a license is needed after completion of the studies proposed in a grant application. When obtaining such a license JBT will get the spiking pattern for the oligonucleotides which will prove useful for patent filing.
4. Submission of NIH grant "Multiple MicroRNA Inhibition for Cardiac Regeneration in Ischemia" September 4th 2015.

JBT has spent $30,000 in 2015 to-date for R&D and patent prosecution, and plans to spend $950,000 in the next year (2016) if funds are raised. JBTs product selection criteria in this case are as follows; relatively low investment requirements, positive return on investment, fit with present strategy, feasibility of development and production, and time to see intended results. R&D will require additional resources in the future as estimated in the Capital and Financial Requirements Section of this document. These will include people and capital expenditures to speed up the development process.

4.3 New and Follow-on Products

The claims of our patent include the following:

1. A method of modulating proliferation of a cardiomyocyte, comprising:

(i) introducing into a cardiomyocyte a nucleic acid encoding an antagonist of a microRNA (miR) 99 microRNA, a nucleic acid encoding an antagonist of a miR-100 microRNA, and a nucleic acid encoding an antagonist of a let-7a microRNA, and a nucleic acid encoding an antagonist of a let-7c microRNA, thereby forming a transfected cardiomyocyte; and

(ii) allowing the transfected cardiomyocyte to divide, thereby modulating proliferation of said the cardiomyocyte.

2. The method of claim 1, wherein the introducing comprises transfecting the cardiomyocyte with a) a lentiviral vector or an adeno-associated viral (AAV) vector comprising the nucleic acid encoding the antagonist of the miR-99 microRNA and the nucleic acid encoding the antagonist of the miR-100 microRNA, and b) a lentiviral vector or an AAV vector encoding the nucleic acid encoding the antagonist of the let-7a microRNA and the antagonist of the let-7c microRNA.

3. A method of modulating proliferation of a cardiomyocyte, said method comprising:

(i) contacting a cardiomyocyte with a small molecule that modulates expression or activity of a miR-99 microRNA-regulated protein, a small molecule that modulates expression or activity of a miR-100 microRNA-regulated protein, a small molecule that modulates expression or activity of a let-7a microRNA -regulated protein, and small molecule that modulates expression or activity of a let-7c microRNA regulated protein, thereby forming a treated cardiomyocyte; and

(ii) allowing said treated cardiomyocyte to divide, thereby modulating proliferation of said cardiomyocyte.

JBT is actively seeking any new licensing opportunities from academic research Institutions including the Salk Institute to develop any promising potential treatments into therapies to treat heart disease. The Company is working with Professor Belmonte at the Salk to determine whether there are complementary miR therapeutics that JBT could license and develop. In Year 2 we intend to have our own laboratory and will develop our own proprietary technology.

4.4 Production

The product is manufactured by a third party vendor. In Year 2 (2017) manufacturing for preclinical studies will require clinical grade drug product that will be manufactured at a Good Manufacturing Practice (GMP) facility. SAFC which is the custom manufacturing and services business unit of Sigma-Aldrich Corporation, could be a potential GMP manufacturer and is leading the field with over 12 years of experience. SAFC works closely with customers to develop and manufacture exciting new treatments for cancer, cardiovascular and central nervous system diseases. SAFC is located at 6219 El Camino Real, Carlsbad, CA 92009, USA. The synthetic antagomiRs will be manufactured at a GMP facility in Germany.

4.5 Uniqueness

The product is unique because there are no commercially available therapies that promote the proliferation of endogenous cardiac myocytes in a mammalian ischemic heart. Manipulation of miR is a first in class therapy and

would be administered with standard of care procedures in the cardiac catheterization laboratory after diagnosis of an AMI. The approach is highly innovative with a large potential for broad clinical applications where regeneration of cardiac muscle is necessary. Successful development will lead to a broad clinical paradigm shift once results are translated into an approved and commercially available clinical product for the treatment of IHD. JBT has an advantage in the Marketplace because of patent, collaborations with academic institutions, experience, and cardiovascular expertise. We have done this before!

5.0 The Market Opportunity

5.1 Market Definition

IHD remains the major cause of death and disability worldwide [1]. Each year, an estimated ≈635,000 Americans have a new heart attack and ≈300,000 have a recurrent attack. With patients having a poor prognosis, there is a significant unmet medical need for the development of new treatment approaches that could regenerate heart muscle. The IHD portion, JBT's targeted market, is currently thought to be in 500,000 patient range for both the virus and synthetic antagomiR therapies. It is expected that patients with AAV antibodies or other contradictions will not be administered with the virus therapeutic. Growth of the IHD market is expected to mirror cardiac disease growth and reflect medical advances that are adopted. Despite a wide therapeutic arsenal, such as restoration of arterial perfusion with thrombolytic and antiplatelet therapy during percutaneous coronary intervention, procedures to open arteries with stents, or surgical revascularization (coronary artery bypass grafting, CABG), that have improved the management of patients with IHD [42-43], recovery of cardiac function and prevention of the transition to heart failure (HF) is unsatisfactory because current treatments do not regenerate heart muscle after an MI as shown in **Table 1** below [44-54]. It remains the leading cause of hospital admissions and the single largest killer of American men and women, causing 1 of every 6 deaths. We expect that JBT-mRI-1 to be administered in conjunction with standard of care procedures after perfusion has been restored to the heart.

Table 1: Current Standard of Care procedures for IHD

Intervention	Timing and Use	Limitation(s)
PCI	90 mins of hospitalization	Minimal, restores coronary blood flow in 90% to 95% of MI patients
CABG	In failed PCI	Higher risk of morbidity and mortality. Limited effect if not within 2 or 3 hours.
Anti-platelet agents	At signs of symptoms	Hemorrhage
Heparin	Within 48 hours	Hemorrhage
Warfarin	At least 3 months after an MI	Not normally recommended. Hemorrhage.
Fibrinolytics	When interventionist unavailable	Not used with Intracranial hemorrhage or malignancy, stroke, aortic dissection, or active bleeding. Effective within first hour of symptoms only.
Oxygen	On recognition of an MI	No studies demonstrate reduction of mortality or morbidity
Vasodilators	For 48 hours	Low BP, headache, and tachyphylaxis
Pain control	At 5 to 15 minute intervals	Can mask ongoing ischemic symptoms, does not treat disease.
Beta Blockers	Within 12 hours and indefinite	Bradycardia, HF, bronchospasm and concerns with hemodynamic instability
ACEI and Angiotensin Receptor Blockers	Within 24 hours and indefinite	Hypotension and declining renal function.
Glycoprotein IIb/IIIa Antagonists	During PCI	Headache, back pain, nausea/vomiting, pain at injection site, bleeding.
Statins	Prior to discharge	Intolerance and pain and inflammation in some subjects.
Aldosterone Antagonists	All post-MI patients	Must use a ACEI, EF<40%, creatinine clearance > 30 mL/min etc.
Implantable cardiac defibrillators	Used only 40 days after an MI	Not recommended for NYHA functional class IV patients or an EF >40%

5.2 Value Proposition

The current costs to treat IHD obtained from *Inpatient Costs Associated with Ischemic Heart Disease Among Adults Aged 18-64 Years in the United States* by Guijing Wang et al. (link http://cdn.intechopen.com/pdfs-wm/29903.pdf) using 2005 statistics showed the following:

- Cost estimates for hospitalizations with a primary diagnosis of IHD : $24,079 on average
- Mean cost for IHD as a primary diagnosis was $46,757 when there was CABG surgery, $19,622 when there was not.
- The cost of heart transplantation: ~$1,000,000

Before clinical trials JBT will conduct formal market research to assess the value proposition of its therapies.

5.3 Administration and Preliminary Channels of Distribution

The sale of this therapy would be direct to the cardiologist community, healthcare providers and to emergency room facilities within the hospitals. Consequently JBT would be expected to either partner with a large pharmaceutical company with the required distribution and sales network or contract with distributors supplying hospitals. JBT intends to publish its advances in order to inform heart and trauma specialists and to engage in frequent public speaking at specialized meetings and seminars to promote its therapy.

6.0 Competition

Our competitors are drugs in development and other early stage technology companies. These include companies that are:

1) Developing stem cell based technologies that can replace lost cardiac muscle cells.
2) Developing microRNA technology and others that may regenerate heart muscle.
3) Developing pharmacological agents that increase heart function or alleviate the symptoms of HF.
4) Large established pharmaceutical companies.

6.1 Replacement of cells using stem cell based technologies

The efficacy of potential sources of replacement cells including autologous [55-56], cardiosphere-derived cardiac stem cells [57] or myocytes derived from pluripotent stem cells and bone marrow derived cells is subject of debate. Inconsistencies in benefits observed across clinical trials are attributed to differences in stem cell methodologies, technical challenges [58-59], and complications such as tumorigenesis and arrhythmogenesis [60-62]. According to Clinicaltrials.gov there are **59 studies listed under the search criteria for** "heart attack and stem cell, Open Studies, Adult**."** The Link accessed October 12th 2015: https://clinicaltrials.gov/ct2/results?term=heart+attack+and+stem+cell&recr=Open&rslt=&type=&cond=&intr=&titles=&outc=&spons=&lead=&id=&state1=&cntry1=&state2=&cntry2=&state3=&cntry3=&locn=&gndr=&age=1&rcv_s=&rcv_e=&lup_s=&lup_e= Our major industry competitors that are developing stem cell technology to treat IHD are shown in **Table 2** below:

Company	Location	Intervention	Strengths	Weakness
CardioCell Altaco	San Diego Astana, Kazakhstan.	Patented ischemia-tolerant mesenchymal stem cells (itMSCs)	In clinical trials for AMI-Phase 2a in the U.S. and Kazakhstan. Have their own GMP facility	Exogenous cells, technically difficult methodologies for production, tumorigenesis and arrhythmia
Teva Pharma Industries	Petah Tikva, Israel	Allogeneic Mesenchymal Precursor Cells (MPC)	Phase 3 for CHF	As above Ongoing, completed in 2018
Mesoblast International Sàrl	U.S, Australia, Singapore	Adult Mesenchymal Stem Cells (MSC) to Treat Acute Myocardial Infarction- Prochymal®	Phase 1 Completed Phase 2	As above No results published No results published
FCB-Pharmicell Co Ltd.	Korea	Intracoronary Adult Human Mesenchymal Stem Cells	Phase 2 and 3 completed	As above No results published
TCA Cellular Therapy	Covington, Louisiana	Combination Stem Cell (MESENDO) Therapy	Phase 1 completed	As above No results published
Stempeutics Research Pvt Ltd	India	Adult mesenchymal stem cells	Phase 1 and 2 completed	As above. No results published
Cytori Therapeutics	San Diego	Adipose-Derived Stem Cells	Phase 1 trials completed in 2012	As above No results published
Stemedica Cell Tech, Inc.	San Diego	Allogeneic Mesenchymal Bone Marrow Cells	Phase 2 Cardiocell subsidiary	As above No results published
Capricor Inc.	Beverly Hills CA	Allogeneic Heart Stem Cells to Achieve Myocardial Regeneration	Phase1-2 Completion December 2015	As above
A. M. Zeiher	Germany	Enriched Progenitor Cells and Infarct Remodeling in Acute Myocardial Infarction	Completed December 2010 Phase 3	As above No results published

Miltenyi Biotec GmbH	Germany	Intramyocardial injection of autologous CD133+ bone marrow stem cells	Phase 3 recruiting	As above
Bioheart, Inc.	Sunrise, Florida	Myoblast Implantation into Myocardium Post Myocardial Infarction	Phase 2 and 3 ongoing	As above
The EMMES Corporation	Rockville, MD	Transplanting progenitor cells Autologous human mesenchymal cells and human bone marrow cells	Phase 1 and 2 In a 30 patient trial, positive effects were seen on Serious Adverse Events and quality of life	As above
Caladrius Biosciences, Inc.	Basking Ridge, NJ	Intracoronary artery administered autologous bone marrow derived stem cells	Phase 2	As above To be completed 2016
Coretherapix	Madrid - SPAIN	Allogeneic Human Cardiac Stem Cells in Patients with AMI	Phase 1 and 2 – To be completed in 2016	As above

Table 2: Competitors developing stem cell technology. Disclaimer: The information above may be subject to changes as development is ongoing. JBT does not know the safety profiles of the above therapies.

6.2 MicroRNA technology for heart disease and other treatments for heart attacks

Competitors listed in **Table 3** have alternative therapies that could potentially regenerate the myocardium after a heart attack. Our major competitor is miRagen Therapeutics. miRagen's lead program in post-MI remodeling targets the miR-15/195 family. In models of MI, inhibitors of this miRNA family reduce heart muscle cell death and promote heart muscle cell regeneration which lead to improved cardiac function. They suggest that miR-15 alone can regenerate heart muscle unlike JBT which is using a combination therapeutic approach.

Company	Location	Intervention	Strengths	Weakness
miRagen Therapeutics	Boulder, Colorado	miR-15 is a preclinical candidates for heart failure	Partnered with Servier at the preclinical stage. Large animal study conducted, potential partner.	Preclinical stage. Suggest that miR-15 alone can regenerate heart muscle unlike JBT which is using a combination therapeutic approach
Isis Pharma	Carlsbad, CA	Targeting Apo(B)-100 Apo(a) Factor XI	Has 4 cardiovascular targets in clinical trials, partnered with Genzyme and Bayer	They targets do not regenerate heart muscle
Zensun USA, Inc.	Shanghai China, San Diego	Recombinant Human Neuregulin-1	Investigated for class II and II CHF in Phase 2 clinical development	Has not been shown to replace damaged myocytes and induce proliferation
Cardiocreate	San Diego	Pim-1 modified cardiac progenitor cells	Could potentially regenerate heart muscle as other stem cell therapies	Will require retransplanation of Pim-1 modified cardiac progenitor cells in to patient's heart, preclinical stage. Disadvantages of stem cell therapies
Polyphor Ltd.	Allschwil, Switzerland	CXCR4 Antagonism for Cell Mobilization and Healing POL6326	In Phase 2 Clinical trials. Investigations in to the mobilization of stems cells in the ischemic heart.	To be completed November 2015. Investigative complementary therapy with stem cells.

Table 3: Other major competitors developing alternatives to stem cell therapy. Disclaimer: The information above may be subject to changes as development is ongoing. JBT does not know the safety profiles of the above therapies.

6.3 Other pharmacological agents that increase heart function

There are other companies that are attempting to transiently increase heart function or alleviate the symptoms of IHD and two are tabulated below in **Table 4**. The disadvantages of these interventions is that they do not replace damaged cardiac muscle or are treatments for IHD.

Company	Location	Intervention	Strengths	Weakness
Cytokinetics	South San Francisco, CA	OMECAMTIV MECARBIL	In Phase 2 trials for HF, data released November 2015. Partnered with Amgen, Oral formulation	Transiently increases heart function, does not regenerate heart muscle. Possible side effect of troponin release.
MyoKardia	South San Francisco, CA	MYK-461	In Phase 1 clinical trials. Partnered with Sanofi and has large investments for inheritable cardiomyopathies	Does not regenerate heart muscle. Focus is not on IHD.

Table 4: Other companies developing treatments for heart failure. Disclaimer: The information above may be subject to changes as development is ongoing. JBT does not know the safety profiles of the above therapies.

6.4 Large pharmaceutical companies

The existing market for heart failure medications is dominated by large worldwide biopharmaceutical companies as shown in **Table 5**. Competitors include, without limitation, Pfizer, Sanofi, AstraZeneca, Novartis, Bristol-Myers-Squibb, (BMS) Merck, Daiichi Sankyo, Abbott, Boehringer Ingelheim (B-I), Servier, Amgen, and others. However, these competitors also represent potential partners and sources for the sale of the product should that alternative be selected. These competitors have established developmental programs, distribution networks, are better financed, and have access to financing sources not available to JBT. They are also subject to changes in developmental direction resulting from management change, changes in strategic priorities, financial market conditions, and other factors. On the other hand, JBT is currently focused on developing therapies for IHD. The pharmacological agents that are currently being administered to patients with IHD do not regenerate heart muscle and cure the disease, they only mitigate symptoms.

Company	2010 Sales $M	2016 Sales $M	2010 Market Share %	2016 Market Share %
Pfizer	16,661	5,915	8.9	3.2
Sanofi	10,527	8,699	6.2	4.6
AstraZeneca	9,365	12,133	5.5	6.5
Novartis	8,574	5,690	5.1	3.1
BMS	8,383	1,055	4.9	0.6
Merck	7,478	6,036	4.4.	3.2
Daiichi Sankyo	5,502	6,505	3.2	3.5
Abbott	3,734	2,681	2.2	1.4
B-I	3,291	3,621	1.9	1.9
Servier	2,848	2,996	1.7	1.6
Total Leading	76,363	55,331	44.8	29.6
Others	94,097	131,570	55.2	70.4
Grand Total	170,460	186,901	100	100

Table 5: Business Insights from Companies Reported Sales. Sales of leading players in the global cardiovascular market ($m), 2010
http://download.bioon.com.cn/view/upload/201303/16084307_4163.pdf

7.0 Risk/Opportunity

7.1 Drug development risks

The drug development road is long, costly and unpredictable with the ever changing landscape. Safety concerns could hinder drug development in the future. The time to commercialize a drug can be between 7-19 years as shown in **Table 6**, however JBT is expecting one of our therapies to be commercialized in 10 years. JBT has structured a preclinical development plan that will enable development through to completion of Phase 2 clinical trials, saving money and time. A great deal of the initial work in Year 1 will be outsourced to UCSD effectively directing resources. JBT is aware of the risks in drug development and is prepared to mitigate risks. To increase the probability of success JBT is actively seeking other investments and patents that may be candidates for cardiovascular drug development, and complementary to our current technology

. **Table 6:** Drug development risks: http://www.fdareview.org/approval_process.shtml

Preclinical	Clinical				Approval	Market
Toxicology	Investigational New Drug Application	Phase I	Phase II	Phase III	New Drug Application	Phase IV / Post market surveillance
		safety	safety dosing efficacy	safety efficacy side effects		
Expenses		$15.2 million	$23.4 million	$86.5 million		
Time		21.6 months	25.7 months	30.5 months		
1 to 6 years	6 to 11 years				0.6 to 2 years	11 to 14 years
Overall probability of success						
		30%	14%	9%	8%	
Conditional probability of success						
	40%	75%	48%	64%	90%	
Sources: Dimasi, Hansen, and Grabowski (2003).						

There are many trials that are ongoing (> 15) using AAV delivery of therapeutics which is considered safe. In 2012 Glybera, a treatment for a rare inherited disorder, became the first treatment to be approved for clinical use in either Europe or the United States after its endorsement by the European Commission. However, AAV delivery of the miR inhibitors may not be effective in patients with AAV antibodies, therefore JBT is also developing soluble synthetic oligonucleotide inhibitors as an alternative therapeutic approach.

7.2 Limited operating history

Although JBT is relatively new, the company has extensive experience since the officers, advisors and consultants of this company have extensive experience in all aspects of drug development including preclinical and clinical development of cardiovascular therapeutics and commercialization of first in class therapeutics.

7.3 Limited resources

JBT has limited resources, financial, manpower and facilities, however it is collaborating with outstanding academic institutions to move its developmental program forward with potential funding from the NIH and others.

7.4 Opportunities

This is a high risk high reward opportunity. Although our business today has its share of risk, we feel we can alleviate these risks with the development of a revolutionary treatment that regenerates heart muscle that could be applicable to any number of diseases where heart muscle regeneration is required. Due to the inconclusive results achieved by stem cell therapies to date and the rising incidence of HF in industrialized countries, finding novel alternatives that replace lost cardiac myocytes after an MI is an urgent necessity and JBTs therapy offers this alternative. Investing at this early stage will require less money and offers the potential of large rewards if successful. The treatment could make a huge impact on society, improving the long-term outcome and quality of life with patients with IHD and other causes of heart failure where cardiac muscle regeneration is necessary such as: Dilated cardiomyopathy, Chemotherapy (adult and pediatric), Restrictive cardiomyopathy, Peripartum cardiomyopathy, Viral myocarditis- 20% of all cases of sudden death in young adults, 50% of HIV deaths, Diabetic cardiomyopathy, Alcoholic cardiomyopathy, Takotsubo cardiomyopathy, Anorexia Nervosa induced cardiomyopathy. This is an opportunity to invest in a:

1. First in class treatment to regenerate heart muscle with proof-of concept preclinical data from outstanding scientific investigators.
2. Highly experienced development and commercialization team with heart failure and drug development expertise and proven success.
3. Company working with the Salk Institute to establish a patent tree stemming from the *METHODS FOR HEART REGENERATION patent option exclusively licensed to JBT [3].*

Market and pricing risk will be addressed by doing a comprehensive study and likely partnering with a larger pharmaceutical company with existing products in this market after preclinical. JBT's focus will be on its technology.

The company has the opportunity to dominate a niche in the marketplace, become a major force in the industry as the only therapy that regenerates heart muscle. It is believed that this can be achieved 5 years. The lead product, JBT-miR1, has the chance to change the industry, affect many lives and improve the outcome, quality of life of patients with IHD and their families.

8.0 Management Team

JBT currently consisted of seven professionals who have 215 years of combined experience in marketing and business development, preclinical development, product development, clinical cardiology and clinical development, and in Chemistry Manufacturing Controls and Quality.

8.1 Officers and Key Employees

- Bhawanjit Brar Ph.D. President and Founder: Has over 20 years in molecular cardiology research experience at outstanding academic institutions including University College London (UK), The Salk Institute (British Heart Foundation Fellow), and University of California, San Diego. She is a former Vice President of a biotechnology company that helped develop a novel therapy for the treatment of CHF from Investigational New Drug Application to Phase 3 clinical trials in 7 years. Dr. Brar has over 30 publications in ischemic reperfusion injury and molecular cardiology and extensive regulatory and clinical operations experience.
- Joseph Hansen. J.D., C.P.A. Chief Financial Officer: has over 25 years of experience serving as a CFO of both public and private companies, a co-founder of three companies, has held various board memberships and executive positions including the biotechnology sector.

8.2 Ownership

JBT was established as a limited liability company with understanding by the founders that depending on the requirements of its funding sources, that it may have to be reorganized as a “C” or “S” corporation to facilitate use of securities or tax laws. JBT has issued no shares. The following persons are owners of the LLC. The company can authorize 44% of the value of the company of common stock as equity.

Bhawanjit Brar Ph.D.	95%
Joseph Hansen J.D., C.P.A.	1%
Professor Kirk Petersen M.D.	1%
Professor Juan Carlos Izpisua-Belmonte Ph.D.	1%
Friends and Family	2%

8.3 Professional Support

We have assembled a team of professionals that includes:

- **Scientific Advisor:** Professor Kirk Peterson M.D. is a current Director Emeritus of the Sulpizio Cardiovascular Center at the University of California, San Diego Health Systems. He is also a Professor of Medicine and Deputy Dean and the Director of the Seaweed Canyon Physiology Laboratory at the University of California, San Diego School of Medicine. He has over 150 publications in cardiovascular science and is the editor and author of numerous book chapters. Professor Peterson is an outstanding translational scientist that specializes in murine ischemic injury models and human cardiac catheterization with over 40 years of experience.
- **Scientific Advisor:** Professor Juan Carlos Izpisua-Belmonte Ph.D. is a current Professor at The Salk Institute, La Jolla in the Gene Expression Laboratory. He received his Bachelors of Pharmacy and Science at the University of Valencia, Spain. He received his Ph.D. at the Universities of Bologna, Italy and Valencia, Spain and was a Postdoctoral fellow at the University of Marburg; The European Molecular Biology Laboratories at Heidelberg, Germany and the University of California, Los Angeles. The questions addressed by the laboratory include: How does one cell give rise to millions of cells, and how do they come to be organized into complete structures such as limbs, a heart or brain? How certain animals are able to regenerate their tissues and organs? He has over 30 years of experience
- **Toxicology Collaborator** (consultant) is Stanley A. Roberts, Ph.D., D.A.B.T President, SAR Safety Assessment has over 40 years of toxicology expertise. He is the former Vice-President, Preclinical Development at CovX Research, LLC (acquired by Pfizer) and was Global Director – Metabolism and Preclinical Pharmacokinetics at Abbot Laboratories.

- **Chemistry Manufacturing and Controls and Quality** consultant is Ms. Shirley Cao has over 20 years of experience in manufacture of drug products.
- **Our Business Development Executive is Mr. Louis Scotti who was a** former Arena pharmaceutical executive responsible for commercialization of an obesity drug. Louis Scotti has over 30 years of experience and has been responsible for over 25 commercialization transactions.
- **Scientific consultant** is Aitor Aguirre who was the lead scientist on publication and patent. He has a Ph.D. from the Tissue Engineering Technical University of Catalonia (Spain), Cum Laude and has 10 years of experience.
- **Basic legal affairs** for JBT are being handled by Joseph Hansen and we are also consulting with patent and business attorneys in the San Diego area.

9.0 Capital and Financial Requirements

9.1 Cost Projections for 3 years

JBT's initial funding has been provided for in the form of loans by its founder. It is hoped but not reflected in the estimates below that JBT will be successful in its NIH grant applications. If successful we estimate that $5.75 million of financing will be necessary to fund JBT for the next three years (**Table 7**). After that time, an estimated additional $15 million will be needed to fund two products through the completion of Phase 2 clinical trials. A preclinical development strategy is planned through to clinical trials, with an expected duration of 3 years. In year 2, potential partners will be approached with the goal of partnering and cost sharing for clinical trials.
As noted in Section 1.9 the funding requirements are dependent on the success of the grant applications.

Year 1 2016	**Total $950,000**
In vivo studies to confirm efficacy of virus and small molecule/synthetic molecules in vivo	$500,000
Operational costs and patent prosecution and licensing	$150,000
Administrative infrastructure, operating costs and insurance	$70,000
Salaries and payroll taxes-various including executive management	$230,000
Year 2 2017	**Total $2,700,000**
Determine whether intracoronary delivery may be as efficacious as intracardiac delivery in an in vivo murine model of ischemic injury	$200,000
Manufacture and determine whether clinical grade virus can promote proliferation of cardiac myocytes isolated from non-rodent species in vitro	$500,000
Patent prosecution and in licensing and running costs of small molecules only after showing efficacy in in vivo mouse model	$250,000
Non Good Laboratory Practice (GLP) survival study in CD1 mice and a non-GLP dose range finding study in the non-rodent species	$500,000
IND submission and writing for virus and small molecules if efficacy is confirmed	$200,000
Salaries, payroll taxes, and operating costs: Business Development Executive, Chemistry and Manufacturing and Controls Director, Toxicologist, Preclinical Development Director and a Staff Scientist, CFO and President	$1,050,000
Year 3 2018	**Total $2,100,000.**
Good Laboratory Practice safety toxicology studies in mice and the identified non-rodent species of virus and small molecules	$1,000,000
Patent prosecution	$50,000
Salaries, payroll taxes, and operating costs for personnel stated in Year 2	$1,050,000
Total costs for 3 years	**$5,750,000**

Table 7: Projected costs over the next 3 years

9.2 Assumptions

Generally, the assumptions inherent in the Financial Plan are based on the experience and knowledge of its President and Chief Financial Officer. They further reflect grant applications to the NIH. Given the 10 plus years it takes to develop and bring a drug to market along with the uncertainties involved in pricing and the competitive environment in 10 plus years, no financial statements have been prepared. Annual cash expenditures are expected to be consistent the totals provided in this Section and will also be dependent on the success of the preclinical trials. All funds expended during the development phase discussed in this plan, 7 years, are expected to result in annual losses and a negative net worth. Milestones reflecting developmental activities are expected to also reflect financial milestones and, to some degree funding activity.

9.3 Valuation

A preliminary valuation has been calculated resulting in an estimated valuation in the neighborhood of $1.8 million at this stage of development. This valuation uses assumptions/estimates are shown in **Table 8**:

Valuation Criteria	Numerical Value
Potential patients	500,000
Drug sales price	$ 3,792
Medicare discount	30%
Medicare patients	70%
Cost of Goods Sold	8%
Royalties	5%
Sales expenses	10%
G & A expenses	7%
Discounts related to risk adjustments	33%
Net present value discount	31.2%
Grants and Equity contributions	Pending

Table 8: Valuation Criteria: All of which assumptions are highly subjective and uncertain.

Nevertheless, the $1.8 million valuation is assumed to be realistic in light of similar valuations of other developmental entities, the expertise of its scientific team, and the patent rights currently held by JBT.

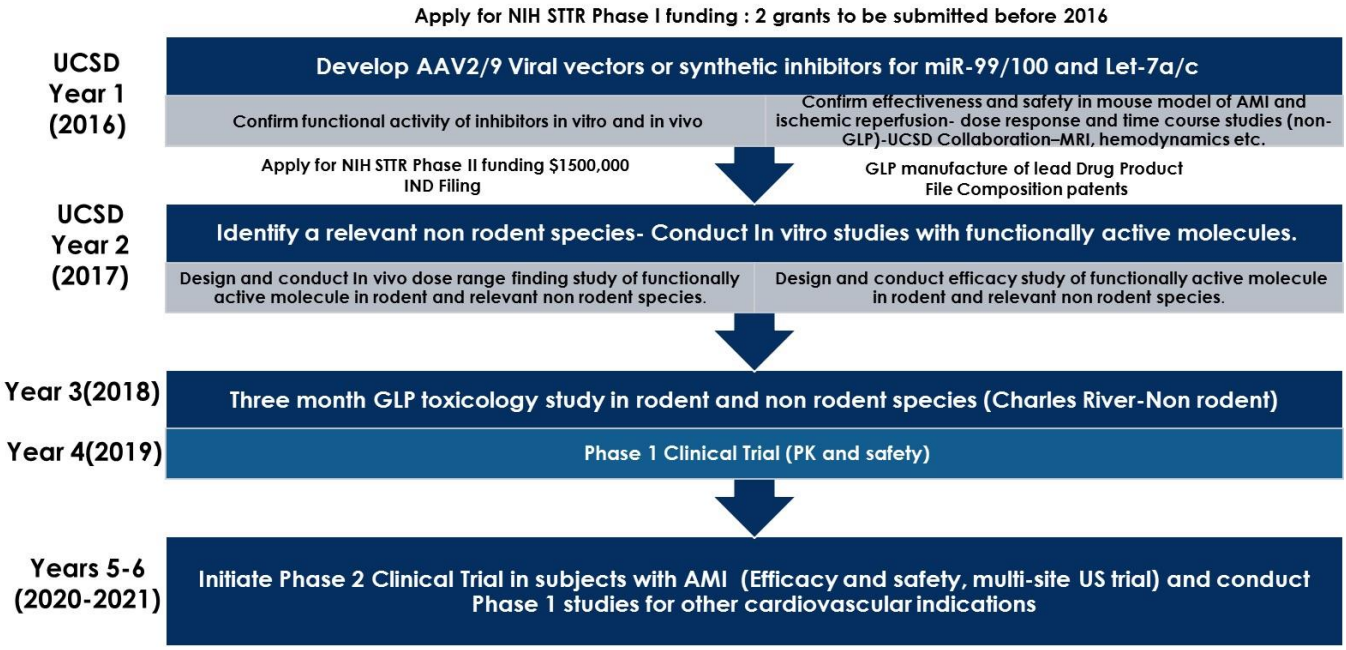
9.4 Exit Strategy

The founders have had extensive experience in the biopharmaceutical industry and have realistic attitudes as to the need for an investors' return. JBT expects to employ a full time business development person in year 2 to begin a search for a phase 1 or earlier partner to carry the burden of future developmental costs or to license the assets developed. Simultaneously, JBT will develop SOX compliant internal controls and FASB compliant financial statements should the opportunity for an initial public offering arise. JBT intends to make every effort to provide a liquidity event.

9.5 Funding Goals

JBT's goal is to raise up to $5.75 million for its research and developmental activities. As part of that goal it intends to raise up to $100,000 as secondary founder equity contributions to be used for immediate research and development and related expenses. As indicated the funding of the primary amount raised is expected to be consistent with R&D milestones. The total amount is also expected to vary with the success of the NIH grant applications already submitted and to be submitted.

10. Time Line for Development



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