



CASE WESTERN RESERVE
UNIVERSITY EST. 1826

Department of Biomedical Engineering
10900 Euclid Avenue, Cleveland, Ohio 44106

OTFBP 10-855

January 25, 2010

Ohio Third Frontier
Ohio Department of Development
Technology Division
77 South High Street, 25th Floor
Columbus, OH 43215-6130

Re: FY2010 Ohio Third Frontier Biomedical Program

Ohio Department of Development:

This letter is to state the intent of the Case Western Reserve University, in conjunction with the partners listed below, to jointly produce and file a full proposal in response to the OTF Request for Proposal released on December 14, 2009.

1. Title: Portable Metabolic Monitoring Platform
2. Contact Person: Colin K. Drummond, PhD, MBA
Director, Coulter Case Translational Research Partnership
Department of Biomedical Engineering
Case Western Reserve University
Cleveland Ohio, 44106
216-368-2639 phone
216-368-4969 fax
email: colin.drummond@case.edu
3. Lead Organization: Case Western Reserve University
4. Legal Structure: Institution of Higher Education, Corporation for Non-Profit, State of Ohio
5. Estimated funds to be requested: \$550,000
6. Collaborating Organizations (as of 1/25/2010):

Breath Measurement Technologies, Inc.
Invacare Corporation

We look forward to submitting a full project proposal to the Third Frontier program in March.

Sincerely,
Case Western Reserve University

Colin K. Drummond
Department of Biomedical Engineering

Portable Metabolic Monitoring Platform

After many years of development in academic and laboratory environments, portable metabolic monitoring devices are gaining credibility within the scientific community for diagnostics and therapy. A combination of minimally invasive sensors and so-called “electronic noses” have been explored in many forms over the years, but a system that can enable the development of low-cost, simple to use, hand-held units in the office of a general practitioner or to the common at-risk cardiovascular patient has escaped commercialization. Our proposal team has completed a proof-of-concept model of a portable metabolic monitoring platform and seeks OTF funding to commercialization of the system into clinical and field trials. Such a

As sensor materials and applications receive more research attention, a broader scope of devices that can monitor metabolic activity can be produced. For instance, those cardiovascular patients pursuing an exercise regime as part of their self-managed recovery could benefit from “instantaneous feedback” on metabolic activity. In some ways the metabolic monitoring field can be overwhelming, from both the large number of publications and specificity of discussion. However, our interest in a hand-held monitoring systems corresponds with a variety of noteworthy research projects that have significantly advanced exhaled breath applications to metabolic monitoring, and is a focused effort to mainstream the technology in the point of care and consumer setting. The portable metabolic monitoring system can be used for existing and at-risk CV populations.

Breath Measurement Technologies, Inc. (BMT) has developed a prototype portable monitoring system composed of a hand-held detection unit and disposable sensor. Hand-held monitoring is made possible by significant technical progress in sensitive and selective advanced sensor technology that can be used to measure markers indicative of metabolic stress. BMT’s partnership with the OFT proposal collaborators will expedite commercialization of the platform technology through field and clinical trials, leading to refined product specifications for an Ohio supply chain partner to complete development and take to the market.

The proposed Platform integrates existing University technology, a small business prototype, and a large company supply chain into an OTF project capable of improving human health through technology. A key metrics of success for this project is a low-cost monitoring system that enters the health care supply chain through the GP; fostering job creation at established Ohio biotech companies.

January 25, 2010

OTFBP 10-856

Lead Applicant: Capsa Solutions LLC.
4800 Hilton Corporate Drive
Columbus, Ohio 43232
614. 864.9966

Contact: Tim Friar
tfriar@artromick.com
614.322.3010

Project Title: Project 11

Grant Funds Requested: \$1,000,000.00

Summary of Proposed Project:

The Artromick product line of Capsa Solutions is in the midst of a strategic growth planning process that will set the product line growth plan for the next few years. The core initiative is the development of a new mobile computing technology platform. Artromick currently manufactures and sells multiple products in this category. Artromick would like to a. cost reduce, b. consolidate, and c. transform / improve the product line through a comprehensive development project. Artromick has knowledge regarding the market and Artromick is beginning some ethnographic research to have a head start on identifying opportunities in the market.

Proposed Product Line

Mobile Computing Cart

- Mobile computing workstations are used to mobilize computers throughout the hospital; ED, surgery, radiology, nursing floor, etc.
- The product will be a highly featured and configurable platform

MedServer Medication Cart

- MCW with the addition of Medication management used primarily on the nursing floor
- The MedServer's basic function beyond the MCW is medication and supply storage and security.

Transfer Cart Line - Development

- Carts used to supply medication on a daily basis from the pharmacy to Medication carts and Medservers
- Transfer carts move Medserver bins or cassettes from the pharmacy to the nursing floor

Project Goals

- Low cost production target of MCW and MedServer
- Product line market ready and available 2011 / 2012
- Development of the highest quality / performance product on the market

Market

- The primary market for the products will be US hospitals
- The secondary market for the product will be US nursing homes
- The third market for the products will be world wide distribution to hospitals and nursing homes



January 25, 2010

The Ohio Department of Development
Technology and Innovation Department
77 South High Street, 25th Floor
Columbus, OH 43215

RE: Letter of Intent to Submit Ohio Third Frontier Biomedical Program Proposal

Dear Sirs:

PneumoSonics Inc., located at 1771 East 30th Street in Cleveland, OH, intends to submit a Ohio Third Frontier Biomedical Program Proposal entitled **Medical Applications for MicroPower Impulse Radar**. Alan Greszler, PneumoSonics' Vice President of Product Development will be the contact for the proposal. Mr.Greszle can be reached at (216) 357-3310 x1007 or agreszler@pneumosonics.com.

The proposal will request approximately \$1 million to develop, test and commercialize different medical devices utilizing micropower impulse radar as the platform technology. The first device, a portable pneumothorax detector, has been prototyped and will begin clinical trials during the third quarter of 2010. The pneumothorax detector will complete clinical trials and be launched by the first quarter of 2012. Additional applications, including a vital signs detector and hematoma detector will be developed based on the same platform technology with modifications to the proprietary algorithm. A one page summary of the proposed project is attached to this letter of intent.

PneumoSonics will be the Lead Applicant. The United States Military, through the Army's Telemedicine and Advanced Trauma Research Center, is expected to be the commercial collaborator for the project. The Ohio State University is expected to be the research collaborator for the project. The University of Cincinnati and Cleveland Clinic Foundation are expected to be clinical collaborators for the project.

We appreciate your consideration of our proposal for funding from this exciting and important program.

Sincerely,

A handwritten signature in black ink that reads "Alan Greszler". The signature is written in a cursive, flowing style.

Alan Greszler
Vice President of Product Development
PneumoSonics Inc.

PneumoSonics Project Summary

PneumoSonics Inc (PSI) is developing medical devices based on micropower impulse radar technology (MIR). MIR technology has been pioneered by researchers at Lawrence Livermore National Laboratory (LLNL). PSI has licensed the MIR technology from LLNL. MIR devices are inherently compact, lightweight (less than one pound), battery operated, robust, and portable. Since current is only drawn during the very short pulse times, the power consumption is extremely low. The power output is also very low, being generally in the range of 250 μ W RMS (about 500 times less than a modern handheld cell phone), and thus the technology is well below the Food and Drug Administration (FDA) established limits and is considered safe for use in medical applications.

Based on these attributes, PSI will utilize the MIR technology to develop portable diagnostic medical devices with applicability in battlefield and civilian field trauma environments as well as hospital-based acute and intensive care unit settings. There is a clear need in these environments for increased diagnostic functionality in the form of low power, portable medical devices, especially in the military where medics are required to make critical life and death decisions in extremely high pressure situations. The benefits of MIR technology will allow PSI to provide increased diagnostic capabilities in these critical environments.

The first product in development is a portable pneumothorax detector device called the PneumoScan. The PneumoScan is a point-of-care, non-invasive, portable, lightweight, low-power diagnostic tool that will be used to rapidly and reliably detect the presence of a pneumothorax (collapsed lung). The technology provides a significant market opportunity and may ultimately become the standard of care in the diagnosis of post-traumatic pneumothorax in pre-hospital and possibly hospital-based settings. The device is conservatively projected to generate \$213 million in revenue and \$40 million in operating profit in seven years with a Net Present Value (NPV) of \$15 million. The PneumoScan will be launched in the first quarter of 2012.

Additional applications exist for various point-of-care, non-invasive, portable, lightweight, low-power diagnostic tools. Two particularly promising applications are a remote vital sign (heartbeat and respiration) detector that does not require use of skin contact leads and a hematoma detector to identify abdominal or thoracic bleeding in battlefield settings. These additional applications are expected to run on the same electronic platform as the PneumoScan. PSI will need to develop application specific algorithms but the intention is to provide increased diagnostic functionality in a single handheld device.

PSI will utilize the funding from Ohio Third Frontier Biomedical Program to complete its clinical studies and launch the PneumoScan product, develop the vital sign and hematoma detection devices, and identify/develop additional portable diagnostic applications based on the MIR technology.

Letter of intent to submit a proposal for the Ohio Third Frontier Biomedical Program 2010

Lead applicant: Cellular Technology Limited (CTL)
20521 Chagrin Blvd
Shaker Heights, Ohio 44122

Contact person: Paul V. Lehmann
President and CEO
216-791-5084
paul.lehmann@immunospot.com

Proposed Project: Characterized human leukocyte libraries as commercially available model organisms for the advancement of cardiovascular and other human disease related research.

Estimated Grant Funds to be requested: \$ 1,000,000.00

Collaborators: HemaCare Corporation

Project summary:

Major cardiovascular diseases such as atherosclerosis are largely defined by the highly variable genetic makeup of susceptible individuals. In addition to the many gene variants involved, the regulation of these genes, as well as the metabolic pathways involved will affect cellular functions that results either in proper cellular activities or aberrant functions that contribute to the development of disease. Individual cells interact in complex ways to participate in processes such as inflammatory or degenerative tissue damage or tissue regeneration. Moreover, many somatic and environmental factors have an influence on the development of diseases such as atherosclerosis.

While the presence of gene variants can be readily studied with extracted DNA, that is, using stable but non-living material, every thing downstream (studies of gene regulation, cellular reactions individually, or the interplay of cells) can be studied only on fully functional living cells and organisms. Based on this the recent logical trend is to use living cells as model organisms on which gene regulation, metabolic pathways, cellular differentiation and cell-cell interactions can be studied. Cellular Technology Limited (CTL) has developed proprietary technology to freeze white blood cells in a way that they fully maintain their functionality after thawing. Such white blood cells contain many cell types that are critically involved in the genesis of atherosclerosis and tissue repair, including stem cells, neutrophils, monocytes/macrophages and lymphocytes. Via leukapheresis, we have been obtaining from our partner, HemaCare Corporation, up to 20 billion white blood cells per human donor and leukapheresis session. We developed strategies for freezing such cell material in up to 2,000 aliquots per draw while fully maintaining the cells functionality after thawing. This will enable industry and researchers to run up to 2,000 screens with the identical cell material; allowing ease of access and reproducibility of results with highly defined materials. Recently CTL showed that when different aliquots of the same cells were tested in different laboratories the results differed by only 40% in a test system that regularly results in up to 3,500% variation without such standardization. Such cells therefore are suited for being used as readily accessible reference standards in different laboratories and entities for harmonizing their data and global research processes.

CTL has processed and frozen white blood cells from 60 human donors. They have been sold to selected commercial entities and members of the immunological research community. The cells of each donor are already characterized for genes of relevance for immune function (HLA) and for immune reactivity to certain environmental antigens (as relevant for reference standard measurements).

We propose here with the help of Third Frontier funds to expand this library to initially 500 donors in a fashion that it can serve as cellular model for cardiovascular research. We believe that providing a choice of cells from a considerable spectrum of humans is a major step towards the appropriate representation of the diversity within the human population. In addition to the cells themselves, we will collect blood plasma and diverse information about cardiovascular family history to screen for potential genetic risk of the donor. DNA will be isolated from each donor and made available. In this way we can offer a library of human material to the cardiovascular research community that encompasses, plasma, DNA, living cellular model organisms, and information on predisposition to disease on individuals, and more importantly, of a sizable genetically diverse population. After the initial phase for which funding is requested, CTL intends to increase the size of library to tens of thousands of individuals to better approximate the spectrum of the human population.

CTL proposes to make all non-personal relevant information on the donors searchable through CTL's internet based data interface "ePBMC". In this way researchers will be able to select online any number of test subjects based on their criteria of interest. Furthermore, this interface will support the addition of data, thus expanding the characterization profile of the cell material.

For the past 5 years we have been successfully marketing such model cell material to the immunology community. Extending the number of donors, and introducing a focus for cardiovascular predisposition will make a major contribution to cardiovascular research (and biomedical research in general). Cellular Technology Limited (CTL) and its collaborator HemaCare Corporation. will combine their strength to support the sustainable growth of CTL and the creation of high paying Ohio jobs over the grant period.

MetalloPharm LLC

1790 Riverstone Drive, Delaware, OH 43035
Tel: 614-306-3960
E-mail: metallopharm@gmail.com

January 25, 2010

Dear Members of the Ohio Third Frontier Commission

I am pleased to submit this letter of intent for a possible proposal submission to the 2010 Ohio Third Frontier BioMedical Program. The proposal would be submitted by MetalloPharm LLC, as detailed below.

Lead Applicant: MetalloPharm LLC, 1790 Riverstone Drive, Delaware, OH 43015.
Contact Person: Dr. Ada S. Cowan
Tel: 614-306-3960
Research Site: Research Laboratories in the Ohio University Innovation Center, Athens, OH
E-mail: metallopharm@gmail.com
Project Title: Development of Novel Cardiovascular Drugs
Estimated Budget: \$1 MM from FY10 OTFBP
\$300 K from WCF
Estimated Timeline: 2 years
Collaborators: Dr. James A. Cowan, The Ohio State University, Department of Chemistry
Dr. Daniel Ely, University of Akron, Department of Biology
Dr. Glen Jackson, Ohio University, Department of Chemistry & Biochemistry

A one-page summary of the proposed project follows.

Sincerely



Ada S. Cowan, Ph.D.
VP, Pharmaceutical Development
MetalloPharm LLC

Development of Novel Cardiovascular Drugs

Cardiovascular disease (CVD) impacts the lives of tens of millions of Americans and is a major drain on the national health budget. Few patients respond well to only one drug and there is a constant need to improve both the efficacy of therapy and minimization of side-effects. In recent years we have worked to develop an approach to drug design that involves both recognition and subsequent irreversible inactivation of therapeutic targets. The basic drug design strategy incorporates a protein recognition domain and a metal binding domain, where the latter mediates irreversible inactivation of the therapeutic target. Inactivation is both catalytic and multiturnover, while the incorporation of both binding and catalytic centers provides a double-filter mechanism for improved target selectivity and lower dosing, with the potential for reduced side effects and toxicity. There is significant interest in identifying cardiovascular drugs that act on multiple targets; including ACE, ECE-1, and NEP. These promise more effective control of hypertension at lower dosage through enhanced specificity. While there is no drug with such a profile currently on the market, MetalloPharm has developed several promising lead metallodrug candidates that demonstrate such. We propose to build on the successes of two prior NIH-funded Phase 1 SBIR proposals and two NIH-funded R01 and R21 programs that led to the development of our catalytic metallodrug platform. These prior efforts demonstrate proof-of-concept, as well as identifying several lead metallodrug candidates that show in vivo efficacy in a hypertensive rat model.

The Aims for this OTFBP proposal are to demonstrate safety and efficacy of our lead cardiovascular drugs for successful commercial applications, as well as understanding the mode of action. The goals include development of the pharmacokinetics (PK) and safety data that will enable MetalloPharm to file an IND in preparation for initiating clinical trials with its lead therapeutic. To accomplish this objective we will first develop PK and initial safety profiles for our set of drug candidates that have already shown in vivo efficacy in a rat model. Studies will include formulation development, and stability studies, as well as dose range-finding using a spontaneously hypertensive rat model. Following these studies, the lead candidate and a backup will be selected for further development in IND-enabling pre-clinical studies. The most effective, stable drug formulation will be selected for the final GLP non-clinical studies and clinical trials. We intend to take at least one of these potent cardiovascular metallodrugs into the clinic to ascertain the most appropriate applications. Once the formulation and non-clinical packages are developed and FDA concurrence is obtained, clinical trials may be conducted in patients with cardiovascular disease through licensing or co-developing with partners.

Successful conclusion of this program will move our cardiovascular drug candidates to a stage where MetalloPharm is ready to seek regulatory approval. This proposal will provide definitive therapeutic strategies and product candidates for formal non-clinical trials, an IND filing and human clinical trials. Fulfilling the research goals will strengthen MetalloPharm's intellectual property position, contributing to its potential value and attractiveness for private investment. Publication of the company's research progress in refereed journals and business publications will bring international exposure to the company and to Ohio as a region where promising biomedical companies can be seeded and grown. If this proposal is successful, MetalloPharm and its collaborators will hire staff to execute this program. The success of this program will allow MetalloPharm to secure additional financial resources needed to commercialize the cardiovascular drug product and ultimately result in the opportunity for significant employment in Ohio within 3 to 5 years of completing the project. It will also further enhance Ohio's growing reputation in cardiovascular R&D.

MetalloPharm is a start-up pharmaceutical R&D company, with research laboratories in the Ohio University Innovation Center. MetalloPharm's drug platform is versatile and applicable to multiple disease treatments. The company seeks growth through development of a metallodrug platform technology with licensing per indication of multiple therapeutic products, and plans to use money received through licensing deals to obtain funding to develop drug candidates for other diseases in the pipeline. The Company's objective over the next two-three years is to generate pharmaceutical interest by demonstrating the robustness of its metallodrug platform, and expects significant job growth as the programs described in this proposal move forward.

Efforts are also underway to develop partnerships with pharmaceutical industry, venture organizations, and VCs such as Roche, through Carole Nuechterlein, Head of the Roche Venture Fund at F. Hoffmann-La Roche; Novartis, through Markus Goebel at the Novartis Venture fund; a Midwest venture capital fund based in Cincinnati; and Unither Virology (part of United Therapeutics) through Urban Ramstedt (Chief Scientist); all of whom have expressed interest in evaluating MetalloPharm's technology for funding through equity exchange.

OTFBP 10-860

This proposal for the Ohio Third Frontier Biomedical Program FY2010 is being led by Cellular Technology Limited (CTL) in collaboration with ReachBio, Inc. CTL is an established biomedical device, contract research and consumable reagent company based in NE Ohio.

Lead applicant: Cellular Technology Limited (CTL)
20521 Chagrin Blvd
Shaker Heights, Ohio 44122

Contact person: Paul V. Lehmann
President and CEO
216-791-5084
paul.lehmann@immunospot.com

Estimated Grant Funds to be requested: \$ 500,000.00

Proposed Project: Development and commercialization of a colony enumeration system for embryonic stem cell (ESC) colony assays and progenitor colony forming cell (CFC) assays.

Project Summary:

According to a report by the U.S. Department of Health and Human Services the global market for the collective sectors within regenerative medicine is estimated at 500 billion. Currently blood and tissue banking including bone marrow, cord blood, and peripheral blood represents a rapidly growing sector within regenerative medicine. With estimates for the 2010 market ranging from 4-10 billion, and projected compound annual growth rates up to 28%, it is a conservative estimate that growth will exceed 15-20 billion within the next five years.

The current state of the art for monitoring regenerative potential in source biological material is based on cell proliferation and colony formation assays under adherent or non-adherent growth conditions. CTL currently markets the BioSpot[®] analyzer product line which supports a broad range of adherent microplate assays including stem cell colony formation assays. In collaboration with ReachBio, Inc. a new instrument in the BioSpot[®] product line will be introduced for non-adherent stem cell assays in semi-solid media. These non-adherent three dimensional stem cell assays are difficult to automate and currently require manual analysis that is subjective, tedious, and time consuming. CTL will leverage it's expertise in high-resolution macroscopic imaging to develop the BioSpot[®] optical system for image capture and analysis of non-adherent stem cell assays. Current instrumentation that is being marketed for these assays rely on capturing multiple images across X, Y and Z axes followed by image stitching to create a composite for analysis. This process is inefficient and introduces processing artifacts that can affect the validity of the counted result. The new product outlined in our proposal will enable analysis of ESC and CFC assays in a single image through a large field of view and depth of field macroscopic optical system.

As the only Ohio company currently marketing instrumentation for stem cell bioassays, CTL is strategically positioned to deliver the first purpose-designed product for the automation of stem cell colony formation assays. CTL anticipates a 30% increase in employment over the grant period that is directly related to the project proposal. This will include high paying technical positions in sales and marketing, production and R&D. Furthermore, the state of Ohio will benefit through our well-established connections with Ohio's precision manufacturing industry, OEM computing vendors, and regional construction resources.



CODONICS

We bring the future into focus

17991 Englewood Drive
Middleburg Heights, Ohio 44130

**Letter of Intent
Ohio Third Frontier Biomedical Program
Fiscal Year 2010**

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, Ohio 43215

To Whom It Concerns:

This document constitutes our Letter of Intent (LOI).

Lead Applicant: Codonics, Inc.
17991 Englewood Drive
Middleburg Heights, OH 44130
440-243-1198

Contact Person: Timothy Jakubisin, Director of Operations
tjakubisin@codonics.com

Project Title: Medical Smart Label Device

Estimated Grant Funds to be requested: \$1,000,000

Known Collaborators: To be determined

Summary of Proposed Project

Codonics proposes the development of a family of related medical devices based on Codonics Smart Label Technology. The devices will improve patient safety and clinician efficiency during drug preparation, drug administration and tissue specimen preparation in the operating room. The scope of the project is the development of devices that utilize Codonics Smart Label Technology for anesthesia and pathology related perioperative applications. The devices will be manufactured, serviced and supported at Codonics facilities in Ohio.

Respectfully submitted,

Timothy E. Jakubisin
Director of Operations
Codonics, Inc.



VIA EMAIL: OTFBP2010@development.ohio.gov
SUBJECT LINE ON EMAIL: "2010 OTFBP LOI"

January 25, 2010

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43215

To whom it may concern:

This letter confirms that it is the intent of Austen BioInnovation Institute in Akron to partner in a collaborative effort with Orthopedic Research Laboratories, Inc., along with the other collaborators listed in this letter, for the purpose of a polymer commercialization project.

This is to also to provide notice that an application will be submitted for review under Ohio Third Frontier Biomedical Program from Austen BioInnovation Institute in Akron (ABIA) as described in the Project Summary attached hereto.

PROJECT TITLE: Ultimate Polymer Project

GRANT FUNDS TO BE REQUESTED:
Ohio Third Frontier Biomedical Program:

- (1) Third Frontier Research and Development Fund: \$1 million
- (2) Wright Capital Fund: \$2 million – ABAI is requesting funds from the Wright Capital Fund for the facilities and equipment to develop ultra high molecular weight polyethylene (UMMWPE) as a bearing surface principally in hip, knee, shoulder, spinal disc and ankle replacement implant systems. Significant commercial opportunity exists in improving its wear and other performance characteristics particular to joint replacement surgery. ABIA is collaborating with the University of Akron Polymer Science Center and Orthopaedic Research Laboratories, Inc., in the development of equipment for two centers of ABIA: MDDC (Medical Device Development Center) and CBMM (Center for Biomaterials and Medical), as well as for construction for Weiner-Landis lab, a University of Akron and Children's Hospital Medical Center collaboration.

LEAD APPLICANT:

AUSTEN BIOINNOVATION INSTITUTE IN AKRON (ABIA)

1 South Main St.

Suite 401

Akron, OH 44308

330-572-7544

Contact: Christine Dodd
Director of Resource Development
Email: cdodd@abiakron.org

Other Key Personnel: Aram Nerpouni, ABIA
Chief Administrative Officer
Austen BioInnovation Institute in Akron
anerpouni@abiakron.org

Jonathan F.I. Greenwald
Business Development Director
Orthopaedic Research Laboratories, Inc.
jon@olr-inc.com

Ali Dhinojwala
Professor, Polymer Science
Ali4@uakron.edu

Known Collaborators:

Orthopaedic Research Laboratories
Northeastern Ohio Universities Colleges of Medicine & Pharmacy (NEOUCOM)
University of Akron
Children's Hospital Medical Center of Akron
Akron General Medical Center
Summa Health System

Sincerely,



Frank Douglas, PhD, MD
President & CEO
Austen BioInnovation Institute in Akron

Enclosure: Project Summary

PROJECT SUMMARY
OHIO THIRD FRONTIER BIOMEDICAL PROGRAM
ULTIMATE POLYMER PROJECT

APPLICANTS: Austen BioInnovation Institute in Akron

The Ultimate Polymer Project seeks to improve the lifespan of joint replacement surgery through employing unique capabilities in polymer science that reside in the Austen BioInnovation Institute in Akron (ABIA). ABIA will collaborate with the Founding Partners and Orthopaedic Research Laboratories, an independent research lab in Cleveland with over 25 years experience in testing and optimizing orthopaedic implant design.

A focal point to innovate in orthopaedic surgery are efforts to extend the longevity of ultra high molecular weight polyethylene (UHMWPE) as a bearing surface principally in hip, knee, shoulder, spinal disc and ankle replacement implant systems. Orthopaedic use of UHMWPE has a decades-long history; however, it has been identified as the technological weak link in joint replacement surgery and a primary causative factor in necessitating costly, high risk revision surgery.

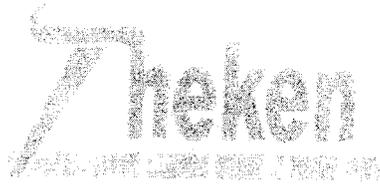
The state-of-the-art in UHMWPE for joint replacement is materials treated with radiation to enhance wear properties. While decreased wear has been demonstrated, so has degradation of certain other material properties including resilience to impact and accelerated breakdown from free radicals.

Alternatives to UHMWPE in joint replacement such as metal or ceramic bearing surfaces offer promise, but come with attendant drawbacks. Metal bearings are associated with high rates of patient sensitivity reactions and with increased cancer risk. Recently, ceramic bearings have revealed a high incidence of audible emissions, or "squeaking", that negatively impact patients' lives.

UHMWPE is the prevailing Gold Standard in orthopaedic surgery and significant commercial opportunity exists in improving its wear and other performance characteristics particular to joint replacement surgery. Worldwide, over 2 million joint replacement surgeries were conducted in 2008 and sales of orthopaedic devices from only the five largest orthopaedic implant manufacturers were in excess of USD 22.1 Billion. Source: American Academy of Orthopaedic Surgeons data & company annual reports.

The Ultimate Polymer Project endeavors to innovate and commercialize next generation material and process improvements leading to better performing, longer lasting joint replacements.

The long-term commercial objective is development of a manufacturing base for next generation polymers for orthopaedic application. Interim objectives include the licensing of material and process improvements to implant manufacturers.



Letter of Intent

Date: January 22, 2010

To: Ohio Department of Development
Ohio Third Frontier Biomedical Program 2010

Subject: 2010 OTFBP LOI

Submitted by:

Theken Spine LLC (dba Integra Spine)
1800 Triplett Blvd
Akron, Ohio 44306

Contact Person:

Richard Navarro, VP Corporate Development
rnavarro@thekenspine.com
330-475-8610

Proposed Title: Spine Implant – Fenestrated Pedicle Screw

Funds Requested: \$1MM

Collaborators: TBD

Summary of Project:

Introduction: Theken Spine, LLC, an Ohio limited liability company (“Theken”) is engaged in the design, manufacturing and sale of implantable titanium rods, pedicle screws, plates and related hardware for spinal fusion. Recently, Theken developed a titanium fenestrated pedicle screw with a partial central cannula (bore) and radial fenestrations (small holes). While currently approved for dye injection by the FDA, these passages allow injection of not only dye but also of bone cement to reinforce the porous bony structure of the vertebrae and directly augment fixation of the screw into low density or compromised bone.

We believe this innovative design will be the first such product approved in the US for use in conjunction with bone cement. The fenestrated screw is intended to expand spine fusion surgery to older osteopenic or osteoporotic patients with poor bone quality that is too weak to anchor conventional screws for the required 6-12 months that bony fusion



requires. This product could also be used in patients who currently are candidates for instrumented fusion to reduce the risk of screw loosening thereby improving overall outcomes. This product is intended to give spine surgeons a new option for improving outcomes and quality of life for an expanded patient population.

The US market for pedicle screws and associated hardware is in excess of \$1B annually. We anticipate that the fenestrated screw will increase the market size by availing more patients to instrumented spine fusion and expect Theken's sales to increase dramatically as a result of introducing this product to a growing demographic of patients over age 60.

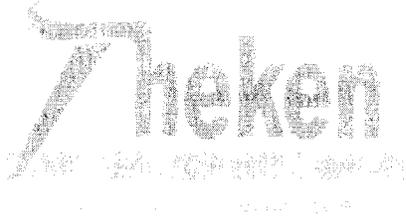
Need for Funds: Theken has nearly completed the investment in the design of the fenestrated screw and its integration with a cement delivery system. Mechanical and cadaveric testing have been conducted to demonstrate the biomechanical efficacy and increased fixation this product has to offer. Although both pedicle screws and bone cement are used currently to treat numerous spinal conditions, our initial 510k application for our fenestrated product in conjunction with bone cement was not granted by the FDA. While accepting all of our design and test information as substantial, the FDA is firm on requiring Theken to conduct a clinical trial to demonstrate the long term (likely 1 year) safety and efficacy of the fenestrated screw. The requirement for a clinical trial of a conventional class 2 spine fusion product is unexpected but due to the conservative viewpoint adopted by the FDA in recent times, not unusual. This product is a high priority, highly differentiated product that stands to be the "first to market" with this approved FDA indication. The proposed funds would definitely accelerate the plan to bring this product to market.

We are asking for \$1M in funds to finish pre clinical testing and support our clinical investigation. The details of the clinical trial and the corporate collaborators that will be engaged during the study are in the process of being determined.

Respectfully Submitted,

A handwritten signature in cursive script that reads 'Ric Navarro'.

Ric Navarro
VP Engineering & Business Development
Theken Spine LLC



Letter of Intent

Date: January 22, 2010

To: Ohio Department of Development
Ohio Third Frontier Biomedical Program 2010

Subject: 2010 OTFBP LOI

Submitted by:

Theken Spine LLC (dba Integra Spine)
1800 Triplett Blvd
Akron, Ohio 44306

Contact Person:

Richard Navarro, VP Corporate Development
rnavarro@thekenspine.com
330-475-8610

Proposed Title: Spine Implant – Compliant Cage

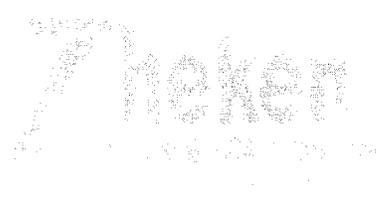
Funds Requested: \$1MM

Collaborators: TBD

Summary of Project:

Introduction: Theken Spine, LLC, an Ohio limited liability company (“Theken”) is engaged in design, manufacture and sale of spine implants. Theken has previously developed and successfully marketed several designs for spine Interbody Devices (IBDs), such devices are commonly referred to as “cages”. When a spinal disc collapses (stenosis) losing much of its normal function and causing pain, an interbody device (IBD) is often used to re-establish and maintain normal disc height as part of permanently immobilizing the segment through instrumented spine fusion. Heretofore, these spine fusion cages have been rigid, ie non-compliant, devices. Theken has designed and developed a new interbody cage device named the Compliant Cage.

This is an innovative product which we believe can become the first such product approved in the US. The product is nearly fully developed at this time and has passed all the interbody cage tests conventionally required by the FDA. This innovation in this design is to add a small amount of compliance through the incorporation of a polyurethane elastomer in to the construction. Adding compliance addresses several objectives not currently addressed by



conventional rigid interbody cages. It is well established that stress on a bone fracture can increase the rate of new bone growth and can increase the quality of bone at the fracture site. The Compliant Cage is designed to avoid stress shielding and promises to increase the rate and quality of the developing spine fusion. This would lead to faster recoveries, and could reduce the use of very costly bone morphogenic protein (BMP) to stimulate growth.

Need for Funds: Theken has already invested in the design and development of this product and is very satisfied with the results. This is a class 2 adjunct to fusion product and is of the same basic mechanical design and meets the same mechanical testing criteria as currently approved products. Further, the Compliant Cage is made from materials currently used in approved products.

We have been advised that this device will require Theken to conduct clinical trials prior to approval. This is a requirement for clinical trials for a conventional class 2 spine fusion product and represents FDA's more recent conservative approach to approvals. With these new costly and unexpected requirements, and in the current economic environment, Theken simply does not have sufficient funds to proceed to market with devices such as this at a pace that will guarantee a "first to market" advantage.

We are asking for the \$1MM in funds to complete in vitro testing and to support these clinical trials. The details of the clinical trials and with whom and with what institutions we will collaborate are in the process of being determined. It is likely that the \$1MM requested will cover most but not all the costs of the trials.

Respectfully Submitted,

Handwritten signature of Ric Navarro in cursive script.

Ric Navarro
VP Corporate Development and Engineering
Theken Spine LLC

Letter of Intent

Ohio Third Frontier Biomedical Program

Fiscal Year 2010 Proposal

Proposed Project Title

COMMERCIALIZATION OF AN ORTHOPAEDIC JOINT SIMULATOR

Lead Applicant

Orthopaedic Research Laboratories
2310 Superior Avenue East
Suite #100
Cleveland, OH 44114
Tel: 216-523-7004
Fax: 216-523-7005
President: A.Seth Greenwald, D.Phil.(Oxon)

Contact: Jon Greenwald
E-mail: jon@orl-inc.com
Website: www.orl-inc.com

Collaborators

Cleveland State University
Department of Mechanical Engineering
2121 Euclid Avenue, SH 247
Cleveland, OH 44115-2214

Contact: Majid Rashidi, Ph.D., P.E.
Distinguished Professor of Mechanical Engineering
Chairman, Engineering Technology Department
Cleveland State University
Website: <http://academic.csuohio.edu/rashidim/>

Estimated Grant Funds to be Requested

\$1M. from Third Frontier Research and Development Fund
\$1M. from Wright Capital Fund

Summary of Proposed Project

Seventy five million Americans annually visit a doctor for help with a musculoskeletal problem.¹ Of those patients, 1,107,200 underwent surgery to replace a hip, knee, shoulder, spinal disc or ankle with an artificial joint implant in 2008. Every one of these implant systems must undergo mechanical testing in a joint simulator as part of their development process and/or as a prerequisite for approval by the U.S. Food and Drug Administration (FDA).

This project seeks to commercialize a joint simulator developed in Ohio that enables significant cost and other advantages in testing implant systems. The joint simulator is presently known as the electromechanical joint simulator, or *EMJS*, and was developed at Orthopaedic Research Laboratories (ORL) of Cleveland under the direction of A.Seth Greenwald, D.Phil.(Oxon) and in conjunction with Majid Rashidi, Ph.D., P.E. of Cleveland State University. ORL is an independent research lab with over 25 years experience testing and optimizing orthopaedic implant systems.

Originally designed to test spinal disc replacement systems, the EMJS has been optimized to test other joints and represents a technology presently in transition from the incubating to demonstrating phase of the Third Frontier Technology Commercialization Framework. The technology has been reduced to practice and intellectual property protection received through award of various patents. Internal proof of concept has been demonstrated through use of the EMJS by ORL to conduct testing in support of multiple successful spinal disc and ankle replacement product submissions to the FDA.

Key project objectives include continued optimization of the EMJS to expand its' application to other joints and enable its' use by outside customers including orthopaedic implant manufacturers and university and private testing labs.

The project also endeavors to establish a manufacturing premises and infrastructure as well as sales, service and marketing functions to support EMJS commercialization.

The EMJS represents paradigm shifting innovation that supplants presently available testing apparatus with high manufacture and acquisition costs as well as complex service and infrastructure demands. The EMJS runs off of a standard 110 volt outlet and features a modular design that enables simple, customizable service and modification as well as performance advantages over alternative systems. Additionally, it can be manufactured at a cost point conducive to a highly competitive pricing model and export to developing markets such as China and India with early stage, rapid growth orthopaedic research, development and manufacturing capabilities.

¹ Healthcare Database Whitepaper, Regional Differences in Healthcare Charges; Pearl Diver Patient Records Database, June 30, 2009.

Cardiox Corporation

4140 Tuller Road, Suite 104
Dublin, Ohio 43017

(614) 791-8118
Fax (614) 791-8221

January 25, 2010

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, Ohio 43215

Subject: 2010 OTFBP LOI

Dear Sir or Madam:

This Letter of Intent is being provided in response to the requirements set forth in Ohio Department of Development's Request for Proposal (RFP) entitled "Ohio Third Frontier Biomedical Program" for Fiscal Year 2010. As specified in paragraph 1.3.3 of the referenced RFP, we are pleased to provide the following requested information.

1. **Lead Applicant:** Cardiox Corporation
4140 Tuller Road, Suite 104
Dublin, Ohio 43017
2. **Phone Number:** 614-791-8118
3. **Contact Person:** Philip E. Eggers, Chief Executive Officer
4. **Contact Person Email Address:** philipeggers@cardioxcorp.com
5. **Title:** Validation and Commercialization of System for Non-Invasive Detection of Right-to-Left Shunts
6. **Estimated Grant Funds to be Requested:** \$1,000,000
7. **Planned Collaborators:** Cleveland Clinic (clinical trial site), QTest Laboratories (pre-clinical evaluation site).
8. **Summary of Proposed Project:**

Stroke represents one of the most significant health problems in the world with 20 million stroke events occurring annually and accounting for 5.7 million deaths. Each year in the U.S. alone, over 780,000 patients suffer strokes with 250,000 deaths related to stroke. An estimated one-third of strokes are attributable to the presence of an undetected congenital right-to-left shunt in the heart. Hence, nearly one-third of strokes could be prevented if the presence of a right-to-left shunt could be detected and closed using recently developed minimally invasive closure methods. The most common type of right-to-left shunt is the Patent Foramen Ovale or PFO. Multiple post-mortem studies have confirmed that over 20% of the general population has a PFO and 7% of the general population has a large PFO. Clinical trials performed in the European Union and the U.S. in recent years have confirmed the significantly higher risk of stroke associated with the presence of a PFO.

Existing methods for the diagnostic confirmation of the presence of a right-to-left cardiac shunt require highly specialized training and expensive equipment. The "gold standard" Transesophageal Echocardiography method must be performed in the catheterization laboratory of a hospital or clinic. However, the false negative rate for even this method can range from 9 to over 30% depending on the cardiologist performing the test.

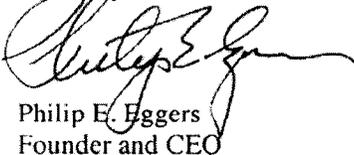
In order to address the need for diagnostic screening and post-closure follow-up, Cardiox has developed proprietary technology which enables a highly sensitive, low-cost shunt diagnostic test to be performed non-invasively in an office setting by a nurse or physician in about 10 minutes. Unlike all existing methods which require the injection of a physician-prepared air bubble/isotonic saline mixture for shunt detection, Cardiox product uses an FDA approved indicator which its proprietary technology can detect transcutaneously at extremely low concentrations in the blood stream. All cardiac/shunt detection methods, including Cardiox' method, require that an indicator being injected into a peripheral vein such that some portion can be detected if it passes from the right side to the left side of the heart without passing through the lungs (i.e., that fraction of indicator which passes through a cardiac shunt). In order to perform a cardiac shunt test, the subject must perform a 5 to 10 second long exhalation procedure know as the Valsalva maneuver. This procedure creates, upon the release of exhalation pressure, the positive right-to-left atrial pressure gradient necessary to induce blood-borne indicator to pass through any clinically significant cardiac shunt that might be present.

Cardiox proprietary method and system has solved a number of the problems which currently limit the sensitivity as well as the ease of use of all existing methods. In particular, one of the principal limitations that limits the sensitivity of all existing methods is selecting the timing of the venous injection of the indicator so that it arrives in the right atrium during the 3 to 4 second window of time that the favorable pressure gradient is present. This favorable gradient is necessary to allow passage of the indicator through the "hole" in the heart and into the arterial circulation. The proposed project will validate Cardiox method and system for determining the optimum indicator injection protocol necessary to assure a high sensitivity level and to allow its broad adoption for diagnostic use. This optimized indicator injection protocol will be fully automated to assure that each shunt detection test is performed in a standardized and highly controlled manner. The requested funding will be used to perform both pre-clinical animal studies and clinical trials to confirm the sensitivity of its method including Cardiox capability to quantify the conductance of the shunt. Cardiox validation studies will include the use of precordial Doppler methods to ultrasonically verify the timing of the arrival of its indicator in the right atrium of the heart. Cardiox development of its optimized injection protocol will then enable the commercial release of its product and ramp-up to large-scale production of its monitor unit and disposable set.

* * * * *

Please contact me if you have any questions.

Sincerely,



Philip E. Eggers
Founder and CEO

PEE:jk

cc: 2010 OTFBP File

Sent via email to OTFBP2010@development.ohio.gov on January 25, 2010 at 1:40 pm (EST)

OTFBP 10-867

January 25, 2010

Dear Ohio Department of Development,

Please accept this Letter of Intent from University Hospitals of Cleveland for our 2010 Third Frontier Biomedical Program proposal.

Lead Applicant: University Hospitals of Cleveland
Address: 11100 Euclid Avenue
Lakeside 1400; Mail Stop LKS 7061
Cleveland, Ohio 44106
Telephone: (216) 844-5577
Contact Name: William Fisher
Contact Email Address: William.Fisher@UHhospitals.org

Project Title: Orifice Pressure Sensing Device

Estimated Grant Funds Requested: \$1,000,000.00

Collaborators: NA

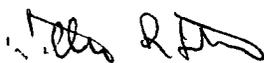
Summary of Proposed Project

Cauda Equina Syndrome (CES) is a condition that results in emergency medical surgery involving severe neural compression of the lumbar or lumbosacral spine. Anyone who visits the emergency room complaining of back pain should be tested for this condition within 48 hours of the incident. Failure to diagnosis and treat can result in permanent loss of Urinary retention, bowel and bladder incontinence, perineal sensory loss, bilateral leg pain, weakness, numbness, and sexual dysfunction. Problems with the techniques used for current diagnosis include:

- Current tests are subjective
- Attending physician and patient discomfort with rectal exams
- Expensive MRI's are often ordered to avoid potential lawsuits (often not necessary, adds significant cost)
- Failure to properly diagnose puts the hospital at risk for significant liability

University Hospitals of Cleveland has developed a proprietary, low cost solution that quantitatively addresses these unmet needs of the physician and emergency room practitioners.

Sincerely,



William Fisher

OTFBP 10-868

January 25th, 2010

Ohio Third Frontier 2010 Biomedical Program Request for Proposals (RFP):
LETTER OF INTENTION

Prospective Lead Applicant's name:
OHIO STATE UNIVERSITY

Address:
473 W. 12th Avenue, Columbus, OH, 43210

Phone number,
614-247-801

Contact person:
NICANOR I. MOLDOVAN, PhD

Email address for the contact:
nicanor.moldovan@osumc.edu

Proposed Project title:
**CellTrap: NOVEL TECHNOLOGY AND DEVICE FOR DETECTING CARDIOVASCULAR
STEM CELLS**

Estimated Grant Funds to be requested:
\$1,200,000

Known Collaborators (in alphabetical order):
APPLIED BIOMOLECULAR TECHNOLOGIES, Inc.
COLUMBUS NANOWORKS, Inc.
DEPARTMENT OF CHEMICAL AND BIOMOLECULAR ENGINEERING, OSU
NANOFIBER SOLUTIONS, Inc.

Summary of the proposed Project.

This proposal is responsive to the Ohio Third Frontier 2010 Biomedical Program Request for Proposals (RFP) in the area “*Development and commercialization of new devices, therapeutics, or diagnostics that can improve delivery or patient outcomes of biomedical technology, or address technical commercialization barriers*”. The focus of our proposal is at the crossroads of *cardiovascular and regenerative medicine*. The result of this activity will be the market-oriented development of a new solid phase assay for cardiovascular stem/progenitor cells. We propose to validate and commercialize a novel device (called ‘**CellTrap**’) for detecting these cells in blood or other cell suspensions, for diagnostic and cell therapy purposes. Our new assay and the accompanying kit aims at a faster, less expensive and more reliable detection of these essential, yet elusive cell populations, which are key for the maintenance of normal vascular function and for organ recovery after injury. Based on an original understanding of progenitor cells biology, we are currently developing a proprietary technology which encompasses protein chemistry, magnetic particle nanotechnology, and biomaterials science. Moreover, assessment of the quality of preparations for cell therapy, as well as their concentrations in peripheral blood of patients after administration, could substantially benefit from this new tool. The assay also could assist the physician in evaluating the wound healing capacity of subjects stratified by lifestyle-related cardiovascular risk factors (smoking, obesity, etc). Furthermore, the cells collected by our method could be directly incorporated into vascular grafts and in other tissue engineering applications. Therefore, the market need for this product is very large. The PI has a synergic background in biophysics, cell biology of vascular wall and cardiovascular translational applications, and leads another major NIH grant in the field of stem/progenitor cells used for tissue engineering. He partnered for the basic science component of CellTrap assay with renowned scientists from the Departments of Chemical and Biomolecular Engineering and Materials Science at OSU. This technology recently won a very competitive RC2/Grand Opportunities ‘stimulus’ award from NIH, covering in large part the research and clinical validation, but not the distribution and business-related phase. For this further product development and commercialization effort, we now enlist the participation of three for-profit Ohio-Based companies: *Columbus Nanoworks* for production of magnetic nanobeads, *Nanofiber Solutions* as supplier of custom-designed assay plates, and *Applied Biomolecular Technologies* for preparing the assay for commercialization. This product development activity will be carried out in three major areas: a) magnetic cell collection; b) scaffold-assisted cell proliferation; and c) advanced colony analysis. A computer modeling approach is also being implemented, in support of the direct experimentation. All these areas will be built on our own or our collaborators proprietary technologies. We anticipate that during completion of the program a new dedicated business will be formed, to integrate the practical aspects of kit production and assay application, and to prepare it for the market. This award would help us to move the manufacturing processes of our biomedical assay and device to a point in the commercialization process where we will be ready to seek regulatory approval. Since there will be no other invasive procedures except blood drawing, we anticipate that at the end of project period, the product will be ready for FDA exemption for commercialization. Thus, this biomedical technology enterprise is very likely to result in significant employment in Ohio within 3 to 5 years of completing the project.

LETTER OF INTENT

Lead Applicant Name	Cleveland Clinic Spine Research Laboratory
Address	1730 West 25 th Street / Luth 2C Cleveland, OH 44113
Phone Number	216/312-9558
Contact Person	Lars G. Gilbertson, PhD
Contact Email Address	GILBERL2@CCF.ORG
Project Title	OPTIMAL DESIGN FOOTBALL HELMET
Estimated Request	\$750,000
Known Collaborators	University of Toledo, Toledo, OH Case Western Reserve University, Cleveland, OH <i>For-profit company Collaborator(s): TBD</i>

PROJECT SUMMARY

Much recent media attention has focused on the “epidemic” of concussion injuries to football players at professional, collegiate, and high school levels. Concussion presents acute and long-term consequences to the athlete, and there is a growing list of high-profile athletes whose careers have ended prematurely due to the effects of concussion. Advances in the materials sciences suggest that football helmet design can be optimized to minimize concussion risk.

On the other hand, neck injuries are of simultaneous concern—again, with many well-known examples of high-profile athletes whose careers have ended due to catastrophic neck injuries and paraplegia. A major concern is that helmets optimized against concussion injury may not optimally protect the athlete against neck injury (due to “competing design criteria” requiring prioritization of the protection).

The proposed project will utilize a multi-objective design strategy to develop a football helmet that offers simultaneous optimization against both head and neck injury. The helmet will be designed and initially evaluated on a computational simulation platform, with the best design advancing to prototyping stage. The resulting prototypes will be experimentally tested under realistic impact scenarios (e.g., helmet-to-helmet contact) to obtain measurements of both head impact forces and neck loads for comparison with existing helmets—demonstrating functionality and supporting market entry.

Successful completion of this project will result in a commercialized football helmet that offers simultaneous protection against both head and neck injury. It is anticipated that the resulting product will have great clinical and societal significance in reducing the incidence and severity of head and neck injuries in football.

OTFBP 10-870

Third Frontier Letter Of Intent

Submitted by:

Explorys, Inc
11490 Euclid Avenue
Cleveland, OH 44106
216-647-0013
Att. Stephen McHale
Stephen.mchale@explorysmedical.com

Project Title: Research Discovery System
Estimated funding request: \$1,000,000
Collaborator: Cleveland Clinic

Summary

Explorys formed in partnership with the Cleveland Clinic Foundation has developed a system that aggregates clinical, EHR, biomedical and lab data from a network of health care providers enabling high speed search engine interrogation to identify opportunities for clinical studies and drug development. The Explorys solution is unique in its ability to increase the quantity and quality of research, while accelerating discovery and driving millions out of the cost of traditionally encumbered processes. In some cases we are able to reduce pre project viability evaluation time by 95%. Traditional systems take weeks to identify the appropriate study cohort group while Explorys can do it in seconds. This translates into significant cost savings in the pre-study process. Additionally the researcher can very quickly determine if an opportunity is valid allowing them to re-direct their efforts on more qualified studies if it is not.

Explorys is a foundational solution which provides underlying support for the Third Frontier objectives:

State of Ohio initiative is catalyzing the growth of existing and emerging industry clusters by:

- Increasing the quantity of high-quality research that has commercial relevance to Ohio companies; ***Explorys accelerates research project viability assessment.***
- Growing and nurturing an increasingly experienced pool of entrepreneurial management talent; ***Our leadership has created over 1400 jobs and developed numerous entrepreneurs and leaders.***
- Addressing the technical needs of existing companies pursuing new products and production processes; ***The Explorys Population Intelligence module provides a key technology in new product identification and development***
- Contributing to the expansion of a technologically proficient workforce; ***Explorys provides breakthrough technology contributing to the skills development and re-training of Ohio's workforce.***
- To help Ohio companies achieve safety and efficacy standards that ultimately help end-users of biomedical technologies define as necessary for successful commercial applications; ***The Explorys solution can provide pharmacovigilance during both during trail and post market launch periods.***

Explorys accelerates collaboration between stakeholders in healthcare by providing a network that bridges the gap between researchers, life sciences, and those delivering care. By organizing clinical data across millions of patients, clinic visits, and outcomes, Explorys is able to extend the power of real-time search and comparative research collaboration to the desktop of virtually anyone involved in research and the advancement of healthcare.

This ubiquitous, yet HIPAA compliant / privacy protected, access to aggregated and analytics enabled healthcare data allows subscribers and partners of the network to identify correlations between patients, diseases, treatments, and outcomes. In turn, these discoveries drive innovation and identify opportunities to reduce costs.

The Explorys leadership team brings with it a proven track record of building successful companies that have deployed some of the world's largest and most scalable data management and security solutions.

Please see www.explorysmedical.com for more information.

CARDIOSTAR INC.

January 25, 2010

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43215

Dear Ohio Department of Development,

Please accept this letter as the indication of our intent to submit a proposal to the Ohio Third Frontier Biomedical Program for the fiscal year 2010.

Lead Applicant: CardioStar Inc.
7772 Metric Drive
Mentor, OH 44060
(440) 255-1155

Contact: Tom Pavsek
tpavsek@frantzgroup.com

Project Title Personal Cardiovascular Non-Invasive Hemodynamic Monitor

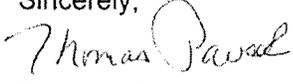
Funds Requested \$1,000,000.00

Known Collaborators Frantz Medical Development, Ltd.
7740 Metric Drive
Mentor, OH 44060
Contact: Mark G. Frantz, President & CEO

The Cleveland Clinic Foundation
Cardiovascular Medicine
Contact: Marc Penn, M.D., Ph.D.

Louis Stokes VA Medical Center
General Surgery
Cleveland, OH
Contact: Melanie Lynch, M.D.

A summary of the product technology and proposal is provided on the next pages.

Sincerely,

Thomas Pavsek
Product Manager

CARDIOSTAR INC.

Project Summary – CardioStar is developing an innovative product pipeline of non-invasive hemodynamic monitoring systems to improve diagnosis and treatment of cardiovascular disease. With seed funding through a grant from the Global Cardiovascular Innovation Center (GCIC), CardioStar has successfully completed the design and prototyping of a non-invasive blood pressure monitoring system that can be easily integrated into the clinician's current practices. This Project will translate the prototype into a commercial product, including completing formal product development per FDA and ISO requirements, partnering with a leading patient vital sign marketer / distributor such as Phillips, and initiating the next development programs. CardioStar has mapped a clear product pipeline, from the hospital to personal home use, which will provide future company growth, translating to economic growth and new jobs for the State of Ohio.

The Company – Formed in 2009, CardioStar Inc. is a joint equity start-up company between an Ohio-based company, Frantz Medical Development Ltd. (FMD) and a Japanese medical device company, X-Cardio, KK. CardioStar's mission is to improve the field of diagnosis and treatment support of cardiovascular disease by providing innovative, non-invasive solutions to beat-to-beat hemodynamic monitoring. In 2009, CardioStar received seed funding through Cleveland Clinic's Global Cardiovascular Innovation Center (GCIC), funded through the Ohio Third Frontier initiative. Its collaboration with Cleveland Clinic and the Louis Stokes VA Center ensures that our Personal Cardiovascular Monitor ("PCM") will meet clinical requirements yet integrate easily into the clinical routine. In addition, these clinical collaborators will be essential in the product's commercialization, penetration and success. As CardioStar is nearing the successful completion of the first year's objectives, it has mapped the product commercialization process and product pipeline that will bring the first product to market in 2011, establish its manufacturing and product sales, and initiate development of next generation products.

The Product Platform - CardioStar is developing the first and only "PCM" – Personal Cardiovascular Monitor – that will be worn at all times on the subject wrist, ultimately as a wrist watch. By an innovative tonometric applanation method, combined with a built-in calibration method, the wrist device provides a non-invasive equivalent to the invasive Arterial-Line. The self calibrating Beat-to-beat Blood Pressure (BP) monitor will store the data and transmit to a server where further analysis will provide needed Cardiovascular parameters like continuous Cardiac Output, relative continuous Ejection fraction, continuous Central BP, continuous peripheral resistance, arterial stiffness, PWV, Endothelial function evaluation, etc.

The Need - Cardiovascular diseases are the No. 1 killer and approximately 1 billion people worldwide are suffering from Hypertension. Estimated at more than \$420 billion, cardiovascular medicine is the largest healthcare market opportunity in the US. The cardiovascular disease burden poses clear medical, scientific, and commercial challenges. CardioStar's partnership with Cleveland Clinic and the Louis Stokes VA Center will facilitate the development and adoption of the Personal Cardiovascular Monitor ("PCM") which is geared towards improving patient care and treatment efficiency. Millions of patients, as well as HMO and Pharmaceutical companies, will benefit from the progress made through this PCM by continuous monitoring, early detection and treatment support of the needed cardiovascular parameters in the hospital and in everyday life.

The Market - Continuous BP Monitoring and extracting Cardiovascular parameters like Cardiac Output, Central BP, etc are associated today with critical condition patients in the OR and ICU. This is because true Beat-to-Beat BP monitoring is done today only invasively, using arterial lines that pose high risks to the patients and high cost to the hospitals. Under this cost-

CARDIOSTAR INC.

effectiveness limitation, doctors settle for the unsatisfactory but inexpensive solution of non-invasive measuring of peripheral Systolic and Diastolic BP once in a while. The existing market consists of 20 million BP monitors annually, with an average cost of about \$100 each. Providing a PCM for the same price range will pave the way to replacing these unsatisfactory devices with the much needed cardiovascular parameters at all times. It is expected that besides replacing the existing devices it will create a much bigger demand, similar to what happened with Oximetry.

CardioStar believes that this new form of Non-Invasive Blood Pressure Monitoring that also provides beat-to-beat, pulse shape and cardiac parameters information in a very affordable price will change the concept of BP and cardiovascular assessment and monitoring, as well as treatment. A number of major medical device companies have expressed a strong interest in selling CardioStar products, further validating this commercial opportunity.



NOTTINGHAM • SPIRK

January 25, 2010

Dear Ohio Department of Development,

Please accept this Letter of Intent from Nottingham-Spirk for our 2010 Third Frontier Biomedical Program proposal.

Lead Applicant Name: Nottingham-Spirk
Address: 2200 Overlook Road
Cleveland, Ohio 44106
Telephone: (216) 231-7830
Contact Person: Robert Hartley
Contact Email Address: bhartley@ns-design.com

Project Title: PSM (Personal Status Monitor)

Estimated Grant Funds Requested: \$1,000,000.00

Collaborators: Blue Highway, LLC, and others to be determined

Summary of Proposed Project

Nottingham-Spirk is a premier design, engineering and testing facility located in Cleveland, Ohio. Nottingham-Spirk was founded in 1972 and is one of the most complete, vertically-integrated product development centers in the U.S., combining product invention, design, engineering, quality assurance and global sourcing of manufacturing.

Nottingham-Spirk has a partner in this wireless patient monitoring technology field that will allow patients' daily health to be monitored remotely by clinicians. This technology platform, known as PSM (Personal Status Monitor), has the potential to reduce hospital re-admissions and unnecessary office visits by providing physicians with more proactive, timely status about the health of their patients at risk.

PSM devices can also provide the following game changing benefits for healthcare:

- Proactively monitor chronic diseases
 - 80% of all US health care spending due to top five chronic diseases
- Proactively monitor commonly seen conditions with the aging population such as:
 - Hypertension (48%)
 - All types of heart disease (32%)
 - Diabetes (16%)



NOTTINGHAM • SPIRK

- Reduce deaths due to medical errors
 - Estimated 44,000-98,000 deaths annually due to medical errors
 - Healthcare costs range from \$17 billion to \$29 billion per year

Sincerely,

Robert W. Hartley

Hansen, Andrew

From: ms_johnson@matsceng.ohio-state.edu on behalf of Jed Johnson
[ms_johnson@matsceng.ohio-state.edu]
Sent: Monday, January 25, 2010 2:01 PM
To: OTFBP2010
Attachments: TFP Summary.docx

Nanofibers Solutions is extending this Letter of Intent to apply for the Third Frontier - Biomedical Program 2010. Our information is blow and attached.

Lead Applicant: Nanofiber Solutions, Ilc

Contact: Ross Kayuha, CEO
1275 Kinnear Road
Columbus, OH 43212
614-975-6646

Project Title: Terahertz Cell Impact Using Aligned and Nonaligned Nanofiber Scaffolds

Est Grant Funds: \$500,000

Collaborators: Dr. Gerald J. Wilmink
711th HPW/RHDR
USAF

Summary of the Proposed Project attached.

Ross Kayuha | CEO | Nanofiber Solutions | 1275 Kinnear Road | Columbus, OH 43212 | **614.975.6646**
Realistic 3-D Ex Vivo Cancer Tools | www.nanofibersolutions.com

SUMMARY

Terahertz imaging is showing a lot of potential to image cells within the human body and distinguish between cancerous and non-cancerous cells. However, safety limits of exposure are largely unknown and current limits are based on extrapolations from current radiation exposures from other sources. More experimental research is needed to determine the effects of terahertz radiation and establish safety limits before this technology can be broadly used.

Gliomas are the most aggressive and least successfully treated brain tumors because of their distinctive ability to infiltrate surrounding brain tissue. Even if the bulk of the tumor is removed, migratory cells left behind are not detected by the immune system and resist current cytotoxic therapies. Tumor recurrence then typically involves a rapid and deadly outcome. Understanding the mechanisms of glioma cell migration and designing novel targeting strategies are major challenges in devising more successful therapies against these tumors. We will expose glioma cells and other non-cancerous cells to terahertz radiation and begin to establish safety and efficacy limits.

Using a highly collaborative, multidisciplinary approach, we will investigate microenvironmental and topographic cues that direct glioma migration on biocompatible nanofibers designed to mimic the substrate topography within the brain. Our specific aims are: 1) optimize a high-throughput *in vitro* migration assay using electrospun fiber mimicking nanoscale neural tissue topography to determine the potential of this model as a predictive bioassay of motility in *ex vivo* clinical glioma samples; 2) utilize the high-throughput assay to explore mechanisms that direct migration of clinical glioma cells and molecular factors regulating motility; and 3) assay anti-migratory strategies against cell dispersion to determine the potential of this model as a predictive bioassay of motility in clinical glioma samples. To pursue these aims we will 1) produce high-throughput multi-well cell culture plates with aligned, electrospun nanofiber on the bottom to mimic the aligned structure of white matter, 2) analyze glioma cell migration and characterize the cellular/molecular changes that occur on nanofibers presenting different topographies, 3) investigate potential molecular targets and anti-migratory chemotherapeutics against glioma migration on these devices, and 4) analyze the migration of *ex vivo* tumor cells and test anti-migratory strategies on those samples to determine the potential of the nanofiber model as a **predictive bioassay with immediate clinical relevance.**

Letter of Intent

Request for Proposal for Ohio Third Frontier/Biomedical Program

Project Title: Cystotrainer Instructional Device

Lead Applicant: OhioHealth
3525 Olentangy River Road
Suite 4300
Columbus, OH 43214-3907
(614) 566-2063

Contact Name: Ben Stobbe
E-mail address: bstobbe@ohiohealth.com

Estimated Grant Funds Requested: \$1,000,000.00

Collaborators: Nottingham-Spirk
2200 Overlook Rd
Cleveland, Ohio 44106
216-231-7830

Proposed Project Summary

OhioHealth's unique training technology, Cystotrainer Instructional Device, will allow advanced procedures to be taught using female cystoscopy at the CME+I (Center for Medical Education and Innovation). Urogynecologic procedures such as basic cystoscopy, bladder/ureteral stone removal, and ureter stenting are primary techniques for training with this potentially patentable device. The training opportunities and procedural skills built around utilization of this device will benefit the education and competency of OhioHealth healthcare professionals as well as local/regional and anticipated national/ international physicians and hospital systems recognizing a need for this training in their systems.

Collaboration with Nottingham-Spirk will enable the CME+I to reach out to clinicians throughout the state of Ohio for beta product validity testing. Additionally, the collaborative will allow for the development of the device. The ultimate goal is to build a device and market inexpensive cystoscopy training.

The Cystotrainer training device will allow:

- Physicians/educators to educate on these techniques using larger audiences, directing a cost- and time-saving benefit compared to the current standard of care
- Opportunity for safe training practice using actual equipment without undue patient harm
- Review of the anatomy of the urogynecologic anatomy
- Utilization of the CME+I to train and observe live surgery through videoconferencing capabilities
- Technology development that could be licensed or marketed through medical training device companies
- Manufactured in Ohio



CASE WESTERN RESERVE
UNIVERSITY
SCHOOL OF MEDICINE

OTFBP 10-875



James E. Dennis, Ph.D.
Assistant Professor
Department of Orthopaedics
Case Western Reserve University
6th Floor Hanna
11100 Euclid Avenue
Cleveland, Ohio 44106

January 22, 2010

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43215

This is my Letter of Intent indicating that I will be submitting a proposal to the Ohio Third Frontier Biomedical Program that is due March 1, 2010. The following is the pertinent information requested in the RFP, including a 1 page summary of the overall research plan in a separate attachment.

Proposal Title: Bioengineering a Cartilage-Tantalum-Bone Interface for Articular Cartilage Repair

Lead Investigator: James E. Dennis (Address, e-mail and phone number above and below)

Contact Person: Phyllis Lie, Administrator; Dept. of Orthopaedics; 6th Floor Hanna, 11100 Euclid Ave., Cleveland, OH 44106; e-mail: pxl3@case.edu; (216)844-3232.

Collaborator: Zimmer, Inc.

Estimated Funds Requested: \$ 700,000 over 3 years including indirect costs.

Sincerely,

James E. Dennis, Ph.D.
Assistant Professor

Title: Bioengineering a Cartilage-Tantalum-Bone Interface for Articular Cartilage Repair
Principal Investigator: Dennis, James E.

While total joint implants have been quite successful for major joint repairs, there remain challenges to improve upon past successes and to develop additional applications for more difficult joints. One approach is to combine tissue engineering of cartilage with implant technology. The goal of this study is to produce a functional bi-phasic joint replacement using Tantalum Trabecular Metal (TTM) combined with human chondrocytes and/or Mesenchymal Stem Cells (MSCs). By combining our tissue engineering capabilities of fabricating cartilage sheets along with implantable TTM, it may be possible to produce a functional joint from a patient's own cells.

HYPOTHESIS and AIMS:

The biomechanical properties Tantalum Trabecular Metal (TTM) make it a very attractive scaffold for the fabrication of a new composite material containing both cartilage and bone forming cells for the repair of articular surfaces. This laboratory has been investigating the use of human chondrocytes and mesenchymal stem cells (MSCs) for the fabrication of large cartilage sheets for tissue engineering, and has applied this technology to other tissue engineering applications, such as the repair of large trachea segments. *It is hypothesized that the combination of this cartilage sheet technology with TTM will allow for the production of a fully functional bi-phasic joint replacement construct.* To address this hypothesis, the following aims are proposed:

Aim 1A: MSC integration into TTM Constructs: MSCs will be applied to TTM constructs either from the top or as a dense layer on the bottom and then assessed for in vivo bone formation in a SCID/NOD model.

Aim 1B: Cartilage sheet/MSC/TTM composite testing: MSCs and cartilage sheets from human chondrocytes will be combined and tested for integration in vivo. Using the optimal MSC method from Aim 1A, MSCs will be seeded into TTM disks, covered or placed on top of cartilage sheets, cultured for up to three weeks and implanted into SCID-17 mice for 6 weeks. At harvest, samples are assessed for integration and biomechanical strength both under compressive load, to measure ability to bear weight, and under shear loads, to measure integration with the TTM.

Aim 2: Development of Shaped Cartilage-TTM Constructs: TTM fabricated into the shape of a rabbit humerus will be combined with cartilage sheets and MSCs in an agarose mold system that conforms to the joint geometry. Constructs will then be tested in the SCID-17 model for integration and structural characteristics and then in a rabbit shoulder repair model.

The results from these studies will test the feasibility of using human chondrocytes and MSCs in combination with TTM to produce a composite joint replacement material that has the advantages of the strength and durability of TTM along with the biomechanical properties of living functional hyaline cartilage. If successful, this study will lead to experimentation in a pivotal study in a large animal model (pig) as a prelude to an FDA trial.

FRANTZ * MEDICAL

Frantz Medical Manufacturing / Frantz Medical Development Ltd.
7740 Metric Drive, Mentor, Ohio 44060 / Tel: (440) 255-1155 / Fax: (440) 255-6975

January 25, 2010

Dear Ohio Department of Development,

Please accept this Letter of Intent from Ohio Health for our 2010 Third Frontier Biomedical Program proposal.

Lead Applicant Name: Frantz Medical Development Ltd.

Address: 7740 Metric Drive
Mentor, OH 44060

Telephone: 440 255-4514

Contact Person: Jennifer Innamorato

Contact Email Address: jinnamorato@frantzgroup.com

Project Title: Portable Handheld Electrical Treatment Wart Treatment Device

Estimated Grant Funds Requested: \$1,000,000

Collaborators: Nottingham-Spirk Contact: Craig Sanders
ML Treatments, LLC Contact: Lawrence Sears
University Hospitals Contact: Dr. Elma Baron

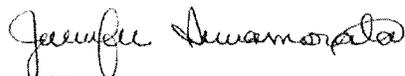
Summary of Proposed Project

There currently lacks an **effective** Plantar wart treatment that does **not require local anesthesia** and has **no morbidity** following treatment. Furthermore, there is no treatment available of this type that is designed for easy portability and use, ideal for consumer and military field applications.

Frantz Medical Development has identified a potential electrical treatment method and device that solves this problem. This invention is a small, handheld, battery operated device that utilizes a high frequency electrical current to eliminate warts, including Plantar warts using the electrosurgery principle of fulguration. This device also includes an integrated miniature filtration system that would reduce smoke and capture particles.

A prototype of the proposed device has been constructed. The funds from this grant would be used to design a next generation device with functional and ergonomic requirements, perform a clinical study to support improved effectiveness with reduced morbidity over current commonly used treatments, and to bring the device through FDA regulatory clearance, into commercialization with a consumer-expert, Nottingham Spirk.

Sincerely,



Jennifer Innamorato
Senior Engineer

MindChild Medical, Inc.
1600 Osgood Street
Suite 2-17
N. Andover, MA 01845
T: 978.975.1160
www.mindchild.com

OTFBP 10-877

1.25.2010

Letter of Intent

This Letter of Intent is in regards to the Third Frontier Biomedical Program (BMP). As the lead applicant, MindChild Medical is excited to submit our proposal by March 1st, 2010. Below is our formal address along with pertinent contact information. If awarded, MindChild Medical will establish a local presence in Northeast Ohio and eventually manufacture components in Ohio.

MindChild Medical, Inc.
1600 Osgood Street Suite 2-17
North Andover, MA 01845
978-975-1160

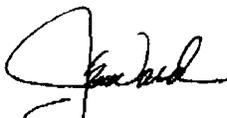
Contact: Jay Ward, Executive Vice President
Email: jay.ward@mindchild.com

Our Project title is Non-invasive Observation of Natal Activity (NONA), which we will be requesting an estimated 1 million dollars in grant funding. We are pleased to include the following Ohio companies as our known collaborators.

1. Orbital Research, Inc. - Cleveland-based research organization with sensor technology
2. Alpha Tool & Mold Incorporated - Cleveland-based manufacturer of medical grade plastic
3. Southworth & Associates - Cleveland-based medical device regulatory affair and compliance consultants
4. Cleveland Clinic Foundation - Top medical facility and research hospital
5. IFW Consulting, FPC - Flat Wire - Mechatronics - representing Freudenberg NOK Mechatronics, consultants for wire management based in Warren, Ohio

I look forward to participating in this exciting opportunity.

Sincerely,



Jay Ward
Executive Vice President
MindChild Medical, Inc.

Project Summary

Non-invasive Observation of Natal Activity (NONA)

The vision for the Non-invasive Observation of Natal Activity system is to develop a non-invasive fetal ECG monitor that will make pregnancy and labor safer for women and their newborns. We will complete development of this monitor and build a garment populated with sensors that the expectant mother can wear on her abdomen during fetal ECG monitoring. Leveraging ongoing research by our collaborative team, we will reduce the cesarean delivery rate and reduce newborn neurologic injury by identifying ECG patterns caused by inflammatory, hypoxic or ischemic insults.

The overall project goal is the development and commercialization of the Non-invasive Observation of Natal Activity (NONA) system. MindChild Medical intends to join its partner, Orbital Research, in Ohio, developing clinical, research, and manufacturing capacity along with a sales force to capitalize on this market need. The NONA system is envisioned to be used in the physician's office during prenatal outpatient check-ups and in all delivery rooms during labor. This NONA system will also allow advanced assessment of the FEECG waveform characteristics, at the level customary to cardiologists, which will mitigate risk to the fetus during growth and delivery. We believe the proposed system will become an essential tool for the physician in the delivery room replacing all invasive fetal scalp electrodes and the less capable ultrasound used in 85% of the delivery rooms. Traditional monitoring methods such as Doppler or scalp electrodes are yesterday's technology. By achieving our project goals we will improve the capability of our caregivers with our advance technology. We will do this by replacing unreliable, expensive ultrasound technology and eliminating the need for potentially harmful, invasive fetal scalp electrodes.

OTFBP 10-878

January 25th, 2010

To: The State of Ohio Department of Development
From: Greatbatch, Inc

Re: Letter of Intent, 2010 OTFBP

Greatbatch wishes to notify the State of Ohio by means of this letter that it intends to submit a proposal for the Ohio Third Frontier Biomedical Program, fiscal year 2010.

Lead Applicant: Greatbatch, Inc.

Address: 1771 E 30th Street
Cleveland, OH 44114

Contact person: Mike Labbe
Tel: 216 325 7454
Fax : 216-937-2812
mlabbe@greatbatch.com

Funds Requested: \$1,000,000

Collaborators: The Cleveland Clinic Foundation

Project Title: Advanced Technology For Sacral Nerve Stimulation

Project Summary

By 2013 it is estimated that over 17 million people in the U.S. will suffer from a controllable form of urinary incontinence. While 90% of the population responds well to drug therapy, the other 10% experiences no benefit. Over the last decade, several non-drug therapies have been clinically evaluated. The most promising is neurostimulation, which features an implanted device that creates a small electric current to stimulate targeted nerves. However, performance limitations of the currently available first-generation technology limit the number of drug-refractory patients who could be receiving treatment.

Greatbatch, which has a successful history of developing neurostimulation components for the heart, intends to leverage this expertise and broaden its reach. In collaboration with the Cleveland Clinic, Greatbatch will develop next-generation components that vastly improve the clinical efficacy of neurostimulation for urinary incontinence.



Cleveland Clinic

William H. Fissell, M.D.
Director
Center for Organ Replacement Engineering
Biomedical Engineering/ND20
The Cleveland Clinic
9500 Euclid Avenue
Cleveland Ohio 44195

January 25, 2010

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43215

In Re: 3rd Frontier BCRP Letter of Intent

Dear Colleagues,

I am extremely interested in submitting a proposal, "Portable Artificial Lung". This device would function as a wearable artificial lung allowing patients awaiting transplant to survive until donor lungs are available. We propose to develop a miniaturized blood oxygenator that will permit patients with respiratory failure to remain mobile and independent in their activities of daily living. Presently there are two technologies to support patients with respiratory failure: (1) positive-pressure ventilation by endotracheal tube, which requires the patient to be sedated and immobilized in bed, but subjects the patient to significant risk of pneumonias and pressure-induced lung injury, (2) extracorporeal membrane oxygenation (ECMO), colloquially known as a "heart-lung machine". Because of the grave risks to the patient inherent in these treatments, they are generally only applied to patients who are gravely ill (intubation and mechanical ventilation) or nearly moribund (ECMO). By the time patients are so ill as to justify use of these treatments, recovery and survival has become unlikely. Even if a patient is relatively well, the sedation and immobilization required by both treatments provokes rapid deconditioning and increases the risk of skin breakdown ("bedsores"). A miniaturized device that could support patients and allow them to avoid mechanical ventilation while minimizing the risk and complexity of a heart-lung machine would be revolutionary and life-saving.

The Cleveland Clinic and H-Cubed, Inc., an Ohio small business, have developed a novel membrane technology with applications to organ replacement. A kidney application of the technology to replace dialysis has been funded by the National Institutes of Health, and that project addresses several fundamental challenges to implementation of these membranes in a blood-contacting device. Thrust areas of that funded project include optimizing membrane porosity, strength, and reliability, and blood-materials interactions. We propose to leverage that research to apply the membrane technology to treatment of patients with lung failure. Over three years, we propose to optimize membrane design parameters for gas transport, finalize membrane surface treatment to maximize blood compatibility and membrane lifetime, and then deploy the membrane as a venoarterial membrane oxygenator in an animal model. At the end of three years, preclinical work supporting an application to the Food and Drug Administration for a Phase I clinical trial will be complete.

Our team has extensive experience with key technologies that act as a springboard for this application, including microscale fabrication, transport phenomena, blood biocompatibility, extracorporeal circulation, and lung transplant. Furthermore, the team includes faculty at Case

The Cleveland Clinic Foundation
Lerner Research Institute
Department of Biomedical Engineering

9500 Euclid Avenue / ND20
Cleveland, OH 44195

Tel: (216) 445-2206
Fax: (216) 444-9198
fisselw@ccf.org

Western Reserve University (who will focus on membrane transport phenomena), engineers at H-Cubed, Inc. University of California, San Francisco (who have vast experience with silicon nanopore membrane fabrication), and Connecticut Reserve Technologies, and investigators and surgeons at the Cleveland Clinic (who are internationally known for their understanding of extracorporeal circulation). We will advance the application of H-Cubed's Ohio-developed technology to develop medical device products and jobs in Ohio.

Our budget will include support for membrane fabrication by H-Cubed, Inc. and University of California, San Francisco, gas transport analysis at Case Western Reserve University, fracture analysis and reliability estimation at Connecticut Reserve Technologies, surface chemistry tasks and analysis at Cleveland Clinic, and bench and animal trials at Cleveland Clinic. From our present status to applying for FDA approval for a Phase I clinical trial we estimate costs to be approximately \$6,000,000- \$8,000,000. We have significant resources already devoted to the fundamental tasks involved in bioengineering medical devices using this new technology, and thus have significant matching funds available already. We are pursuing SBIR, philanthropic, and venture capital support for the project as well.

This initiative addresses important problems facing patients with advanced lung disease. The technology developed under this proposal would allow for an extremely functional outpatient bridge-to-transplant device for these patients, who presently have no effective therapeutic options.

Please feel free to contact me if you have any questions regarding this proposal.

Contact Information

Dr. William H. Fissell
Biomedical Engineering ND20
Cleveland Clinic
9500 Euclid Avenue
Cleveland OH 44195

216-445-2206
fisselw@ccf.org

Michael Villalobos
Sr. Commercialization Officer
Cleveland Clinic Innovations
9500 Euclid Avenue
Cleveland, OH

216-445-0812
villalm@ccf.org

sincerely,

William H. Fissell MD

Letter of Intent

Ohio Third Frontier Biomedical Program

Fiscal Year 2010 Proposal

Proposed Project Title

***INFRASTRUCTURE DEVELOPMENT PLAN FOR THE CLEVELAND MEDICAL MART
CONVENTION CENTER: AN IDEA WHOSE TIME HAS COME***

Lead Applicant

Orthopaedic Research Laboratories
2310 Superior Avenue East
Suite #100
Cleveland, OH 44114
Tel: 216-523-7004
Fax: 216-523-7005
President: A.Seth Greenwald, D.Phil.(Oxon)

Contact: Jon Greenwald
E-mail: jon@orl-inc.com
Website: www.orl-inc.com

Collaborators

Greg Sanker
Vice President of Leasing
Cleveland Medical Mart & Convention Center
The Higbee Building
100 Public Square, Suite 210
Cleveland, OH 44113

Tel: 216-875-6615
E-mail: gsanker@mmart.com

Estimated Grant Funds to be Requested

\$1M. from Third Frontier Research and Development Fund

Summary of Proposed Project

A Medical Mart for Cleveland; long the subject of developers, public inquiry and a tax levy seems closer to project initiation during calendar year 2010. Although the vision for what it may bring to the city and the region have long been espoused, very little has emerged particular to the infrastructure required for its' success.

This summary describes a development project based on the continuing medical education of healthcare professionals which serves as a focus for attraction of regional,

national and international healthcare manufacturers of medical devices, diagnostics and drugs. Using as a base of experience the largest international joint arthroplasty meeting in the world, Current Concepts in Joint Replacement (CCJR), whose origin resides in Cleveland, and the significant experience of the Orthopaedic Research Laboratories in education, research and bioskills laboratory development.

While orthopaedics is a single specialty within a larger medical continuum, it serves as a basis for significant commercial activity which is easily enlarged. The continuing medical education of healthcare professionals involved in orthopaedic surgery is inclusive of surgeons, residents and fellows, nurses and members of allied healthcare industries.

This project involves the development of continuing education meetings at the Cleveland Medical Mart built around the attraction of large numbers of technical exhibitors across the nation and the world. The opportunity to meet their end product users and decision makers is a powerful incentive to be there and exhibit.

Coincident with their presence and interest is the development of a significant bioskills laboratory facility housed within the Medical Mart. This is an essential part of product introduction and product learning by healthcare professionals, both cadaveric and simulated means will be utilized.

In addition to both exhibitor floor space and bioskills laboratory, an auditorium suitable for 1,000 people in both theater and schoolroom seating will be required.

The exposure of regional manufacturers to their national and international peers creates business development and expansion opportunities for the orthopaedic supply chain in Ohio. This will culminate in contract manufacturing, technology licensing and potential facility establishment in the region.

The Third Frontier Grant will be used to establish an operational infrastructure which will enable the projected 2013 opening of the Medical Mart to achieve success.