OTFBP 10-801

Syncro medical innovations

Enhancing the Healing Hands of Medicine Worldwide

GARY WAKEFORD
PRESIDENT

January 12, 2010

FY2010 Ohio Third Frontier Biomedical Program (OTFBP)
Ohio Department of Development
Technology Division
77 South High Street, 25th Floor
Columbus, Ohio 43215-6130

This **Letter of Intent** is provided by **Syncro Medical Innovations, Inc.** (Lead Applicant) in anticipation of a proposal for the 2010 Ohio Third Frontier Biomedical Program (OTFBP).

Lead Applicant:

Syncro Medical Innovations, Inc.
20 West Federal
Suite M-5B
Youngstown, Ohio 44513
Phone (234) 855-1605
Fax (716) 809-350

Lead Applicant Contact:

Mr. Gary Wakeford
Syncro Medical Innovations, Inc.
Gary.Wakeford@Syncromedical.com
Office (234) 855-1605
Cell (330) 766-1173

Project Title:

Development of the Tracheal Avoidance Enteral Feeding Tube with Positive Confirmation Technology (PCT).

Budget request estimate: $950,000.00

Known Collaborators: **Youngstown State University**
Telemedicine & Advanced Technology Research Center (Dept of Defense)
John J. Turner Research Fund, Northside Hospital Youngstown Ohio

Project Summary (See Attachment A)

Sincerely,

Gary Wakeford
President
Syncro Medical Innovations, Inc.

(ATTACHMENT A)

Project: Development of the Tracheal Avoidance Enteral Feeding Tube with Positive Confirmation Technology (PCT)

The Enteral Feeding Tube (EFT) market is fraught with complications and cost over runs that are both very serious and very expensive. There is growing evidence that the prevalence of inadvertent placement of feeding tubes into the lung is becoming a serious problem. Independent clinical studies from 4 U.S Teaching Hospitals each clearly demonstrate that 2% of all feeding tubes are mal-positioned in the trachea and/or lung. With over 6 million feeding tubes placed each year in the U.S. the number of serious complications becomes staggering. These misplaced tubes account for serious injury, millions of dollars in increased complication rates, and are the direct cause of nearly 5,000 deaths per year.

Beginning with the development and market entry of the Syncro BlueTube ™, (Ohio 3rd Frontier Research and Commercialization Grant # TECH 08-079), Syncro Medical Innovations has completed Phase I of the longer term goal of providing a more accurate placement of small bowel feeding tubes while avoiding serious and costly complications associated with misplacement of the tube. The high incidence of feeding tubes placed in the lung is the primary reason that x-rays are required during this procedure. The total number of x-rays associated with feeding tube placements exceeds 8 million per year in the U.S. Using a conservative fully burden cost figure of $150.00 per x-ray the cost to the U.S healthcare market of these x-rays alone is over a billion dollars per year. The Syncro BlueTube™ is successfully capturing the small bowel feeding tube market. It also provides the product platform from which Syncro will develop the technology to eliminate this serious complication from the market place, while simultaneously removing the need for an x-ray during the insertion of feeding tubes.

The initial clinical studies were designed to demonstrate the effectiveness of the Syncro BlueTube™ in achieving small bowel placement. These studies have been very positive and are helping to launch the Blue Tube™ into the market place. During the administration of these clinical trials it was noted that the magnetic characteristics of the BlueTube™ offered the clinician the ability to effectively avoid the trachea upon insertion. Further developments in the basic construct of the tube are necessary to make the tube applicable for both gastric and small bowel placements. The ability of the tube to safely negotiate the esophageal passageway is only one half of the equation. It will be necessary to develop a Positive Confirmation Technology (PCT) to confirm to the clinician at bedside when the tube has safely passed the trachea. Such a confirmatory device is what will ultimately allow for the elimination of x-rays. It is also important to note that many of the more serious and costly complications associated with enteral feedings are the result of significant delays in the initiation of feeding regimens.

The Department of Defense has committed $2.1 Million dollars in funding to Syncro Medical to further our progress in this area. The contract was signed as of September 21, 2009 and we estimate that $1.25 Million of this award will be used as matching funds on this project. The completion of the Tracheal Avoidance TrueTube™ and the corresponding Positive Confirmation Technology will further solidify the reputation of Northeast Ohio as the new epicenter for medical device companies. This project will further enhance a critical goal of the Third Frontier program of transitioning Ohio's workforce to the Bio- technologies. The project will have an immediate and significant impact on the local economy as it will sponsor a professorship at the Youngstown State University; it will expand upon the Engineering internship program already in place with the university; and it will bring another manufacturing process from Dresden Germany to the Interplex Company of Milford Ohio.

January 22, 2010

2010 Ohio Third Frontier Biomedical Program
Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, Ohio 43215

This **Letter of Intent** is provided by AxioMed Spine Corporation in anticipation of a proposal for the 2010 Ohio Third Frontier Biomedical Program.

1. **Lead Applicant Contact:**
   Mrs. Kari B. Zimmers
   AxioMed Spine Corporation
   5350 Transportation Blvd., Suite 18
   Garfield Heights, OH 44125
   E-mail address: kzimmers@axiomed.com
   Phone number: 216-587-5566, ext. 104
   Fax: 216-587-3388

2. **Project Title:** Development of a Facet Replacement or Augmentation Device for the Lumbar Spine

3. **Budget request estimate:** $1,000,000.00

4. **Lead Organization and Legal Structure of the Organization:** AxioMed Spine Corporation (ASC) is an Ohio for- profit biomedical device developer and manufacturer and is the lead organization for the application.

5. **Collaborating Organization:** The Cleveland Clinic Foundation

6. **Project Description:**

   Low back pain affects 80% of the adult population at some point in their lives, with a total annual cost to the US economy of over $100 billion. While the majority of episodes are short and self-limiting, over $26 billion is spent annually on back pain-specific treatment expenditures. On average, individuals with back pain incurred health care expenditures about 60% higher than individuals without back pain. Injury and degeneration of intervertebral discs and facet joints are among the main causes of back pain in adults.

   The primary objective of this research is to develop a viscoelastic device to replace or augment degenerated lumbar facet joints, restoring lumbar spinal function in a minimally invasive manner. The aim of the project is to develop a facet replacement or

augmentation implant which will align and stabilize the spinal segment, while maintaining normal motion in axial rotation, lateral bending, extension and flexion. The primary market for this technology are patients with facet degeneration due to trauma and ageing. Additionally, the technology may be used as an adjunct to total disc replacement devices in patients with degenerated discs and facets. This technology will further advance the facet replacement device developments under investigation which restore facet motion but do not replicate the stiffness and function of the healthy human lumbar facet.

This project will allow AxioMed Spine Corporation, a company established in Ohio in 2001, to expand its product line to benefit patients with facet degeneration in addition to intervertebral disc degeneration. AxioMed Spine Corporation will partner with the Cleveland Clinic Foundation to develop this new technology. AxioMed Spine Corporation will provide project management, materials and engineering expertise, and unique and proprietary bonding techniques developed internally. In addition, the vast experience and expertise of the Cleveland Clinic will be critical in developing this advanced technology for facet replacement. Several Ohio companies will be participating in the project during manufacturing of prototypes and to manufacture mechanical test fixtures. Upon its completion, the project will strengthen Ohio's presence in the area of biomedical devices.

Sincerely,

Kari B Zimmers

Kari B. Zimmers
Director, Research & Development
AxioMed Spine Corporation
5350 Transportation Blvd., Suite 18
Garfield Heights, OH 44125

OTFBP 10-803

Ohio Third Frontier Biomedical Program (OTFBP) – Letter of Intent

Lead Applicant's Name: Cleveland Clinic
Contact Person: Vadim F Lvovich, Ph.D.
Address: 9500 Euclid Ave, Mail Code ND20, Cleveland Clinic, OH 44195
Office Phone: (216) 445-3577
Fax: (216) 444-9198
Email: lvovicv@ccf.org

Proposed Project Title: Lab-on-a-Chip Clinical Diagnostic of Thrombosis Risk

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

Known Collaborators:
ZIN Technologies, Inc.
CWRU Department of Chemical Engineering

Summary of the Proposed Project:
This proposed OTFBP initiative addresses the important medical problem of point-of-care diagnostics and non-invasive risk determination for thrombosis (blood clots). Blood cell-derived microvesicle biomarkers (MVBs) are linked specifically to cardiovascular conditions such as venous and arterial thrombosis through well-known pathogenic mechanisms. This project is dedicated to commercial near-term development of a clinical lab-on-a-chip device for electrochemical detection and characterization of MVBs in clinical samples (blood and biological fluids) and as a laboratory research tool for thrombosis diagnostics. Introduction of a specific, affordable, robust and reliable diagnostic technology for *in vitro* and *in vivo* detection and quantification of cell-derived MVBs gives this project high clinical value. Commercial development will result in production of a miniaturized point-of-care clinical diagnostic platform device for a selective, sensitive, rapid and inexpensive diagnostics of cardiovascular, immunology and cancer related conditions. The technology will also have significant impact in facilitating translational clinical research for common human diseases such as sickle cell anemia, coronary disease, aortic aneurysm, lupus, cancer, obesity and diabetes.

PeriTec

OTFBP 10-804

Date: January 20, 2010
Ohio Department of Development
Technology and innovation division
77 South High Street, 25th Floor
Columbus, OH 43215

RE: Letter of Intent and Summary for the Ohio Third Frontier Biomedical Program

On behalf of Peritec Biosciences Ltd., We would like to submit this letter of intent to apply for funds through the "Ohio Third Frontier Biomedical Program". The title of the proposed project is "Establish Pilot Manufacturing Facility for Tissue Lined Stent". This project will create key biomedical engineering jobs in northeast Ohio, and facilitate efforts for future jobs.

We are collaborating with Cleveland Clinic, Dr. Sarac (Department of Vascular Surgery, Cleveland Clinic Innovations), Nitinol Device and Components, Inc. (NDC) and Proxy Biomedical, Cleveland, Ohio. Peritec Biosciences will have a 1:1 matching for cost sharing with Cleveland Clinic. The proposed budget for this project will be $1Million.

The key personnel who are involved in this project are:

1. Don Gustavon, CEO, Peritec BioSciences
2. Timur Sarac, M.D, Department of Vascular Surgery, Cleveland Clinic Innovations
3. Nancy Rubin, CFO, Peritec BioSciences
4. Brenda Cho, Ph.D., Dir. Comm./Engr., Peritec BioSciences
5. Michelle Poole, Lab Manager, Peritec BioSciences
6. Mallika Sattiraju, Intern, Peritec BioSciences

The Principle Investigator for this project is Mr. Donald Gustavson.
Address: 10265 Carnegie Avenue, Cleveland, OH 44106
Email: labcaseworks@aol.com
Phone: 216-870-1512

Contact person for this grant is Ms. Mallika Sattiraju
Address: 10265 Carnegie Avenue, Cleveland, OH 44206
Email: m.sattiraju@peritecbio.com
Phone: 216-334-4420
216-444-5004

Sincerely,

Donald Gustavson
CEO, Peritec Biosciences Ltd.

PeriTec™

PROJECT SUMMARY

PeriTec Biosciences' mission is to create and develop innovative vascular and cardiovascular surgical products that improve blood vessel surgery outcomes through product longevity and cost effectiveness. The company's technology involves the incorporation of a superior biological tissue, the peritoneum, into minimally invasive peripheral vascular stents. This is a platform technology which include the iliac and femoral arteries of the legs, liver TIPS procedures, dialysis access grafts, tibial PAD, and saphenous vein coronary grafts. .

The Company is focused on producing a peritoneal lined stent graft for treatment of peripheral artery disease, particularly the SFA (superficial femoral artery). While good solutions exist for cardiac related artery and valve diseases, there is no consensus solution for SFA peripheral artery disease. The market for just the SFA is $1 billion alone, and growing each year. Similar markets exist for each of saphenous vein grafts, TIPS/biliary, renal, iliac, and carotid. The combined $6Bn market is increasing at a very quick pace owing to the aging, diet and exercise habits of the populace in the Western countries.

Technology and Products

The company's technology offers important advantages. A variety of complications arise from older products including neointimal hyperplasia, thrombosis (or clotting), and susceptibility to infection. PeriTec's proprietary peritoneum material - the tissue lining all mammals abdominal wall - is strong yet flexible and is only 150 microns thick. It has the same cellular structure as that of the endothelium, the inner lining of blood vessels, and pericardium which surrounds the heart and is used in heart valves. These characteristics allow for size customization, less likelihood of obstruction, and a greater product life expectancy. In addition to these attributes, the bovine peritoneum material is in abundant in supply and competitively priced in relation to other biologic tissues.

Intellectual Property

The inventor of PeriTec's technology, Timur P. Sarac, M.D., is a vascular surgeon at the Cleveland Clinic Foundation ("CCF"). As a result of this relationship, PeriTec has executed a license agreement with the Cleveland Clinic in order to proceed with the development and commercialization of the technology applications. U.S. Patent No. 6,579,307 was awarded to CCF in May 2003, and covers the use of peritoneum as graft or biological conduits, and stent linings. CCF and the Company had an additional patent granted in 2006 for construction (U.S Patent No. 7,137,947), a divisional patent granted for tissue processing and use as a drug delivery mechanism (7,559,953) Also three patents filed for novel crimping mechanisms and delivery catheters covering the architecture, construction and deployment of biologically covered stents (filed 2006).

PeriTec seeks funds to establish a pilot manufacturing facility for product manufacturing in accordance with appropriate ISO standards. The first goal is to begin the process of European CE mark validation and subsequent sales. This will also serve as the precursor for larger IDE/PMA work. This will not only create jobs, but also serve as a spring board for many more biomedical engineering jobs.

OTFBP 10-805

FTA

Norm Chagnon
Executive Director Third Frontier Commission
Ohio Third Frontier Biomedical Program

01/21/10

Subject: 2010 OTFBP LOI

Dear Director,

Our company, FTA Bioscience, is requesting $10 Million in funding from the Ohio Third Frontier program to finance the development and commercialization of our new pathogen Silver Dihydrogen Citrate.

It is our intent to perform the clinical trials in Ohio, and create an Ohio based operating entity that would include but is not limited to manufacturing, marketing and distributing our finished medical formulations. Our company holds the medical pathway rights to twelve issued worldwide patents covering the anti-microbial properties of Silver Dihydrogen Citrate. We intend to formulate novel compounds that demonstrate improved safety and toxicity profiles with high efficacies. Our final products will provide improved methodologies for treating and remediating Acne, Chronic Wounds, and Biofilms. We believe the maximum returns are possible for SDC product versions that are FDA approved. Our SDC molecule enjoys a competitive advantage over current treatments in that its aqueous form allows for accurate delivery of the active ingredient, it attacks the infectious organisms in a non-toxic, odorless, tasteless, and colorless delivery system, and its stabilized silver ion complex has up to 24 hour residual kill efficacy.

We have received a letter of intent for capital investment from Great Lakes Ventures Fund. In July of 2009 we entered into a services agreement with The Cleveland Clinic in exchange for equity. We are currently being advised by BioEnterprise of Cleveland. Our medical director is Mahmoud A. Ghannoum M.Sc., Ph.D., EMBA.

The founding Doctors of FTA Bioscience are Frank Papay MD, FACS, FAAP of the Cleveland Clinic and Tony Balsamo MD of Geisinger Health System.

Our business contact information is as follows:

Brian V. Sokol, President. FTA Bioscience
812 Huron Rd. Suite 240
Cleveland, Ohio 44115
216-952-4030
bsokol@innodirect.com

11000 Cedar Ave.
BioEnterprise, Suite 100
Cleveland, OH 44106
www.theravasc.com

January 21, 2010

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

Dear Sirs:

TheraVasc intends to submit an application in response to your recent Biomedical Program 2010 RFP. Following is the information requested as part of this RFP:

Lead Applicant's Name: TheraVasc Inc.

Address: 11000 Cedar Ave., BioEnterprise, Suite 100, Cleveland, OH 44106

Phone Number: 318-349-3851

Contact Person: Tony Giordano

Email of Contact Person: tgiordano@theravasc.com

Proposed Project Title: Clinical Development of TV1001 for the Treatment of Peripheral Artery Disease

Estimated Grant Funds to be Requested: $1,000,000.

Known Collaborators: Although not identified at present, upon submission of the application, collaborators will include an Ohio cGMP manufacturing facility; an Ohio clinical contract research organization; and, and Ohio medical institution capable of carrying out the project.

Proposed Project Summary: TheraVasc Inc. is a Delaware C-Corp formed in 2009, originally established in Shreveport, LA and relocated to Cleveland, OH. The Company has raised $650,000 to date from founders, GLIDE (Loraine, OH), Portal Capital (Beachwood, OH) and JumpStart (Cleveland, OH) to carryout Phase I clinical trials on a non-enteric coated and an enteric coated formulation of TV1001. The focus of this trial is to better understand the pharmacokinetics of TV1001 in diabetic/peripheral artery disease patients. TV1001 is an oral formulation of sodium nitrite. Sodium nitrite has been shown in animal models of diabetes and peripheral artery disease (PAD) to stimulate new blood vessel growth specifically in the ischemic limbs of the animals. Since many of the problems associated with diabetes and PAD result from loss of blood vessels, this strategy represents the first real hope for the 12-15M patients suffering from PAD in the US.

The proposed project will be a Phase IIa dose-escalating study in diabetic/PAD patients. An IND is being drafted and will be submitted prior to the start of this trial. In the proposed study, four dosages, 20,

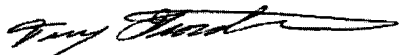
40, 80, 160 mg, of enteric coated sodium nitrite will be administered, twice daily. These dosages should provide therapeutic benefit without resulting in side effects.

Thirty patients will be enrolled in the trial and randomly assigned to placebo (10 subjects) or treatment (20 subjects) groups. After informed consent has been obtained, subjects will be scheduled for their Baseline Study Visit (BSV). Subjects will be NPO (nothing by mouth) after midnight for the first visit and PK assessment will be carried out after administration of the first treatment. 20 mg of enteric coated sodium nitrite will be given to patients for taking orally twice daily and the patients' blood chemistries will be assessed the following week. In addition, all patients will be given blood pressure kits and instructed to monitor their blood pressure daily and immediately report any changes of more than 10% or any feelings of dizziness. If blood chemistries are within acceptable levels and no changes are reported by the patients in blood pressure, the dose will be increased the following week (2-weeks on each dose). During administration of the first and last dose, pharmacokinetics will be assessed. Although the primary objective of this chronic, dose-escalation study is to assess safety following long-term administration to diabetic patients, the study is also being designed to give some indication of efficacy. To that end, during each weekly visit the patients ankle-brachial index (ABI) will be measured to assess whether there are changes in blood flow to the ischemic limb, biomarkers will be analyzed from blood samples and the SPY Imaging System will be used to monitor new blood vessel formation.

During this project period the Company will also work on development of a sustained release formulation of the drug. This will involve development of new formulations and testing the formulations in rabbit models of diabetes and ischemia. TheraVasc's management believes that a sustained release formulation will provide greater safety by reducing methemoglobin levels and additional patent protection from potential generics.

Please let me know if you require any additional information at this time.

Sincerely,



Tony Giordano, Ph.D.
President and CEO

OTFBP 10-807

LETTER OF INTENT
Ohio Third Frontier Biomedical Program - 2010

Lead Applicant:
Jon J. Snyder
President and CEO
Neuros Medical, Inc.
4230 State Route 306, Suite 305
Willoughby, OH 44094

Email: jsnyder@neurosmedical.com

Phone: 440-951-2565

Project Title: Commercialization of peripheral nerve block stimulation technology for chronic pain applications.

Estimated Grant Funds to be Requested: $1M

Known Collaborators:
Case Western Reserve University, Cleveland Clinic

This project focuses on the commercialization of our platform technology, peripheral nerve block stimulation for patients suffering from chronic pain. Chronic pain affects nearly 75 million patients in the U.S. according to the National Pain Foundation. Chronic pain is also met with a poor prognosis that is poorly treated by conventional therapies. Our novel nerve block neurostimulation technology, invented by Drs. Kilgore and Bhadra of the Biomedical Engineering Department at Case Western Reserve University, has the potential to provide relief to millions of patients suffering from chronic pain. Our patented nerve block portends to stop the pain signal near the point of origination, rendering it intransmissible and unable to be received by the central nervous system as a pain signal.

Our project will contain three phases over two years. The first phase is completion of product development, transforming this technology from the research stage to a form to be used by patients. The second phase will focus on a human clinical study, confirming safety and efficacy. The final phase will support commercial launch of the product including launch support activities, growing our organization via new job creation and hiring, as well as product manufacturing to fulfill launch initiatives. In all phases, we will continue to augment our strong intellectual property position.

Our clinical study activity will be led by Dr. Michael Stanton-Hicks of the Cleveland Clinic's Pain Management Program, a world renowned specialist in chronic pain. The clinical study is a pivotal piece of our commercialization and its effective execution will lay the groundwork for product launch, staffing, and related support activities.

Micropyretics Heaters International

www.mhi-inc.com

January 22, 2010

OTFBP 10-808

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

Dear Ohio Department of Development:

Please accept this letter of intent from Micropyretics Heaters International ("MHI") for our Fiscal Year 2010 Ohio Third Frontier Biomedical Program ("OTFBP") proposal.

Lead Applicant Name:	Micropyretics Heaters International Inc.
Address:	750 Redna Terrace, Cincinnati, Ohio, 45215
Telephone:	(513) 772-0404
Contact Person:	Dr. Anu Vissa, President
Contact Email:	avissa@mhi-inc.com
Project Title:	Commercialization of Nanostructured Biomedical Coatings in Ohio
Estimated Grant Amount:	$1,000,000
Known Collaborators:	Collaborators to be determined

Summary of Proposed Project:

An overwhelming need to suppress hospital-acquired infection rates in the U.S. is a serious concern in the health care industry. The U.S. Centers for Disease Control and Prevention (CDC) estimates that the infections acquired in hospitals alone affect approximately 2 million persons annually. In the U.S., between 44,000 and 98,000 people die every year from infections they picked up in hospitals. The alarming rate of patient infection due to ineffective antimicrobial techniques and the high costs associated with retroactive infection treatment is a significant problem.

Further compounding the problem, Medicare and Medicaid no longer reimburse expenses related to most hospital-acquired infections. Therefore, the costs to treat patient infections must be covered by the healthcare institution. This has created a significant opportunity for biomedical antimicrobial coatings companies. The demand for antimicrobial coatings is growing at a rapid pace all over the world. In the U.S. alone, the market for these products is expected to grow from $175 million in 2005 to over $550 million in 2012.

Micropyretics Heaters International
www.mhi-inc.com

Infection control in a hospital environment depends heavily upon the use of a variety of specialized antimicrobial formulations. Current disinfectant techniques such as chemical sprays and wipes, and heat, steam, pressure, and radiation treatments have been proven costly, ineffective, and temporary. Other disinfectant techniques utilize disposable components, resulting in increased costs as well as bio-contaminant waste management and safety issues. The biomedical industry must permanently mitigate harmful microorganisms with a low cost, safe and durable antimicrobial coating solution.

Headquartered in Cincinnati, Ohio, Micropyretics Heaters International is a world leader in the energy and materials sector. The company was an early recipient of the Governor's Energy Award and has won the R&D 100 award four times. The company manufactures a range of materials and has three main areas of operations, namely, biomedical, materials and energy. Several of its products are derived from its core molybdenum disilicide (MoSi2) heating products. MHI has patented its recent discoveries (over 10 applications filed world-wide) based on the anti-microbial (biocidal) properties of molysilicide and closely related materials. These may be used for bio-medical applications on duplex and multiplex surfaces throughout the biomedical industry. MHI is a global supplier of high quality goods and products with over four hundred customers including fifty Fortune 500 customers.

With support from the OTFBP, MHI and project collaborators propose to further develop and commercialize this novel, low cost, durable, nanostructured biocidal biomedical coating. This durable MoSi2 coating, when applied to the surface of biomedical devices manufactured in Ohio, will safely, efficiently, and cost-effectively eliminate harmful microbes. Unlike other antimicrobial materials, MHI's patented MoSi2 coating material is permanently welded to the surface of the medical device and possesses exceptional anti-microbial properties.

Building upon a strong foundation of experience and knowledge in the biomedical sector, MHI along with its collaborators will successfully develop and commercialize a multipurpose novel antimicrobial coating initially focusing on biomedical device applications in the State of Ohio. The project aligns with the purpose, goals and objectives of the OTFBP as it relates to adapting or modifying biomedical products produced in Ohio that can improve delivery and patient outcomes through improved safety and efficacy of biomedical products.

MHI's project will benefit Ohio's robust biomedical device cluster, further solidify Ohio at the forefront of the biomedical industry, and generate technology based economic development for the citizens of Ohio.

Sincerely,

Dr. Anu Vissa

750 Redna Terrace • Cincinnati, OH 45215 USA • Office (513) 772-0404

OTFBP 10-809

us endoscopy
listening
phone
fax
customer service

January 25, 2010

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

Subject: 2010 OTFBP LOI
VIA: E-mail to OTFBP2010@development.ohio.gov

To Whom It May Concern:

Please let this letter serve as notice of intent for US Endoscopy to apply for the fiscal year 2010 Ohio Third Frontier Biomedical Program (OTFBP). Below is the information requested in Section 1.3.3 of the Request for Proposal for the OTFBP. The attached project summary provides additional details about our project.

Lead applicant: US Endoscopy
Address: 5976 Heisley Road, Mentor, OH 44060
Telephone: 440-639-4494
Contact: Peter Brumbergs, Chief Financial Officer
E-mail: pbrumbergs@usendoscopy.com
Proposed project title: Advanced Urological Diagnostic & Therapeutic Accessories Project
Estimated grant funds to be requested: $1 million
Potential Collaborator(s): Cleveland Clinic, University Hospitals and other thought-leading healthcare providers and industry partners

Thank you for your assistance. Please feel free to contact me if you need additional information.

Sincerely,

Peter Brumbergs
Chief Financial Officer

Attachment: Project Summary

US Endoscopy
Advanced Urological Diagnostic & Therapeutic Accessories Project
2010 Ohio Third Frontier Biomedical Program
Project Summary

US Endoscopy, located in Mentor, Ohio (Lake County) is a prolific designer and supplier of urgently needed, niche diagnostic, therapeutic and support accessories for the Gastrointestinal (GI) Endoscopy market. The Company employs over 300 individuals at its headquarters and sole manufacturing location in Mentor, where the company has been located since its founding in 1991. US Endoscopy develops and manufactures equipment primarily used in the Gastrointestinal Endoscopy procedure, which allows a doctor to see the lining of the digestive tract. This examination is performed using an Endoscope which is a rigid or flexible fiber optic tube with a tiny camera at the end. The Endoscope not only allows diagnosis of gastrointestinal disease, but treatment as well. US Endoscopy's product range of approximately 140 items is primarily concentrated in Endoscope accessories that allow diagnosis and therapy such as suction, irrigation, injection, tissue sampling and foreign body management.

Technologies and devices currently being developed by US Endoscopy have tremendous potential for use in the field of Urology, or more specifically Endourology or Cystoscopy, as well. The Company's expansion into this large and growing industry will involve significant research and development, product testing, regulatory approvals and certifications. The Company's proposed project represents one of the most significant R&D undertakings in its history.

The proposed Third Frontier Biomedical project would take the development of the technology to the point of market entry within two years. Development of the technology would occur at the Company's facility in Mentor, OH and the finished product would be produced there as well. Intellectual property protection would be secured during the grant period to ensure that a lasting competitive advantage would be created for the State of Ohio and the Company. Significant job creation at the Company's headquarters and manufacturing facility would occur at the end of the Third Frontier project.

The Company's development and commercialization processes are highly collaborative, and involve significant input from major healthcare organizations such as the Cleveland Clinic and Mayo Clinic, individual doctors, and the Company's industry partners. For this project, the Company may collaborate with the Cleveland Clinic, University Hospitals and other thought-leading healthcare providers engaged in product design, testing, and certification.

OTFBP 10-810

Spine Form

January 23, 2010

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

Dear OHIO DOD,

RE: Letter of Intent - Ohio Biomedical Program FY2010 (2010 OTFBP LOI)

SpineForm LLC is an Ohio limited liability company intending to submit a Third Frontier Biomedical Program funding proposal entitled: **"Clinical Study of Non-Fusion Spinal Implant Treatment of Progressive Idiopathic Scoliosis"** in the cluster specific development program of orthopaedics. The following is contact information for the lead applicant and a list of known collaborators:

Lead Applicant:
SpineForm LLC
Joseph E. Reynolds
President
4480 Lake Forest Dr., Suite 414
Cincinnati, OH 45242
jreynolds@spineform.com; (513) 769-1916 x15

Known Ohio Based Collaborators:
Cincinnati Children's Hospital Medical Center

University Hospital Case Medical Center, Rainbow Babies & Children's Hospital, Cleveland, OH

University of Cincinnati

E-Prime LLC; Cincinnati, OH

SpineForm's emerging and innovative technology, known as the HemiBridge™ System addresses an unmet clinical need for non-fusion treatment of progressive scoliosis (deformity of the spine during juvenile and adolescent growth). SpineForm was created in 2004 and began operations with an exclusive patent licensing agreement with Cincinnati Children's Hospital Medical Center (CCHMC).

The research staff at CCHMC won the highest award from the Scoliosis Research Society for their research in 2003 of endoscopic mechanical modification of spine growth. According to the National Scoliosis Foundation, 38,000 spinal fusion surgeries are performed for scoliosis correction in the US annually which translates into a product potential market of $650 Million in the US or $850 Million world wide.

Extensive mechanical testing, animal and cadaver studies were conducted at Ohio testing facilities that have validated the pre-clinical safety and potential effectiveness of the spinal implant construct, surgical instruments and surgical procedure. Based on these pre-clinical studies, testing and the design of the clinical study, SpineForm received an Investigational Device Exemption (IDE) in November of 2009 from the US FDA. The IDE is regulatory approval to study first use in humans of the HemiBridge™ System. The FDA approval is a key project milestone and positions SpineForm as the world's leader in the field of compressive spinal growth modulation. The planned clinical studies are expected to position Ohio collaborative institutions as the world leaders in the non-fusion surgical treatment of spinal deformity and bring significant revenue and therefore employment opportunity to the State of Ohio.

The HemiBridge™ System is transitioning from the "Incubating" to the "Demonstrating" phase of commercial development. The funds will be used for the clinical studies, intellectual property prosecution, regulatory market clearance, and perhaps enable European market entry. SpineForm intends to request $1 Million in matching funds (that is a total funded budget of $2 Million) for the clinical study. The program funding will be matched with project dedicated company funds, committed private funding, and in-kind support from collaborators.

Please provide an identification number for submitting our proposal.

Sincerely,

Joseph E. Reynolds
President
SpineForm LLC

Via: e-mail OTFBP2010@development.ohio.gov

Ohio Third Frontier Biomedical Program

Letter of Intent

Project Title: ***Safety and Efficacy Studies for the Next Generation of Insulin Analogs***

Lead Applicant

Thermalin Diabetes Incorporated
Cleveland Clinic **Cardiovascular** Innovation Center
10265 Carnegie Avenue
Cleveland OH, 44106
O: 617-695-0523
F: 617-928-0523

Contact Person

David Tischler
David@venzyme.com

Grant Funds Requested: $965,930

Known Collaborators

Case Western Reserve University. Case Western will assist in performing some of the necessary studies for this project.

Aclairo Pharmaceutical Group. Aclairo will design clinically relevant pre-clinical safety and efficacy studies based on their extensive experience in this field.

Project Summary

Overview

Thermalin has clinically superior second-generation insulin analog candidates for both the $8B rapid-acting and $4B long-acting insulin markets. We are requesting funds that, along with matching dollars from identified angel investors, would support studies of safety and efficacy prerequisite to IND applications. Such validation and proof-of-concept will enable our developing Thermalin into a robust biotechnology company in Ohio.

Diabetes mellitus (DM) is a major risk factor for virtually all types of cardiovascular disease (CVD). Advanced patients must inject insulin subcutaneously to prevent chronic hyperglycemia (high blood sugar), which causes oxidative stress in blood vessels throughout the body. DM doubles CVD risk[1]; 70% of diabetes-related deaths are from CVD[2]; and MI patients are almost fourfold more likely to be diagnosed as pre-diabetic or diabetic[3].

Thermalin has two patent-pending lead candidates: **70-001** is a single chain, ultra-rapid-acting analog demonstrated to be stable for many months at high temperatures (98° F). This novel stability eliminates the refrigeration currently required to delay formation of fibrils (or insulin "clumps") that destroy the functionality of insulins. **62-002F2** is an analog formulation with long-acting kinetics (demonstrated in diabetic rats) similar to that of insulin glargine (the market-leading long-acting insulin). Glargine has elevated binding to a cancer-related receptor (IGF1-R), and there is evidence of a dose-dependent cancer risk. 62-002F2 has been shown to have dramatically lower binding to IGF1-R – making it a long-acting analog with a significantly reduced cancer risk.

Market Need

Over the next 20 years, the WHO predicts that worldwide insulin sales will grow from $12B to $54B: doubling in the US, tripling in the EU, and expanding 12 fold in the rest of the world. Novo, Lilly, Sanofi, Merck, Abbott, and others are shopping for superior analogs in preparation for the next big market share shake-up when existing analogs go off-patent in 2013/14. Each of these companies will seek to partner on an insulin analog to compete in the next innovation cycle. In a $12B market there is room for several "blockbuster" drugs.

Benefits to Ohio

As a successful company, Thermalin Diabetes will create biotechnology jobs in Ohio: more than 100 highly skilled employees by 2015, many involved in expanding and managing our relationships with our partners. Our products will have a significant impact on the treatment of DM and the reduction of CVD complications. Thermalin's insulins will enable next-generation insulin pumps that will revolutionize glycemic control and further reduce CVD side-effects. Thermalin's thermostable analog will also have a significant impact on world health, particularly in developing countries where refrigeration is not widespread; this will bring significant humanitarian repute to Ohio biotechnology. Along the way, Thermalin will engage several institutional investors and corporate partners while helping to raise the profile of Ohio's technology cluster.

Project Specifics

These funds will enable bioequivalence studies in rabbits and safety studies in rats and dogs for both candidates 70-001 and 62-002F2. We have detailed specifications for project costs and timelines and expect to finish both sets of studies within 18 months for a total expenditure of 2X the funds requested ($965,930 + matching funds).

Principals

Michael Weiss, M.D., Ph.D., *Founder & CSO*. Professor and Chairman of Biochemistry at Case Western Reserve University School of Medicine, Michael has more than 150 publications and is chair of the NIDDK's Board of Scientific Councilors. He earned his A.B., *summa cum laude* in Physics in 1978, his M.D., *summa cum laude*, in 1985, and a Ph.D. in biophysics in 1986, all from Harvard University.

Richard Berenson, *Executive Chairman*. Rick has been building organizations for twenty-five years; he has been CEO or COO of ten companies and CFO/Treasurer of several more. Rick received a JD-MBA from Harvard Law and Business Schools in 1984 and is a graduate of Harvard College.

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[1] http://www.worldheart.org/cardiovascular-health/cardiovascular-disease-risk-factors/

[2] http://www.servier.com/App_Download/JFax/Cardiovascular/Kub27ang.pdf; Diabetes and Cardiovascular Disease : A Statement for Healthcare Professionals from the AHA: Grund S; Benjamin I, Burke G, Chait A, Eckel R, Howard B, Mitch W, Smith S Sowers J *Circulation* 1999;100;1134-1146

[3] http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(07)61343-9/abstract

OTFBP 10-812

January 22, 2010

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

Letter of Intent to Submit a Proposal for Funding
Ohio Third Frontier Biomedical Program
Fiscal Year 2010

Lead Applicant: Sonix Therapeutics
11257 Willowwood Drive
San Diego, California 92127
858.775.1723

Contact Person: Ross Tsukashima
Co-Founder / Sonix Therapeutics
11257 Willowwood Drive
San Diego, California 92127
858.775.1723
rossmail@gmail.com

Proposed Project Title: Percutaneous Ultrasonic Drug Delivery System

Estimated Grant Funds: $500,000

Known Collaborators: Sonix Therapeutics - San Diego California
Cleveland Clinic Lerner Research Institute - Cleveland Ohio

One Page Summary See Page 2

One Page Summary:

Sonix Therapeutics has developed an innovative ultrasonic drug delivery catheter platform for the improved treatment of coronary artery and peripheral vessel disease Sonix has also secured commitments from nationally prominent cardiologists at the Cleveland Clinic to help develop the technology into a commercial product. Sonix intends to conduct its development at the new Global Cardiovascular Innovation Center incubator facility as a tenant, will conduct its preclinical research at the Atrial Fibrillation Innovation Center (AFIC), and subsequently will conduct its initial phase I pilot study at the Cleveland Clinic.

Current methodologies for treating stenotic lesions, including drug eluting stents, only affect the innermost layer of the arterial wall. The strategy of Sonix Therapeutics is to utilize ultrasonic pressure waves coupled with a proprietary balloon drug coating to actively and evenly infuse anti-restenosis medication throughout the vessel strata. Targeted volumetric dosing reduces drug overloading along the interior vessel lining which can increase the likelihood of late thrombus formation, and allows for drug penetration deep into the interior and exterior vasculature where the genesis of smooth muscle cell proliferation occurs.

Sonix Therapeutics has developed and tested a laboratory "proof of concept" ultrasonic drug delivery model. This device has been used to validate the concept of using an ultrasonic transducer as a drug transport mechanism and has been instrumental in the creation of our intellectual property portfolio. Experimental results obtained from this system have clearly demonstrated the ability of the device to actively drive drug elution outwardly from the balloon surface. Provisional patents have filed to secure intellectual property.

Dr. E. Murat Tuzcu and Dr.Samir Kapadia, both of the Cleveland Clinic, have committed to oversee the preclinical testing and clinical trials for the system.

Murat Tuzcu, M.D. is a Professor of Medicine, Vice-Chairman, Department of Cardiology in the Sydell and Arnold Heart & Vascular Institute, an Interventional Cardiologist at Cleveland Clinic. Dr. Tuzcu's research interest involves the use of various imaging modalities to elucidate the development and progress of atherosclerosis. Dr. Tuzcu has agreed to be the Principal Investigator for this project.

Samir Kapadia, MD, is the Director of the Sones Cardiac Catheterization Laboratories in the Robert and Suzanne Tomsich Department of Cardiovascular Medicine. He is board-certified in internal medicine, cardiology and interventional cardiology. As an interventional cardiologist, Dr. Kapadia has a special interest in complex coronary, structural heart disease-related cardiac interventions as well as carotid and peripheral interventions. Dr. Kapadia will lead the preclinical research effort needed to secure FDA approval to proceed into a human clinical study.

Funds obtained from the Third Frontier grant program and other matching will be funneled into further Research and Development of our ultrasonic frequency drug delivery apparatus. This technology will be developed for maximum effectiveness of drug delivery and vascular penetration and objective performance testing will be published on an ongoing basis to demonstrate feasibility.

Coronary heart disease remains the leading cause of death in both men and women in the United States. The aging of the United States population contributes to the high prevalence of this affliction. By the year 2020, it is estimated that ischemic heart disease will be the number one cause of disability and death worldwide. It is estimated that in the United States over 800 thousand deaths annually are directly attributed to some form of cardiovascular disease.

CR-2,526: NOVEL NON-ANXIOGENIC BROAD SPECTRUM ANTI-EMETIC

The current medical need for the development of more effective treatment of nausea/emesis, with an improved side effect profile, is enormous. Broadly categorized, the market potential can be divided into medical indications and exaggerated physiologic responses to motion (motion sickness), which can occur both in civilian and military populations. Major categories of medical conditions include: adverse effects of medications, toxic etiologies (cancer chemotherapy, radiotherapy), infections, disorders of the gastrointestinal tract, central nervous system, or endocrinologic/metabolic systems, post-operative settings, and multiple advanced chronic diseases. For example, the prevalence of nausea and the number of US patients in the following advanced disease categories is large: incurable cancer (31%; 565,650), heart disease (48%; 4,790,000), renal failure (26%; 651,330), and diabetes (5%; 20,800, 000). Finally, poorly controlled nausea is a common symptom of the terminally ill patient in the palliative care setting. The market size for nausea and vomiting in hospice settings alone is estimated to be $50 to $100 Million.

Cenomed's and Wright State University's scientific development teams have discovered a novel non-anxiogenic, anti-emetic (CR-2,526) with multi-receptor pharmacology acting at the common final target for emesis. CR-2,526 has a benign side effect profile, including the absence of the induction of either anxiety or sedation. In fact, the induction of anxiety and panic attacks in humans has limited the further clinical development of a number of potential candidates. Following the completion of the remaining pre-IND enabling studies, Cenomed and Wright State University are poised to take the lead compound, CR-2,526 into early clinical development and proof of concept studies in the palliative care setting.
The request will be for one million dollars.

ADVANTAGES

- Small molecule
- Multi-receptor pharmacology
- Novel mechanism(s) of action
- Targets central emesis center
- Robust preclinical dose-dependent efficacy
- Non-anxiogenic (potential anxiolytic)
- Effective in both and acute and subacute preclinical conditions
- Benign pre-clinical safety profile at projected clinically efficacious doses
- Wide therapeutic window (60:1)

TECHNOLOGY STATUS

- US patent filed
- Remaining IND enabling studies (Toxicology, PK/PD, CMC) required
- Phase 1/2 proof of concept clinical trial in end of life palliative care patient population: Collaboration and commitment established at the Institute for Palliative Medicine

CONTACT:

James B. Lucot, Ph.D.
Department of Pharmacology and Toxicology
3640 Col. Glenn Hgwy
Dayton, OH 45435
(937) 775-3700
james.lucot@wright.edu

OTFBP 10-814

Letter of Intent for 2010 Ohio Third Frontier Biomedical Program

Lead Applicant: Copernicus Therapeutics, Inc.
Address: 11000 Cedar Avenue, Suite 145 Cleveland, OH 44106
Contact person: Mark J. Cooper, M.D., mcooper@cgsys.com, 216 231-0227
Title: Senior Vice President, Science and Medical Affairs
Project Title: Treatment of the Lung Manifestations of Cystic Fibrosis using Compacted DNA Nanoparticles
Estimated grant funds: $1M Academic Collaborator: Case Western Reserve Medical School

This Letter of Intent describes a joint proposal from Copernicus and Case Western Reserve Medical School for late stage development-track studies leading to submission of an IND application for a phase I/II lung aerosol trial of our DNA nanoparticle therapeutic for Cystic Fibrosis (CF). This proposal is based on significant improvements in our DNA nanoparticle technology since completion of our initial phase I human trial in the nares of CF subjects, and builds on prior Ohio awards in our technology, including a 2002 Technology Action Fund grant (02-064, DNA nanoparticle aerosol development) and a current BRCP award (08-055, GMP manufacturing facility funding).

CF is caused by mutations in the CFTR gene, which encodes for a membrane-bound chloride channel that is expressed by lung epithelial cells (and nasal epithelium). Aberrant CFTR protein leads to thick pulmonary secretions, recurrent lung infections, and respiratory failure (typically in the third decade). Although candidate small molecules to improve function of specific CFTR gene mutations are under development, there currently is no FDA-approved product to treat the underlying cause of CF, and all approved drugs are for supportive care.

The Copernicus-sponsored initial CF trial administered DNA nanoparticles encoding a wild-type human CFTR gene to the nares of subjects with CF. No adverse events were attributed to the DNA nanoparticles, there was substantial evidence of gene transfer, and most subjects (8/12) had electrophysiologic evidence of CFTR chloride channel function. A CMV promoter element was used to transcribe hCFTR cDNA in these nanoparticles, and the duration of improved CFTR activity was about a week. This result was not surprising, since the CMV promoter generates short-term expression in the lung using our technology. Since completion of the clinical trial, Copernicus has optimized the CF platform by improving both the level and duration of hCFTR expression. Levels of hCFTR gene expression in the lung of CF knockout mice were increased by: i) development of a synthetic hCFTR gene sequence that is codon-optimized and CpG-depleted; ii) various expression plasmid improvements, including promoter, intron, chromatin barrier elements, and optimized prokaryotic backbone. Using this plasmid, day 2 levels of hCFTR transgene mRNA were >100% of endogenous lung murine CFTR mRNA. The duration of gene expression was then optimized by testing a series of novel strategies. One of these was successful, generating high level hCFTR mRNA for the lifetime (~100 days) of the lung epithelial cell. These developments led to new patent applications covering high level and prolonged duration of hCFTR expression.

Aerosols of compacted DNA can be generated by several devices and compacted DNA is stable in these mist droplets. In studies partially funded by an Ohio TAF grant, outsourced lung dosing studies (at Battelle) demonstrated excellent gene transfer in the lungs of intubated rabbits. In other studies, excellent gene transfer was observed in the lungs of ferrets and sheep, further demonstrating the activity of our nanoparticles in the lungs of multiple species.

The optimized hCFTR expression plasmid, compacted as a DNA nanoparticle, is now ready for final IND-track studies for a phase I/II lung aerosol clinical trial. The steps required for IND submission include: i) research level toxicology in the lungs of normal mice following aerosol administration; ii) GLP toxicology and DNA biodistribution studies after lung aerosol dosing in mice (and possibly another species based on discussions with the FDA). In addition, we feel that one research study is needed, which is to be performed by our long-standing collaborators at Case Medical School. Since patients with CF have chronically-infected lungs, we propose to determine how lung infection may alter the level and/or duration of hCFTR mRNA expression. Using a well-described Pseudomonas aeroginosa lung infection model, CF knockout mouse will be dosed with our hCFTR DNA nanoparticles and levels and duration of hCFTR expression will be measured.

In summary, we proposed IND-track studies for a phase I/II CF clinical trial of our DNA nanoparticle therapeutic. Since the CF marketplace is substantial (> $2B/year), we feel support of this program will not only provide a much needed therapeutic that may prolong life, but will generate substantial finances to NE Ohio as the DNA nanoparticle industry expands into the CF marketplace and other indications.

OTFBP 10-815

January 24, 2010

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

Re: *Ohio Third Frontier Biomedical Program Letter of Intent*

Dear Ohio Department of Development:

Please accept this letter of intent from CardioInsight Technologies, Inc. for the Fiscal Year 2010 Ohio Third Frontier Biomedical Program ("OTFBP").

Lead Applicant: CardioInsight Technologies, Inc.
11000 Cedar Ave., Ste. 210
Cleveland, OH 44106
216-453-5950

Contact person: Dr. Harold Wodlinger, VP Product Development
(216) 453-5959 x108
harold@cardioinsight.com

Project Title: Atlas Electrocardiographic Mapping System

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

Collaborators: Cleveland Clinic Foundation and others to be determined

Project Summary:

CardioInsight Technologies, Inc. ("CardioInsight") is an Ohio company that has licensed IP developed by Case Western Reserve University in the area of Electrocardiographic mapping, and is in the process of commercializing this technology. CardioInsight has successfully developed a pre-commercial version of the device and has begun clinical studies in sites in the United States and Europe. CardioInsight seeks funding from the OTFBP to develop the commercial version of the device and bring it to market.

An Electrocardiographic mapping system measures and displays the electrical activation system of the human heart. It is used to diagnose the mechanism of cardiac arrhythmias and to guide therapy. The procedure involves placing a disposable array of 252 electrodes on the chest of the patient, and then obtaining a CT image of the patient's heart. The electric field on the surface of the heart is derived from the measured electric field on the chest, and then is displayed on the CT image. The physician is able to visualize the conduction abnormality, and then direct an ablation catheter or a pacing lead to the appropriate site in order to resolve the problem.

Existing commercial cardiac mapping systems are all based on invasive catheter localization. The physician generates a map of the conduction system by physically moving the catheter around one chamber of the heart (called point-to-point mapping). The procedure takes up to 20 minutes to generate a map and new maps must be generated after ablation therapy, since ablation permanently changes the electrical activation system.

In contrast, the CardioInsight EC Mapping system is non-invasive, generates a map in a single heart beat, and generates that map for all four cardiac chambers. The CardioInsight EC mapping system has the potential to substantially reduce procedure times. The CardioInsight EC mapping system also has the unique ability to map cardiac arrhythmias that are transient or unstable, and to map arrhythmias that involve more than one cardiac chamber. These capabilities will allow more effective treatment for a number of common arrhythmias and will create a very large market for the device.

CardioInsight has a world-class management team with extensive experience in medical device development, manufacturing, and marketing. CardioInsight's Medical Advisory Board includes some of the most widely respected Electrophysiologists in the world. Management recently closed a round of financing that will be committed as cost share for the proposed OTFBP project.

Building upon a strong foundation of experience in the biomedical sector, CardioInsight and its collaborators will successfully develop and commercialize the Atlas Electrocardiographic Mapping System. The project aligns with the purpose, goals and objectives of the OTFBP and will benefit Ohio's robust biomedical device cluster, further solidifying Ohio at the forefront of biomedical innovation.

Sincerely,

Dr. Harold Wodlinger
VP Product Development

OTFBP 10-816

OHIO THIRD FRONTIER BIOMEDICAL PROGRAM LETTER OF INTENT

Lead Applicant: SpineMatrix, Inc.
202 Montrose West Avenue
Suite 306
Akron, OH. 44321
Telephone: (330) 665-6780

Contact Person: Timothy G. Biro
Chief Technology and Chief Scientific Officer
Telephone (Office): (330) 665-6780 ext. 229
Telephone (Mobile): (216) 533-3082
Email: tbiro@spinematrix.com

Project Title:
Development and Clinical Validation of an Algorithm for the Diagnosis and Prognosis of Low Back Pain using Computerized Electrophysiological Reconstruction of Spinal Regions (CERSR®)

Funds Requested: $1,000,000

Known Collaborators:
Lead Applicant: SpineMatrix, Inc.
Collaborators:
1. University of Cincinnati, Department of Biomedical Engineering, Scott Wampler, Dr. Donita Bylski-Austerow
2. University of Cincinnati, Department of Environmental Health, Division of Occupational and Environmental Medicine, Dr. Trang Nguyen, MD, FAADEP
3. Midwest Occupational Health Management, Inc., Milford, Ohio, Dr. David C. Randolph, President, MD, FAADEP; Past President American Academy Disability Evaluating Physicians

Development and Clinical Validation of an Algorithm for the Diagnosis and Prognosis of Low Back Pain Using Computerized Electrophysiological Reconstruction of Spinal Regions (CERSR®)

Summary of Proposed Project: Low Back Pain (LBP) is the leading cause of work-related disability in persons younger than 45 years, and responsible for more than one-third of all disability costs in the U.S. An estimated 60 million Americans have one or more episodes of LBP each year. The diagnosis and prognosis of LBP is challenging; anatomical evaluation including x-ray, MRI and CT can identify the source of LBP in less than 15% of patients. Many healthy patients (no low back pain at time of evaluation) will have abnormal anatomical features, and many patients experiencing LBP will have normal anatomical features[1]. In addition, x-ray and MRI findings have no predictive value and do not correlate with clinical symptoms or work capacity[2]. There is a need for a diagnostic test that can evaluate low back physiology, and enable the Physician to determine if the LBP patient is responding to treatment, and evaluate if the patient can return to work.

SpineMatrix, Inc., an Ohio-based company has developed CERSR®, a non-invasive technology which has been FDA cleared to *monitor and display the bioelectric signals produced by muscles to aid in the diagnosis and prognosis of muscular disease and dysfunction.* Based on the results of primary market research in the form of Physician Roundtables, Physical Therapy Roundtables, and Workers' Compensation Roundtables, there is a need and a demand for an objective test to determine if a patient with LBP is responding to treatment, to create a baseline for the health and physiology of an employee at the time of hiring and to observe changes from the baseline after injury and to return to the baseline following successful treatment, and to develop a tool that can be shared with the patient to help them return to work. The results of a CERSR® test can provide the baseline for the employee at the time of hiring or after injury. The purpose of this project is to develop an algorithm that can clinically establish the physiology of the low back as either normal (consistent with the results for patients without back pain) or not normal (consistent with results for patients with low back pain). This algorithm can be used as a clinical tool by the Physician to determine if the physiology of the low back has changed from baseline following a claim of low back pain and injury, to determine if the physiology of the low back has responded to treatment (change from not-normal as a result of injury, to normal following treatment), and to share with the patient as an objective measurement for positive reinforcement if the treatment is effective and the patient can return to work on restricted or full, normal duty.

SpineMatrix (SMI) will provide the CERSR® systems for clinical testing, and will submit the clinical study results to the FDA for expansion of the 510(k) label to include normal and not normal LBP claims. SMI will also be responsible for the commercialization of the platform. Dr. Donita Bylski-Austrow (University of Cincinnati Department of Biomedical Engineering, Children's Hospital Department of Orthopedics) will collaborate on biomechanical aspects of low back injury and pain. Scott Wampler, Assistant Professor of Biomechanical Engineering at UC will collaborate on medical device design. Dr. Trang Nguyen and Dr. David Randolph will collaborate on the clinical studies (protocol design through clinical study completion).

From: jslindsey@roadrunner.com
Sent: Sunday, January 24, 2010 8:40 PM
To: OTFBP2010
Subject: 2010 OTFBP LOI

Lead Applicant:
Atypigene Biomedical Research Institute
340 West State Street
Athens, Ohio 45701
206-619-9077

Contact person: J. Suzanne Lindsey, PhD, President and Chief Scientific Officer email address: jslindsey@roadrunner.com

Proposed Project title: Tumor cell-specific targeting for cancer therapies

estimated grant funds to be requested: $1,200,000.

Collaborator: Ohio University Innovation Center

Summary of the proposed project:

Metastasis, the destructive spread of tumor cells to multiple sites of the body, is the lethal stage of carcinomas. Yet no current therapies target this process. When tumor cells leave the primary tumor they become resistant to cell death. In addition, it is widely believed that recurrence of cancer is caused by residual tumor cells that have migrated away from the primary tumor and are resistant to most if not all current therapies. This is a problem because there are no FDA-approved treatments that target invading tumor cells, the cause of metastasis. In addition, current therapies target proteins overexpressed on or in tumor cells; these proteins are also expressed on normal cells. This is a problem because unwanted side effects are caused by targeting these overexpressed proteins. If tumor cell- specific proteins can be targeted, especially with a preventative vaccine, direct and associated costs will be greatly reduced and quality of life as well as productivity i mproved.

A metastasis target, Mig-7, is apparently tumor cell-specific and not merely overexpressed compared to normal cells. Mig-7 is expressed by all types of solid cancers and melanomas analyzed to date. Targeting Mig-7 inhibits growth as well as tumor cell invasion (Molecular Cancer Therapeutics, 2009,vol 8, pgs 2412-2423). In addition, a peptide vaccine can be employed because of Mig-7 expression specificity and should not cause autoimmunity as a side effect.

Funding for this project will test Mig-7 peptide vaccine in vivo. This vaccine was tested ex vivo and significantly increased human immune cell killing of human breast carcinoma cells (see Molecular Cancer Therapeutics, 2009,vol 8, pgs 2412-2423). In addition, Mig-7 monoclonal antibody will be tested in vivo. Mig-7 antibody significantly decreases tumor cell invasion in vitro (Molecular Cancer Therapeutics, 2009,vol 8, pgs 2412-2423).

OTFBP 10-818

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.

OTFBP 10-819

January 25, 2010

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

Subject: LETTER OF INTENT

JointVue, LLC intends submit a proposal to the Ohio Third Frontier Biomedical Program as requested in The Ohio Department of Development's FY2010 RFP released December 14, 2009.

Applicant Information

Lead Applicant:	JointVue, LLC
Address:	1275 Kinnear Rd. Columbus, OH 43212
Contact:	Mark Byrne, COO
Phone:	614-340-3350
Email:	mark@primedicus.com
Project Title	Noninvasive Dynamic Knee Diagnostics
Estimated Grant Amount:	$1,000,000
Known Collaborators:	Ohio Willow Wood OhioHealth Research & Innovation Institute University of Tennessee

1275 Kinnear Rd. Columbus, OH 43212
614.340.3350 phone
614.340.3351 fax

JOINT VUE

Project Description

The JointVue is commercializing a patent pending medical device for diagnosing musculoskeletal abnormalities. It consists of a non-invasive brace coupled to an instrumentation system for three dimensional ultrasound imaging and joint sound analysis. The technology is applicable to all major joints including knee, hip and spine. The proposed project, *Noninvasive Dynamic Knee Diagnostics*, is intended to develop and commercialize a medical device for dynamic assessment and diagnosis of the knee joint. The outcome of this project will be a system that enables physicians to identify specific causes of knee pain thereby allowing for personalized non-operative or minimally invasive treatment.

Today, knee pain is assessed using static imaging such as x-ray, CT, MRI or fluoroscopy, which provides a limited understanding of the specific underlying problem source. This leads to a reliance on aggressive (and expensive) treatments such as total joint replacements for a wide range of knee pathology. In contrast, JointVue enables dynamic ultrasound imaging of the knee in three dimensions combined with audio signature analysis for identification of specific knee joint pathology. Knowing the underlying causes of knee pain will enable physicians to select appropriate rehabilitative, non-operative or minimally invasive treatments, improving patient outcomes and reducing cost.

JointVue has developed technology demonstration prototypes and proposes to use the Biomedical Program award to develop a market-ready product. The project summary below outlines the five phase of the proposed project. The outcome of this project will be a product and manufacturing system ready for regulatory submission and market introduction.

Project Summary

Phase	Year 1	Year 2	Year 3
1) **Product Design**	X		
2) Pilot Manufacturing	X		
3) **Clinical Evaluation**		X	
4) Manufacturing Scale-Up		X	
5) **Regulatory Submission**			X

Sincerely,

Ray C. Wasielewski, MS MD
Chief Executive Officer

1275 Kinnear Rd. Columbus, OH 43212

614.340.3350 phone

614.340.3351 fax

OTFBP 10-820

Hansen, Andrew

From: hongyan he [hehongyan1974@gmail.com]
Sent: Monday, January 25, 2010 1:30 AM
To: OTFBP2010
Subject: 2010 OTFBP LOI
Attachments: Project Summary.doc

Dear OTF Officer:

I am writing to inform OTF of our intent to submit a 2010 OTFBP proposal in response to the recent announcement of RFP.

1. The Lead Applicant: BioLOC LLC.

   1381 Kinnear Rd. Suite 100

   Columbus, Ohio 43212

   Phone: 614-329-1394

2. Contact person: Dr. Hongyan He, Email: hehongyan1974@gmail.com

3. Project title: Microfluidic ELISA System for Biomedical Applications

4. Estimation of Fund Requested: $850,000

5. Known collaborators:

TEC Institute, Fisher College of Business, The Ohio State University will provide incubation and managerial services for the new venture including interim executive leadership, administrative oversight, fund raising support, and technical and business development.

Advanced Research Technologies will provide market development and technology evaluation services.

OSU Medical Center will conduct clinical testing for analysis and comparison of conventional and CD-ELISA technologies.

Everfavor will design, fabricate and test the analyzer system and the automated sample-handling system by charging only the material and labor cost.

6. A project summary has been attached in this email.

Thank you for your help in administering this request,

Sincerely,

Hongyan He, Ph.D.

BioLOC LLC.

Project Summary

Miniature medical systems such as 'lab-on-a-chip' (LOC) devices and advanced drug delivery systems are a rapidly-growing market, with annual sales of >$20 billion and a high growth rate. Currently, the most prominent market niche is genetic, protein, and immunoassay analyses for pharmaceutical development. Applications on the horizon include advanced medical diagnostics and therapy, toxicology, and homeland security. Although microarray and microfluidic biosensors/chips have reached commercialization in recent years, highly automatic and efficient devices that can be mass produced at low-cost are still very few on the market.

We propose to commercialize a novel and affordable proteomic sensor system for rapid disease detection, diagnosis and therapy by leveraging the existing technical strengths in BioMEMS and polymer/biomaterial engineering at the Ohio State University. Product development and commercialization will be carried out by the start-up company, BioLOC focusing on a fully automated Compact Disc (CD)-Enzyme-Linked ImmunoSorbent Assays (ELISA) protein detection and diagnosis system for a combined US market of over $1B annually. OSU medical center will perform clinical testing for analysis and comparison of conventional and CD-ELISA technologies. OSU's Center for Entrepreneurship and the Technology Entrepreneurship and Commercialization Institute will provide business support and business project management for the proposal team. BioOhio, located at TechColumbus, will also support integration of BioLOC into the emerging Ohio biotechnology market.

This disc-like biochip system is built on patented nanobiotechnology platforms developed in the Center for Affordable Nanoengineering of Polymeric Devices (CANPBD) at OSU. The CD based immunoassay chips are a joint project with several Ohio and non-Ohio companies including world largest CD producer, RITEK. BioLOC has developed the total instrumentation, including an inexpensive CD-ELISA chip and a highly automated analyzer. For this system, the proposed research and commercialization efforts will focus on ß-testing at OSU's Medical School and Hospital, and further data generation for both non-clinical and clinical applications with the ultimate goal of pushing these products close to market entry.

In summary, a multidisciplinary collaboration with OSU and Ohio and non-Ohio biotechnology companies will allow BioLOC to convert a number of 'demonstrating to market entry' technologies into new products for the >$2B/yr. well-defined medical and pharmaceutical device markets, and facilitate job creation in Ohio.

University Hospitals
Case Medical Center

CASE WESTERN RESERVE UNIVERSITY EST. 1826

January 24, 2010

The Research and Commercialization Program
The Ohio Department of Development
Technology Division
77 South High Street, 25th Floor
Columbus, OH 43215
OTFBP2010@development.ohio.gov

RE: 2010 Research Commercialization Program Letter of Intent

To Whom It May Concern:

Through this Letter of Intent, we wish to inform the Technology Division of The Ohio Department of Development of our planned application for support through The Ohio Third Frontier Biomedical Program. The proposal, described in brief in the attached summary, represents a unique opportunity that will leverage an existing international partnership and facilitate growth of a new Ohio-based industrial partner whose mission will be the commercialization of shared technologies. This program will bring recognition to The Third Frontier Commission through a successful new initiative in regenerative medicine that aims to bring lead molecules from bench to bedside, while establishing a commercialization path for novel agents currently under development. This initiative is currently titled "The Case-Korean Consortium for Regenerative Therapeutics", for which the partnering academic and commercial institutions will request $1.0 million in grant funds that will be exceeded by matching investments through participating organizations. We greatly appreciate your consideration.

The Applicant Organization is:

Case Western Reserve University
School of Medicine
1900 Euclid Avenue
Cleveland, OH 44106-4904

Point of Contact (POC):
For proposal related matters

John J. Letterio, M.D.
(Lead Applicant)
The Jane & Lee Seidman Chair in Pediatric Cancer Innovation / Professor of Pediatrics
Rainbow Babies & Children's Hospital
Case Western Reserve University
Cleveland, Ohio 44106
Phone (216) 844-3345
Fax: (216) 844-5431
e-mail: john.letterio@case.edu

The Case - Korean Consortium for Regenerative Therapeutics

Case Western Reserve University (CWRU), University Hospitals Case Medical Center and their Korean-based partner Regulon Pharma will leverage their expertise in fundamental cell biology, medicinal chemistry, developmental therapeutics, and clinical medicine to benefit patients throughout Ohio and globally through the development of novel regenerative therapeutics that promote wound healing through stimulation of angiogenesis and resolution of inflammatory disease. The effort capitalizes on the known linkages between wound healing and inflammation by design, development and commercialization of novel agents that target molecular pathways central to these disorders.

This effort will capture distinction as a new initiative for the Research and Commercialization Program, and capitalize on the investments of both regional institutions and an international collaborator in the discovery, preclinical development and commercialization of novel agents protected through patents that cover composition of matter and methods of use. The opportunity is timely, focused on untapped new drug discoveries and a select number of novel compounds that are ripe for commercial development. The collaborative effort engages a Korean-based industrial partner, who through the establishment of an Ohio-based for-profit affiliate, will engage the Ohio-based academic institutions in the initiation and conduct clinical trials. This effort is focused squarely on the demonstration of clinical utility and aims to advance agents to the IND stage and to secure FDA approval for the introduction of these novel agents into clinical practice. The disease areas targeted by the designated therapeutics include conditions with delayed wound healing, including cancer and chronic inflammatory disease (diabetes, vasculitis, arthritis, inflammatory bowel disease, psoriasis) and related areas in which the participating clinical center (University Hospitals Case Medical Center) ranks among the best in the United States.

The principal projects in this proposal place a high priority on late stage pre-clinical and early clinical applications of novel agents / emerging technologies. Individual projects are each anchored by a strong partnership between the academic and commercial teams of investigators who together will design, develop and demonstrate the clinical utility of novel agents with well-defined benchmarks and commercialization strategies that ensure the establishment of new commercial ventures and jobs in Ohio.

Collaborating Institutions:

Academic Medical Centers
Case Western Reserve University
University Hospitals of Cleveland
Rainbow Babies & Children's Hospital
Lee Gil Ya Cancer and Diabetes Research Institute (Inchon, Korea)

Commercial / Industry Partners
(preliminary list)
Regulon Pharma (Inchon, Korea)
Regulon-Ohio (anticipated affiliate)
Ricerca (Concord, Ohio)

Phone: 513-985-1920
Fax: 513-985-0999

www.akebia.com

Akebia Therapeutics, Inc.
10300 Alliance Road
Suite 510
Cincinnati, OH 45242

Company: Akebia Therapeutics, Inc., 10300 Alliance Rd., Suite 510, Cincinnati, Ohio 45242

Contact: Robert Shalwitz, MD, Sr. Vice President and Chief Medical Officer

Email: rshalwitz@akebia.com

Phone: 513-985-1922

Title: Novel Therapeutics for Topical Therapy of Acute and Chronic Infections and Wounds

Amount Requested: $750,000 over two years

Collaborators: TBD

Akebia THERAPEUTICS

Phone: 513-985-1920
Fax: 513-985-0999
www.akebia.com

Akebia Therapeutics, Inc.
10300 Alliance Road
Suite 510
Cincinnati, OH 45242

Summary:

Akebia Therapeutics, Inc. is a venture capital backed pharmaceutical development company, founded in 2007 and located in Cincinnati, OH. Its primary intellectual property was licensed from Proctor and Gamble Pharmaceuticals (Cincinnati, OH). Since its founding, Akebia's scientists and collaborators have substantially extended the potential for the original P&G compounds. Though Akebia has venture capital to pursue its two primary programs (anemia and vascular stabilization), it is seeking additional capital to continue its wound healing program. This topical therapeutic program will utilize several of Akebia's novel compounds to help treat complex acute and chronic wounds due to infection (particularly MRSA), vascular compromise, diabetes, trauma, and immune suppression. Although other Akebia programs may be licensed to large pharmaceutical companies for final development and marketing, Akebia intends to fully develop and market its wound healing programs so that it will become a **self-sustaining company in the State of Ohio**.

The foundation of this proposal is based on the transcription factor hypoxia inducible factor-1 (HIF-1) as a master regulator of host innate immune function. HIF-1 is induced by bacterial infection and regulates the production of key immune effector molecules including granule proteases, antimicrobial peptides, nitric oxide and proinflammatory cytokines such as TNF-α. This in turn regulates the inflammatory and broad-spectrum bactericidal capacities of macrophages and neutrophils.

The bactericidal capacity of the phagocytic cells can also be augmented through pharmacologic targeting of HIF-1. Therefore, rather than designing drugs to target the bacteria, medications that promote HIF-1 activity could be used to boost the natural immune defenses and the bacterial killing ability of white blood cells to promote resolution of infection. The highly potent HIF-1 agonist AKB-4924, which works through the inhibition of prolyl-hydroxylase, is a doubly innovative therapy with the pharmaceutically induced boost in HIF-1 enhancing both bactericidal activity as well as promoting wound healing.

HIF stabilizing drugs accelerate wound closure through promotion of vascularization and wound healing. In a diabetic mouse model of chronic wounds, stabilization of HIF-1 improved several parameters of the wound healing process (granulation, vascularization, epidermal regeneration, and recruitment of endothelial precursors). In a normal mouse skin puncture wound model, the HIF agonist AKB-6548 (orally available HIF-1 and HIF-2 agonist) demonstrated significantly improved rate of wound healing.

In addition to the HIF stabilizing compounds, Akebia has a large series of vascular stabilizing compounds that will promote revascularization of acute and chronic wounds without inducing systemic changes.

Therefore, the goal of this program is to integrate and develop the array of Akebia's compounds for the many varieties of infections, wounds (acute and chronic), and injuries that are treatable through topical therapy. The potential markets for topical therapeutics are vast, with some requiring relatively short and comparatively inexpensive development programs. Akebia will initially target short term programs to enable ongoing income to support continued research, marketing and general operations.

OTFBP 10-823

January 22, 2010

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

To Whom It May Concern:

This is a Letter of Intent for submission of a proposal for Ohio Third Frontier Funding for Fiscal Year 2010. The application information is as follows:

NitAn Biotech, LLC
Srikanth Vedamoorthy, PhD, President, Founder, and Chief Scientific Officer
1381 Kinnear Road
Columbus, OH 43212
614-893-3137
Contact: Joshua Young, Business Strategy Manager
614-746-8098
Josh@NitanBiotech.info

Project: Development of Antibodies to Detect Redox Modulated Proteins
Estimated Funds Requested: $250,000.00
Project Summary: Attached

Sincerely,

Srikanth Vedamoorthy, PhD, President, Founder, and Chief Scientific Officer

NitAn Biotech LLC currently provides custom products to researchers at academic institutions, research firms, biotechnology companies, and pharmaceutical companies. Our proposed project is the development of unique antibodies that detect redox modulated proteins. The first one that we will develop is an antibody to detect S-nitrosylation (SNO-P). S-nitrosylation is a factor in the regulation of post-translational modification in almost all major classes of protein, meaning it has relevance to research in many major diseases such as atherosclerosis, hypertension, carcinomas, and diabetes. The other antibody that NitAn Biotech is developing detects Protein S-Glutathiolation (PSSG). PSSG is a post-translational modification that involves the conjugation of glutathione to protein cysteine residues which is the critical mechanism of redox based signalling. Levels of both proteins, PSSG and SNO-P, increase under conditions of oxidative stress, and detecting these reactive groups that are modified will be a key in identifying the oxidation of specific proteins in order to intervene early in disease processes to prevent further damage. The antibodies that we are developing should be ready for market within a few months and will be a key tool for researchers. They will be a breakthrough for research in cardiovascular and other disease types.

Another part of our business development will be the production of unique, disease based, biomarker antibody sampler kits for cardiovascular research. These tools are critical to research for the treatment of heart failure and other vascular diseases that can lead to serious heart complications such as stroke and atherosclerosis. In the market today, antibodies are sold individually, but our sets will contain smaller quantities of five to eight selected antibodies to monitor the expression and post translational modifications of five to eight proteins that are critical to a particular disease state or pathway. Our purification methods ensure the highest quality of these antibodies, and the availability of these antibodies in the specific sets will improve research efficiency by targeting critical proteins for a particular disease type at once. We will also add the new antibodies that we are developing to these kits.

The tools that we are developing will accelerate the study of critical disease state and cell function pathways. The detection of redox modulated proteins facilitates understanding of the processes of redox that are occuring early in disease processes,allowing earlier intervention and the prevention of further damage. Thiol dependent redox systems are involved in the regulation of diverse biological processes, like response to stress, signal transduction, and protein folding. The roles of thiol redox control in cardiovascular diseases, inflammatory diseases, aging-related diseases like Parkinson's and Alzheimer's disease and other pathophysiological processes have also been described.

Both of these novel antibodies will open the door to unraveling the functional significance of PSSG/SNO-P in human diseases where changes in redox balances have been documented.

The funds that we are seeking will be used for:

- Antibody materials, consumables, and reagents for the research and development of the new antibodies
- Science personnel to assist in the research and development
- The establishment of expanded facilities
- Equipment for the facilities
- Hiring of additional lab personnel

Ohio Third Frontier Biomedical Program - FY 2010
Letter of Intent

Lead Applicant:

ChanRx Corporation
14656 Neo Parkway
Cleveland, OH 44128
Phone: 216-332-1665
Fax: 216-332-1706
Contact: Arthur M. Brown, M.D., Ph.D.
E-mail: abrown@chantest.com

Proposed Project Title:

New Technologies for Discovering Cardiovascular Drugs

Estimated Grant Funds Requested:

$1,000,000 over two years

Known Collaborators:

Ricerca Biosciences, LLC, Concord, OH

Summary:

ChanRx is a Cleveland-based drug discovery company focused on the need for discovering new drugs to treat common cardiovascular (CV) diseases such as cardiac arrhythmias and congestive heart failure. *ChanRx* executes its strategy in three novel ways. First, *ChanRx* repurposes drugs that have been successful in Phase 1 clinical trials for diseases of non-CV systems but have been suspended, discontinued or withdrawn for lack of efficacy or commercial success. The most important advantage of repurposing is the shortcut to Phase 2a proof of concept clinical trials bypassing the many years and expenses required before first in man studies. Second, ion channels are major targets for arrhythmias, heart failure, hypertension and other CV diseases and *ChanRx* screens libraries of repurposed drugs against the world's largest library of ion channel-expressing cell lines. Repurposed drugs that block or activate ion channels linked to CV disease by channelopathies or off-target effects but not heretofore considered as therapeutic CV targets are quickly identified and a mechanism of action hypothesized. Third, *ChanRx* does its secondary screens using stem cell-derived human cardiomyocytes (HESC-CMs) and human vascular smooth muscle cells to initially validate the proposed mechanism of action. .Thus, the present proposal is pertinent to both CV medicine and a practical application of regenerative medicine to drug discovery, two of the preferred subjects for the present RFA. The remaining step before the proof of concept Phase 2a clinical trial is a test of the hypothesis in an animal model of the disease. *ChanRx* has used its program to develop vanoxerine which has completed a successful Phase 2a trial for atrial fibrillation. *ChanRx* is considering a Term Sheet from a specialty pharmaceutical company for this drug or spinning it out as a stand-alone company. A west coast VC is in the process of submitting a Term Sheet for funding the Vanoxerine Development Company. A second antiarrhythmic drug is about to go into humans overseas. Two additional drugs for CV indications have been identified. With award of the present proposal, *ChanRx* will advance drugs already in its pipeline, add new drugs to its pipeline, be in a strong position to partner with big Pharma companies and their extensive repurposing libraries, and become a major Ohio born and bred pharmaceutical company. *ChanRx* leads this OTFBP and its Ohio partner is Ricerca Biosciences, a company that is well-known for its expertise in IND-enabling services. Ricerca will provide medicinal chemistry, manufacturing and animal model support to the proposal. We expect that the two businesses will add hundreds of high-paying jobs for citizens of Ohio.

LANX

OTFBP 10-825

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

January 20, 2010

Dear Ohio Department of Development:

Thank you for the opportunity to submit this letter of intent for the Fiscal Year 2010 Ohio Third Frontier Biomedical Program ("OTFBP").

Lead Applicant Name:	Lanx, Inc.
Address:	390 Interlocken Cresent, Suite 890 Broomfield, CO 80021-8053
Telephone:	(303) 443-7500 x8482
Contact Person:	Mr. Stuart Born, Director of Clinical Studies
Contact Email:	stuart.born@lanx.com
Project Title:	Lumbar Motion Monitor Commercialization in Ohio
Estimated Grant Amount:	$1,000,000
Known Collaborators:	The Ohio State University and others to be determined

Summary of the Proposed Project:

Lanx, Inc. ("Lanx") was founded in 2003 by two physicians who created a patient focused culture of quality and innovation. As one of the largest privately held spinal companies in the U.S., Lanx is committed to providing spine surgeons innovative solutions for the challenges they face every day. Lanx proposes to culminate over 25 years of research and development by commercializing a diagnostic medical device in Ohio capable of quantifying the extent of a low back disorder by monitoring the motion functional characteristics (kinematic signature) of a patient's low back. This Lumbar Motion Monitor ("LMM") device provides a quantifiable functional assessment of lumbar spine disorders.

Lanx, Inc. will continue its partnership with the Biodynamics Laboratory at Ohio State University to commercialize the Lumbar Motion Monitor (LMM). The objective of the proposed OTFBP project is to move this innovative technology from the laboratory to the clinical environment to help clinicians more accurately diagnose low back pain. A more accurate diagnosis by physicians earlier in the clinical workup will result in fewer diagnostic medical scans and unnecessary surgeries. This will help reduce the extremely high cost associated with the treatment of lower back pain.

The LMM is a non-invasive device that a patient wears on a harness that takes measurements of the lumbar spine in motion. These spine motions represent a "motion signature" of the patient and this signature is believed to represent a "proxy" of important functional information relating lumbar spine functional status. The LMM has extensive scientific backing with over 40 peer reviewed journal articles to support its capabilities, including:

- Quantifying the extent of a low back disorder;
- Indicate the probable nature of the low back disorder (structural or muscular);
- Identifying need for further more expensive follow-up tests (e.g. MR imaging);
- Quantifying treatment success or failure and indicating when maximal medical improvement has been achieved; and
- Determining a patient's sincerity of effort.

When the kinematic signature is combined with the spine model under development by the OSU Biodynamics Laboratory, it will provide a surgeon with information never before available. The combination of these two projects will allow surgeons to conduct surgery 'in silico' and provide them with patient specific biomechanical information to aid in their decision process to determine the best surgical option for their patient. Lanx has the

exclusive rights to commercialize both the LMM and the spine model. Lanx is requesting a $1,000,000 OTFBP grant to bring the device to full commercialization in the State of Ohio. Taken together, OTFBP and match funding will:

- Test and validate of the production version of the LMM;
- Achieve LMM FDA approval;
- Establish a fully staffed Lanx diagnostic division in Columbus, Ohio;
- Create marketing, sales and business development to support a formal product launch;
- Establish production capabilities; and
- Develop backend software systems to support both the interpretation and presentation of the LMM data and support company operations.

Collaboration with the OSU Biodynamics Laboratory provides Lanx with the engineering research expertise and investigations of low back pain causality that are essential to understanding the cause of low back pain. The OSU team provides a systems perspective which includes factors such as the occupational cause and the effect of muscle activity on spine loading.

Building upon a strong foundation of experience and knowledge in the biomedical sector, Lanx will successfully develop and commercialize a novel LMM device. The project aligns with the purpose, goals and objectives of the OTFBP. This project will benefit Ohio's robust biomedical cluster and generate continued technology based economic development throughout Ohio.

Sincerely,

Stuart Born
Director of Clinical Research
Lanx, Inc.

OTFBP 10-826

Accord Biomaterials
Delivering Biocompatibility

Accord Biomaterials Inc.
3550 West Liberty, Suite 3
Ann Arbor, MI 48103

phone: 734.995.9089
fax: 734.995.0840
www.accordbiomaterials.com

January 25, 2010

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

Re: Ohio Third Frontier Biomedical Program Letter of Intent for Proposal 'Point-of-Care Diagnostic for Pulmonary Hypertension'

Dear Ohio Department of Development:

Accord Biomaterials is pleased to submit this Letter of Intent for the 2010 Ohio Third Frontier Biomedical Program for Proposal 'Point-of-Care Diagnostic for Pulmonary Hypertension'. Requested information is provided below:

Lead Applicant Name:	Accord Biomaterials, Inc.
Lead Applicant Address:	3550 W. Liberty, Suite 3, Ann Arbor, MI 48103
Lead Applicant Phone Number:	734-995-9089 x229
Contact Person:	Kristyn R. Aalto, President
Contact Person Email:	kaalto@accordbiomaterials.com
Proposed Project Title:	Point-of-Care Diagnostic for Pulmonary Hypertension
Estimated Grant Funds Requested:	$1,000,000
Known Collaborators:	SNS Nano Fiber Technology, Akron, OH The Cleveland Clinic Z-Tech Scientific, San Jose, CA Manufacturer to be selected from Ohio candidates Frantz Medical, Valtronic and Parker Hannifin

The proposal summary is provided on the following page. Please contact me with any questions or concerns. I will await receipt of the proposal identification number.

Sincerely,

Kristyn R. Aalto
President
Accord Biomaterials, Inc.

Summary:

Abstract: The goal of this proposal is to develop and validate a non-invasive diagnostic for pulmonary hypertension using Accord Biomaterials, Inc.'s ('Accord's') proprietary Nogen™ *S*-nitrosothiol (RSNO) sensing system, resulting in a practical, point-of-care tool for clinical diagnostic applications. RSNO's are a primary carrier and reservoir of nitric oxide (NO), a critical cardiovascular signaling and regulation molecule, *in vivo* and are a potential *pre-symptom* marker for hypertensive disorders, endothelial dysfunction, cardiovascular risk and inflammation. RSNO concentration in blood has already been established as an early, independent and statistically-significant predictor of mortality from cardiovascular events in a prospective clinical study[1]. RSNO concentration in breath exhalates has also been quantitatively linked to the pulmonary arterial pressures which indicate and classify pulmonary hypertensive disease state[2]. Pulmonary hypertension—and the differentiation of *primary* pulmonary hypertension (also called pulmonary arterial hypertension, PPH or PAH) from elevated pulmonary arterial pressures secondary to left-heart disease—is currently diagnosed only via right heart catheterization with its inherent costs, risks and lack of widespread access to symptomatic patients early in the diagnosis algorithm. However, the clinical significance of endogenous RSNO levels cannot be fully realized without a quick and convenient assay for RSNO's. Compared to existing RSNO assay techniques, the proposed electrochemical RSNO sensor is highly sensitive and selective, free from nitrate interferences, is capable of rapidly measuring RSNO's in blood without separation or pretreatments and is suitable for simple and robust point-of-care use as a clinical diagnostic. A novel catalytic sensor will be developed and validated in collaboration with SNS Nano Fiber Technology, LLC ('SNS') in Akron, OH, the Cleveland Clinic and Z-Tech Scientific ('Z-Tech') in San Jose, CA. The system is slated for a clinical trial in 2011 to be led by Raed Dweik, MD, Director of the Cleveland Clinic's Pulmonary Vascular Program and for FDA 510(k) clearance in 2013.

Commercial Rationale and Opportunity: PAH, a terminal cardiovascular disease, affects well over 200,000 patients throughout the world and pulmonary hypertension impacts more than 460,000 U.S. hospital visits annually[3,4]. Disease experts and health authorities largely agree that the costs and risk of complication associated with heart catheterization significantly limit diagnostic detection efforts and therefore ***reported prevalence figures are grossly understated.*** Accord's RSNO sensor diagnostic could be integrated into the evaluation of patient groups with high risk for PAH and could be used as a precursor or replacement to improve outcomes over those with more costly, invasive, and non-confirmatory tests. Therapeutics marketed or under investigation for PAH, including Pfizer's Revatio and Actelion's Tracleer and Ventavis, are projected to represent a $2B market by 2014[5] and are well-positioned for companion diagnostics that allow optimized medical management.

Specific Aims of Third Frontier Funding: Program proceeds of approximately $1,000,000, along with matching Accord and partner cost share, fund the three-year program to bring the diagnostic to market via the FDA 510(k) clearance pathway. It is expected that roughly $900,000 of the requested funding will go toward operational costs while the remaining $100,000 will go toward capital equipment acquisition and/or improvements. This will include the opening of Accord's Akron, OH engineering office to leverage the efficiency of Accord's working relationships with SNS, the Cleveland Clinic and candidate manufacturing partners such as Frantz Medical, Valtronic, Parker Hannifin and others within the greater Cleveland region. Collectively this program will introduce a needed cardiovascular tool to the market that can improve the outcomes of millions, reduce healthcare system costs and increase Ohio's medtech jobs base through both Accord's relocation to and expansion in Ohio and increased work volume for partner companies already established within Ohio.

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[1]Massy, ZA et al, 'Increased Plasma S-Nitrosothiol Concentrations Predict Cardiovascular Outcomes among Patients with End-Stage Renal Disease: A Prospective Study,' *J Am Soc Nephrol* 15: 470-476, 2004.

[2]Kaneko et al, 'Biochemical Reaction Products of Nitric Oxide as Quantitative Markers of Primary Pulmonary Hypertension,' *Am J Resp Crit Care Med* 158: 917-923, 1998.

[3]Agency for Healthcare Research and Quality. Online. www.changehealthcare.com. 2009.

[4]Frost and Sullivan. US Pulmonary Arterial Hypertension Markets. December 2006.

[5]Datamonitor, 2006.

OTFBP 10-827

Accord Biomaterials
Delivering Biocompatibility

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January 25, 2010

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

Re: Ohio Third Frontier Biomedical Program Letter of Intent for Proposal 'Smart Materials for Cardiovascular Devices that Reduce Clotting, Infection and Vascular Narrowing'

Dear Ohio Department of Development:

Accord Biomaterials is pleased to submit this Letter of Intent for the 2010 Ohio Third Frontier Biomedical Program for Proposal 'Smart Materials for Cardiovascular Devices that Reduce Clotting, Infection and Vascular Narrowing'. Requested information is provided below:

Lead Applicant Name:	Accord Biomaterials, Inc.
Lead Applicant Address:	3550 W. Liberty, Suite 3, Ann Arbor, MI 48103
Lead Applicant Phone Number:	734-995-9089 x229
Contact Person:	Kristyn R. Aalto, President
Contact Person Email:	kaalto@accordbiomaterials.com
Proposed Project Title:	Smart Materials for Cardiovascular Devices that Reduce Clotting, Infection and Vascular Narrowing
Estimated Grant Funds Requested:	$1,000,000
Known Collaborators:	SNS Nano Fiber Technology, Akron, OH University of Akron Polymer Science Battelle Manufacturer to be selected from Ohio candidates including Frantz Medical and Parker Hannifin

The summary is provided on the following page. We await receipt of the proposal identification number.

Sincerely,

Kristyn R. Aalto
President
Accord Biomaterials, Inc.

Summary:

Abstract:

The goal of this proposal is to develop and validate a family of smart, biomimetic polyurethanes for vascular devices using Accord Biomaterials, Inc.'s ('Accord's') proprietary Nogen™ nitric oxide (NO) materials technology. Nogen technology utilizes nitric oxide to reduce clotting, tissue overgrowth and potentially infection on and around implanted devices in contact with circulating blood. Nitric oxide's critical health role was recognized by the 1998 Nobel Prize in Medicine; this work proved that nitric oxide was the critical signaling molecule known as endothelium-derived relaxing factor (EDRF) that regulates many aspects of vasodilation and blood pressure, vascular narrowing and healing, infection control, platelet activity and clotting response. Mark Meyerhoff *et al* at the University of Michigan invented the Nogen technology as a practical way to generate nitric oxide locally on a medical device surface. The Nogen technology is unique in that it catalyzes the in vivo production and release of nitric oxide in the same manner and concentration delivered by native vascular endothelium (blood vessel cells). Nogen active sites can be incorporated into common medical device materials, such as polyurethane, and are compatible with standard fabrication and sterilization processes--unlike previous attempts to harness nitric oxide for medical device applications. A novel family of implant-grade polyurethanes with Nogen NO technology will be developed and validated in collaboration with SNS Nano Fiber Technology, LLC ('SNS') in Akron, OH, the University of Akron, Battelle and a manufacturer to be selected from Ohio candidates such as Parker Hannifin and Frantz Medical.

Commercial Rationale and Opportunity:

Smart biomaterials incorporating the Nogen technology have wide applicability across many growing medical device markets—prime candidates include vascular stents, grafts, catheters and intravascular blood analyte monitors—representing over $5 billion in annual sales. The medical device coating market itself is worth $3 billion. ***The inherent financial value in smart Nogen biomaterials arises from the ability to deliver a desired biological response for significantly improved cardiovascular device performance without embarking on a costly and extended pharmaceutical or biologics development program.*** Several Nogen applications have a desirable 510(k) path to FDA clearance. Specifically, Accord is well-positioned to be the first company to bring a biomimetic, nitric oxide material to clinical utilization.

Specific Aims of Third Frontier Funding:

Program proceeds of approximately $1,000,000, along with matching Accord and partner cost share, fund the two-year program to bring the smart materials to commercialization through an Ohio-based manufacturing partner. It is expected that roughly $900,000 of the requested funding will go toward operational costs while the remaining $100,000 will go toward capital equipment acquisition and/or improvements. This will include the opening of Accord's Akron, OH engineering office to leverage the efficiency of Accord's working relationships with SNS, the University of Akron and candidate manufacturing partners such as Frantz Medical, Parker Hannifin and others within the greater Cleveland region. In total this program will introduce sought, biomimetic materials for critical cardiovascular devices that can improve the outcomes of millions of patients, reduce healthcare system costs and increase Ohio's medtech jobs base through both Accord's relocation to and expansion in Ohio and increased work volume for partner companies already established within Ohio.