Colorado
Office of Economic
Development and
International
Trade

Bill Ritter, Jr., Governor

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HOUSE FINANCE COMMITTEE

SENATE FINANCE COMMITTEE

BIOSCIENCE DISCOVERY EVALUATION CASH FUND PROGRAM UPDATE

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Legislative Report to House and Senate Finance Committees
per CRS 24-48.5-108
Bioscience Discovery Evaluation Grant Program
By the Colorado Office of Economic Development and International Trade

State funds have been targeted to the advancement of bioscience research and the commercialization of that research in Colorado with the aim of creating new companies and quality jobs in the state over the long-run. In terms of economic development, the biosciences take longer to develop than other industries, but the long-term payoff means stronger academic and research institutions, new R&D and manufacturing companies, and high-quality jobs. The Bioscience Discovery Evaluation Grant Program has been praised for its effectiveness in leveraging a limited state investment to move promising commercial technologies to market.

The program was initiated when HB06-1360 authorized $2.0 million for the support of bioscience research at Colorado's research institutions and program administrative costs. The bioscience research funds, totaling $1,960,000, were awarded in CY2007 and the research is either completed, or nearing completion. Through HB07-1060, an addition $2.5 million dollars was dedicated to the advancement of the bioscience industry with grants continuing to fund proof-of-concept research with commercial potential, and also early-stage company development for those businesses that had federal Small Business Innovation Research or Small Business Technology Transfer grants. The program currently operates per HB08-1001 which continues to provide poof-of-concept grants, but has changed the requirements for early-stage company grants, and added opportunities for adding infrastructure to support the bioscience industry in the state. Under HB08-1001 $5 million is available in state fiscal year (SFY) 2008-09 – 2 grant cycles for early-stage companies have been held, the 2nd grant cycle for proof-of-concept proposals is about to close as is the cycle for infrastructure projects. Many projects have received approval, and preliminary commitments have been made for a majority of the funds available in SFY 2008-09.

Since the first grants under the program were made in SFY 2006-07, the direct initial results of the state's investment are very promising. Fifty-two jobs have been created along with four new companies. The most impressive short-term return, however, is the additional capital that has been leveraged in matching funds, and the follow-on funding that further advances the subject technologies. Slightly over $3 million in state funds leveraged more than $4 million in matching funds. Results obtained with these project funds have brought in a reported $10 million in additional grants, angel or venture capital that moves these Colorado technologies closer to market.

The following tables summarize the grants and preliminary results in terms of jobs, companies created and follow-on capital.

Bioscience Discovery Evaluation Grant Program

Bill	Program	Recipient	PI	Title	Awarded	Final	Match	Status	Jobs	Companies	Follow-on $
HB06-1060	POC	Bonfils Blood Center	Ambruso	Transfusion Related Acute Lung Injury Identification Test Kit (Neutrophil Priming Activity)	$78,275	$78,275	$78,275	complete	1		
HB06-1060	POC	Colorado State University	Bartels	Development of a well-engineered proof of concept nonlinear imaging instrument	$78,536	$78,159	$78,536	complete			
HB06-1060	POC	Colorado State University	Monnet	Evaluation of a dynamic external cardiac device for the treatment of functional mitral valve regurgitation	$99,533	$99,533	$99,533	complete			
HB06-1060	POC	Colorado State University	Puttlitz	Instrumented cervical intervertebral disc space distractor	$107,285	$107,285	$107,285	complete			
HB06-1060	POC	Colorado State University	Dernell/Gustafson	Evaluation of lymphactic drainage and uptake following intracavitary chemotherapy administration for mammary carcinoma	$61,646	$61,646	$61,647	complete	2		$350,000
HB06-1060	POC	Colorado State University		Evaluation of phytodetectors	$94,000		$94,000	no report			
HB06-1060	POC	University of Colorado	Stevens	New treatment for ineffectively treated schizophrenia patients	$91,832	$91,833	$98,167	complete	1.4		
HB06-1060	POC	University of Colorado	Anderson	Suppression of irradiation –induced salivary gland dysfunction by IGF	$68,632	$68,631	$73,369	complete	1		$1,926,022
HB06-1060	POC	University of Colorado	Larson	Device for laser fusion of septal tissue	$46,883	$46,087	$49,266	complete	1	1	
HB06-1060	POC	University of Colorado	Hodges/Holmes	Validation of SARS coronavirus antibody technology of influenza virus	$90,382		$96,618	in-process	1		
HB06-1060	POC	University of Colorado	Ross	Hydroquinone ansamycins as novel anticancer Hsp90 inhibitors in pancreatic cancer	$89,744		$89,744	in-process			
HB06-1060	POC	University of Colorado	Shapiro	Infusion of alpha-1-antitrypsin (ATT) to suppress Human Immunodeficiency Virus Type 1 (HIV) replication in patients	$45,916	$43,916	$46,979	complete	3	1	
HB06-1060	POC	University of Colorado	Brodsky	In vivo analysis of a cardiac and skeletal muscle stem cell activator	$91,832	$91,832	$98,169	complete			yes
HB06-1060	POC	University of Colorado	Holt	Biomarker enabled development of PARP inhibitors for cancer therapies	$78,916	$78,916	$84,362	complete	3.5	1	$139,293
HB06-1060	POC	University of Colorado	Graham	Novel biology targeted agent for the treatment of non-small cell lung cancer	$91,832	$91,831	$98,169	complete	2		yes
HB06-1060	POC	University of Colorado	Bowman/Sikes	Redox-Initiated Radical Chain Polymerization for the Detection and amplification of biological recognition events	$92,819	$92,819	$99,223	complete			$300,000
HB06-1060	POC	University of Colorado	Dempsey	Moving Bryostatin-1 from the lab to the clinic for the treatment of pulmonary hypertension	$85,549	$58,962	$63,031	in-process	2		
HB06-1060	POC	University of Colorado	Koch	New targeted drug for the treatment of lung cancer.	$91,349		$97,651	in-process	1		
HB06-1060	POC	University of Colorado	Hunsucker	Protein biomarkers to differentially diagnose follicular thyroid carcinoma and follicular thyroid adenoma	$63,314		$67,686	in-process	1		
HB06-1060	POC	University of Denver	Shouresi	Development of a gait monitor for fall	$81,960		$81,960	no report			
HB06-1060	POC	University of Denver	Kutataledze	Encoding and screening of solution phase	$80,505	$80,505	$80,505	complete			
HB06-1060	POC	National Jewish Health	O'Brien	experiments to determine whether soluble	$20,986	$20,986	$20,986	complete			
HB06-1060	POC	National Jewish Health	Day	Instrumented Cervical	$36,981	$36,964	$36,981	complete			

Bill	Program	Recipient	PI	Title	Awarded	Final	Match	Status	Jobs	Companies	Follow-on $
HB06-1060	POC	National Jewish Health	Gelfand	Heat shock proteins modify lung allergic inflammatory responses	$48,421	$48,418	$48,418	complete			
HB06-1060	POC	National Jewish Health	Born	Inhaled and T-cell-receptor antibodies for the treatment of airway hyper-responsiveness and inflammation	$55,093	$54,981	$54,981	complete			
HB06-1060	POC	National Jewish Health	Nick	A method for the prevention and treatment of pseudomonas biofilm infections	$34,502	$34,502	$34,502	complete			
HB06-1060	POC	University of Northern Colorado	Mackessy	a proteomics approach toward the development of drugs from toxins	$53,260		$53,260	in-process			
HB07-1360	POC	University of Colorado		ALD Catalytic Microchannel Reactor - Converting Biosyngas to Biofuels	$86,777	$86,777		in-process	1.5	1	
HB07-1360	POC	University of Colorado	Gill/Medlin	Molecular Biorefining to Liquid Alkanes and Alcohols	$85,771	$85,771		in-process	2		
HB07-1360	POC	Colorado State University	Henry	Glucose/Xylose Sensor for Cellulosic Biomass Processing	$17,000		$17,000	in-process			
HB07-1360	POC	Colorado State University	Ali	In Planta Degradation of Lignin Using Fungal Enzymes	$42,455		$42,455	in-process			
HB07-1360	POC	University of Northern Colorado	Basu	Copabia for Biodiesel	$49,463		$49,634	in-process			
HB07-1360	POC	Colorado State University	McKay	Modification of Camalina Sativa & Development of Straight Vegetable Oil as Fuel	$100,000			contract not yet executed			
HB07-1360	SBIR/STTR	Colorado State University/Advanced MicroLabs, LLC		Microchip Assay for Serum Creatinine, Advanced MicroLabs, LLC	$49,855		$99,710	in-process	1		
HB07-1360	SBIR/STTR	Colorado State University/Advanced MicroLabs, LLC		Rapid Determination of Homocysteine by Michochip CE-PAD, Advanced MicroLabs, LLC	$50,700		$101,400	in-process	1		$750,000
HB07-1360	SBIR/STTR	University of Colorado/Sundrop Fuels	Perkins	Hydrogen Production from Biomass	$62,285		$150,000	in-process	15		$5,000,000
HB07-1360	SBIR/STTR	University of Colorado/Sundrop Fuels	Perkins	Syngas Production from Biomass	$75,000		$150,000	complete			
HB07-1360	SBIR/STTR	University of Colorado/ApopLogic Pharmaceuticals	Bellgrau	Fasaret for Cancer Treatment	$100,000		$674,771	in-process			$1,000,000
HB07-1360	SBIR/STTR	University of Colorado/Endoshape	Shandas	Shape memory Polymer TCD Devide	$49,500		$99,250	in-process	3		$500,000
HB07-1360	SBIR/STTR	University of Colorado/Tissue Genetics	Holt	BRCA 2 ovarian Cancer Marker	$27,424		$54,849	in-process	2.5		
HB07-1360	SBIR/STTR	University of Colorado/Tissue Genetics	Holt	BRCA 2 Breast Cancer Marker	$80,839		$161,678	in-process	2.5		
HB07-1360	SBIR/STTR	University of Colorado/Quest Product Development	VonOhlsen	Micro-Flex Surgical Device	$68,980		$149,774	in-process	1		$34,003
HB07-1360	SBIR/STTR	University of Colorado/Locomotion	Kram	Leg Swing Assist Device	$50,000		$100,000	in-process	0.5		
HB07-1360	SBIR/STTR	University of Colorado/Aktiv Dry	Quinn	Inhalable Vaccine Delivery	$49,990		$99,990	in-process	2		
HB07-1360	SBIR/STTR	University of Colorado/BlueSun		Journey to Disaster Recovery	$90,500		$181,000	contract not yet executed			
				PROGRAM TOTAL	$3,096,522	$1,538,629	$4,124,814		51.9	4	$9,999,318

Narrative – Project Summaries

As required by the statutes, the following project descriptions and funding amounts are provided. All HB06-1360 and HB07-1060 projects are grouped according to the focus of the research or technology. The Bioscience Discovery Evaluation Grant Program provides gap-funding to advance promising research from Colorado's outstanding research institutions into the market place. Colorado's researchers are leading advancements in the detection and treatment of lung disease and cancer. Novel drugs and devices are being explored and proven with the support and leverage of state funds. Biofuels production is being taken to the next level by improving native grasses for better fuels and improving processing techniques. Ultimately, it is expected that the bioscience industry will be strengthened by such efforts, resulting in long-term job creation and company formation.

Biofuels

University of Northern Colorado – Primary Investigator (PI), Basu $49,634
This grant supports the cloning of oleoresin producing genes from the diesel tree and then genetically transforms oilseed crops with these genes to produce an ideal source of biodiesel. Oleoresin producing tissues will be used to construct a copy DNA library. An expressed sequence tags library will be developed as an approach to gene discovery. An approach known as polymerase chain reaction will be used to identify terpene synthase like genes from the diesel tree. Collaborations with other institutions has begun, results of the research are being shared, while strategic industry partnerships are being developed. Additional grant funds to continue development of the technology are being sought.

University of Colorado – PI, Gill/Medlin $86,777
This project aims to produce catalytic microchannel reactors using atomic layer deposition (ALD) methods to convert syngas from cellulosic biomass to fuels. The goal is to demonstrate economically-efficient, small-scale production of biofuels from syngas generated close to the biomass source. Project activities include the design and construction of a microchannel reactor, constructing a reactor system, ALD development, and conducting an experimental program for converting bio-syngas to both useable gaseous and liquid fuels. Progress thus far includes construction of the microchannel reactor lab test system and development of ALD methods for depositing iron oxide and platinum based catalyst materials.

University of Colorado – PI, Henry $85,771
Molecular Biorefining to Liquid Alkanes and Alcohols
This project will use engineered microorganisms to produce a single fuel molecule containing functional groups that improve bioprocessing and subsequent catalytic processing into a variety of separate product streams that each have established markets. Specifically, the project involves demonstrating molecular biorefining for biogasoline production and demonstrating hydrogenolysis of metabolic engineered fatty acids. The researchers will demonstrate molecular biorefining for biogasoline production, and they will demonstrate hydrogenolysis of metabolic engineered fatty acids.

Colorado State University – PI, Henry $17,000
Work has just begun on this project with the goal of developing a sensor for the measurement of glucose and xylose produced during the processing of cellulosic biomass. Glucose and xylose are generated during the breakdown of cellulose and hemicellulose and can be further used as fermentable sugars for production of ethanol. It is important for processing purpose to have a real-time measurement of glucose and xylose to reduce energy use and increase throughput rate. The goal is to use microchip capillary electrophoresis coupled to pulsed amperometric detection to analyze the sugar content for cellulosic biomass processing.

Colorado State University – PI, Ali $42,455
This project is focused on improving the effectiveness of the production of biofuels by improving the release of monomeric sugars in plant biomass for fermentation to ethanol. The project involves testing fungal ligninolytic enzymes to determine if they can be expressed, and then to determining if these enzymes can be targeted at extracellular spaces in a plant system. As an outcome, the researchers will determine the best combination of enzymes with maximum lignin-degradation capability. The targeted expressed genes from groups of ligninolytic enzymes will be expressed in tobacco and switchgrass and assayed for the degradation of lignin. To-date, researchers have established white rot fungus culture, and isolated total RNA and RT-PCR for the lignin-degrading enzyme genes from P. chrysosporium.

University of Colorado/Copernican Energy - $62,285
This project aimed to develop a business and commercialization plan for developing renewable hydrogen generation technology. Key deliverables were a market research report on hydrogen, evaluation of potential investors/licensees in the field, a market strategy for implementing the technology on an industrial scale, and submission of a commercialization plan as part of an NSF Phase II proposal. The project goals have been completed at this date - submission of the NSF Phase II proposal will take place in July 2009.

Copernican Energy was acquired in July 2008 by Sundrop Fuels who was looking for a solar thermal chemical platform technology on which to build. The company relocated from the San Francisco, CA and Santa Fe, NM areas to be headquartered in Louisville, CO. The main research facility is in the Colorado Technology Center in Louisville, and the company is investing $5M in a solar thermal pilot research plant already under construction in Broomfield, CO.

University of Colorado/Copernican Energy - $75,000
This grant was used to develop a commercialization plan, seek investors, and develop a Phase II STTR proposal for solar thermal gasification of biomass into useful fuels (methanol, methanol-to-gasoline, FT diesel, hydrogen, ammonia). This technology is continuing to be developed under Sundrop Fuels, who purchased Copernican Energy in July 2008.

Blood Transfusion
Bonfils Blood Center – PI, Ambruso $78,275
Under this project an easy, low-cost test kit was created to test patients post blood transfusion for Transfusion Related Acute Lung Injury - currently the number one cause of death related to transfusions. Platforms for measuring neutrophil priming were established, and a technique for isolating neutrophils from anti-coagulated human blood was verified. The results of the work were promising, so future work will be to validate all platforms.

Cancer
Bone
University of Colorado/Apoplogic Pharmaceuticals - $100,000
This company is working to develop a product, Fasaret, for the treatment of bone cancer. The state funded grant is being used for: (1) oncology clinical drug development to aid with planning and clinical trial design for Fasaret; (2) FDA regulatory expertise to arrange and prepare for a pre-IND meeting with the FDA and to plan for the manufacture and required toxicity testing of Fasaret that would include contractor selection and oversight; and (3) freedom-to-operate analysis and strategic planning around the Fas ligand intellectual property.

Breast

University of Colorado – PI, Holt $78,916

This project studied a molecular defect found in patients with inherited breast cancer and controls for the cancer. PARP inhibitor treatment, which has been an effective therapy for these patients was found to also be effective for some patients without a family history. An inexpensive, and timely immunohistochemistry (IHC) test was developed to identify patients who would be likely responders to PARP treatment.

University of Colorado/Tissue Genetics - $27,424

This grant is funding the commercial deployment of an immunohistochemistry (IHC) test to screen for hereditary breast cancer. Independent lab tests have given positive results for the company's clinical antibodies, moving the company toward development of a test-kit. Tissue Genetics is in the process of acquiring market research to confirm domestic and international ovarian cancer demographics. The company has recruited noted oncologist and pathologists for its medical advisory board. Investor meetings have been held and will continue through the project period. Some patent work has been conducted and will continue. Regulatory planning is still required.

Head and Neck

University of Colorado – PI, Anderson - $68,632

This project looked at minimizing the negative impacts of irradiation treatment for head and neck cancer patients. The studies conducted under the grant were promising, and therefore studies have been expanded.

Kidney

Colorado State University/Advanced MicroLabs - $49,855

Advanced MicroLabs, LLC (AML) was awarded a Phase I grant by the National Institutes of Health (NIH) to develop a novel point-of-care, in-vitro diagnostic medical device for the determination of serum creatinine concentrations, the most common determination for kidney function. The state grant is providing AML funds to evaluate the market, plan for FDA approval, understand third-party reimbursement, and protect intellectual property (IP). Deliverables include a formal business plan for a serum creatinine stand-alone diagnostic medical device, as well as, complimentary diagnostic markers.

Lung

University of Colorado – PI, Koch $91,349

This project is focused on developing a new targeted drug for the treatment of lung cancer. Researchers will administer systemically inactive peptide-linked doxazolidine, which will be activated by plasmin released at the site of tumor metastases. Thus, normal tissue will be exposed to the inactive pro-drug, while the tumor will be exposed selectively to the released, and highly toxic, cytotoxin.

University of Colorado – PI, Graham $91,831

Non-small cell lung cancer (NSCLC) is the primary cause of cancer mortality in the United States. Less than 25% of patients treated on current chemotherapy protocols survive 2 years. This project supported testing to identify targeted biologic therapies which will synergistically interact with standard chemotherapy to enhance patient survival. The completed studies in this project support an oncogenic role for the Axl and Mer receptor tyrosine kinases in NSCLC. The research has shown the role of these receptor tyrosine kinases in survival and proliferation in NSCLC. They also found that their novel biologic inhibitor, AxlFc, blocks Axl activation in NSCLC. The in vitro studies accomplished with the aid of the state grant enabled them to move forward with preclinical evaluation of the biologic inhibitors in animal models of NSCLC. Furthermore, these data helped provide support

for the filing of a provisional patent in the previous year and have led to additional grant support to continue this project.

University of Colorado – PI, Bowman/Sikes $92,819
Early detection of cancer in clinical settings requires the development of novel, pragmatic detection assays that are capable of high-throughput evaluation of biomarkers in a highly sensitive and specific manner, necessitating creative and innovative approaches to signal amplification. Through the duration of this grant, successful research has been performed in the development of polymerization-based amplification (PBA) to meet such needs. The specific aims have focused on A) developing PBA towards the visual, sensitive detection of clinically relevant DNA and antibody biomarkers indicative of early stage cancer, B) developing PBA towards achieving high gains in quantitative fluorescent and colorimetric signals, C) implementing PBA into new applications significant for early cancer detection, including direct detection of cancerous cells in tissue samples.

Lymphatic
Colorado State University – PI, Dernell/Gustafson $61,646
Sustained release of anticancer chemotherapy from a biodegradable polymer system placed in the surgical site during breast-sparing surgery for breast cancer was tested. It is thought polymer technology may be adapted to other cancers and non-cancer diseases that preferentially spread to the lymphatics. The following tests were conducted: 1) the regional lymphatic drainage and uptake of paclitaxel following polymer delivery into the mammary tissue of non-tumor-bearing nude mice. 2) determine human mammary cancer cell lines which show lymphatic metastasis, 3) control of lymphatic metastasis following polymer delivery of paclitaxel into the wound cavity following mammary tumor removal of tumor-bearing nude mice.

Ovarian
University of Colorado/Tissue Genetics - $80,839
This state grant is supporting the commercial deployment of an immunohistochemistry (IHC) test to screen for hereditary ovarian cancer. Independent lab tests have given positive results for the company's clinical antibodies. Tissue Genetics is in the process of acquiring market research to confirm domestic and international ovarian cancer demographics. The company has recruited noted oncologist and pathologists for its medical advisory board. Investor meetings have been held and will continue through the project period. Some patent work has been conducted and will continue. Regulatory planning is still required.

Pancreatic
University of Colorado – PI, Ross $89,744
To-date results from this project have demonstrated that treatment of human pancreatic cancer cells with benzoquinone ansamycins (BA) results in Hsp90 inhibition and cell death. Treatment of human pancreatic cancer cells with BA's resulted in compensatory increases in Hsp70 and decreased ERK phosphorylation, molecular biomarkers of Hsp90 inhibition. These results also demonstrated the formation of hydroquinone anasamycins in human pancreatic cancer cells and a role for NQO1 in hydroquinone formation. Increased BA concentrations (quinone and hydroquinone) were detected in human pancreatic cancer cells expressing NQO1 compared to NQO1 null cells. These data suggests that human pancreatic cancer cells metabolize BA's to their corresponding hydroquinone derivatives leading to more effective Hsp90 inhibition and cell death.

Thyroid

University of Colorado – PI, Hunsucker $63,314

The aim of this project is to develop assays and validate protein biomarkers that can differentially diagnose follicular thyroid carcinoma (FTC) and follicular thyroid adenoma (FTA). Such a clinical assay will provide sufficient diagnostic power to correctly distinguish FTC and FTA when fine-needle aspiration biopsy results are indeterminate and can be performed on a blood sample from the patient. Such an assay could save the healthcare system on the order of $250 million per year and prevent tens-of-thousands of unnecessary thyroidectomies.

Cardiac

University of Colorado – PI, Brodsky $91,831

This project evaluated a compound to therapeutically induce stem cell-mediated growth and repair of damaged heart muscle for the treatment of chronic lung and heart disorders, including chronic obstructive pulmonary disease (COPD) with complicating pulmonary hypertension (PHTN).

The research uncovered difficulties in producing prelamin A peptide, and researchers are still working to confirm peptide structure/activity relationship. These studies have, however, led to the development of highly sensitive, accurate and reproducible assays to characterize and confirm peptide identity and chemical structure. The studies have also led to the development of an appropriate synthesis and purification protocol for the production of structurally correct and biologically active peptide. The protocols developed have now been employed in the synthesis and purification of a large scale preparation of the covalently modified prelamin A pre-peptide needed to perform the remaining experiments in this research project, and initial chemical characterization indicates the desired peptide species has been correctly synthesized and purified to homogeneity. At the conclusion of this project, the peptide species identity is still in doubt and early studies have not been replicated with later batches of the peptide. More work will need to be done to understand the exact peptide species of prelamin A required to achieve the expected biologic activity.

University of Colorado – PI, Dempsey $85,549

This project tested the hypothesis that Bryostatin-1, alone or in combination with other emerging drugs, will exert striking protective and attenuating effects on the pulmonary circulation exposed to chronic hypoxia and other injurious stimuli. Bryostatin-1 is in a family of macrocyclic lactones that can be isolated from the murine bryozoan, *Bugula neritina* The research aimed to resolve questions about potential early and late effects on vascular tone that could not be studied in mice by using more invasive hemodynamic techniques in a larger rat model and determine an optimal drug dosing regimen; identify a readily measurable biomarker of drug effect and disease activity in serum or circulating progenitor cells; establish efficacy of Bryostatin-1 in both preventing and promoting regression in rat models of PHTN, and screen for potential synergistic interactions between Bryostatin-1 and other emerging treatment strategies by using panels of mouse, rat, cow and human PA SMCs and endothelial cells and growth assays followed by selective testing in the same hypoxic rat model. The project also covers planning for testing in a large animal model of hypoxic PHTN as a step toward a clinical trial in patients.

Colorado State University – PI, Monnet $99,533

This grant supported the development of an epicardial device for the treatment of functional mitral regurgitation in human patients. The device will have the potential to address the most important underlying cause of functional mitral valve regurgitation which is tethering of the papillary muscle following severe dilation of the left ventricle. Product development is moving forward.

Colorado State University/Advanced MicroLabs - $50,700
Cardiovascular disease (CVD) is the number 1 killer in the United States and much of the Western world. Homocysteine (HCY) is a confirmed independent risk factor for CVD. Advanced MicroLabs, LLC (AML) was awarded a Phase I grant by the National Institutes of Health (NIH) to develop a novel point-of-care, in-vitro diagnostic medical device for the determination of serum HCY concentrations. The NIH Phase I research was completed March 2008 and final report submitted and accepted by the NIH in May 2008. A Phase II application was awarded by the NIH in September 2008 for $750,000. The state grant is providing funds to advance the commercialization of a point-of-care diagnostic to determine serum HCY concentrations. Grant funds are provided to evaluate the market and protect intellectual property (IP). Deliverables include a formal business plan for an HCY stand-alone diagnostic medical device as well as complimentary diagnostic markers. The business plan will evaluate competition; define the strengths and weaknesses of the proposed product; identify industrial partners; propose a company structure, finance strategy, and 5-year strategic plan. Scientific Advisory Board members will be recruited. Project funds may be spent for Patent Office Action responses and/or Division Applications. Project funds will also be used to manage project activity.

Degenerative Disc Disease
Colorado State University/Advanced MicroLabs - $107,285
Spine fusion and disc replacement are common procedures to treat degenerative disc disease of the cervical spine. The surgical outcome is highly-dependent upon the size of the implant and compression across the disc space. If the graft/implanted device is too tight there is an increased risk of subsidence (penetration of the graft/implant into the endplate) and fracture of the vertebral bodies (in osteoporotic and osteopenic patients). If the graft/implanted device is too loose there is an increased risk of pseudarthrosis (fibrous nonunion) and graft/implant dislodgement. Currently the degree of distraction, and hence graft fit, is determined solely by the operating surgeon's subjective evaluation. There is currently no data relating structural stiffness to surgical outcome.

Under this grant researchers are developing an instrumented cervical intervertebral disc distractor that provides the surgeon with real-time measures of distraction force in order to improve the outcome of these surgical procedures. This project is comprised of two main segments; a clinical trial (currently underway) and the Caspar pin distractor redesign incorporating the new instrumentation - including internalization of the device's electronic components and associated wiring, packaging of the software and digital readout components and associated wiring, packaging of the software and digital readout components and associated wiring, packaging of the software and digital readout information, and additional intra-operative experiments to further demonstrate the clinical value of the device. Such a prototype has been created – clinical trials are identifying new improvements.

Drug Development
University of Denver – PI, Kutataledze $80,505
Via the state grant, researchers have further developed a technology that creates a library of drug candidates, each of which is uniquely identified by a chemical tag. This technology is being analyzed for development into a manufacturing and servicing company.

University of Northern Colorado –PI, Mackessy $53,260
The applications of protein drugs are rapidly growing and are projected to continue growing in the foreseeable future. Snake venoms have long been recognized as sources of actual and potential drugs and are complex mixtures consisting primarily of proteins. Through this grant, the goal is to discover valuable new compounds with therapeutic and/or biomedical applications. To date, researchers have identified a number of lead compounds with promising activities which may have potential for

development as drug candidates. There are still many biochemical and *in vitro* analyses which are required before these could be considered for clinical trials.

Environmental Pollutants
Colorado State University – $94,000
Evaluation of phytodetectors (plants designed to be highly specific detectors of environmental pollutants). It is currently impractical to monitor large areas such as metropolitan areas, sports arenas, transportation hubs, shopping malls, and areas around chemical plants for threats from terrorists or the presence of environmental pollutants. Researchers have produced plants with a high specificity to sense substances such as explosives. This project proposes to evaluate this technology.

HIV
University of Colorado HB06-1360
Infusion of alpha-1-antitrypsin (ATT) to suppress Human Immunodeficiency Virus Type 1 (HIV) replication in patients. Current antiretroviral therapy for HIV is subject to the mutation-induced escape of drug resistant HIV strains. Researchers plan to infused AAT into 7 volunteers infected with uncontrolled HIV in an attempt to suppress viral replication. At the conclusion of the state grant, researchers still have plans to recruit more volunteers.

Infection
National Jewish Health – PI, Gelfand $48,418
A class of non-toxic compounds was tested to disrupt and prevent the formation of a biofilm that often leads to severe infection for contact wearers, those with severe burns, and those with cystic fibrosis. The project results support further work, and additional grants have been awarded and are being applied for. NJH is working on a licensing opportunity with a CO start-up.

Influenza
University of Colorado – PI, Hodges/Holmes $90,382
This project draws on a unique strategy developed to block SARS to develop a similar antibody to the influenza A virus fusion protein. The researcher is currently progressing and showing promise.

Lung Disease
National Jewish Health –PI, O'Brien $20,986
This proof of concept project looked at altering inflammatory responses to protect tissues from damage and destruction. Though this T cell receptor based approach did not prove effective, the findings advance the search for new inflammatory treatments. The technology has been marketed to various companies throughout the U.S., but no licensing deals are executed.

National Jewish Health – PI, Day $36,998
This project evaluated two compounds to increase glutathione levels in the lungs, and thereby decrease inflammation for the treatment of various lung diseases. Understanding of the mechanisms and model were advanced, and encourage further research. A venture capital firm is reviewing the merits of the technology, and confidentiality agreements have been executed with two companies.

National Jewish Health – PI, Gelfand $48,418
This grant funded proof of concept research into gene therapy for the treatment of and improvement of lung function for asthma. The project is complete, and results were positive, improving the commercial potential of this treatment approach. The technology has been marketed to various companies throughout the U.S., but no licensing deals are executed.

National Jewish Health – PI, Born $55,093
T cell receptor antibodies administered to mice lungs have proven effective in treating features of asthma and other diseases of the lung. This project tested inhalation of these antibodies in nonhuman primates, and found the selected aerosolized antibody effective in abrogating airway hyper responsiveness. Thus, the technology has progressed forward in its commercial potential. NJH has executed confidentiality agreements with 4 companies (1 Colorado-based) interested in the potential of this technology.

Pathology
Colorado State University – PI, Bartles $78,536
Under this project a prototype laser-scanning THG microscopy with vibrational contrast through coherence—modulated perturbations to coherent nonlinear scattering was designed and constructed. Third harmonic generation (THG) microscopy is used to make dynamic images of living systems. Out of this work a novel approach to improving the imaging resolution of THG microscopy arose. This technique enables a new class of nano-scale imaging. The high resolution will make possible imaging of sub-cellular structure, such as organelles with great detail. Moreover, this technique could find application in many areas of nanoscience and tracking of functional behavior of macromolecules. With a slight modification of the prototype, we were able to demonstrate this new technique which greatly expands the possible utility of this technology.

RSV
University of Colorado/Aktiv-Dry - $49,990
This project advances a technology that delivers small interfering RNA (siRNA), targeted to the treatment of respiratory syncytial virus (RSV), a leading cause of bronchiolitis, pneumonia, and respiratory failure in infants. Grant funds have been used to explore the potential of Bubble Dryer manufacturing/assembly to administer siRNA or other dry powder pharmaceuticals. Engineering analysis has led to design improvements. Market analysis and the search for investors continues.

Schizophrenia
University of Colorado – PI, Stevens $91,832
Under this project, researchers reformulated clozapine, a highly effective medication for schizophrenia, for central administration to achieve a better therapeutic effect and reduce side effects. The project results provided further support for central administration, but further studies are required.

Sterilization
University of Colorado/EndoShape, Inc. - $49,500
Trans-cervical tubal sterilization device (TCD)
EndoShape is developing a TCD fabricated from unique shape memory polymer (SMP) technology. With the state grant, the company has 1) completed an intellectual property assessment, 2) completed a regulatory plan, 3) conducted a market assessment. Within the scope of the grant, the following are pending: 1) FDA visit, 2) external market review.

Surgical Device

University of Colorado/Quest Product Development - $68,980

This grant supports moving MicroFlex technology for endoscopes for minimally invasive surgery toward a commercially available product. Initial market research has been completed providing useful market feedback, numerous interested candidates for the Medical Advisory Board, and direct contact with several primary potential licensees. Upcoming or just started tasks include: 1) formation of the Medical Advisory Board, 2) market research into new applications is in progress, 3) FDA regulatory overview work has begun, 4) with a subcontract being negotiated for some of the work. A first-draft of a business plan was completed, but will be updated. Travel to strategic partners has been waiting for more technical progress by the CU research team, which has been slow, but is moving forward. Funds have been committed for an optics/image guide consultant and a microfabrication study to aid with the challenging technological aspects.

Tissue

University of Colorado – PI, Larson $46,883

Under this project, a prototype device for joining tissue in surgical procedures involving the nasal septum was created, tested and optimized for joining tissue. This new tailored device provides an economical new solution for a common procedure. A new company headquartered in Colorado Springs has been created as a result of this work.

Walking/Stability

University of Denver – PI, Shoureshi $81,960

This project supports further development of a gait monitor for fall prevention, including incorporating a self-power mechanism, testing on human subjects and production of commercial versions of this device for demonstration, further verification, marketing and attracting capital investment.

University of Colorado/Locomotion - $50,000

This grant allows Locomotion to expand the potential market for a leg-swing-assist device (LSA) from testing on incomplete spinal cord injury patients (conducted under an SBIR grant) to stroke, traumatic brain injury, and cerebral palsy patients. Product design under the SBIR grant has been completed, and the evaluation of other markets under the state grant has begun.