



LETTER OF INTENT
Ohio Third Frontier Biomedical Program - 2011

Lead Applicant:

Jon J. Snyder
President and CEO
Neuros Medical, Inc.
4230 State Route 306, Suite 105
Willoughby, OH 44094

Email: jsnyder@neurosmedical.com

Phone: 440-951-2565

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

Estimated Grant Funds to be Requested: \$1M

Known Collaborators:

Case Western Reserve University, Cleveland Clinic, The Ohio Pain Clinic

Chronic pain affects nearly 75 million patients in the U.S. according to the National Pain Foundation. Chronic pain often has a poor prognosis when treated by conventional therapies. Our novel neurostimulation platform technology invented by Drs. Kilgore and Bhadra of the Biomedical Engineering Department at Case Western Reserve University has the potential to provide relief to millions of patients suffering from chronic pain. Our patented electrical nerve block portends to intercept the pain signal near the point of origination, preventing it from reaching the central nervous system.

Our project will contain two phases over two years. The first phase will focus on a human clinical study, confirming safety and efficacy. The second phase will support commercial launch of the product including launch support activities, growing our organization via new job creation and hiring, as well as product manufacturing to fulfill launch initiatives. In both phases, we will continue to augment our strong intellectual property position.

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

December 10, 2010

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

Re: Letter of Intent Ohio Third Frontier Biomedical Program -2011

Dear Sir/Madam:

This letter of Intent confirms that our intention to submit a proposal to Ohio Third Frontier Biomedical Program for year 2011. Project details and project summary are included in this letter of intent.

Lead Applicant's Name: The University of Toledo Health Science Campus
3000 Arlington Avenue
Toledo, OH 43614

Tel: (419) 383-4252
Fax: (419) 383-4262
Email: reseachadmin.hsc@utoledo.edu

Contact Person: A. Champa Jaysuriya, Ph.D.
Associate Professor, Department of Orthopaedic Surgery
Tel: (419) 383-4252
Fax: (419) 383-3526
Email: a.jayasuriya@utoledo.edu

Title of Project: Evaluation of Injectable Bone Grafts for Bone Regeneration

Estimated Budget Request: \$1,000,000.00 Third Frontier Fund
\$ 100,000.00 Wright Capital Fund

Known Collaborators: Profit collaborator will be identified.

Project Summary

United States bone and joint decade was declared the years of 2002-2011, providing national recognition to the fact that musculoskeletal disorders and diseases are the leading cause of physical disability in this country. Approximately 6.2 million fractures occurred in US annually from 1992-1994. The fractures increased to 7 million in 1998. The cost for musculoskeletal conditions was 215 billion in 1995 [9]. As our population aged these numbers are increased dramatically with economic burden for the all communities. Osteoporotic fractures have doubled in the last decade, so that 40% of all women over 50 will eventually suffer from one.

This proposal is based on our ongoing research related to injectable bone grafts based on natural biopolymer chitosan. We have our initial proof of evidence related to our bone grafts, such as *in vivo* biocompatibility and ability to heal the bone defects in a rat model. We also possess a patent related to this technology. In general, chitosan evoke a minimal foreign body reaction, with little or no fibrous encapsulation. Biodegradability and biocompatibility are very important properties that make chitosan a useful material for bone regeneration. We can fabricate the spherical shape microparticles in the size range of 40-700 μm depending on the application type. These bone constructs will possess injectability, biodegradability, biocompatibility, osteoconductivity, antibacterial activity, and mechanical integrity.

This project will align with the goals of OTFBP since the project involve in regenerative medicine and orthopaedic disciplines. The objective of this project is to commercialize the developed bone constructs at the end of the project period. This project will benefit to improve the Ohio's economy by partnering with Ohio's residents.

The developed bone constructs can be administered with a small gauge needle injection, making possible filling defects of different shapes and sizes through minimally invasive surgery (MIS). The MIS limits pain, prolonged hospitalization, recovery time, blood loss, morbidity, and scar formation compared with open surgeries, which require implanting existing treatments of autografts, allografts or conventional scaffolds. The proposed bone constructs can be applied into different size and shape of orthopaedic bone defects including spine fusion.

Sincerely,

A. Champa Jayasuriya, Ph.D.
Associate Professor, Director of Orthopaedic Research
University of Toledo Health Science Campus
Department of Orthopaedic Surgery
Mail Stop 1094, 3065 Arlington Avenue
Dowling Hall, Suite 2447
Toledo, OH 43614-5807

Tel: 419-383-6557

Fax: 419-383-3526

Email: a.jayasuriya@utoledo.edu

December 13, 2010

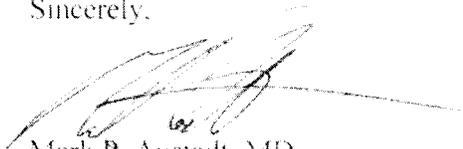
The Ohio Department of Development, Technology Division
77 South High Street 25th Floor
Columbus, OH 43215

Subject: 2011 OTFBP LOI

This letter is submitted to express the commitment of LifeBridge Technologies, LLC to submit a proposal to the Ohio Third Frontier Biomedical Program. This proposal will request \$1,000,000 of support for a proposed cost-shared budget.

Lead Applicant:	LifeBridge Technologies, LLC
Address:	30 E. Apple St., Suite 6252 Dayton, OH 45409
Phone:	937. 269.6452
Contact person:	Mark P. Anstadt, M.D.
Email:	mpanstadt@aol.com
Proposed Project Title:	Mini Heart Pump for Lifesaving Neonatal and Pediatric Circulatory Support
Estimated Request	\$1,000,000
Known Collaborators	Wright State University Dayton, OH 45435 Applied Sciences, Inc. Cedarville, OH 45314 Nationwide Children's Hospital Columbus OH 43205 Qtest Labs Columbus, OH 43212

Sincerely,



Mark P. Anstadt, MD
President
LifeBridge Technologies, LLC

Project Title: Mini Heart Pump for Lifesaving Neonatal and Pediatric Circulatory Support

Project Description:

While there is a need for cardiac transplantation in approximately 350 children each year, donor organs are limited. Children awaiting heart transplantation face frequent complications culminating in death rates above 50% for those who do not receive a heart transplant expeditiously. The need for mechanical circulatory support has therefore increased for pediatric patients with congenital or acquired heart disease over the past decade. However, the unsuitable characteristics of these systems prevent their use in most children who could benefit from it. The morbidity and mortality associated with mechanical circulatory support in children is essentially imparted by the requirement of blood contact, necessitating full anticoagulation, leading to excessive bleeding or thrombosis.

LifeBridge Technologies, LLC is developing a proprietary, non-blood contacting heart pump for support of neonatal and pediatric patients. The device has unique efficacy for supporting the small neonatal to the pediatric sized failing heart. The company will work with four collaborators to complete the development and testing of a miniaturized mechanical support system for marketing in the United States. Wright State University, Nationwide Children's, and Qtest Labs will provide related resources for required pre-clinical testing and initial clinical trials. Drive manufacturing, device distribution and related technical support is anticipated to create significant job opportunities in Ohio.

11-544

Sparton Medical Systems
22740 Lunn Road
Strongsville, OH 44149



Ohio Third Frontier Letter of Intent

December 12, 2010

The Ohio Department of Economic Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43125

Dear Ohio Department of Economic Development:

Please accept this proposal and following summary for Sparton Medical System's intent to submit an Ohio Third Frontier Biomedical Program ("OTFBP2011").

Lead applicant:	Sparton Medical Systems, Inc.
Address:	22740 Lunn Road
Phone number:	440.878.4630
Contact Person:	Kevin Webb
Email:	kwebb@sparton.com
Proposed Title:	BioSamples – DNA <i>Extractor</i>
Est. Grant funds:	\$500,000
Known collaborators:	BioSample Solutions, LLC Multiple Qualified Ohio Based Supplier-Partners

We are looking forward to taking the next steps and a one page summary follows within this document.

With best regards,

A handwritten signature in cursive script, appearing to read "Duane K. Stierhoff".

Duane K. Stierhoff
VP/General Manager



Project Summary

All molecular diagnostics require DNA extraction. The current methods have been proven over the past twenty years but were originally designed for isolating and archiving DNA samples for research labs and never intended for diagnostics. Though the current methods work, they require a high level of manual control and large samples which takes additional time and increases the risk of contamination.

There is a need within this \$5 billion dollar diagnostics market to develop, perfect, and mass produce a system which decreases the process time and mitigates contamination. While the need also exists in today's research lab, this need is becoming a necessity for the growing diagnostics market which is currently monopolized by one European company with out-dated technology.

Therefore, Sparton Medical Systems in conjunction with BioSample Solutions is planning to launch a rapid DNA extraction platform which will reduce the sample preparation time from forty minutes to fifteen minutes while being robust and user-friendly in resolving the contamination issues which continues to plague this field.

Specifically, Sparton Medical will design, prototype, and manufacture market desired hardware to automate the sample preparation while BioSample further develops and commercializes their patented consumable Bio-Cookies™ which is user-friendly, thus decreases process and training time of operators. Also, the Bio-Cookies™ technology requires a very small sample amount which is the driving force to resolve errors with contamination.

Sparton Medical and BioSample will integrate the hardware and the consumable into a bench-top platform to be clinically trialed for research labs by the second year. In the third year, a 510k will be submitted and the plan is to penetrate the multi-billion dollar diagnostics field while both the hardware and the consumable is being produced here in Ohio, utilizing Ohio based supplier-partners.

About Sparton Medical: Located in business and family friendly Strongsville, Ohio and a former recipient of the Third Frontier Initiative for job growth, Sparton Medical Systems, Inc. is an FDA-registered and ISO 13485 certified contract design, development, and manufacturing company. The company specializes in diagnostic laboratory instrumentation and therapeutic point-of-care devices and is responsible for launching and delivering finished medical products globally.

About BioSamples: Founded by Chiu Chau whom previously pioneered a molecular diagnostics platform for blood group genotyping, BioSample Solutions, LLC was formed early this year to commercialize their patented BioCookie™ technology for pre-analytical DNA extraction. Mr. Chau brings not only his vast experience to further develop both needed and desired consumables, but he also has a solid track record with his last venture by growing from a start-up company to being successfully acquired for \$120 million in 2008.

In partnership, Sparton Medical and BioSample plan to penetrate this market by combining our core competencies while benefiting Ohio in retaining and growing the talent here in our State.

2011 Request for Proposals

Application Information Page

Letter of Intent (LOI) Notification Number (Issued by ODOD)	LOI #: OTFBP 11-_____
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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 and commercial development of MultiStem®, an adult stem cell product, in solid organ transplantation		
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 #	Preclinical validation of genetically modified, nanofiber-expanded hematopoietic stem cells for osteoporosis therapy Development of the StemMed Closed System for Hematopoietic Stem Cell Expansion
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Holly Lipkovich

Typed Name of Authorizing Agent

**Associate Director, Office of Grants and Contracts -
School of Medicine**

Title of Authorizing Agent

Signature

Date

For ODOD Use Only

Date Received

Proposal
ID #

Ohio Third Frontier Biomedical Program

Lead Applicant Contact Information

Authorizing Agent	Name	Holly Lipkovich		
	Title	Associate Director, Office of Grants and Contracts - School of Medicine		
	Organization	Case Western Reserve University		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106-4919		
	Telephone	216-368-4432	Fax	216-368-4805
	E-Mail	medres@case.edu		

Project Director	Name	Stanton L. Gerson		
	Title	Director of Case Comprehensive Cancer Center, NCRM		
	Organization	University Hospitals Case Medical Center		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106		
	Telephone	216-844-8565	Fax	216-368-1166
	E-Mail	slg5@case.edu		

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

Grant Administrator	Name	Michael Gilkey, MBA MS		
	Title	Acting Executive Director, National Center for Regenerative Medicine		
	Organization	Case Western Reserve University		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106		
	Telephone	216-368-2079	Fax	216-368-6020
	E-Mail	meg14@case.edu		

Authorizing Agent – the individual authorized by the Lead Applicant to accept the terms and conditions of an award of Grant Funds.
 Project Director – the individual authorized by the Lead Applicant to direct the Project for which the Grant Funds have been awarded.
 Fiscal Agent – the individual authorized by the Lead Applicant to sign Grant-related financial documents, e.g., Requests for Payment, Grant financial reports, etc.
 Grant Administrator – the individual authorized by the Lead Applicant to oversee the day-to-day administration of the Grant Funds, including preparing progress reports, monitoring project progress, etc.
Note: The same individual may hold more than one of these positions.

Ohio Third Frontier Biomedical Program Collaborator Information

Name	Stanton Gerson		
Title	Director of Case Comprehensive Cancer Center, NCRM		
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	Slq5@case.edu		

Name	Michael Gilkey, MBA MS		
Title	Acting Executive Director, National Center for Regenerative Medicine		
Organization	Case Western Reserve University		
Address	10900 Euclid Avenue		
City, State, Zip	Cleveland, OH 44106		
Telephone	216-368-2079	Fax	216-368-6020
E-Mail	Meg14@case.edu		

Name	Wouter van't Hof		
Title	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	wouter@athersys.com		

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	Telephone
E-Mail	RDeans@athersys.com		

Name	John J. Fung		
Title	Chairman, Department of General Surgery, Director of the Transplant Center, Cleveland Clinic, Professor of Surgery at Case		
Organization	Cleveland Clinic		
Address	9500 Euclid Avenue		
City, State, Zip	Cleveland, OH 44195		
Telephone	216-444-6664		
E-Mail	funj@ccf.org		

Name	Kenneth R. McCurry		
Title	Assistant Professor of Surgery		
Organization	Cleveland Clinic		
Address	9500 Euclid Avenue		
City, State, Zip	Cleveland, OH 44195		
Telephone	216-444-6664		
E-Mail	mccurk@ccf.org		

Ohio Third Frontier Biomedical Program

Letter of Intent

Athersys, Inc., a founding, collaborative member of the Ohio Wright Center for Regenerative Medicine, has developed a proprietary adult stem cell product, MultiStem[®], 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[®] in several pre-clinical disease models including stroke, acute myocardial infarct (AMI), and in Graft vs. Host Disease (GVHD). The FDA has approved the manufacturing and basic safety profile of MultiStem[®] for use in humans in multiple indications. Athersys has completed enrollment in a Phase I AMI study and is anticipating completion of GVHD trial accrual in 2011. Earlier in 2010 Athersys and Pfizer received approval for a Phase II clinical study testing MultiStem efficacy in ulcerative colitis. This was accomplished within the first year of collaboration, underscoring ability of the Company to utilize its prior experience for rapid advancement of clinical MultiStem studies in new indications.

Athersys has secured strong IP positions in the US and Europe, covering the use of MultiStem in the solid organ transplant (SOT) setting. We propose to support new preclinical R&D activity to obtain regulatory approval for clinical studies evaluating the safety and therapeutic effectiveness of **MultiStem[®] in SOT**, through regional collaboration between Athersys and the Cleveland Clinic (CCF), including the world-renowned expert transplant teams of Drs. John Fung and Kenneth McCurry. CCF is ranked first in number of lung transplants, and third in number of heart transplants, currently performed in the United States. It is anticipated that this SOT proposal could address significant unmet medical need, has great potential for rapid entry into late stage clinical evaluation, and also represents a significant commercial opportunity.

Recent estimations indicate that the market for a stem cell therapy in the SOT space, just for kidney transplantation alone, exceeds \$700 million per year. Calcineurin inhibitor (CNI) therapy is considered the backbone for standard of care for all organ recipients. One of the therapeutic hypotheses for MultiStem is that it will enable reduction or omission CNI immunosuppressive therapy (IS), potentially saving upwards of \$2.4 billion per year in IS drug costs alone. MultiStem therapy may also enable increased use of allogeneic organ transplantation where patients and donors are less well matched, shortening ever-growing transplant waiting lists, further improving patient morbidity/mortality, and quality of life.

The underlying scientific hypothesis for the SOT research program is that MultiStem has ability to provide benefit via modulation of ischemia-reperfusion injury and prevent acute graft rejection. Preliminary preclinical findings show that MultiStem can prolong the survival of allogeneic heart grafts in heterotopic rat transplant models. Specifically, when combined with certain IS therapy, MultiStem guides long-term graft acceptance in a manner that is not accomplished with treatment of individual therapies, and enables reduction or even elimination of immunosuppressive regimens. These data support the concept that MultiStem therapy can help induce tolerance in the recipient, such that the donor graft is not attacked by the immune system of the recipient. These are significant preliminary findings for MultiStem which, when developed in the proper translational environment, have great potential to revolutionize the standard of care in clinical transplantation.

The funds applied for herein will be used to support two main research activities in established *in vivo* preclinical models of heart and lung transplantation in the laboratories of Drs. Fung and McCurry, specifically; 1) additional safety and efficacy studies required for regulatory approval of MultiStem evaluation in heart or lung transplantation, and; 2) mechanistic studies to further assess mode of action of MultiStem in enabling allograft protection. Studies to be performed include assessment of maximal effective MultiStem dose, optimal window of administration, and optimal number of administrations, with read-out of prevention of ischemia-reperfusion injury and acute allograft rejection. In addition, immunosuppressive drug titration experiments will be designed to establish the optimal, safe and efficacious combinations of MultiStem and IS therapy. Data generated from animal studies in the first 24 months will be used as part of a pre-clinical data package to apply to the FDA for use of MultiStem[®] for support of SOT patients in a Phase I/II IND clinical study.

It is the intention of Athersys to secure a development partner for commercial marketing and distribution of MultiStem for SOT as it has already done for AMI with Angiotech Pharmaceuticals, and for treatment of Inflammatory Bowel Disease with Pfizer, with the objective of closing this partnership to support pivotal Phase 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 Ohio.

Application Information Page

Letter of Intent (LOI) Notification Number
(Issued by ODOD)

LOI #: OTFBP 11-_____

This Application: Does Does NotInclude information considered a "trade secret" under Ohio Revised Code
Section 1333.61 (D)Lead Applicant Name
Marco A Costa, M.D., Ph.D.Lead Applicant Address
10900 Euclid Avenue
Case School of Medicine

City: Cleveland

State: OH

Zip: 44106

County: Cuyahoga

Project Title: Development of the StemMed Closed System for Hematopoietic Stem Cell
Expansion

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 #Preclinical validation of genetically modified, nanofiber-expanded hematopoietic
stem cells for osteoporosis therapyClinical and commercial development of MultiStem®, an adult stem cell product, in
solid organ transplantation

Holly Lipkovich

Typed Name of Authorizing Agent

Associate Director, Office of Grants and Contracts -
School of Medicine

Title of Authorizing Agent

Signature

Date

For ODOD Use Only

Date Received

Proposal
ID #

Ohio Third Frontier Biomedical Program Lead Applicant Contact Information

Authorizing Agent	Name	Holly Lipkovich		
	Title	Associate Director, Office of Grants and Contracts - School of Medicine		
	Organization	Case Western Reserve University		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106-4919		
	Telephone	216-368-4432	Fax	216-368-4805
	E-Mail	medres@case.edu		

Project Director	Name	Marco A Costa, M.D., Ph.D.		
	Title	Professor of Medicine, Director, Center for Research and Innovation Harrington-McLaughlin Heart and Vascular Institute		
	Organization	University Hospitals Case Medical Center		
	Address	11100 Euclid Ave. LKS 3001		
	City, State, Zip	Cleveland, OH 44106		
	Telephone	216-844-5480	Fax	216-368-1166
	E-Mail	slg5@case.edu		

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

Grant Administrator	Name	Michael Gilkey, MBA MS		
	Title	Acting Executive Director, National Center for Regenerative Medicine		
	Organization	Case Western Reserve University		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106		
	Telephone	216-368-3614	Fax	216-368-6020
	E-Mail	dsg12@case.edu		

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

Ohio Third Frontier Biomedical Program Collaborator Information

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

Attach additional forms as needed.

Name	Marco A. Costa, M.D., Ph.D.		
Title	Professor of Medicine, Director, Center for Research and Innovation Harrington-McLaughlin Heart and Vascular Institute		
Organization	Case Western Reserve University, University Hospitals		
Address	11100 Euclid Ave. LKS 3001		
City, State, Zip	Cleveland, OH 44106		
Telephone	(216) 844-5840	Fax	(216) 844-8954
E-Mail	marco.costa@uhhospitals.org		
Name	Jane Reese Koç, MBA, MT		
Title	Operations Director, Cell Therapy Service		
Organization	University Hospitals		
Address	2103 Cornell Road		
City, State, Zip	Cleveland, OH 44106		
Telephone	216) 368-1007	Fax	216) 368-2855
E-Mail	jsr5@case.edu		
Name	Michael Gilkey, MBA MS		
Title	Acting Executive Director, National Center for Regenerative Medicine		
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	meq14@case.edu		
Name	Masakazu Ishikawa, M.D., PhD.		
Title	VP of R&D		
Organization	StemMed West, LTD.		
Address	2103 Cornell Road,		
City, State, Zip	Cleveland OH 44106-7290		
Telephone	216-3683747	Fax	216-368-0556
E-Mail	mxi87@case.edu		
Name	Takayuki Asahara, M.D., PhD		
Title	Chief Scientific Officer		
Organization	StemMed West, LTD.		
Address	2103 Cornell Road, Cleveland OH 44106-7290		
City, State, Zip	Cleveland OH 44106-7290		
Telephone	216-3683747	Fax	216-368-0556
E-Mail	a4shr@mac.com		

Ohio Third Frontier Biomedical Program Letter of Intent

Cardiovascular disease (CVD) is the leading cause of death and disability in the western world, accounting for 40% of our nation's mortality and much of its morbidity. CVD have claimed more lives each year in the United States than cancer, respiratory diseases, accidents, and diabetes mellitus combined since 1900; except for the year 1918. CVD accounted for 17.5 million deaths around the world in 2005 and is projected to remain the leading cause of death in the future. Peripheral arterial disease (PAD), the most common form of CVD, affects a high fraction (29%) of patients 70 years and older, or aged 50 to 69 years with a history of cigarette smoking or diabetes. In particular, critical limb ischemia (CLI), the advanced presentation of PAD caused by severe compromise of blood flow to the affected extremity, is a growing vexing and costly problem in the western society, accounting for more than 400,000 hospital discharges a year in Europe and North America. Despite the advances in revascularization strategies (angioplasty or bypass surgery), amputation is still necessary in about 30% of patients, a procedure that is associated with significant disability, perioperative mortality, and poor overall prognosis. Patients with CLI have quality of life indices similar to that for terminally ill cancer subjects. These alarming figures illustrate the pressing need to develop safe, feasible and cost-effective therapeutic approaches for such patients in the greatest need.

Dr. Takayuki Asahara (key collaborator) made the first scientific observation that endothelial progenitor cells circulated in peripheral blood and were able to promote angiogenesis in vivo. These cells have been characterized by the expression of CD133 and CD34, based on their close relationship to Hematopoietic stem cells (HSC). These early observations provided the foundation for the development of autologous stem/progenitor cell therapy. The CD34+ cell is likely the most studied cell fraction for CVD therapeutics with angiogenesis and has been the preferred cell candidate for therapeutic angiogenesis due to its well known mechanism of action and experience. Dr. Marco Costa (Project Director) was one of the main investigators in the largest double-blind, placebo-controlled Phase II FDA clinical trial to date (ACT34-CMI sponsored by Baxter, Identifier: NCT00300053) where patients with chronic ischemic heart disease were treated with intramyocardial injection of fresh isolated CD34+ cells. Results presented at the 2009 Annual Scientific Session of the American Heart Association showed improved myocardial perfusion and symptoms in patients randomized to cell therapy. We and our collaborators completed successful pilot studies using the same standard fresh CD34+ cell-based approach to treat patients with CLI (ACT34-CLI Identifier: NCT00616980). These studies have shown similar positive angiogenesis results in patients with CLI. From these and other studies, our group developed a closed system for HSC expansion maintaining angiogenic potential in order to overcome some of these critical limitations that hamper the use of cell-based therapy in the clinical setting.

The concept of expanding CD34+ cells ex-vivo (EX) is appealing, as it would promote both increase in cell number and fortification in cellular bioactivity. If successful, this would eliminate the need for costly and risky large volume blood aphaeresis or bone marrow aspiration that require tertiary specialized centers. Previous attempts used animal-serum and proved unpractical for clinical application, due to the difficulty in isolating and harvesting adherent cells, and need to use open, bench top culture system. Drs. Asahara and Masuda originally developed and validated a serum-free bench top culture system to enhance/expand CD34+ cells EX by using a proprietary combination of growth factors/cytokines. Unlike previous approaches, the EX system was designed to maintain cell immaturity and fortify angiogenic potential of *non-adherent CD34+ cells*. Further improvements were made by Drs. Costa and Ishikawa at CWRU, and the new CD34-EX system uses exclusively FDA approved serum-free medium and animal-free growth factors/cytokines within a closed-system (specialized bag/cartridge for suspension culture), which makes the process extremely simple (i.e. "office"-based approach) and feasible for large-scale applications in the clinical setting. Extensive pre-clinical testing has been conducted. In-vitro data showed enhanced expression of angiogenic markers in CD34+ post-expansion, and enhanced tube formation in matrigel. In-vivo testing was also conducted in different animal models, including acute MI myocardial infarction, diabetic wound healing and CLI. The results showed improved neovascularization and healing in animals treated with EX-CD34+ compared to fresh, pre EX CD34+ cells (standard method) and placebo.

In this OTFBP grant application, we propose to repeat these pre-clinical experiments according to GLP standards in order to obtain IND clearance by the FDA and start Phase I-IIa clinical trials by year 3. The EX-CD34+ cell product (a closed, specialized bag or cartridge contained proprietary media) will be manufactured and quality controlled by the Ohio Wright Center for Regenerative Medicine's Cell Therapy Integrated Service (CTIS) which operates under FACT and FDA guidelines for Phase I-IIa clinical trials. Experiments to be performed will include: optimizing dose and dose regiments, cell persistence, biodistribution and safety experiments. Data generated from these animal studies in the first 12 months of the award will be used as part of a pre-clinical data package to apply to the FDA for use of StemMed West EX-CD34+ cell product for treatment of patients suffering from CLI in a Phase I-IIa IND clinical study.

It is the intention of NCRM and StemMed West to secure a development partner for commercial marketing and distribution of the cell product. In this initial phase, the focus will be on CLI, but the plan is to make this a platform cell-therapy product for other forms of CVD and orthopedic applications (data not shown). Baxter has been identified as a potential commercial partner for this project. StemMed West technology adds significant value to Baxter's current cell therapy portfolio based on CD34+ cell line (ACT-34 studies), which is starting its Phase III clinical trial in 2011. The goal would be to close the partnership to support pivotal Phase IIb-III clinical trials, which could account for a \$300 million long-term financial investment in cell manufacturing and therapeutic product development in Ohio.

2011 Request for Proposals

Application Information Page

Letter of Intent (LOI) Notification Number
(Issued by ODOT)

LOI #: OTFBP 11-_____

This Application: Does Does NotInclude 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

Cleveland

Cleveland

Cleveland

Cleveland

County:

Cuyahoga

Cuyahoga

Project Title:

Preclinical validation of genetically modified, nanofiber-expanded hematopoietic
stem cells for osteoporosis therapy

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 #Development of the StemMed Closed System for Hematopoietic Stem Cell
ExpansionClinical and commercial development of MultiStem®, an adult stem cell product, in
solid organ transplantation

Holly Lipkovich

Typed Name of Authorizing Agent

Associate Director, Office of Grants and Contracts -
School of Medicine

Title of Authorizing Agent

Signature

Date

For ODOT Use Only

Date Received

Proposal
ID #

Ohio Third Frontier Biomedical Program Lead Applicant Contact Information

Authorizing Agent	Name	Holly Lipkovich		
	Title	Associate Director, Office of Grants and Contracts - School of Medicine		
	Organization	Case Western Reserve University		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106-4919		
	Telephone	216-368-4432	Fax	216-368-4805
	E-Mail	medres@case.edu		

Project Director	Name	Stanton L. Gerson		
	Title	Director of Case Comprehensive Cancer Center, NCRM		
	Organization	University Hospitals Case Medical Center		
	Address	10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106		
	Telephone	216-844-8565	Fax	216-368-6020
	E-Mail	slg5@case.edu		

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

Grant Administrator	Name	Michael Gilkey, MBA MS		
	Title	Acting Executive Director NCRM		
	Organization	Case Western Reserve University		
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	City, State, Zip	Cleveland, OH 44106		
	Telephone	216 368 2079	Fax	216-368-6020
	E-Mail	meg14@case.edu		

Authorizing Agent – the individual authorized by the Lead Applicant to accept the terms and conditions of an award of Grant Funds.
 Project Director – the individual authorized by the Lead Applicant to direct the Project for which the Grant Funds have been awarded.
 Fiscal Agent – the individual authorized by the Lead Applicant to sign Grant-related financial documents, *e.g.*, Requests for Payment, Grant financial reports, *etc.*
 Grant Administrator – the individual authorized by the Lead Applicant to oversee the day-to-day administration of the Grant Funds, including preparing progress reports, monitoring project progress, *etc.*
Note: The same individual may hold more than one of these positions.

Ohio Third Frontier Biomedical Program Collaborator Information

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

Attach additional forms as needed.

Name	Hiranmoy Das, PhD		
Title	Associate Professor, Director, Stem Cell Research Laboratories,		
Organization	The Ohio State University Medical Center, NCRM		
Address	BRT # 382, 460 W 12 th Avenue		
City, State, Zip	Columbus, OH 43210		
Telephone	614-688-8711		614 293-5614
E-Mail	hiranmoy.das@osumc.edu		
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	Slg5@case.edu		
Name	Michael Gilkey, MBA MS		
Title	Acting Executive Director NCRM		
Organization	Case Western Reserve University		
Address	School of Medicine 10900 Euclid Avenue		
City, State, Zip	Cleveland, OH 44106		
Telephone	216 368 2079	Fax	216-368-6020
E-Mail	meg14@case.edu		
Name	John J. Lannutti		
Title	Professor		
Organization	Department of Materials Science and Engineering		
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City, State, Zip	Columbus, OH 43210		
Telephone	216-426-3594	Fax	216-361-9495
E-Mail	lannuttj@matsceng.ohio-state.edu		
Name	Rebecca D. Jackson, MD		
Title	Professor, Chair. Women's Health Initiative, Washington. Director, Clinical and Translational Research, OSU		
Organization	The Ohio State University Medical Center		
Address	485 McCampbell Hall, 1581 Dodd Hall		
City, State, Zip	Columbus, OH 43210		
Telephone	(614) 292-3800	Fax	(614) 292-8289
E-Mail	jackson.20@osu.edu		
Name	Richard T Hart, PhD		
Title	Professor, Chair, Dept Of Biomedical Engineering		
Organization	The Ohio State University Medical Center		
Address	270 Bevis Hall 1080 Carmack Road		
City, State, Zip	Columbus, OH 43210		
Telephone	(614) 292-1285 Fax: (614) 2927301		
E-Mail	hart.322@osu.edu		

Ohio Third Frontier Biomedical Program

Letter of Intent

Osteoporosis is a systemic metabolic bone disease manifested by fractures and skeletal deformity characterized by low mineral density and micro-architectural deterioration of the skeleton. It is a major contributor to mortality, morbidity and medical expense worldwide. Bone is a dynamic organ, constantly remodeling. It consists of dense organic, inorganic, and mineral components, and at a cellular level, remodeling is coordinated by bone forming cells (osteoblasts) (1) and bone resorbing cells (osteoclasts) (2). Osteoporosis can result from decrease in number or activity of osteoblasts and/or increase in number or activity of osteoclasts. Bone augmenting therapies, such as hormone replacement, bisphosphonates, and implantation of osteoinductive biomaterial, and changes in lifestyle, only temporarily augment bone mineral density yet induce side effects. Stem cell therapies for osteoporosis are currently being investigated, but clinical success is not yet established. Stem cells are pluripotent cells that can be differentiated into any lineage, determined by molecular cues they receive from their microenvironment. Animal studies for bone diseases have used stem cells derived from bone marrow, peripheral blood, and human embryonic stem cells. However, there are limitations to harvesting stem cells from bone marrow; it requires a painful and invasive procedure and stem cell function declines in aged patients, imposing hurdles in autologous stem cell therapy. However, stem cells derived from human umbilical cord blood (UCB) have the great advantage of being able to create numerous distinct tissues, less immunogenic than bone marrow, readily harvested without risk to the donor and far less likely to induce host-versus-graft rejection. The problem with UCB as a cell source is dosing – you need to have a certain amount of cells in order to get a desired effect. Historically expansion of these cells has been difficult. We have established nanofiber-based, ex vivo expansion technology for CD133+/CD34+ hematopoietic stem cells derived from human umbilical cord blood to provide useful numbers of functional therapeutic stem cells with the help of Dr. John Lannutti's group (who has started-up a company called 'Nanofiber Solutions'). Subsequently, we demonstrated that overexpression of pro-angiogenic growth factors in the stem cells enhances their beneficial effects in ischemic diseases.

Nanofiber Solutions was founded by Dr. John J Lannutti and Dr. Jed Johnson in April of 2009 at The Ohio State University. The company was established as an LLC in the State of Ohio in April of 2009 and has received University Technology Transfer Company status from The Ohio State University, which allows the company to operate completely independent of the university with sole access to the proprietary technology developed while affiliated with the university. Nanofiber Solutions' IP is protected by provisional patents filed through the Technology Licensing and Commercialization Office at OSU. The technical expertise of Drs. Johnson Lannutti was combined with Ross Kayuha's extensive senior executive management and entrepreneurial experience to develop a business plan that won first place in the 2009 Deloitte Business Plan Competition at the Center for Entrepreneurship in the Fisher College of Business at The Ohio State University and over \$90,000 in cash and in-kind services. Because of this achievement, Nanofiber Solutions was invited to participate in the DFJ Cisco Global Business Plan competition.

Nanofiber Solutions develops and markets patented electrospun fiber multi-well plate technologies for cell culture and cancer research. Historically, cell culture has been performed on flat, tissue culture polystyrene (TCPS) because it is cheap, optically clear, and many cells grow well on it. In reality, however, living organisms are made up of an extracellular matrix that supports cells. TCPS lacks three-dimensional (3-D) component and cells behave very differently on this flat, smooth substrate than they do in true biological settings.

We hypothesize that osteoporosis will be reversed by genetically modified hematopoietic stem cells from UCB resulting in increased bone remodeling, bone mineral density and neovascularization thereby establishing bone homeostasis. Our long-term goal is to establish the use of such nanofiber-expanded cells for the clinical treatment of osteoporosis. Our earlier preclinical studies with hind limb ischemia have generated a successful ongoing clinical trial (10 patient critical limb ischemia trial (NIH/NHLBI - SBIR R44HL092706, Cooper PI), and we plan for this proposal to lead us to an IND in 3 years and a clinical trial for osteoporosis by year 5. We also propose to develop a bioreactor for large scale expansion of clinically compatible cells using FDA approved GMP facility that might be marketable not only for clinical application but also for research use.

2011 Request for Proposals

Application Information Page

Letter of Intent (LOI) Notification Number
(Issued by ODOD)

LOI #: OTFBP 11-_____

This Application: Does Does Not

Include information considered a "trade secret" under Ohio Revised Code Section 1333.61 (D)

Lead Applicant
Name

Larry C. Lasky, M.D.

Lead Applicant
Address

310 Doan Hall

410 West 10th Avenue

City:

Columbus

State:

OH

43210

County:

Franklin

Project Title:

Development of a human platelet production device for clinical use

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 #

Amanda H. Gibbs

Typed Name of Authorizing Agent

Sponsored Program Officer

Title of Authorizing Agent

Signature

Date

For ODOD Use Only

Date Received

Proposal
ID #

Ohio Third Frontier Biomedical Program Lead Applicant Contact Information

Authorizing Agent	Name	Marta L. Morris		
	Title	Director, Grants and Contracts		
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	City, State, Zip	Columbus, Ohio 43210		
	Telephone	614 292 2655	Fax	614 292 4315
	E-Mail	Morris.6@osu.edu		

Project Director	Name	Larry C. Lasky, M.D.		
	Title	Associate Professor of Pathology and Internal Medicine		
	Organization	The Ohio State University		
	Address	310 Doan Hall 410 West 10th Avenue		
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	Telephone	614 293 3020	Fax	614 293 4591
	E-Mail	Lasky.4@osu.edu		

Fiscal Agent	Name	Richard Bradbury		
	Title	Director, fiscal services		
	Organization	The Ohio State University		
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	City, State, Zip	Columbus, Ohio 43210		
	Telephone	614 688 8125	Fax	614 292 7505
	E-Mail	bradbury.1@osu.edu		

Grant Administrator	Name	Michael Gilkey, MBA MS		
	Title	Acting Executive Director NCRM		
	Organization	Case Western Reserve University		
	Address	School of Medicine 10900 Euclid Avenue		
	City, State, Zip	Cleveland, OH 44106		
	Telephone	216 368 2079	Fax	216 368 6020
	E-Mail	meg14@case.edu		

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

Ohio Third Frontier Biomedical Program Collaborator Information

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

Attach additional forms as needed.

Name	Larry C. Lasky, M.D.		
Title	Associate professor of Pathology and Internal Medicine		
Organization	The Ohio State University		
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	410 West 10th Avenue		
City, State, Zip	Columbus, Ohio 43210		
Telephone	614 293 3020	Fax	614 293 4591
E-Mail	lasky.4@osu.edu		

Name	Michael Gilkey, MBA MS		
Title	Acting Executive Director NCRM		
Organization	Case Western Reserve University		
Address	School of Medicine		
	10900 Euclid Avenue		
City, State, Zip	Cleveland, OH 44106		
Telephone	216 368 2079	Fax	216 368 6020
E-Mail	meg14@case.edu		

Name	Alvin H. Schmaier, M.D.		
Title	Professor of Medicine, Oncology, and Pathology		
Organization	Case Western Reserve University		
Address	10900 Euclid Avenue WRB2-130		
City, State, Zip	Cleveland, OH 44106		
Telephone	216 368 1172	Fax	216 368 3014
E-Mail	schmaier@case.edu		

Name	Stanton Gerson		
Title	Director of Case Comprehensive Cancer Center, NCRM, CSCRM		
Organization	Case Western Reserve University		
Address	School of Medicine		
City, State, Zip	10900 Euclid Avenue		
Telephone	Cleveland, OH 44106	Fax	216-368-6020
E-Mail	216-844-8565		

Name			
Title			
Organization			
Address			
City, State, Zip			
Telephone			
E-Mail			

Ohio Third Frontier Biomedical Program

Letter of Intent

We propose further development of a device to produce human platelets for clinical use. The **Imagining** phase of this project was funded in part by the 3rd Frontier program, from 2003 to 2009; the requested funds will help carry the project through the **Incubating** phase. The proof-of-concept work already performed will be advanced through the preclinical animal testing phase, to the point at which FDA IND approval can be sought and clinical testing begun by 2014 (the **Demonstrating** phase).

Allogeneic platelets for transfusion and other clinical applications are currently obtained from volunteer donors. While the donors are screened by history and blood tests for a variety of known diseases, unknown and multiple known diseases are not tested for or detected. These platelet units are far from uniform in purity, potency, and effectiveness. Their 5 to 7 day shelf life means that a far larger supply than that actually used needs to be collected. Ex vivo production of platelets for transfusion would address many of these problems. Currently, platelets for transfusion are either isolated from collected whole blood, yielding a platelet concentrate, or are collected using a machine directly from the donor. The total annual US market for platelets for transfusion is currently approximately \$990 million.

Our Specific Aims are to 1) optimize platelet number and quality produced in the modular bioreactor system, and 2) demonstrate that the platelets produced are safe and functional using in vitro and in vivo testing. Dr. Larry Lasky, who will direct device development, is an expert in collection and culture of blood-forming stem cells, and his work in laboratory production of platelets has been internationally recognized. Dr. Alvin Schmaier, who will direct platelet evaluation, is an internationally recognized expert in elucidation of the mechanisms of platelet function and in angiogenesis.

The proposed work will take the platelet production system through application for an IND from the FDA. During years 2 and 3 we will actively seek outside investments to supplement the 3rd Frontier funding and other grant support. The potential market for a device that will produce disease-free, well-controlled and functioning, plentiful platelets for transfusion or other clinical uses will be very large. There are a number of companies that specialize in blood banking supplies and machines, including Baxter, Caridian BCT (formerly Gambro BCT), and Haemonetics that would be a good fit for commercialization and production of the platelet production system. End users for the device and the platelet concentrates produced include large platelet suppliers, notably the American Red Cross, as well as community blood centers and large hospital blood bank/transfusion services and our military. We expect that the device will also be of interest to drug companies as a way to test drugs and therapies regarding possible deleterious or positive effects on thrombopoiesis and platelet function.

We will seek clinical trial funding to begin at or near the end of the 3 year funding requested herein, from agencies including Department of Defense and the NIH, as well as the companies mentioned above and others active in the field. Given the need for the large volume of platelet transfusions given, we expect to collaborate with clinicians caring for malignancy patients. Depending on the state of the art, we expect to also collaborate with those with difficult-to-heal wound infection patients. We expect that initial deployment into blood centers in the US could begin as early as years 5 and 6 of the grant period.

11-549

NDI

NDI Medical

NeuroStim Design and Innovation

December 14, 2010

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

Re: 2011 OTFBP LOI

Dear Sir or Madam;

This letter is to indicate our intent to submit a proposal under the Ohio Third Frontier Biomedical Program for the project titled: Neurostimulation for Pain Relief.

The Lead Applicant, SPR Therapeutics, will direct a collaboration that will develop and commercialize novel technologies and methods that will be applied to create therapeutic products for pain relief. These technologies have the potential to treat numerous painful symptoms arising from orthopedic and neurological conditions.

The collaboration will bring together the talents and services of several Ohio organizations including medical product development and sales companies (NDI Medical, LLC (Cleveland, OH), Checkpoint Surgical (Cleveland OH)), contract manufacturing facilities (Delta Systems (Streetsboro OH)), advanced circuit technologies (Valtronic Technologies (Solon OH)), and world-renowned academic researchers (the FES Center at CASE (Cleveland, OH) and clinicians (MetroHealth Medical Center (Cleveland, OH)).

Our proposal will request approximately \$1 million in grant funds to commercialize our proprietary pain management systems. A one page summary of our proposed project is attached.

Lead Applicant: SPR Therapeutics, LLC.
22292 Millcreek Boulevard, Suite 110,
Cleveland, OH 44122
216-378-9106

Contact person: Maria Bennett, President and CEO
mbennett@sprtherapeutics.com

Sincerely,



Maria Bennett

The Neurostimulation for Pain Relief Program will be directed by the Lead Applicant, SPR Therapeutics, in collaboration with device engineering development, contract manufacturing, academic, and clinical partners to bring to market a pipeline of therapies and technologies to relieve orthopedic and neurological pain.

SPR Therapeutics is the latest company formed by the management team of NDI Medical, LLC, a medical device incubator. SPR Therapeutics is working to commercialize proprietary neurostimulation pain therapies. Neurostimulation is a \$4.6B estimated market segment of the \$220B medical device market that has consistently outperformed other common areas of investment. One of the largest 2012 neurostimulation markets will be pain management, representing ~30%. NeuroInsights Report considers Cleveland "among the neurotechnology regions to watch worldwide" as Northeast Ohio is rated #5 worldwide for neurotech healthcare and #6 for neurodevice companies.

SPR is launching commercialization of its proprietary short-term peripheral nerve stimulation therapy for orthopedic and neurological pain, the Smartpatch System. It is non-narcotic, minimally-invasive, easily deployed and has demonstrated clinical benefit. The next product to be commercialized is a long-term, chronic pain therapy, which utilizes the Smartpatch short-term, trial system, and a fully implantable long-term therapy.

SPR and its collaborators have developed the first generation technology, conducted initial clinical studies, completed independent market studies, filed an FDA 510(k) application for Smartpatch market clearance, obtained FDA IDE approval to conduct a commercialization study for our long-term therapy, and filed patent and trademark applications to supplement our already issued patents.

For the Smartpatch to be commercially successful, we must identify and hire key resources to support product sales and training; develop a pricing strategy based upon reimbursement, cost effectiveness, manufacturing costs and other factors; complete successful manufacturing and product build; identify initial customers within target market segments; and conduct post-market clinical studies to enhance marketing capabilities to various market segments.

While initiating manufacturing and sales activities for the Smartpatch System, the Neurostimulation for Pain Relief Program will also advance the technology and therapy delivery methods through research and development. Our collaboration is already initiating studies to address painful conditions arising from multiple etiologies, and we are working on next generation technologies that will be more easily deployed, provide enhanced functionality, and be highly durable.

Funding through the OTFBP will enable SPR to initiate sales and marketing activities and transfer and begin pilot manufacturing with our Ohio contract manufacturing partner. These activities will result in opportunity for significant employment in Ohio within 3 to 5 years of initiating the project. Further, we will continue to develop a pipeline of new products and indications to address pain arising from numerous orthopedic and neurological conditions.



11-550

ApneiCare, LLC
6185 Huntley Road, Unit B
Columbus, Ohio 43229-1098

December 13, 2010

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

Dear Ohio Department of Development:

Please accept this letter of intent from ApneiCare, LLC for our Fiscal Year 2011 Ohio Third Frontier Biomedical Program proposal.

Lead Applicant: ApneiCare, LLC
Address: 6185 Huntley Road, Unit B
Columbus, Ohio 43229-1098
Telephone: (614) 410-1266
Contact Person: Mr. Craig Pickerill, President
Contact Email: craig@sleepcareinc.com
Project Title: Development and Commercialization of a Relational
Thermorespirometer Spot Vitals Monitor
Estimated Grant Amount: \$1 million
Known Collaborators: OhioHealth and others to be determined

Summary of Proposed Project:

Monitoring spot vitals is an important part of patient management in all healthcare settings and especially in the acute care hospital settings. Spot vitals often include objective *automated* digital collection of temperature, blood pressure, pulse rate, and oxygen saturation and subjective *manual* methods of determining respiratory rate (usually by counting chest movement or listening to lung sounds with a stethoscope), methods which have both been proven to be only intermittent and unreliable. Respiratory rate is a vital indicator of ventilation in the assessment of patients, and is a sensitive early indicator of progressing physiological instability such as Congestive Heart Failure, Sepsis, cardiac and respiratory arrest. Despite its importance there remains a lack of objective and reliable methods of spot collection.

In addition, although early detection of these conditions results in higher survival rates, shorter hospital stays, and improved patient outcomes these warning signs can be overlooked by medical



ApneiCare, LLC
6185 Huntley Road, Unit B
Columbus, Ohio 43229-1098

professionals because vital signs are measured and recorded independent of each other and oftentimes must be manually examined by a medical professional to make an assessment and possible diagnosis.

ApneiCare proposes to continue the development of a Relational Thermo-respirometer Spot Vitals Monitor that will compare the relationship between all vital signs and will examine trends to provide early warning before a critical event. In addition to the vital signs measured by a traditional spot monitoring device, the ApneiCare monitor will use Plethysmography and other methods to objectively measure respiratory rate and amplitude. This allows the respiratory rate to be measured more precisely while also saving time. The device will examine and compare vital signs and provide alerts if additional clinical assessment or medical intervention is necessary. The ApneiCare monitor will be compatible with Spirometry and Capnography instruments for collection of additional clinical data, providing hospitals with a powerful analytical tool for assessing patient conditions and implementing the necessary interventions.

The proposed project aligns with the purpose and goals of the Ohio Third Frontier Biomedical Program.

Sincerely,

Mr. Craig Pickerill,
President

11-551

2011 Biomedical Program Letter of Intent

Lead Applicant's Name: Cleveland Clinic

Contact Person: Wael Barsoum, M.D.

Address: 9500 Euclid Ave., Mail Code A41, Cleveland, OH 44195

Office Phone: 216/444-7515

Fax: 216/445-6255

E-mail: barsouw@ccf.org

Proposed Project Title: *Interactive Visual Health Record*

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

Known Collaborators:

To Be Determined

Summary of proposed project:

The “Interactive Visual Health Record” (iVHR) will focus on the development of an innovative, software-based physician assistance solution. This novel platform will function as a layer above the electronic health record (EHR) to translate standard clinical workflows into accurate, structured documentation that supports physicians in optimizing clinical care and improving patient outcomes. It will enable healthcare providers to achieve appropriate reimbursement, reduce operating expenses, and pursue new revenue opportunities. As a result, iVHR will deliver immediate positive return on investment to hospitals and healthcare providers and enable them to keep pace with evolving meaningful use requirements, quality measures, and payor standards.

iVHR’s core components include:

- **Real-Time Data**
- **Discrete Data Capture**
- **Problem List Validation**
- **Outcomes-Based Predictive Models**
- **Interactive Data Visualization**

The iVHR project team will be led by a team of physician inventors from Cleveland Clinic (the Clinic). The grant funds will be used to support development of the iVHR platform and deployment and validation of pilots at the Clinic for cardiovascular and orthopedic indications.



Dec 14, 2010

FY2011 Ohio Third Frontier Biomedical Program (OTFBP)
Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th floor
Columbus, OH 43215

Sub: Letter of intent by Renovo Neural, Inc. to submit a proposal for FY2011 OTFBP

Lead Applicant: Renovo Neural, Inc.
10000 Cedar Avenue
3rd Floor
Cleveland, OH 44106
Phone: 216-445-4252
Fax: 216-445-2981

Lead Applicant Contact: Satish Medicetty
President
smedicetty@renovoneural.com

Project Title: Three-Dimensional Nanohistology

Funds Requested: 1,000,000

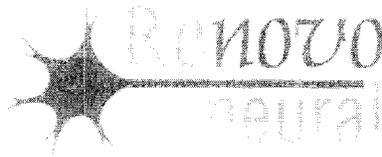
Known collaborators: Cleveland Clinic (Dr. Bruce Trapp, Chairman of Department of Neuroscience, and Dr. Grahame Kidd, Staff in the Department of Neuroscience)
Case Western Reserve University

Project Summary: See page 2

Sincerely,

A handwritten signature in blue ink, appearing to read "Satish Medicetty", with a horizontal line extending to the right.

Satish Medicetty, DVM, PhD, MBA
President
Renovo Neural, Inc.



Project Summary:

Automated 3-dimensional electron microscopy (3D-EM) is a new technology spawned by advances in gigapixel imaging and new SEM instrumentation to support nanotechnology and recently adapted for 3D electron microscopy of biological samples (nanohistology). It is revolutionizing sub-cellular analysis and is currently recognized as a rapid growth area in basic, translational and diagnostic medical sciences. Through collaborative efforts in Cleveland, we have become pioneers in the development and application of this technology. The purpose of this proposal is to obtain funds to commercialize this technology through the Third Frontier funded contract research organization, Renovo Neural Inc (RNI). There is an unmet international market for 3D-EM products, both in preclinical testing and in biomedical research, and we intend to develop NE Ohio as an international center for 3D-EM services and products.

RNI was established by Third Frontier funds to develop and commercialize preclinical assays to test drugs for Multiple Sclerosis (MS). Currently, RNI has commercialized two assays: (a) In vitro high content and high throughput cell-based screening to identify and evaluate novel MS drugs and (b) In vivo efficacy test in a mouse model of demyelination (a characteristic feature of MS). RNI has been successful in creating jobs (currently 9 employees) and revenue by offering its services (assays) to pharmaceutical companies that are developing MS drugs.

This grant will provide the assets and funding to purchase a 3D-EM system and expand our expertise. We will develop and market 3D-EM-based assays in our area of strength - MS research. These new assays will improve and expand RNI's product line for testing MS-related pharmaceuticals. Through collaborations with researchers at the Cleveland Clinic, Case Western Reserve University, and other Ohio Institutions we will develop 3D-EM expertise and products in other disciplines.

Lead Applicant Name: Cleveland Clinic
Maria Siemionow MD, PhD, PI
Applicant's address: 9500 Euclid Ave
Department of Plastic Surgery, desk A-60
Cleveland, OH 44195
216-445-4572
siemiom@ccf.org

Contact person: Agata Matejuk, PhD
9500 Euclid Ave
Department of Plastic Surgery, Desk A60
Cleveland, OH 44195
216-444-4652
madajkm@ccf.org

Proposed project title: Tolerogenic properties of chimeric cells

Estimated grant funds to be requested: \$1 million

Collaborators: Stanton Gerson MD; Tolera Therapeutics, LLC

Project description

Each year, more than 5,000 people awaiting a transplant die in the U.S. because a suitable organ donor cannot be located. Further, nearly 80% of transplant recipients who have received an organ with 1 degree of mismatch will develop Graft Versus Host Disease, which can cause organ failure and death. Even in uncomplicated transplants, chronic administration of immunosuppressive drugs can cost the in excess of \$20,000 per year, and result in chronic co-morbidities that total several times that amount. Primary graft failure is an even more devastating complication of Bone marrow, solid organs and vascularized transplants, since the original donor may be unwilling or unavailable to donate further cells or organ. One of the most effective approaches for inducing tolerance of transplanted organs without immunosuppression is through the establishment of mixed hematopoietic chimerism. The new therapeutic approach and products embodied by the proposal will have direct clinical applicability in the following situations: (i) in organ and CTA transplants to induce transferable tolerance in recipients requiring primary graft replacement with second graft transplanted from unrelated donors; (ii) for induction of donor-specific immune non-responsiveness in recipients of multi-organ transplants from two different unrelated donors; (iii) when a highly selected cell population is preferred, but unavailable.

The market for human chimeric cell technology is the broadly defined immunosuppressants market. The overall market is estimated at over \$10 billion and includes medical market segments such as oncology, autoimmune disease, and transplantation (5). These medical segments are underserved by current therapeutic approaches, which offer broad non-targeted immunosuppressant solutions that often carry significant side-effect risk.

This Program's initial focus will be the transplantation segment, estimated at \$3 billion, and expected to grow to \$4 billion by 2015. The transplant market is a strong global market, for which the greatest opportunity lies in the chronic immune suppression market. In the US, several hundred thousand organ recipients are maintaining their allografts through some degree of chronic immune suppression. The projected global market for de novo solid organ transplants is summarized in the table below.

Table C.1. Global Incidence of Organ Transplants (Kidney, Liver, Heart)

	2005	2006e	2007e	2008e	2009e	2010e	2011e	2012e	CAGR
%Transplant Incidence (number of patients)									
United States	27,609	28,164	29,295	30,500	31,789	33,169	34,654	36,257	4
Europe	16,312	16,860	17,428	18,017	18,627	19,260	19,917	20,598	3
Japan	171	173	175	177	180	183	186	190	2
Rest of World	25,763	25,855	26,146	26,442	26,742	27,046	27,356	27,670	1
Total	69,855	71,052	73,044	75,136	77,338	79,658	82,113	84,715	3

e= Morgan Stanley Research estimates

Source: 2005 actuals from The Organ Procurement and Transplantation Network (US), UK Transplant (UK), The Tran(RoW), Organizacion Nacional de Transplantes (Spain), Centro Nazionale Trapianti (Italy), Agence de la Biomedicine

To achieve the objectives of this project the following tasks have been identified:

1. Optimize in vivo and ex-vivo technique for producing multi-donor chimerism in rats.
2. Characterize the tolerogenic potential of in vivo and ex vivo created multi-chimeric cells.
3. Create human chimeric cells using ex vivo cell fusion techniques.

Task 1 has been underwritten by the US Army through the AFIRM program. We propose to utilize Third Frontier funding to push this technology to the initiation of human clinical studies in conjunction with Dr. Stanton Gerson at the Case Comprehensive Cancer Center and Tolera Therapeutics as the commercial licensee of the technology.



December 14, 2010

Ohio Third Frontier Wright Project Program

Ohio Department of Development

Technology Division

77 South High Street, 25th Floor

Columbus, OH 43215-6130

Re: Letter of Inquiry - Wright Project FY 2011

Please accept this Letter of Inquiry from Cleveland State University (CSU) indicating our intent to submit a proposal to the Third Frontier Commission for an Ohio Third Frontier Biomedical Program, Fiscal Year 2011 (Wright Project) with the requisite information as follows.

Project Title	Recombinant Expression of Bio-active Therapeutic Proteins
Lead Applicant Name	Cleveland State University
Address	2121 Euclid Avenue, SR 353 Cleveland, OH 44115
Phone Number	(216) 687-5580 (College of Sciences and Health Professions)
Contact Person	Sailen Barik, PhD Professor and Director, Center for Gene Regulation in Health and Disease, (216) 523-7326 s.barik@csuohio.edu
Estimated Grant Funds	\$2,000,000 (\$1M TFRD + \$1M WCF)
Known Collaborators	DAPCEL, Inc. http://dapcel.com/

PROJECT DESCRIPTION

This application represents an Academia-Industry Consortium, consisting of faculty members of the Center for Gene Regulation in Health and Diseases (GRHD), an Ohio Center of Excellence at Cleveland State University (CSU), and DAPCEL, Inc., a highly promising new Biotechnology company housed at BioEnterprise, a local business acceleration initiative designed to grow health care companies and commercialize bioscience technologies. The Consortium is dedicated to the common goal of discovery and development of biomedically important molecules and technologies. Substantial extramural grants of the GRHD members and investment by DAPCEL, Inc will provide the matching funds.

The Technology

A major challenge in biotechnology today is how to produce pharmacologically active macromolecules, particularly proteins, in active forms, since heterologous expression generally leads to poor solubility, activity and stability. In this application, we will combine novel biochemical and bioinformatic approaches recently developed and tested by various members of our group. Our proposed research is comprehensive, and will involve the novel gene re-design technology of DAPCEL, Inc for optimal protein expression, combined with post-translation modifications and the use of protein chaperones by the GRHD scientists to generate human and parasitic proteins of pharmacological importance. Results obtained with this funding will form the cornerstone of larger endeavors in the future, leading to commercialization of a potentially wide variety of protein products for Pharmaceutical, and Biotechnology industry.

This project will include GRHD faculty members with active Federal funding and therapeutically-relevant translational research in the following areas:

Name	Bio-active proteins and their relevance
Sailen Barik	Heat shock protein (Hsp): Anti-cancer, anti-parasitic drugs
Valentin Boerner	Chromatin-regulatory proteins: Anti-cancer; gene regulation
Anton A. Komar	Therapeutic proteins for cardiovascular disease (CVD), hemophilia
Bibo Li	Trypanosome telomere complex: Sleeping sickness, aging, cancer
Barsanjit Mazumder	Translational silencing of ribosomal protein, L13a: CVD
Xue-Long Sun	Liposomal thrombomodulin: Anti-thrombotics, heart disease

DAPCEL, Inc. is a research biotechnology company focused on the development of strategies for optimization of enhanced protein production in any desired host organism. To this end, DAPCEL, Inc. utilizes unique approach for gene redesign that takes into account the importance of rare codons for protein folding¹⁻³ and results in high yields of correctly folded and active soluble proteins⁴.

The recent successes of DAPCEL, Inc. in recombinant protein production are reflected in high profile publications utilizing DAPCEL, Inc. thechnology⁴ and its successful partnership with PeproTech, Inc. (<http://www.peprotech.com/content/links.htm>), a world leader in providing highest quality cytokine products (interleukins, chemokines, interferons, defensins, etc.) for biotechnology research.

Completion of this project will allow to perfect the design process developed by DAPCEL, Inc., achieve its full automation by developing a computer software, and accomplish the development of a number of highly active recombinant proteins, including but not limited to Interferon beta-1a and Oct-4 used in the treatment of cancer/multiple sclerosis and for promoting cell self-renewal and cell differentiation, respectively.

References

1. Komar, A.A. (2007) SNPs. Silent but not invisible, *Science*, 315, 466-467.
2. Komar, A.A. (2008) Protein translation rates and protein misfolding: Is there any link? In "Protein Misfolding: New Research" Ed. Frank Columbus, Nova Science Publishers, Inc. NY, pp. 61-80.
3. Komar, A.A. (2009) A pause for thought along the co-translational folding pathway. *Trends Biochem Sci.* 34, 16-24.
4. Skabkin, M.A., Skabkina, O.V., Dhote V., Komar, A.A., Hellen, C.U. and Pestova, T.V. (2010) Activities of Ligatin and MCT-1/DENR in eukaryotic translation initiation and ribosomal recycling. *Genes Dev.* 24, 1787-1801.



11-555

December 14, 2010

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

Subject: 2011 OTFBP LOI

VIA: E-mail to OTFBP2011@development.ohio.gov

To Whom It May Concern:

Please let this letter serve as notice of intent for Huneo to apply for the fiscal year 2011 Ohio Third Frontier Biomedical Program (OTFBP). Below is the information requested in Section 1.3.3 of the Request for Proposal for the OTFBP. The attached project summary provides additional details about our project.

Lead applicant: Huneo

Address: P.O. Box 336, Gates Mills, OH 44040

Telephone: 440-832-0331

Contact: Phil Ryder, Chief Executive Officer

E-mail: phil@huneo.com

Proposed project title: Wireless, integrated acquisition of biophysical data streams for real-time processing, analysis and retrieval

Estimated grant funds to be requested: \$1 million

Potential Collaborator(s): MetroHealth Systems, Cleveland Ohio

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

Sincerely,

Phil Ryder
CEO, Huneo, LLC

Attachment: Project Summary



Huneo

Project Title: Wireless, integrated acquisition of biophysical data streams for real-time processing, analysis and retrieval

2011 Ohio Third Frontier Biomedical Program

Project Summary

HUNEO, LLC is a two year old start-up company focused on delivering integrated systems for capturing, wirelessly transmitting, and storing human biophysical data. Our products include wireless sensor units (of our own design), as well as an entire infrastructure for the storage of data captured, as well as for real-time dissemination of this data to interested health professionals. To date, Huneo's Cleveland office has coordinated all development of our wireless sensor units and biophysical sensors. This office will expand greatly with the implementation of the proposed project. We estimate that within the first year we will employ an additional ten to twenty high level engineers and technicians, with virtually all of the activities related to this project being carried out in Ohio.

Technologies and devices currently being developed by HUNEO have tremendous potential for use in:

- Providing a wireless system for comprehensive and continuous real-time tracking of vital sign data throughout a patient's stay in a medical facility, regardless of where their location in the hospital or clinic
- Diagnosis of Obstructive Sleep Apnea
- Collection of much more extensive cardiac data than is typically gathered in an in-clinic EKG / stress test
- The fusion of time-series data from existing disparate (and often near-obsolete) systems found in a typical medical facility. These devices can range from simple blood-pressure measurement cuffs found on the clinic wall, to existing anesthesia information management systems found in operating rooms within large hospitals.

Huneo's development and commercialization processes are highly collaborative, and involve significant input from major healthcare organizations. For this project we will collaborate extensively with MetroHealth Systems located in Cleveland. For proof of the capabilities of the devices and interfaces that we are developing as a part of this project, the following studies have been suggested by our colleagues from MetroHealth:

1. Collection of waveform data at the central monitor system and then processing the data in real time for decision support (as Sessler - CCF "triple low" and other real time warning applications)
2. Dynamic, real time flow measurements by recording the pressure drop across a resistive element: i.e. in-line filter in a patient breathing circuit or the oxygenator/heat exchanger of the CP Bypass Pump
3. Accelerometer measurement of the chest wall motion produced during manual CPR either in our Operating Rooms or in Simulator training sessions.

The proposed Third Frontier Biomedical project would take the development of our technology to the point of market entry within two years. Development of this technology would occur at the Company's facility in Cleveland, OH. All interaction with the FDA and submittals of 510(k) approval requests would also be managed in this office. Finally, all assembly, and shipping and support for the finished product will also take place in Ohio. Intellectual property protection for key technology developed as a part of this grant will be secured so as to ensure that a lasting competitive advantage would be created for the State of Ohio and Huneo. Significant job creation at the Company's Ohio headquarters and manufacturing facility would occur at the end of the Third Frontier project.

PHOSPLATIN
THERAPEUTICS

Letter of Intent

*Pursuant to the November 1, 2010 Request for Proposals
Ohio Third Frontier Biomedical Program, Fiscal Year 2011
Dated: December 14, 2010*

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

Summary Information:

Prospective Lead Applicant: Phosplatin Therapeutics LLC
1350 Avenue of the Americas, 3rd Floor
New York, NY 10019-4703

Contact: Matthew R. Price
Executive Vice President
T: (646) 380-2441
E: mprice@phosplatin.com

Proposed Project title: Development of Phosphaplatins: A Novel Class of non-DNA
Binding Oncology Therapeutics

Estimated Grant Funds to be requested: \$1,500,000.00
Est. Matching Funds to be committed: \$1,500,000.00

Known Collaborator: – Ohio University, Edison Biotechnology Institute, Athens, OH

Possible Collaborators: – Battelle Memorial Institute, Columbus, OH
(discussions in progress) – Charles River Laboratories International, Inc., Spencerville, OH
– Ricerca Biosciences LLC, Concord, OH

Primary scientific/technical field(s): Biomedical – drug development, therapeutics.

Respectfully submitted,



Matthew R. Price
Executive Vice President
Phosplatin Therapeutics LLC

One-page Summary of the Project:

Phosplatin Therapeutics LLC is pleased to submit this letter of intent (LOI) related to its existing research and development program for phosphaplatins, a new class of anti-cancer agents. Phosphaplatins have been discovered by Dr. Rathindra Bose, Vice President of Research and Dean of the Graduate College at Ohio University, and are the result of over twenty-five years of investigation into the effects of metals on cancer, primarily into the mechanism of action of platinum cancer therapies. By adding to this work the emerging understanding of intracellular genetic signaling pathways, Dr. Bose has been able to design a class of compounds which, according to preliminary results in several human tumor cell lines, are more effective and less toxic than the current standard of care.

Phosplatin Therapeutics was launched in 2010 in order to commercially develop phosphaplatins into a new class of cancer therapeutics, and has entered a license agreement with Ohio University. As part of this agreement, the company has committed to fund research in the Edison Biotechnology Institute at Ohio University, and has in fact already created three jobs in Ohio with its funding within the lab.

Phosplatin Therapeutics is requesting funds to support to the development of this oncology therapeutic, which as of today shows promise in treating a variety of cancer indications. Phosphaplatins have been shown to effectively kill ovarian, testicular, colorectal, and head-and-neck cancers both *in vitro* and *in vivo*. Of particular note, these compounds are also effective towards resistant cancers where other available drugs fail. Existing platinum therapies, though widely used in hospitals around the world, are limited in their application due not only to severe toxicity, but to the resistance which largely results from their mechanism of action: DNA-binding leading to cell death. Phosphaplatins, however, were designed not to bind DNA, and show no measurable sign of such binding. We believe they are for that reason able to avoid stimulating the cells' own repair function, which is one of the primary modes of cellular drug resistance, and thus one of main limitations of platinum drugs for patients. Furthermore, preliminary results show that phosphaplatins exhibit minimal toxicity compared to existing marketed chemotherapeutic agents. Part of this tolerability may be attributed to the compounds' desirable physiochemical properties. They are soluble, exhibit much lower protein-binding than other drugs in the therapeutic category, and are stable in physiological conditions. This class of compounds is designed to, and has demonstrated an ability to, activate a set of genes in the cell membrane that are related to programmed cell death in cancer cells. To our knowledge, there is no single drug on the market that safely exhibits these combined characteristics, and we believe a successful development plan can lead to a paradigm-changing therapeutic of medical and commercial importance.

The forthcoming proposal will outline a development strategy that meets the regulatory requirements for an Investigational New Drug (IND) application with the Food and Drug Administration by the end of project year two. The development plan includes ongoing investigation at Ohio University of the compounds' mechanism of action; comprehensive animal pharmacology, pharmacokinetic, and toxicology studies, to be carried out by Battelle Memorial Institute and/or Charles River Laboratories (Ohio location); and chemistry manufacturing and controls, to be carried out by Ricerca Biosciences.

With Phosplatin Therapeutics' matching financial commitment, and its desire to relocate the company's technology management to a principal office within the Ohio University Innovation Center, the project will create Ohio employment opportunities within the university, the company, and at contract research organizations conducting the necessary testing prior to IND application submission. In addition, the company will develop a clinical plan and explore clinical partners among leading medical centers in Ohio, for its first-in-human trials after the IND. Thus the company's plan will support further long-term employment opportunities during the clinical testing and scale-up manufacturing phases. In addition to the operating funds, capital funds will be proposed for acquisition of laboratory analytical equipment to support further understanding of the compounds' unique mechanism of action, as well as allowing Phosplatin Therapeutics' collaborator, Ohio University, to use the equipment in future applications in the advanced life sciences.

Strategic Technology Enterprises, Inc.

A Subsidiary of STERIS Corporation

December 10, 2010

11-557

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

Dear Ohio Department of Development:

Please accept this letter of intent from Strategic Technology Enterprises, Inc. (STE), a subsidiary of STERIS Corporation, for our Fiscal Year 2011 Ohio Third Frontier Biomedical Program (OTFBP) proposal.

Lead Applicant Name: Strategic Technology Enterprises, Inc.,
A subsidiary of STERIS Corporation

Address: 5960 Heisley Road
Mentor, OH 44060

Telephone: (440) 392-7113

Contact Person: Mr. Lewis I. Schwartz, Vice President, Defense & Aerospace

Contact Email: lew_schwartz@steris.com

Project Title: Vaporized Hydrogen Peroxide (VHP[®]) Medical
Decontamination System

Estimated Grant Amount: \$1,000,000

Known Collaborators: The Cleveland Clinic Foundation

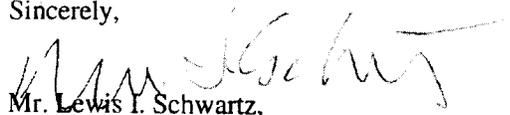
Summary of the Proposed Project:

Recent emerging infectious diseases, including antibiotic resistant strains such as *Clostridium difficile* and Methicillin-resistant *Staphylococcus aureus* (MRSA), represent a challenge to infection control professionals. Frequent, thorough decontamination of medical facilities and patient transport vehicles is essential to slow the spread of infections and minimize cross-contamination. Yet the alarming rate of hospital-acquired infections (HAI) attests that current decontamination methodologies are inadequate.

Strategic Technology Enterprises, Inc. (STE), a subsidiary of STERIS Corporation, is working to adapt STERIS's gaseous decontamination technology—Vaporized Hydrogen Peroxide (VHP[®])—into a decontamination system for the unique challenges of military medical environments. For the FY2011 OTFBP, STE will propose a project that builds upon this VHP[®] decontamination work with the United States military. STE will work closely with the Cleveland Clinic Foundation and other OTFBP project collaborators to perform an evidence-based evaluation of the routine use of VHP[®] decontamination on patient HAI outcomes.

STERIS recognizes the strength of the Ohio biomedical cluster, represented by the world-class institutions and companies throughout the state. The STERIS project aligns with the goals and objectives of the OTFBP and will generate continued technology based economic development for the citizens of Ohio.

Sincerely,


Mr. Lewis I. Schwartz,
Vice President, Defense & Aerospace





Phone: 513-985-1920

Fax: 513-985-0999

www.akebia.com

11-558

Akebia Therapeutics, Inc.

9987 Carver Road

Suite 420

Cincinnati, OH 45242

December 14, 2010

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

To Whom It May Concern:

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

Lead Applicant: Akebia Therapeutics, Inc.

Address: 9987 Carver Rd., Suite 420
Cincinnati, OH 45242

Telephone: 513-985-1934
513-544-8868 (cell)

Contact Person: Kevin Peters, MD
Vice President and Chief Scientific Officer

Email: kpeters@akebia.com

Project Title: Tie2 activators for Severe Sepsis and Septic Shock

Estimated Funding Request: \$1,000,000

Known Collaborators: Charles River
Medpace
Aroz Technologies, LLC

Project Summary:

Severe sepsis places a large and growing burden on the health care system, with an incidence ranging from 50 to 300 cases per 100 000 population and a short-term mortality of 20% to 25%, reaching up to 50% when shock is present. The average cost per case of sepsis has been estimated at \$22,100 with total costs of \$16.7 billion nationally. Unfortunately, treatment of sepsis is still largely dependent on prompt and appropriate antibiotic therapy and diligent supportive care. Thus, more effective therapies for severe sepsis and septic shock represent an enormous unmet medical need.

Akebia Therapeutics, Inc. has developed a small-molecule therapeutic, AKB-9778, that has demonstrated efficacy and minimal side effects in animal models of sepsis. In a cecal ligation, puncture and excision model of sepsis which caused 50 % mortality in vehicle treated animals, AKB-9778 provided complete protection from mortality. Vascular leak is a hallmark of sepsis and is a major contributor to morbidity and mortality. Mechanistically, vascular leak is associated with a dramatic increase in angiopoietin-2, an antagonist of the Tie-2 receptor-like kinase. Blockade of Tie-2 signaling leads to vascular destabilization and results in vascular leak. AKB-9778 overcomes Ang-2-induced blockade and restores Tie-2 signaling by inhibiting protein tyrosine phosphatase β (PTP β), the negative regulator of Tie-2 signaling. AKB-9778 and its analogs are potent and selective inhibitors of PTP β .

Akebia is submitting this Letter of Intent to request funds for part of the research required to carry AKB-9778 through Investigational New Drug (IND) and Phase Ia, as required by the U.S. FDA. These funds will then be matched by money derived from venture capital. Together, they will provide Akebia with the means to complete IND enabling studies and initiate a Phase 1 clinical study with AKB-9778 within the next year and a half.

In the past three years Akebia has grown from four employees to seventeen, and has collaborated with many Ohio biomedical companies and institutions. Akebia will continue those practices with the AKB-9778 project by supporting more Ohio employment, working with Charles River in Spencerville, Medpace and Aroz Technologies in Cincinnati, and other Ohio companies.

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

Sincerely,



Kevin Peters, MD

Vice President and Chief Scientific Officer

11-559

**Ohio Third Frontier Biomedical Program
Letter of Intent
December 14th 2010, 2:00PM**

The Ohio Department of Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43215
OTFBP2011@development.ohio.gov

Lead Applicant:

The Ohio State University
Office of Sponsored Programs
1960 Kenny Road, Columbus, OH 43210
Contact: Jill E. Richards, DVM, CRA, Senior Sponsored Program Officer
richards.832@osu.edu
614-292-1475

Principal Investigator and Contact Person:

Alicia L Bertone, DVM, PhD, ACVS
Comparative Cell Therapy Research
College of Medicine and Veterinary Medicine
The Ohio State University
Bertone.1@osu.edu
614-292-7449
Role: Cell Therapy Research and Development

Project Title:

Commercialization of Cell Regenerative Technology for Orthopaedic and Veterinary Applications

Funds Request:

\$1M OTFRDF

Collaborators:

OSU

Wright Center for Innovation in Biomedical Imaging
College of Medicine
The Ohio State University
2050 Kenny Road
Columbus, OH 43221

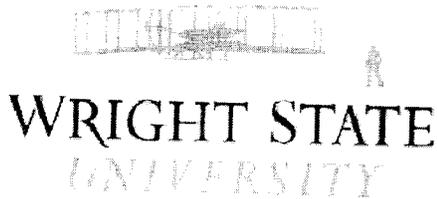
Center for Entrepreneurship
Fisher College of Business
The Ohio State University
256 Fisher Hall
2100 Neil Avenue
Columbus, OH 43210

For-Profit Business Partners

Biodontos Cell, LLC
Neuracrest, LLC
Dublin, Ohio

The goal of this proposal is to immediately commercialize regenerative cartilage cell-based therapies in veterinary medicine to facilitate rapid commercialization to humans. Osteoarthritis is a common degenerative cartilage condition of joints, affecting over 20 million Americans, costing the U.S. economy nearly \$125 billion per year; it also affects 1/3 of 1.8 million horses [an estimated \$3.6 billion market] and \$11 million dogs [an estimated \$14 M-20M market]. Current therapies, including surgery, have unacceptable complication rates or limited effectiveness. Regenerative cell technology has proven commercial success for cartilage repair in humans internationally [SewonCellonech, Co., Ltd, RMS Chondron™] and in veterinary medicine for use in tendon repair [VetStem, VetCell, CelaVet]. We propose to capitalize on the uniqueness at The Ohio State University College of Veterinary Medicine, OSU Medical Center Orthopaedics, and Wrights Center of Innovation in Biomedical Imaging to immediately utilize a GMP cell processing center and enter this market offering cell-therapy approaches to directly patch injured cartilage and deliver stem cells/biologics containing healing proteins to joints via injection. Our program will uniquely capitalize on existing corporate and Third Frontier investments, including 1) GMP infrastructure for biomedical imaging, 2) an explored scientific and business model in animal regenerative medicine for research and veterinary applications, 3) a robust medical, research and business community for intellectual property (IP) development and human clinical trial application, and 4) Ohio Board of Regents investment in business, academic, and continuing medical education. OSU will offer cell services, facility access, and collaborative research to commercial partners and end user clinical customers, first in animals and then humans. OSU can provide the scientific, medical, and entrepreneurial leadership to grow this business and create intellectual assets to establish spin-off companies for sustainable growth. Our founding Ohio for-profit commercialization partner [Biodontos Cell, Inc./Neuracrest, Inc.] will contribute funds to support this business and serve as the first platinum customer for the growth and development of their stem cell business in bone and joint repair.

The Comparative Orthopaedic Research focus at OSU is a leader in the use of cells, including genetically engineered cells, for bone and cartilage regeneration for medical application. The result is proven efficacy for bone regeneration using engineered bone-forming cells, including in clinical trials in animals, and early efficacy for cartilage restoration using an equine model and dynamic contrast Magnetic Resonance Imaging in a collaboration between the Wrights Innovation Center for Biomedical Imaging and the College of Veterinary Medicine. The OSU location of this project capitalizes on the unique central resource of a comprehensive medical, dental, and veterinary Health Sciences Center and the Ohio Third Frontier project at the Wrights Center for Innovation in Biomedical Imaging. Net revenue is anticipated within year 1 from research (preclinical) and veterinary customers. With GMP certification (Yr2) exponential growth in net revenue is anticipated as new commercial entities spin off for human applications due to the immediate gap filled by proposed center that meets regulatory standards for commercialization of cellular products for use in joints. The proposed program will combine assets of commercial partners, the State of Ohio and a premier state academic institution (OSU) to provide cells for research and clinical patients. It is anticipated that at least 12 new jobs for this business, 40 new jobs at Biodontos Cell, Inc. and new end-user companies, and greater than 100 new jobs state-wide in other commercial partners will be generated in less than 5 years. OSU will perform research and generate intellectual assets, serve as the initial medical site for application in people, and provide training (education) for practitioners and business students. The impact of this facility is a high return on investment (\$1M for 100 jobs) using Ohio resources with a high likelihood of serving as a sustainable magnet for jobs in the State of Ohio.



11-560

Dayton, Ohio 45435
(937) 775-2425
Fax: (937) 775-3781
E-mail: marianne.shreck@wright.edu
14 December 2010

Lead Applicant: Wright State University (WSU)
3640 Colonel Glenn Highway
Dayton, OH 45435-0001

Contact Name: Elliott Brown, Ph.D.
elliott.brown@wright.edu
937-775-4903

Title: THz-Radar-Guided Prosthetic Fitting
Estimated grant funds requested: \$1,000,000 over two years

Known Collaborators: Optimus Prosthetics, Inc (Dayton, OH), Mr. Scott Schall

Executive Summary:

The goal of this project will be to advance the state-of-the-art in prosthetic technology for the Orthopedic Medical Industry. The ultimate goal of prosthetic device designers is to precisely replicate the construction, function and feel of a natural limb. The interface design — uniting together device with residual limb — plays an integral role in that ability. Experts and prosthetic users alike agree that the functionality of the prosthesis means little if it does not seamlessly attach to the body. The interface design process begins with obtaining a model of the residual limb; it is desirable to obtain a model of the limb under *weighted* conditions to mimic weight-bearing on the prosthesis. Obtaining a digital model of the residual limb under weighted conditions has never been accomplished. Current methods of obtaining a model of the limb require casting or mechanical measurements that are time consuming and subject to dimensional error.

Independent of prosthetics, THz sensor technology has evolved that provides unique biomedical capabilities. Our proposal is to develop and commercialize a hand-held THz impulse radar to acquire the weighted residual limb surface data to enhance the process of designing the prosthetic interface. The THz radar brings four key benefits to the prosthetics application: (1) precise range resolution based on the short pulses (~5 ps) it transmits, (2) good penetration of plastics, cloths, and various ceramics used in pre-weighting the residual limb in the prosthetic interface design process, (3) very exact reflection at the interface between these materials and the human epidermis (based on large hydration levels in physiological skin) and (4) complete lack of ionization or other damage to human tissue of all sorts. Furthermore, through research carried out by the PI (Brown), the THz impulse transmitter and receiver can be compacted into a small transceiver “head” unit that can be scanned manually around the human subject of interest, similar to the “wand” in ultrasonic imaging systems. Strong leverage against the high-frequency electronics, photonics, and fiber-optics industries come to bear in this approach.

Our proposal entails further research and development of the THz impulse radar and demonstrative “proof-of-concept” on human phantoms at the WSU THz Sensors Laboratory (created through the Ohio Research Scholars Program). This R&D will be guided by the commercial partner, Optimus Prosthetics, Inc., located in Dayton conveniently close to WSU. After eight months of tailoring the radar for this specific application, a prototype will be transferred to the Optimus Prosthetics facility for demonstration on human subjects and for commercialization assessment during the second eight-month period. Various issues will be addressed, such as packaging, user interface, compliance with FDA requirements, etc. Then during the last eight months of the project, an optimized brassboard system will be constructed at WSU and transferred to Optimus Prosthetics for the mandatory FDA-approval process, tentatively scheduled to start upon completion of the 3rd-Frontier Project.

Ohio Third Frontier Letter of Intent

December 14, 2010

The Ohio Department of Economic Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43125

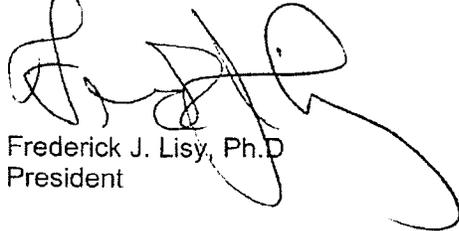
Dear Ohio Department of Economic Development:

Please accept this proposal and following summary for Orbital Research Inc. intent to submit an Ohio Third Frontier Biomedical Program ("OTFFBP2011").

Lead applicant:	Orbital Research, Inc.
Address:	4415 Euclid Avenue, Suite 500, Cleveland, OH 44103-3757
Phone number:	(216) 649-0399
Contact Person:	Fred Lisy
Email:	lisy@orbitalresearch.com
Proposed Title:	Versatile Vital Sign Monitoring System
Est. Grant funds:	\$1,000,000
Known collaborators:	Body Media Nottingham-Spirk Design Associates

We are looking forward to taking the next steps and a one page summary follows within this document.

Sincerely,
Orbital Research Inc.



Frederick J. Lisy, Ph.D
President

Project Summary

Orbital Research in collaboration with Nottingham Spirk, BodyMedia, and our Ohio based manufacturer and clinical testing partners will design, develop, test and commercialize a third generation, state-of-the-art disposable physiological assessment system. The components of this non-invasive monitoring system will be manufactured in Ohio.

About Orbital Research: Orbital Research specializes in two core technologies: Advanced Controls and MEMS (Micro-Electro-Mechanical Systems). Since our inception in 1991, Orbital Research has developed a strong foundation composed of intellectual assets, expertise/know-how and resources around these two core technologies. We have capitalized on these assets to become a fast growing company providing custom solutions across multiple application areas in consumer, commercial, medical and military markets.

About BodyMedia: Founded in 1999, BodyMedia, Inc. is the pioneer in developing wearable body monitoring systems designed to help people lose weight, improve performance, and live a healthier lifestyle. Our patented multi-sensor technology has been adapted for a variety of markets, enabling us to deliver validated products that monitor calorie expenditure, amount of physical activity, number of steps taken, and sleep efficiency. No other comfortable, convenient, continuous body-monitoring product can measure physical activity and calories burned with BodyMedia's greater-than-90% accuracy.

About Nottingham-Spirk: Nottingham-Spirk Design Associates develops user-desired products to become market leaders for clients to gain a competitive advantage to grow sales. The company is responsible for inventing and commercializing over 570 patents within the last 30 years which has generated over \$30 billion in sales for medical, consumer, and industrial clients.



Project Summary:

Intelligent Brain Monitor for the ICU

The overall goal of this program is **to develop and market our new NeuroFAST brain monitor dedicated to Intensive Care Units (ICUs)**. The NeuroFAST is 2-channel state-of-the-art electroencephalographic (EEG) acquisition and processing device for real-time seizure detection and sedation monitoring . Particularly simple to use, it can be deployed in the ICU by any nurse or physician with no prior expertise in Neurology. The device displays at all time the patient status, and output alerts in case of detected neurologic abnormalities.

The challenges that ICU patients and critical care physicians routinely face are very serious and multifaceted. Across different ICUs, up to 40% of these patients were reported to die despite intensive care medicine. Recent study in 3077 critically ill patients evaluated the causes of death in the ICU and independent risk factors for death were identified. *Interestingly, neurologic failure increased the risk of death most significantly, even more so than the cardiovascular failure.* Neurological problems are very common among critically ill patients. A third of ICU admissions have a neurological complication detrimental to outcome, which double both the length of stay in hospital and the likelihood of death.

Seizures are among the most common neurological complications in the ICU (28.1%) and can severely and irreversible damage the brain if not timely detected and treated. The sedation is another significant problem in the ICU since critical illness requires ventilation which is not possible without sedation. Due to the lack of means to directly assess level of sedation, patients are typically overdosed. This leads to prolonged mechanical ventilation (≥ 96 hrs), which numbered to about 300,000 cases in 2003 and \$16 billion in hospital costs annually, while its volume is projected to more than double by year 2020. Over-sedation further leads to a failure to awaken the patient for routine neurological assessments, which in turn contributes to a delayed detection of neurological injury.

NeuroWave Systems Inc. has worked diligently in bringing to market new technologies and devices in brain monitoring. In particular, NeuroWave has received in 2010 the CE clearance to market its Anesthesia/Sedation Brain Monitor in European countries. NeuroWave has recently signed a distribution agreement with CareFusion, a leading global distributor of medical devices, and has started selling the NeuroSENSE in Europe. In addition, NeuroWave has also developed a real-time Seizure Monitor (supported by grants from the US Army and the NIH). Finally, we have recently received the 510k FDA-clearance to market a 2-channel EEG monitor in the US, that incorporates advanced algorithms for superior quality of acquired EEG recordings to enable their automated interpretation.

The Ohio Third Frontier Biomedical Program will help NeuroWave to leverage its existing products and technology, and bring them together into a single innovative device for the European market, which will fulfill a gapping clinical need for timely detecting neurologic complications in the ICU and their timely treatment by providing a unique decision support tool to ICU staff.

About NeuroWave:

NeuroWave Systems Inc.'s mission is to develop, manufacture, and market monitoring products using advanced signal processing of brain waves (electroencephalogram - EEG) and other biosignals for Neurology, Anesthesia, Critical Care and Emergency Medicine, in order to improve patient outcome and quality of life.

11-563

Lead Applicant Name: Maria Siemionow MD, PhD

Applicant's address: 9500 Euclid Ave
Department of Plastic Surgery, desk A-60
Cleveland, OH 44195
216-445-4572
siemiom@ccf.org

Contact person: Maria Madajka, PhD
9500 Euclid Ave
Department of Plastic Surgery
Cleveland, OH 44195
216-444-4652
madajkm@ccf.org

Proposed project title: Restoration of Peripheral Nerves with Epineural Sheath and Bone Marrow Stromal Cells (BMSC) therapy

Estimated grant funds to be requested: \$ 1 million

Collaborators: Arnold I Caplan, Ph.D.

Summary of the Proposed Project

Restoration of Peripheral Nerves with Epineural Sheath and Bone Marrow Stromal Cells (BMSC) therapy

Peripheral nerve injury can result in a significant burden for the patient, family and medical community. Majority of cases are the result of car accidents, home/work accidents, cancer or genetic defects and require over 50,000 peripheral nerve repair procedures/year. The annual overall cost of treatment for these patients exceeds \$7 billion in the USA. High cost and long post-operative recovery demand the development of new techniques and therapies for optimal nerve regeneration.

Nerve repair requires neuron growth, extension of new axons across the damaged area and fusion with the distal nerve segment. Currently several methods are used including cable nerve grafts, vein grafts, and conduits from biodegradable polymers. Their success rate is limited to post-operative complications such as sensory loss, scarring and painful neuroma formation, but most importantly, the grafts often fail entirely when the nerve damage exceeds 4cm. Limited efficacy requires novel approaches.

We propose to use a surgical approach with the use of a decellularized nerve sheath, harvested from cadaver donors, together with a bone marrow stem cell therapy as a new protocol for the treatment of peripheral nerve damage. Our proposal will lead to the development of the method which is low cost, easily accessible, not rejected by the body, promotes nerve growth, and eliminates scar tissue formation.

The project will also create the quantitative and qualitative evaluation of factors released in vitro by epineural sheath and BMSC in order to generate the optimal media conditions which will enhance the therapeutic results. The priority for us will be to measure the concentrations of NGF, VEGF due to their known neurotrophic activity. This step will be performed using BMSC cultures during different time points. Quantitative data will serve later as a template to produce the optimally enriched media used further for epineural sheath incubation. Such approach can significantly enhance the regenerative potential of the epineurial sleeve construct and reduce the time of nerve regeneration. Additionally, the creation of enriched media for epineural sheath might be a good alternative in the future to serve as supportive medium for sheath storage. Due to its content created by us medium will maintain and enhance the regenerative potential of epineurium and might be useful in case of patients requiring multiple surgeries.

Our proposal will contribute significantly to the development of new therapies for the treatment of peripheral nerve damage by lowering the risk of immunological rejection, cost of treatment, and easy accessibility of required materials. In partnership with an emerging commercial partner, we intend to make our first product available based on this technology within 24 months of commencement.

11-564

Sparton Medical Systems
22740 Lunn Road
Strongsville, OH 44149



Ohio Third Frontier Letter of Intent

December 14, 2010

The Ohio Department of Economic Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43125

Dear Ohio Department of Economic Development:

Please accept this proposal and following summary for Sparton Medical System's intent to submit an Ohio Third Frontier Biomedical Program ("OTFBP2011").

Lead applicant:	Sparton Medical Systems, Inc.
Address:	22740 Lunn Road Strongsville, OH 44149
Phone number:	440.878.4630
Contact Person:	Kevin Webb
Email:	kwebb@sparton.com
Proposed Title:	Non Invasive Continuous Hemodynamic Monitoring
Est. Grant funds:	\$1,000,000
Known collaborators:	University Hospitals Case Medical Center Nottingham-Spirk Design Associates

We are looking forward to taking the next steps and a one page summary follows within this document.

With best regards,

A handwritten signature in black ink, appearing to read "Duane K. Stierhoff".

Duane K. Stierhoff
VP/General Manager



Project Summary

Continuous BP monitoring of critical care patients requires the invasive placement of an intra-arterial catheter. However, the placement of an intra-arterial catheter may lead to serious complications such as the formation of a hematoma, arterial thrombosis, necrosis, vessel perforation and infection. Currently the Centers for Medicare & Medicaid Services (CMS) have stopped paying hospitals for catheter related blood stream infections (CRBSI). A single incident of CRBSI can cost as much as \$56,000 to treat, once the cost of pharmacy charges, catheter changes, lab tests and an additional hospital stay in the ICU are totaled up. Hence, the ability to non-invasively, yet accurately measure BP and arterial waveforms for clinical applications is an unmet clinical need which can minimize patient distress, reduce the risk of life-threatening complications and infections, and result in huge savings to the healthcare system.

In collaboration with University Hospitals Case Medical Center (UH-CMC), Case Western Reserve University (CWRU), Nottingham-Spirk, and Sparton Medical Systems are proposing to perform the commercial development of groundbreaking Navy technology which adapts laser Doppler vibrometer (LDV) interferometry technology to measure the pulsatile velocity waveform of skin in proximity to an artery, and converts it into a high fidelity representation of the continuous blood pressure waveform of the underlying artery. The system comprises of a disposable optical fiber connecting patch and a reusable laser source. It is completely non-invasive and multifunctional and can be used for continuous monitoring of critical care patients without the risk for infections or other costly complications. Using an off the shelf prototype, data sets for waveform calibration have been collected from more than 100 human subjects who underwent cardiac catheterization, demonstrating proof of concept. In this current proposal, the collaboration between Sparton Medical Systems, Nottingham-Spirk, UH-CMC and CWRU seeks an investment to build upon this existing data and secure 510k clearance within the project period. Nottingham-Spirk will be responsible for designing the optical interface between the patient and the laser source as well as the monitor and software interface between the user and the data. Sparton Medical will use this design input to execute the necessary product verification, process validation, and manufacturing release within strict cGMP regulations. UH-CMC and CWRU will carry out the preclinical and clinical testing required to supplement the data for FDA submission as well as for validation of the device.

About Sparton Medical: Located in business and family friendly Strongsville, Ohio and a former recipient of the Third Frontier Initiative for job growth, Sparton Medical Systems, Inc. is an FDA registered and ISO 13485 certified contract design, development, and manufacturing company specialized in launching and delivering "first-of-kind" medical products globally.

About University Hospitals Case Medical Center: University Hospitals Case Medical Center is a tertiary medical center specializing in adult and pediatric medical and surgical care. Located in the heart of Cleveland's University Circle on a beautiful and accessible 35-acre campus, University Hospitals Case Medical Center includes three major medical centers: UH Ireland Cancer Center, UH MacDonald Women's Hospital and UH Rainbow Babies & Children's Hospital.

About Nottingham-Spirk: Nottingham-Spirk Design Associates develops user-desired products to become market leaders for clients in gaining a competitive advantage and grow sales. The company is responsible for inventing and commercializing over 550 patents within the last 30 years which has generated over \$30 billion in sales for medical, consumer, and industrial clients.

All together, the collaborator's goal is to successfully launch this product by using Ohio's talent.

December 14, 2010

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

Subject: 2011 OTFBP LOI

Dear Madam or Sir:

Thank you for the opportunity to submit this Letter of Intent from NanoLogix, Inc. for our 2011 Ohio Third Frontier Biomedical Program (OTFBP) proposal. We are pleased to provide the following, requested information:

- Lead Applicant Name: NanoLogix, Inc.
- Address: 843 North Main St
Hubbard, Ohio 44425
- Phone Number: 330-534-0800
- Contact Person: Bret Barnhizer, President and CEO
- Contact E-mail: bbarnhizer@me.com
- Project Title: Commercialization of Rapid Diagnostic Kits
Against Bacterial Pathogens
- Estimated Grant Amount: \$1,000,000
- Planned Collaborators: Battelle, Columbus, OH; others TBD
- Summary of Proposed Project:

Rapid clinical diagnosis is a critical element for treatment of infectious diseases. Currently, diagnosis of an infected patient may take 48 to 72 hours, which for some pathogens may be beyond the time for effective therapeutic treatment. A rapid diagnostic kit capable of identifying bacterial pathogens within 6 hours or less is needed to ensure that proper, specific treatment is quickly administered to infected patients. This type of early detection of infection would not only be useful in the clinical setting, but also applicable for Homeland Security and the Department of Defense following a malicious release.

Current methods of detection involve traditional culturing of the bacterial pathogens that can take days to propagate, identify, and quantitate, leading to subsequent treatment strategy. Although there are methods available for rapid detection, such as polymerase chain reaction (PCR) assays, additional tests and specialized equipment are required to complement the PCR results and provide diagnosis

NanoLogix has two diagnostic kits, BioNanoPore (BNP) and BioNanoFilter (BNF), that address the need for rapid detection and confirmation of pathogenic organisms without having to rely on special equipment or facilities to perform the work. NanoLogix has demonstrated the ability to identify and quantitate pathogenic organisms such as *Escherichia coli* and *Bacillus anthracis* within 5 to 6 hours compared to normal culturing methods of 18 to 24 hours. Additionally, NanoLogix is working with the University of Texas Health Science Center in an ongoing clinical trial to study the speed and accuracy of NanoLogix technology. The trial is designed to compare NanoLogix technology to current methods in use for detection and identification of Group B Streptococcus (GBS) in pregnant women. Initial results obtained last spring at UTHSC-Houston show the technology identifies GBS in 2 to 6 hours. This is 8 to 24 times faster than the conventional methods of PCR and traditional Petri culturing, either of which can take 48 hours or more.

The work funded by OTFBP would further develop and test the speed and accuracy of BNP and BNF technologies for an array of pathogenic organisms. The data would be used for submission filings at regulatory agencies for validation and approval in clinical settings. NanoLogix would be to capture multiple markets for rapid testing once third party validations are complete. The market for Group B Strep in pregnancies alone is roughly \$150 million in the US and significantly more internationally. Such business

would lead to expansion and job creation within Ohio. All of the domestic market would be served from Ohio, with licensing internationally and revenue to the company in Ohio from that segment.

Sincerely,

Bret Barnhizer

President and CEO

NanoLogix, Inc.

Ohio Third Frontier Letter of Intent

December 14, 2010

The Ohio Department of Economic Development
Technology and Innovation Division
77 South High Street, 25th Floor
Columbus, OH 43125

Dear Ohio Department of Economic Development:

Please accept this proposal and following summary for Orbital Research Inc. intent to submit an Ohio Third Frontier Biomedical Program ("OTFFBP2011").

Lead applicant:	Orbital Research, Inc.
Address:	4415 Euclid Avenue, Suite 500, Cleveland, OH 44103-3757
Phone number:	(216) 649-0399
Contact Person:	Fred Lisy
Email:	lisy@orbitalresearch.com
Proposed Title:	NONA – Non-Invasive Observation of Natal Activity
Est. Grant funds:	\$400,000
Known collaborators:	MindChild Medical Terrazign IFW Consulting

We are looking forward to taking the next steps and a one page summary follows within this document.

Sincerely,
Orbital Research Inc.



Frederick J. Lisy, Ph.D
President

Project Summary

Orbital Research in collaboration with MindChild Medical, Terrazign, and IFW Consulting will design, test and manufacture, NONA after the Roman god of pregnancy, this innovative fetal ECG (FECG) monitoring system which will mitigate the risk to the child during pregnancy and childbirth by non-invasively identifying signs of cardiac irregularity. The current non-invasive fetal monitoring equipment uses trans-abdominal Doppler ultrasound which is unreliable and subject to frequent signal loss due to maternal or fetal movement. The invasive alternative system (scalp-electrode) poses a health risk and provides limited information. The fetal scalp-electrode (current gold standard) is a problematic technology, because it can only be used in a very limited clinical scenario when a patient is in labor, has ruptured amniotic membranes and has a dilated cervix. Therefore, the fetal scalp-electrode cannot be used for monitoring of the vast majority of pregnant and laboring patients. Since the electrode is screwed into the fetal scalp, this invasive fetal ECG monitoring system has risks, as rare cases of fetal scalp abscess have been reported after its use.

The proposed non-invasive fetal monitor will reliably acquire fetal ECG signals, and identify characteristic ECG patterns that predict impending fetal injury caused by inflammatory, hypoxic, or ischemic insults. Analysis of fetal ECG entropy (Society of Maternal-Fetal Medicine, abstract 2008) distinguished intrapartum fever better and earlier than beat-to-beat variability, and therefore we are optimistic that similar analyses made possible the the non-invasive NONA system device will provide relevant clinical information that will allow clinicians to predict intrapartum fever, and move toward delivery before chorioamnionitis develops. Chorioamnionitis is associated with a nine-fold risk of cerebral palsy.our Ohio based manufacturer and clinical testing partners will design, develop, test and commercialize a third generation, state-of-the-art disposable physiological assessment system. The components of this non-invasive monitoring system will be manufactured in Ohio.

About Orbital Research: Orbital Research specializes in two core technologies: Advanced Controls and MEMS (Micro-Electro-Mechanical Systems). Since our inception in 1991, Orbital Research has developed a strong foundation composed of intellectual assets, expertise/know-how and resources around these two core technologies. We have capitalized on these assets to become a fast growing company providing custom solutions across multiple application areas in consumer, commercial, medical and military markets.

11-567



Thomas Neenan
Vice President, Business Development
7100 Euclid Ave.
Cleveland, OH 44103
216.658.4101 Main
216.658.4102 Fax
781-266-7297 Mobile
e-mail: thomas.neenan@proxybiomedical.com

December 14, 2010

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

Dear Sir/Madam,

Proxy Biomedical is pleased to submit this Letter of Intent pursuant to the 2011 Ohio Third Frontier Biomedical Program RFP. The title of our proposal is:

“The Development and Commercialization of a Novel Biomaterials Therapy for Stress Urinary Incontinence”

Lead Applicants:

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

Firouz Daneshgari M.D. F.A.C.S.
Lester Persky Professor & Chair,
Department of Urology,
University Hospitals, Case Medical Ctr.
11100 Euclid Ave Suite 4554
Cleveland, OH 44106
Tel: 216-844-5504

Collaborators:

Cleveland Clinic

Proxy Biomedical will request \$1M through the FY11 OTFBP.

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 Gingras", with a long, sweeping horizontal line extending to the right.

Peter Gingras
President & CEO



The Development and Commercialization of a Novel Biomaterials Therapy for Stress Urinary Incontinence.

Our proposal seeks to commercialize a novel therapeutic approach to urinary incontinence in women. Proxy Biomedical, a leader in the development of surgical products for the women's health market will manufacture and commercialize the therapy, based upon technology developed by the Cleveland Clinic. University Hospitals, Case Medical Center, a leader in health care services will provide pre-clinical and clinical support for the therapy. Together we believe that our groups will bring a significant new product to this growing market that will combine minimally invasive surgery, cutting edge regenerative medicine and the promise of optimal outcomes for a condition with significant unmet medical need.

Urinary incontinence is one of the most prevalent conditions of the lower urinary tract, affecting approximately 40% of women in the United States. Stress urinary incontinence (herein abbreviated SUI) accounts for a large portion of these women. SUI is the loss of small amounts of urine associated with movements, such as coughing, sneezing, laughing, and exercise that cause increased pressure on the bladder based on increased intra-abdominal pressure. It is generally accepted that that deficient or weakened pubo-urethral ligament (or PUL), with attachments between the ventral surface of the urethra and the lower pubic bone leads to urethral mobility and SUI or mixed urinary incontinence in women. Surgical treatments for SUI have led to the development of mid-urethral slings, pioneered by the transvaginal tape sling procedure. This procedure has enjoyed worldwide popularity with excellent long term efficacy. It is estimated that over one million sling procedures have been performed worldwide, with approximately 160,000 surgical procedures being performed annually alone in the United States. Proxy Biomedical, as a producer of surgical meshes, is a significant player in the field through relationships with large multi-nationals in the woman's health field. However, the sling procedure is not without morbidity, and a more simplified procedure with the potential to reduce morbidity and pain for the patient would be desirable.

An attractive approach to SUI is to introduce a bulking agent into the vicinity of the PUL that serves to strengthen and maintain positional stability. Bulking agents such as autologous fat, silicone beads, collagen, carbon particles, and polytetrafluoroethylene (Teflon®) paste have all been used experimentally, with mixed degrees of success. However, none have proven effective over time and have been associated with side-effects. The ideal material should be non-immunologic, biocompatible, and hypoallergenic. It should retain its bulking characteristics for a prolonged interval and not biodegrade or migrate. Additionally, it should be easy to prepare and implant, ideally using minimally invasive surgical techniques. The most common complications are pain during injection and transient urinary retention, and voiding dysfunction after implantation. Our therapeutic approach addresses many of the deficits of current approaches. Additionally, Proxy Biomedical brings a deep understanding of, and experience in, this market and will seek to commercialize this opportunity through continued development and regulatory efforts, leading to US approval in 2-3 years. Our likely commercialization strategy would be to partner with a large player in the woman's health market (Boston Scientific etc.) or with a conventional large pharmaceutical company with a strong interest in regenerative medicine (Pfizer, GSK etc).



Letter Of Intent for FY 2011 Ohio Third Frontier Biomedical Program

Lead Applicant (prospective): Center for Innovative Food Technology (CIFT)
Street Address & Telephone: 5555 Airport Hwy, Ste 100, Toledo OH 43615; 419.535.6000
Contact Name & Title: Stephanie A. Smith, Ph.D., CIFT Food Scientist
Contact Telephone & E-mail : 419.708.5647; ssmith@eisc.org
Project Title (proposed): Validation and Commercialization of a Premium, Standardized, Isoflavone-Rich, Phytosterol-Rich, Organic, Ohio-Grown, Red Clover Ingredient for Nutraceutical and Other Products
Grant Funds (estimated): \$370,000
Known Collaborators Graminex, LLC
Corporate Office: 95 Midland Rd., Saginaw, MI 48638
Manufacturing & R&D: 2-300 Road C, Deshler, OH 43516

Proposed Project Summary

Phytosterols, also called plant sterols, are plant-derived compounds similar in structure and function to cholesterol that inhibit the intestinal absorption of cholesterol. Daily consumption of foods enriched with at least 0.8g of phytosterols has been shown to lower serum LDL-cholesterol and reduce the risk of coronary heart disease prompting the U.S. Food and Drug Administration (FDA) to designate foods containing plant sterols eligible to make an FDA-approved health claim (21 CFR 101.83). Isoflavones are compounds with estrogenic activity that have shown potential health benefits for age-related and hormone-dependent diseases. Consequently, ingredients containing high concentrations of phytosterols and isoflavones command a premium price. While many plant species contain isoflavones, including soybean and clover, the predominating chemical forms and amounts differ.

Graminex has identified certain red clover varieties rich in phytosterols with favorable isoflavone profiles that are well-suited to be grown organically in Ohio. Using its innovative, proprietary cultivation-harvesting-drying process, Graminex has developed a red clover ingredient superior to any currently available, the bulk of which is now sourced from China. Graminex' unique process is less energy-intensive than similar drying operations and is gentle on the plant material allowing maximum retention of the phytosterol and isoflavone compounds. Graminex is already a successful manufacturer of a non-solvent flower pollen extract for the global market. The company is developing a premium, standardized, phytosterol-and-isoflavone-rich, organic, red clover extract for the food and beverage, dietary supplement, and cosmetics sectors to meet the demands and requirements of the domestic and international markets. Graminex is expanding its operations in Deshler Ohio to accommodate the expected market demand for a premium, standardized red clover product. The technical challenges to be addressed in the proposed study are in optimizing the process once the construction is complete and developing analytical methods to be validated by international standard-setting bodies, such as AOAC International and USP. The red clover ingredient will be grown and processed exclusively in northwestern Ohio.

11-569

 | USB[®]
Products

26111 Miles Road | Cleveland, OH 44128
Phone: 800-321-9322 | Fax: 216-464-5075

Lead Applicant:

Affymetrix

USB Molecular Biology Reagents and Biochemicals

26111 Miles Road

Cleveland, Ohio 44128

Phone: +1-216-765-5000

Fax: +1-216-464-5075

Contact: Matthew Lawes Ph.D.

Matt_Lawes@affymetrix.com

216-378-5930

Project Title:

Radical Innovation in Transfection Products for Medical Research and Genetic Therapeutics.

Estimated Grant Funds: \$640K over 2 years

Collaborators:

Techulon

Joshua Bryson Ph.D.

joshua.bryson@techulon.com

www.techulon.com

2200 Kraft Drive, Suite 2475

Blacksburg, VA 24060

540-443-9254

Radical Innovation in Transfection Products for Medical Research and Genetic Therapeutics.

USB has been a Cleveland based life science company for over 30 years with expertise in commercialization of research reagents and technology. Anatrace, a 25 year old company based in Maumee (Toledo) is an internationally recognized leader in developing and manufacturing reagents for membrane protein studies and was acquired by USB in 2005. USB/Anatrace was in turn acquired by Affymetrix, the pioneer in commercial microarray technology in 2008 and the company is now poised to increase its product portfolio by introducing new research tools which compliment Affymetrix microarray solutions for scientific and medical discovery. Affymetrix microarrays are now being introduced for clinical screening and the company is completing ISO 13485 Medical Device Quality Standards throughout the organization, including the Ohio locations.

The Affymetrix/USB site in Cleveland is now the sole worldwide manufacturer of reagent kits for use with Affymetrix microarrays, as well as the site of manufacture and distribution of USB Molecular Biology Products. The company now seeks to leverage our unique position as the exclusive owner or licensor of molecules with great potential as non toxic transfection reagents. Most transfection formulations currently in the market are lipid based and unfortunately as effectiveness increases, so does cell toxicity. This makes them useless for work with primary cells, stem cells and for regenerative and therapeutic in vivo applications. In contrast our molecules promise the highly differentiated properties of high effectiveness with extremely low cell toxicity. Transfection is the process of importing nucleic acids into cells through nonviral methods to manipulate gene expression and protein levels at the cellular level. Potential applications include gene-therapy, manipulation of stem cells, regeneration of neural cells etc – thus making this a valuable tool for research at clinical laboratories and potentially a front line medical treatment methodology.

Affymetrix has already approved R&D funds for chemical synthesis of transfection candidate compounds in 2011, but the purpose of this grant application is to build the capability in Ohio for the functional testing need to screen, develop and commercialize entirely new categories of transfection reagents. Product lines to be developed from existing molecule library will be specialized for delivery of one or more molecular types, e.g. plasmids, vectors, or siRNA and will permit us to aggressively innovate and enter the stable and mature transfection market currently worth \$200 million annually on the medical research side alone. Therapeutic market estimates – as yet undeveloped, are closer to \$6-8 billion annual potential. If we successfully capture the lead share in these two submarkets, additional employment is sure to be added in R&D in both Maumee and Cleveland, as well as production and manufacturing jobs in both locations. Ohio could derive the essentially exclusive economic benefit of futuristic gene therapy medicine in this manner.

The Affymetrix R&D appropriation for this project in 2011 is \$320K and we are seeking grant funds from OTF to match this amount in 2011 and 2012 (\$640K over two years) for a two year project life. Product will be launched to market (research use only) by the end of this two year project window. We are currently negotiating collaborative R&D agreements with Techulon Inc. (Blacksburg, VA) to further secure our molecule library position.

12/14/2010

Lead Applicant: Teraphysics Corporation
110 Alpha Park
Dayton, OH 45435-0001

Contact Name: JT Tan
jttan@teraphysics.com
440-573-0008

Title: Wound Healing via High Frequency Light
Estimated grant funds requested: \$2,000,000 over three years

Known Collaborators: Cleveland Clinic (Dr. Maria Siemionow), Wright State University (Dr. Elliott Brown)

To whom this may concern,

Teraphysics Corporation, in collaboration with the Cleveland Clinic and Wright State University, would like to submit a \$2 million proposal to the Ohio Third Frontier Biomedical Program to bring to market a safe, light-based wound healing device.

Our project, entitled "Wound healing via high frequency light", builds upon existing research which shows decreases across all important wound healing metrics using the same high frequency light that Teraphysics' product line produces.

With our partner organizations, we intend to leverage our respective expertise to bring our wound healing device to clinical trials by the end of the project period.

If there are any questions or comments, do not hesitate to be in touch.

Best Regards,
JT Tan
Lead Applicant, OTF-BP 2011
jttan@teraphysics.com

From: vladimir.perlov@ifwconsulting.com
Sent: Tuesday, December 14, 2010 1:59 PM
To: OTFBP2011
Subject: 2011 OTFBP LOI

15 December 2010
Ohio Department of Development
77 S. High St. PO Box 1001
Columbus ,Ohio 43216-1001

To whom it may concern,

This letter is to confirm the intent of IFW Consulting, INC (Warren, Ohio) to submit a proposal to the 2011 Third Frontier Request for Proposals.

Lead Applicant: IFW Consulting
Address 2145 Brittainy Oaks Trail NE, Warren OH 44484
Telephone 330-881-8376
Contact information: vladimir.perlov@ifwconsulting.com
Funds requested \$500,000

Collaborators:
Freudenberg NOK Mechatronics, Weinheim Germany
Terrazign, Portland Oregon

Project Summary:
IFW is an Ohio Based company, leading the design and distribution of innovative flat wiring solutions and integrated electronics for the automotive industry. IFW intends to leverage their expertise and resources to design and fabricate custom and innovative wiring solutions for medical applications. There is need for IFW technology in hospital, out-patient, triage, home based medical monitoring. IFW will lead develop the capability for turnkey medical manufacturing in Warren, Ohio area.

Sincerely,

Vladimir Perlov

IFW Consulting
FPC - Flat Wire - Mechatronics
2145 Brittainy Oaks Tr.
Warren, OH 44484
Phone: 330-881-8376
E-mail: vladimir.perlov@ifwconsulting.com

BREATH 2010 RCP LOI

2010 Research Commercialization Program Letter of Intent

Lead Applicant's Name: Raed A. Dweik, M.D.

Institution: Cleveland Clinic

Contact Person: Raed A. Dweik

Address:

Department of Pulmonary, Allergy and

Critical Care Medicine

Desk A-90

Cleveland Clinic

Office: 216/445-5763

Fax: 216/445-8160

E-mail: dweikr@ccf.org

Proposed Project Title: Commercialization of a Versatile, Packaging System for Mobile Breath-based Health Care Diagnostics

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

Known collaborators:

NASA Glenn Research Center

Case Western Reserve University

Ohio State University

Makel Engineering

Summary of the proposed project:

Human breath is a very complex mixture of molecules that provides a signature of human health. Analysis of a particular molecule or a combination of molecules in breath has the potential for disease diagnosis and treatment as well as is a determinant of general health conditions. Thus, breath analysis is rapidly evolving as the new frontier in medical testing and is now used to diagnose and monitor asthma, to check for transplant organ rejection, and to detect lung cancer, to mention a few applications. Over the last decade, the push has been to develop sensor platforms that are mobile such that point-of-care health information is available. Even though there have been numerous publications and patents in this area, there are still very few commercial portable breath monitoring devices that are available. Much of the published research has focused on development of new sensor technology. In a Third Frontier project including Cleveland Clinic, NASA, Case Western Reserve University, and Ohio State University and Makel Engineering, we are developing a portable NO_x sensor. Our research and development has shown that packaging the sensor into a portable device for reliable breath monitoring is a significant technological problem, and is possibly the reason for the paucity of commercial sensors. The packaging that we have developed has the potential advantage of incorporating single or multiple electrochemical sensors. We now have an unique opportunity to provide this packaging technology to the community for incorporation of existing and new sensors and are requesting funds to support the development and commercialization of these packaging systems. The project's emphasis will be on sensors already produced in Ohio, and to attract companies from outside Ohio to have their sensors tested and commercialized employing our packaging, and this strategy should accelerate new products for the commercial marketplace and help solidify Ohio's leadership position in this rapidly growing field. Through the success of our projects, we have the opportunity to make Ohio the hub for the rapidly evolving field of breath diagnosis. We cannot afford to miss this opportunity.

December 13, 2010

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

Re: Ohio Third Frontier Biomedical Program (OTFBMP) – Letter of Intent

Dear Ohio Department of Development:

PercuVision, LLC. Intends to submit an application in response to your recent Biomedical Program 2011 RDP. The following is the information requested as part of this RFP:

Lead Applicant's Name:

PercuVision, LLC
6264 S. Sunbury Rd.
Westerville, Ohio 43081
O: 614-891-4800
F: 614-891-3500

Contact Person:

Errol Singh, M.D., CEO
Email: eos@percuvision.com

Project Proposed Title: DirectVision System Component Integration and Miniaturization

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

Known Collaborators:

- OhioHealth and Riverside Methodist Hospital
- Scott and White Hospitals, Temple Texas

Summary of the Proposed Project:

PercuVision's mission is to improve patient outcomes by advancing the standard of care through the application of vision technology to medical procedures. PercuVision® LLC was founded in 2007 by Dr. Errol Singh, a practicing urologist. His motivation to develop this innovative technology and achieve a first-to-market product position was driven from seeing patients in discomfort, pain, and with injuries, which result from blind urinary catheterizations. Dr. Singh was motivated to come up with a better and safer way to catheterize patients as a result DirectVision™ was developed.

Urethral injuries that are caused by blind insertions of a catheter are generally deemed to be inevitable under the current state-of-the-art blind insertion. With PercuVision®'s real-time visualization of the urethra during insertion of the catheter, injuries that were once inevitable become avoidable. **The goal for this project is to use PercuVision®'s existing technology to lower the cost for routine use which will change the standard of care.** The project will advance PercuVision®'s DirectVision® technology by consolidating and miniaturizing electronic components and advancing techniques for visualizing the urethra. These improvements will offer healthcare providers a safe and low-cost alternative for performing difficult urinary catheterizations and should lead to a paradigm shift for performing all urinary catheterizations in the future.

DirectVision™ is applicable to both male and female markets and is currently released in the U.S. market with respective FDA 510Ks. DirectVision™ is less expensive when compared to the state-of-the-art medical procedures for difficult "blind" placements. DirectVision™ is about 82% less. PercuVision anticipates that as DirectVision™ is utilized by more healthcare professionals, a paradigm shift will occur in the use from primarily difficult catheterizations to routine, of which the latter represents 80% of all urinary catheterizations. The DirectVision System is developed around three patents held by the organization.