

## SpineMatrix Ohio Third Frontier Biomedical Program Grant Letter of Intent

Lead Applicant: SpineMatrix, Inc.  
4480 Lake Forest Drive, Suite 412  
Cincinnati, OH. 45242

Contact Information: Timothy G. Biro, Chief Technology Officer  
Mobile: 216-533-3082  
Email: [Tbiro@spinematrix.com](mailto:Tbiro@spinematrix.com)

Project Title: Development and Commercialization of Disposable Array for Diagnosis of Upper Back and Shoulder Pain

SpineMatrix intends to apply for \$1,000,000 from the Biomedical program Ohio Third Frontier grant, to develop and commercialize a disposable array to aid the Physician in the diagnosis and prognosis of upper back pain and shoulder pain. The array will be used in combination with the FDA 510k cleared SpineMatrix CERSR<sup>®</sup> (Computerized Electrophysiological Reconstruction of the Spinal Regions) hardware and software. The \$1,000,000 grant will support the product design of the array, development of prototypes for clinical testing, clinical testing of the array, software enhancements to use the array on the CERSR<sup>®</sup> platform, and modifications to the manufacturing operation for array production. The timeline to complete the above is estimated at 24 months; SpineMatrix will seek FDA 510k approval upon completion of the clinical trials, and SpineMatrix anticipates initial sales within 30 months of grant award.

SpineMatrix is the commercialization partner for this grant application. Potential collaborators include University of Akron for biomedical engineering expertise (product design and conductive gel for array,), Akron Children's Hospital (Dr. Joseph Congeni, confirmed) for product design and clinical evaluation of the array, Nordson Corporation (confirmed) for manufacturing line modifications, and Austen BioInnovation Institute (preliminary discussions) for clinical trial studies. The \$1,000,000 grant will be matched by \$1,000,000 in a blend of cash from SpineMatrix, and support and in-kind from the collaborators.

This grant will enable SpineMatrix to have a second product to complement out initial array for aiding the Physician in the diagnosis of low back pain. Upper back / neck and shoulder pain are very common medical disorders in the United States. More than 1 million cervical sprain and strain injuries occur annually due to whiplash, and more than 4 million Americans seek medical treatment for shoulder problems. Primary market research indicates that 20-25% of shoulder pain is related to upper back injury, and diagnosis is often missed as a result. This grant will contribute to the development of an array that will aid the Physician in the diagnosis, resulting in better treatment and therefore better clinical outcomes, lowering the cost of medical care to society.

The grant will have significant economic impact, creating additional engineering and manufacturing jobs, and attracting additional investment capital to SpineMatrix, an Ohio-based company.



# 11-502

December 7, 2010

FY 2011 Ohio Third Frontier Biomedical Program (OTFBP)  
Ohio Department of Development  
Technology and Innovation Division  
77 South High Street, 25th Floor  
Columbus, OH 43215

This **Letter of Intent (LOI)** is provided by the University of Toledo in anticipation of a proposal for the FY 2011 Ohio Third Frontier Biomedical Program (OTFBP).

**1. Lead Applicant Contact:**

Dr. Krishna Shenai, Professor  
Electrical Engineering and Computer Science Department  
MS 308, 2801 W. Bancroft Street  
The University of Toledo  
Toledo, OH 43606-3390  
TEL: (419) 530-8144; FAX: (419) 530-8146  
E-MAIL: [krishna.shenai@utoledo.edu](mailto:krishna.shenai@utoledo.edu)

**2. Project Title:** Minimally Invasive Spinal Surgical (MISS) Robot

**3. Budget Request Estimate:** \$1,000, 000 from Third Frontier &  
\$1, 000, 000 from Wright Capital Funds

**4. Lead Organization and Legal Structure of the Organization:** The University of Toledo is one of the nation's leading research universities.

**5. Collaborating Organizations:** X-spine Systems, Inc., Miamisburg, OH 45342;  
Toledo Orthopaedic Surgeons, Toledo, OH 43615; Ohio Supercomputer Center,  
Columbus, OH 43212.

**6. Project Description:**

This project will commercialize our new minimally invasive spinal surgical (MISS) robotic concept [1] integrated with advanced imaging and tracking technologies. The robotic action is controlled in a closed-loop manner using the sensing and feedback signals obtained by real-time modeling of the spine on a high-performance computing platform. The technique employs accurate three-dimensional (3D) finite element (FE) spine modeling as the spine is being displaced or deformed by the robotic action. A prototype of this robotic surgical concept has been built and tested as functional; the system needs further improvement to be deployed in a surgical environment. In this project, a patient-specific spine model will be developed and integrated into Class II

College of Engineering

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419.530.8140 Phone • 419.530.8146 Fax • [eeecs@eng.utoledo.edu](mailto:eeecs@eng.utoledo.edu) • [www.eecs.utoledo.edu](http://www.eecs.utoledo.edu)

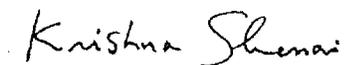
FDA approved robotic system to improve the accuracy of robotic movement; and, the speed of control of the robot will be dramatically improved by reducing data transmission time, by using improved model reconstruction methods, and by using improved markers in order to render this surgical concept practical. An *in situ* spine imaging technology will be integrated in order to provide additional flexibility and greatly enhanced surgical accuracy.

This project brings together diverse yet overlapping interests and expertise of an electrical and computer engineer, an orthopedic biomechanical engineer, a practicing spinal surgeon, and a commercialization entity for exploring new methods to facilitate rapid development of a robust intelligent spinal robotic surgical system. The overall research builds on a cyber platform that integrates (i) advanced imaging and computer modeling; (ii) line-of-sight ultrasonic tracking and position monitoring; and (iii) real-time control and precision-guidance of the robot. The two most important intellectual contributions of the research include a new integrated hardware (*e.g.*, demonstration of a complex, intelligent, adaptive, surgical robotic system) and software (*e.g.*, accurate patient-specific 3D spine modeling using real-time, line-of-sight tracking and imaging of the spine).

With the advent of computing and design tools, it is now possible to integrate high-performance computers in a closed-loop system, perform real-time modeling of complex objects, and remotely navigate robotic systems with high degree of precision. The proposed surgical robotic system has the potential to significantly advance the current state-of-the-art of spinal surgery as it reduces the patient trauma and cost of surgery, and minimizes radiation exposure to the personnel in the surgical operating room. The same concept can be extended to perform other types of surgeries and to increase the efficiency of manufacturing operations and surveillance/detection functions.

[1] B. R. Lilly, K. Shenai, V. Goel and A. Biyani, "Robotic Surgical System Utilizing FE Model Coupled with Ultrasonic Tracking," in *Proceedings of 2010 IEEE International 53rd Midwest Symposium on Circuits and Systems*, Seattle, WA, August 1-4, 2010, pp. 997-1000.

Sincerely,



Krishna Shenai, Ph.D.  
Professor

# PerGenix, LLC

19 Stonemark Drive  
Henderson, NV 89052

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(702) 269-6527

Fax (702) 269-1596

December 10, 2010

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

**Subject: 2011 OTFBP LOI**

Dear Sir or Madam,

This Letter of Intent is being provided in response to the requirements set forth in Ohio Development's Request for Proposal (RFP) entitled "Ohio Third Frontier Biomedical Program" for fiscal year 2011. As specified in paragraph 1.3.3 of the referenced RFP, we are pleased to provide the following requested information.

1. **Lead Applicant:** PerGenix, LLC  
29 Stonemark Drive  
Henderson, NV 89052  
Note. Headquarters facility and R&D/clinical laboratory will be moved to Ohio; address yet to be undetermined.
2. **Phone Number:** (702) 269-6527
3. **Contact Person:** Robert Case, President and Chief Executive Officer
4. **Contact Person's Email Address:** [rcase@pergenix.net](mailto:rcase@pergenix.net)
5. **Title:** Integration of clinical laboratory controlled and physician monitored remote diagnostic testing for home monitoring of chronically ill patients and clinic based telemedicine.
6. **Estimated Funds to be requested:** \$1,000,000
7. **Planned Collaborators:** Sparton Medical Systems, Strongsville, OH (contract development and production of remote testing devices and network/lab software).
8. **Summary of Proposed Project:** (Page 2)

### ***The Problem***

Government and private entities in the US, Europe and Asia are searching for solutions to increase access to health care, facilitate timely and informed physician intervention and realize a reduction in total cost of care for their growing and aging populations.

- 21 million people visited 400 convenient care clinics at Wal-Mart, Walgreens and CVS-Caremark pharmacies in 2009 – AP
- Chronic disease home monitoring provides superior outcomes and reduced cost – CTO, Kaiser Permanente
- \$277B US chronic disease expenditures in 2008 – Milken Institute
- Developing regions do not have access to diagnostics and healthcare treatment – WHO

Diagnostic testing is employed more than 70% of the time as the first step in determining the need for medical treatment, eg. cardiac testing. However, professionally controlled and verified testing is only available in hospital or commercial laboratories, typically the least accessible and most costly venues for much of the world's population.

### ***The Solution***

PerGenix LLC was formed to more accurately and cost-effectively deliver lab-controlled diagnostic testing directly to patients and clinicians for rapid determination of the need for medical intervention and treatment. An estimated \$2.5B US market exists for a diagnostic information platform which is:

- **Patient-Driven** – Improved Access, Convenience & Compliance
- **Physician-Directed** – Improved Patient Management & Clinical Outcomes
- **Lab-Verified** for Professional QC, Interpretation & Reporting
- **Payer Approved** for Lower Initial & Long-term Cost

The PerGenix Remote Diagnostic Module & Software transforms standard computers & smartphones into remote diagnostic testing terminals. PerGenix delivers low cost, real-time diagnostic testing for the consumer home and professional diagnostics markets. The proprietary point-of-use diagnostic system connects testers to designated licensed clinical laboratories, treating physicians, Healthcare 2.0 databases and on-line EMS's anywhere in the world. Testing is analyzed, quality controlled, interpreted and reported by designated licensed clinical laboratories. The secure and HIPAA-compliant network will deliver immediate, lab-validated test results for healthcare screening, disease identification, disease monitoring and prognostics.

Strategic markets and partners include:

- State Telemedicine Programs
- Convenient Care Clinics
- HMO Home Chronic Disease Monitoring Programs
- Physician's Office Testing
- Employer Wellness Programs
- OTC Wellness Management



Phone: 513-985-1920

Fax: 513-985-0999

www.akebia.com

Akebia Therapeutics, Inc.

9987 Carver Road

Suite 420

Cincinnati, OH 45242

# 11-504

December 9, 2010

Ohio Department of Development  
Technology and Innovation Division, Attention: OTFBP  
77 South High St, 25<sup>th</sup> Floor  
Columbus, OH 43215-6130

To Whom It May Concern:

The following is our Letter of Intent regarding the Ohio Third Frontier Biomedical Program for fiscal year 2011.

**Lead Applicant:** Akebia Therapeutics, Inc.

**Address:** 9987 Carver Rd., Ste 420  
Cincinnati, OH 45242

**Telephone:** 513-985-1922  
513-226-9316 (cell)

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

**Email:** [rshalwitz@akebia.com](mailto:rshalwitz@akebia.com)

**Project Title:** A new therapeutic for severe attacks of ulcerative colitis

**Estimated Funding Request:** \$1,000,000

**Known Collaborators:** Charles River  
Medpace

**Project Summary:**

There are approximately 300,000 people diagnosed with ulcerative colitis (UC) in the U.S., with about 86,000 hospitalizations each year. Although mild or moderate forms of UC are manageable and do not impact mortality rate, about 15% of those diagnosed suffer from acute, very severe attacks of the disease. These attacks can be life-threatening and in 30% of the cases a colonectomy is required which can significantly reduce quality of life. The treatment for these severe attacks is a course of high dose corticosteroids – a treatment that has changed little since the 1950s. While the corticosteroids can be effective, about 15% of the patients are resistant to treatment, and there is a high incidence of corticosteroid-related adverse side effects. Other, less potent drug treatments have proven to be ineffective.

Akebia Therapeutics, Inc. has developed a small-molecule therapeutic, AKB-4924, that has demonstrated efficacy and minimal side effects in animal models of colitis. AKB-4924 has been shown to significantly reduce severity of colitis symptoms and reverse disease expression after treating animals with full-blown disease. Therefore, AKB-4924, as a fast-acting, non-steroidal drug, could prove to be an excellent first response to severe attacks of colitis in place of high dose corticosteroids.

Akebia is submitting this Letter of Intent to request funds for part of the research required to carry AKB-4924 through Investigational New Drug (IND) and Phase Ia, as required by the U.S. FDA. These funds will then be matched by money derived from venture capital and grants from the U.S. Department of Defense and the NIH. Together, they will provide Akebia with the means to complete IND enabling studies and initiate a Phase 1 clinical study with AKB-4924 within the next year and a half.

In the past three years Akebia has grown from four employees to seventeen, and has collaborated with many Ohio biomedical companies and institutions. Akebia will continue those practices with the AKB-4924 project by supporting more Ohio employment, working with Charles River in Spencerville, Medpace in Cincinnati, and other Ohio companies.

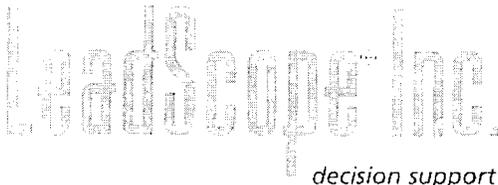
We look forward to working with the Ohio Third Frontier on this exciting grant proposal.

Sincerely,



Robert Shalwitz, MD

Sr. Vice President and Chief Medical Officer



**11-505**

December 10, 2010

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

Dear Sirs,

This letter is to express Leadscope's intent to submit an Ohio Third Frontier Biomedical Program proposal.

Lead applicant name: Leadscope, Inc.  
Address: 1393 Dublin Road, Columbus, Ohio 43215  
Phone number: 614 675 3768  
Contact person: Michael Conley  
Email: [mconley@leadscope.com](mailto:mconley@leadscope.com)  
Proposed title: Development of an integrated testing strategy for cardiac toxicity  
Estimated Grant Funds: \$1,000,000  
Known collaborators: ChanTest, U.S. Food & Drug Administration

A summary of the proposed project is attached.

Sincerely,

Michael Conley  
Chief Financial Officer

Cc: Glenn Kirsch, ChanTest

## **Development of an integrated testing strategy for cardiac toxicity**

It is essential that any chemical products with human exposure, such as drugs, do not cause cardiac toxicity, which includes adverse effects on the heart muscle, valves or production of arrhythmias. It is one of the major areas of concern in the development of new drugs as well as one of the main reasons drugs receive use-restrictions or are taken off the market. The industry's inability to identify and rectify these issues puts patients' lives at risk and costs the pharmaceutical industry billions of dollars every year in delayed product launches or withdrawals. In recent years, a number of new approaches have been developed, including in vitro and computer-based models. These approaches are able to screen large numbers of chemicals against molecular or cellular human cardiac safety targets at low cost. Leadscope and ChanTest are two Ohio-based companies at the forefront of this technology. Leadscope develops and markets toxicology databases and computer models including products developed in collaboration with the US Food and Drug Administration. ChanTest provides pre-clinical cardiac risk assessment services, including human ion channel and GPCR services (GLP and non-GLP), cell lines, membranes and reagents. Both companies will collaborate to develop a series of new products and services, including high quality cardiac toxicity databases and methods for predicting cardiac toxicity using a combination of computer models and in vitro testing. This will include the development of the most comprehensive cardiac toxicity database ever generated. This database will be data mined to understand relationships between pre-clinical indicators and adverse cardiac events in humans. Using these tools throughout research and development in the pharmaceutical, consumer products, and chemical industry as well in the regulatory process will increase the development of new products by allowing researchers to focus on the most promising candidates, as well ensuring safe products reach and stay on the market. This represents a significant commercial opportunity for both Leadscope and ChanTest. The projected revenue from these new products and services will allow Leadscope and ChanTest to create high-tech jobs in Ohio and solidify Ohio as a center of excellence on the forefront of advanced cardiac risk assessment.



Joe G. Hollyfield, PhD  
Lura and Gordon Gund Professor  
of Ophthalmology Research

December 10, 2010

Cleveland Clinic Foundation  
9500 Euclid Avenue  
Cleveland, OH 44195

The Ohio Department of Development  
Technology Division  
7 South High Street, 25<sup>th</sup> Floor  
Columbus, OH 43215

Project Title:

**“Drug Delivery & Clinical Research Testing Center”**

Grant Funds Sought:

**One Million Dollars (\$1,000,000)**

The Cleveland Clinic Foundation, along with its partners, is honored to provide this Letter of Intent for the 2011 Research Commercialization Program (RCP). Our initiative, entitled “Drug Delivery and Clinical Research Testing Center” intends to build upon the success of the BRCP “Age-related Macular Degeneration Initiative for Prevention and Cure” (AMD-*i*PAC) in order to achieve the goal of making northeast Ohio the premier site for integrated ophthalmology commercialization, research and service.

The individual initiatives covered in this grant request trace their roots to the success of the AMD-*i*PAC. These newly proposed programs expand the focus from AMD to include a wider range of ophthalmic diseases and multiple partners have also been added to our efforts including two start-up companies that were formed as a result of the AMD-*i*PAC. Finally, we will build on the research tools, biomarkers, genetic database and models created with the help of the AMD-*i*PAC and form a unique Clinical Research Testing Center in the vicinity of the Cleveland Clinic. This for-profit will offer ophthalmic focused contract research and services for preclinical studies, through phase IV clinical trials.

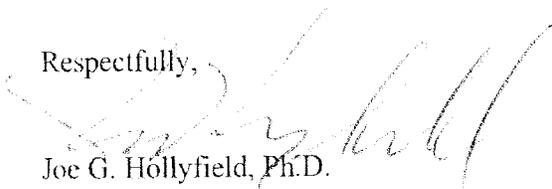
In this proposal, Buckeye Ocular and AngioQuest will collaborate to develop and commercialize the first non-invasively delivered therapeutic for age-related macular degeneration. Both Buckeye and AngioQuest have made significant progress in their commercial development. Buckeye has achieved this through a strategic collaboration with Parker Hannifin and AngioQuest through state supported Ohio Biovalidation Fund Support. At this stage the two companies are poised to join efforts on delivery of AngioQuest’s lead compound, TIMP3 for non-invasive drug delivery. We are confident

that IND approval will occur in the timeframe required by this proposal and 510k approval of the delivery device alone will be well within the first eighteen months of funding this project.

The program for contract research and services provides a good example of the business oriented focus of this application. In this model, a specialty contract research program will be set up using animal models, biomarkers, a genetic database and other research tools developed under AMD-iPAC. Ophthalmic industry leaders such as Genentech/Roche, Novartis, Merck, and Johnson and Johnson subsidiary Vistakon have already approached Cleveland Clinic about developing further relationships with such a center. This business model is efficient in that it leverages the Cleveland Clinic's current capabilities and allows for continued expansion and provides a high rate of return for future support.

In summary, this letter of intent by the Cleveland Clinic Cole Eye Institute serves as an affirmation of the State of Ohio's previous efforts to support technology-based economic development as well as an opportunity for Ohio to continue to grow this endeavor by supporting the proposal.

Respectfully,



Joe G. Hollyfield, Ph.D.  
Research Chairman  
Cole Eye Institute  
Cleveland Clinic Foundation

Contact information:  
Neema Mayhugh, Ph.D.  
Cleveland Clinic  
9500 Euclid Avenue  
Cole Eye Institute, i20  
Cleveland, OH 44195  
216-445-7176  
mayhugn@ccf.org

December 10, 2010

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

**Re: Ohio Third Frontier Biomedical Program Letter of Intent for Proposal 'Diagnostic and Therapy Monitoring Tool for Pulmonary Hypertension and Other Cardiovascular Diseases'**

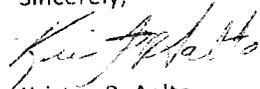
Dear Ohio Department of Development:

Accord Biomaterials is pleased to submit this Letter of Intent for the 2011 Ohio Third Frontier Biomedical Program for Proposal 'Diagnostic and Therapy Monitoring Tool for Pulmonary Hypertension and Other Cardiovascular Diseases'. Requested information is provided below:

Lead Applicant Name: Accord Biomaterials, Inc.  
Lead Applicant Address: 5703 N. Main St., Suite E, Sylvania, OH 43560  
Lead Applicant Phone Number: 419-517-7303 x202  
Contact Person: Kristyn R. Aalto, President  
Contact Person Email: kaalto@accordbiomaterials.com  
Proposed Project Title: Diagnostic and Therapy Monitoring Tool for Pulmonary Hypertension and Other Cardiovascular Diseases  
Estimated Grant Funds Requested: \$1,000,000  
Known Collaborators: The Cleveland Clinic, The University of Toledo, Battelle

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 primary 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 and therapy monitoring 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<sup>1</sup>. RSNO concentration in breath exhalates has also been quantitatively linked to the pulmonary arterial pressures which indicate and classify pulmonary hypertensive disease state<sup>2</sup>. 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 the Cleveland Clinic, Battelle, the University of Toledo and other to be determined collaborators. The system is already in a feasibility-phase clinical trial led by Raed Dweik, MD, Director of the Cleveland Clinic's Pulmonary Vascular Program and is slated for FDA 510(k) clearance in 2013. Program activities will also support follow-on development of preeclampsia and cardiovascular risk stratification products.

**Commercial Rationale and Opportunity:** PAH, a terminal cardiovascular disease and Accord's entry market, affects well over 200,000 patients throughout the world and pulmonary hypertension impacts more than 460,000 U.S. hospital visits annually<sup>3,4</sup>. 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 conventional, more costly, invasive, and non-confirmatory tests. Additionally, current invasive tests are rarely used for therapy monitoring due to their costs and risks. Therapeutics marketed for PAH represented a \$2.7B market in 2009 that is expected to reach \$3.6B by 2015<sup>5</sup>; these drugs are well-positioned for companion diagnostics that allow optimized medical management. Follow-on cardiovascular markets represent significantly larger commercial opportunities.

**Specific Aims of Third Frontier Funding:** Program proceeds of approximately \$1,000,000, along with matching Accord cash cost share and Series B venture capital investment, fund the three-year program to bring the diagnostic to market via the FDA 510(k) clearance pathway. Collectively this program will introduce a needed cardiovascular tool to the market that can improve the outcomes for millions of patients with PAH and other cardiovascular diseases, reduce healthcare system costs and increase Ohio's biomedical jobs base through both Accord's expansion in Ohio and increased work volume for partner companies already established within Ohio.

<sup>1</sup>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.

<sup>2</sup>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.

<sup>3</sup>Agency for Healthcare Research and Quality. Online. [www.changehealthcare.com](http://www.changehealthcare.com). 2009.

<sup>4</sup>Frost and Sullivan. US Pulmonary Arterial Hypertension Markets. December 2006.

<sup>5</sup>Globaldata, June 2010.



**11-508**

Ohio Third Frontier Biomedical Program  
Letter of Intent

December 10, 2010

Lead Applicant: NanoAxis, LLC  
626 North French Road, Suite #5  
Buffalo, NY 14228  
716.908.2392

Contact: Dr. Krishnan Chakravarthy, PhD  
[krishnan.chakravarthy@nanoaxisllc.com](mailto:krishnan.chakravarthy@nanoaxisllc.com)  
716.908.2392

Project Title: Project 11

Grant Funds Requested: \$1,000,000

Summary of Proposed Project:

In 2008, Dr. Krishnan Chakravarthy, PhD formed NanoAxis as a University of Buffalo spin-off company to pursue the commercialization of nanoparticles (i.e. quantum dots). NanoAxis mission from inception has been to develop nanomaterials for nanomedicine applications. Our long term goal is to provide nanomaterials for biomedical applications and to deliver high-quality, cost-competitive nanomaterial-based products to the medical, research, and general population.

The projected market for the nanomedicine sector within the nanotechnology market space is 6.8 billion dollars as last assessed in 2006. Of this, 5.4 billion dollars rests on the drug delivery market. Based on these figures, NanoAxis plans to become a player and significant contributor to this market by propelling its patent pending technology using controlled release biodegradable nanoparticles for targeted gene and drug therapy. The goal of NanoAxis is to advance our targeted gene therapy process into the clinical setting. Unlike industry alternatives in regards to gene delivery methods, our technology is unique in that it addresses key impediments to achieving drug delivery in a clinical setting mainly systemic toxicity issues using an paradigm of targeted controlled release with biodegradability of the carrier (nanoparticle). This has been a major roadblock in the gene therapy commercialization pipeline which our technology addresses.

With this grant from Ohio Third Frontier NanoAxis intends to commercialize a novel gene therapy for post-arthroscopic knee osteomyelitis using controlled release biodegradable polymer nanoparticles in conjunction with the Department of Orthopedic Surgery at Albert Einstein School of Medicine who will serve as collaborators. The grant will begin production of this product in the greater Cleveland area that will lead to major job and economic growth in that region particularly with respect to manufacturing labor.

A rare but devastating problem is infection after placement of hardware whether after a knee replacement or after fracture treatment with metal. Incidence of infection after an elective knee replacement is 1%. Medicare spends 25 billion dollars in treatment of pre-prosthetic infections and osteomyelitis. Most infections require long courses of antibiotics (4-8 weeks) and require expensive nursing care for administration of these intravenous drugs. Our grant proposal employs an innovative delivery technique (nanotechnology) along with intra-articular injection of plasmid delivery to induce production of endogenous vancomycin, a high dose of local antibiotic given where it is most efficacious to reduce the incidence of renal complications from systemic exposure of vancomycin, while maintaining sustained and controlled release. The proposed research will foster the development of a clinically feasible methodology and therapy for treating pre-prosthetic infections, and can have huge cost savings in health care delivery.

Our team of chemists and research scientists in conjunction with our management team have the expertise to synthesize hyperbranched biodegradable nanoparticles using our proprietary method, perform associated gene complexation, and interpret the corresponding biological outcomes for this project. We are poised to see the development of these nanoplex based gene therapy through Phase 1-4 human clinical trials, and believe that the greater Cleveland area will benefit from promoting this product line. This delivery methodology can then be applied to a wide array of diseases with a genetic etiology, propagating a growing product line and job creation in the greater Cleveland area. We also feel that the Cleveland area with its strong medical community inclusive of Cleveland Clinic and University Hospitals will be the ideal environment to foster this project. We look forward to an opportunity to file a full proposal to Ohio Third Frontier.

Sincerely,

Krishnan Chakravarthy PhD  
President/CEO  
NanoAxis, LLC  
Email: [krishnan.chakravarthy@nanoaxisllc.com](mailto:krishnan.chakravarthy@nanoaxisllc.com)  
Phone: 716-908-2392



PeriTec Biosciences Ltd.  
Cleveland Clinic Innovations Building  
1000 Cedar Avenue  
Cleveland, Ohio 44106  
(216) 444-1293

**11-509**

Date: December 12, 2010  
Ohio Department of Development  
Technology and Innovation Division  
77 South High Street, 25<sup>th</sup> Floor  
Columbus OH, 43215

This letter of intent is submitted by Peritec Biosciences, Ltd. for the Ohio Third Frontier Biomedical Program

**Lead Applicant:**

Peritec Biosciences, Ltd  
10000 Cedar Avenue, Suite 3  
Cleveland, OH, 44106  
Ph: 216-445-0961

**Lead Applicant Contact:**

Donald Gustavson  
Peritec Biosciences, Ltd  
dgustavson@peritecbio.com  
Phone Number: 216-870-1512

**Project title:** Commercialization of Tissue Lined Stent for Treatment of Peripheral Artery Disease and Dialysis Access Stenosis.

**Budget Request Estimate:** \$ 1,000,000.00

**Known Collaborators:** Parker Hannifin  
Tower tools  
NDC  
Cleveland Clinic  
Proxy Biomedical  
Tactx Creganna

**Summary:** Attached

Sincerely,

A handwritten signature in black ink, appearing to read "DGustavson".

Donald Gustavson  
CEO



PeriTec Biosciences Ltd.  
Cleveland Clinic Innovations Building  
1000 Cedar Avenue  
Cleveland, Ohio 44106  
(216) 444-1293

## Summary of the Project

Cardiovascular disease is the leading cause of death in the United States and atherosclerosis is its major cause. Based on statistics for aging population alone, a conservative prediction is there will be approximately 190,000 peripheral vascular procedures performed in 2020. This disease has significant adverse effects on the quality of life and survival with a high mortality rate. A major component of peripheral arterial disease (PAD) is obstruction of blood flow to the lower extremities from atherosclerosis. The superficial femoral artery (SFA) is the most commonly affected artery by PAD with over 50% of all PAD involving the SFA. The challenge with the current grafts is their high potential for clotting and restenosis, and high potential for causing an infection. They frequently develop stenoses at the venous anastomosis and have a high rate of failure.

Similarly, an estimated 11.5 percent of adults (approx 23 million people) suffer from chronic kidney disease. Among people suffering from end-stage renal disease (ESRD), the mortality is approximately 163.8 deaths per 1,000 patient years. Hemodialysis is the leading treatment for more than 341,000 patients in the United States with ESRD, or kidney failure, which can be caused by common chronic conditions such as diabetes and hypertension. The market for AV grafts is increasing since not all patients can wait the length of time for the fistula to mature or it cannot be used for people with fragile veins. Thus, as the number of Americans with end-stage renal disease (ESRD) continues to rise, the use of grafts will continue to be employed as a means of vascular access. Despite enthusiasm for PTFE and other biological grafts, there currently is no ideal solution to treating ESRD, and there have been only three stents that are currently approved by FDA for PAD.

To meet this growing unmet need, PeriTec Biosciences has developed a novel peritoneum lined stent (PLS). The PLS has shown excellent performance in animal and international human clinical studies for both dialysis access failure and femoral artery occlusive disease. Peritec now aims to develop the stent graft to use as a treatment method to improve dialysis access stenosis. These unique tissue lined stents require special handling in a novel delivery system developed by PeriTec to maintain their physical and biological integrity. Peritec has developed a safer and more efficient stent scaffold specifically designed to accommodate the tissue with desired characteristics that include different radial forces and flared ends.

This project will provide jobs to staff for our new pilot manufacturing facility for tissue lined stents. In the first year, a tissue processing lab will be set up to process tissue for stent manufacturing. Along with this, a mechanical testing lab will be set up to perform mechanical testing on each manufactured lot of the tissue. In the second year, we will set up our stent integrated testing facility to perform lot fatigue tests with the objective of determining the relationship between the stress range and number of cycles before failure. Laboratories will be designed to the standards of ISO 13485:2003. This will allow the use of the unique biocompatible PLS to meet a serious and growing unmet need in the treatment of vascular atherosclerosis in the lower extremities and as a dialysis access. This project will not only create job in the region of Ohio, but also serve as a spring board for many biomedical engineering jobs.



6217 Centre Park Drive  
West Chester, Ohio 45069  
Tel. 513-755-4100  
Fax 513-755-4108

December 13, 2010

**11-510**

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

Dear Ohio Department of Development:

Please accept this Letter of Intent from AtriCure, Inc. for our Fiscal Year 2011 Ohio Third Frontier Biomedical Program ("OTFBP") proposal.

**Lead Applicant Name:** AtriCure, Inc.

**Address:** 6217 Centre Park Drive  
West Chester, OH 45069

**Telephone:** (513) 755-5762

**Contact Person:** Mr. Salvatore Privitera, Vice President of Engineering & Product Development

**Contact Email:** SPrivitera@atricure.com

**Project Title:** Development and Commercialization of a Minimally Invasive Left Appendage Exclusion System

**Estimated Grant Amount:** \$1 million

**Known Collaborators:** The Ohio State University, Deaconess Hospital, Battelle, R&R Tool, Inc. and others to be determined

**Summary of Proposed Project:**

Since the incorporation of West Chester, Ohio-based AtriCure® in November 2000, AtriCure's commitment to innovation has been relentless. AtriCure has assembled experts in the medical device industry to form a highly effective team dedicated to serving patients, medical professionals, and investors.

AtriCure is a unique Ohio medical device manufacturer that takes products from concept to market. At its Cincinnati facilities, AtriCure has a team of experts that develops technology concepts, manufactures the devices, and markets its products across the world. Nearly 80-90 percent of AtriCure's device components are sourced from within the State of Ohio.

AtriCure has a successful track record of developing and commercializing products. Over the last five years, the company has released over 25 product codes across six product platforms, and under ten FDA 510K clearances. AtriCure's bipolar ablation system, released in 2003, is a standard treatment alternative during open-heart surgical procedures to safely, rapidly and reliably create lesions in cardiac tissue to block the abnormal electrical impulses that cause atrial fibrillation ("A-Fib"), a rapid, irregular quivering of the upper chambers of the heart. Since that time, AtriCure has built upon its suite of product offerings to include complimentary products that aid in the treatment and prevention of cardiac abnormalities and ailments.

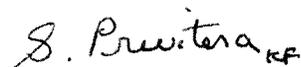
The American College of Cardiology issued guidelines indicating that A-Fib surgical patients, and others at high risk for stroke or developing A-Fib, should be treated with Left Atrial Appendage ("LAA") exclusion to reduce long-term risks of stroke. Current techniques for LAA exclusion carry procedural and efficacy risks, limiting compliance to these guidelines. As such, AtriCure has developed the AtriClip—a parallel closing, non-piercing, epicardial implant—which quickly and safely excludes the LAA by excluding fluid communication. Originally conceptualized by the Cleveland Clinic's Drs. Gillinov and Cosgrove, the device received 510K clearance in June 2010, and AtriCure is now working to secure broad labeling clearance to market the AtriClip. While this device is effective, the current device configuration and indications limit clinical use to a small subset of the patients that could benefit from the technology.

AtriCure plans to seek OTFBP funding to support the development and clinical study of a specialized AtriClip delivery system which will allow "thoroscopic or robotic occlusion of the LAA". While this new device is based on AtriCure's currently marketed product, the delivery system will be new and the resulting delivery system product and indications will address a much larger patient population to market the device.

The proposed project will build upon AtriCure's internal manufacturing capabilities by bringing "in-house" the manufacturing of critical AtriClip components. In addition to scaling up device manufacturing, AtriCure will design and develop a thoroscopic clip deployment tool and will develop and execute a feasibility phase clinical study. AtriCure will simultaneously complete a Good Laboratory Practices ("GLP") study and will ultimately seek FDA 510K approval for thoroscopic or robotic occlusion of the LAA.

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,



Salvatore Privitera  
Vice President of Engineering & Product Development

## Letter of Intent for Application to the Ohio Third Frontier Biomedical Program--Fiscal Year 2011

**Application Title:**

**Development of a Transport Mechanism to Improve Bioavailability of Drugs for Diseases of the Brain**

**Lead Applicant:** Case Western Reserve University School of Medicine

**Address:** 11000 Euclid Avenue Cleveland, Wearn B-42, OH 44106, (216) 983-3264

**Contact person:** James P. Basilion, Ph.D., Associate Professor of Radiology, Biomedical Engineering, and Pathology, Contact Info: [James.basilion@case.edu](mailto:James.basilion@case.edu), 216-983-3264

**Project Title:** Development of a Transport Mechanism to Improve Bioavailability of FDA Approved Drugs for Diseases of the Brain

**Estimated grant funds:** \$1M

**Collaborators:**

- Curragh Chemistries, Inc.,
- Ricerca Inc.
- Hydrophobic Transport, Inc.,
- Case Western Reserve University (Gary Landreth, Department of Neurosciences; Clemens Burda, Department of Chemistry; and Michael Haag, TTO)

This Letter is to notify the State of Ohio of our intention to submit an application in response to the RFP entitled "Ohio Third Frontier Biomedical Program, Fiscal Year 2011". This application will describe a novel gold nanoparticle approach to deliver blood-brain-barrier (BBB) impermeable drugs into the brain interstitium. This application will expand upon significant preliminary data demonstrating the utility of nanogold particles as carriers for anti-cancer drugs directed against brain tumors.

This application will build upon a RO1 funded research program that is developing and characterizing different design features for gold nanoparticles as highly efficient drug delivery systems. These studies have led to a phase one particle design of a gold nanoparticle that efficiently can transport hydrophobic anti-cancer drugs preferentially into brain tumors. Follow on studies have demonstrated the potential for these same nanoparticles to cross intact BBB and therefore suggest that these particles may have merit for transfer of therapeutic agents into the blood with out the need for a disrupted BBB found within tumors. These findings would potentially enable two distinct but related development paths: 1) these nanoparticles may make delivery of potent anticancer

therapeutics, which are currently not able to cross the BBB or the brain tumor-blood barrier (BTBB), potential drugs for brain tumor therapy; and 2) the ability of these particles to cross the intact BBB may provide a mechanism to resurrect many promising drugs for other neuronal diseases (e.g. Alzheimer's disease) that were abandoned because of poor biodistribution into the target brain tissues. For this proposal we intend to drive forward three candidate drug complexes to nanogold carriers to provide therapy to either brain tumors or Alzheimer's disease. In each of the three cases mouse models for human disease will be used to assess efficacy of the complex compared to delivery of "free" compound. Synthesis of the most likely successful candidate will be scaled up and a preclinical toxicology package will be designed and implemented to drive towards an IND approval from the FDA by 3 years from the start of the research support by this application.

To accomplish these goals we have put together a research team from the lead organization (Case Western Reserve University) consisting of an expert in chemistry of gold nanoparticles (Dr. Clemens Burda), an expert in neurosciences (Dr. Gary Landreth) and an expert in imaging of nanoparticles (Dr. James P. Basilion). This effort will be supported by collaborations with at least two Ohio companies, Curragh Chemistries, for scale up support and synthesis and Ricerca Inc, for toxicology and pharmacology assessment in small animals.

If the effort is funded and successful, we expect the development of:

- Development of novel drug approaches to cure brain cancers and
- Development of novel drug approaches for Alzheimer's disease
- Formation of a company, Hydrophobic Transport Inc., with a potential for outstanding growth potential
- Development of novel phase I-III clinical trials and drug to market development

# 11-512



December 14<sup>th</sup>, 2010

FY2011 Ohio Third Frontier Biomedical Program (OTFBP)  
Ohio Department of Development Technology Division  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, Ohio 43215-6130

This **letter of intent** is submitted by **LyoGo LLC**. (Lead Applicant, [www.LyoGo.com](http://www.LyoGo.com))  
in anticipation of a proposal for the 2010 Ohio Third Frontier Biomedical Program (OTFBP).

**Lead Applicant Information:**

LyoGo LLC.  
3315 Edgerton Street  
West Lafayette Indiana, 47906  
[www.LyoGo.com](http://www.LyoGo.com)

**Lead Applicant Information:**

Rush Bartlett, Co-Founder  
LyoGo LLC.  
[Rush.Bartlett@LyoGo.com](mailto:Rush.Bartlett@LyoGo.com)  
Phone: (918) 688-4303

**Project Title:**

Second phase product development and pilot manufacturing of easy to use drug delivery devices that inject freeze dried substances which would otherwise require complex mixing and or refrigeration.

**Budget Request Estimate:** \$1,400,000

**Intended Collaborator:** Battelle Memorial Institute

**Project Summary:** See Attachment A

At LyoGo we are looking forward to sharing more about our award winning innovations with the Third Frontier Program. Our goal is to generate synergistic relationships in Ohio with organizations like Battelle Memorial Institute and Third Frontier to positively enhance economic impact in the buckeye state to enhance patient quality of life around the world. Our vision is to help ensure US citizens, and especially our armed forces and other safety and security professionals, have immediate access to therapies, vaccines, and antidotes which are easy to use, safe, and efficacious.

Sincerely,

A handwritten signature in black ink, appearing to read "Rush Bartlett".

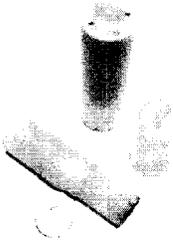
Rush Bartlett, Co-Founder

## ATTACHMENT A

**History:** LyoGo started as GlucaGo LLC. when three graduate students licensed technology from Purdue University and invested \$30,000 of their own money for prototyping with Rose Hulman Ventures ([www.rhventures.org](http://www.rhventures.org)). The team gained traction and funding with business plan competitions where GlucaGo (first name of the company) won 7 internationally recognized competitions, and was featured in FORTUNE Magazine. Realizing that glucagon was just a \$250 million dollar segment of a larger \$350 billion dollar global injectable drug market the team changed the name to LyoGo or lyophilized (freeze dried) drugs to go. LyoGo secured \$100,000 from competitions, a life science grant from NASA (\$20,000), the Qualified Therapeutic Discovery Grant from the US Government, and a highly experienced business team.

**The Problem:** \$350 billion dollars of drugs are given with 40 billion injections worldwide annually. Freeze drying an average injected drug enhances its shelf life at room temperature from a few hours to a year or more making it easier to store and transport. For most injected drugs freeze drying could reduce the need to refrigerate the compound during storage. This can be vital for anything from vaccine stockpiles to cancer drugs. However, once freeze dried a solvent has to be added to turn the drug back into a liquid so that it can be injected. Over 200 different drugs, vaccines, and antibiotics are freeze dried but, manual mixing and administration is dangerous and difficult. Current schemes to alleviate this problem add \$8-\$16 per injection due to custom manufacturing and require 4-6 user steps to activate. As a result, secondary disease transmission, misuse, drug wastage, and spoilage cost billions annually.

**The LyoGo Solution:** LyoGo's platform of drug mixing and delivery devices make it easier to administer these drugs through our "One Step Inject" operation. Simply remove the cap and press to inject the drug, simple enough that anyone, even a child, can use it. Our devices are engineered to fit existing filling equipment and are their own self contained sharps containers meaning low cost manufacturing and safe disposal, vital traits for drug delivery markets.



Left is our Intramuscular injection device but we are also using our core mixing technology to develop additional devices for subcutaneous, intradermal, intranasal, oral dropping, and intravenous delivery of freeze dried medication. The main mixing device works with a standard lyophilization vial where the glass bottom is removed and replaced by our proprietary mixing membrane. This drug container slides into the device which then uses one fluid motion of compression to first inject the needle and then second inject the drug.

**Intellectual Property:** LyoGo has the exclusive worldwide license from Purdue. A prior art search has been conducted and as a result LyoGo filed 3 provisional patents that were converted to a PCT and an additional 2 provisional patents that will be converted to a PCT in 2011. No negative feedback from the USPTO has been received on the first PCT application.

**Current State of the Technology:** We have offers of collaborations test devices at Purdue University and Indiana University Medical Center. Several companies have expressed strategic partnership interests in LyoGo, e.g. Pfizer, Becton Dickenson and many others (confidential). Their primary goal is to see our product come through pilot manufacturing. To make that happen we are communicating with prospective partners. The current front runner is Battelle Memorial Institute, who immediately suggested we apply for Third Frontier Funding.



Thermedx, LLC  
31200 Solon Rd, Unit #1  
Solon, OH 44139  
Phone: (440) 542-0883 x 14  
Fax: (440) 542-0920  
Cell: (216) 577-1716  
MHaritakis@Thermedx.com

December 14, 2010

**VIA EMAIL** ([OTFBP2011@development.ohio.gov](mailto:OTFBP2011@development.ohio.gov))

**11-513**

The Ohio Department of Development  
Technology and Innovation Division  
Attention: OTFBP  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, Ohio 43215

**Subject: 2011 OTFBP LOI for New Orthopedic Medical Device from Thermedx, LLC.**

Dear Ohio Third Frontier Commission:

In response to the November 1, 2010 Request for Proposals (“RFP”) from the Ohio Third Frontier Biomedical Program (“OTFBP”), please accept this Letter of Intent (“LOI”) from Thermedx, LLC (“Thermedx”), as the prospective Lead Applicant for the proposed development and commercialization of a new and proprietary version of an orthopedic medical device known as a Pulse Lavage (the Thermedx “Pulse Lavage System”). As requested in the RFP, please find enclosed the following information for the submission of this LOI:

<b>OTFBP RFP Requested Information</b>	
The Prospective Lead Applicant's Name:	Thermedx, LLC
Address of Lead Applicant:	31200 Solon Road, Unit #1, Solon, Ohio 44139
Phone Number of Lead Applicant:	(440) 542-0883
Contact Person at Lead Applicant:	Michael A. Haritakis, Executive Vice-President
Email Address of Contact Person:	<a href="mailto:mharitakis@thermedx.com">mharitakis@thermedx.com</a>
Proposed Project Title:	Thermedx “Pulse Lavage System”
Estimated Grant Funds To Be Requested:	One-Million Dollars (\$1,000,000)
Known Collaborator(s):	An Ohio Healthcare Organization(s) and/or Company(ies)
One Page Summary of the Proposed Project:	See enclosed THERMEDX SUMMARY OF PROPOSED PROJECT

THERMEDX SUMMARY OF PROPOSED PROJECT

Thermedx ([www.thermedx.com](http://www.thermedx.com)) is a for-profit, early stage medical device company headquartered in Solon, Ohio that has been a member of BioEnterprise ([www.bioenterprise.com](http://www.bioenterprise.com)) since 2007. Thermedx is focused on the development and commercialization of proprietary Fluid Management & Patient Temperature Management Products for Orthopedic and other clinical applications, which includes a multi-functional Surgical Irrigation System that received FDA 510(k) clearance in July 2010. Thermedx currently has eighteen employees comprised of engineering, sales, business development, and administrative personnel, which collectively have significant commercialization experience with medical devices and other technology products.

In response to the RFP, Thermedx is intending to submit a Proposal as the Lead Applicant for the development and commercialization of a new and novel version(s) of a medical device known as a "Pulse Lavage", which is used in Orthopedic Joint Replacement and other procedures. As part of developing its own proprietary Pulse Lavage System, Thermedx will adapt and modify the platform technology of its existing FDA 510(k) cleared Surgical Irrigation System and will: (i) Reduce Healthcare Costs, and (ii) Improve Patient Outcomes. The development of the Pulse Lavage System will also involve: (i) Ohio Collaborators, who will provide various services and technology, (ii) Ohio Committed End Users, who intend on using the Pulse Lavage System, and (iii) Ohio Suppliers, who will provide key components.

The Thermedx Pulse Lavage System is anticipated to quickly have a significant Job Creation and Economic Development impact on the State of Ohio, resulting from Thermedx's participation in the \$200 Million US Pulse Lavage Market, generated from the 1.3 Million orthopedic surgeries completed annually. Thermedx will design and manufacture the Pulse Lavage System at its headquarters in Solon, Ohio, and is planning to use Ohio Suppliers where financially feasible to support the development and production of the Thermedx Pulse Lavage System, both of which will lead to significant job growth within the State. Since the Pulse Lavage itself is currently classified by U.S. Food & Drug Administration as a "Jet Lavage" that is "510(k) Exempt", and Thermedx has progressed through its initial Intellectual Property evaluation, it is anticipated that the Thermedx Pulse Lavage System will rapidly enter the Market Entry Phase of the Technology Commercialization Framework.

If the above described Thermedx Pulse Lavage System initially meets the criteria of the OTFBP, please provide an identification number for the anticipated Proposal to be submitted by January 18, 2011. Please let me know if there any questions regarding the Pulse Lavage System. We look forward to the opportunity to submit a Proposal for the Thermedx Pulse Lavage System in response to the OTFBP RFP. Thank you.

Sincerely,



Michael A. Haritakis, Executive Vice-President



11-514

**COLLEGE OF MEDICINE**

THE UNIVERSITY OF TOLEDO

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

December 13, 2011

RE: LOI Ohio Third Frontier Biomedical Program

Dear Sir/ Madam,

This letter serves as notification of our intent to submit a project proposal to the Ohio Third Frontier Biomedical Program for Fiscal Year 2011.

**Lead Applicant:** University of Toledo Health Sciences Campus

**Address:** 3000 Arlington Ave, Toledo, OH 43614  
Phone: 419-383-4252

**Contact Person:** Beata Lecka-Czernik, PhD  
Professor, Department of Orthopaedic Surgery  
Phone: 419-383-4140  
E-mail: [beata.leckaczernik@utoledo.edu](mailto:beata.leckaczernik@utoledo.edu)

**Project Title:** Application of micro-computed tomography for pre-clinical testing of biosafety and biocompatibility of medical devices

**Funds Requested:** \$480,000 Third Frontier Research and Development (TFRD)  
\$260,000 Wright Capital Funds (WCF)

**Collaborator:** North American Science Associates, Inc.  
Northwood, OH 43619

## **Application of micro-computed tomography for pre-clinical testing of biosafety and biocompatibility of medical devices**

The assessment of safety and biocompatibility is an obligatory step in the development of new medical devices and it comprises of extensive testing in animal models. This step is required by the FDA as an important component of application for the use of such devices in humans. Methods which are currently used, although precise and accurate in producing results, are generally limited to an analysis of small sample of tissue surrounding the foreign material. Such approach does not allow for full assessment of tissue/device interactions.

We are proposing a development of quantitative volumetric non-destructive methods for the analysis of tissues contacting the entire surface of an implant or biomaterial. The methods will focus on the pathologic changes in the surrounding tissue resulting in calcification, development of fibrotic tissue, and accumulation of fat. These methods will be developed with the use of state-of-the-art high resolution micro-computed tomography (mCT) and in collaboration with the North American Science Associates, Inc., (NAMSA).

NAMSA is a global company specializing in testing of biosafety and efficacy of medical devices for biomedical industry. Its World Headquarters and research facility is located in the Toledo area. NAMSA strongly supports a development of new methods of biosafety assessment and sees it as an important avenue for attracting new customers from biomedical industry. Our laboratory is specializing in the analyses of orthopedic medical devices and materials using mCT methodology, with successful and ongoing partnership with NAMSA. The novelty of this application relies on the development of new applications of mCT for quantitative visualization of pathologic changes resulting from interactions of soft tissue organs with artificial materials. The strategic partnership between the University of Toledo and NAMSA will assist in commercialization of high impact product.

Sincerely,



Beata Lecka-Czernik, PhD  
Professor, Department of Orthopaedic Surgery  
University of Toledo College of Medicine  
3000 Arlington Avenue, Mail Stop 1008  
Toledo, OH 43614  
Phone: (419) 383-4140  
Fax: (419) 383-2871  
<http://www.utoledo.edu/med/depts/ortho/bonelab/>





Surgeons speak. We deliver.®

products designed by our internal research and development group of engineers (with extensive input from our medical advisory board consisting of world class thought leaders in the orthopedic industry) and manufactured by inter- and intrastate vendors. Ohio-based headcount is currently 44, which is nearly 4 times the 12 heads the company employed when the application for the Innovation Ohio Loan Fund was submitted in March 2007. OrthoHelix has been able to attract individuals within Ohio as well as recruit talent from highly respected orthopedic companies outside of state, including our CEO and VP of Research and Development, both of whom relocated to Ohio.

In 2009, the company sold to over 700 hospitals and surgery centers in over 30 states mostly through an independent sales force selling our consigned inventory and instruments. Over 600 different surgeons performed over 7,000 surgical procedures with our products in 2009 alone. We continue to expand our sales force, the inventory and instruments available, as well as our product portfolio so that we can continue to generate the exceptional sales growth that we have demonstrated historically. While a number of product lines have contributed to this growth, our most significant growth figures have come from one particular product line consisting of universal and indication-specific implants with foot and ankle applications called MaxLock Extreme. This product line currently generates nearly 70% of the company's sales and resulted in 230% sales growth in 2009.

While our current MaxLock Extreme product offers many options to fulfill a host of applications, there are needs currently unmet with the available implants in this product line. In fact, our products currently compete in about 1/3 of the \$1.6 billion extremity market.

An Ohio Third Frontier Biomedical Program award would create the resources necessary for OrthoHelix and its collaborators to create a new implant system to complement the existing successes of our MaxLock Extreme product line. The proposed system will build on our initial successes utilizing plates that include intra-medullary fixation options.

The proposed project requires extensive design work, prototyping, testing, manufacturing and quality support. However, with the addition of these products, OrthoHelix will continue to expand market share in the 1/3 of the extremity market in which we currently compete, as well as begin to open up the other 2/3 of the market. The proposed project will create technology-based economic development benefits, attract additional investment, and contribute to making Ohio a leader for orthopedic industry innovation.

Sincerely,

A handwritten signature in black ink, appearing to read 'Dennis Stripe', with a long horizontal flourish extending to the right.

Dennis Stripe  
CEO

## 2011 OTFBP LOI

**Prospective Lead Applicant's name, address, phone number:**

Oasis Consumer Healthcare, LLC  
812 Huron Road East, Suite 235  
Cleveland, OH 44115-1123

**Contact person, including email address for the contact:**

Afif Ghannoum, JD  
[aghannoum@oasisrx.com](mailto:aghannoum@oasisrx.com)

**Proposed Project title:** Development and commercialization of an oral spray to prevent oral infections and cardiovascular disease.

**Estimated Grant Funds to be requested:** \$1 million

**Known Collaborators,**

Dr. Mahmoud Ghannoum, School of Medicine, Case Western Reserve University  
Dr. Richard Jurevic, School of Dentistry, Case Western Reserve University  
Dr. Hussein Assaf, School of Dentistry, Case Western Reserve University  
Dr. Pranab K. Mukherjee, School of Medicine, Case Western Reserve University

## Summary of the Proposed Project.

Coronary heart disease (CHD) is the most important clinical manifestation of atherosclerosis. It is the single greatest cause of mortality in Western countries. For example, 33% of all annual deaths in the US are due to CHD. CHD afflicts 7 million Americans and is responsible for over 500,000 deaths annually. Association between dental infections and advanced coronary atherosclerosis has been well-established. Therefore, development and commercialization of products that can prevent dental/oral infections and associated cardiovascular diseases is needed.

Oasis Consumer Healthcare has developed a novel product (spray formulation) using an innovative approach that combines their proprietary Tri-Hydra™ technology with an active antimicrobial agent. This technology possesses a unique delivery mechanism that addresses the two clinical objectives of hydrating the mouth and delivering antimicrobial agent over an extended period of time. This formulation hydrates the mouth because of its aqueous base, allows hydrogen bonding with the hydrophilic polymers to trap the water within the polymer network, and slows its loss into the oral cavity, and a humectant coating of the oral surface which forms a barrier that prevents loss of the antimicrobial agent. As a result, the antimicrobial agent in the formulation is retained over an extended period of time, allowing for prolonged activity against microbes associated with cardiovascular diseases.

Preclinical testing of this product showed that it possesses activity against: (1) bacteria including *Streptococcus sanguis*, *S. oralis*, *S. mitis*, *S. salivarius*, *S. gordonii*, *Staphylococcus aureus*, *Actinobacillus actinomycetemcomitans*, and *Fusobacterium nucleatum*, with MIC<sub>50</sub> of 0.4%, (2) *Candida* species, with minimum concentration that inhibited 50% of the tested isolates (MIC<sub>50</sub>) was 0.0125%, (3) viruses (EBV, HIV), as shown by inhibition of viral replication at concentrations as low as 1.56%, and (4) bacterial and fungal biofilms (plaques) as shown by culturing (colony forming units, CFUs) and microscopy (electron and confocal microscopy). In addition, (5) electron microscopy analysis showed that exposure of *S. sanguis*, *S. oralis* and *C. albicans* to the product affected the morphology of these oral pathogens, resulting in deformed morphology and cell disruption. These studies demonstrate that the developed product is active against bacteria, fungi, and viruses as well as against microbial biofilms.

In the current proposal, we will conduct a clinical trial to evaluate the safety, tolerability and efficacy of the developed formulation in the prevention and treatment of periodontal infections associated with cardiovascular complications.



## 2011 Ohio Third Frontier Biomedical Program – Letter of Intent

Lead Organization: SironRX Therapeutics, Inc.  
Address: 10000 Cedar Avenue, Cleveland, OH 44106  
Contact Person: Tim Miller, Ph.D.  
Title: Director of Product Development  
Email: [Tmiller@sironrx.com](mailto:Tmiller@sironrx.com)  
Phone: 216-445-5588

This Letter of Intent confirms that SironRX Therapeutics will submit a proposal titled “SDF-1 treatment to induce vascular and epithelial regeneration in sternotomy wounds”. requesting approximately \$1,000,000 from the Ohio Third Frontier Biomedical Program. SironRX Therapeutics, a clinical-stage, venture backed regenerative medicine company, will collaborate with Juventas Therapeutics and the Cleveland Clinic to develop and commercialize JVS-100 to accelerate wound repair and prevent scarring after cardiovascular surgery.

JVS-100 expresses human Stromal cell-Derived Factor 1 (SDF-1), a naturally occurring chemokine that is rapidly over-expressed in response to tissue injury. SDF-1 is a strong chemo-attractant of stem and progenitor cells that promote tissue preservation by promoting vasculogenesis. The therapeutic potential for SDF-1 is well established in wound healing, cardiovascular disease and peripheral vascular disease. With an estimated 1.5 million general thoracic surgeries performed in 2008, surgeons are turning to regenerative therapies in an attempt to improve outcomes, enhance the rate of healing and limit the disfigurement associated with major surgical procedures. SironRX seeks to address this unmet need by evaluating the safety and efficacy of its lead product, JVS-100, to accelerate wound closure and prevent scarring in patients having recently undergone a median sternotomy after cardiac surgery.

JVS-100 is being successfully developed by Juventas Therapeutics for clinical use for treatment of heart failure and critical limb ischemia (CLI). Specifically, Juventas received IND #14203 from the FDA for use of JVS-100 to treat patients with heart failure and has completed enrollment of a 16-person multi-center, open-label, dose-escalation study. Also, an IND for a Phase IIa clinical trial evaluating the use of JVS-100 for the treatment of patients with CLI was submitted to the FDA in November 2010. SironRX was recently formed as a Juventas spinoff company to develop JVS-100 as a biopharmaceutical to promote healing and reduce scarring of hard-to-heal acute and chronic wounds. **The studies proposed in this grant will yield large animal dosing and efficacy data necessary to file an IND within 9 months of study completion for a Phase II clinical trial evaluating use of JVS-100 to accelerate wound closure and reduce scarring of median sternotomies following open-chest surgery.**

Sincerely,

A handwritten signature in black ink that reads "Timothy J. Miller". The signature is written in a cursive, slightly slanted style.

Timothy J. Miller, Ph.D



**11-518**

December 14, 2010

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

**Subject: 2011 OTFBP LOI**

**VIA: E-mail to [OTFBP2011@development.ohio.gov](mailto:OTFBP2011@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 2011 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](mailto:pbrumbergs@usendoscopy.com)

**Proposed project title:** Advanced Urological Diagnostic & Therapeutic Accessories Project

**Estimated grant funds to be requested:** \$1 million

**Collaborator(s):** University Hospitals and industry partners

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

Sincerely,

A handwritten signature in black ink, appearing to read "Peter Brumbergs". The signature is written in a cursive style.

Peter Brumbergs  
Chief Financial Officer

Attachment: Project Summary



**US Endoscopy**  
**Advanced Urological Diagnostic & Therapeutic Accessories Project**  
**2011 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 approximately 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 University Hospitals and Mayo Clinic, individual doctors, and the Company's industry partners. For this project, the Company expects to collaborate with University Hospitals, and long-time industry partner firms engaged in product design, testing, and certification.

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Monday, December 13, 2010

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

This Letter of Intent is provided by Gerard Ventures, dba Ischemia Care in anticipation of a proposal for the Ohio Third Frontier Biomedical Program.

Lead Applicant: Gerard Ventures, LLC dba Ischemia Care ("Ischemia Care" or "ISC" herein)  
347 S College, Suite B  
Oxford, OH 45056  
866.517.1966  
[www.ischemiacare.com](http://www.ischemiacare.com)

Contact Person: Jeffrey June, CEO  
513.255.7868  
[jeff.june@iscdx.com](mailto:jeff.june@iscdx.com)

Project Title: Blood test for the diagnosis of ischemic stroke

Grant Funds: \$1,000,000

Collaborators: Advanced Testing Laboratory, Kendle International, Medpace, NanoString, UCLA, University of California – Davis, UCSF, Miami University, nationally recognized prescription benefits manager (TBA) and a nationally recognized center for personalized medicine (TBA).

Project Summary: Attachment A

Thank you for your consideration,

Jeffrey June  
CEO  
Ischemia Care

Attachment A: Project Summary – Blood test for the diagnosis of ischemic stroke

Submitted on December 13, 2010 *via email* to [OTFBP2011@development.ohio.gov](mailto:OTFBP2011@development.ohio.gov)

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**Attachment A: Project Summary – Blood test for the diagnosis of ischemic stroke.**

795,000 Americans suffer a stroke annually and 195,000 are recurrent attacks. The diagnosis of causes of stroke is complex and typically based upon clinical exam, imaging and other tests. The cause of stroke is usually presumptive with no specific blood test available. In up to 35% of cases, the cause of ischemic stroke remains unknown. Timely diagnosis would assure the most appropriate acute treatments or prevention plans were adopted.

Ischemia Care (ISC) is a molecular diagnostics company developing a blood test for the accurate diagnosis of ischemic stroke leading to timely adoption of proper acute therapies. **The funding contemplated herein will allow the company to commercialize a gene expression based blood test as an outsourced service through a single company owned CLIA lab offering the test to hospitals, stroke centers and research facilities.**

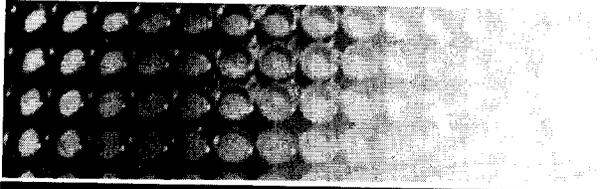
Specifically, the test is a gene expression test used to differentiate cardio embolic (origin in heart) cause of stroke through athero embolic (origin in large vessel) cause, when hemorrhagic stroke is ruled out. Strokes of cardio embolic origin may be treated with an anticoagulant therapy (warfarin) and strokes of athero embolic origin are treated with antiplatelet therapy (clopidogrel or Plavix). In summary, the ISC test will align diagnosis, therapy adoption and responsiveness.

Progress to date includes collected human data on over 500 patients (including peer reviewed publications), \$5M in research funding, closed Series A funding June 2010, relationships with world class research institutes, outstanding management team and board, executed license agreements, filing of three US patents and filing of related international patents, formulated regulatory and reimbursement strategy, developed lab operations plan and in early stages of pilot programs at leading neurology programs. Additionally, the management team has collective experience selling into over 600 hospitals, medical centers and research facilities.

The funding will focus on the following commercialization activities during a 12 to 24 month period:

1. Building CLIA lab and hiring (training) laboratory personnel.
2. Validate CLIA lab using samples previously collected through a clinical trial.
3. Design and run prospective multicenter pilot program for 200+ patients.
4. Gain reimbursement at pilot locations and build pharmaco economic endpoints into pilot activities.
5. Develop the physician interface and results reporting system (HIPPA compliant).
6. Software algorithm development.
7. Build therapeutic responsiveness information in the public domain into the ISC test.
8. Create minimum six full time positions.

# 11-520



Combining the Best of 3D and 2D Cell Culture.

 **Nanofiber**  
SOLUTIONS

December 13, 2010

Ohio Department of Development  
Technology Division  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, OH 43215  
Attention: "2011 OTFBP"

Subject: Letter of Intent for 2011 Ohio Third Frontier Biomedical Program

Dear ODOD Representative:

Please accept this Letter of Intent for the above-mentioned project. Below is the information required by the 2011 OTFBP Request for Proposals:

**Lead Applicant:** Nanofiber Solutions

**Address:** 1275 Kinnear Road, Columbus, OH 43212

**Phone Number:** 937-631-3596

**Contact Person:** Jed Johnson

**E-mail address:** [jed.johnson@nanofibersolutions.com](mailto:jed.johnson@nanofibersolutions.com)

**Project Title:** Commercialization of Aligned Nanofibers for Cell Culture Research

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

**Known Collaborators:**

Nanofiber Solutions is interacting with a broad cross section of Ohio industrial leaders (who can either be part of the supply chain or have a biomedical use for aligned nanofiber material) including Celartia and BioWorld as well as Ohio State University researchers to form an attractive team to commercialize this unique aligned nanofiber material for cell culture products. The final collaborator list will be transmitted in our proposal in January.

**Proposed Project Summary:**

Nanofiber Solutions develops and markets electrospun nanofiber substrates for cell culture and drug development applications in standard multiwell plates or in scalable configurations. Historically, general cell culture has been performed on flat, tissue culture polystyrene (TCPS) because it is cheap, optically clear, and many cells grow well on it. In reality, however, living organisms are made up of an extracellular matrix (ECM) that presents both aligned physical structure and mechanical support to the cells. Adherent cells are complex, self-sustaining units that require ECM anchorage to proliferate and undergo differential function and TCPS lacks this aligned three-dimensional (3-D) component and cells behave very differently on this flat, smooth substrate than they do in

true biological settings. Not surprisingly, drugs developed using TCPS as an *in vitro* substrate experience a >90% failure rate in clinical studies.

Aligned 3-D substrates mimic specific human *in vivo* environments and thus facilitate faster screening and more effective cancer and stem cell research. As a result, researchers are able to more accurately study the effects of various chemical compounds on cell behavior. This is especially true as researchers attempt to model and measure cell migration (i.e. metastasis) from the primary tumor. This technology allows high-throughput testing previously possible only in small, niche labs.

By allowing researchers to measure cell mobility for cancer research and providing physiologically relevant cell culture substrates for faster cell expansion, Nanofiber Solutions' technology allows earlier breakthroughs and fewer failures to significantly decrease time to market.

The requested Third Frontier funding will allow Nanofiber Solutions to:

- 1) Complete additional laboratory testing to further validate the value propositions associated with the new technology.
- 2) Interact with collaborators who will use our technology in their product lines.
- 3) Establish a commercial domestic/international distribution channel and supply chain.
- 4) Begin commercial operation and third party sales in the second half of the project.

If you have any additional questions or require any additional information, please contact me at 614-975-6646.

My warmest regards,



Ross Kayuha  
Chief Executive Officer  
Nanofiber Solutions LLC

Ohio  
2131 Aetna Road  
Ashtabula, Ohio 44004  
440.940.4001

Pennsylvania  
10600 North Star  
Van Nuys, CA 91411  
818.709.1999

San Diego  
3550 Camino del Rio South  
San Diego, CA 92108

# 11-521



December 10, 2010

2011 Ohio Third Frontier Biomedical Program  
Ohio Department of Development  
Technology and Innovation Division  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, OH 43215

## Letter of Intent

**1. Lead Applicant Contact:**

David R. Lewis, Managing Director  
Spinal MetRx Corporation  
2131 Aetna Rd.  
Ashtabula OH 44004  
[dave@spinalmetrx.com](mailto:dave@spinalmetrx.com)  
440.940.4001

**2. Project:** Repetitive Progressive Motion (RPM) device and treatment for spinal pain and injury.

**3. Funding Requested:** \$1,000,000 Project; \$850,000 Infrastructure/Facility

**4. Lead Organization:** Spinal MetRx Corporation is an Ashtabula OH based for-profit corporation specializing in the research, development and manufacture of spinal rehabilitation solutions for the biomedical market. The company has moved from Mercer PA where it operated under the name of Blacktown NC LLC to be located near its research institutions and component manufacturers.

**5. Collaborators:**

BioOhio  
Kent State University  
Youngstown State University  
The Cleveland Clinic Foundation, Spine Research Lab  
Pittsburgh Life Sciences Greenhouse

## The Project

Back pain is considered the second most common health complaint worldwide. Despite the prevalence of back pain, medical practitioners have no effective, predictable mechanized approach for back pain therapy. As a result there are limited treatment options for patients with chronic back pain. Hands-on physical therapy is often prescribed, but results are unpredictable and practitioner dependent. Spinal surgery is only utilized as a last resort due to the uncertainty of a successful outcome and economic cost. The marketplace seeks a safe and cost effective solution.

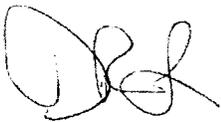
Spinal MetRx Corporation is a spinal disorder treatment company developing validated rehabilitation solutions through innovative devices. Located in Ashtabula, Ohio and Mercer, PA, its mission is to address the growing concerns over efficacy and safety of back pain treatment and management by offering FDA-approved products validated by the highest level of medical research, creating a new standard of care. The company's first product, the **Repetitive Programmed Motion Therapy (RPM™)**, is a computer-controlled rehabilitation device that will revolutionize the management of back pain by combining recognized physical therapies with the latest robotic control methods. This new therapeutic approach will precisely measure the range of spinal movement and record each session for tracking and documenting a patient's individual therapeutic progression.

Though originally conceived to treat the lower back, the RPM™ may have expanded utility. Initial clinical evaluations have shown the potential to treat a variety of vertebral conditions currently considered untreatable by other rehabilitation devices. The company is filing numerous patents and has a strong IP position.

The chronic back pain market in the US exceeds \$100 billion annually, with an expected CAGR of 10%. Spinal MetRx can participate in this segment through the more than 40,000 facilities in the US providing back therapy to patients, including general and surgical hospitals, physical rehabilitation facilities, extended care facilities, physical therapy clinics, and individual practitioners. The company has positioned itself to successfully bring this product to market within two years through collaborative efforts with major research hospitals (providing medical validation), major universities, the Pittsburgh Life Science Greenhouse (providing business and fundraising guidance), BioOhio, and federal and state business development agencies.

We thank you for this opportunity.

Sincerely,



David R. Lewis, Managing Director

# VASOSTAR INC.

Reaching New Frontiers in Vascular Medicine

December 13, 2010

## 11-522

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

**Subject: 2011 OTFBP LOI**

Dear Ohio Department of Development,

Please accept this letter as our official Letter of Intent (LOI) to submit a proposal to the Ohio Third Frontier Biomedical Program for fiscal year 2011.

**Lead Applicant:** VasoStar Inc.  
7740 Metric Drive  
Mentor, OH 44060  
(440) 266-8226

**Contact:** Paul Erickson  
perickson@frantzgroup.com

**Project Title:** Vibrating Tip Guidewire System for Penetrating Chronic Occlusions

**Funds Requested:** \$1 million

**Known Collaborators:** Frantz Medical Development, Ltd.  
Mentor, OH 44060  
Contact: Stephanie Harrington, Vice President

Interplex Medical LLC  
Milford, OH 45150  
Contact: Matt Otten, Vice President

The Cleveland Clinic Foundation  
Cardiovascular Medicine  
Contact: Kiyo Fukamachi, M.D., Ph.D.

Stanford University School of Medicine  
Cardiovascular Medicine  
Stanford, CA 94305  
Contact: Peter Fitzgerald, M.D., Ph.D.

The next page contains a summary of the proposed program.

Sincerely,



Paul Erickson  
Senior Manager, Product Development  
VasoStar Inc.

# VASOSTAR INC.

Reaching New Frontiers in Vascular Medicine

*VasoStar's mission is to develop and commercialize electromagnetically driven guidewire systems that safely improve the success rate for crossing Chronic Total Occlusions.*

**The Need** – VasoStar has developed a unique vibrational guidewire system for penetrating hard arterial blockages, known as chronic total occlusions (CTOs). Current manual techniques for crossing CTOs are complex and generally require long procedure times with high contrast loads and radiation exposure. By and large, success ultimately depends on the skill and persistence of the clinician. As such, these procedures remain primarily the domain of diehard CTO specialists. New devices which can simplify, systematize, and speed the treatment of such cases would be an important addition to the arsenal of the interventionalist and allow many patients, who might otherwise be referred for bypass surgery, to be treated percutaneously.

**VasoStar Inc.** – VasoStar Inc. has developed a solution to this unmet need: a miniaturized electromagnetic engine that produces longitudinal vibrations at the guidewire tip for safely penetrating CTOs and passing through chronically stenosed lesions without changing the interventionalist's standard guidewire technique and feel.

VasoStar has exclusively licensed this technology from EYoCa Medical Ltd., an Israeli company. Frantz Medical Development (FMD), an Ohio-based medical device developer and manufacturer established in 1979, has ownership of VasoStar Inc. and has leveraged FMD engineering and operational resources to seed VasoStar's initiative.

With support of seed funding from the National Institutes of Health (NIH), the Global Cardiovascular Innovation Center (GCIC), and Frantz Medical, VasoStar has successfully designed and refined a guidewire and catheter system that can safely and effectively penetrate CTOs as demonstrated by benchtop testing, in vivo evaluations, and clinician assessments. In addition, VasoStar has established a clear path through the final phases of development, regulatory approval, and commercialization.

**Innovative Technology** – The VasoStar Vibrating Tip Guidewire (VTG) System incorporates a 0.014" guidewire with integrated micro magnets and a microcatheter fitted with electromagnetic (EM) coils that together form a magnetic engine. By driving the coils with pulses of alternating current, an alternating magnetic field is established that vibrates the guidewire tip like a miniature jackhammer for breaking through arterial blockages.

A unique advantage of the VTG technology is the fact that the workflow of the interventionalist remains essentially unchanged. Other active CTO devices deliver their energy via a bulky catheter, which prevents their use in small vessels, or they have a handpiece that attaches to the guidewire. The handpiece adds a layer of separation between the clinician and the guidewire and severely detracts from the tactile feedback and handling of the guidewire which the clinician depends on.

**Collaboration** – In Ohio, VasoStar has partnered with Frantz Medical Development to leverage medical device development and manufacturing capabilities, especially quality systems infrastructure, device design, and device assembly. For catheter manufacturing, VasoStar has partnered with Interplex Medical in South West Ohio. In addition, with the Cleveland Clinic and Stanford collaborations, this technology will be well vetted and optimized for clinical utility and effectiveness and will add a valuable revascularization tool for our leading vascular clinicians.

**Economic Growth** – While initially focused on cardiovascular, this platform technology also has application in peripheral and neurovascular procedures, as well as multiple product configurations; therefore, we are confident that the long term economic impact of the VasoStar program on the State of Ohio will be significant – by growing jobs in Ohio, expanding technical and manufacturing expertise, and building on local manufacturing and product development capabilities.



## Biomedical Informatics

John J. Hutton, MD  
Director

## Faculty

Bruce J. Aronow, PhD  
Karen Davis, PhD  
Mark Halsted, MD  
Michael Jansen, PhD  
Anil G. Jegga, DVM, MS  
Michal Kouril, PhD  
Long (Jason) Lu, PhD  
Jun Ma, PhD  
Keith Marsolo, PhD  
Mario Medvedovic, PhD  
Jarek Meller, PhD  
John P. Pestian, PhD, MBA  
Jerry L. M. Phillips, MS  
Andrew Spooner, MD  
Michael Wagner, PhD  
Yan Xu, PhD

Eszter Jakab Belcher, MS  
Business Director

**Date:** December 13, 2010

**Purpose:** Letter of Intent to submit an Ohio Third Frontier Biomedical proposal

**Contact:** John P. Pestian, Ph.D. ([john.pestian@cchmc.org](mailto:john.pestian@cchmc.org))

**Title:** Neuropsychiatric Drug Selection Using Advanced Clinical Decision Support

**Known Collaborators:** Cincinnati Children's Hospital Medical Center, AssureRx, Diamond Healthcare Corporation

**Summary:** This proposal will focus on the distribution and commercialization of advanced technology that is used for the identification and selection of neuro-psychiatric drugs. The collaborators includes expertise in algorithm development, product development, reimbursement and commercialization. Together they will deploy these technologies to support clinical decision.

Cincinnati Children's Hospital Medical Center is one of the top pediatric academic centers in the nation. As an Ohio based institution it employees more than 12,000 people and has a \$2.72 billion dollar regional impact.

Cincinnati-based AssureRx Health, Inc. is a personalized medicine company that specializes in pharmacogenetics and is dedicated to helping physicians determine the right drug at the right dose for individual patients suffering from medical conditions. The proprietary technology is a result of Third Frontier support and is based on pharmacogenetics - the study of the genetic factors that influence an individual's response to drug treatments - as well as evidence-based medicine and clinical pharmacology.

Diamond Healthcare Corporation is the national leader in the planning, development and operation of high quality behavioral health services in partnership with healthcare organizations. Diamond's client relationships span a diverse geographic and demographic range — from rural critical access hospitals to urban academic medical centers, from sole community hospitals to multi-hospital health systems, including faith-based healthcare organizations, not-for-profit systems and for-profit hospital companies.

Sincerely,

John Pestian, Ph.D.  
Associate Professor  
Director, Computational Medicine Center



## Project Summary

# 11-524

### 2011 OTFBP LOI

Lead applicant name	<b>The Turning Point, LLC</b>
Address	<b>87 Drummer Lane Redding, CT 06896</b>
Phone number	<b>203.938.3939</b>
Contact person	<b>F. Alan Schultheis, Founder and CEO</b>
Contact e-mail address	<b>aschultheis.tpbiotech.com</b>
Project Title	<b>Biomarker to Predict Risk for Back Pain and to Quantify Existing Back Pain</b>
Estimated grant funding request	<b>\$1,000,000</b>
Known collaborators	<b>University of Toledo (Toledo, OH) Cleveland Clinic (Cleveland, OH) Ohio State University (Columbus, OH) University of Akron (Akron, OH) University of Findlay (Findlay, Oh)</b>

## Project Summary

It is estimated that everyday, more than 30 mil. Americans suffer from back pain, 1.5 mil. disabled.<sup>1</sup>

*“While no one dies from mechanical back pain, it is one of the most common reasons for work disability. The bill for lost productivity and back-related health care is about \$100 billion a year.”<sup>2</sup>*

Core (axial) rotation is one of the most fundamental musculoskeletal movements and weakness in core rotation one of the leading causes of back pain.

*“Not only during gait is rotation of the spine involved but also during various daily routine activities [and essentially all sports] . . . It is also a known fact that excessive rotation of the spine in the industrial area is cause for 60% of major back injuries.”<sup>3</sup>*

Ever increasing expenditures to treat back pain have had little impact, the National Health Interview Survey showed low back and neck pain increased from 3.2% of the population in 1998 to 8.3% in 2006.

The Turning Point, LLC (Turning Point) proposes this project, **Biomarker to Predict Risk for Back Pain and to Quantify Existing Back Pain**. It will develop research based correlations between limitations in various measures of axial rotation as a predictor of future back problems and as quantifiable proof of existing problems causing back pain. Turning Point and its collaborators anticipate three key outcomes; 1) the first ever quantifiable process for predicting future, and evaluating and verifying back pain, 2) improved effectiveness in the non-invasive “pre-habilitation” and the treatment of existing back pain through more precise, measurable therapy and conditioning, and 3) the macro-economic potential to significantly reduce the very expensive lost productivity and insurance related costs.

Doctors, physical medicine specialists and therapists have limited measurement options for identifying musculoskeletal conditions that could lead to future back problems and for correlating existing back pain to underlying musculoskeletal limitations. Using its patented *Turning Point 4.0* therapy/conditioning device, Turning Point will work with the collaborators to:

1. Perform research to develop normative functional standards for back/core musculoskeletal rotation. The research will collect and validate data related to core/axial range of motion, symmetry, strength, and endurance. This new medical scholarship will result in normative functional standards for the healthy.
2. Perform research to develop functional standards for back pain sufferers. This research will collect and validate data on the same measures as item 1 above for individuals with varying levels of back pain and lumbar degenerative disease. Both efforts will require large populations to represent the demographics most affected by back pain.
3. Undertake and complete the statistical analysis needed to establish the correlations to link back pain to the underlying musculoskeletal conditions.
4. Actively engage the FDA at appropriate junctures during the project.

At the conclusion of this project, Ohio, five of its leading institutions and Turning Point, headquartered in Toledo, will bring the evaluation and care of non-surgical back pain from the “art” it is today to a quantifiable science that will help improve “pre-habilitation” and improve the effectiveness of treatment and potentially result in significant reductions to the associated costs.

It is anticipated that this project will require 3 years and \$1,000,000 to complete.

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<sup>1</sup> Healthvideo.com, Robert Bazell, NBC Universal, 2008.

<sup>2</sup> Dr. Timothy S. Carey, Professor of Medicine, University of North Carolina, published February 10, 2009

<sup>3</sup> Dr. Shrawan Kumar, Professor- Manipulative Medicine, University of North Texas, Health Science Center, 2003

December 14, 2010

**Letter of Intent - Ohio Third Frontier Biomedical Program**

**To:** Technology and Innovation Division, Ohio Department of Development  
**From:** Cleveland Clinic  
**Subject:** Biomedical Program Letter of Intent

**Lead Applicant Information:**

Cleveland Clinic  
Department of Neurological Surgery  
9500 Euclid Avenue / Mail Code S4  
Cleveland, Ohio 44195

**Contact Person:**

Edward Benzel, MD  
Office Phone: 216/445-6797  
Fax: 216/636-0325  
E-mail: benzele@ccf.org

**Proposed Project Title:** *Intelligent Mouthguard* for In Vivo Brain Injury Monitoring in Sports

**Estimated Grant Funds to Be Requested:** \$1,000,000 TFRD

**Known Collaborators:** Sportsguard Laboratories, Inc.

**Summary of Proposed Project:**

Concussion is the signature injury for participants in modern contact sports. Advancements in athletic performance, pace of play, and increases in the size and strength of athletes have made head impacts more violent. Increasing awareness of concussion prevalence in sports, along with its potential long term negative implications on brain health, have led to heightened demands from Congress, regulatory bodies, and players' groups to consider changes in protective equipment, rules of play, and athlete participation as a means to mitigate the risks associated with concussion. The lack of a reliable and accurate method to quantify in vivo athlete head impact dynamics in real time and a standard means to correlate this data to clinical outcomes have been two fatal flaws undermining initiatives designed to protect athletes from concussion and brain injury.

Scientists in the Cleveland Clinic Department of Neurosurgery, Neurological Institute and Spine Research Laboratory have developed technology that can reliably and accurately capture in vivo dynamic head impact data for correlation to clinical outcomes. The *Intelligent Mouthguard* captures impact data, transmits data wirelessly to sideline or ringside, processes the data into a clinically relevant format and enables data pairing with outcomes from physical exam, brain imaging, blood tests and neurocognitive and motor testing. The Cleveland Clinic *Intelligent Mouthguard* development team, in collaboration with commercial partners, is submitting this Third Frontier Biomedical Program proposal to assist *Intelligent Mouthguard* transition from the current-stage robust laboratory prototypes to commercially available *Intelligent Mouthguard* products by July 2012.

Respectfully submitted,

Edward Benzel, MD  
Department Chair, Neurological Surgery  
Cleveland Clinic

11-526

*PolyOne*

**PolyOne Corporation**  
33587 Walker Road  
Avon Lake, OH 44012  
440.930.1000  
www.polyone.com

December 14, 2010

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

Dear Sir/Madam,

Subject:

This letter transmits PolyOne Corporation's Letter of Intent to submit a proposal for the

Lead Applicant's name: PolyOne Corporation  
Address: 33587 Walker Road, Avon Lake, Ohio 44012 (Lorain County)  
Phone number: 440-930-1000  
Contact person: Thomas W. Hughes  
Email address for the contact: [thomas.hughes@polyone.com](mailto:thomas.hughes@polyone.com)  
Proposed Project title: **Development Of Self-Lubricating Catheters**  
Estimated Grant Funds to be requested: \$1,000,000  
Known Collaborators: Austen BioInnovation Institute of Akron, others  
One page summary of the proposed project: See Attached

Sincerely,



Dr. Cecil C. Chappelow  
Vice President, Chief Innovation Officer  
PolyOne Corporation

**Abstract:**

**Development Of Self-Lubricating Catheters**

Catheters typically are provided with an insertion lubricant to facilitate use. The lubricant is designed to liquefy at body temperature, providing reduced friction to aid with insertion. Lubricant is typically applied after the catheter has been extruded via a dip-coating process. This process has disadvantages in that it requires an added step in production, and also results in a potentially mobile lubricant on the surface. This can result in unintended coating of the lubricant on packaging materials during storage and handling.

Our proposed research is to utilize an emerging extrusion compounding technology to incorporate the lubricant directly into a neat resin or into a compounded radiopaque catheter resin material. Prior work shows that both small molecule and polymeric additives can be compounded wherein one modifier is intended to bloom to the compound surface, but the migration can be controlled through incorporation into the polymer. This approach would remove the need for a second process step, and would additionally ensure that the lubrication remains on the catheter surface when needed.

11-527

*PolyOne*

**PolyOne Corporation**  
33587 Walker Road  
Avon Lake, OH 44012  
440.930.1000  
[www.polyone.com](http://www.polyone.com)

December 14, 2010

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

Dear Sir/Madam,

Subject:

This letter transmits PolyOne Corporation's Letter of Intent to submit a proposal for the

Lead Applicant's name: PolyOne Corporation  
Address: 33587 Walker Road, Avon Lake, Ohio 44012 (Lorain County)  
Phone number: 440-930-1000  
Contact person: Thomas W. Hughes  
Email address for the contact: [thomas.hughes@polyone.com](mailto:thomas.hughes@polyone.com)  
Proposed Project title: **Development Of Alternate Radiopaque Technologies For Minimally Invasive Devices**  
Estimated Grant Funds to be requested: \$1,000,000  
Known Collaborators: Austen BioInnovation Institute of Akron, others  
One page summary of the proposed project: See Attached

Sincerely,



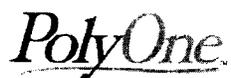
Dr. Cecil C. Chappelow  
Vice President, Chief Innovation Officer  
PolyOne Corporation

## **Abstract:**

### **Development Of Alternate Radiopaque Technologies For Minimally Invasive Devices**

Catheters for minimally-invasive procedures often are made radiopaque so that the specific location of the catheter in the body can be determined through fluoroscopic methods. These catheters are typically thermoplastic polyurethane or other elastomers filled with tungsten or barium sulfate. The high filler levels required to achieve good contrast in use can compromise the extrudability of the compounding as well as impact the physical properties. The high filler levels can make it difficult to extrude complex geometries with tight tolerances. Likewise, the high filler loadings negatively impact elasticity and tensile strength, which are desirable for physical maneuverability during use.

With the desire for reduced radiation levels, it is critical to improve the contrast observed during use while maintaining superior mechanical properties. Our proposed research is to identify alternate radiopacifier systems through two concurrent approaches. First is to develop and understanding of the radiopaque properties of mixed filler systems, which may provide synergies while providing for improved dispersion in the polymer matrix. Second is to identify techniques to attach non-particulate radiopacifiers to a polymer backbone, which could then subsequently be compounded with traditional radiopaque fillers. Both approaches may allow for higher contrast at reduced filler loadings.



11-528

**PolyOne Corporation**  
33587 Walker Road  
Avon Lake, OH 44012  
440.930.1000  
www.polyone.com

December 14, 2010

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

Dear Sir/Madam,

Subject:

This letter transmits PolyOne Corporation's Letter of Intent to submit a proposal for the

Lead Applicant's name: PolyOne Corporation  
Address: 33587 Walker Road, Avon Lake, Ohio 44012 (Lorain County)  
Phone number: 440-930-1000  
Contact person: Thomas W. Hughes  
Email address for the contact: [thomas.hughes@polyone.com](mailto:thomas.hughes@polyone.com)  
Proposed Project title: **Development Of Bio-Resorbable Compounds For Implant Applications On PLA, PGA, And PCL Compounding**  
Estimated Grant Funds to be requested: \$1,000,000  
Known Collaborators: Austen BioInnovation Institute of Akron, others  
One page summary of the proposed project: See Attached

Sincerely,

Dr. Cecil C. Chappelow  
Vice President, Chief Innovation Officer  
PolyOne Corporation

**Abstract:**

**Development Of Bio-Resorbable Compounds For Implant Applications On PLA, PGA, And PCL Compounding**

Bio-resorbable materials are increasingly used in orthopedic implants such as tissue and bone fixation devices, bioabsorbable stents, sutures, as well tissue scaffolding. The bio-resorbable materials used in these applications range from polylactides (PLA) to polyglycolides (PGA) as well as polycaprolactides (PCL).

Compounding fillers into these materials to achieve functionalization such as radiopacity, cell structure engineering, bone regeneration, as well as advantageous melt rheology characteristics is becoming an important area of focus for these materials as a one size fit's all scenario does not work in today's world of bio-resorbable materials.

We propose to utilize our extensive knowledge of blending and functionalization to develop technology and expertise that will help to optimize these materials for the applications areas listed above and extend their use beyond what the current constraints imposed by processing as well as fillers will allow.

## 2011 Biomedical Program Letter of Intent

Lead Applicant's Name: Cleveland Clinic

Contact Person: Joseph Iannotti, M.D., Ph.D.

Address: 9500 Euclid Ave., Mail Code A-41, Cleveland, OH 44195

Office Phone: 216/445-5151

Fax: 216/445-6255

E-mail: iannotj@ccf.org

Proposed Project Title: TIOSO technologies and concepts for other orthopedic applications

Estimated Grant funds to be requested: \$1,000,000 TFRD + \$1,000,000 WCF

Known collaborators:

Astro Manufacturing

Simbionix

Summary of the proposed project:

This intended Biomedical Program project is a follow-on to the TIOSO BRCP project awarded to the Cleveland Clinic in 2009. Since that award, our team has made great progress developing and testing product concepts for innovative Patient Specific Instruments (PSIs) to facilitate hip and shoulder joint replacement surgeries. We have received strong industry feedback about the clinical value of our TIOSO project, and plan to achieve FDA approval of our first device by the end of 2011. We have submitted 7 patent applications for the software, patient specific instrumentation, and novel surgical tools, and have identified additional patentable technologies that will be protected. Our development plan includes use of the current funding to develop a knee arthroplasty system and finance the further development of all these products for FDA approval which we expect will take through 2012.

Following this initial success, we are requesting additional 3<sup>rd</sup> Frontier funds to pursue additional related commercial opportunities:

- Applying the technologies and concepts developed in the TIOSO **project to other orthopedic applications, such as foot & ankle, hand & wrist, and trauma and deformity surgery**. These applications of pre operative software and tools to assist the surgeon in execution of the surgery is a very active area of development across the world. We believe we have developed a complete advantage for both the software applications and tools that we have developed. To maintain this advantage to protect our initial investment and shoulder and hip we must continue to innovate to make these products better and deliver a better product as well as expand the tools to other areas to produce an intergraded platform multiple tools for multiple clinical applications.
- **Developing and improving the manufacturing processes required to give our TIOSO products additional competitive advantage over similar products on the market.** Specifically, we have been able to develop a production process that allows us to go from software approval by the surgeon to PSI products (including sterilization) within 4 – 5 work days; the current industry standard is 4-6 weeks. We realize that our ability to achieve this rapid turnaround is in some measure because we are working closely with our internal development team and partners. We now need to develop processes and tools to allow us to bring our current level of turnaround to surgeons not part of the development team. This will require development of internet sites for transfer or images with the protection of patient specific information, improved process for development and approval of the surgical plan with external surgeons and then scale up to manufacture, quality assessment, packaging, sterilization and delivery of product and support of those products to the end user. We must develop infrastructure and process to do this faster and better than our competitors. We will use the additional funding to support these processes while using the current funding to develop and study the efficacy ( pre clinical and clinical trials) for the hip, shoulder and knee products defined in the original BRCP grant.

**11-530**

# **Cardiox Corporation**

4140 Tuller Road, Suite 104  
Dublin, Ohio 43017

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

December 14, 2010

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

**Subject: 2011 OTFBP Letter of Intent (LOI)**

Dear Sir or Madam:

This Letter of Intent is being provided in response to the requirements set forth in the Ohio Department of Development's Request for Proposal (RFP) entitled "Ohio Third Frontier Biomedical Program" for Fiscal Year 2011. As specified in paragraph 1.3.3 of the referenced RFP, we are pleased to provide the following referenced information.

- 1. Lead Applicant:** Cardiox Corporation  
4140 Tuller Road, Suite 104  
Dublin, Ohio 43017
- 2. Phone Number:** 614-791-8118
- 3. Contact Person:** Philip E. Eggers, Chief Technical Officer
- 4. Contact Person Email Address:** <philieggers@cardioxcorp.com>
- 5. Title:** Validation and Commercialization of System for Cardiac Output and Total Circulating Blood Volume Monitoring
- 6. Grant Funds Requested:** \$1,000,000
- 7. Planned Collaborators:** Nottingham-Spirk, QTest Laboratories and Ohio Hospitals
- 8. Summary of Proposed Project:**

The need for critical care is expanding rapidly in the U.S., as an aging population and shortened hospital lengths-of-stay increase the number of very sick patients and the intensity of care in acute-care hospitals. At the same time, hospitals have been plagued with personnel shortages, declining reimbursements, a shortage of critical care beds, and rising costs. Critical care units are the most expensive sites in the healthcare system, accounting for 28% to 35% of a hospital's total budget. Although hospital cost-cutting efforts have impacted the critical care

industry, the market for critical care products is still expected to grow substantially in the years ahead. The U.S. market for critical care products is projected to increase from \$1.97 billion in 2002 to an estimated \$2.6 billion in the year 2006, a compound annual growth rate of 7.2%.

In the hospital setting, over 30 million operations are performed annually in the U.S. of which 2.4 million are considered high risk. The mortality rate of high-risk patients in the month following surgery is reported to be in the range from 20 to 30 percent. One of the principal risks for such patients is a reduction in global oxygen delivery during and following surgery. Studies have shown that the cardiac output and total circulating blood volume during and after surgery are critical to maintaining oxygenation levels adequate to minimize morbidity and mortality risks. The continuous monitoring of total circulating blood volume particularly important in the management of patients suffering from renal failure, sepsis and septic shock, acute liver failure, kidney failure, acute respiratory distress syndrome, following trauma, during surgery and to allow early detection of post-operative hemorrhaging. Managing the patient during these critical situations is further complicated by the fact that administering either too much or too little fluid during hemodynamic crises or rapidly changing hemodynamic conditions can lead to an increased risk of morbidity or mortality.

Approximately 1.6 million patients require cardiac output measurement each year in the U.S and 3 million require such monitoring in the combined US/EU/Japan market. This represents a market potential for Cardiox product of over \$300 million in the U.S. and over \$600 million worldwide for disposable sales alone. In addition, Cardiox estimates that over 3.5 million patients per year in the U.S. and 7 million patients per year worldwide could also benefit from the availability of an accurate total circulating blood volume monitoring method. This represents a market of \$700 million per year in the U.S. and \$1.4 billion, worldwide.

Cardiox Corporation has previously developed and patented a highly accurate, minimally invasive, automatic, and continuous system to measure cardiac output and total circulating blood volume. Cardiox has invested over five years of research and development on a first-generation, minimally invasive method and system which is based on the same proven indicator/dilution principles used in current thermodilution and dye dilution methods. Cardiox proprietary method and system solves a number of problems which currently limit the accuracy and ease of use of all existing methods for measuring cardiac output on the continuing basis required for patient monitoring. The current gold standard for cardiac output measurement requires three or more injections of 5 to 10 ml of ice-cold isotonic saline into a pulmonary artery catheter which must be placed within the heart and entrance into the lungs. This existing method (known as the cold-bolus thermodilution method) is both labor intensive and exposes the patient to the additional risks associated with a catheter residing in the heart for typically three days or more. Also, the amount of injected liquid per test prevents the use of this method for continuous monitoring due to the problem of fluid overload in the patient. In addition, no accurate method currently exists for the continuous monitoring of a second critical parameter related to the total circulating blood volume. Cardiox method and system will allow both parameters to be simultaneously measured each time the small indicator injection is performed.

The proposed project will build upon Cardiox' platform technology, originally developed for its first product for detecting cardiac shunts, to validate and commercialize a product for the non-invasive continuous monitoring of cardiac output and total circulating blood volume. The existing Cardiox product for detection of cardiac shunts will be modified to incorporate an automated intravenous injection pump while utilizing all of the other non-invasive indicator detection functions of the existing Cardiox Controller/Monitor. This method and system for the continuous monitoring of cardiac output and total circulating blood volume utilizes Cardiox proven non-invasive technology for detecting blood-borne ICG indicator combined with an additional optical, transcutaneous measurement of hematocrit which enables the essential determination of the ICG concentration in the blood.

The scope of this proposed work will include both in vivo animal studies and clinical trials. The in vivo pig experiments will be conducted at QTest Labs in Columbus while the clinical trials will be performed in hospital sites within Ohio. The project team will include Nottingham-Spirk whose focus will be on the development of an automated infusion pump to deliver highly accurate, small doses of the FDA-approved indocyanine green (ICG) dye indicator at regular intervals. In this critical care patient monitoring product, very small amounts of ICG (e.g., 0.1 mg per injection) will be injected into a vein in the patient's arm about every 5 minutes. The known dose of each ICG injection combined with the measured change in ICG concentration vs. time as well as a hematocrit level (as detected non-invasively at the ear) will enable the accurate measurement of both cardiac output and total circulating blood volume based on established indicator-dilution principles.

The requested funding for the proposed project will be used for the validation and commercial release of Cardiox method and system for the continuous monitoring of cardiac output and total circulating blood volume for use in hospital settings for critical care patients.

\*\*\*\*\*

Please contact me if you have any questions.

Sincerely,

Philip E. Eggers  
Founder and Chief Technical Officer

Sent via email to OTFBP2011@development.ohio.gov

# IR Diagnostyx Inc

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December 14, 2011

# 11-531

The Ohio Department of Development

Subject : 2011 OTFBP LOI

Dear Sir or Madam,

This letter of intent is being provided in response to Request for Proposal (RFP) for the "Ohio Third Frontier Biomedical Program" 2011.

**Lead Applicant** : IR Diagnostyx Inc

**Address** : 1275 Kinnear Road, Columbus OH 43212

**Telephone** : 614-340-1686

**Contact Name** : Gary Smith

**Contact Email** : [smithg@irdiagnostyx.com](mailto:smithg@irdiagnostyx.com)

**Project Title** : Diagnosis of a disease condition using Infrared Spectroscopy

**Funds Requested** : est. \$1.0 million

**Collaborators** : Ohio State University, University of Toledo, Glickman Urology Institute-CCF, Beaumont Hospital Dept of Urology, Riverside Hospital, Morrison Medical, IC Association

**Summary of the Project** : IR Diagnostyx Inc., (IRDx) is a Columbus, Ohio based, early stage medical diagnostics company developing for market, an innovative minimally invasive diagnostic platform for medically challenging functional disease (MCFD) diagnoses. Medical trends toward personalized and preventive medicine are driving significant demand to reduce costs and provide early-stage disease diagnosis. The healthcare system currently lacks cost effective, accurate diagnostic methods for over 40 functional diseases (MCFD). Most significant of these are: Irritable Bowel Syndrome (IBS), Interstitial Cystitis (IC) - also known as Painful Bladder Syndrome (PBS), Fibromyalgia, and Chronic Fatigue Syndrome (CFS), which combined, affect over 85 million Americans. IRDx is developing a minimally invasive, serum based diagnostic test(s) that significantly shortens the time and reduces the cost to confirmatory diagnosis. IRDx technology will replace the current "rule-out" diagnostic approach which can take over 5 years, thousands of dollars and require interactions with multiple physicians before an accurate diagnosis. IRDx is currently focusing its efforts on commercializing the test for Interstitial Cystitis. The company requests the funds from the third frontier program to conduct a multi-site clinical trial in order to secure FDA approval for its diagnostic test(s). Specifically the funds will be used for developing clinical protocol, establishing IRB, setting up laboratory, recruiting 300-500 patients, processing the tissue samples, preparing a 510(k) submission, and stabilizing quality system. The company intends to complete the process of FDA approval in 2011 and launch the diagnostic platform in early 2012.

Please see [www.irdiagnostyx.com](http://www.irdiagnostyx.com) for more information.

11-532



**BETTCHER Industries, Inc.**

6801 State Route 60, Birmingham, OH 44816 USA • P.O. Box 336, Vermilion, OH 44089 USA

Phone: (800) 321-8763 or (440) 965-4422 • Fax: (440) 965-4900 • [www.bettcher.com](http://www.bettcher.com)



December 13, 2010

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

**Subject: 2011 OTFBP LOI**  
**VIA: E-mail to [OTFBP2011@development.ohio.gov](mailto:OTFBP2011@development.ohio.gov)**

To Whom It May Concern:

Please let this letter serve as notice of intent for Bettcher Industries to apply for the fiscal year 2011 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:** Bettcher Industries  
**Address:** 6801 State Route 60, Birmingham, OH 44816  
**Telephone:** 440-965-4422  
**Contact:** Timothy McNeill, Chief Financial Officer  
**E-mail:** [timmcneill@bettcher.com](mailto:timmcneill@bettcher.com)  
**Proposed project title:** Bettcher Medical Debridement Technology  
**Estimated grant funds to be requested:** \$1 million  
**Potential Collaborator(s):** Community Tissue Services

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

Sincerely,

Timothy McNeill  
Chief Financial Officer

Attachment: Project Summary





**Bettcher Medical Debridement Project  
2011 Ohio Third Frontier Biomedical Program  
Project Summary**

Bettcher Industries (“Bettcher” or the “Company”), located in Birmingham, Ohio (Erie County) has been an innovative market leader in the design and manufacture of meat processing and foodservice equipment since its founding in 1944 by Louis A. Bettcher. Originally located in a small machine shop in Cleveland, Ohio, Bettcher Industries relocated to Vermilion, Ohio in 1958. Today, the Company is still family-owned and operated, and employs over 160 individuals at its headquarters and sole Ohio location in Birmingham, where the company has been located since 1972. Bettcher has traditionally been focused on the design and manufacture of equipment primarily used in the meat processing industry. As a testament to the quality and innovative design features of its products, many of the original *Bettcher Carcass Splitters* are still in use after more than 50 years of service! More recently, Bettcher has proactively sought to expand and diversify its product offerings into other sectors, most notably the rapidly growing medical device industry. Towards this end, Bettcher is applying its decades of knowledge and expertise in the design and manufacture of meat processing equipment to an impressive portfolio of new products. The Company’s new products are currently positioned at various stages of the commercialization process.

Technologies and devices currently being developed by Bettcher Industries have tremendous potential for use in the fields of tissue and bone recovery, burn treatment, plastic reconstructive surgery, and dermolipectomy surgery. Bettcher’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 technologies and devices to the point of market entry within 18 months. Development of the technologies and devices would occur at the Company’s facility in Birmingham, 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 Bettcher’s headquarters and manufacturing facility in Birmingham, OH would occur throughout the duration of the Third Frontier project period.

The Company’s development and commercialization processes will be highly collaborative, and involve significant input from several healthcare organizations. For this project, Bettcher is collaborating with Community Tissue Services of Dayton, Ohio, and is exploring opportunities with other potential collaborators.



December 14, 2010  
Ohio Department of Development  
Technology and Innovation Division  
77 South High Street, 25th Floor  
Columbus, OH 43215

**Subject: 2011 Ohio Third Frontier Biomedical Program**

Dear Sir or Madam:

Please accept this Letter of Intent from Austen BioInnovation Institute in Akron for our Ohio Third Frontier Ohio Third Frontier Biomedical Program proposal. The relevant information about our proposal is as follows:

**Lead Applicant:** Austen BioInnovation Institute of Akron  
1 South Main Street, Suite 401  
Akron, OH 44308

**Contact Person:** Brian L. Davis, Ph.D.  
Vice President, Director Medical Device Development Center  
(330) 572-7547  
bdavis@abiakron.org

**Proposed Project Title:** Material Optimization for Biomedical Interfaces In Lower Extremity  
Prosthetics (Mobile prosthetics)

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

**Known Collaborators:** The University of Akron  
Ohio Willow Wood  
PolyOne Corporation

**Summary of Proposed Project:**

The amputee population in the U.S. is approximately 1.2 million people and is dominated by patients with diabetes. In contrast, the foreign market has a far higher percentage of traumatic amputations. In all cases, a major factor affecting the usage of prosthetic limbs is the quality of the skin at the interface with the prosthetic socket. If the skin is damaged or experiences pain due to chafing, maceration or other reasons, the amputee patient is unable to maintain an acceptable quality of life. Transfemoral amputations, in particular, can readily lead to sedentary lifestyles, which can compound health risk factors such as peripheral vascular disease or diabetes that often were the cause of the initial amputation. It is therefore imperative that amputee patients maintain an active lifestyle as a means of controlling the burden on the healthcare system.

The focus of the current project will be on biomaterials that permit an optimal interface between a patient's limb and their prosthetic limb. The market for such technologies is significant, particularly because the issues cut across all prosthetic componentry. The team that has been assembled to create an optimal prosthetic interface include faculty from the renowned polymer program at the University of Akron, leaders in polymer chemistry from Ohio's PolyOne Corporation, and engineers with a track record of commercializing prosthetic medical devices.

Sincerely,



Brian L. Davis, Ph.D  
VP, Medical Device Development Center

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

Please accept this letter of intent from Sensible Medical Innovations for our Fiscal Year 2011 Ohio Third Frontier Biomedical Program (“OTFBP”) proposal.

**Lead Applicant:** Sensible Medical Innovations  
**Address:** 5a Giborei Israel Street, Netanya, Israel 42504  
**Telephone:** 011-972-9-865-4402  
**Contact Person:** Samuel Goldberg  
209 Lake Bluff Drive  
Columbus, Ohio 43235  
614-396-6553  
**Contact Email:** [sgoldberg@sggslc.com](mailto:sgoldberg@sggslc.com); [amirr@sensible-medical.com](mailto:amirr@sensible-medical.com)  
**Proposed Project Title:** Commercialization of a Novel Non-Invasive Device for Congestive Heart Failure Diagnostics and Management  
**Grant Fund Requested:** \$1 million  
**Known Collaborators:** The Ross Heart Hospital, headed by the internationality acclaimed Dr. William Abraham  
The ElectroScience Laboratory (ESL), headed by the internationally acclaimed Dr. John Volakis, The Ohio State University;  
The Global Cardiovascular Innovation Center (GCIC)

## **One Page Summary:**

Sensible Medical Innovations is developing a breakthrough product line employing a novel sensing technology that is geared to revolutionize the treatment of Congestive Heart Failure (“CHF”). CHF is the number one cause of hospitalizations in the US and worldwide; it is considered the largest and most costly chronic disease accounting for 43% of Medicare spending. Sensible’s technology addresses the missing link in CHF management and treatment and is predicted to prevent over 40% of all hospital admissions. Preventing these hospitalizations is the key to significantly reducing one of America’s leading healthcare costs and improving the quality of life and mortality for millions of heart failure patients.

Sensible’s ReDS™ technology is the first to enable effective, non-invasive and continuous monitoring of CHF in both hospital and home environments. While implantable devices such as St Jude CardioMEMS technology and Medtronic OptiVol have recently proven that CHF monitoring dramatically reduces hospital admissions (by 38%), these invasive devices are applicable to a relatively small portion of the CHF population (around 15%), are expensive (above \$15,000) and involve the higher risks of a surgical procedure. Sensible’s products are a

non-invasive solution that matches the accuracy of implantable devices. As a result, Sensible will address the broader CHF population without the risk associated with implantable invasive technologies and with production costs of only a few dollars per unit.

Sensible's technology has an advanced ability to "see through walls." Derived from home-land security applications for through-wall imaging, Sensible is the first and leading company applying this technology to medical applications. Progress thus far has enabled Sensible to commence clinical trials in three sites and prove first-in-human feasibility.

Sensible's vision is to establish headquarters in Columbus, Ohio that will include a research center of excellence involving hightech radar and antenna research, a corporate center for business development, as well as a hub for manufacturing, marketing, and sales for international sales and distribution. The headquarters will also oversee multi-site clinical trials. To achieve large scale operations, Sensible will draw upon Ohio's wealth of educated, technical workforce talent. To date, Sensible has been working closely with world renowned cardiologist Dr. William Abraham, Director of the Division of Cardiovascular Medicine at The Ohio State University Medical Center. This project will also be in partnership with internationally acclaimed antenna expert Professor John Volakis, Director of the ElectroScience Laboratory at The Ohio State University.

Sensible's technology is a platform technology with a wide range of applications. It is geared to become the cornerstone modality for meeting the growing need for continuous monitoring and preventive mobile healthcare. Sensible's vision is to become a leading medical device corporation headquartered in Columbus, Ohio.

**11-535**

**Letter of Intent for 2011 Ohio Third Frontier Biomedical Program**

**Name:** Joseph P. Giuffrida, PhD

**Company:** Cleveland Medical Devices Inc.

**Address:** Cleveland Medical Devices Inc.  
4415 Euclid Avenue  
Cleveland, Ohio 44103

**Phone:** 216-619-5904

**Contact Person:** Joseph P. Giuffrida, PhD

**Contact Email:** [jgiuffrida@clevemed.com](mailto:jgiuffrida@clevemed.com)

**Proposed Project Title:** Web Integrated Exercise Technology for Motor Symptom Management in Parkinson's Disease

**Estimated Grant Funds:** \$500,000

## **Project Summary**

Parkinson's disease (PD) affects over 1.5 million people in the United States and its incidence continues to increase with 50,000 new cases reported each year. Parkinson's disease disrupts the motor system and is characterized by cardinal symptoms of tremor, bradykinesia (slowed movements), and rigidity. The disease most frequently occurs between 50 and 65 years of age. Symptoms directly affect a patient's quality of life and activities of daily living by impeding higher motor function required for coordination of multiple limbs and fine dexterity. Patients are prone to falling and increased risk for falling/hip fracture, decreased mobility, and social isolation. A five year study of nearly 1.9 million Medicare claims showed that PD patients incurred almost double the number of broken bones and hip fractures than non-PD patients. While traditional methods of treating PD motor symptoms include pharmaceutical interventions and deep brain stimulation, these methods are both associated with significant costs and adverse side effects including motor fluctuations and dyskinesias (involuntary, irregular movements), and patient outcomes often rely on their access to movement disorder specialists. This can create geographic or socioeconomic disparities in patient care. Preliminary data has documented that exercise performed at specific intensity levels can help minimize motor symptom severity both acutely and chronically and may even provide neuroprotective effects to slow disease progression. Therefore, the aim of this proposal, to develop a standardized and web integrated exercise system easily implemented in community-based settings to minimize motor symptoms for PD patients, could have a significant and wide spread impact to both improve intervention access and quality of life for disparate PD populations, as well as significantly reduce healthcare costs for the over 1.5 million people affected by the disease.

An effective system for exercise-based PD motor symptom therapy should 1) Provide intensity feedback to ensure a patient reaches levels required to alleviate motor symptoms, 2) Monitor motor symptom severity to ensure effective symptom control, 3) Be cost effective and simple to replicate in community settings across the country, and 4) Integrate centers and patients through web-based access. Providing widespread access to systems with these features should reduce Medicare usage costs and improve patient quality of life and overall health by providing a convenient means for the older adult population to participate in effective exercise programs tailored to the PD lifestyle. PD-fit development will leverage existing CleveMed technology for capturing Parkinson's disease motor symptoms with new hardware and software integration to provide a standardized exercise platform with motor symptom severity detection and closed loop patient exercise intensity feedback. The current symptom evaluation standard is the Unified Parkinson's Disease Rating Scale (UPDRS), a qualitative ranking system used to evaluate tremor, bradykinesia, rigidity, balance, and gait, in which clinicians subjectively assess severity and assign integer scores from 0 to 4. CleveMed has previously developed Kinesia™, an objective, patient-worn motion sensor-based technology platform, to automatically generate quantitative PD motor symptom scores highly correlated to expert clinician ratings during in-clinic exams. This proposed project will integrate Kinesia technology with exercise equipment and biometric exercise physiology measures, intensity training displays, and closed loop feedback in a compact package that can be easily translated to local community settings. User interface software will be developed to integrate system components and track and report patient progress. An exercise protocol for the older adult PD population will be developed and integrated into the software application. A web-based application will be developed to link data from community centers to other centers or clinicians, and also allow patients to track their own progress online. Finally, the system will be implemented and evaluated in several community settings. Throughout development, this project will leverage clinical expertise at several movement disorder centers throughout Ohio, as well as several community-based Parkinson's support groups across the state.

In terms of economic impact, this proposed technology will positively impact the State of Ohio economy in several ways. First, both in Ohio and across the nation, this system has the potential to improve access and decrease healthcare costs for the large Parkinson's disease population. More directly, the technology developed as part of this project has the potential to create significant new jobs in the state in the areas of manufacturing, clinical training, sales and marketing, and customer support. Finally, the technology will help drive a new commercial revenue stream to the State from the sale of hardware and software technology, web-based subscription access, and support and training packages.

CARDIOSTAR INC.

December 14, 2010

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

**Subject: 2011 OTFBP LOI**

Dear Ohio Department of Development,

Please accept this letter as the indication of our intent to submit a proposal to the Ohio Third Frontier Biomedical Program for the fiscal year 2011.

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

**Contact:** Tom Pavsek  
[tpavsek@frantzgroup.com](mailto:tpavsek@frantzgroup.com)

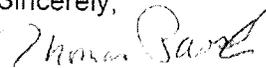
**Project Title:** Personal Cardiovascular Non-Invasive Hemodynamic Monitor

**Funds Requested:** \$1 million

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

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

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

Sincerely,  


Thomas Pavsek  
Product Manager  
CardioStar Inc.

## CARDIOSTAR INC.

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

**The Company** – Formed in 2009, CardioStar Inc. is a joint equity start-up company between an Ohio-based company, Frantz Medical Development Ltd. (FMD) and a Japanese medical device company, X-Cardio, KK. CardioStar's mission is to improve the field of diagnosis and treatment support of cardiovascular disease by providing innovative, non-invasive solutions to beat-to-beat hemodynamic monitoring. In 2009, CardioStar received seed funding through Cleveland Clinic's Global Cardiovascular Innovation Center (GCIC), funded through the Ohio Third Frontier initiative. Its collaboration with Cleveland Clinic ensures that our Personal Cardiovascular Monitor ("PCM") will meet clinical requirements yet integrate easily into the clinical routine. In addition, the clinical collaborator will be essential in the product's commercialization, penetration and success.

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

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

**The Market** - Continuous BP Monitoring and extracting Cardiovascular parameters like Cardiac Output, Central BP, etc are associated today with critical condition patients in the OR and ICU. This is because true Beat-to-Beat BP monitoring is done today only invasively, using arterial lines that pose high risks to the patients and high cost to the hospitals. Under this cost-effectiveness limitation, doctors settle for the unsatisfactory but inexpensive solution of non-invasive measuring of peripheral Systolic and Diastolic BP once in a while. The existing market is of 20 million BP monitors annually, with an average cost of about \$100 each. Providing a PCM for the same price range will pave the way to replacing these unsatisfactory devices with

## CARDIOSTAR INC.

the much needed cardiovascular parameters at all times. It is expected that besides replacing the existing devices it will create a much bigger demand, similar to what happened with Oximetry.

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



11-537

December 13, 2010

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

RE: Letter of Intent to submit a proposal for the Ohio Third Frontier Biomedical Program

This will serve as our LOI to submit a proposal for the above program.

Lead Applicant

Name: Chemsultants International  
Address: 9079 Tyler Blvd., Mentor, Ohio 44060  
Telephone: 440-974-3080  
Contact Person: Joseph T. Mausar  
Email: jmausar@chemsultants.com

Proposed Project Title: Adhesion-releasable skin contact adhesive for wound care and other medical applications

Estimated Grant Funds: \$ 450,000

Known Collaborators: American Medical Adhesives LLC.  
230 Pheasant Run Drive, Chagrin Falls Ohio 44022

A Summary of the proposed project follows on page 2 of this letter.

Best regards,

A handwritten signature in cursive script that reads "Gary A. Avalon".

Gary A. Avalon  
Chief Operating Officer

9079 Tyler Boulevard  
Mentor, OH 44060  
P: 440.974.3080  
F: 440.974.3081  
info@chemsultants.com  
www.chemsultants.com



## Summary of the Proposed Project

**Title:**

**Adhesion-releasable skin contact adhesive for wound care and other medical applications**

This project proposes to complete development of a medical grade adhesive that will adhere adequately to a wide variety of skin types under various wear conditions yet is able to be removed without excessive pain or damage/trauma to the skin area when required by significantly reducing the adhesion properties of the adhesive on demand. The successful adhesive product must avoid the use of harsh chemicals, or extraordinary steps to accomplish removal. The successful adhesive product must also stand up to human perspiration / bathing / water contact for up to seven days without losing its adhesion effectiveness.

Most likely path to success is a combination of approaches. Initial work has identified likely avenues or approaches with the most promising being:

- An engineered sharp glass transition polymer approach - crystalline melting of the adhesive to facilitate removal
- Employing a balance of polymer functional groups for adhesion with glass transition temperature and polymer structure engineering to facilitate removal
- A change-in-adhesion resulting from a change-in-wound-dressing-temperature approach utilizing an external warming process to facilitate removal
- Time duration adhesive migration into the supporting wound care dressing layer with applied heat, and shrinkage of film to help debond the adhesive to facilitate removal

The project will complete evaluation of these approaches, identify the most promising approach and begin development of a commercializable medical grade adhesive.

Applications for the proposed adhesive include wound care dressings and bandages, ostomy mounts, surgical drapes and transdermal patches for pharmaceutical, nutraceutical and cosmeceutical applications.

9079 Taylor Boulevard  
Mentor, OH 44060  
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**11-538**

December 14, 2010

2011 Ohio Third Frontier Biomedical Program (OTFBP)  
Ohio Department of Development  
Technology and Innovation Division, Attention: OTFBP  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, Ohio 43215

This Letter of Intent is being submitted by Tendon Technologies, LTD, DBA Ortheon Medical. (Lead Applicant) in anticipation of a proposal for the 2011 Ohio Third frontier Biomedical Program (OTFBP).

Lead Applicant:  
Tendon Technologies, LTD, DBA Ortheon Medical  
777 West Swan Street  
Columbus, Ohio 43212  
(614) 228-8008 (office)  
(614) 228-8088 (fax)

Lead Applicant Contact:  
Michael Ward  
[MWARD@ORTHEON.COM](mailto:MWARD@ORTHEON.COM)  
(614) 570-9614 (cell)

Project Title: TenoFix

Budget request estimate: \$1,000,000.00

Known Collaborators:  
Lawrence Lubbers M.D.  
Warren Williamson IV  
Richard Coleman M.D.

The overall goal of this project is to further develop the TenoFix tendon repair system to allow for additional surgical techniques in the repair of torn/lacerated flexor tendon while keeping with a procedure that is easy to perform, does not cause bunching or gapping of tissue, does not compromise vascularity and is strong enough to allow for immediate active motion therapy as needed.

In our submission we will be requesting funds to significantly enhance the existing TenoFix tendon repair system to allow for the development of a bone anchor for more distal repairs and an enhanced soft tissue anchor that will allow for enhanced holding power so that the system can be used in more highly loaded tendons throughout the patient. The work will be completed in a manner that is consistent with the process needed (systematic steps & proper paperwork) allowing for submission of applications to the proper regulatory bodies (FDA) for approval of the enhanced TenoFix tendon repair system.

Tendon Technologies TenoFix tendon repair system is currently on the market and has been used by over 350 surgeons in the US to repair in excess of 2,500 tendon injuries over the past 5 years with no reported failures.

Traditional tendon repair methods require lengthy immobilization after surgery to avoid tearing of the newly repaired tendon. Lengthy immobilization often leads to scarring that restricts flexibility and often requires repeat surgeries.

The TenoFix tendon repair system utilizes a small (2mm x 3mm) proprietary soft tissue core and coil combination which is pre-loaded into an installation instrument. As it is corkscrewed into a damaged tendon, it gathers the tendon fibers as it turns, in effect, harnessing the intrinsic strength of the tendon. A braided 2.0 stainless steel suture is then inserted through the anchor and passed through to the other side where the process is repeated. The severed ends of the tendon are then approximated or pulled together. The corkscrew action holds the key to the concept behind the anchoring system. Where traditional techniques utilize sutures that can be pulled delicate tendon fibers leading to separation called "gap", the anchoring system provides additional support for the tendon allowing motion therapy to begin without placing undue stress on the tendon.

The degree of difficulty in repairing tendon lacerations differs for each of the five zones. Zone lacerations are the most difficult to repair because of the complex anatomical structure and mechanical performance of the flexor tendons in the region. Post operatively, management and rehabilitation of zone II repairs are complicated because of the involvement of the sheath and pulleys so restoring function after flexor tendon injuries is one of the greatest challenges to hand surgeons and therapists.

The integrity of the tendon repair and the degree of restoration of; range of motion, grip strength and functionality of the affected digit(s) each contribute to the success or failure of the flexor tendon repair.

The TenoFix tendon repair system is a proven technology that will continue to evolve with additional research and the development of enhancements of the soft tissue anchoring system allowing for a bone anchor mechanism for more distal repairs. In addition, the proposed development for final commercialization of a stronger anchor will open up a market that is over a magnitude larger than the current market that is being served by the TenoFix.

Tendon Technologies is solely focused on the further development of enhancements of the TenoFix tendon repair system. Tendon Technologies is owned by a partnership of engineers and surgeons.

The research and development efforts of this proposed effort will be managed by Ward Engineering. Manufacturing of the commercial technology will take place at Ward Engineering until such time as commercial success will allow tendon Technologies to build and operate its own facilities. Ward Engineering has developed a commercialization plan for this technology based on significant experience in taking a number of concepts of medical technology through the process of FDA approved and commercial sales.

Ward Engineering is an ISO 13485-certified medical research and development engineering firm, founded in 1991 and located in Columbus, Ohio just west of The Ohio State University. Ward Engineering is housed in a 20,000 sq. ft. facility and employs just under 30 engineers, technicians and support staff. In addition, Ward Engineering is a FDA registered medical manufacturing facility that currently manufactures two class 2 medical devices. Ward Engineering's expertise in design control and creative problem solving has flourished, completing projects including clinical equipment, disposables, surgical instruments, therapy delivery devices and implants.

Ward Engineering's quality system complies with FDA's 21 CFR part 820 and is designed to provide its clients with well documented, risk assessed medical products. In addition, Ward Engineering also provides precision components manufacturing and assembly services in their ISO Class 8 clean rooms (ISO 14644-1 standard) which are designed and used for assembling medical devices.

Ward Engineering has extensive experience in taking concepts for medical devices through the 510K regulatory submittal process of the FDA. Approved devices that are currently on the market with a portfolio of medical devices including:

- TenoFix Tendon Repair System\*
- Sakura Automated Embedding System Auto-Tec\*\*
- Sakura Accu-Edge Grossing Tools\*\*
- Pedimed Drug Delivery Device
- Sakura Automated Immuno-Histological Stainer \*\*
- Minimally Invasive Devices ClearVU \*\*
- Vertebraion \* \*\*
- Tubal Ligation System
- Anastomic Clip and Delivery System\*\*
- Gastrointestinal Stapler Device\*\*
- Methods for Implantable Bone Prosthesis\*\*
- Minimally Invasive Lung Disease Implant and Delivery System\*\*
- Tissue Stabilizer for Open Heart Surgery\*\*
- Minimally Invasive Heart Valve Delivery System\*\*

\*Privately Held, Company name withheld

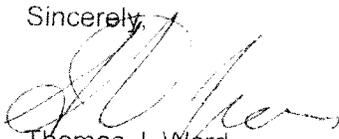
\*\* Products being sold internationally today

The Proposed effort submission will include the following:

- Description of Manufacturing of the TenoFix.
- Description of GMP facilities located in Columbus, Ohio where TenoFix development work and manufacturing will be completed.
- A listing of all Ohio based companies involved in the development and manufacturing of the TenoFix.
- A projection of sales and growth of TenoFix, including investments in proposed jobs created.
- Presentation of marketing efforts completed to date, including a description potential market for the TenoFix.
- Design of the improvements to TenoFix that will allow for significant market share increase.
- Presentation of external verification and validation of the performance of the TenoFix.
- Review of regulatory work completed to date and presentation of the regulatory plan for the Commercialization of the new features of the TenoFix.
- Plan for the completion of the efforts to take TenoFix from its current commercial position to an enhanced position, including budget, schedule and manpower.

A laboratory dedicated to Tendon Technologies has been setup at Ward Engineering in which to complete the commercialization of the TenoFix technology. This fully equipped laboratory has been established in a manner consistent with Ward Engineering facilities including: quality control, inspection facilities, computer systems, communication, offices, conference rooms and all additional amenities required by Tendon Technologies. In addition all Ward Engineering personnel including engineering, fabrication, administrative, bookkeeping and quality control are available to support Tendon Technologies.

Sincerely,



Thomas J. Ward  
President  
Tendon Technologies

777 West Swan Street ~ Columbus, Ohio 43212

Phone: 866-TENOFIX ~ Fax: 407-671-5380

[www.orthcon.com](http://www.orthcon.com)

## PreCelleon, Inc.

777 West Swan Street  
Columbus, Ohio 43212-3864

614-228-8008 (VOICE)  
614-228-8088 (FAX)

December 14, 2010

2011 Ohio Third Frontier Biomedical Program (OTFBP)  
Ohio Department of Development  
Technology and Innovation Division, Attention: OTFBP  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, Ohio 43215

This Letter of Intent is being submitted by PreCelleon, Inc. (Lead Applicant) in anticipation of a proposal for the 2011 Ohio Third frontier Biomedical Program (OTFBP).

Lead Applicant:  
PreCelleon, Inc.  
777 West Swan Street  
Columbus, Ohio 43212  
(614) 228-8008 (office)  
(614) 228-8088 (fax)

Lead Applicant Contact:  
Michael Ward  
[MWARD@PRECELLEON.COM](mailto:MWARD@PRECELLEON.COM)  
(614) 570-9614 (cell)

Project Title: CellGenus

Budget request estimate: \$1,000,000.00

Known Collaborators:  
Ohio State University - Department of Chemical and Biomolecular Engineering  
Cleveland Clinic

The goal of this proposed project is to complete the development for commercialization of the CellGenus, a robust negative depletion system for the enrichment of circulating tumor cells (CTC) and circulating endothelial cells (CEC) from the blood of cancer patients. Interest in the potential of identification and enumeration CTC for diagnostic, prognostic and research utilities continues to grow and yet current commercial technology has significant limitations including limited CTC identification and absorbent costs. In our submission we will be requesting funds to complete FDA required development efforts to demonstrate the CellGenus performs to an equivalent or superior standard as compared to the current instruments being utilized in the market.

The ability to accurately detect, identify and quantify blood-borne CTC and CEC could, in addition to diagnostic/prognostic importance, be additional keys to clarifying the angiogenic and metastatic processes from primary tumors for a variety of cancers. Accurate enumeration of CTC will provide a commercially viable clinical diagnostic to be used for the treatment of tumor growth and regression, metastasis and disease progression.

We submit that the CellGenus instrument is a significant improvement in detection technology and our proposal will be focused on: 1) design changes to further enhance the technology, 2) further clinical verification and validation required by the FDA, and 3) completion of business challenges such as completion of IP filings, ramping up of manufacturing, and initiating distribution of the CellGenus

PreCelleon is solely focused on the commercialization of the technology that is licensed from OSU and the Cleveland Clinic. The research and development efforts of this proposed effort will be managed by Ward Engineering. Manufacturing of the commercial technology will take place at Ward Engineering until such time as commercial success will allow PreCelleon to build and operate its own facilities. Ward Engineering has developed a commercialization plan for this technology based on significant experience in taking a number of concepts of medical technology through the process of FDA approved and commercial sales.

Ward Engineering is an ISO 13485-certified medical research and development engineering firm, founded in 1991 and located in Columbus, Ohio just west of The Ohio State University. Ward Engineering is housed in a 20,000 sq. ft. facility and employs just under 30 engineers, technicians and support staff. In addition, Ward Engineering is an FDA registered medical manufacturing facility that currently manufactures two class 2 medical devices. Ward Engineering's expertise in design control and creative problem solving has flourished, completing projects including clinical equipment, disposables, surgical instruments, therapy delivery devices and implants.

Ward Engineering's quality system complies with FDA's 21 CFR part 820 and is designed to provide its clients with well documented, risk assessed medical products. In addition, Ward Engineering also provides precision components manufacturing and assembly services in their ISO Class 8 clean rooms (ISO 14644-1 standard) which are designed and used for assembling medical devices.

Ward Engineering has extensive experience in taking concepts for medical devices through the 510K regulatory submittal process of the FDA. Approved devices that are currently on the market with a portfolio of medical devices including:

- Sakura Automated Embedding System Auto-Tec\*\*
- Sakura Accu-Edge Grossing Tools\*\*
- Pediamed Drug Delivery Device
- Sakura Automated Immuno-Histological Stainer \*\*
- Minimally Invasive Devices ClearVU\*\*
- Vertebration\* \*\*
- Tubal Ligation System\*
- Anastomic Clip and Delivery System\*
- Gastrointestinal Stapler Device\*
- Methods for Implantable Bone Prosthesis\*
- Minimally Invasive Lung Disease Implant and Delivery System\* \*\*
- Tissue Stabilizer for Open Heart Surgery\*
- Minimally Invasive Heart Valve Delivery System\*
- TenoFix Tendon Repair System\*

\* Privately Held, Company name withheld

\*\* Products being sold internationally today

The PreCelleon Proposed effort submission will include the following:

- Description of Manufacturing of both the CellGenus and disposables.
- Description of GMP facilities located in Columbus, Ohio where CellGenus development work and manufacturing will be completed.
- A listing of all Ohio based companies involved in the development and manufacturing of the CellGenus and disposables.
- A projection of sales and growth of PreCelleon, including investments in proposed jobs created.
- Presentation of marketing efforts completed to date, including a description potential market for the CellGenus and disposables.
- Post beta design of the proposed commercial version of the CellGenus.
- Presentation of external verification and validation of the performance of completed prototype, alpha, and beta CellGenus designs.
- Review of regulatory work completed to date and presentation of the regulatory plan for the Commercialization of the CellGenus.
- Plan for the completion of the Cell Genus from its current position to complete commercialization, including budget, schedule and manpower.

A laboratory dedicated to PreCelleon has been setup at Ward Engineering in which to complete the commercialization of the CellGenus technology. This fully equipped laboratory has been established in a manner consistent with Ward Engineering facilities including: quality control, inspection facilities, computer systems, communication, offices, conference rooms and all additional amenities required by PreCelleon. In addition, all Ward Engineering personnel including engineering, fabrication, administrative, bookkeeping and quality control are available to support PreCelleon.

Sincerely,



Thomas J. Ward  
President  
PreCelleon, Inc.



# ARTERIOCYTE

Commercialization of GMP Grade NANEX™ Kit. In this phase Arterioocyte will setup a GMP production facility and work with different suppliers to supply a GMP grade product for HSC Expansion, which can be marketed into clinical laboratories for their clinical research projects and human trials. 2) In the meantime, a Prototype of a fully closed clinical culture system with NANEX™ coating will be developed and tested through pre-clinical studies. The data from this study, as well as the on-going clinical trial from Arterioocyte using NANEX™ technology for Critical Limb Ischemia, will be used to obtain FDA 510(k) Approval by the end of the project. Arterioocyte expects to have the regulatory approval within five (5) years, and start manufacturing and distributing such products to hospitals as a medical device to expand HSCs *ex vivo* for bone marrow transplantation. Through this project, Arterioocyte expects to create Ohio-based jobs in manufacturing, quality, sales and marketing, and generating revenue through its GMP grade product within the project period. With the company's successful track record in the past Ohio Third Frontier Programs, Arterioocyte is confident in creating more jobs and revenues to the State through its commercialization efforts.