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SBIR: Advancing Medical Breakthroughs

Statement of

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Good afternoon, Chairman Altmire, Ranking Member Gohmert, and members of the Subcommittee. My name is Jo Anne Goodnight. I am the Coordinator of the Small Business Innovation Research (SBIR) and the Small Business Technology Transfer (STTR) programs at the National Institutes of Health (NIH), an agency of the Department of Health and Human Services. Among the eleven Federal agencies that participate in the SBIR program, the NIH is one of the largest funders, second only to the Department of Defense, and the single largest supporter of biomedical research. Thank you for the invitation and the opportunity to discuss the NIH SBIR program's contribution to the development of important medical advances.

NIH SBIR Program - Ideally suited for Advancing Medical Breakthroughs

The NIH SBIR program is part of a complex innovation ecosystem that provides dedicated funding for small businesses to engage in innovative, early-stage biomedical and behavioral research and development (R&D) projects with commercial potential for medical solutions and breakthroughs. The program plays an important role in achieving our mission of improving human health, particularly in translating research findings and advancing medical discoveries into tangible products and services.

The NIH SBIR program encompasses 23 of NIH's 27 Institutes and Centers (ICs), each of which has a mandate to address science and health from a specific perspective, disease area (e.g., cancer), or area of concern (e.g., aging). The SBIR program is one means by which the ICs accomplish their R&D objectives. The unique feature of the SBIR program is a focus on commercialization of the outcomes of research. Thus, the SBIR program supplements the approach of the traditional research programs of NIH.

The many scientific medical advances achieved by NIH-funded researchers investigating the prevention, causes, treatments, and cures for common and rare diseases allow people to live longer. We are moving from a system of "sick care" to "health care." As the age of our population shifts, so too does the landscape of health challenges – from acute to chronic diseases such as diabetes, congestive heart failure, and stroke – all compounded by rapidly increasing healthcare costs. The key to overcoming these challenges is through rapid translation of transformative medical breakthroughs. The NIH SBIR program focuses on precisely that – the development of tangible products resulting from innovative R&D approaches that assist with predicting, preventing, diagnosing, and treating diseases and disabilities.

Overall, the SBIR program has complemented NIH's mission to advance science while reducing the burden of illness on public health. NIH is committed to maintaining the integrity of its SBIR program and ensuring continued development and dissemination of technologies for the benefit of all.

The NIH SBIR program is poised to fund early stage, high-risk research from which important medical advances are developed. Below are some examples of how tangible scientific benefits can result from a small investment of SBIR funds in early-stage ideas with commercial potential but uncertain verification or feasibility.

- **Altea Therapeutics (GA)**, with the help of NIH SBIR funding, was able to test the feasibility of a needleless infusion patch, a breakthrough technology that enables fast, cost-effective, controlled, and painless delivery of drugs (e.g., insulin) and vaccines through the skin. Altea Therapeutics received the 2007 Frost & Sullivan Technology Innovation Award in the field of transdermal drug

delivery for its development of the *PassPort™ System,* which has dramatically extended the range of diseases that can be treated using transdermal patches. This novel technology presents great opportunity for Altea Therapeutics in addressing important medical needs using a method of drug administration proven to lead to high patient compliance.

- **Genaera Corporation (PA)** is focused on advancing the science and treatment of metabolic diseases. Genaera's discovery of aminosterols, a novel class of small molecules discovered in dogfish shark tissues, has led to several research programs that have been funded, in part, from NIH SBIR awards. Genaera, like many other biotech firms, has multiple lines of research at different stages of development (e.g., pre-clinical, Clinical Phase I trials, Clinical Phase II trials) Genaera now has three products in development for cancer, age-related macular degeneration, asthma, and cystic fibrosis:
    - Squalamine, an anti-angiogenesis treatment for cancer and "Wet" age-related macular degeneration disease;
    - Interleukin-9 antibody, a respiratory treatment for asthma; and
    - LOMUCIN™, a mucoregulator to treat the overproduction of mucus and secretions involved in many forms of chronic respiratory disease.

- **RedPath Integrated Pathology (PA)**, a woman-owned biotech firm, is focused on earlier detection of cancer using a technology that will result in an important advancement in personalized medicine. Cancer death rates have declined since 2001, making cancer one of the most preventable and increasingly curable life-threatening diseases, if detected early. Funded in part by NIH SBIR funding, RedPath researchers developed patented techniques to extract objective and

quantitative genetic information from minute biological specimens. By integrating traditional pathology analysis with genetic mutational analysis, RedPath developed a topographic genotyping (TG) technology called *PathFinderTG*®, a specialized cancer diagnostic platform that resolves diagnostic dilemmas.

- **GlycoFi Inc. (NH)**, a biotherapeutics company, used the NIH SBIR program to explore the feasibility of making injectable proteins, so called "biotech drugs", using a glycoengineered yeast strain. GlycoFi's work is an example of exciting translational research using an innovative approach called *GlycoDesign*™ to control a protein's glycans (sugars) to optimize a therapeutic protein. GlycoFi demonstrated successfully the technical feasibility of developing a yeast system for producing therapeutic drugs on a large scale. In May 2006, this six-year-old company was acquired by Merck & Co. for about $400 million in cash, the largest such deal ever reported for a private biotechnology company.

It is important to note that the NIH SBIR program funds a wide diversity of promising ideas and companies, not just those focused on drug development and therapeutics. For example, NIH SBIR projects have supported the development of medical devices, assistive technologies, and research tools.

One medical advance of note is a device called the TandemHeart™ PTVA System. The TandemHeart™, manufactured by **CardiacAssist (PA)**, is an adult-use device for temporary use during surgery that increases blood flow and reduces demands on weakened or damaged hearts. A pediatric version is being developed by the company through NIH SBIR funding.

An exciting assistive technology resulted from more than a decade of R&D. Supported by the NIH SBIR program, **Boston Medical Product's (MA)** *Montgomery® Thyroplasty Implant System,* which improves the quality of life for individuals with communication disorders. It is the first standardized thyroplasty implant device for the treatment of vocal cord paralysis that requires no suturing, reduces trauma and surgery time, and is reversible.

NIH SBIR projects are stories of discovery.

A 3-year-old girl grabs a frying pan of boiling-hot oil off the stove . . . a 5-year-old boy ignites his pajamas while playing with matches . . . the tip of an 80-year-old woman's housecoat catches on fire as she reaches for a teakettle on the stove.

Each year in the United States, more than 2 million burn injuries result from situations such as these. Twenty years ago, second- and third-degree burns covering half the body were routinely fatal. Today, patients with severe burns over 90 percent of their body surface typically survive. With NIH SBIR support, researchers at **Integra LifeSciences Corporation (NJ)** developed an artificial skin system called *Integra™ Matrix Wound Dressing*. Developed by a trauma surgeon and a mechanical engineer, *Integra™* exemplifies the extraordinary value of collaborative research supported by NIH SBIR funding. The product is now being manufactured and sold by Integra. After extensive clinical testing and FDA clearance, the product is now widely used for the treatment of severe burns and other serious skin injuries, saving and improving lives of millions of affected Americans. Today, *Integra™* is the top-selling skin substitute in the world.

A BRIEF OVERVIEW OF NIH'S SBIR FUNDING FOR "ORPHAN" DISEASES

Many of the scientific advances described thus far have focused on more common diseases—cancer, diabetes, heart. Let me now focus on the less common diseases, often called "orphan" diseases. An orphan disease may be a rare disease, defined in statute as, in general, any disease, syndrome, or disorder affecting fewer than 200,000 people in the United States. There are more than 5,000 such rare disorders.

Rare "orphan" diseases include such better-known names as sickle cell anemia, Tay-Sachs, hemophilia, Tourette syndrome, Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's disease), and systemic scleroderma. They also include obscure diseases such as Trisomy 13 syndrome and Progeria.

NIH supports research, both basic and applied, in rare diseases and related conditions, and the awards to SBIR and STTR recipients help facilitate NIH's research mission related to these rare diseases. From fiscal years 1983 through 2007, the NIH SBIR and STTR programs awarded $637.4 million for orphan or rare disease projects. This is 9.8 percent of the $6.5 billion awarded by NIH for SBIR and STTR projects during that period. Further, of the total $637.4 million awarded for orphan or rare disease projects over that 25-year span, $575.1 million, or 85.3 percent, came from NIH SBIR/STTR projects over the last ten years. Such projects included research for identification of a compound that is a potential treatment for ALS, diagnosis of Urea Cycle disorders, and development of vaccines for malaria.

Following are some descriptions of NIH SBIR projects for which R&D is being supported or products have been developed in the area of rare or "orphan" diseases.

- **Dyax (MA)** develops and commercializes innovative biopharmaceuticals for medical needs. Funded under the NIH SBIR program, Dyax used its core proprietary phage display technology to rapidly identify compounds that bind with very high affinity and specificity to therapeutic targets. Its lead product candidate is *DX-88*, a recombinant small protein that is currently in clinical trials for its therapeutic potential in both hereditary angioedema (HAE) and prevention of blood loss during on-pump coronary artery bypass graft (CABG) procedures. *DX-88* has orphan drug designation in the United States and European Union, as well as FDA Fast Track designation for the treatment of acute attacks of HAE. In addition to supporting their own commercialization goals, Dyax leverages its technology broadly with more than 70 revenue generating licenses and collaborations for therapeutic discovery.

- **Angion Biomedica Corporation (NY)** is a biopharmaceutical company focused on R&D solutions for diseases relating to tissue and organ injury and fibrosis. Angion used the NIH SBIR program to evaluate a lead small-molecule drug candidate with potential to treat systemic scleroderma, a rare chronic autoimmune disease that causes skin to thicken and tighten. For some patients, it also causes life-threatening damage to internal organs. Currently, there is no known cure for scleroderma. Angion identified a small molecule compound, *Ang1170,* which showed antifibrotic effects both *in vitro* and *in vivo*.

- **Azevan Pharmaceuticals (PA)** received multiple NIH SBIR awards that enabled the company to identify and validate novel drug candidate molecules from vasopressin receptor antagonists. Vasopressin has been implicated in aggression. Azevan has focused on the most promising candidates to develop

drugs for the treatment of stress-related disorders and depression and to treat impulsivity, violence, and self-injurious behavior in patients with autism, Tourette syndrome, and mental retardation.

INITIATIVES ASSOCIATED WITH THE RECRUITMENT OF SBIR APPLICANTS

Although the NIH SBIR program remains a vibrant and robust program, over the past few years the number of new small business concerns participating in the program has been decreasing, with only about one-fourth of the awardees being new to the program in fiscal year 2006 -- the lowest proportion within the last decade. SBIR application numbers also have been declining. To build on our successes and to reverse the trend of declining NIH SBIR applications and diminishing new firms in the program, the NIH has enhanced its outreach efforts aimed at recruitment of SBIR applicants pursuing innovative research ideas that could improve human health.

We participate in national, regional and state conferences around the country, especially those focused on increasing the participation of small firms owned by women or socially disadvantaged individuals. Our recent participation in Maryland's Minority Research and Development Initiative, "SBIR: From Awareness to Awards and Commercialization" (January 2008) and the Alabama A&M University 2008 SBIR/STTR Small Business Conference (January 2008) are just two recent examples of these efforts. NIH will hold its 10th Annual SBIR/STTR conference in Atlanta, Georgia, on July 22-23, 2008; we expect to draw 600-800 attendees. Attendees can learn about the programs and also have an opportunity to meet one-on-one with NIH staff to discuss the "fit" of their technology within our agency. Other SBIR conferences are planned to be held in Louisiana, Kentucky, and New York. NIH's average annual outreach activities extend to more than 30 states per year. We also have begun to utilize other forms of

outreach like interactive videoconferencing (Vermont Small Business Development Center) and Webinars (University Start-ups and University Angel Investor Groups). We have seen some benefit from these outreach and recruitment efforts, particularly from states where applications to NIH have historically been low. The number of states receiving zero or one Phase II award declined from 28 in 1995 to 16 in 2003.

In addition, the NIH Small Business Research Funding Opportunities Web site which receives about 15,000 monthly hits and the NIH SBIR/STTR ListServ, with more than 14,000 subscribers, are key outreach tools. They are important avenues for communicating to broad audiences information about the programs' procedures such as solicitations, research topics, application process, technical assistance, partnering opportunities (e.g., NIH Pipeline to Partnerships), and other useful information.

Recruitment efforts have their limits, especially if incentive opportunities are not clearly identified. One major challenge for many small businesses is the long funding gap (six months or more) between the end of Phase I and the beginning of Phase II. It is often difficult for companies to hold a team together through this funding gap. To address this challenge, NIH offers several gap-funding programs, such as a Phase I/II Fast-Track option and Phase II competing renewal awards, for Phase II awardees to receive additional R&D funding to meet certain FDA regulatory milestones along the product development pathway. NIH SBIR applicants have an opportunity to submit a Phase I or Phase II application on any of our three annual, standard due dates. Moreover, NIH SBIR applicants are afforded the opportunity to resubmit unfunded applications twice. We have found that many firms are either not aware, or are not taking advantage of the

opportunity to submit investigator-initiated ideas or to revise an application. Therefore, we are continually assessing new avenues to recruit more SBIR applicants.

Although 11 federal agencies participate in the SBIR program, it is not a one-size-fits-all program, given our varying missions and needs. Procedures distinguishing the NIH SBIR program from those at other agencies are primarily due to the flexibility that the Small Business Administration has provided to accommodate the changing nature of biomedical and behavioral research. One of the most appealing features of our programs is the opportunity for firms to propose R&D in the fields that have the most biomedical promise, rather than to restrict their ideas to projects that can only be conducted under a prescribed amount of time and money.

Local or state organizations that have dedicated resources to support the R&D of innovative, technology-based projects or the commercialization of those projects also can enhance the recruitment and retention of SBIR applicants.

ENTREPRENEURIAL AND BUSINESS SKILLS TRAINING AVAILABLE TO PHASE I GRANTEES

NIH offers several entrepreneurial and business training programs -- some for Phase I and some for Phase II awardees. As permitted by the SBA's SBIR Program Policy Directive, the NIH has developed a menu of technical assistance programs that are targeted to companies' individual needs. The programs enhance the current phased award structure, provide commercialization assistance, facilitate partnering opportunities, and are essential in helping small businesses cross the proverbial commercialization "valley of death."

Niche Assessment Program: Often, scientists lack the entrepreneurial skills to assess whether there are other applications or niches for their SBIR-developed technology.

Often, true market value is underestimated. The Niche Assessment Program helps Phase I awardees assess the market opportunities and the needs and concerns of end-users and assists them in discovering potential new markets.

COMMERCIALIZATION AND MANUFACTURING ASSISTANCE PROGRAMS FOR NIH PHASE II GRANTEES

As noted in the recent National Research Council (NRC) SBIR study, a meaningful 40 percent of NIH SBIR-funded projects reach the commercial market. The NRC also noted that this is an impressive figure for such early stage research. Recent data from NIH's Performance Outcomes and Data System (PODS), a dynamic monitoring system that enables NIH to document the continued achievements of SBIR awardees over time, indicates that estimated cumulative sales increased over 200%, showing about 50% of SBIR awardees funded from 1992 to 2001 have achieved commercial sales.

Although commercialization is one metric for judging program success, NIH considers other metrics equally valuable in demonstrating success of its SBIR projects; these include published papers, patents, conduct of FDA-regulated trials, FDA approval/clearance of drugs and devices, Initial Public Offerings, and the use of the technology in other research projects. We have learned through the PODS outcomes updates from the 1992-2001 cohort of SBIR awardees that the number of those awardees receiving additional non-SBIR funding or capital increased 33%, and the number of awardees with FDA-approved projects increased 51%.

The commercialization pathway is long, arduous, and costly. Therefore, NIH has undertaken a series of initiatives to foster and assist NIH SBIR awardees in developing effective commercialization strategies.

The **NIH Commercialization Assistance Program (CAP)** provides entrepreneurial training assistance and one-on-one business counseling to Phase II awardees in order to develop and implement an appropriate business strategy aimed at commercializing the products resulting from their SBIR research projects. CAP culminates with an investment event at which the participants present their business opportunities to a targeted group of potential investors and/or strategic partners. A recent enhancement to the CAP makes available publicly the abstracts and company presentations upon completion of the CAP to facilitate the identification of commercialization partners after the opportunity forum. NIH is tracking each participating company's commercialization progress for 18 months following completion of the program. Although investments and deals take time to mature, we believe the CAP is having positive impacts on SBIR companies seeking investments and partnerships. For example, one company is developing a technology to create a living blood vessel. This exciting medical advancement holds promise for coronary bypass candidates, lower limb amputation candidates, and hemodialysis patients. As a CAP participant, the company has raised $17 million in private equity financing to fund some of their clinical studies.

We have found that 39 NIH-CAP companies have been able to raise over $68M in funding. In addition, the NIH-CAP has facilitated over 1400 contacts with investors, over 1100 meetings with investors and partners, 558 Confidentiality Disclosure Agreements signed, 302 negotiations with investors and partners, 138 initial proposals and term sheets, and 109 deals.

The **Manufacturing Assistance Program (MAP)** is aimed at helping SBIR Phase II awardees to identify, address, and develop a strategy to overcome the manufacturing

issues related to the commercialization of SBIR-developed products. In partnership with the National Institute of Standards and Technology's Manufacturing Extension Partnership (MEP) program (http://www.mep.nist.gov), participants will have access to MEP's nationwide network of non-profit manufacturing centers, which were established to assist small manufacturers in becoming globally competitive, supporting greater supply chain integration, and improving productivity. Each MAP participant is assigned to a MEP center that provides technical support, including but not limited to: method of scale up; cost estimation; quality control; prototyping; design for manufacturability; facility design; process development/improvement; vendor identification and selection; and plant layout.

A company participating in the MAP, Luxel Corporation, is working on an NIH SBIR project to improve specimen supports for Transmission Electron Microscopes (TEMs). A main objective is to design a manufacturing process that can mass produce TEM supports made of nano-thin polyimide membranes at a competitive price and in a clean sanitary environment. A MEP Center assisted Luxel in considering automation (e.g., robots), costing, and market size estimations. The Center saved Luxel engineering time and shortened their learning curve. Luxel now has a robot-controlled clean environment in which to mass produce nano-thin polyimide membrane specimen supports for TEMs.

The **NIH Pipeline to Partnerships** (P2P) is a virtual space for NIH SBIR/STTR awardees and NIH licensees to showcase technology and product development for an audience of potential strategic partners, licensing partners and investors. P2P helps NIH in advancing its mission by furthering the development of its own licensed technologies

or those for which it has provided SBIR/STTR funding. Currently, there are over 100 technologies in the searchable/indexed database.

CONCLUSION

In conclusion, I want to reemphasize that NIH is dedicated to improving the health of Americans through medical research. We are looking to small businesses to help us face new challenges and to produce not only new knowledge but also tangible benefits that touch the lives of every individual. We are confident that our continuing outreach efforts and actions to modernize the NIH SBIR/STTR programs will be helpful in that regard.

This concludes my statement, Mister Chairman. I will be pleased to answer any questions you may have.