



January 25, 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
Proposed title:	Predicting cardiac toxicity in humans
Estimated Grant Funds:	\$1,000,000
Known collaborators:	ChanTest Corporation

A summary of the proposed project is attached.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael Conley", is written over a white background.

Michael Conley  
Chief Financial Officer

Cc: G. Kirsch, ChanTest Corporation

## **Predicting cardiac toxicity in humans**

For chemical products such as drugs, cosmetics, and pesticides to reach and stay on the market they must be safe. Today, this assessment is primarily performed using animal experiments on species such as rats and mice. Unfortunately, the results are not always relevant to human health considerations. These experiments are also time-consuming, expensive, and require the use and sacrifice of large numbers of animals. This in turn directly influences the rate at which new products reach the market. The costs of these tests are, however, dwarfed by the potential risk of exposing the general population to a dangerous agent.

It is essential that any product does not cause cardiac toxicity, which includes adverse effects on the heart muscle, valve or production of fatal arrhythmias. It is one of the major areas of concern in the development of new drugs as well as one of the leading causes that drugs are taken off the market. In the last 30 years approximately 28% of all drugs were removed from the market as a result of cardiac problems.

In recent years, a number of new approaches have been developed as alternatives to traditional animal testing, including in vitro and computer-based models. These approaches are able to screen considerably larger numbers of chemicals at lower costs. 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 develop in collaboration with the US Food and Drug Administration. ChanTest provides pre-clinical cardiac risk assessment services, including 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. These approaches will focus on the development of tools that are predictive of cardiac toxicity in humans.

Using these tools throughout research and development in the pharmaceutical, cosmetics, 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 hire additional employees in Ohio and solidify Ohio as a center of excellence that is at the forefront of alternative methods for cardiac safety assessment.



# Medical Center

Cardiovascular Medicine

## OTFBP 10-829

Davis Heart & Lung Research Institute  
473 West 12th Avenue, Suite 200  
Columbus, OH 43210-1252

Administrative Office: 614.293.4967  
TollFree: 1.877.478.2478  
Fax: 614.293.5614

Physician Referral: 614.293.7677  
Toll Free: 888.293.7677

January 22, 2010

*Specializing in:*

*Arrhythmia Monitoring  
Cardiac Catheterization  
Cardiovascular Clinical Trials  
Cardiovascular Rehabilitation  
Clinical Cardiovascular Disease  
Congenital Heart Disease  
Coronary Bypass  
Diagnostic Services  
Echocardiography  
Electrocardiography  
Electrophysiology  
Heart Failure Program  
Heart Transplant Program  
Interventional Cardiology  
Mitral Valve Repair  
Pacemaker Services  
Preventive Cardiology  
Pulmonary Hypertension  
Therapeutic Services  
Vascular Angiography  
Vascular Medicine  
Women's Health*

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

Re: LOI Ohio Third Frontier Biomedical Program

Dear Ohio Department of Development:

This letter serves as notification of our intent to submit a project proposal to the Ohio Third Frontier Biomedical Program for Fiscal Year 2010.

**Lead Applicant:** The Ohio State University

**Address:** 410 West 10<sup>th</sup> Ave.  
Columbus, OH 43210

**Telephone:** 614-293-0739

**Contact person:** Orlando P. Simonetti, PhD  
Associate Professor, Internal Medicine and Radiology

**Email:** [simonetti.9@osu.edu](mailto:simonetti.9@osu.edu)

**Project Title:** Novel sensor technology for physiological monitoring during magnetic resonance imaging

**Estimated Funding Request:** \$1,000,000 Third Frontier R&D Fund  
\$ 100,000 Wright Capital Fund

**Known Collaborators:** SRICO, Inc.  
Siemens Healthcare, Inc.

**Project Summary:**

Magnetic resonance imaging (MRI) is becoming increasingly important in the diagnosis and evaluation of patients with cardiovascular disease. MRI of these patients requires accurate and reliable sensing of the electrocardiogram (ECG) both for patient safety as well as for accurate synchronization of image acquisition to the cardiac cycle. The expanding applications of interventional and intra-operative MRI also require accurate patient monitoring, as do the imaging of critically ill and sedated patients. Additionally, new developments in functional brain imaging (fMRI) could benefit from simultaneous electroencephalographic (EEG) monitoring. Easy and accurate monitoring of these electrophysiological signals in the high magnetic field environment within an MRI system remains an elusive target of research and development efforts.

SRICO, Inc., located in Columbus, Ohio, specializes in the design, development, manufacture, and worldwide marketing of high performance optical integrated circuit components and optoelectronic subsystems that dramatically improve optical signal transmission and electrical measurement in communication and sensor networks. SRICO has developed proprietary sensor technology (US patent 7,447,534) that will enable easy and accurate acquisition of physiological electrical signals in the high magnetic field environment created by the MRI system. The aim of the proposed collaborative project between SRICO and The Ohio State University will be to develop patient monitoring devices based on this novel sensor technology. Siemens Healthcare will also partner in this effort and support the integration of monitoring devices with MRI systems at OSU. The SRICO sensors will also offer advantages in ECG and EEG monitoring outside of the MRI environment; these additional applications will also be explored.

Sincerely,



Orlando P. Simonetti, PhD  
Associate Professor  
Internal Medicine and Radiology  
The Ohio State University



**2010 Ohio Third Frontier Biomedical Program - Letter of Intent**

Lead Organization: Juventas Therapeutics, Inc.  
Address: 10265 Carnegie Avenue, Cleveland OH 44106  
Contact Person: Rahul Aras, Ph.D.  
Title: President & CEO  
Email: [Rahul@juventasinc.com](mailto:Rahul@juventasinc.com)  
Phone: 216-445-0830

This Letter of Intent confirms that Juventas Therapeutics will submit a proposal entitled **Novel Epidermal Wound healing: SDF-1 Treatment for Advanced Regenerative Therapy (NEW START)** requesting approximately \$1,000,000 from the Ohio Third Frontier Biomedical Program. Through NEW START, Juventas Therapeutics, a clinical-stage, venture-backed regenerative medicine company will collaborate with The Cleveland Clinic Heart Center to develop and commercialize ACRX-100 to accelerate wound repair and prevent scarring after cardiovascular surgery.

Juventas Therapeutics has already developed its lead product, ACRX-100, through pre-clinical studies and has initiated a Phase I clinical trial evaluating the safety and efficacy of this product in patients with heart failure with approval from the Food & Drug Administration (FDA). ACRX-100 is a non-viral DNA plasmid engineered to express human Stromal cell-Derived Factor 1 (SDF-1). SDF-1 triggers a number of protective molecular cascades that are both anti-inflammatory and anti-apoptotic. Furthermore, SDF-1 is a strong chemo-attractant of stem cells and progenitor cells that promote tissue preservation and blood vessel development. As part of the regulatory package submitted to the FDA, Juventas demonstrated that ACRX-100 is both safe and efficacious at promoting cardiac function in a porcine model of heart failure. Expanding its cardiovascular applications, Juventas has gone on to show that ACRX-100 also promotes new blood vessel growth, accelerates repair and prevents scarring in porcine acute full-thickness wounds. NEW START will build upon these findings to develop ACRX-100 for wound repair and scar prevention through completion of human clinical trials in patients having undergone median sternotomies. The developed product will address the broader unmet clinical needs in the multi-billion dollar wound healing market specifically related to acute traumatic wound care, cosmesis, and military combat care.

Sincerely,

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

Rahul Aras, Ph.D.

# OTFBP 10-831

CardioQuickSys™  
11785 Highway Dr., Suite 100  
Sharonville, Ohio 45241  
513.759.4333  
L. Ross Love  
[rlove@bluechip-enterprises.com](mailto:rlove@bluechip-enterprises.com)

January 22, 2010

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

Project Title: CardioQuick Patch® Commercialization  
Grant Funds Requested: \$1,000,000  
Current Collaborators: Dr. Ed Goldman  
Joe Myers, President/CEO JM Capital Ventures, LLC  
Bernard Anderson, President Anderson Financial Solutions

Dear Sir/Madam:

This letter has been prepared by CardioQuickSys™ to announce our company's intention to apply for an Ohio Third Frontier Biomedical Grant. The grant would be used in partnership with private investment to assist in commercializing and bringing to the healthcare market the Company's first product, the CardioQuick Patch®, a significant breakthrough in electrocardiogram (EKG) electrode placement.

The CardioQuick Patch® has the potential to become a new "best practice" for securing a 12-lead EKG reading, creating the potential to save the lives of tens of thousands of heart attack patients each year who might otherwise take longer to accurately diagnose and treat. The Patch is a breakthrough medical device that delivers significantly more accurate and rapid placement of the precordial (chest) electrodes when performing a 12-lead electrocardiograph (EKG), compared to the age-old practice of using individually-placed single electrodes.

Why is this important? For patients experiencing a cardiac event, accuracy and speed in securing an accurate EKG reading to guide diagnosis and treatment is the most important factor for improving outcomes, including survival. The current practice is to manually place the six individual electrodes on the chest to get the EKG reading, with most practitioners "approximating" the electrode location based on past experience. Approximating electrode placement is an 'accepted' bad practice that can lead to inaccurate placement which alters the EKG reading and leads to errors in diagnosis and treatment, adversely effecting patient morbidity and mortality levels.

In a year-long, independent study utilizing EMT Basics conducted by the EMS Medical Director for Region 5 in the State of Ohio, there was a 97.4% accuracy rate when applying the precordial leads using the Patch. In addition in this study, the CardioQuick Patch® reduced "door-to-balloon" time by 31 minutes versus the time for patients on whom single electrodes were used. (Note that "door-to-balloon" time, i.e. the time from patient pick-up to initial treatment, is becoming a critical performance measure for hospitals and EMS units.)

This new medical device is protected by multiple patents (no comparable competitive products exist).

The CardioQuick Patch® is now being introduced broadly. The Cleveland Clinic will conduct an extended trial of the Patch in one or more of its regional hospitals. The Summa Health System (Akron) has scheduled use of the Patch in a lead hospital (Western Reserve). St. Luke's Episcopal Hospital in Houston, ranked #5 in the country for heart care by U.S. News & World Report, has committed to begin an extended trial. In addition, use of the Patch is also being considered by decision-makers at a number of hospitals including: University's Case Medical Center and MetroHealth Medical Center in Cleveland.

Please send an application and written questions to CardioQuickSys™, in care of L. Ross Love, at the address listed above. Our company is prepared to file its application by the March 1, 2010 submission date.

Sincerely,

L. Ross Love  
Chairman, Board of Members

# OTFBP 10-832

January 25, 2010

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

**2010 OTFBP LOI  
Ohio Third Frontier Biomedical Program  
Fiscal Year 2010 Request for Proposals (RFP)**

RFP Manager:

This reply represents our Letter of Interest (LOI) as a response and intention in regards to an invitation to participate in the Request for Proposal (RFP) for a Third Frontier BioMedical grant.

The Future Path Medical BioMedical mission includes effective and complete recovery monitoring of cardiac patients while in post-operative intensive care that is essential to both the health of the patient and controlling costs and post-surgical complications.

Vital signs are continuously monitored and relayed for real-time monitoring to identify anomalies as quickly as possible. Unfortunately, not all available information is readily integrated and incorporated to provide the most complete picture possible of the patient as they recover from cardiac surgery.

This project will research and develop the necessary enhancements to existing Future Path Medical patented technologies to deliver hospital-grade devices for real-time monitoring of critical kidney functions for patients following cardiac and other surgeries.

Future Path Medical will be partnering with Ohio technology companies and medical institutions in the design, development and refinement of existing home care devices for the subsequent commercialization and manufacture of integrated wireless medical devices for the hospital market.

The company will leverage its several years of product development experience in the medical market to develop these highly-reliable integrated monitoring devices for kidney function and recovery.

Applicant Name: Future Path Medical, LLC  
Applicant Address: 3020 Hinsel Drive, Columbus, OH 43232  
Applicant Phone Number: 614-863-5651  
Applicant Contact Person: Ty Bryant  
Applicant Contact Person Email: [ty@future-path.net](mailto:ty@future-path.net)  
Project Title: Cardiac Recovery Monitoring System (CRMS)  
Estimated Funds Requested: \$400,000  
Known Collaborators: Accelerated Data Concepts, LLC, New Life Foundation

Thank you for including our company and collaborators in your assessment and consideration for an opportunity to help create jobs here in Ohio.

Regards,  
Ty

Ty Bryant  
Chairman, Founder  
Future Path Medical Holding Company, LLC  
3020 Hinsel Drive  
Columbus, OH 43232  
614-863-5651  
[ty@future-path.net](mailto:ty@future-path.net)

## 2010 Request for Proposals

## Application Information Page

Letter of Intent (LOI) Notification Number (Issued by ODOT)	LOI #: OTFBP 10-_____
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This Application:  Does  Does Not Include information considered a "trade secret" under Ohio Revised Code Section 1333.61 (D)

Lead Applicant Name	Stanton L. Gerson, M.D.		
Lead Applicant Address	10900 Euclid Avenue Case School of Medicine		
City:	Cleveland	State: OH	Zip: 44106
County:	Cuyahoga		

Project Title:	Clinical Development of MultiStem® for Treatment of Spinal Cord Injury		
State Funds:	OTFRDF\$ \$1 Million Wright\$ \$0 Total\$ \$1 Million	Cost Share:	\$1 Million

Is the Lead Applicant the lead in any other proposal submitted under this RFP?  Yes  No

If yes, provide the following information:

Project Title/LOI #	Clinical Production of Induced Pluripotent Stem Cells for Neurodegenerative Disorders
---------------------	---

**Robin L. Bissell**

Typed Name of Authorizing Agent

**Director of Research, Accounting and Forecasting -  
School of Medicine**

Title of Authorizing Agent

Signature

Date

For ODOT Use Only

Date Received

Proposal  
ID #

# Ohio Third Frontier Biomedical Program

## 2010 Request for Proposals

### Lead Applicant Contact Information

<b>Authorizing Agent</b>	<b>Name</b>	Robin L. Bissell		
	<b>Title</b>	Director of Research, Accounting and Forecasting - School of Medicine		
	<b>Organization</b>	Case Western Reserve University		
	<b>Address</b>	10900 Euclid Avenue		
	<b>City, State, Zip</b>	Cleveland, OH 44106-4919		
	<b>Telephone</b>	216-368-4432	<b>Fax</b>	216-368-4805
	<b>E-Mail</b>	<a href="mailto:medres@case.edu">medres@case.edu</a>		

<b>Project Director</b>	<b>Name</b>	Stanton L. Gerson		
	<b>Title</b>	Director of Case Comprehensive Cancer Center, NCRM, and CSCRM		
	<b>Organization</b>	University Hospitals Case Medical Center		
	<b>Address</b>	10900 Euclid Avenue		
	<b>City, State, Zip</b>	Cleveland, OH 44106		
	<b>Telephone</b>	216-844-8565	<b>Fax</b>	216-368-1166
	<b>E-Mail</b>	<a href="mailto:slg5@case.edu">slg5@case.edu</a>		

<b>Fiscal Agent</b>	<b>Name</b>	Robin L. Bissell		
	<b>Title</b>	Director of Research, Accounting and Forecasting – School of Medicine		
	<b>Organization</b>	Case Western Reserve University		
	<b>Address</b>	10900 Euclid Avnue		
	<b>City, State, Zip</b>	Cleveland, OH 44106-4919		
	<b>Telephone</b>	216-368-4432	<b>Fax</b>	216-368-4805
	<b>E-Mail</b>	<a href="mailto:medres@case.edu">medres@case.edu</a>		

<b>Grant Administrator</b>	<b>Name</b>	Debra S. Grega		
	<b>Title</b>	Executive Director, Center for Stem Cell and Regenerative Medicine		
	<b>Organization</b>	Case Western Reserve University		
	<b>Address</b>	10900 Euclid Avenue		
	<b>City, State, Zip</b>	Cleveland, OH 44106		
	<b>Telephone</b>	216-368-3614	<b>Fax</b>	216-368-6020
	<b>E-Mail</b>	<a href="mailto:dsg12@case.edu">dsg12@case.edu</a>		

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**Note:** The same individual may hold more than one of these positions.

# Ohio Third Frontier Biomedical Program

## 2010 Request for Proposals

### Collaborator Information

List each Collaborator identified in the proposal, including a contact name and contact information for each.

Attach additional forms as needed.

Name	Stanton Gerson		
Title	Director of Case Comprehensive Cancer Center, NCRM, CSCRM		
Organization	Case Western Reserve University		
Address	School of Medicine		
	10900 Euclid Avenue		
City, State, Zip	Cleveland, OH 44106		
Telephone	216-844-8565	Fax	216-368-6020
E-Mail	<a href="mailto:Slq5@case.edu">Slq5@case.edu</a>		

Name	Debra Grega		
Title	Executive Director CSCRM		
Organization	Case Western Reserve University		
Address	School of Medicine		
	10900 Euclid Avenue		
City, State, Zip	Cleveland, OH 44106		
Telephone	216-368-3614	Fax	216-368-6020
E-Mail	<a href="mailto:Dsg12@case.edu">Dsg12@case.edu</a>		

Name	Robert Deans		
Title	VP of Regenerative Medicine		
Organization	Athersys		
Address	3201 Carnegie Avenue		
City, State, Zip	Cleveland, OH 44115		
Telephone	216-426-3594	Fax	216-361-9495
E-Mail	<a href="mailto:RDeans@athersys.com">RDeans@athersys.com</a>		

Name	Robert Mays		
Title	Sr. Director of Regenerative Medicine		
Organization	Athersys		
Address	3201 Carnegie Avenue		
City, State, Zip	Cleveland, OH 44115		
Telephone	216-431-9900	Fax	216-361-9495
E-Mail	<a href="mailto:Rwmays@athersys.com">Rwmays@athersys.com</a>		

Name	Jerry Silver		
Title	Professor in Neurosciences		
Organization	Case Western Reserve University		
Address	School of Medicine		
	10900 Euclid Avenue		
City, State, Zip	Cleveland, OH 44106		
Telephone	(216) 368-2150		
E-Mail	<a href="mailto:jxs10@case.edu">jxs10@case.edu</a>		

# Ohio Third Frontier Biomedical Program

## Letter of Intent

The treatment of spinal cord injuries and related paralysis and disability is an unmet medical condition of significance in the United States. A study recently completed by the Christopher and Dana Reeve Foundation indicates that nearly 1 out of every 50 people living in the United States suffers from some form of paralysis, a total of almost 5.6 million Americans. Approximately 25 percent of all paralysis is due to spinal cord injury (SCI); direct medical costs associated for treating SCI patients is estimated at over \$40 Billion annually, with estimated indirect costs for caring for these patients at a staggering \$300 Billion annually. There is currently no FDA approved treatment for SCI and associated paralysis. The numbers of affected individuals, the costs necessary to facilitate their care and rehabilitation and the lack of current therapies reiterate that SCI represents a current significant unmet medical need.

Athersys, Inc., as a founding, collaborative member of at the Center for Stem Cell and Regenerative Medicine (CSCRM), has developed a proprietary adult stem cell product, MultiStem<sup>®</sup>, which is a Multipotent Adult Progenitor cell (MAPC) product manufactured under strict specifications and release criteria approved by the FDA. Athersys has demonstrated safety and efficacy using MultiStem<sup>®</sup> in several pre-clinical disease models including stroke, acute myocardial infarct (acute MI), and in treating Graft vs. Host Disease (GVHD) symptoms in allogeneic bone marrow transplant.

The FDA has approved the manufacturing and basic safety profile of MultiStem<sup>®</sup> for use in humans in multiple indications: for prevention of GVHD in allogeneic bone marrow transplantation settings, for treatment of acute myocardial infarction, in addition the treatment of acute ischemic stroke.

Dr. Jerry Silver, (CWRU Department of Neuroscience) has been pioneering reparative approaches to spinal cord injury (SCI). Based on the successful results in animal studies using MultiStem<sup>®</sup> for treatment of ischemic stroke, Athersys and Dr. Jerry Silver, (CWRU) undertook a focused series of pilot experiments both *in vitro* and, subsequently *in vivo*, to test the benefit of MultiStem<sup>®</sup> for treatment of SCI in rats. The results from these preliminary studies suggest that cells provide novel benefit and support to neurons in representative *in vitro* models of SCI. *In vivo* transplantation of the cells into rats following SCI, suppress the progression of neuroinflammation and axonal “dieback” normally observed post SCI-injury, as well as promoting growth of the axons into and through the lesion core of the injury.

In this OTFBP grant application, we propose to perform extend these pre-clinical animal experiments facilitating the translational application of these cells into patients who have suffered a SCI. Experiments to be performed will include: determining the optimal route of administration, optimizing dose and dose regimens and determining the window of optimal therapeutic benefit for the MultiStem<sup>®</sup> product. These experiments will be performed collaboratively between Dr. Silver and Athersys. After optimizing the clinically relevant translational experiments, cell persistence, biodistribution and safety experiments will be performed in collaboration with additional researchers at CSCRM and the CSCRM Core Facilities.

Data generated from these animal studies in the first 24 months of the award will be used as part of a pre-clinical data package to apply to the FDA for use of MultiStem<sup>®</sup> for treatment of patients suffering a SCI in a Phase I IND clinical study.

It is the intention of Athersys to secure a development partner for commercial marketing and distribution of the cell product for SCI as it has already done for acute MI with Angiotech Pharmaceuticals, and for treatment of Inflammatory Bowel Disease with Pfizer, with the objective of closing this partnership to support pivotal Phase II-III clinical studies. Based on Athersys' prior experience, this partnership could comprise \$250 - \$300 million of long term financial investment to the company and support cell manufacturing and therapeutic product development in the region.

## 2010 Request for Proposals

## Application Information Page

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State Funds:	OTFRDF\$ \$1 Million Wright\$ \$0 Total\$ \$1 Million	Cost Share:	\$1 Million

Is the Lead Applicant the lead in any other proposal submitted under this RFP?  Yes  No

If yes, provide the following information:

Project Title/LOI #	Clinical Development of MultiStem® for Treatment of Spinal Cord Injury
---------------------	--

**Robin L. Bissell**

Typed Name of Authorizing Agent

**Director of Research, Accounting and Forecasting -  
School of Medicine**

Title of Authorizing Agent

Signature

Date

For ODOT Use Only

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# Ohio Third Frontier Biomedical Program

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	<b>E-Mail</b>	<u>medres@case.edu</u>		

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	<b>Title</b>	Executive Director, Center for Stem Cell and Regenerative Medicine		
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# Ohio Third Frontier Biomedical Program

## 2010 Request for Proposals

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Attach additional forms as needed.

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Title	Director of Case Comprehensive Cancer Center, NCRM, CSCRM	
Organization	Case Western Reserve University	
Address	School of Medicine 10900 Euclid Avenue	
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Name	Debra Grega	
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Organization	Case Western Reserve University	
Address	School of Medicine 10900 Euclid Avenue	
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Telephone	216-368-3614	Fax 216-368-6020
E-Mail	<a href="mailto:dsg12@case.edu">dsg12@case.edu</a>	

Name	Robert Miller	
Title	Professor in Neurosciences	
Organization	Case Western Reserve University	
Address	School of Medicine 10900 Euclid Avenue	
City, State, Zip	Cleveland, OH 44106	
Telephone	216-368-6269	
E-Mail	<a href="mailto:rhm3@case.edu">rhm3@case.edu</a>	

Name	Bruce Trapp	
Title	Chairman of Neurosciences	
Organization	Cleveland Clinic	
Address	Lerner Research Institute / NC30 9500 Euclid Avenue	
Telephone	(216) 444-7177	
E-Mail	<a href="mailto:trappb@ccf.org">trappb@ccf.org</a>	

Name	Jeffrey Cohen	
Title	Staff in Mellen Center for Multiple Sclerosis Treatment and Research	
Organization	Cleveland Clinic	
Address	Cleveland Clinic Main Campus / U10 9500 Euclid Avenue	
Telephone	(216) 445-8110	
E-Mail	<a href="mailto:cohenj@ccf.org">cohenj@ccf.org</a>	

<b>Name</b>	<b>Paul Tesar</b>
<b>Title</b>	<b>Assistant Professor in Genetics</b>
<b>Organization</b>	<b>Case Western Reserve University</b>
<b>Address</b>	<b>School of Medicine</b>
	<b>10900 Euclid Avenue</b>
<b>City, State, Zip</b>	<b>Cleveland, OH 44106</b>
<b>Telephone</b>	<b>(216) 368-6225</b>
<b>E-Mail</b>	<b><a href="mailto:pjt5@case.edu">pjt5@case.edu</a></b>

# Ohio Third Frontier Biomedical Program

## 2010 Request for Proposals

### Letter of Intent

There is a clinical and commercial opportunity to advance cell therapy for neurodegenerative disorders utilizing a relatively new technology, induced pluripotent stem (iPS) cells. We propose to utilize iPS cell technology to derive patient-specific iPS cells and differentiate them into oligodendrocytes for use in regenerative medicine.

Neurodegenerative disorders are a broad class of diseases and many are caused by the improper functioning of supporting cells such as oligodendrocytes. Oligodendrocytes provide an electrical insulation, myelin, around nerve fibers and thus allow the proper conduction of impulses along the nerve fiber. Without myelin, there is improper or lost communication between the brain and other regions of the body. This disruption is readily apparent in genetic diseases such as Pelizaeus-Merzbacher Disease (PMD), Adrenoleukodystrophy (ALD), Alexander's Disease, and Krabbe Disease as well as Multiple Sclerosis. There are no curative or restorative therapies for these myelin-based neurodegenerative disorders. Curative therapy would require remyelination and protection or restoration of associated axons

We propose an interdisciplinary approach that combines the strengths in stem cell transplantation, iPS cell derivation and differentiation, oligodendrocyte development and function at Case Western Reserve University (CWRU), University Hospitals Case Medical Center (UHCMC), and the Cleveland Clinic (CCF). The focus is to develop patient-specific iPS lines from tissue samples from patients with myelin-defective, neurodegenerative diseases. The processes, procedures and quality control and assurance will be established in conjunction with the Cell Therapies Integrated Services (CTIS) of the Wright Center for Stem Cell and Regenerative Medicine (CSCRM) and UHCMC while leveraging opportunities for collaborating with commercial partners.



Three Commerce Park Square  
23230 Chagrin Blvd, 9<sup>th</sup> Floor  
Beachwood, Ohio 44122

Phone: 216.359.0165  
Fax: 216.360.7333

January 25, 2010

To: Technology and Innovation Division, Ohio Department of Development

From: Perfusion Solutions Inc.

Subject: Letter of Intent, Ohio Third Frontier Biomedical Program, FY 2010

Perfusion Solutions, Inc. (PSI) is pleased to announce our intention to submit a proposal to the 2010 Ohio Third Frontier Biomedical Program with focus on cardiovascular medicine, regenerative medicine, and orthopedics. PSI is the developer of innovative technologies in the field of ventricular assist and heart replacement. As such, our program is focused on technology and procedural innovation in the cardiovascular arena.

Heart failure has been referred to as a new epidemic. The population of the United States and all developed nations is aging, and heart failure is a disease whose incidence and prevalence increases with age. Today, medicine's ability to address more acute forms of death from heart disease and stroke results in greater numbers of patients surviving to experience long term congestive heart failure. The associated costs are staggering. The cost of all heart disease to the United States in 2009 is estimated to be \$475B; the fraction specifically attributable to heart failure is estimated to be \$37B.

The current treatment standards (drugs) often result in the survival of heart failure patients, while leaving them with a poor quality of life as even small effort leaves them short of breath. Currently available ventricular assist devices (VADs) require highly invasive thoracic surgery with long recovery times, high cost and available only to the sickest patient population suffering from heart failure. A miniaturized, minimally invasive implantable, cost effective VAD that is capable of one-half or two-thirds of normal cardiac output would provide enormous benefit to these as well as "healthier" patients.

Looking forward to expanded indications for use of VADs, even under the most optimistic scenarios for regenerative medicine (stem cell and gene expression treatments), these therapies require an incubation period after application during which the failing heart needs significant functional support. This period provides an alternative market opportunity not yet measurable in economic terms. Finally there will always be a patient segment with fundamental structural cardiac defects that mandate VAD support or even total functional replacement of both ventricles; in some cases the ventricles may be so pathological as to require replacement with a donor heart or a total artificial heart.

Over the last decade, minimally invasive surgical approaches have been developed and optimized for a wide range of surgical fields including orthopedics, gynecology, urology, general and cardiac surgery. The benefits of these procedures to patients, including reduced recovery time, reduced pain, shorter hospital stay, reduced post procedural complications, and overall improved Quality of Life (QoL), are well documented. In the cardiac arena, coronary artery bypass grafting (CABG) and valve replacement and

repair procedures are routine surgeries increasingly conducted using minimally invasive approaches of which benefits to patients include reduced trauma and pain in the acute post-operative period, more rapid recovery and earlier mobility particularly in the elderly population. An equivalent VAD database cannot yet be established, but the patient population and complexity of the surgical maneuvers is likely to be similar to a mitral valve repair, suggesting that a small device placed by minimally invasive surgery could significantly reduce post-surgical complications, hospital stays and costs, as has been demonstrated for other procedures using minimally invasive techniques.

The **Program Point Of Contact** will be:

Mr. T. Stephan Weber, MSBME, MBA  
Chief Executive Officer  
Perfusion Solutions Inc.  
Three Commerce Park Square  
23230 Chagrin Blvd, 9<sup>th</sup> Floor  
Beachwood, Ohio 44122  
Office: 216.359.0165  
Fax: 216.360.7333  
Email: [sweber@perfsolinc.com](mailto:sweber@perfsolinc.com)

**Proposed Project Title:** Product Development And Testing Of A Miniaturized Ventricular Assist Device

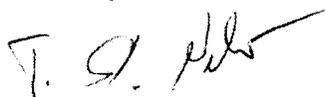
**Anticipated Requested Budget:**

PSI Personnel + Fringes (5)	\$ 188,217
Materials & Supplies	\$ 32,787
Equipment	\$ 45,101
Subcontracts	\$ 631,714
Indirect Cost	\$ 53,221
TOTAL (requested)	\$ 951,041
PSI Cost Share	\$1,793,668

**Proposed Collaborators:**

Perfusion Solutions, Inc., Beachwood, Ohio (Lead Applicant)  
Department of Biomedical Engineering, Cleveland Clinic, Cleveland, Ohio  
Omnitek LLC, Beachwood, Ohio  
Ward Engineering, Inc., Columbus, Ohio

Sincerely,



T. Stephan Weber  
Chief Executive Officer  
Perfusion Solutions, Inc.

**Program Summary** – The proposed program represents a logical transition from research to product development. The M2F technology has been invented, prototyped and extensively tested (bench and preclinical animal tests) over the last 4 years at the Cleveland Clinic under support from the National Heart, Lung and Blood Institute (NHLBI).

The goal of the proposed program is to complete final development of clinical product prototypes of the implantable M2F VAD system and to demonstrate system operation *in vitro* and *in vivo*, preparatory to regulatory preclinical development program initiation. Development activities will be conducted in compliance with applicable FDA regulations for medical device design and development to support subsequent clinical trial and product commercialization.

The OTF funds will be applied to achieve the following technical goals:

1. Development of the commercial version of the implantable pumping unit and its supervisory and power delivery systems, performed under the PSI quality system as mandated by FDA for the medical device design and development.
2. Bench and preclinical animal testing of the system, performed under the PSI quality system to ensure compliance with Good Laboratory Practice and Animal Welfare requirements overseen by the Cleveland Clinic Institutional Animal Care and Use Committee.

The technical program will be conducted over a period of 18 months. Within the first 6 months, an integrated design review, component design revision and functional expansion will be completed. Within the center portion (months 7 through 12) of the program, initial intermediate prototypes will be fabricated and functional bench testing will be completed, with initiation of final product prototype fabrication by program month 11. Months 13 through 18 of the program facilitate extensive testing of the final prototype systems including bench performance and durability testing and limited animal testing to verify device performance in a true physiologic environment and absence of adverse events such as hemolysis and thrombosis. Five (5) full systems will be fabricated and tested under this program.

PSI will create 2 engineering and 2 support staff positions with focus on mechanical and electrical design, device testing, and administrative support. PSI's collaborators will retain and continue to support a total of 6 full time employment positions through salary contributions from a successful grant application.

The requested OTF funds will be matched by contributions from PSI and its private shareholders, with a matching ratio (OTF:PSI) of 1:1.88. Throughout the program, PSI will raise series B funds to support this preclinical development program and to achieve clinical trial readiness. A series C investment round will be required to support subsequent clinical trials in the US and outside. Interactions are underway to secure these funds during the proposed program.

PSI, the lead applicant, will have ultimate, development and system integration responsibility and program control. It serves as design and specification developer as well as business development entity charged with continued fund raising, strategy implementation and device commercialization. PSI will maintain oversight of the activities of all subcontractors with executive decision rights on technical and business aspects and regulatory compliance.

The Cleveland Clinic (CC), as original technology developer and long-term commercial partner, will provide design and test support and special fabrication services through collaborative access to staff and facilities, and will be responsible for the conduct of the animal testing program.

Ward Engineering, Inc. is an ISO 13485 certified and FDA registered medical device manufacturer with an established track record of medical device design, fabrication, assembly, packaging and distribution. Ward has previously collaborated with CC and PSI on device prototyping, and will continue to apply its expertise to this program, device fabrication and assembly.

Omnitek LLC is the electronics developer for this program, responsible to revise and finalize the electronic supervisory and power system. Like Ward, Omnitek has collaborated with CCF on board development on prototyping for this application. Omnitek will closely coordinate with PSI on functional requirements development and design implementation.

# VASOSTAR INC.

January 25, 2010

## OTFBP 10-836

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

Subject: 2010 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 the fiscal year 2010.

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

Contact: Paul Erickson  
[perickson@frantzgroup.com](mailto:perickson@frantzgroup.com)

Project Title: Miniaturized Distal Vibration System for Penetrating Vascular Occlusions

Funds Requested: \$1,000,000

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

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

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

Stanford University School of Medicine  
Cardiovascular Medicine  
Stanford, CA  
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's mission is to develop and commercialize electromagnetically driven guidewire systems that safely improve the success rate for crossing Chronic Total Occlusions.*

# VASOSTAR INC.

**The Need** – Crossing chronic total occlusions (CTOs) and safely navigating through highly stenosed, tortuous arteries remains a major challenge for interventionalists. Current techniques are complex and diverse 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 with percutaneous techniques.

**VasoStar Inc.** – VasoStar Inc. was established to develop and commercialize a solution to this unmet need: a miniaturized electromagnetic solenoid that produces longitudinal vibration at the guidewire tip for safely penetrating CTOs and passing through tortuous, stenotic 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 majority ownership of VasoStar Inc. and has leveraged FMD engineering and operational resources to seed VasoStar's initiative.

With support of seed funding by the Global Cardiovascular Innovation Center (GCIC), funded by Ohio Third Frontier, and FMD, VasoStar has successfully designed and optimized a guidewire and catheter system that is effective in penetrating CTOs and crossing tortuous, stenotic lesions, as demonstrated through bench-top efficacy and safety testing and clinician assessment. In addition, VasoStar has established a clear path through the next phases of development, regulatory approval, and commercialization.

**Product Technology** – The VasoStar Vibrating Tip Guidewire (VTG) System features a 0.014" guidewire embedded with integral miniature magnet beads and a microcatheter fitted with electromagnetic (EM) coils that together form a magnetic engine. When the EM coils are powered by an alternating electric current, an oscillating magnetic field is created that causes the guidewire tip to vibrate back and forth like a piston.

A unique advantage of the VTG technology is the fact that the workflow of the interventionalist remains essentially unchanged. Interventionalists would begin the catheterization with the VTG magnetic guidewire (having a standard 0.014" diameter). Upon reaching a stenotic lesion that is hard to cross, they would insert the EM microcatheter over the guidewire to initiate vibration of the guidewire's distal tip. After crossing the lesion, the EM microcatheter is swapped for an over-the-wire balloon to complete the procedure, without the need to exchange the guidewire.

**Collaboration** – In Ohio, VasoStar has partnered with Frantz Medical Development to leverage medical device development and manufacturing capabilities, especially for injection molded components, automation, and finished device assembly. For catheter manufacturing, VasoStar has partnered with Interplex Medical in SW 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.

**Growth** – While initially focused on cardiovascular, this platform technology also has application in peripheral revascularization 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.



**OTFBP 10-837**

January 25, 2010

Dear Ohio Department of Development,

Please accept this Letter of Intent from OrthoHelix Surgical Designs, Inc. for our 2010 Third Frontier Biomedical Program proposal.

**Lead Applicant Name:** OrthoHelix Surgical Designs, Inc.

**Address:** 1065 Medina Road, Suite 500  
Medina, Ohio 44256

**Telephone:** (330) 247-1441

**Contact Person:** Mr. Cameron Rubino, VP of Finance

**Contact Email:** [crubino@orthohelix.com](mailto:crubino@orthohelix.com)

**Project Title:** Mini/Mega MaxLock Extreme Orthopedic Implants

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

**Known Collaborators:** Austin Bioinnovation Institute in Akron, and others to be determined

**Summary of Proposed Project:**

OrthoHelix is a medical device company located in Medina, Ohio and is committed to the design and commercialization of small bone fixation implants and instrumentation for trauma and deformity. The company was founded in 2004 with a vision of developing fixation plates that are designed to fit the anatomical shape of small bones.

The company is privately held and was initially funded by friends and family and later by Ohio-based venture capital and angel investors. Over \$20 million in equity has been infused into the company since inception in addition to a \$1.2 million loan through the Innovation Ohio Loan Fund (which has since been repaid). Proceeds have been used to (a) develop innovative products and then (b) make these products available to orthopedic surgeons and podiatrists at hospitals and surgery centers all over the United States.

OrthoHelix' sales have increased at rates far exceeding industry standard including 79%, 88%, and 210% in 2009, 2008, and 2007, respectively. These sales increases have come from a number of products designed by our internal research and development group of 8 degreed engineers (with

Surgeons speak. We deliver.



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 34, which is nearly 3 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 65% 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 expand the already-proven MaxLock Extreme product line to additional upper and lower extremity applications. The scaled up and scaled down versions of the implants and instruments will be modeled after our current MaxLock Extreme product.

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".

Dennis Stripe  
CEO

Surgeons speak. We deliver.

# OTFBP 10-838

**SUBJECT: 2010 OTFBP LOI**

Lead Applicant: Midmark Corporation 60 Vista Drive, P.O. Box 286 Versailles, OH 45380-0286 1-800-643-6275	Contact Person: Thomas Schwieterman, M.D., Director of R&D 60 Vista Drive, P.O. Box 286 Versailles, OH 45380-0286 937-526-8722 tschwieterman@midmark.com
Estimated Grant Funds Requested: \$1,000,000.00	Collaborators: TBD

**Project Title: A New Cardiovascular Disease Management Platform Solution with a Focus on Improving the Identification and Management of Patients Suffering from Obstructive Sleep Apnea**

**Company Summary:** Based in Versailles, OH, Midmark is a privately-held, physician-led, manufacturer of medical equipment and cardiovascular diagnostic devices. Midmark has four divisions, all of which are healthcare-focused: medical, dental, imaging, and veterinary. Midmark serves the front line of today's health-care system, predominantly the office-based physician and office-based dentist. Midmark products can be found in well over 90 percent of ambulatory physician offices and a majority of dental offices. Midmark's vision is to be, "A global leader providing products and services for the healthcare provider, integrating value-added technology for efficient and effective patient care."

**Project Summary:** At Midmark, we take seriously our opportunity to be an integrator of technologies to improve patient outcomes. That's why we believe we are uniquely positioned to lead the development of a new system and platform that addresses unmet needs in the diagnosis and management of cardiovascular patients suffering from obstructive sleep apnea (OSA). OSA is a serious disease, affecting millions of Americans, yet only 20% of affected patients are currently being diagnosed and even fewer are receiving effective treatment. Why? Diagnosing OSA is tedious, expensive, and time consuming. Effective treatment is difficult to achieve because the most efficacious therapeutic interventions require significant collaboration between primary care, specialists, and dentists. Unfortunately, the requisite collaboration and patient coaching needed to improve outcomes is not happening in today's healthcare system.

Primary care physicians and cardiologist have long recognized the implications and sequelae of OSA. Cardiovascular diseases are the leading cause of death in the United States and in most European countries. "Although obstructive sleep apnea and cardiovascular disease have common risk factors, epidemiologic studies show that sleep apnea increases risks for cardiovascular disease independently of individuals' demographic characteristics (i.e., age, sex, and race) or risk markers (i.e., smoking, alcohol, obesity, diabetes, dyslipidemia, atrial fibrillation, and hypertension). Individuals with severe sleep apnea are at increased risk for coronary artery disease, congestive heart failure, and stroke. [However,] the underlying mechanisms explaining associations between obstructive sleep apnea and cardiovascular disease are not entirely delineated."<sup>1</sup>

The physicians and dentists who can help improve diagnosis and treatment of OSA are current Midmark customers. If provided with a solution integrating a range of third-party OSA diagnostic and therapeutic devices and emphasizing collaboration, we believe that dramatic improvements can be made to help OSA patients get the care they need. The proposed solution will be complemented by our market leading cardiovascular diagnostic devices (ECG, holter, spirometer) and our market-leading digital intraoral imaging devices. Our unmatched device integration with over ninety electronic medical record systems will ensure the clinical data created becomes part of the patient's electronic medical record and can be leveraged to help minimize long-term cardiovascular diseases.

The primary benefits of the proposed system will be:

- Improved detection of OSA by integrating innovative home based sleep diagnostic solutions into primary care
- Improved care-coordination of OSA between dentists, doctors, and specialists, and patients
- Improved compliance to OSA therapies with virtualized care management strategies that compliment and augment the efforts of the patient's local care team
- Significant contributions to clinical data about OSA, enabling comparative effectiveness of various diagnostic and therapeutic options for treating OSA.
- Reduced healthcare system costs through proactive management of OSA and the reduction of long term morbidities known to be consequences of inadequate sleep apnea treatment.

We are actively working to identify the right collaborators for this project from our network of contacts in Ohio.

---

<sup>1</sup> Jean-Louis G, Zizi F, Clark LT, Brown CD, McFarlane SI. Obstructive sleep apnea and cardiovascular disease: role of the metabolic syndrome and its components. J Clin Sleep Med. 2008;4(3):261-272.

## Ohio Third Frontier Biomedical Program Letter of Intent January 25, 2010

The Ohio Department of Development  
Technology and Innovation Division  
77 South High Street, 25<sup>th</sup> Floor  
Columbus, OH 43215  
[OTFBP2010@development.ohio.gov](mailto:OTFBP2010@development.ohio.gov)

### **Lead Applicant:**

The Ohio State University  
Columbus, OH 43210

### **Principal Investigator and Contact Person**

Alicia L Bertone DVM, PhD, ACVS  
Comparative Orthopedic Cell and Molecular Laboratories  
College of Veterinary Medicine  
The Ohio State University  
614-292-7449  
[Bertone.1@osu.edu](mailto:Bertone.1@osu.edu)

### **Project Title:**

Commercialization of Cell Regenerative Technology for Orthopedics

### **Funds Request:**

\$1,000,000 Research and Development Funds  
\$ 500,000 Wright Capital Funds

### **Collaborators:**

#### **OSU**

Michael Knopp MD, PhD  
Wright Center for Innovation in Biomedical Imaging  
College of Medicine  
The Ohio State University  
614-293-9998 (Office)  
[knopp.16@osu.edu](mailto:knopp.16@osu.edu)  
Role: Facility Development, Medical Research

S. Michael Camp MBA, PhD  
Center for Entrepreneurship  
Fisher College of Business  
The Ohio State University  
614-292-3045  
[camp\\_1@fisher.osu.edu](mailto:camp_1@fisher.osu.edu)  
Role: Business Strategy

#### **For-Profit Business Partners**

Biodontos  
Stem Cell Technology Company  
Dublin, OH 43017  
614-789-1758  
[www.biodontos.com](http://www.biodontos.com)  
[info@biodontos.com](mailto:info@biodontos.com)  
Role: Commercial Partner

### ***Commercialization Plan and Collaboration for Development***

We propose a collaborative biomedical economic development program that proactively fills a regulatory/safety and marketing gap for the medical application of cell regenerative technology, initially for orthopedic tissue regeneration. Our program will “drop into” already established OSU initiatives and expertise to optimize the impact and success of the funds requested in this TFP proposal. Our plan supports the OTF investment in the biomedical clusters of both Regenerative Medicine and Orthopedics in the state of Ohio. Our goal for economic development, new jobs, and commercialization is to establish an Ohio-based GMP (Good Manufacturing Practices) FDA (Food and Drug Administration)- certified facility (CellSite™) for distribution, processing and storage of cells used for commercial enterprise and innovative regenerative medicine. We will create the cell product and market the service of cell biomedical therapy. OTF investment in our proposed facility will synergize immediately with previous Ohio investment in the Third Frontier Programs; “Wright Center of Innovation in Biomedical Imaging” and “Center for Stem Cell and Regenerative Medicine”. The proposed central location of this facility adjacent to the OSU campus will uniquely capitalize on established corporate and third frontier investment in: 1) GMP infrastructure for biomedical imaging (Dr Knopp), 2) an explored scientific and business model in animal regenerative medicine for research and veterinary application (Dr Bertone), 3) a robust medical, research and business community for intellectual property (IP) development and human clinical trial application (Drs Bertone, Knopp, Camp, and others), and 4) Ohio Board of Regents investment in business academic education (Dr Camp). OSU will establish CellSite™ and provide the scientific, medical and entrepreneurial leadership for the entity to grow into corporate independence, as well as establish spin-off companies for sustainable growth of the program. Our established Ohio-based commercialization partners will provide the corporate management and distribution infrastructure, as well as invest in product development.

### ***Innovation and Science***

The focus of the Comparative Orthopedics Research Laboratories (Dr Bertone) has been the development of cells, including genetically engineered cells, for bone and cartilage regeneration for medical application. In 2009 and 2010, scientific publications and patent applications from this laboratory have proven efficacy for bone regeneration. Engineered bone-forming cells are now being used clinically on a smaller scale at the OSU College of Veterinary Medicine (CVM). Dr Bertone and Biodontos have established collaborations on scientific investigations using innovative cell sources and cell differentiation strategies. Dr Bertone also serves as Director of Research for the OSU Sports Medicine Center and is a Professor in the OSU Department of Orthopedics in the College of Medicine with many established collaborations necessary for rapid human application. Active work and IP from her laboratory is for human application. Cell regenerative medicine for orthopedics is ready for commercialization and is already a clinical and research investment at OSU.

### ***Business Proposal Summary***

The OSU location of this project capitalizes on the unique central resource of a comprehensive medical, dental, and veterinary Health Sciences Center. Commercial entities will invest in the human applications due to the immediate gap filled by such an FDA approved center that meets regulatory standards for manipulation and manufacturing of cellular devices (i.e. bench cell sorting technologies), cellular products (cell-based off the shelf injectables and scaffolds), gene therapy products with a cellular component (growth factor engineered cells) or any combination product resulting in a biologic drug or device. An investment of capital by the OTFBP; matched by capital from corporate partners and commitments from OSU will be used to build CellSite™, hire business management, and establish the commercial use of proven cell therapy for bone regeneration in animals and humans.



# OTFBP 10-840

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

January 25, 2010

**VIA EMAIL** ([OTFBP2010@development.ohio.gov](mailto:OTFBP2010@development.ohio.gov))

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

**Subject: 2010 OTFBP LOI For Proposed New Orthopedic Medical Device From Thermedx, LLC In Possible Collaboration With The Cleveland Clinic Foundation.**

Dear Ohio Third Frontier Commission ("OTFC"):

In response to the December 14, 2009 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, 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):	The Cleveland Clinic Foundation ("CCF")
One Page Summary of the Proposed Project:	See enclosed 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 with FDA 510(k) clearance pending. Thermedx currently has ten (10) 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 routinely used in orthopedic surgeries to allow the surgeon end-user to deliver pulsed jets of irrigation fluid to remove blood and debris, penetrate into the cancellous bone, supply an improved bone-to-cement interface for joint replacement procedures, and reduce the risk of fat embolism. As part of its own proprietary Pulse Lavage System, Thermedx may also adapt and modify its existing, FDA 510(k) pending, Surgical Irrigation System to be compatible with its new Pulse Lavage. As a direct result of such adaptation and modification, the cost, safety, and efficacy of the Thermedx Surgical Irrigation System, together with the patient outcomes resulting from its use, will be improved upon.

Thermedx's Pulse Lavage System will be a potentially significant technological advancement that orthopedic surgeon end-users have determined to be a potentially "game changing" improvement in safety and efficacy, in comparison to the competitive basic versions currently in the marketplace. Thermedx is currently completing its proprietary functional specifications for its Pulse Lavage System, which includes significant input from Dr. Mark Froimson, MD, MBA ([http://my.clevelandclinic.org/staff\\_directory/staff\\_display.aspx?doctorid=2955](http://my.clevelandclinic.org/staff_directory/staff_display.aspx?doctorid=2955)), an Orthopedic Surgeon with The Cleveland Clinic Foundation ("CCF"), and Jim Ciccone, RN, an Orthopedic Nurse with CCF. In addition to CCF's continued collaboration on the Pulse Lavage System, the development of the Pulse Lavage System may also involve other Collaborators, possibly including one or more Ohio Suppliers of 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 only Ohio Suppliers 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 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 March 1, 2010. Please let me know if there are 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, Vice-President



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**Letter of Intent to the FY2010 Ohio Third Frontier Biomedical Program**

**Lead Applicant:** Faraday Technology, Inc., 315 Huls Drive, Clayton, OH 45315

**Phone number:** 937-836-7749

**Contact person:** Dr. EJ Taylor, [jenningsstaylor@faradaytechnology.com](mailto:jenningsstaylor@faradaytechnology.com)

**Proposed Project title:** Manufacturing of Medical Devices and Implants

**Estimated Grant Funds to be Requested:** \$500,000

**Known Collaborators:** Dayton Development Coalition

**Summary of the Proposed Project:**

Faraday Technology proposes the development and commercialization of a surface finishing process that will address the issues of cost and yield in the production of medical components, such as stents and orthopaedic implants. Specifically, Faraday will develop its' FARADAYIC ElectroPolishing Process that provides rapid, robust surface finishing of such components. This project will advance state-of-the-art manufacturing in Ohio.

The targeted technology subject areas are cardiovascular medicine and orthopedics. Faraday has demonstrated the feasibility of surface finishing of a variety of alloys applicable to these medical markets, such as titanium alloys, niobium alloys and stainless steels. Specifically, Faraday has developed a process that eliminates the need for hydrofluoric acid in polishing titanium and niobium alloys and the need for phosphoric/sulfuric acid in polishing of stainless steels. This process will improve worker safety, lower device cost and improve yield. Furthermore, Faraday has an upcoming project investigating FARADAYIC Through-mask Etching/ElectroPolishing of Nitinol stents.

Faraday seeks partners in the biomedical industry who are seeking innovative, environmentally-benign, cost-effective processes for manufacturing of medical devices and implants.



**Peter Gingras**

**CEO**

7100 Euclid Ave.  
Cleveland, OH 44103  
216.658.4101 Main  
216.658.4102 Fax  
216.272.5250 Mobile  
e-mail: peter.gingras@proxybiomedical.com

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

Jan 25<sup>th</sup> 2010

Dear Sir/Madam,

Proxy Biomedical is pleased to submit this Letter of Intent pursuant to the 2010 Ohio Third Frontier Biomedical Program RFP. The title of our proposal is:

***“Regenerative Orthopedic Products Comprising Biodegradable Scaffolds Combined with Multipotent Adult Progenitor Cells: Development of Therapies for Bone and Cartilage Repair.”***

**Lead Applicant:**

Thomas X. Neenan Ph.D.  
Vice-President, Business Development,  
Proxy Biomedical,  
7100 Euclid Avenue,  
Cleveland, OH 44103  
Tel: 216-658-4101; Fax: 216-658-4102  
Email: thomas.neenan@proxybiomedical.com

**Collaborators:**

Mr. Robert Perry,  
Senior Director, Manufacturing and Operations,  
Athersys, Inc.  
3201 Carnegie Ave,  
Cleveland, OH 44115  
Tel: 216-431-9900; Fax: 216-361-8495  
Email: [rperry@athersys.com](mailto:rperry@athersys.com)

Proxy Biomedical will request \$1M through the FY10 OTFBP. We anticipate a request of a further \$1M for each of FY11 and FY12.

We look forward to submitting a full proposal and, with the assistance of the OTFBP, to accelerating the introduction of our innovative products into the marketplace.

Sincerely Yours,

A handwritten signature in black ink, appearing to read "Peter H. Gingras". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

Peter Gingras  
Managing Director, Proxy Biomedical



## **Regenerative Orthopedic Products Comprising Biodegradable Scaffolds Combined with Multipotent Adult Progenitor Cells: Development of Therapies for Bone and Cartilage Repair.**

The global market for orthopedic products in 2007 was \$32B and continues to grow at a double digit rate. The US, European and Japanese markets, driven by a combination of aging populations, obesity and improved technologies and procedures account for more than eighty per cent of the global market. In recent years there have been two accelerating trends in orthopedic treatment: (1) A gradual replacement of permanent implants such as metal and ceramics with biodegradable polymers and materials; (2) The increasing success of regenerative medicine wherein healing of damaged parts of the body is promoted via introduction of reparative tissue, cells or proteins.

Our proposal seeks to commercialize novel orthopedic products that utilize patented and proprietary technologies to promote more effective tissue repair and healing through the combination of resorbable polymers and cell therapy induced regenerative medicine. Specifically, we will develop products that combine proprietary biomaterial scaffolds developed by Proxy Biomedical in conjunction with an advanced adult stem cell platform, MultiStem<sup>®</sup>, that has a demonstrated capacity to form bone, cartilage and other tissues relevant to orthopedic treatment.

With four FDA approved products Proxy Biomedical is a leader in the field of surgical materials (meshes and scaffolds) designed for minimally invasive surgery. Our philosophy is to combine structural function with optimal tissue generation. We have an established interest in orthopedic products as a major source of future growth, particularly as it pertains to bone and cartilage repair.

Athersys, Inc. has developed a patented and proprietary adult stem cell product MultiStem<sup>®</sup>, a Multipotent Adult Progenitor cell (MAPC) product manufactured under strict specifications and release criteria approved by the FDA. In the context of appropriate biological conditions, (e.g. an osteoinductive matrix) MultiStem<sup>®</sup> has the established potential to form bone, cartilage as well as a range of other cell types. Importantly, MultiStem<sup>®</sup> can be expanded extensively *ex vivo* (i.e. manufactured at scale) resulting in a consistent and well characterized product, and is administered without tissue matching or immune suppression. The FDA has evaluated the manufacturing and basic safety profile of MultiStem<sup>®</sup> and has authorized administration to human patients in clinical trials in multiple indications, including treatment of acute myocardial infarction, in cancer treatment support (i.e. leukemia and myelodysplasia patients undergoing bone marrow transplantation that are at risk for Graft Versus Host Disease (GVHD) and other complications), and ischemic stroke.

The hypothesis behind our proposal is that the combination of biodegradable polymers with MultiStem<sup>®</sup> will afford a suite of orthopedics products with superior technological, clinical, regulatory and commercial success. Specifically, over the course of three years we will develop:

- A bone plate product for the treatment of fractures wherein we will combine Proxy's well developed technology in weight-bearing erodible polymer implants with MultiStem<sup>®</sup>;
- A bone repair product targeting non-healing bone voids that combines Proxy's HydroxyColl platform (hydroxyapatite plus collagen) with MultiStem<sup>®</sup> for optimal bone regeneration;
- A cartilage repair product combining MultiStem<sup>®</sup> with novel polymeric scaffolding targeting osteoarthritis.



Research and development work related to the proposal would be conducted at Proxy Biomedical's and Athersys' facilities in Cleveland. Success in any of the three programs would allow Proxy and Athersys rapid access to several multi-billion market segments. Our likely commercialization strategy would be to partner with a large player in the orthopedics market (e.g. Zimmer, Stryker etc.) or with a conventional large pharmaceutical company with a strong interest in regenerative medicine (Pfizer, GSK etc).

# OTFBP 10-843

**Hansen, Andrew**

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**From:** Kevin Snape [kfsnape@yahoo.com]  
**Sent:** Monday, January 25, 2010 12:29 PM  
**To:** OTFBP2010  
**Subject:** LOI

Ohio Third Frontier Staff,

This is our Letter of Intent to apply within the context of the Third Frontier Biomedical RFP. We are:

Body Phyx International  
20370 Lorain Rd,  
Fairview Park, Oh 44126  
330-356-2315 (p)  
216-392-3920 (c)

Contact: Kevin Snape, Ph.D.  
kfsnape@yahoo.com

Title:  
Nerve Mobilization for Pain Relief

Collaborators:

Glide: The Innovation Fund  
CHC Physical Therapy  
Cuyahoga County New Product Loan Fund  
Astro Manufacturing  
LogiSnych

Budget:

Kevin Snape  
216-392-3920

**Hansen, Andrew**

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**From:** Kumar Parekh [kumar@irdiagnostyx.com]  
**Sent:** Monday, January 25, 2010 12:46 PM  
**To:** OTFBP2010  
**Subject:** 2010 OTFBP LOI  
**Attachments:** Letter of Intent.docx

Hello Sir/Madam,

We would like to submit a proposal for the Ohio Third Frontier grants. Below is the information required for the letter of intent.

Lead Applicant's name: IR Diagnostyx Inc.  
Address: 1275 Kinnear Road, Columbus, OH - 43212  
Phone number: 614-296-4213  
Contact person: Gary Smith  
Email address: [smithg@irdiagnostyx.com](mailto:smithg@irdiagnostyx.com)  
Proposed Project title: Diagnosis of Interstitial Cystitis and other functional diseases  
Estimated Grant Funds to be requested: \$500,000  
Known Collaborators: The Ohio State University

Attached is the 1 page summary of the proposed project. Please let us know if you have any questions.

Warm Regards,  
Kumar Parekh

IR Diagnostyx Inc.  
1275 Kinnear Road  
Columbus, OH 43212  
Phone: 859-229-7803  
[kumar@irdiagnostyx.com](mailto:kumar@irdiagnostyx.com)

## **Company Background**

IR Diagnostyx, Inc. is a Columbus, Ohio-based startup company that specializes in providing accurate, painless, and rapid diagnostic services for several functional diseases. IR Diagnostyx will initially establish a laboratory in Columbus that will provide diagnostic services to the United States and abroad. We anticipate creating as many as 30 jobs in central Ohio in the first five years of operation. The executive team includes Gary Smith, Hardik Desai and Kumar Parekh.

## **Intellectual Property**

Dr. C. A. Tony Buffington and Dr. Luis Rodriguez-Saona, distinguished faculty and research professionals at The Ohio State University (OSU) have developed a biomarker discovery platform technology for the diagnosis of Interstitial Cystitis and other functional syndromes. The technology is based on Spectroscopic analysis of the blood specimen observed under an **Infrared Microscope**. This patent-pending analysis clearly indicates whether or not the patient suffers from the particular disease. More than \$100,000 has already been invested in this research. OSU has filed a patent application for the technology that is applicable to over 40 functional diseases most of which currently have no easy diagnostic test. IR Diagnostyx has established a partnership with OSU and has secured an option for the development and commercialization of this technology for the use of the greater medical community.

## **Unmet Needs**

The healthcare system currently lacks accurate diagnostic methods for over 30 functional diseases including Interstitial Cystitis (IC), Irritable Bowel Syndrome (IBS), Fibromyalgia, and Chronic Fatigue Syndrome (CFS). Combined, these four diseases affect over 110 million Americans. A typical patient may have painful symptoms for more than four years and interact with as many as five physicians before achieving a correct diagnosis. Patients spend thousands of dollars trying to find the cause of their illness. Preliminary analysis shows that average cost to diagnose these diseases is above \$5,000. These costs do not include the cost of misdiagnosis and subsequent treatment of misdiagnosis, if any, in the process. The medical community, insurance providers and patients are all very frustrated currently because of the lack of reliable, accurate and conclusive diagnosis.

## **Service Description**

The company is working with the lead scientists in completing the development of the technology. After that the company will be providing diagnostic services to the medical community. The diagnostic test provided by the company will work as a replacement for the complicated set of diagnostic procedures currently performed. The physicians will typically order this test series of tests for their patients to determine whether or not the patient is suffering from the particular diseases mentioned above or not. The IR Diagnostyx test will replace most of this series of tests currently being used.

## **Competition**

Currently, the only way to diagnose these diseases is through the traditional exclusion method used by physicians around the world. These procedures are expensive, inaccurate, and take years to reach a conclusion. In the mean time, patients suffer unnecessarily. All of the 40 diseases that we have identified have similar existing diagnostic methods.

## **Market Opportunity**

In United States alone, there are about 85 million people suffering from IBS, 13 million suffering from IC, 10 million people suffering from Fibromyalgia and about 4 million people suffering from CFS. The prevalence (% of total population) of these diseases is very similar in Canada, UK, Europe and other developed countries as well. In a simplified survey of urologists in central Ohio, the physicians indicated that they would use our diagnostic test to test for IC only as many as 8 times per week. When extrapolated across the 12,000 urologists in the US, the market for IC only is approximately \$100 million at \$200 per test. This does not include the dozens of other functional diseases for which our patent-pending diagnostic procedure is applicable.

2010 OTFBP LOI  
Cleveland Clinic Spine Research Laboratory  
(L.G. Gilbertson, PhD)

## LETTER OF INTENT

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

## **PROJECT SUMMARY**

Head and neck injuries in sports represent an ongoing challenge to the sideline physician who must rapidly evaluate an athlete for injury and implement an appropriate injury management protocol. Knowledge of the likely "injury mechanism" allows the physician to anticipate the orthopaedic and neurological injuries sustained by the athlete even before a detailed physical examination has been performed.

The broad objective of this project is to develop a head-mounted system that will register impacts to the head and output data to the sideline physician to enable a rapid assessment of head/neck injury risk. The system thus will function as an "early warning system" for the detection of head and neck injuries. The head-mounted system is to be implementable for non-helmeted sports (boxing, mixed martial arts, soccer) as well as helmeted sports (baseball, football, ice hockey, cycling).

The project will (a) perform biomedical research to define the optimal sensor type, configuration, and mounting location for the reliable measurement of head impact, (b) carry out technology developmental work to produce prototypes of the head/neck injury diagnostic system, (c) field-test the system under realistic sports conditions to demonstrate functionality and support market entry.

Successful completion of this project will result in a commercialized head/neck injury diagnostic system with significant potential to reduce sports-related head and neck injuries.

# OTFBP 10-846



January 25, 2010

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

Dear Ohio Department of Development,

Please accept this Letter of Intent from Enhanced Systems Technologies, Inc. for our Fiscal Year 2010 Ohio Third Frontier Biomedical ("OTFBP") Program.

<b>Lead Applicant Name:</b>	Enhanced Systems Technologies, Inc.
<b>Address:</b>	6168 Cochran Rd Solon, OH 44139
<b>Telephone:</b>	(440) 785-2298
<b>Contact Person:</b>	Mr. Jim Ohneck
<b>Contact Email:</b>	<a href="mailto:johneck@valtronictechnologies.com">johneck@valtronictechnologies.com</a>
<b>Project Title:</b>	Laser Wound Healing Device Commercialization
<b>Estimated Grant Amount Requested:</b>	\$1,000,000
<b>Known Collaborators:</b>	Valtronic Technologies, Inc. Akron General University of Toledo MAGNET

## Summary of Proposed Project:

Solon, Ohio-based Enhanced Systems Technologies, Inc. develops and commercializes laser light based medical-therapeutic equipment. The use of lasers therapeutically to treat chronic pain has grown significantly over the past several years. The acceptance of this technology has been due in part to the introduction of a liquid light guide technology to deliver the laser beam, which was developed by EST and its collaborators under a prior Third Frontier Grant Program. This system, used to treat chronic pain, is currently manufactured by Valtronic Technologies in Solon and sold by Avicenna Laser Technology, Inc. in Bainbridge, Ohio.

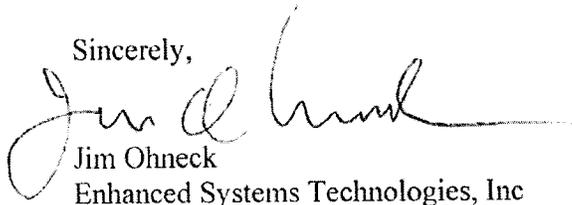
EST intends to further develop and commercialize its liquid light technology, either directly or through one of its channel partners, for the purpose of wound healing and tissue regeneration. The University of Toledo, a previous project collaborator, as well as Akron General Hospital have both completed scientific studies strongly indicating that EST's laser accelerates the healing of cells and thus can be used to heal wounds and regenerate healthy tissue.

EST and its collaborators, Akron General Hospital, The University of Toledo, Valtronic Technologies, Inc. and MAGNET are seeking OTFBP funds to enable a broad clinical trial of the laser in preparation for FDA submission and approval for use in wound healing and modification of the laser for specific use in this application. EST and its collaborators strongly believe that OTF funding will enable commercialization of the laser within the projected project period.

The market for regenerative laser technology offers a substantial, viable and growing market opportunity with a solution that has already been developed and proven commercially successful in other medical applications.

EST's proposed project aligns with the goals and objectives specified by the OTF Biomedical Program with regards to device modification in the field of regenerative medicine. EST believes that the state of Ohio will benefit from this project through the creation of professional and manufacturing jobs, economic development and the reduction of health care costs.

Sincerely,



Jim Ohneck  
Enhanced Systems Technologies, Inc

## Hansen, Andrew

---

**From:** Walcer, Louis [WALCERL@ccf.org]  
**Sent:** Monday, January 25, 2010 12:50 PM  
**To:** OTFBP2010  
**Cc:** Muschler, M.D., George; Hoover, Brett; Sump, Elizabeth; Vasanji, Ph.D., Amit; Kiderman, Sam; Bernat, Susan; Coburn, Christopher; Nic.Copley@Parker.com  
**Subject:** 2010 OTFBP LOI  
**Importance:** High

Lead Applicant's Name: Cleveland Clinic (CC)  
Contact Person: George F. Muschler, MD  
Address: 9500 Euclid Ave, Mail Code ND20, Cleveland Clinic, OH 44195  
Office Phone: (216) 444-1055  
Fax: (216) 444-9198  
Email: muschlg@ccf.org

Proposed Project Title: Development and Commercialization of a Cellular Imaging, Analysis and Processing Tool for Application in Regenerative Medicine

Estimated Grant Funds to be requested: \$1,000,000  
Known Collaborator(s): Parker Hannifin Corporation (PHC); University of Cincinnati (UC)

### Summary of the Proposed Project

Cell-based regenerative medicine has been widely touted as the “next frontier” in the treatment of human disease and injury. Cell-based therapies have not, however, yet achieved wide commercial use, in part because their manufacture and regulatory approval is labor-intensive and not standardized. Progress in the field to date has been hamstrung by cost-, labor- and infrastructure-intensive manual methods of cell culture, selection, and subsequent expansion. There is also a dearth of purification and quality control systems suitable to support the needs of scaled-up “in-house” manufacturing. Lastly, even the best manual methods yield highly variable data, and fail to produce the robust safety and efficacy audit trail necessary to streamline the regulatory path from R&D to FDA approval. With this in mind, there is a need for a cost-effective means for the rapid preparation of therapeutic cells for research and clinical use.

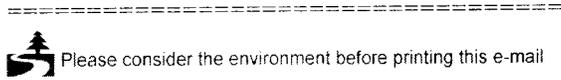
The underlying tenet of this proposal is that an automated, modular, scalable platform technology for culture, identification, isolation, selection and expansion of stem and progenitor cells will provide a much needed standard upon which pre-existing and future cell-based therapies can be manufactured with precision. Such a system will also provide a comprehensive audit trail to streamline regulatory approval. The platform technology (*Accellerator-CPS*®) will be based upon the modular integration of a proprietary cell (identification) imaging and analysis technology from Cleveland Clinic with a successful commercialized automation technology into a fully integrated platform for stem cell selection and expansion for academic and clinical applications.

In this proposal, Cleveland Clinic (CC), with its academic collaborator University of Cincinnati (UC) and its commercial partner Parker Hannifin Corporation (PHC), will integrate emerging state-of-the-art cell imaging and manipulation technologies to develop, validate and commercialize a novel platform technology to address the significant technical and commercialization barriers associated with regenerative medicine by significantly reducing the cost, labor and infrastructure required to process and manufacture cell-based products.

Cleveland Clinic, and its team of academic collaborators and commercial partners, is uniquely positioned to play a pivotal role in establishing the quality standards (still being developed by the FDA) applied to cell therapy products, and to enable growth and innovation in an industry that will change healthcare as we know it.

LW (OBO Dr. Muschler)

**Lou Walcer** | Sr. Commercialization Officer  
Cleveland Clinic Innovations | New Ventures  
Cleveland Clinic | Mail Code D20 | 9500 Euclid Ave. | Cleveland, OH 44195  
(O): (216) 445-1943 | (F) 216-445-6514 | (C): 216-312-4243



Cleveland Clinic is ranked one of the top hospitals in America by U.S.News & World Report (2009). Visit us online at <http://www.clevelandclinic.org> for a complete listing of our services, staff and locations.

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# OTFBP 10-848

## Letter of Intent for OTFBP Program

**Name of the Lead Applicant:** Zhenguo Liu, MD, PhD, Assistant Professor of Medicine.

**Addresses:** Division of Cardiovascular Medicine, Davis Heart and Lung Research Institute and Department of Medicine, The Ohio State University Medical Center, Suite 200, DHLRI, 473 West 12<sup>th</sup> Ave., Columbus.

**Phone numbers:** 614-247-8435

**Emails:** [zhenguo.liu@osumc.edu](mailto:zhenguo.liu@osumc.edu)

**Proposed Project Title:** Development and commercialization of AT-6: a novel drug for the Treatment of Ventricular Tachycardia/Fibrillation and heart failure

**Estimated Grant Funds:** 1.0 million dollars.

**Name of the Collaborator:** Robert L. Hamlin, DVM, PhD. Stanton Youngberg Professorship of Veterinary Medicine

**Addresses:** Department of Veterinary Biosciences, The Ohio State University, 480 VMAB  
1900 Coffey Rd. Columbus, Ohio 43210

**Phone numbers:** (614) 292-8122

**Emails:** [Robert.Hamlin@cvm.osu.edu](mailto:Robert.Hamlin@cvm.osu.edu)

**Name of the Collaborator:** David Hamlin, BA, President of QTest Labs

**Addresses:** QTest Labs, 6456 Fiesta Drive, Columbus, Ohio 43235

**Phone numbers:** (614)-581-9256

**Emails:** [dhamlin@qtestlabs.com](mailto:dhamlin@qtestlabs.com)

## Project Summary:

### Project Title: Development and commercialization of AT-6: a novel drug for the Treatment of Ventricular Tachycardia/Fibrillation and heart failure

Ventricular arrhythmias (ventricular tachycardia and fibrillation) are the primary cause of sudden cardiac death, and the number one killer in USA with 450,000 sudden cardiac deaths each year. Heart failure is also a serious problem with about 5 million people suffering from this condition with 1,101,000 hospitalizations each year with heart failure in USA in 2004. About 550,000 new cases of heart failure are diagnosed each year in US. There is no cure for heart failure at this time. More than 287,000 people in US die with heart failure annually. **The estimated direct annual cost for heart failure in 2006 is \$29.6 billion in the United States.** Of note, ventricular arrhythmias often develop in the patients with heart failure, and may lead to tachycardia-induced heart failure or make heart failure worse. The treatment for both ventricular arrhythmias and heart failure has been very limited due to significant side effects or toxicities for the limited available drugs.

**AT-6** is a natural product. Our preliminary data showed that this compound was very effective on preventing and treating ventricular arrhythmias in chemically-induced ventricular arrhythmia animal model and ischemia-induced arrhythmia animal model. **AT-6** also dramatically increased heart pumping function and relaxation without any adverse hemodynamic effects (no changes in heart rate and blood pressure). It also improved organ perfusion during heart failure. In addition, this compound shortened QT interval (QT prolongation is considered a key element for triggering ventricular arrhythmias). There were no known toxicities or side effects for this compound from our acute toxicity studies. This will be an ideal drug to develop for the treatment of ventricular tachycardia, and congestive heart failure (both systolic and diastolic).

This project is proposed to develop and commercialize this compound AT-6 for the prevention and treatment of ventricular arrhythmias, and congestive heart failure. This project will involve the joint efforts from **Dr. Zhenguo Liu**, a board certified clinical cardiac electrophysiologist at the Ohio State University Medical Center, **Dr. Robert Hamlin**, a well known veterinary electrophysiologist at the Ohio State University College of Veterinary Medicine, and **Mr. David Hamlin**, President of QTest Labs in Columbus, Ohio.

The proposed project will consist of two phases: phase 1, and 2. During **Phase 1** of the development, efforts will be focused on the preparations of materials for FDA approval for Phase 1 Clinical Trial including chronic toxicity studies and chemical identification by spectroscopic and/or chromatographic fingerprints, as well as bioavailability studies. It will take 12 to 18 months for this phase. During **Phase 2** of this project, FDA approval for Phase 1 clinical trial for the product will be obtained. The Phase 1 clinical trials will be completed at this stage. It will take 6 to 12 months for this phase. After completion of this phase, the product will be moved to the stage of Phase 2 Clinical Trial. The proposed project will be completed within 3 years.

**Hansen, Andrew**

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**From:** Sump, Elizabeth [sumpe@ccf.org]  
**Sent:** Monday, January 25, 2010 1:01 PM  
**To:** OTFBP2010  
**Cc:** Siemionow, M.D., Ph.D., D.Sc., Maria; James Herrmann; John Puisis  
**Subject:** 2010 OTFBP LOI

**Lead Applicant's Name:** Cleveland Clinic (CC)  
**Contact Person:** Maria Z. Siemionow, MD, PhD, DSc.  
**Address:** 9500 Euclid Ave, Mail Code A60, Cleveland Clinic, OH 44195  
**Office Phone:** (216) 445-2504  
**Fax:** (216) 444-9419  
**Email:** siemiom@ccf.org

**Proposed Project Title:** Clinical Trial of an Advanced Therapy to Confer Donor-Specific Immune Tolerance in Transplant Patients

**Estimated Grant Funds to be requested:** \$1,000,000  
**Known Collaborator(s):** Tolera Therapeutics, Inc (Tolera)

**Summary of the Proposed Project:**

Approximately 30,000 solid organ and tissue transplants are performed in the United States each year. Each of these transplants requires that the recipient receive a cocktail of drugs to prevent rejection of their transplanted organ or tissue. Traditional "triple therapy" against acute immune rejection has proved effective to control rejection, but is associated with multiple co-morbidities, including Type II Diabetes, Lymphoma, and severe viral infections. The co-morbidities associated with multiple drug therapies have spurred a trend toward long-term single-drug therapies in recent years. Unfortunately, these single drug therapies have not proved to be efficacious.

TOL101 is a murine IgMk isotype, anti-human T-cell monoclonal antibody (mAb) that recognizes the  $\alpha\beta$ -T cell receptor (TCR) complex on human CD3<sup>+</sup> T cells. In previous human clinical trials, it has been shown to effectively deplete the alloreactive T-cells involved in the pathogenesis of donor organ tissue rejection. Due to its observed immune modulating properties, and potential as a tolerance inducing agent, **Tolera Therapeutics (a Cleveland Clinic Spin-off) is developing TOL101 specifically for the prophylaxis of organ allograft rejection in kidney transplant recipients and more generally as an immune modulator with potential across a wide range of tissue transplantation opportunities, potentially reducing or eliminating the need for life-long immunosuppression.**

Since June of 2008, Tolera has invested \$8 million in preparations for human clinical study. Within 14 months, the company has established an effective development team, received orphan drug designation from the FDA, developed commercial scale GMP manufacturing, completed animal toxicology studies, produced TOL101 drug product for the proposed clinical trial, held a pre-IND meeting with the FDA, and developed a creative, "adaptive-design" protocol for its first-in-human kidney trial. The company has submitted its IND and expects FDA approval presently for the company to enter human clinical studies in the first quarter 2010.

**Tolera aims to receive full market approval for TOL101 by 2013.** To accomplish this, Tolera has developed a creative adaptive-design Phase 1/2 human clinical study to accelerate the development program. The study was designed to provide an accelerated path to market by accumulating the necessary safety and mechanistic data to close out Phase 2 by the end of 2010. This aggressive program sets out to achieve the following objectives:

- 1) rapid assessment of drug PK and PD in human subjects

- 2) determination of a high effective and low effective dose regimen, establishing a range of safe dosing.
- 3) confirmation of tolerance inducing mechanisms, including assessments of organ tissue function, immune and inflammatory responses and efficacy in hitting its biomarker target.
- 4) seamless transition into a broad multi-center study to build a robust safety database with sufficient support to permit initiation of registration trials in 2011.

**The proposed clinical trial is Part B of a Phase 1/2, open label, adaptive, two-part (Part A and Part B) dose escalation and pharmacokinetic/safety study.** The patient population is renal transplant patients receiving living or cadaveric donor kidneys, and the investigational drug is to be administered as a prophylactic agent against allograft rejection, with dosing to begin at the time of the transplant surgery and to extend for 5 or 9 further doses. Part A (previously funded by Tolera and AFIRM) will consist of 4 or more cohorts of 3 patients each in a dose-finding portion that is designed to establish two potential therapeutic dosing regimens; Part B will consist of 3 arms randomized 3:3:2, TOL101 dose 1 to TOL101 dose 2 to Thymoglobulin (an active comparator), respectively. A Data Monitoring Committee (DMC), in concert with the principle investigator at each site, will be responsible for making decisions regarding dose escalations, safety data, administration of concomitant medicines, and general patient care.

**The current request is for \$1,000,000 to provide for site set-up, data collection and monitoring, drug supply, and patient care for six to eight of a total of twenty-four patients for the Part B study.** These patients will generate the necessary dose, PK, PD, and safety data to support continued study. In the absence of this funding, the study sponsor, Tolera, will need to raise 100% of the funds from venture capital. Availability of the \$1.0 M funds requested will both significantly reduce the overall fund-raising need and **will significantly reduce barriers to private fundraising, permitting initiation of the trial and collection of critical safety and dosing data.**

#### **Timeline:**

The full trial design is expected to require 6 to 8 months of enrollment, with 6 months of patient follow up. Therefore, the entire trial may be completed within 12 – 14 months from the date of first patient – first visit. This estimate is based on a conservative enrollment rate of 2 transplants per month per medical center (large centers may do 15 to 20 kidneys per month). Part A dosing may be completed within 120 days. Tolera currently plans to initiate dosing early in 2010 and have the Part A trial closed by the end of 2010. **The requested funding would allow Tolera to begin trial enrollment for the Part B trial in early 2011, with a target of enrollment completion by early 2012.**

#### **Benefit to the State of Ohio**

All trials using State of Ohio funding would be conducted in the State of Ohio, with targeted facilities at the Cleveland Clinic, Ohio State University, University of Cincinnati, and University Hospitals Cleveland. **This will directly benefit Ohio transplant patients.** In addition, the leverage provided by the State of Ohio funds would greatly facilitate private equity fundraising for the remaining trial costs, resulting in **a net inflow of \$10-14 million in new private equity, much of which will be expended in the treatment of patients in Ohio** medical facilities. In addition, some of the matching funds for this trial are provided by an Ohio based venture capital fund – Triathlon Medical Ventures. With a successful trial, a significant portion of the value of the project will accrete to Ohio investors, providing more capital for future Ohio ventures. Finally, Tolera has engaged a clinical research organization from Cincinnati, Ohio to provide clinical trial project management and medical monitoring for the entire program, requiring approximately 2 – 3 full time equivalent employees in the state.

On behalf of Dr. Siemionow,



Elizabeth Sump | Executive Director, Clinical Tissue Engineering Center  
Chief Commercialization Officer, AFIRM

Cleveland Clinic | 9500 Euclid Avenue | Mail Stop ND20 | Cleveland, OH 44195  
16-445-4145 Fax: 216-444-9198  
www.ctecohio.org



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# OTFBP 10-850

Prospective Lead Applicant: Ohio University  
120 RTEC  
Athens, OH 45701  
(740) 593-0370  
Rathindra Bose, Professor Biomedical Sciences and  
Chemistry & Biochemistry  
[bose@ohio.edu](mailto:bose@ohio.edu)

Proposed Project title: Cancer Therapeutics for Treating Resistant Ovarian,  
Testicular and Head & Neck Cancers.

Estimated Grant Funds to be requested: \$2 million (including \$1 from Wright capital Fund)

Known Collaborators: Battelle Memorial Institute (Columbus, OH)

Ohio University is requesting funds to support the drug development of a new class of cancer chemotherapeutics, phosphaplatins – discovered by Rathindra Bose – that have been shown to effectively kill ovarian, testicular, head and neck cancers both *in vitro* and *in vivo*. These compounds are also effective towards resistant cancers where other available drugs have failed. Furthermore, these compounds exhibit minimal toxicity compared to other drugs available in the market.

**Background:** Platinum metal-based anticancer drugs, cisplatin, carboplatin, and oxaliplatin are widely used for the treatment of a variety of cancers including ovarian, testicular, small cell lung, and colorectal cancer. In addition, these compounds are used in conjunction with other therapeutic regimens, including radiation therapy to treat an expanded array of cancers. Although platinum-based chemotherapeutics are widely used, severe side effects including nephro-, neuro- and oto-toxicities limit their applications. Moreover, approximately 10% of patients become resistant to platinum drug treatment. Although carboplatin reduces some side effects, acquired resistance remains a major problem, leading to poor survival rates. Currently, oxaliplatin is approved to treat colorectal cancer; however its resistance is largely unexplored. Severe side effects stated above are largely due to the apparent facile reactivity of platinum compounds with a number of proteins and enzymes. Furthermore, resistance to platinum drugs is mainly due to the efficient removal of platinum from platinum bound DNA by nucleotide excision repair (NER) enzymes.

Dr. Bose has identified two lead compounds– pyrodach-2 and pyrodach-4– that are less toxic and more effective anticancer agents. The development strategy was based on the premise of creating a class of non-covalent DNA binding platinum antitumor agents that appears to circumvent the DNA-repair based resistance but activates cell surface genes to maximize tumor cell death. Furthermore, the antitumor agent exhibits weaker affinity to proteins and small molecules to avoid rapid deactivation in intra- and extra-cellular milieu, which allows the use of lower doses and may also lead to reduction of severe toxicities. ***This strategy is is a paradigm shift*** from conventional platinum drug development approaches in that DNA binding has been the central theme in developing more efficient platinum anticancer agents, and most studies to date have sought positive correlation between drug efficacy and the extent of DNA binding.

**Regulatory Development Strategy:** Dr. Bose is working in collaboration with Battelle to finalize the regulatory plans, which detail the regulatory strategy, requirements, and scheduling for animal pharmacology and toxicology studies, chemistry, manufacturing and control, and clinical testing, that will allow for Investigational New Drug (IND) Application filing by the end of the three-year project period. Battelle will conduct the animal pharmacology and toxicology studies, prepare the pre-IND meeting package and the IND to support the initial clinical study. Ohio University is currently in negotiations to partner with a pharmaceutical company to cost share and develop the drug through clinical testing.

**Outcomes:** During the three-year project period, the project will create employment opportunities within the companies and at contract research organizations conducting the necessary testing for IND application submission. Long-term, the equity created will support additional employment opportunities during the clinical testing and scale-up manufacturing phases.

## Ohio Third Frontier Biomedical Program

Letter of Intent  
January 25, 2010

### ***Lead Applicant***

Dr. Lonnie King  
Dean, College of Veterinary Medicine  
The Ohio State University  
1900 Coffey Rd  
Columbus, OH  
614-688-8749

### ***Contact Person***

Dr. Lawrence Mathes  
Associate Dean of Research & Graduate Studies  
College of Veterinary Medicine  
The Ohio State University  
1900 Coffey Rd  
Columbus, Ohio  
614-292-5179  
[mathes.2@osu.edu](mailto:mathes.2@osu.edu)

### ***Project Title***

Commercialization of EPR Imaging Technology for Cardiovascular Safety Assessment

### ***Funds Request***

\$1,000,000 Third Frontier Research & Development Program  
\$1,000,000 Q-Test/Ohio State University College of Veterinary Medicine  
\$2,000,000 TOTAL

### ***Collaborators***

Q-Test  
OSU College of Veterinary Medicine  
OSU Center for Biomedical EPR Spectroscopy and Imaging, Davis Heart and Lung  
Research Institute  
OSU College of Pharmacy

### ***Concept***

Q-Test is an established small business concern whose primary product is safety assessment for the pharmaceutical industry. Safety assessment in laboratory animals is a necessary step for FDA approval of new drugs. The current approach to safety assessment involves a treatment phase during which physiological measurements are taken followed by phenotyping of target tissues for toxic effects. This approach is costly and not broadly compatible with parallel testing in human subjects. Q-Test proposes to modernize the Safety Assessment approach by incorporating Electron Paramagnetic Resonance (EPR) imaging technology that identifies sites of oxidative stress in small animal models. The expected outcome is a radical change in Safety Assessment that will use non-invasive tools to measure toxic oxygen free radical formation in tissues. Once toxic outcomes in drug escalation protocols are blueprinted in the animal models, those outcomes could be used to monitor drug toxicity during treatment of human subjects to identify real-time toxic variations often seen in human trials. With this method, the treatment protocols could be personalized to attain the greatest effect with minimal collateral toxicity.

### ***Background***

Safety Assessment is a necessary step in the development of new compounds for human use as they move through the FDA approval process. Q-Test is unique in their approach to Safety Assessment because they use animals with disease conditions to assess toxicity rather than normal animals (without disease) as is commonly used by other providers of drug safety assessment. Diseased animals (usually mouse models of disease) often have different sensitivities to drug toxicity than normal non-diseased animals. Q-Test has a number of disease animal models, particularly cardiovascular disease, that place its services in high demand. Q-Test is limited by the company size and technology to conduct their toxicity studies in a traditional manner where physiologically or histological measures are used to assess toxicity. EPR Spectroscopy and Imaging, similar to MRI, measures the resonance absorption of magnetically aligned electrons or protons, respectively. For EPR, electron resonance absorption is altered by unpaired electrons that occur in free radicals. Thus, sites of oxygen free radical formation resulting from inflammation, hypoxia and drug toxicity can be imaged. Q-Test proposes to work with Dr. Periannan Kuppusamy at the Center for Biomedical EPR Spectroscopy and Imaging, Davis Heart Lung Research Institute and Dr. Robert Hamlin, Department of Veterinary Biosciences, to utilize EPR technology to measure oxidative stress as a surrogate marker for toxicity. This approach to Safety Assessment is novel but based on proven technology.

### ***Business Proposal Summary***

David Hamlin, President and CEO of Q-Test, an Ohio-based corporation with sales of \$1.5 million and a national reputation for their unique service, approached The Ohio State University with a proposal to form a joint-venture business with the objective of finding applications for EPR oxidative imaging in Safety Assessment and patient monitoring. The Colleges of Veterinary Medicine and Pharmacy have a strong interest in incorporating safety assessment into an interdisciplinary graduate program in translational medicine. At the same time, the Center for Biomedical EPR Spectroscopy and Imaging is promoting translation of its EPR technology to clinical applications. Together, OSU and Q-Test have the potential to advance Safety Assessment to a new level and at the same time form a new and truly unique graduate program in safety assessment using state-of-the-art technology. The prospective generation of business in the state of Ohio includes the establishment of a new business model, employment of personnel to operate the new imaging technology center in Ohio, and partnership with other businesses within and outside Ohio to utilize this technology. In this regard, OSU College of Veterinary Medicine, College of Pharmacy, and Heart and Lung Research Institute have held joint meetings with Q-Test focused on this first step in transforming Safety Assessment.



1034 S. Broadway, Akron, Ohio 44311

## Letter of Intent

**Date:** January 25, 2010

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

**Subject:** 2010 OTFBP LOI

**Submitted by:** Akron BioMaterials Inc  
1034 S Broadway  
Akron, Ohio 44311

**Contact Person:** David Russell, Director  
ddr1034@yahoo.com  
330-310-9534

**Proposed Title:** Biomedical Polymer Manufacturing

**Funds Requested:** \$400,000

**Collaborators:** TBD

## Summary of Project:

**Introduction:** Akron BioMaterials Inc. ("ABM") is a woman owned Ohio corporation, operating in Akron Ohio since 2003. ABM develops and manufactures medical grade and other specialty polymers; primarily polyurethanes. Our scope includes coatings, sponge, and thermoplastics with primary emphasis on thermoplastic polyurethanes. Our novel technologies include nano-silver based anti-microbial formulations, nano-carbon filled conductives, and biodurable and pharmaceutical resistant PurCarb™ implantable polycarbonate based thermoplastic polyurethanes (TPUs). These are specialty materials which sell for as much as \$100/lb or more depending on volume. Typical commercial volumes range from 5000lb per year to 20,000lb/year.

Commercializing the PurCarb materials is our current priority. We currently produce this in up to 50lb batches and have had replicate successful evaluations at major medical device manufacturers for use in long term orthopedic implants and for use in implantable vascular access catheters. Compared to current art polycarbonate type TPUs such as Bionate, used for long term implants in the orthopedic field; the aromatic type TPUs based upon PurCarb chemistry have



demonstrated improved fatigue resistance, creep resistance, and in vitro biodurability. Chronoflex is the polycarbonate type polyurethane used today for indwelling port catheters which deliver anti-cancer drugs. The aliphatic type PurCarbs have demonstrated greatly superior strength and resistance to drug uptake. In particular, when exposed to aggressive anti-cancer drugs such as etoposide preparations, PurCarb has shown up to 50% improved strength retention compared to currently used TPUs.

We are at the stage where we need to install proper environmental controls and pilot scale equipment to produce market development quantities of PurCarb in the 100 to 500lb scale. We have active interest from two out of state firms who wish to acquire the technology and manufacture these and other formulations. However, we are committed to keeping the business local if possible.

Our overall business plan includes not only making the PurCarb TPU but also producing catheters and molded device subassemblies. We have observed that many of the major device manufacturers have their catheters and molded assemblies produced by toll manufacturers. We believe we can add value by streamlining the supply chain and more importantly we can accelerate the development and approval process by having extrusion and molding capabilities in house as opposed to being under the control of a third party.

**Need for Funds:** Our first priority is to hire staff then we have specific capital equipment needs. We have (4) active commercial development projects in house which have just moved from the bench scale to the 50lb scale quickly.

Specifically, we intend to add an additional polymer technician to contribute to both production and QC and we need capital to expand our QC lab. Additional staff will be added as production demand indicates. We need to build out a 500sq ft controlled environment room for primary manufacturing which includes HEPA filtration units. Our choice is to move the operation from the current building at 1034 S. Broadway in Akron to the Canal Place Akron Global Business Accelerator. Affordable space to suit our needs is currently available at the Accelerator.

In terms of capital equipment our first priority is an underwater pelletizer to replace our strand pelletizer which severely limits our throughput rate. With core equipment and staff the funds requested will provide we will be positioned well for next stage of growth adding additional production personnel as demand warrants.

Respectfully Submitted,

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

David Russell

January 25, 2010

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

**To:** Technology and Innovation Division, The Ohio Department of  
Development  
**From:** Cleveland Clinic  
**Subject:** Letter of Intent, Biomedical Program, FY 2010

Please accept this correspondence as an indication of our intention to submit a proposal for the 2010 Biomedical Program to advance the commercialization of a Trans-Catheter Mitral Valve Stent Implant Technology, invented by Jose Navia, M.D., a CC cardiothoracic surgeon. As required, information regarding our proposal follows.

**1. Lead Applicant Information:**

The Cleveland Clinic  
D-20  
9500 Euclid Avenue  
Cleveland, Ohio 44195  
Tel: 216-444-5757  
Fax: 216-445-6514

**2. Contact Person:**

Jennifer Boland, New Ventures  
Officer  
CC Innovations  
Phone: 216-445-1014  
e-mail: [bolandj@ccf.org](mailto:bolandj@ccf.org)

**3. Proposed Project Title:**

Trans-Catheter Mitral Valve Stent Implant

**4. Estimated Grant Funds to Be Requested:**

\$750,000

**5. Known Collaborators:**

TBD

## **6. Summary of Proposed Project:**

The Trans-Catheter Mitral Valve Stent Implant technology invented by Jose Navia, M.D., F.A.C.C., a Cleveland Clinic cardiothoracic surgeon, has been under development for several years and has recently achieved several significant clinical and technical milestones.

The Clinic conducted a number of cadaveric and ex vivo studies to achieve proof of concept for the device in early 2009. Follow-on acute animal studies with the valve stent conducted by the Clinic over the past 6 months have demonstrated excellent delivery, positioning and functioning of the valve stent in beating heart procedures. Funding from the Third Frontier Program would be used to develop the device further by providing for 1) optimization of the stent design and materials, including performance testing; 2) development of a catheter based delivery system, 3) fabrication of valve stents for use in chronic animal studies; and 4) conducting chronic animal studies.

It is our intention to submit a proposal to advance the technology and commercialization of the Trans-Catheter Mitral Valve Stent Technology. An internal review of literature and patents indicates that this is leading edge technology. While there are other catheter-based mitral valve technologies under development, we are not aware of any human clinical studies involving such valves. Dr. Navia has received positive feedback from both clinicians and potential investors on the results of the acute animal studies.

A grant from the Biomedical Program will be critical to ensure that this promising cardiovascular technology has a solid development opportunity to secure the follow-on investment necessary to transition to the next phase of commercialization and generate a significant economic impact for the State of Ohio.



**NanoMed Systems, Inc.**

January 25, 2010

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

Dear Ohio Department of Development,

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

Lead Applicant: NanoMed Systems, Inc.  
7740 Metric Drive  
Mentor, OH 44060  
(440) 266-8246  
Contact: Michael Wiggins  
mwiggins@nanomedsystems.com

Project Title: Nanoporous Thin Films for Enhancement of Implantable Electrode Performance

Funds Requested: \$1,000,000.00

Known Collaborators: Frantz Medical Development, Ltd.  
7770 Metric Drive  
Mentor, OH 44060  
Contact: Stephanie Harrington, VP

Cleveland Clinic Foundation  
Department of Biomedical Engineering  
Contact: Cameron McIntyre, Ph.D.  
Associate Staff

The attachment contains a brief summary of the project's goals and collaborators.

Regards,

Michael J. Wiggins, Ph.D.  
Principal Engineer  
NanoMed Systems, Inc.



# NanoMed Systems, Inc.

## Project Summary

**Objective:** The objective of this project is to significantly improve the electrical performance of existing implantable electrodes by adapting our existing novel nanoporous thin film technology. While this technology has the potential to have broad impact on the implantable electrode field, initial efforts will be focused on developing and commercializing enhanced electrodes for deep brain stimulation.

**Background:** Electrical stimulation of tissue is being used to treat a variety of medical conditions. For example, stimulation of cardiac tissue is used to treat tachycardia and sudden cardiac arrest while stimulation of neural tissue is used to treat chronic pain, bladder control, Parkinson's diseases, and traumatic brain injury. One ongoing challenge in the design of electrodes is the maximizing the delivery efficiency of the electrical stimulation from the electrode to the tissue. Higher efficiency means either smaller batteries, less frequent replacement of batteries, or both. Efficiency may be improved by increasing the surface area of the electrode, but long-term efficiency may be compromised by fibrous tissue that grows around the lead increasing its impedance. We propose a nanoporous coating that would not only significantly increase the surface area of the electrode but also serve as a reservoir that would slowly release a drug that would diminish the growth of fibrous tissue around the electrode.

**Enabling Technology:** NanoMed Systems (NMS) has developed a proprietary platform manufacturing process where two elements or alloys are co-deposited as a solid film onto a substrate using physical vapor deposition. One component of the film is subsequently removed through a novel process to produce a nanoporous coating (NPC), see Figure 1. Through a partnership with Medtronic, we have successfully demonstrated that this NPC, when applied to a cardiovascular stent, is a metallic alternative to polymeric coatings to control local drug delivery.

**Approach:** We believe our NPC can bring significant improvement in the performance of electrodes. First, the NPC has a much higher surface area than a smooth surface and, as such, should immediately improve the electrical efficiency. Second, in subsequent product applications, the NPC can be tuned to control the release of a therapeutic drug selected to control the inflammatory response around the electrode and reduce the formation of a fibrous capsule.

Our proprietary manufacturing process offers a distinct commercial opportunity for providing a platform coating process to the range of currently available and future implantable electrode technologies. Collaborators have been identified to complement NMS' expertise in thin film processes. From Cleveland Clinic Lerner Institute, Dr. Cameron McIntyre has agreed to assist in the design of the electrodes using his understanding of neurophysiology, neuroanatomy, and neurostimulation modeling. Frantz Medical Development has the expertise and infrastructure in development and manufacturing to produce a marketable final product under ISO 13485 and FDA Quality System Regulations and has also agree to join NMS as a collaborator. There are a number of electrical stimulation companies that have developed out of Northeast Ohio's premier academic and clinical institutions that NMS may pursue as potential collaborators to further enhance the team's strength – Intelect Medical (deep brain stimulation), Synapse Instruments (diaphragm pacing), Neuros (chronic pain control), and NDI Medical. These complementary strategic partnerships will assist in the commercialization of a high impact product.

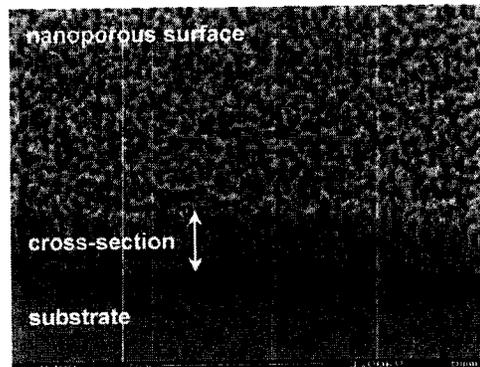


Figure 1: NMS Platinum Nanoporous Coating