SUBCOMMITTEE HEARING ON SBIR: ADVANCING MEDICAL BREAKTHROUGHS

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT
COMMITTEE ON SMALL BUSINESS
UNITED STATES HOUSE OF REPRESENTATIVES

ONE HUNDRED TENTH CONGRESS

SECOND SESSION

FEBRUARY 13, 2008

Serial Number 110-70

Printed for the use of the Committee on Small Business

Available via the World Wide Web: http://www.access.gpo.gov/congress/house

U.S. GOVERNMENT PRINTING OFFICE
39–790 PDF WASHINGTON : 2008

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

HOUSE COMMITTEE ON SMALL BUSINESS

NYDIA M. VELÁZQUEZ, New York, *Chairwoman*

WILLIAM JEFFERSON, Louisiana
HEATH SHULER, North Carolina
CHARLIE GONZALEZ, Texas
RICK LARSEN, Washington
RAUL GRIJALVA, Arizona
MICHAEL MICHAUD, Maine
MELISSA BEAN, Illinois
HENRY CUELLAR, Texas
DAN LIPINSKI, Illinois
GWEN MOORE, Wisconsin
JASON ALTMIRE, Pennsylvania
BRUCE BRALEY, Iowa
YVETTE CLARKE, New York
BRAD ELLSWORTH, Indiana
HANK JOHNSON, Georgia
JOE SESTAK, Pennsylvania
BRIAN HIGGINS, New York
MAZIE HIRONO, Hawaii

STEVE CHABOT, Ohio, *Ranking Member*
ROSCOE BARTLETT, Maryland
SAM GRAVES, Missouri
TODD AKIN, Missouri
BILL SHUSTER, Pennsylvania
MARILYN MUSGRAVE, Colorado
STEVE KING, Iowa
JEFF FORTENBERRY, Nebraska
LYNN WESTMORELAND, Georgia
LOUIE GOHMERT, Texas
DEAN HELLER, Nevada
DAVID DAVIS, Tennessee
MARY FALLIN, Oklahoma
VERN BUCHANAN, Florida
JIM JORDAN, Ohio

MICHAEL DAY, *Majority Staff Director*
ADAM MINEHARDT, *Deputy Staff Director*
TIM SLATTERY, *Chief Counsel*
KEVIN FITZPATRICK, *Minority Staff Director*

SUBCOMMITTEE ON INVESTIGATIONS & OVERSIGHT

JASON ALTMIRE, PENNSYLVANIA, *Chairman*

CHARLIE GONZÁLEZ, Texas
RAUL GRIJALVA, Arizona

VACANT, *Ranking*
LYNN WESTMORELAND, Georgia

CONTENTS

OPENING STATEMENTS

WITNESSES

APPENDIX

SUBCOMMITTEE HEARING ON SBIR: ADVANCING MEDICAL BREAKTHROUGHS

Wednesday, February 13, 2008

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON SMALL BUSINESS,
SUBCOMMITTEE ON INVESTIGATIONS & OVERSIGHT
Washington, D.C.

The Subcommittee met, pursuant to call, at 10:00 a.m., in Room 2360 Rayburn House Office Building, Hon. Jason Altmire [chairman of the Subcommittee] presiding.

Present: Representatives Altmire and Graves.

OPENING STATEMENT OF CHAIRMAN ALTMIRE

Chairman ALTMIRE. I call this hearing to order. Mr. Graves is going to be joining us shortly, but I don't want to delay the proceedings any more. If we start into the testimony and he arrives, I'll halt it at the end of who is ever speaking and we'll allow him to make his opening statement at that time.

I am calling this hearing this morning through the Subcommittee on Investigations and Oversight and we will continue to review the Committee on Small Business Investment Research Program.

This hearing examines how SBIR is laying the foundation to fight disease and advance medical breakthroughs. Through this initiative to date nearly $600 million has gone to small firms researching national health and wellness priorities. There are many examples of health care therapies that have been developed as a result of SBIR funding. These include vaccines for biodefense and food safety, novel anesthesia delivery devices to relax children during medical procedures and improved monitors to control blood glucose levels.

SBIR has also spearheaded the discovery of safer methods for laser vision correction, needle-less infusion patches to deliver drugs such as insulin and improved research tools for studying dementia. These examples make it clear that SBIR is on the cutting edge of improving the quality of health care. We must, however, take steps to make it more responsive to today's medical challenges. This includes expanding the number of companies replying to research solicitations. This is an important issue for at least two reasons. First, the National Institutes of Health reports an alarming decrease in SBIR applications since 1994; and second, a recent National Academies of Science study recommends that all federal agencies increase their efforts to encourage women and minority-owned businesses apply for SBIR awards.

This Subcommittee will also focus on initiatives that the NIH has developed to support the successful commercialization of SBIR-funded research. The Pipeline to Partnership database, NIH's pilot program in conjunction with the manufacturing extension partnership and the Agency's decision to support promising projects with multiple SBIR awards are initiatives that other participating agencies should consider as potential avenues to encourage higher rates of commercialization.

Finally, we will consider how to further encourage research in fields that suffer from chronic under-funding including orphan diseases which are not receiving the capital they need to advance new therapies.

Going forward, the Committee will look at ways to address these funding shortfalls. The region I represent in western Pennsylvania boasts some of the best medical research and development in the nation and last year the State brought in nearly $75 million in SBIR grants, ranking ninth nationally.

We have tools and infrastructure necessary to lay the groundwork for the development of innovative medical technology, equipment, and therapies. RedPath Integrated Pathology, a small company based in Pittsburgh, Pennsylvania, is a prime example of how the SBIR program can take an innovative idea to corporate success. RedPath was awarded an SBIR grant that enabled it to compete and validate key aspects of the molecular-based tests that could facilitate earlier, more personalized and more definitive cancer diagnosis.

The positive result of this research led RedPath to introduce Pathfinder TG, a diagnostic tool that is now being used to combat one of the leading diseases affecting the American public. It also spawned an enterprise that created more than 40 highly-skilled jobs in just four years with a goal of doubling its growth this year. However, without the initial grant from SBIR, RedPath may never have been able to survive and grow into the successful company that it is today.

This is just one example of medical breakthrough technology that is a result of SBIR illustrating the importance of the program and all it has to offer. Should we fail to support our innovative researchers and technological advancements we will lose the technological edge that allows this nation and our economy to expand, and in RedPath's case to improve patient care.

With the Committee working to reauthorize SBIR this year today's hearing will provide testimony central to the SBIR program's on-going effectiveness. During this time, it's important that we modernize the program so that it can create the medical breakthroughs of tomorrow, while still promoting job creation in our local communities.

Over the last 25 years, the SBIR program has contributed to the emergence of some of the world's most innovative and successful life science companies: Amgen, Biogen, and Chiron are all graduates of the SBIR program. At it's most effective, the SBIR program provides seed funding that will provide the next decade's Amgen with its start, while also incorporating America's small life science research firms to help reduce the burden of illness on the American public.

So I thank the witnesses for being here today and look forward to all of your testimony.

And at this time, if he's ready, I recognize Mr. Graves for his testimony.

OPENING STATEMENT OF MR. GRAVES

Mr. GRAVES. Thank you, Mr. Chairman. Thank you very much. Good morning, everyone. I'd like to welcome all of you to this hearing on the Small Business Innovative Research Program or SBIR, and its role in the development and commercialization of innovative health care technologies.

I'd also like to extend a special thanks to each of our witnesses who have taken the time to provide this Subcommittee with their testimony. I also especially would like to welcome Dr. Nicholas Franano who is the Founder and Chief Scientific Officer for Proteon Therapeutics, Incorporated, a biotech company located in Kansas City, Missouri. Welcome, Doctor. I appreciate you being here.

As part of the 2000 SBIR program reauthorization, Congress required the National Academy of Sciences, the National Research Council to conduct a comprehensive review and assessment of the SBIR program. Using the NRC report as a starting point last month, the House Small Business Committee started its review of the SBIR program which was last fully examined by this Committee in 1999 and reauthorized in 2000. It should be noted that the core finding of the NRC report is that the SBIR program is sound in concept and effective in practice.

Today's hearing represents a continuation of this Committee's work to review and reauthorize the SBIR program and we'll focus on how SBIR reauthorization can better structure the program to address its role as a vehicle in the early stage development of innovative medical technologies, therapies, products and drugs.

Created in 1982, the development of the SBIR program is not only critical to the unique needs of each of the participating federal agencies, but also to our national economy. Small biotech businesses play a key role in innovative research resulting the commercialization of cutting edge medical technologies. For the small business biotech entrepreneur, it is a vehicle that provides essential early stage development funding for promising biotech drugs with the added benefits of ensuring there is no dilution of ownership and that no repayment is needed like in traditional modes.

Agile investors, venture capital investors, and other early stage investors rely on the data developed from this early stage discovery and initial development to establish a promising proof-of-concept in order to make investments to support the further development of such technologies.

At last month's hearing, it was pointed out that the SBIR program's current eligibility requirements effectively prevent some small business biotech firms from participating in this program. One of the structural barriers is based on the biotech industry's need for access to large sums of capital. This and other barriers can prevent pursuit of innovative medical therapies, causing a good amount of these products never be fully developed and marketed.

Today's hearing is part of the Committee's fact-finding process to find ways of making the SBIR program more efficient and effective in its role in innovative health care research resulting in the commercialization of cutting edge biotech technologies.

Mr. Chairman, I look forward to working with you on this important issue. Again, thank you to each of you for being here today. I know some of you traveled a fair distance and I appreciate it.

Thanks, Mr. Chairman.

Chairman ALTMIRE. Thank you, Mr. Graves. And I'm going to recognize the witnesses one at a time. We'll give the introduction and then the witness will speak and then we will introduce the second witness and so forth.

So at this time I want to recognize—well, let me explain the light system first. You'll have five minutes to give your remarks when you see the green light. That means you're okay. when you see the yellow light you have one minute left; if you could start to sum up your remarks at that time and at the red light, your five minutes would be up.

At this time I would like to introduce Ms. Jo Anne Goodnight who serves as the Small Business Innovation Research and Small Business Technology Transfer Program Coordinator at the National Institutes of Health. NIH is the primary federal agency for conducting in supporting medical research and administers one of the federal government's largest SBIR programs.

During her 25 years of service, in addition to her positions at NIH, Ms. Goodnight has held positions at the USDA and the Food and Drug Administration.

Welcome, Ms. Goodnight, and we look forward to your testimony.

STATEMENT OF MS. JO ANNE GOODNIGHT, SBIR PROGRAM COORDINATOR, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MD

Ms. GOODNIGHT. Thank you. Good morning, and thank you for the opportunity to discuss the NIH SBIR program and its contribution to the development of important medical advances.

Part of a complex innovation ecosystem, the SBIR program provides dedicated funding for small businesses to conduct early stage research and development on innovative projects with commercial potential for medical solutions and breakthroughs.

Overall, the SBIR program has complemented NIH's mission to advance science while reducing the burden of illness on public health. However, 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 ideally suited for stimulating technological innovations funding early stage high-risk research and advancing medical breakthroughs. As mentioned, Altea Therapeutics is developing the passport system, a needleless infusion patch for painless delivery of drugs such as insulin and vaccines, such as Hepatitis B antigen through the skin.

NIH-SBIR projects are stories of discovery. We've all read headlines such as these: a three-year-old grabs a frying pan of boiling hot oil off the stove. The tip of an 80-year-old woman's housecoat

catches on fire as she reaches for a tea kettle. Twenty years ago, second and third-degree burn injuries from such situations were routinely fatal. With NIH support, Integra Life Sciences Corporation developed an artificial skin system called Integra Matrix Wound Dressing, a wound care product that helps create a scaffold for damaged cells to regenerate and capillaries to grow. This product is saving and improving lives of millions of affected Americans.

Also, as already mentioned in your opening statement, RedPath Integrated Pathology is focused on early detection of cancer, using a technology that will result in an important advancement in personalized medicine for resolving diagnostic dilemmas.

It is important to note that the NIH SBIR program funds a wide diversity of promising ideas and companies beyond drug development and therapeutics. Examples include medical devices, assistive technologies and research tools which are described in more detail in my written statement.

Many of these scientific advances 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 general as any disease, syndrome, or disorder affecting fewer than 200,000 people in the United States. NIH supports research in rare diseases and related conditions and awards to SBIR and STTR recipients help facilitate NIH's research mission in regard to these rare diseases.

Since 1983, the NIH, SBIR, and STTR programs awarded about $630 million for orphan or rare disease projects. This is nearly 10 percent of the $6.5 billion awarded for those projects during that period.

Some projects underway include the development of a malaria vaccine, a potential treatment for amyotrophic lateral sclerosis, commonly known as Lou Gehrig's Disease and potential treatments of patients of autism of Tourette's Syndrome.

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 deceasing and the number of applications declining. There are outreach efforts and program enhancements. We are aiming to recruit more SBIR applicants that have innovative research ideas that could improve human health.

We participate in national, regional and state conferences all around the country, especially those focused on increasing the participation of small firms owned by women or socially-disadvantaged individuals. Our participation in Maryland's Minority Research and Development Initiative, SBIR from Awareness to Awards and Commercialization, and Alabama A&M University's 2008 SBIR Conference are just two recent examples.

We're also very excited about our tenth annual NIH SBIR Conference to be held in Atlanta on July 22nd and 23rd. To reach a broader audience, we've started using other outreach avenues, including interactive video conferencing and webinars. And we find the NIH small business research funding opportunities web site to be key in communicating information such as programs, procedures, technical assistance and partnering opportunities such as NIH pipeline to partnerships.

Recruitment efforts may be impacted if incentive opportunities and program enhancements are not clearly identified or understood. One major challenge for small businesses is the long gap between the end of Phase 1 and the beginning of Phase 2, so to address this challenge we offer several gap funding programs and the opportunity for applicants who are unfunded to resubmit their application twice. We're continually assessing new avenues to recruit more applicants and make them more aware of our programs.

Turning now to the topic of programs aimed at helped SBIR awardees cross the proverbial commercialization "Valley of Death", currently we offer three programs, a technology Niche Assessment Program for Phase I awardees; and for Phase II awardees, a commercialization assistance program and a manufacturing assistance program. Under CAP, just one example is a company developing a technology for creating living blood vessels, a medical advancement that holds promise for coronary bypass and lower limb amputation candidates and hemodialysis patients. This company has raised $17 million in private equity financing to fund some of their clinical studies.

In conclusion, I want to re-emphasize that NIH is dedicated to improving the health of Americans through medical research and we're looking to small businesses to help us face new challenges and to produce not only new knowledge, but also products that will allow people to live longer and healthier lives. We're confident that our continuing research outreach efforts and actions to modernize the NIH SBIR and STTR programs will be helpful in that regard.

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

[The prepared statement of Ms. Goodnight may be found in the Appendix on page 29.]

Chairman ALTMIRE. Thank you, Ms. Goodnight. I would now like to introduce Ms. Amy Comstock Rick. She is the Chief Executive Officer of the Parkinson's Action Network. Before joining PAN in 2003, she served as the director of the U.S. Office of Government Ethics, having accepted the nomination to the Senate confirmed position in 1999. Prior to her appointment to the Office of Government Ethics, Mrs. Rick was associate counsel to the President in the White House Counsel's Office. Welcome, Ms. Rick, and we look forward to your testimony.

MS. AMY COMSTOCK RICK, CHIEF EXECUTOR OFFICER, PARKINSON'S ACTION NETWORK, WASHINGTON, D.C.

Ms. RICK. Thank you. Thank you, Chairman Altmire, Congressman Graves for inviting me to testify on behalf of the Parkinson's Action Network about the SBIR program.

The Parkinson's Action Network represents the entire Parkinson's community on public policy issues, so I am here on behalf of the Michael J. Fox Foundation, the Parkinson's Alliance, the Parkinson's Disease Foundation, the National Parkinson's Foundation, and the American Parkinson's Disease Association.

Quite briefly, let me give you a picture of Parkinson's disease. It is the second most common neurological disease. It is a chronic,

progressive disease that results from the death of the dopamine-producing cells in the brain.

We don't really know the cause yet, although we think it's a combination of genetic and environmental and there is no cure. And in fact, the treatment that we currently have it's quite sobering. The treatment that we currently have was approved about 40 years ago. It is still the primary treatment and it is only a symptomatic treatment. We have nothing that slows the progression of the disease. And in fact, the symptomatic treatment only tends to work well for five to eight years.

I tell you this to get a picture of the Parkinson's community and the want and sometimes desperation for better therapies for Parkinson's disease.

Before I begin to discuss the SBIR program specifically, it is helpful, I believe, for me to explain the context in which the Parkinson's community views all NIH, National Institutes of Health programs. As you know, I am sure, NIH is the largest single source of Parkinson's disease research dollars in the world. And the basic discoveries coming out of NIH, of course, are very important. But it is our belief, as I've testified before the House Appropriations Committee in the past, that NIH should focus more of its resources on therapeutic outcomes rather than basic research. And again, if you'll bear with me for a second to talk a little bit, the drug development time line can be phenomenally long. The fastest might be 15 years depending on where you begin with your basic research idea. It could be 40. And it begins with NIH funded research, and of course ends with the pharmaceutical companies shepherding their products through, hopefully through the door in approval by FDA.

But that's a very long time-line and where there is a drop-off after NIH funded research at academic institutions with basic research, where the expectation in our country is that the private market, the free market companies, would pick up those bright, potentially bright ideas and move them through the pipe line. But in fact, there is nobody who shepherds these ideas through and it is very possible that a potentially promising therapy or bright idea might drop off or languish for some time before a company, private researcher, privately funded researcher picks it up and then can move it through.

I tell you this because it is that potential drop off that is referred to as the "Valley of Death", which is quite sobering for the Parkinson's community. And in fact, the Parkinson's Action Network's position for a number of years has been to try and get the NIH to move more into that black hole, that "Valley of Death" to translate more basic discoveries into possible therapies. In fact, we have not seen that kind of movement at NIH and with recent flat-funding for NIH, Dr. Zerhouni has even testified that the cuts will have to come in the area of translating discoveries from the laboratory to patients.

In my position as the CEO of the Parkinson's Action Network, I often will have to explain to people with Parkinson's that in fact, in our country, there is no process for shepherding drugs and bright ideas directly through and that sometimes a potential therapy can languish while waiting for a company to pick it up and run

with it. So having said this about our, the Parkinson's Action Community's vision of a greater need to focus more resources on turning young and bright ideas into therapies, it should be clear while the Parkinson's communities is so strongly supportive of the SBIR program. The SBIR program supports cutting edge research where other sources of funding are difficult and if not impossible to obtain.

But in fact, as we look at it, it is not just a question of funding sources. It is actually for some of what we believe the SBIR program funds, it is the difference between this research happening and not happening. Having stated our strong support for the NIH SBIR program, however, I do want to offer a recommendation for the future. As this Committee is well aware and as Ms. Goodnight referred, there was a 2003 SBA ruling regarding SBIR eligibility based on majority ownership by individuals and this has had, in our view, a negative impact on the biomedical research community. It is my understanding that since that ruling application have dropped precipitously, about 12 percent in 2005, 15 percent in 2006, and then 21 percent in 2007. And given the increase in most applications at NIH, it is fair to assume that this drop is a direct result of the eligibility ruling.

From a patient perspective, it does not seem logical and it is in fact scary to eliminate from eligibility research projects that otherwise merit funding because of the financial structure of the company. And the reasoning, quite frankly, even becomes more muddled to us when you talk about that fact that we're focusing on the companies that are being excluded are in fact the very same companies that are attracting venture capital funding. So they are clearly considered to be efficient, moving forward. They're doing something well if they're attracting funding and then we eliminate them from federal funding.

It is also scary because when we talk about high-risk funding, that SBIR can fund, Parkinson's Disease, as I've said, is a disease of one million people and that is not considered to be a large market. Alzheimer's disease is four and a half million, for example. So we are the population that is sometimes considered high risk. Not the science, but we're not a big market.

I do want to quickly before I wrap up give you a sense of the impact of the SBIR program. There, as I've told you, Parkinson's disease is still being treated very much as is it was in 1967. That is kind of scary. But we have a clinical trial right now going on Phase II. Spheramine actually takes retinal cells that do have an impact on dopamine production and injects them surgically into the brain and it promotes additional dopamine production in the brain. It is still early, but so far the results are promising and the community is excited about it.

But the early research for this now Phase II clinical trial was funded by an SBIR grant, the animal research as well as Phase I. And we fear and it is our understanding, before 2003, that this research would not now be funded and we fear then that it would have languished as others do.

As PAN continues working towards better treatments and cures for Americans, we respectfully seek the support of this Committee for the SBIR program. SBIR is an essential program for funding for

patient-oriented research, currently languishing in what we call the "Valley of Death." We respectfully request your support to include, however, revision to not eliminate small companies simply based on their financial structure.

Thank you again for this opportunity to testify and my more complete written record has been submitted.

[The prepared statement of Ms. Rick may be found in the Appendix on page 44.]

Chairman ALTMIRE. Thank you, Ms. Rick.

I would now introduce Dr. Mel Billingsley from my home state of Pennsylvania. He is President and CEO of the Life Sciences Greenhouse. The Life Sciences Greenhouse of central Pennsylvania has a goal to advance the life sciences within the Commonwealth of Pennsylvania. The organization supports new and expanding commercial entities in Pennsylvania through direct investment and selective delivery of business development services. Dr. Billingsley also serves as Professor of Pharmacology at Pennsylvania State University's Milton S. Hershey College of Medicine and Professor of Biotechnology and Entrepreneurship at Penn State's Harrisburg Campus. Dr. Billingsley is testifying on behalf of the Pennsylvania Biotechnology Industry Organization and I welcome Dr. Billingsley. We look forward to hearing you.

STATEMENT OF MR. MEL BILLINGSLEY, PH.D., PRESIDENT AND CEO, LIFE SCIENCES GREENHOUSE, HARRISBURG, PA, ON BEHALF OF PENNSYLVANIA BIO

Dr. BILLINGSLEY. Thank you Chairman Altmire, Ranking Member Graves, and other Member of the Committee for giving us this opportunity to address the importance of the SBIR program for the development of medical innovations in our country and in our state in specific.

I represent the Life Sciences Greenhouses of Pennsylvania, my fellow CEOs John Manzetti of Pittsburgh, Barbara Schilberg of BioAdvance, and also Pennsylvania Bio which is an organization that represents over 300 companies involved in the life sciences, medical devices and the like.

I also represent the State of Pennsylvania which is one of the larger funded entities from the National Institutes of Health representing the fifth highest state of NIH basic research funding in the past year.

What I'd like to point out are the needs of the emerging companies and how SBIRs help them, some of the issues that are raised as mentioned in the "Valley of Death", some of the issues raised by eligibility and possibilities of how to fix them by being more flexible and allowing larger amounts that are determined by individual programs which support the SBIR program.

Emerging companies are incredibly fragile. It takes a large sum of money and a lot of time and a lot of risk to bring a drug or a therapeutic device to the market. Pennsylvania Greenhouses were formed specifically to aid that process and we have seen, as you can see in our written testimony, incredible demand for our services. We've invested well over $35 million into over 100 separate small companies, all of which have leveraged over $500 million of

follow-on investments in a range of these companies. This is a leverage greater than 10 to 1, and it has provided 2600 new, sustaining jobs in Pennsylvania.

Federal funding like the SBIR programs have been critical to these developing companies by both validating their technology and leading to additional investments from outside sources such as ourselves and venture capital. We need venture capital to advance therapeutics because of the incredible costs and time. In addition to the time, the cost of bringing a therapeutic, even in an orphan area, are in the tens of millions of dollars to advance a clinical trial, far beyond that which could be provided by an SBIR program.

Let me give you an example of three companies successfully funded by SBIRs in the State of Pennsylvania. In the Philadelphia area, Yaupon Therapeutics, supported by BioAdvance, has garnered well in excess of $10 million of federally-sponsored SBIR funding including $700,000 for orphan drug development for a specific drug for lymphoma. They've been successful and have now gone on to get $15 million in venture funding.

Azevan, supported by LSGPA, received $800,000 in phase two support from NIMH to develop a drug for treating aggression. They are now venture funded and are proceeding to the clinic. And in Pittsburgh, which has an aggressive SBIR training program, they developed a series of companies, one of which is the company Cohera. Cohera is developing a surgical glue for use in intra-surgical procedures, now has SBIR funds and leveraged that into venture-backed funding to develop their product for the clinic.

Clearly, though, improvements are needed for successful programs. One is obvious: the eligibility for venture-backed programs needs to be reconsidered and restored. It is the case that venture funding is necessary and in fact, the sign of approval that a company is moving forward. As mentioned before, excluding these companies is counter intuitive and illogical.

The second point is that there are needs for larger grant programs. Specific cases are best administered by the programs that are funding them such as the NCI or the NIH. The set amounts that are used span across the agencies from DOD to NIH; it is not a one size fits all and I believe that providing flexibility within the institutes themselves gives greater jurisdictional control and a greater sense of the funding needs.

To give you a specific example of venture-backed company being excluded from the SBIR program—BioRexus was a successful Philadelphia-based bio company that was developing a protein drug for diabetes. It became venture backed but subsequently, in that same time frame, had a program to develop a botulism anti-toxin that was highly favored by the DOD. They could not pull down that SBIR funding; that program came to a grinding halt, even though BioRexis was successful.

And as we all know, companies have failed on their first attempts. Cephalon and Centocor are two prime examples, of highly successful companies where both first drugs failed. So to limit the program to just one time, one shot at goal really limits the chance of the company's success and is illogical.

"Valley of Death." We have a saying in the Greenhouse, ″build bridges not piers.″ So we're trying to build a bridge over the "Valley

of Death", not a pier to drop people off in deep water and what often happens is that the funds provided by the SBIR and other entities at the early stages are not sufficient to cross the valley, so companies wind up at a critical period in the middle of a very deep pond of water.

So, we think that programs such as the NSF phase two B program that provides additional funding, highly competitive, selective, but matched by outside capital, may be the way to think about developing programs that can bridge this.

So in summary, I would say that the SBIR program has had an unbelievably positive impact on the development of novel medical therapeutics, on health and well being. These investments are worthy and they are peer reviewed. They get a cache of scientific respectability and, importantly, they provide the fundamental basis for other investors, like ourselves and venture groups, to provide the next stage of funding in order to develop successfully.

So we welcome the opportunity to weigh in on these issues and thank you for your time.

[The prepared statement of Mr. Billingsley may be found in the Appendix on page 48.]

Chairman ALTMIRE. Thank you, Dr. Billingsley, and as you probably all noticed the vote buzzer went off while you were speaking. So we have one vote. It's a procedural vote and then we're going to run back. I'm going to recess for the vote and I will say at 10:45, we will reconvene. Thank you very much.

(Off the record.)

Chairman ALTMIRE. This hearing will come back to order. I was pretty close. We may have continuing procedural votes, it appears throughout the day, so we're going to try to move quickly, but please take your time and say what you have to say. When you hear the buzzer, don't hurry up. We'll worry about the schedule.

So at this point, I would like to thank Dr. Billingsley for his testimony and Dr. James Stefansic is our next witness. He is the Chief Operating Officer at Pathfinder Therapeutics, a medical device company focused on improving patient outcomes during therapeutic procedures through the use of medical imaging.

Before joining Pathfinder, Mr. Stefansic, am I pronouncing that correct? Dr. Stefansic worked as a research assistant in the Surgical Navigation Apparatus Research Lab, a division of the Center for Technology Guided Therapy in the Department of Biomedical Engineering at Vanderbilt University.

Dr. Stefansic is testifying on behalf of AdvaMed. Welcome and we look forward to hearing your testimony.

STATEMENT OF MR. JAMES D. STAFANSIC, PH.D., M.B.A., CHIEF TECHNOLOGY OFFICER, PATHFINDER THERAPEUTICS, INC., NASHVILLE, TN, ON BEHALF OF ADVAMED

Dr. STEFANSIC. Thank you, Mr. Chairman. We thank the Subcommittee for holding this important hearing today on the SBIR program and its role in advancing medical breakthroughs. I'm going to talk a little bit about my experiences as a company that receives several SBIR grants.

First, let me tell you a little bit about AdvaMed. Pathfinder is a member of AdvaMed, the Advanced Medical Technology Association which represents over 1,600 of the world's leading medical technology innovators and manufacturers of medical devices, diagnostic products, and medical information systems. Over 70 percent of AdvaMed's member companies are relatively small, with sales of less than $30 million a year. Our constant innovation leads to the introduction of new technologies that prevent illness, allow early detection of diseases, and treat patients as effectively and efficiently as possible.

Pathfinder is a surgical technology company focused on the world's first image guided surgery systems for soft tissue applications. Pathfinder was incorporated in July 2004 through a partnership with Vanderbilt University, where the initial technology was developed by six current and former clinical and engineering faculty members, including myself. With support and guidance from Vanderbilt, Pathfinder was fortunate to acquire a very modest seed round investment to launch the company. In 2005, Pathfinder was awarded a $1.5 million SBIR grant from the National Cancer Institute. These funds had been used to develop the SurgiSight image guided therapy platform for multiple applications with an initial focus on liver surgery.

In 2006, Pathfinder received a second SBIR grant worth $1.9 million to conduct a three site clinical trial. One of our sites, by the way, is the University of Pittsburgh Medical Center. With our Linasys device, which is an image guided liver surgical system that can be used to pinpoint and accurately resect or ablate tumors located deep within the organ. Essentially, this like a GPS system for surgery. Our greatest achievement to date was being granted FDA clearance in late December 2007 for our Linasys device. Pathfinder now has overcome much of the technology and regulatory risk associated with bringing a new medical device to market. But these risks would not have been conquered without both SBIR grants and the modest seed round investment in the company.

The costs of these risks can be staggering and are often not supported in full by early stage venture capital or angel funding. To place the SBIR's value in perspective, note that seven of our eight current employees are funded at least in part by the SBIR grant. Considerable R&D expenditures, in addition to some corporate overhead and other expenses, have been and continue to be covered with SBIR funding. Still, many challenges remain to ensure that our technology could improve the lives of those suffering from abdominal cancer, and those challenges will continue to require a combination of both SBIR and other funding sources such as venture capital

First, we will continue to need funds for all the overhead side of the business, beyond research and development, including accounting, legal, quality, regulatory, marketing, and sales issues. These activities are critical to the success of the company in bringing new technologies to patients. They are largely not covered by SBIR funding.

Second, we will continue to need SBIR funding for further research and development to develop the next applications of our image-guided technology. Unfortunately, the 2003 interpretation of

SBA regulations may exclude Pathfinder from seeking SBIR grants even though we are still in need of assistance. The SBA's ruling is completely at odds with the intent of the SBIR program to assist small businesses like ours with enormous tasks of developing promising early-stage technologies so they can be brought to market for the benefit of patients.

It also overlooks the nature of venture capital investment today. Venture capitalists are becoming more and more risk averse. They are now investing in later stage companies in order to reduce their risk profile and focus on companies that are already generating revenue or have completed human clinical trials.

Unfortunately, because we have continued to be provided with bridge financing of our seed round venture capital investors, Pathfinder will very soon no longer be eligible for any additional SBIR funding given the change of our ownership structure. We hope Congress will address this issue soon so companies like Pathfinder can continue to grow and bring technologies to market for the benefit of all patients.

I do want to commend the NIH and NCI for their additional initiatives to help bring small companies, to help small companies get their novel technologies to market. For example, Pathfinder has recently benefited from the NIH SBIR manufacturing assistance program. This assistance will not only ensure that we meet all necessary national and international regulations in the manufacturing of the Linasys device, but also improve the overall quality of our facility.

Although this program is beneficial, it is very small compared to a phase two SBIR grant and will not fill in all the gaps necessary to commercialize our medical technology. We believe that addressing the venture capital issue should be a top priority if Congress intends to help small companies like Pathfinder that rely on SBIR funding to develop new medical technologies for patients.

We thank you, Mr. Chairman, Chairwoman Velázquez, and Congressman Graves for your leadership in the reauthorization of the SBIR program and for your strong support for restoring SBIR eligibility for small businesses like ours that also have venture capital investment. We also want to thank Congressman Chabot for his willingness to work with us to resolve this important issue.

We look forward to working all of you to ensure that small businesses will continue to drive medical innovation in developing promising new technologies for patients. Thank you.

[The prepared statement of Mr. Stefansic may be found in the Appendix on page 53.]

Chairman ALTMIRE. Thank you, Dr. Stefansic, and Mr. Graves wanted me to again recognize Dr. Franano. Dr. Nicholas Franano is founder and Chief Scientific Officer at Proteon Therapeutics. Founded in 2001, Proteon Therapeutics is a privately-held biopharmaceutical company developing novel pharmaceuticals to address the medical needs of patients with renal and vascular diseases. Proteon Therapeutics' first drug candidate is in development for the improvement of blood flow following vascular surgery procedures.

Dr. Franano holds an M.D. and an M.A. in Biomedical Research from Washington University, St. Louis, and a B.S. in Cell Biology from the University of Kansas.

Welcome, Dr. Franano.

STATEMENT OF NICHOLAS FRANANO, M.D., FOUNDER AND CHIEF SCIENTIFIC OFFICER, PROTEON THERAPEUTICS, INC., KANSAS CITY, MO

Dr. FRANANO. Thank you, Chairman Altmire, Ranking Member Graves and other Members of the Committee. I do thank you for the opportunity to share some thoughts with you today and I think it's an excellent topic and excellent panel. I concur with almost everything that's been said today and would like to provide some personal experiences that might help highlight the issues that we're discussing today.

I've been in that position where you make an invention. And it's a really interesting thing that happens. I was a biologist, went to medical school. Was recruited to Hopkins by Dr. Zerhouni when he was in the Radiology Department there, now the Chairman of the NIH and he provided me the opportunity to do a substantial amount of laboratory work while I was in my residency training. And so some days I would go to the Interventional Radiology Suite and do patient care and other days I would go to the laboratory and it was a great environment in that I could see problems in the clinical side and then think about how to solve those problems on the research side.

So in interventional radiology, we're basically glorified plumbers. We open up blood vessels and keep them open. I mean you like to think it's exciting, but it's really plumbing at its basic level. With expensive tools. And so the big problem we have is often the pipes are too small and so we put in stents and we use balloons and we do bypass grafts, we do all these mechanical things, because we have patients who can't get enough blood flow and not enough blood flow is bad in a lot of situations.

So what you find is you do an angioplasty. You do a stent. You do a bypass graft. All that fails. You amputate a person's leg and you put it in a bucket and that really drives home failure. Nothing is worse than having a patient come to your office with a problem and is wheeled out of the hospital without a leg. That tends to really focus your mind on why you're failing.

So when I was in the laboratory, I started looking at how the body naturally dilates blood vessels and discovered a drug that could dilate blood vessels without any mechanical effect at all, which was very exciting to me and Hopkins was very excited and we filed patents and I left to go into private practice. I started a family. I went back to Kansas City and the thought was a biotech company is going to pick this up and develop it.

When it came time to file the world-wide patents they have offered the technology to several biotech companies, but none had picked that up and the message was there wasn't enough data to support a $50 million investment in the drug at an early stage. And so Hopkins asked if I wanted to buy the technology back and start a company myself which was a very provocative thought to me. When I had the invention I knew right away that this would

work. I was absolutely convinced that this would work. I'd seen it with my own eyes. I had—couldn't find a problem with it. So— but it's a very difficult kitchen table conversation to have with your husband or wife that I'm going to quit my job which is paying well, and I have a baby on the way and I'm going to quit my job. I'm going to borrow money from my friends and family and start a biotech company with the hope that things are going to work out. That's a tough conversation to have.

My wife was supportive, remarkably, but a big question was how are you going to fund the first year? And how are we going to live while you go chase this idea? And so the SBIR program for me was an argument that I could use to say I'm going to apply for these grants and if we're successful in getting the grants, there will be some money to get the company off the ground and that was a really big part of it for me and one of the things I would emphasize to the Committee is people have novel and innovative ideas all the time.

Today, as we sit here, somebody is having a novel idea that could lead to an important therapy that could help people. And then the question becomes can I—how hard is it for me to start a company and commercialize that technology? The barrier is getting people started and the SBIR program can help get people started.

So we did apply for those grants. We were successful. We got $157,000 grant and then a $100,000 follow-on grant and we were able to use that grant money to build out our own laboratory which was absolutely vital for our company to get its venture capital financing and move this product into clinical development. Without that initial grant, we would not have built out our laboratory and we would not have I don't believe been able to get the venture capital investment that got our drug into the clinic.

So absolutely, the program was vital to Proteon. I think we're a success story. Our drug is going to go into clinical development this year. It looks very good. But we are again caught in the same problem others are now as we have some innovative new drugs that we would like to develop. And I'm going to go to a board meeting later today and I'm going to advocate that the company devote a substantial amount of money to one of these new programs. And I'm a decent vote counter. I'm going to lose that argument, so I've made the argument before and lost and I'm going to make the argument again. The venture capitalists invested $19 million in Proteon and they devoted that money to our lead drug program and it's very hard for me as Chief Scientific Officer to get $50,000, $100,000, $150,000, $200,000 for a new program when we need $50 million more to develop our lead.

And so normally prior to the rule change I would have applied for an SBIR grant and gotten that program started, but now I can't, so I can't move the new technologies forward, but I can't leave them behind. So I do think that it's surprising the drop off in SBIR grants. I think that should be a warning. That's a canary in the coal mine that there's something wrong with the company. And I think eligibility is a big part of that. So I would encourage the reauthorization of the program with the changes in eligibility to go back to the old rules because I think technologies are not

being developed and that has both a human and a financial impact on the country.

I think venture-backed companies are the most innovative companies and we're 20 people. We have a little lab off the plaza in Kansas City. We're a small business. Four years ago, we were in my basement. The idea that we look just like a small business looks except that we have some very powerful investors.

And I think it seems unfair to me that the rules allow—say that we're not a small business, that somehow the employees of our venture capitalists and the employees of the other companies that they invest in somehow count towards our total to me is I think nonsensical. I think really stretches the credibility of the people making that argument.

I couldn't go and get help from a company that our venture capitalists invest in. They're not part of us any more than I could go to another place. So I would concur with the prior remarks and would say that although it's been a success for us, I think that the program can be more successful if we went back to the old rules.

Thank you very much.

[The prepared statement of Dr. Franano may be found in the Appendix on page 59.]

Chairman ALTMIRE. Thank you. And I was going to—I'm still going to talk about how Mr. Graves and I work together hand in hand on this bill. It's a great example of bi-partisan cooperation. Chairwoman Velázquez and Ranking Member Chabot, same thing. Unfortunately, on the floor today, we're debating an issue on which there is some disagreement. So that is why these procedural votes are taking place and I do apologize, but I believe, is there a vote on—okay, there's another vote and I have a lot of really good questions, so I'm going to have to make it suspenseful for you and go vote and maybe find Mr. Graves or maybe have a surprise person if I can find someone to come back. But I have questions, so if any of you have to leave or your staff have to leave, I understand and I apologize for this, but I will return to reconvene the hearing at approximately 20 after 11. Thank you.

(Off the record.)

Chairman ALTMIRE. We will reconvene, and you can imagine my excitement. I came back and there is a huge line over there. There's a lot of TV cameras and I thought wow, we're generating a lot of interest. Then I heard it is because Roger Clemens is testifying in the next room over. So when you leave, you may want to go the other way. I recommend it.

(Laughter.)

Thank you for waiting. Sorry, and I'm told there may be further votes that are going to be coming up shortly.

My first question is for Ms. Goodnight, and again, thank you all very much for your testimony. Ms. Goodnight, research has found that SBIR grants encourage University based Ph.D. researchers to found companies. Of course, running a company demands skills that not all Ph.D. researchers possess. How important are available business skill training initiatives to the eventual success of a company founded with an SBIR award?

Ms. GOODNIGHT. Those types of skills are extremely important and so much so that we offer a commercialization assistance program to assist those companies that don't necessarily have the business savvy on seeing products that have done well and met certain milestones through the R&D reach the marketplace. And so, for example, our commercialization assistance program is about a nine or ten month entrepreneurial business skills and strategic training that helps businesses kind of focus on what their strategy will be to bring that idea to the marketplace.

It is actually a really rigorous program and the companies realized very early on that they have certain milestones and homework assignments that they need to accomplish to succeed in this program. But it is useful and it does help them either to realize they need to bring on other employees to help address those business aspects. We can't forget the B in the SBIR program.

Chairman ALTMIRE. Thank you, and with all these questions, if any of the other panelists have comments they want to make, feel free to jump in. Is there anyone who wants to weigh in on that?

Dr. Billingsley?

Dr. BILLINGSLEY. Well, I think it is critical whenever you get to the point—

Chairman ALTMIRE. If you could turn your microphone on. Is it on?

Dr. BILLINGSLEY. I think so.

Chairman ALTMIRE. Okay, good.

Dr. BILLINGSLEY. Critical whenever you get to the point of commercialization that the equivalent talent and business skills are matched with the equivalent talent in science. I've noticed we have an MBA/Ph.D. here and that's certainly one way to go. But it does take somebody who is seasoned in drug development or in device development in order to carry it forward to get a successful company. A lot of what happens is there is a transition, usually a time of first significant institutional financing, where the investors and the Board change, and I believe, people become, founders become chief science officers and people who are more experienced run it. It is very critical.

Dr. STEFANSIC. Can I add something there too?

Chairman ALTMIRE. Certainly.

Dr. STEFANSIC. If you think about the goals of the SBIR program, it's in my opinion, if a company gets an SBIR, they have to start thinking about those business things right away. They can't put those things on the back-burner, and a lot of times you don't have anybody with any business acumen working for the company. The PI is so focused on getting the technology to market they don't think about regulatory, quality issues, all of those other issues that a small business almost has to think of from the beginning, and this is where if you have the venture backing behind it, that could bring in the seasoned management that Dr. Billingsley talked about to sort of help accelerate both tracks, both the research track and the business track.

Dr. FRANANO. I would say that the number of potential people who could be entrepreneurs in this business is much larger than the number of people currently making a run at it. There are a lot of natural entrepreneurs out there. I think sometimes the industry

tends to focus so much on experience that it misses the people who have real potential, but who need that first start of understanding a business plan. There is a lot of competence, but not experience. I find that in biotech, those people can be really powerful entrepreneurs if given the right opportunity and the right initial training and mentoring.

Because in biotech, I think people ask me, well, how much impact can the small business, SBA program have? It's $100 million dollars to get a drug to market. What does $100 or $150,000 dollars really mean, or a million for a phase II. Biotech companies do really well with small teams.

Innovation in biotech comes from teams of five or ten or fifteen people and that's one of the areas where biotech has a huge advantage over pharma. It's hard to get a really innovative drug through a thousand person department, even if you have $5 billion. Because everything gets chopped down to the lowest common denominator, and that's why if Pfizer, I mean, I don't want to imply, pharma has done a lot of great things, but they have enormous research budgets, huge numbers of people, and are producing precious few novel drugs; whereas, these biotech companies which are small and have very limited budgets are actually producing a lot of the innovative products and I think it goes down to in biotech, small teams are very innovative and the SBIR program can assemble those small teams to get something like our compound from heresy initially, which a lot of innovative therapies are to interesting. That's what your program does is take something outside of the box that someone has invented and make it—move it on the path, give it enough data for the data-driven people to go. That looks really interesting, I'll invest.

And so I think that programs that can assist entrepreneurs, get people with an entrepreneurial mindset on the path to being an entrepreneur is very helpful.

Chairman ALTMIRE. Ms. Goodnight.

Ms. GOODNIGHT. I'm just sitting here thinking back to the days when I was at the National Cancer Institute and we had one company, Endocyte, who Dr. Phil Low had started. And he was working on his basic R&D, had an idea of using the vitamin folate for treating or even potentially curing ovarian cancer. And he was really in this conundrum. Do I start my own company? Do I sell everything off to investors? Do I do go outside of my home state of Indiana? What to do?

And he actually had support through the university and through some of their facilities that they provide to entrepreneurs and they even have things like entrepreneurial leave models. So he was able to start his own company, but he did impart a very important piece of advice. He said I do really good basic research and R&D to get the science done under this SBIR. But I don't have the business acumen, so he hired a CEO and he hired people who could take care of that of those types of activities. But the point being that he also was utilizing resources within the state and so sometimes the state can provide some very important resources to help bolster some of the business aspects of the program.

Chairman ALTMIRE. Thank you. Dr. Franano, the guidelines for phase one and phase two grant sizes have not increased since 1992

and some observers have noted that the inflation-eroded awards allow for significant less research than they did in 1992. Do you believe increasing the average award size is likely to strengthen the contributions of SBIR-funded research?

Dr. FRANANO. I do. I think that we're do for an inflation adjustment. Certainly, the costs of developing drugs continues to rise certainly above the rate of inflation and so the grants are not providing as much developmental support as they previously were.

I think the most important—probably of the two phases, I think the second phase is more important. That's where $1 million, you take to say it, $1 million doesn't go as far as it used to— it's a silly thing to say, but for phase two especially, I think some flexibility in making larger awards for technologies that are pretty costly, but very potentially powerful would be better because the phase two is where you really struggle to fit the second part of your program into the current structure.

The $100,000 to $200,000 phase ones are still relevant. I mean you adjust them somewhat, but I'd say the second phase is where you could really make an impact on companies because the second phase grants are harder to write. They're longer. They require a lot more effort and when you start to fold what you can fold in there, you realize you come up pretty short most of the time.

Chairman ALTMIRE. Ms. Rick, as I understand it, when—let me just say I'm going to reset the clock also. We're about four minutes over on the first round. We'll consider this to be the second round, just so we can keep track.

As I understand it, when the NIH develops research project topics for SBIR awards it is in effect directing millions of dollars to research to a specific scientific area.

Do representatives of patient groups like yours have an opportunity to work with the NIH SBIR office with respect to the development of SBIR research topics and interests?

Ms. RICK. While I understand that that is the case, we have not had an opportunity to do that and I will say that I'm torn sitting here because I am a representative of a particular disease.

One of the rules that we live by in my office, however, is that we don't compete diseases. And I think SBIR, while they certainly need to receive input on areas of great need and gaps, the SBIR applications are, in fact, peer reviewed, and by colleague scientists. And I think it's hugely important that the SBIR program with its vision of commercialization focus on the best science with the best opportunity. And so sitting here, I will tell you that it is my view and the view of many of my colleagues with other diseases that the key is creating a culture where we're getting things out the door. And if that means there isn't an SBIR grant for the next few years for Parkinson's, needless to say I'm sad, but the focus is on the culture and the speed of getting what is needed actually into patients and it doesn't require necessarily equal representation at every moment for every disease.

I may lose my job now.

(Laughter.)

Chairman ALTMIRE. Ms. Goodnight, do you have a comment on that?

Ms. GOODNIGHT. I have an important distinction, so NIH is comprised of 27 institutes and centers, 23 of which participate in the SBIR and STTR programs. And each of those institutes and centers currently has a mandate to address science and health from a perspective, whether it's a disease area such as cancer or Parkinson's, whether it's an area of concern such as aging.

The one unique feature about our agency is our applicants can propose research in any areas that relate to our over-arching mission of improving human health and we certainly welcome those types of applications that are in addition to any specific topics and that's fairly clearly laid in our solicitation, but perhaps we need to be including that even stronger in our outreach efforts.

Chairman ALTMIRE. Thank you. Similar to the question I asked Dr. Franano earlier, this would be directed to Dr. Billingsley, the National Academies of Science has recommended increasing the SBIR award amounts for phase one and phase two grants. Do you believe that an increase in the average dollar amounts granted by NIH and other federal agencies with SBIR programs would encourage more life science companies like yours to apply for the SBIR awards?

Dr. FRANANO. The answer in the short phase is yes. It costs more to do more, but I'd also echo the notion of more flexibility with the need for larger grants and larger entities at the program and institute level.

Having read the GAO report, it was a financial analysis across the board comparing DOD and NIH as if all SBIR grants were created equal. They're not. All projects are not equal. They're not.

This is a highly regulated, highly risky, long-term commitment to bring a product to market whereas for a software or hardware project, it's very short term and it's market-driven. So that same yardstick that was used to analyze those sets of data doesn't really apply and I think the NIH has shown some discretion on occasion at increasing amounts of phase two and/or the notion that there are other ways in which this can be done to support pre-clinical trials.

Let me give you a real particular number. It takes at least $1 million to do some pre-clinical toxicology on a compound in order to prepare it to be submitted to the FDA for approval as an investigational new drug. That's almost a fixed cost of doing business. And that's low.

Dr. FRANANO. Try $5 million.

Dr. BILLINGSLEY. Well, it depends on the compound, but it's at least that much money must be generated. So there are increasing costs and you don't want to undercut the value of the need for that kind of toxicology.

So yes.

Dr. FRANANO. And often, I think it's that initial money that is—that will lead you to the larger investment that can bring your drug into clinical development and put it on the way to patients is that investors are very reluctant to invest until they see that the drug or the device works and that it has an acceptable risk in terms of toxicity.

And it's really hard to generate that data with $50,000 and $100,000 investments from your friends and family. That's a lot of

friends and family. I don't have that many. So that grant programs sometimes can step into that breach and provide some additional investment that can help you get to the point where you are ready for that large investment to take you to the next level.

Dr. BILLINGSLEY. And there are related programs also by the federal government such as the National Toxicology Program, the RAID program or Rapid Access to Investigational Drugs through different agencies, that may dovetail and may help alleviate some of the pain, but that takes a fair amount of coordination between and among the agencies. So it is an expensive proposition. It has not gotten cheaper to develop a drug or device.

Chairman ALTMIRE. Thank you. Ms. Rick?

Ms. RICK. Can I just add something that a concept that we talk a lot about in the Parkinson's community is time. Obviously, we've discussed the drug development time line and how long it is. But anything that this program can do to shorten, a year and a half or two years, that it might take for someone to find private funding if they can for a stage of development, to the extent that SBIR can come in and fully or partially fund that, can be the difference for a person with Parkinson's between being Stage III and Stage IV. It can be the difference between working and not working, being in a wheel chair and not being in a wheel chair.

In fact, the people who are being diagnosed with Parkinson's disease today, and there's people out there being diagnosed today, probably will not even benefit with our current time line from the drugs that are just being thought of now. It takes too long, 15 or 20 years for drug development, 15 or 20 years you live post diagnosis. So whatever we can do with this program to shorten the time line makes a huge difference in people's lives.

Chairman ALTMIRE. Thank you. I will ask one more question and several Members of the Committee who couldn't be here today expressed interest in communicating directly with you with their own questions, so please look for some questions through the mail or through your offices that other Members may have and if you could respond in a timely way, that would be appreciated.

Last question for Ms. Goodnight. It can cost a small company thousands of dollars to prepare and submit a well-written phase I application. Undoubtedly, the cost of preparing the application is prohibitive for a number of potential applicants, similar to what we've talked about. Has the NIH considered developing a preliminary application process whereby an applicant provides a relatively brief white paper and receives an assessment of the likelihood of success before they go through the full application process?

Ms. GOODNIGHT. We haven't used that type of a process and it could be that the reviewers would not necessarily see all of the details in the research plan for assessing the full scientific and technical merit of the proposed research. What we have done is to try to work with states who offer these Phase 0 programs to help companies prepare more competitive applications. We do a lot of outreach to do some one-on-one assistance, and also I think the electronics submission process, although in the beginning it may have been somewhat difficult, analogous to the first time you ride a bicycle, it has actually helped to simplify that whole process.

Chairman ALTMIRE. Okay, any other comment on that?

Dr. BILLINGSLEY. I think from our state, representing Pennsylvania, there are several programs that have been initiated to deal with this initial barrier. Some of it is mechanical and technical submissions through egov.com. Others are more substantive, what people want to see, and offering pre-review. It is a barrier, several thousand dollars to do that, but hopefully that is not a complete barrier to entry. It would be of concern if a company could not find either the resources or several thousand dollars of consultants that could help them to do that.

But I would agree that the real value of the SBIR review process is the peer review, which needs the full scientific vetting. Without that, you don't have the kind of the blessing of peer review, as painful and lengthy as it may be.

Chairman ALTMIRE. So as I understand it, you're both expressing concern that if you go through the process that I described in the question, that you would leave out, you would have an initial decision that might leave out someone who really did have a chance of success?

Dr. BILLINGSLEY. Correct. If they wrote the white paper in a way that was either too descriptive or not technical enough, it could be dismissed out of hand, and I don't know who would be comfortable to make a scientific decision based on a white paper.

Chairman ALTMIRE. How about if you had a process where anyone could submit a grant, that you could submit a pre-grant where you would get an award of two or three or five thousand dollars and a road map for how to prepare a grant as a way to lower the barrier for someone to at least get interested in the program and start the process, that you didn't have to go through that as prescreen, but that it was available to those individuals. Because that would allow, if it was a three thousand dollar grant, someone could use that then to hire a consultant to help them write the grant. I'm all for anything that lowers the barrier for that person sitting in their office to start a company, because that is a huge barrier that we don't think about much. There's a lot of people out there thinking about starting a company who aren't. And anything we can do to make those stairs flatter and shorter to get up to the top, to make those first few steps, would be good. So you were you thinking about that, where they might be some small assistance that you would submit a one-page saying I've got this kind of idea for a grant application, but I need some assistance in getting the grant together and could you administer a small check like that? I don't know.

Chairman ALTMIRE. It sounds like that's what we're trying to get over that first hurdle to allow especially the smaller companies the ability to move forward in a reasonable and cost-effective way, but we don't want to diminish their chances of success if they really do have a chance of making it through the process. Obviously, it's worth their while to submit the full application.

Did you have a comment, Ms. Goodnight?

Ms. GOODNIGHT. Sorry, just a real quick comment. We really encourage our applicants to contact our program staff, our program administrators to call and talk about their idea. They're not playing the role of peer review, but they certainly can give some good

guidance on whether it's an area of research that we would likely support if the proposal is deemed to be scientifically meritorious.

I'm also thinking back to the days when the federal and state—what was it called, FAST, Federal And State Technology program, I believe, was in existence and that again went back to the states in providing assistance to small companies for a very small amount of funds to prepare those proposals. And so there are still, even today, after FAST has ended, a number of states who are providing that type of assistance.

Dr. STEFANSIC. I just want to add something. Most scientists that write a grant, especially if you're in the academic setting, you can almost expect that you're going to have to submit it at least twice. You need that initial feedback.

I think one thing that the NIH has done and the NCI and some of these federal institutions in having the electronic submission program, from what I understand, this cycle, this first cycle is moving more quickly. So you get feedback back and you can resubmit—you can maybe hit the next cycle instead of having to wait two cycles. So that—having that in place, I think, will help a lot. And it's the same program for the SBIR or for academic grants. So getting that—I think getting that peer-review feedback though is really, really important because you can't really in a one page or summary or a white paper. It's really going to be very difficult to determine the scientific validity of what's being presented.

Ms. RICK. There are other Parkinson's disease research centers at NIH and that program does accept letters of intent, early on before the grant application process and my understanding is that that's been very helpful to people either to weed out some who don't spend a lot of money and time filling out a grant application and it's not going to go anywhere, or people with great ideas and may not be that good at it.

The point is to start the dialogue and it sounds like they do that at SBIR to help someone through the process to the bright ideas are not lost for what is in the application as opposed to the quality of the idea. And that open dialogue, as long as it can advertised and people know it is available is what is important, I think.

Chairman ALTMIRE. Thank you, and I know I said that was my last question, but I do have one more. For Ms. Goodnight, again. The majority of SBIR awards go to firms based in technology-rich states and localities. Is the NIH taking steps to encourage more life science researchers and biomedical firms from states and regions that win few SBIR grants to apply for future awards?

Ms. GOODNIGHT. We are and we are doing that through our outreach at various workshops and conferences held throughout the United States. We have actually offered to go to states like Wyoming to do some hands on workshops just to help them get over that, you know, black box kind of impression that they might have. We're also doing those types of things so they understand there is this opportunity to revise and resubmit their application, because we want to see those states who have not participated in the past to really take advantage and take advantage of every opportunity to improve an application if it is not funded the first time through.

Chairman ALTMIRE. And if you could talk about the SBIR program, FAST, where states were given the opportunity to apply for

federal grants to support efforts to build their state's applicant pool, and during the years this initiative received funding, in your view, did it expand the number of SBIR applicants from states that win fewer awards?

Ms. GOODNIGHT. I believe it did. We could certainly probably look more to the states to give those metrics, because that was part of their proposal as I recall in having to review those. So that was a program that was supported through the Small Business Administration and administered by those, but I definitely think that it was helping to improve the applicant pool in those states.

Chairman ALTMIRE. That was a question that was of great interest to a Member of the Committee who is unable to be here today, so just for your staff that are here, you may be receiving further questions about that issue.

Dr. FRANANO. We got assistance from the Missouri Fast organization, which was outstanding in addition to Jo Anne's work at NIH has been great. Our head of research and development, I think has talked to you several times and come back with glowing, you know, feedback, that the program that you put together really makes the program accessible. Because there can be a black box phenomenon for people who are approaching a big program like this for the first time and to the extent that you do outreach and you send out your newsletters and you are accessible for people who are just getting started without making them feel foolish.

Because when you start, you are raw and you, you know, it is a bit embarrassing how bad your first business plan is and how bad your first grant is and I think the organization does a nice job in making people feel like everybody is bad the first time, you know. I guess Roger Clemens is next door, right? You're going to give up home runs in the minor leagues. It's good for people to have that accessibility to the program, because I do think that the goal of encouraging the formation of new businesses and the development of new technology is an important goal for the country for people and for our economy, and to the extent that these are really high-risk ventures, and I think it is fair for the taxpayers to share in the risk of this high-risk or early-stage development, because they will, in the end, get the rewards. I think it is a reasonable thing for the taxpayer to invest in, because I often find that our individual angel investors are really philanthropic, early stage investors. They are people who have made a fair amount of money at a business and are investing because they would love the idea that they invested in something early that had a big impact on people's lives. They are really being, I never tell them that, I always tell them that they're going to make money. But at base they know that I think they're going to make money, but at some level it is philanthropy, and it is asking a lot of individual angel investors to accept the risk when the benefit of the technology is going to benefit everyone.

So I do think to the extent that the SBIR program can help spread that risk to the population that's going to benefit from, and I think it is a legitimate use of the taxpayer's money.

Chairman ALTMIRE. Just to continue the mutual admiration society and wrapping it up, I do want to again recognize Mr. Graves, who is one of the leaders in the entire Congress on these research

issues and biotech and life sciences firms are important to him and his District, and I've worked very closely with him on those issues and I really wanted to thank him in his absence for helping set this hearing up and for his leadership on the issues. I want to thank the entire panel. I apologize for the couple of breaks we had to take, which were beyond our control. I know you have other commitments on your time, and the fact that you stayed the whole time and your staff was here, I really appreciate it on the behalf of the committee. Thank you, and this hearing is now adjourned.

[Whereupon, at 11:49 a.m., the hearing was concluded.]

JASON ALTMIRE, PENNSYLVANIA
CHAIRMAN

LOUIE GOHMERT, TEXAS
RANKING MINORITY MEMBER

Congress of the United States

U.S. House of Representatives
Committee on Small Business
Subcommittee on Investigations and Oversight
2361 Rayburn House Office Building
Washington, DC 20515–0515

Statement of the
The Honorable Jason Altmire, Chair
Subcommittee on Investigations and Oversight
Committee on Small Business
"SBIR: Advancing Medical Breakthroughs"
Wednesday, February 13, 2008

This morning the Subcommittee on Investigations and Oversight will continue the Committee's review of the Small Business Innovation Research (SBIR) program. This hearing will examine how SBIR is laying the foundation to fight disease and advance medical breakthroughs. Through this initiative, to date nearly $600 million has gone to small firms researching national health and wellness priorities.

There are many examples of health care therapies that have been developed as a result of SBIR funding. These include vaccines for biodefense and food safety purposes, novel anesthesia delivery devices to relax children during medical procedures; and improved monitors to control blood glucose levels. SBIR has also spearheaded the discovery of safer methods for laser vision correction; needle-less infusion patches to deliver drugs such as insulin; and improved research tools for studying dementia.

These examples make it clear that SBIR is on the cutting edge of improving the quality of health care. We must, however, take steps to make it more responsive to today's medical challenges.

This includes expanding the number of companies replying to research solicitations. This is an important issue for at least two reasons. First, the National Institutes of Health reports an alarming decrease in SBIR applications since 2005 and, second, a recent National Academies of Science study recommends that all federal agencies increase their efforts to encourage woman- and minority-owned businesses to apply for SBIR awards.

The Subcommittee will also focus on initiatives that the NIH has developed to support the successful commercialization of SBIR-funded research. The Pipeline-to-Partnership database, NIH's pilot program in conjunction with the Manufacturing Extension Partnership and the agency's decision to support promising projects with multiple SBIR awards are initiatives that other participating agencies should consider as potential avenues to encourage higher rates of commercialization.
Finally, we will consider how to further encourage research in fields that suffer from chronic under-funding, including "orphan" diseases, which are not receiving the capital they need to advance new therapies. Going forward, the Committee will look at ways to address these funding shortfalls.

The region I represent in western Pennsylvania boasts some of the best medical research and development in the nation, and last year the state brought in nearly $75 million in SBIR grants, ranking ninth nationally. We have the tools and infrastructure necessary to lay the groundwork for the development of innovative medical technology, equipment and therapies. RedPath Integrated Pathology, a small company based out of Pittsburgh, Pennsylvania, is a prime example of how the SBIR program can take an innovative idea to corporate success. RedPath was awarded an SBIR grant that enabled it to complete and validate key aspects of a molecular-based test that could facilitate earlier, more personalized, and more definitive cancer diagnosis. The positive results of this research led RedPath to introduce PathFinderTG, a diagnostic tool that is now being used to combat one of the leading diseases affecting the American public. It also spawned an enterprise that created more than 40 highly-skilled jobs in 4 years, with a goal of doubling its growth in 2008. However, without the initial grant from SBIR, RedPath may never have been able to survive and grow into the successful company that it is today. This is just one example of medical breakthrough technology that is the result of SBIR, illustrating the importance of the program and all it has to offer. Should we fail to support our innovative researchers and technological advancements, we will lose the technological edge that allows the national economy to expand and, in RedPath's case, to improve patient care.

With the Committee working to reauthorize SBIR this year, today's hearing will provide testimony central to the SBIR program's on-going effectiveness. During this time, it is important that we modernize the program so that it can create the medical breakthroughs of tomorrow, while still promoting job creation in our local communities.

Over the last 25 years, the SBIR program has contributed to the emergence of some of the world's most innovative and successful life science companies. Amgen, Biogen, Genzyme and Chiron are all "graduates" of the SBIR program. At its most effective, the SBIR program provides seed funding that will provide the next decade's Amgen with its start, while also incorporating America's small life science research firms to help reduce the burden of illness on public health.

I thank the witnesses for being here today and look forward to all of your testimony."

U.S. House of Representatives
SMALL BUSINESS COMMITTEE
Subcommittee on Investigations and Oversight
Wednesday,
February 13, 2008

Opening Statement of Ranking Member Sam Graves

Small Business Innovation Research Program: Advancing Medical Breakthroughs

Good morning. I would like to welcome all of you to this hearing on the Small Business Innovation Research, or SBIR, program and its role in the development and commercialization of innovative healthcare technologies. I'd like to extend a special thanks to each of our witnesses who have taken the time to provide this subcommittee with their testimony. I would also especially like to welcome Doctor Nicholas Franano, who is the Founder and Chief Scientific Officer, Proteon Therapeutics, Inc., a biotech company located in Kansas City, Missouri. Welcome Dr. Franano to the Small Business Committee's Subcommittee on Investigations and Oversight.

As part of the 2000 SBIR program reauthorization, Congress required the National Academy of Sciences' National Research Council (NRC) to conduct a comprehensive review and assessment of the SBIR program. Using the NRC report as a starting point, last month, the House Small Business Committee started its review of the SBIR program which was last fully examined by this committee in 1999 and reauthorized in 2000. It should be noted that the core finding of the NRC Report is that the SBIR program is sound in concept and effective in practice.

Today's hearing represents a continuation of this committee's work to review and reauthorize the SBIR program and will focus on how the SBIR reauthorization can better structure the SBIR program to address its role as a vehicle in the early stage development of innovative medical technologies, therapies, products, and drugs.

Created in 1982, the development of the SBIR program is not only critical to the unique needs of each of the participating federal agencies, but also to our national economy. Small biotech businesses play a key role in innovative research resulting in the commercialization of cutting edge medical technologies. For the small business biotech entrepreneur, it is a vehicle that provides essential early stage development funding for promising biotech drugs with the added benefits of ensuring there is no dilution of ownership and that no repayment is needed like traditional loans.

Angel investors, venture capital investors, and other early stage investors rely on the data developed from this early stage discovery and initial development to establish a promising proof of concept in order to make investment decisions to support the further development of such technologies.

At last month's hearing, it was pointed out that the SBIR program's current eligibility requirements effectively prevent some small business biotech firms from participating in the SBIR program. One of the structural barriers is based on the biotech industry's need for access to large sums of capital. This and other barriers can prevent pursuit of innovative medical therapies, causing a good amount of these products to never be fully developed and marketed.

Today's hearing is part of the Committee's fact finding process to find ways of making the SBIR program more efficient and effective in its role in innovative healthcare research resulting in the commercialization of cutting edge biotech technologies.

Mr. Chairman, I look forward to working with you on this important issue. Again, I thank each of you for being here today and I yield back.

###

Testimony
Before the
Subcommittee on Investigations and Oversight
Committee on Small Business
United States House of Representatives

SBIR: Advancing Medical Breakthroughs

Statement of
Jo Anne Goodnight
SBIR/STTR Program Coordinator
National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 10:00 a.m.
Wednesday, February 13, 2008

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.

Testimony of the Honorable Amy Comstock Rick, J.D.
Chief Executive Officer
Parkinson's Action Network
Washington, DC

For the U.S. House of Representatives
Committee on Small Business Subcommittee on Investigations and Oversight
Hearing on "SBIR: Advancing Medical Breakthroughs"

February 13, 2008

Thank you, Chairman Altmire, and Ranking Member Gohmert for inviting me to testify on behalf of the Parkinson's Action Network regarding the Small Business Innovation Research (SBIR) program. As you know, I am the Chief Executive Officer of the Parkinson's Action Network, also known by our acronym, PAN.

PAN represents the entire Parkinson's community, including the more than one million Americans currently fighting Parkinson's disease (PD), the estimated 60,000 newly diagnosed every year, and their families, and all the national Parkinson's organizations, including The Michael J. Fox Foundation for Parkinson's Research, Parkinson's Disease Foundation, National Parkinson Foundation, Parkinson Alliance, and American Parkinson Disease Association.

Parkinson's disease is a chronic, progressive neurological disorder that results from degeneration and premature death of dopamine-producing brain cells. It is the second-most common neurodegenerative disease in the United States. The cause of PD is unknown, although research points to a combination of genetic and environmental factors. PD is currently without known cure.

Parkinson's patients experience devastating physical and mental symptoms such as tremors, debilitating slow movements, postural instability (balance problems), sleep disturbances, and a variety of cognitive impairments. Today, treatment options only provide some symptomatic relief but are in no way neuroprotective; halting or reversing the progression of the disease. Current state-of-the-art treatment for people with Parkinson's disease is rooted in levodopa and its derivatives. Levodopa was approved almost 40 years ago and, sadly, is still the primary treatment for Parkinson's. Yet, levodopa and the derivatives only treat the symptoms of the disease and are only effective in treating symptoms for a limited period of time. We still have nothing that will actually slow the progression of Parkinson's or that will ward off ultimate and complete disability. As Parkinson's progresses, even with treatment, substantial disability -- including the inability to maintain balance, walk, speak, and move -- is inevitable and makes assisted living and nursing home care necessary. Parkinson's disease sufferers are desperately awaiting an innovative neuroprotective treatment that will relieve their pain and halt the disease.

Before I begin to discuss the Small Business Innovation Research (SBIR) program specifically, it is helpful to understand the context in which PAN views all National Institutes of Health (NIH) programs. As you may know, NIH is the single largest source of Parkinson's disease research funding in the world, and the basic discoveries coming out of NIH are very important, but it is our belief that NIH is not funding enough research that aims to translate basic scientific discoveries into therapies for people living with diseases. As I testified before the House Appropriations Committee in 2006, the primary focus at NIH is on basic research – research that is not necessarily geared towards therapeutic outcomes – rather than research that will advance scientific innovation towards needed therapies.

The drug development process takes many years from beginning to end. At the beginning you have basic research supported by NIH. At the end, one hopes, you have a drug, biologic, or treatment, approved by the FDA, that is available to those afflicted with a particular disease. Unfortunately, between these two bookends of well-understood areas of federal oversight, you have a process that is often-times confusing, inefficient, and not geared toward improving the public health. Currently, no one in the federal government is responsible for ensuring that the scientific baton (promising early NIH-funded research) is passed from basic discovery onto private development, generally a pharmaceutical or biotechnology company, that will pick up the project and see it through to the end of the FDA approval process. This middle part of the process, where promising drugs can be lost and no one is ensuring that good ideas in the lab are "translated" into real possibilities for patients, is referred to as the "Valley of Death."

It has been the position of the Parkinson's community for quite some time that NIH should focus on patient-oriented outcomes by doing more to combat the "Valley of Death." We have suggested that more of the NIH extramural grant program should be focused on potential therapies for particular diseases. Unfortunately, however, due to a lack of funding and in order to maintain basic research grants, NIH has not only not focused more on translational research, but has actually cut these programs. As Dr. Zerhouni said in his Senate Labor, Health and Human Services, and Education Appropriations Subcommittee testimony on March 19, 2007, "the impact [of NIH budget cuts] is primarily in our ability to translate from the laboratory to the clinic to the bedside into the community what we need to do to prevent diseases."

It is disconcerting for people living with Parkinson's and other un-treated or under-treated conditions to know that many potential drugs are languishing in the "Valley of Death" simply because there is not enough funding to move basic research to product development. This science is some of the most difficult and costly research needed to develop therapies and meet the public health need, including developing pre-human testing, efficacy trials, production design and a range of other steps needed to determine whether a drug will be safe and effective. It is also essential for reducing the burden of disease and disability for millions of Americans.

Having heard our vision of the need for NIH to refocus some of its grantmaking, it should be clear why I and the Parkinson's community are so strongly supportive of the SBIR

program. SBIR grants have a significant role to play in the drug development arena called the "Valley of Death. The Parkinson's Action Network strongly supports the entire NIH SBIR program, but there are several important elements of the program that I will highlight and a few suggestions of areas that would benefit from improvement.

NIH SBIR grants, of course, are awarded to small companies that conduct biomedical research. In order to address the NIH SBIR program from a biomedical perspective, it important to understand in a little more detail, the how these small biomedical companies function. Generally, these companies have one or two lead projects for which they are able to raise funds through private investors. These research projects are investigations into promising products or therapies that investors have determined to be worthy of their money. But, like many things in life, there is often a second tier. The second tier includes research that is also promising, but which, for one reason or another, is not as appealing to private investors. The lack of appeal to investors may occur for a number of reasons – it can be that the science at issue, while worthy, is less certain and more of a risk so private investors are more leery. Or, the lack of appeal to private investors may be because of the size of the potential market. This is a very real issue for a disease like Parkinson's that, while between one and one and a half million people, is not a sizeable market that is appealing for potential profit.

Companies may have trouble attracting private investors to support this second category of projects, which are scientifically valuable research projects but are less certain in terms of the potential return on investment. I cannot emphasize to you enough how troubling it is to a person with Parkinson's or their loved one that there are potentially hundreds of bright ideas out there for better treatments for Parkinson's disease that are not being pursued because our system does not have a process for ensuring that good ideas are not lost. In fact, in a perfect world there should be a way of ensuring that promising ideas move through the pipeline as quickly as the science dictates and the potential benefit to the public health demands. But this is not the case. There is no guarantee that a promising therapy for a disease with a very small population, for example, will move through the pipeline at all. Similarly, there is no guarantee that a risky idea for a disease that affects a larger population, let's say Alzheimer's Disease, with a population of about 4.5 million and growing, will be pursued.

This is where SBIR comes in. The SBIR program supports cutting-edge research where other sources of research are difficult if not impossible to obtain. But when you turn that thought around and look at it from a patient perspective, it is not that this program is about funding, it is that this program makes possible research for many diseases that would not otherwise occur. That is invaluable.

Having stated our strong support for the NIH's SBIR program, however, I do want to offer an important recommendation for the future. As this committee is well aware, the 2003 SBA ruling regarding SBIR eligibility based on majority ownership by "individuals" has had a negative impact on the biomedical research community. It is my understanding that, since that ruling, applications to the NIH SBIR program have dropped precipitously. SBIR applications, we have been told, are down 11.9% in 2005, 14.6% in

2006, and 21% in 2007. And, given the increase in most applications to NIH, it is fair to assume that this drop is a direct result of the eligibility ruling.

From a patient perspective it does not seem logical, and is in fact scary, that we eliminate from eligibility research projects that otherwise merit funding, because of the financial structure of the company. And, the reasoning becomes more muddled when one focuses on the fact that the companies that are being excluded by the SBA rule are the very ones that are doing work that is good enough, for whatever reason, to have attracted venture capital money. The very companies that are doing a good enough job in one area are, because of that success, barred from federal support for other promising research. This policy doesn't penalize companies, it penalizes patients.

Let me give you an example of the impact of this ruling. It is a sad reality that there is a lot we still do not understand about neurological diseases. There are many investigations into compounds that show therapeutic promise in pre-clinical and even early clinical stages in which the research is dropped and no actual therapies are developed. That is why our community is heavily invested in any potential therapy that is beginning to show real promise. We have one now, Spheramine, that is in Phase II clinical trials. Spheramine, quite simply, injects retinal cells into the brain, surgically, to provide a continuous source of dopamine. While this trial is now in Phase II and our community is quite enthusiastic about its promise, the animal research and Phase I research was funded through an SBIR grant. We are fearful that keeping the eligibility ruling as it now stands will keep this kind of promising research from going forward. In fact, who knows what promising therapies are sitting now, unfunded and not moving?

I would like to make one final point in support of revisiting the ruling SBIR ineligibility based on venture capital investment. At NIH, as with SBIR throughout the government, 2.5 percent of the extramural grant monies are set aside for this program. By eliminating a large percentage of private, innovative researchers, we are left with a much smaller pool of applicants from which NIH can draw when funding these grants. And, while all applications are peer-reviewed so, presumably, are all good science, it just seems logical to me that we would want to do everything we could to invite as many applications as possible to go into that peer-review process so that we are assured that what comes out is the best science, with the most promise, that we can fund.

As PAN continues working toward better treatments and cures for Americans, we respectfully seek the Small Business Committee's support for a robust SBIR program at NIH. SBIR is an essential program that provides key funding for patient-oriented research currently languishing in the "Valley of Death" of the biomedical research system. We respectfully request that your support include a revision to not eliminate small companies simply based on their financial structure.

Thank you again for this opportunity to provide testimony. I look forward to working with the Committee on this critical issue for the Parkinson's community, the small business community, and all American families facing disease and disability.

Hearing Testimony
Melvin Billingsley, Ph.D.
President and Chief Executive Officer
Life Sciences Greenhouse of Central Pennsylvania

On behalf of
Pennsylvania Bio
and The Pennsylvania Life Sciences Greenhouse Program

Before the House of Representatives Committee on Small Business
Subcommittee on Investigations and Oversight

SBIR: Advancing Medical Breakthroughs

February 13, 2008

Chairman Altmire, Ranking Member Graves, and Members of the Subcommittee:

Thank you for the opportunity to provide testimony before you regarding the nation's Small Business Innovation Research (SBIR) Program and its impact on advancing medical breakthroughs.

I am Dr. Melvin Billingsley, president and Chief Executive Officer (CEO) of the Life Sciences Greenhouse of Central Pennsylvania (LSGPA). I am the founding CEO of LSGPA, and, along with my fellow CEOs John Manzetti of the Pittsburgh Life Sciences Greenhouse and Barbara Schilberg of BioAdvance, have worked diligently to support and invest in emerging life science companies in Pennsylvania. I have considerable experience with the National Institutes of Health (NIH) grant system, and have been grant recipient from NIH. I have served as a reviewer for the United States Department of Defense (DoD), for NIH, and for NIH SBIR awards; thus, I am familiar with the importance of the SBIR program as a key catalyst for commercialization of innovative, life-saving technologies.

Pennsylvania's Life Sciences Greenhouse (LSG) program was created through a one-time set aside of $100 million of Pennsylvania's share of the Tobacco Master Settlement Agreement. The LSGs were designed as a flexible mechanism for the commercialization of life science business opportunities by accelerating technology transfer, enhancing collaboration, and attracting new business. There are three regional greenhouses in Pennsylvania: the Pittsburgh Life Sciences Greenhouse; BioAdvance: the Biotechnology Greenhouse of Southeastern Pennsylvania; and the Life Sciences Greenhouse of Central Pennsylvania. Each provides services based on the needs of our respective regions; however, we each provide direct early-stage investment for emerging companies. I have provided with this testimony a fact sheet on each greenhouse.

I am testifying today at the request of Pennsylvania Bio, the statewide life science association representing the interests of the Commonwealth's research, biotechnology, medical device, diagnostic and pharmaceutical industry. The Association represents more than 300 organizations across the commonwealth. Pennsylvania is a major recipient of funding from the NIH, ranking fifth overall in the past year with more than $1.4 billion in funding. In addition, in

2005, Pennsylvania companies received significant SBIR funding from the NIH; there were 45 Phase I projects totaling $6.9 million, and 31 Phase II projects totaling $15.3 million.

Needs of Emerging Companies in Bringing Therapies to Patients

Before we engage in a discussion about the value of the federal SBIR program, it is important to review the needs of emerging companies. I recognize that you may have heard this in other forums, but to bring a new therapy to patients, which is the goal of every company that is engaged in medial research, it takes an enormous amount of patience, time and capital. The Tufts Center for the Study of Drug Development estimates between 8 to 12 years and between $800 million to $1.2 billion to bring a product through clinical trials to FDA approval, if a company is fortunate.

Emerging companies are going through this process without any product revenue and rely solely on other means to fund the company and the research. The intellectual property of emerging life science companies is often the only basis for future value. Consequently, many of these companies will need to access the capital markets at some point in order to advance their products.

Companies first need early-stage risk capital, which is often the toughest to find in the market. The Life Sciences Greenhouses can address this gap. As a result, the three Pennsylvania Greenhouses collectively have seen a huge demand for this funding. The greenhouses have committed $35 million to 149 projects in Pennsylvania, but the need for investment far exceeds the funds available. As of June 2007, the greenhouses have received 814 applications requesting a total of $314.6 million. Our early-stage funding helps companies reach that next step in funding and product development:

- The Greenhouses' portfolio companies have attracted more than $500 million in additional funding beyond the greenhouse investment.
- Each dollar invested by the greenhouses has leveraged currently at least $10 dollars from additional sources, and this number continues to increase. This is a greater than 10:1 leverage, which is exceptional.
- The greenhouses have helped to create/retain 2,363 jobs in the commonwealth, nearly 700 of which were created through the greenhouses' investment portfolios.
- SBIR and other Federal funding remains a critical funding mechanism for emerging companies. From 2003-2007, LSG-supported projects have attracted more than $78 million in Federal funding (2007 Annual Report).

After seed funding from the LSGs and other programs such as SBIRs, most companies need funding that is often best met via professional venture capital (VC) investment. In Pennsylvania, VC investment in the life science industry has been on the rise, reaching a high of $476 million in 2006. According to Pennsylvania Bio's 2007 report on the life sciences industry in the Commonwealth, the life sciences accounted for 60 percent of all VC funding in Pennsylvania in 2006.

Outstanding, life-saving research is happening in our young companies in Pennsylvania, and we need to advance this research to the commercial market, where it can impact the health of our citizens.

Role of SBIR Funding

The SBIR program was enacted in 1982, and for nearly 20 years small, domestic life science companies successfully competed for these grants. SBIR grants, along with other government programs, can play a significant role in the funding continuum for emerging life sciences companies.

For example, in Pennsylvania, Yaupon Therapeutics, a BioAdvance-supported company, has progressed four therapeutic programs using approximately $14 million in funding over the last five years. Yaupon has benefited from the larger Phase II SBIR grants, including a $920,000 Phase II SBIR grant for a tobacco addiction compound in 2005. The company also received a $700,000 Orphan Drug grant in 2006 for a different program. Finally, the NIDA has been funding the development of a therapeutic agent to treat methamphetamine addiction, which is scheduled to begin Phase II trials. This funding assistance has been critical to the company's ability to move these programs concurrently. Now that the programs have progressed into the clinic, the company has been able to attract $15 million in venture capital.

Similarly, Azevan Pharmaceuticals, Inc, supported by LSGPA, has received an $800,000 NIH Phase II SBIR grant to develop novel therapeutics for aggression and anxiety. The company's lead compound has just completed Phase I clinical trials, and several of the pre-clinical studies were supported in part by the National Toxicology Program via the NIMH. This company has also attracted venture investment, which is needed to progress through Phase II clinical studies. Although the SBIR funding is significant, the amount of funds needed to complete clinical trials is a significant hurdle, and one best met via venture capital.

Launched in 2002, the Pittsburgh Life Sciences Greenhouse (PLSG) SBIR Advance Program is the only southwestern Pennsylvania resource dedicated to the specific needs of life sciences entrepreneurs. SBIR Advance is designed to enhance an entrepreneur's existing understanding of the SBIR Phase 1, Phase II, and Fast-Track proposal processes. Since inception, 110 companies have participated in the SBIR Advance Program which is directly responsible for bringing $13 million of non-dilutive SBIR funding into the region. One of those companies, Cohera Medical, Inc. is a PLSG supported medical device company whose patented product, TissuGlu™, is currently in pre-clinical testing and is designed to adhere tissues to prevent fluid accumulation in deep wounds. Cohera has closed a series A financing for $6.79 million and has been awarded two Phase I grants for $309,838 and was just funded a Phase II grant for $1.6 million with total SBIR support nearing $2 million. The SBIR funding has been critical to TissuGlu™'s pre-clinical testing and use to create a variety of products that meet surgeons' needs across many specialties.

Improvements to the program

Even the most successful program can be improved, and since recent administrative rulings by the Small Business Administration have weakened the SBIR program's ability to support life science innovation, we see areas for improvement within the SBIR program. Two specific areas need to be addressed in order to strengthen the program:

- Eligibility for venture-backed companies needs to be restored.
- Larger grant programs need to be fostered to help address "the valley of death" as companies seek venture capital funding.

Restore eligibility for venture-backed companies

New interpretations set in place in 2003 preclude many companies that are more than 51 percent venture backed from competing for SBIR grants. We've seen this impact in Pennsylvania, where companies have had to turn down SBIR grants and in turn terminate promising research. BioRexis Pharmaceutical Corporation is one such company. BioRexis had received VC funding to advance its lead product for Type II diabetes. The company had an additional program it was researching for a botulism anti-toxin. This was a program of great interest to the Department of Defense and in 2004, BioRexis received a $980,000 SBIR grant to explore the development of a long-acting inhibitor of botulism. Because of the company's venture capital investment, it was unable to draw down this grant, and the program was halted.

The BioRexis experience illustrates a particular need for venture backed companies. When venture capitalists invest in a company, it is often to advance the company's lead product and move the company more quickly to an "exit": an IPO, FDA approval, an acquisition or merger. Companies, though, are often looking at other indications for their technology or are advancing a second research project, as was BioRexis. SBIR funding can be enormously important for a second project. There is always the risk that a company's lead product will fail. We have many examples of this in Pennsylvania, most notably two of our successful "Pennsylvania-born" companies, Cephalon and Centocor. Each failed to receive FDA approval on their very first products, but because each company was able to successfully advance another project, both are successful, thriving companies today.

Since 2003, the life science industry has been seeking to redress this interpretation. We greatly appreciate Congressman Altmire's support with HR 3567, the Small Business Investment Expansion Act, and we thank the House for passing this legislation. I encourage the Senate to take up this legislation at its earliest convenience.

Address the "Valley of Death"

Many of you may have heard the term the "valley of death" as it relates to life science company financing. Companies can use the early-stage risk funding and government grant programs to advance companies to the point of human clinical trials, but large amounts of capital are needed to bring a promising product through the development process. Venture capitalists in recent years are trending toward coming in later in the development process. The period between when a company completes preclinical work and the later stage research and development is known as the "valley of death."

Phase I and Phase II funds can often be insufficient to get to the early clinical stages. A larger grant pool, such as a Phase II B program can help bridge this funding and attract venture capital earlier. This was the original intent of the federal SBIR program—early stage support leading to commercialization and higher capitalization. However, the long timelines and regulatory atmosphere for life science products presents a unique challenge for an SBIR-funded company. It is important to recognize that the significant capital risk occurs well beyond the early stage trials and preclinical development.

To this end, the NIH needs to maintain its flexibility in the SBIR program. Different award sizes are needed for different kinds of research support. For some Agencies, award sizes may not need to be as large. For some life science research, awards will need to be much larger. Flexibility is critical to maintaining a successful SBIR program. The amounts should always be commensurate with what the science and technology require. Artificial caps could threaten innovation.

Summary

The changes proposed by the Small Business Committee will greatly enhance the impact of SBIR companies in the life science area. SBIR grants have several positive impacts. First, Phase I capital can be used to develop products to the point of proof of principle, allowing key data to be generated in support of commercialization and technology transfer. This early validation of a technology via the peer-review system affords a level of technical approval and acceptance. Second, the critical SBIR phase II funds allow the leap to more extensive data generation that can warrant early stage investments such as those by the LSGs. This stage still lacks sufficient funding to complete all of the necessary preclinical trials needed prior to initiation of regulated trials, however. Programs such as the competitive Phase II B program provide enhanced levels of funding, matched at least 1:1 with private funds, to carry on preclinical trials needed to receive FDA approval to move the drug or device into the clinical trials area. Third, the SBIR programs need to recognize that venture-backed and other professional equity funds are needed to generate the amounts of funding needed to propel a company into the early stages of clinical trials. This is a high risk, high cost endeavor.

Thus, the research and development supported by the basic investments in NIH and National Science Foundation can be translated towards commercialization via programs such as the SBIR and Small Business Technology Transfer (STTR) grants. However, in order to maximize the impact of innovative technologies on human health, and to recognize the significant risk involved in new product development, we strongly recommend that SBIR programs reflect the intrinsic risks and rewards in the complex and costly system of regulatory approval of new products to treat disease.

701 Pennsylvania Ave NW, Suite 800
Washington, DC 20004
Tel: 202 783 8700
Fax: 202 783 8750
www.AdvaMed.org

HOUSE SMALL BUSINESS

SUBCOMMITTEE ON

INVESTIGATIONS AND OVERSIGHT

FEBRUARY 13, 2008

STATEMENT BY

JAMES STEFANSIC, PHD, MBA

CHIEF TECHNOLOGY OFFICER, PATHFINDER THERAPEUTICS, INC.

ON BEHALF OF
THE ADVANCED MEDICAL TECHNOLOGY ASSOCIATION (AdvaMed)

We thank the Subcommittee for holding this important hearing today on the Small Business Innovation Research (SBIR) grant program and its role in advancing medical breakthroughs. My name is Jim Stefansic, co-founder and Chief Technology Officer for Pathfinder Therapeutics, Inc., a small medical device company located in Nashville, TN.

Pathfinder is a member of AdvaMed, the Advanced Medical Technology Association, which represents over 1,600 of the world's leading medical technology innovators and manufacturers of medical devices, diagnostic products and medical information systems. Over 70% of our member companies are relatively small companies with sales of less than $30 million per year. Our members are devoted to the development of new technologies that allow patients to lead longer, healthier, and more productive lives. Together, our members manufacture nearly 90 percent of the $86 billion in life-enhancing health care technology products purchased annually in the United States, and nearly 50 percent of the $220 billion in medical technology products purchased globally.

The medical technology industry is a critical component of the U.S. health sector. In addition to the profound contributions of medical technology to the health and well-being of the public, in 2006 the industry employed 357,700 workers; paid $21.5 billion in salaries; and shipped $123 billion worth of products. Taking into account the national multiplier impacts, the industry created (direct plus indirect plus stimulated impacts): 1.96 million jobs; payrolls that totaled $93 billion; and $355 billion in shipments/sales. However, we are not just a major contributor to the U.S. economy based on revenues and jobs. The devices we make also help patients stay healthier longer as well as recover more quickly after treatment, thus allowing patients to participate more fully at work and in the community.

The medical technology industry is fueled by intense competition and the innovative energy of small companies – firms that drive very rapid innovation cycles among products, in many cases leading new product iterations every 18 months. Our constant innovation leads to the introduction of new technologies that prevent illness, allow earlier detection of diseases, and treat patients as effectively and efficiently as possible.

Overview of Pathfinder Therapeutics, Inc.

Pathfinder Therapeutics, Inc. (PTI) is a surgical technology company that is focused on developing the world's first image-guided surgery systems for soft tissue applications. Image-guided surgery essentially describes the interactive use of images during a medical procedure and is often referred to as a "global positioning" system (GPS) for surgery. In an automobile GPS, the current position of a vehicle is accurately localized or "registered" onto an electronic roadmap located on the dashboard. As the automobile moves, its position is updated on this roadmap. The driver can use the GPS as a guide to determine where his or her vehicle has been and where it is headed. In image-guided surgery, the current surgical position is registered onto medical images that are used as a guide to conduct a therapeutic procedure.

PTI was incorporated in July 2004 through a partnership with Vanderbilt University, where the initial technology was developed by six current and former clinical and engineering faculty members, including myself. Note that the surgical guidance device was developed over a seven year period at Vanderbilt before the company was formed, so much of the technology risk associated with bringing a novel medical device to the market was eliminated. With support and

guidance from the technology transfer office at Vanderbilt, PTI was extremely fortunate to acquire a modest seed round investment to launch the company. Note that when PTI was formed, none of the founders had any small business experience. As I was the one founder finishing my part-time MBA at Belmont University and was inclined to work in industry, I left my position as a faculty member at Vanderbilt to run operations at the company. The other founders remained in their respective career academic positions.

In under four years, PTI has grown to eight employees and acquired $3.4MM in SBIR funds from the NIH / NCI. Our greatest achievement to date was being granted FDA clearance in late December, 2007 for our Linasys device, an image-guided liver surgical system that can be used to pinpoint and accurately resect or ablate tumors located deep within this organ. Given that tumor resection clearly provides the best chance of long-term survival for patients suffering from liver cancer, our device is of great benefit as it assists physicians performing these very difficult surgical procedures.

Although PTI has overcome much of the technology and regulatory risk associated with bringing a new medical device to market, many other challenges remain to ensure that our technology can improve the lives of those suffering from abdominal cancer. It is important to note that these risks would not have been conquered without both the SBIR grants and the modest seed round investment in PTI. Both of these funding sources are described in more detail below.

The Impact of SBIR for Pathfinder

Given that the expertise of the founders in successfully acquiring academic federal grant funding, we were encouraged by our seed round investors in the summer of 2004 to raise additional early-stage funds through the SBIR mechanism. With teamwork and considerable effort from all the founders, in early 2005 PTI was fortunate to land on our first attempt a fast-track SBIR grant from the National Cancer Institute (NCI) to develop a commercial software and hardware platform for a variety of image-guided therapeutic applications that target cancer. As the principal investigator on this grant, I have been able to focus part of my time and energy on taking the technology from the founders in the academic setting to commercialization without being concerned about salary support and other R&D resources for my engineering staff. The $1.5MM in grant funds have been primarily used to develop the SurgiSight image-guided therapy platform and will enable PTI to grow from one specific therapeutic area (liver surgery) to the broader field of surgical oncology (kidney and colorectal) to the broadest field of general surgery (vascular/soft tissue applications throughout the body). The key to unlocking this potential is the stability and versatility of our software platform and its ability to seamlessly interact with multiple hardware configurations. This versatility will enable Pathfinder to release products that are amenable to applications that employ either an open or minimally invasive surgical approach.

Although it took longer to acquire, PTI was fortunate in late 2006 to land a second fast-track SBIR grant from the NCI worth $1.9MM to conduct a 3-site clinical trial with our Linasys device and demonstrate its efficacy. To our knowledge, this will be the first formal clinical trial ever conducted by a company in the field of image-guided surgery. After considerable preparation, including the planning and actual replication of three Linasys systems, we are now set to launch the clinical trial at three premier cancer centers in the U.S. – Memorial Sloan Kettering, Univ. of Pittsburgh Medical Center, and Shands at the Univ. of Florida . The feedback we will acquire

from the thought-leader surgeons at these sites and data acquired will help us improve the quality of our device and successfully market our product for its now FDA-cleared indicated use.

The positive impact of the SBIR grants for PTI cannot be overstated. We would not have survived the critical and difficult stage of transferring the product from a research to a commercial environment without this funding. The costs can be staggering and are often not supported in full by early stage venture capital or angel funding because of the considerable technology risk and scientific unknowns.

To place their value in perspective, note that 7 of our 8 current employees are funded at least in part by the SBIR grants. Considerable R&D expenditures, in addition to some corporate overhead and other expenses, have been and continue to be covered with the direct, indirect, and profit components of this federal funding.

The Need for Venture Capital Funding

As stated previously, PTI secured an early stage seed round investment, which includes both angel and venture capital funding. Given the challenging environment for the acquisition of early stage funding for medical technology, this was a critical source of capital that PTI was fortunate to secure at the onset of incorporation.

Unless one has "been in the trenches" of a start-up medical device company, it is difficult to imagine all the time and financial resources that are required to initiate and maintain this type of business beyond product R&D. Note that many scientists who apply for and obtain NIH SBIR funding are starting their very first businesses. Although these individuals are intelligent and motivated, they usually do not have the experience or time to handle the "overhead" side of the business beyond R&D, including accounting, legal, quality/regulatory, and marketing & sales issues. They are so focused on handling the technology risk that all other risks are put on hold, sometimes indefinitely. To guarantee success, it is important for start-up medical device companies to consider these issues and more importantly their costs at the onset of launching their businesses. Unfortunately, most of their financial costs are not covered by SBIR grants.

With the help of our Board of Directors, PTI hired appropriate lawyers and accountants with experience launching and building medical device companies. This included lawyers skilled in the art of intellectual property prosecution. We also started a search for experienced management early in 2005. By January 2006, we hired our CEO & current President Paul MacDonald, a seasoned executive with industry-specific experience. We hired appropriate consultants to assist with regulatory issues related to FDA clearance. Finally, some limited resources were used to establish a FDA-compliant quality system.

As mentioned previously, the SBIR funding aids in reducing the technology risk associated with creating a sustainable medical device company. Unfortunately, there are many other types of risk that must be considered concurrently, including management (people) risk, regulatory risk, and market risk. Although Pathfinder only received a modest seed round investment from venture capital sources, we were at least able to consider these risks at the earliest stages of corporate development while taking advantage of the SBIR mechanism. This does not ensure that the

R&D efforts successfully executed with the SBIR money will lead to commercial and market success, but our chances are much greater.

The Impact of SBIR Eligibility Rules

A series of rulings from 2001 – 2003 by the Small Business Administration's Office of Hearings and Appeals resulted in the determination that small businesses that were majority-backed by venture capital investors were no longer eligible for SBIR grants. This interpretation of SBA regulations excludes many small medical technology companies from participating in the SBIR program – including many that have received SBIR grants in the past and are emblematic of the success of the program – even though these small businesses still have a tremendous need for assistance. It is at odds with the original intent of the SBIR program to assist small businesses with the enormous task of developing promising, early stage technologies so they can be brought to market for the benefit of patients. It also shrinks the competitive pool of SBIR applicants and hinders SBIR's goal of funding the most promising breakthroughs in medical technology to improve public health.

It is important to note that venture capitalists are becoming more and more risk averse. They are now investing in later stage companies in order to reduce their risk profile and put larger amounts of capital to work in companies that are already generating revenue or have completed human clinical trials. For Pathfinder, this trend has been very frustrating. Note that we have successfully navigated the technology and regulatory risks using a combination of both angel and institutional investors and SBIR funds, and even considered other risks as much as financially possible. However, in order to diversify appropriately, our current venture capital investors can only allocate a small portion of their funds to extremely high risk early stage medical device portfolio companies such as PTI. They are now looking for other venture capital firms to share in the risk moving forward and cannot fully support PTI's financial needs.

Unfortunately, new venture capital investors continue to wait on the sidelines for the risk to be even lower before they invest in PTI. For example, one key risk factor for these investors involves the size of the liver cancer market. Although liver cancer is one of a few cancers in the U.S. that is actually growing in rate and the NCI realizes that there is a need for new technology to combat this, the market is still very small compared to the large investor markets in orthopedics or cardiology. The investors are not convinced that their investment in PTI would provide an acceptable return given this market size. PTI has considered this and is prepared to launch the commercial liver surgery image-guided application first while continuing to focus on other higher volume image-guided surgical applications for colorectal or kidney cancer.

Of course, this strategy will still require additional R&D funding for both engineering and clinical costs. Because we continue to be provided with bridge financing by our seed round venture capital investors, PTI will very soon no longer be eligible for any additional SBIR funding given the change of our ownership structure. This is frustrating both to us and our seed round angel and venture capital investors who took a high amount of risk to bring our technology to its current stage and would appreciate future R&D funds to grow the company. PTI will continue to take advantage of current SBIR funding awarded to the company and work to lower the risk so new investors will consider our opportunity.

The Impact of New NIH & NCI SBIR Programs

Fortunately for SBIR companies, the NIH and NCI have recognized that companies need further resources beyond SBIR R&D funds to get their novel medical technologies to market. For example, PTI has recently benefited from the NIH SBIR Manufacturing Assistance Program (MAP). Assistance for developing a FDA and ISO quality facility at PTI will be provided by the Tennessee Manufacturing Extension Partnership (TMEP). In particular the Univ. of Tennessee Center for Industrial Services will provide PTI with 171 hours of consulting in the next 6 months that is paid for by the NIH. This assistance will not only ensure that we meet all necessary national and international regulations in the manufacturing of the Linasys device, but also improve the overall quality of our facility. Although this award is beneficial, it is very small compared to a Phase II SBIR grant and will not fill in all the gaps necessary to commercialize federally funded medical technology.

The NCI is also involved in new programs and is seeking to establish a financial bridge program to move SBIR companies through the "Valley of Death," or period in between the completion of significant technology milestones accomplished with SBIR funding and the FDA approval process. By providing funding beyond the end of the SBIR, the NCI seeks to share in the investment risk and incentivize venture capitalists to fund earlier stage projects. Note that Pathfinder has been able to somewhat navigate the "Valley of Death" through careful planning with venture capital support provided concurrently with the SBIR funding.

Legislation to Restore SBIR Eligibility for Small Businesses

These new programs at NIH are promising and will help assist small medical technology companies as they move from product development to commercialization. However, addressing the venture capital issue remains of utmost concern to Pathfinder and other small companies that rely on SBIR funding to develop new medical technologies for patients.

Mr. Chairman, we thank you for your leadership in the reauthorization of the SBIR program and for your strong support in restoring SBIR eligibility for small businesses like ours that also have venture capital investment. We also thank you, Congressman Graves, for your longstanding efforts and leadership to restore SBIR eligibility for the past several years. We also want to thank Chairwoman Velazquez for her leadership in moving SBIR reauthorization forward this year and for her support on the venture capital issue. And we also want to thank Congressman Chabot for his willingness to work with us to resolve this important issue. We look forward to working with all of you to ensure that small businesses will continue to drive medical innovation and develop promising new technologies for patients.

I want to thank the Subcommittee again for holding this important hearing. We look forward to working with you as SBIR reauthorization moves forward. I'll be happy to answer any questions you may have.

Hearing Testimony
F. Nicholas Franano, M.D.
Founder and Chief Scientific Officer
Proteon Therapeutics, Inc
Before the House of Representatives on Small Business
"SBIR: Advancing Medical Breakthroughs"
Wednesday, February 13, 2008

Chairman Altmire, Ranking Member Graves, and Members of the Committee:

Thank you for providing me the opportunity to testify before you today regarding the Small Business Innovation Research Program (SBIR). My name is Nicholas Franano. I am a physician, scientist, and founder of Proteon Therapeutics, an early stage biotechnology company with operations in Kansas City, Missouri and Waltham, Massachusetts. My familiarity with the SBIR program began in 2003 when Proteon Therapeutics first applied for an SBIR grant from the NIDDK. In 2004, Proteon was awarded a Phase I STTR grant from the NIDDK and in 2005 Proteon won a Phase I SBIR grant from the NHLBI. I have served as the principal investigator for both grants. In 2007, I went to the other side of the table and served as a member of a scientific review committee tasked with evaluating SBIR grants for the NIDDK, and so I have now seen the program both from the vantage point of applicant and reviewer.

In preparation for this testimony, I reviewed the excellent remarks by Douglas Doerfler, the CEO of Maxcyte, Inc, that were presented to the committee on January 29th. In my opinion, Doug's testimony provided an excellent summary of the strengths and weaknesses of the current SBIR program. His comments are almost entirely consistent with my personal experiences. Rather than remake the points Doug emphasized, I would like to relate my personal story and the story of the Company that I founded, as a way to provide additional depth to your understanding of the issues.

In 1993, I was a medical student at Washington University, St. Louis and had just completed the requirements for a master's degree program in biomedical research. While applying for a residency position in Radiology at Johns Hopkins University, I had the good fortune to meet Dr. Elias Zerhouni, who was then an associate professor. Elias wanted to bring more individuals to the Radiology Department at Hopkins who had a background and interest in research. As you may know from the size of his NIH budgets, Elias is a hard man to say no to. In 1997, after four years of medical training at Hopkins, Dr. Zerhouni asked me to apply for a physician research training grant from the NIH and devote half of my time to laboratory research for a period of two years. The grant paid 50% of my salary, freeing up the

time for research, an incentive that was necessary for the department to let me go into the lab.

When I sat down with Elias at the start of the project and asked him what he would like me to focus on, he gave a remarkable answer. Although I don't remember the specific words, his message was clear and memorable. Identify an important medical problem that interests you and that you could be passionate about, and then try to find a better way to treat it. It sounded so simple and straightforward, I thought. As an interventional radiologist, I had spent many hours unclogging vascular access sites for patients on hemodialysis and was interested in studying this problem. The difficulty begins when a patient's kidneys stop working. Without treatment, they will die within days. Fortunately, there are machines that can filter the blood of patients with kidney failure, allowing them to live. In order to get blood out of a person to filter through the machines and then give the cleaned blood back to the person, a surgeon must create a site in the body where blood can be removed and returned rapidly. Although these access sites are relatively straightforward to make, they don't last. The sites need to be repeatedly cleaned out and opened up, and eventually replaced. It is miserable for patients and expensive for Medicare to deal with this chronic problem, accounting for more than $1B in costs each year. During my time working as a physician at Hopkins, it occurred to me that the clogging occurs in a pretty short and predictable segment of blood vessel in the access site and the clogging is often a direct cause of the blood vessel being too small in diameter. During my time working as a researcher at Hopkins I invented a drug and methods that could be used at the time an access site was created that could enlarge the diameter of the key blood vessel segments and reduce the chance of clogging. Not surprisingly, Hopkins asked me file for a patent on the invention, which I did. The patent lawyers told me the University would almost certainly license this invention to a biotechnology or pharmaceutical company for development. After this, I left Baltimore in 2000 and went back home to Kansas City to start a family and a private medical practice. Life was good. In 2001, the Technology Transfer Office at Hopkins contacted me about the patent application. The Office had offered a license to the invention to a few companies but they had declined. My contact at the Technology Transfer Office indicated that the deadline for worldwide patent filings was coming up in the next few months and that without a licensee, Hopkins would likely abandon the patent rather than pay the additional fees. I implored them to keep investing in the technology. They responded by asking if I was interested in buying the patents from Hopkins and starting a biotechnology company myself.

I spent the next several weeks talking with individuals with biotechnology experience about whether I should do this. To my surprise, nearly all of the individuals I contacted recommended against it. First, they said it is really hard to find capital and talent for a biotech company in a place like Kansas City and that I would likely have to move to Boston or San Francisco to get a company started. Second, they worried that without formal business experience I would not be able to attract enough investors to be successful. Third, they said that even if I could get

past these two barriers, the odds that a pre-clinical drug candidate would make it to the market is very low, and that I could harm my medical career by spending a lot of time working on it.

One bright spot in this discussion, however, was learning about the SBIR program and understanding how the SBA could help support an early stage biotechnology company with a novel approach to an important unmet medical need. With that in mind, I got just enough courage to discuss the idea with my wife. To my surprise, she was cautiously supportive. I committed to continue working as a physician initially and see how the Company and technology came along. In the fall of 2001, Proteon Therapeutics was born. I attracted an experienced business partner and co-founder and quietly started moving money from my savings to the Company to generate additional data that we might use to attract investors. I set up an office in the basement of my house and started reading every research paper I could find on the topic. I worked nights and weekends, slept through parties, and missed a lot important events. Then in the fall of 2003, Proteon secured its first round of external capital, a total of $265K. We squeezed every last bit of progress out of each dollar and applied for an SBIR grant to help. We took no salary. Our first grant was rejected without review. We sent in a revised grant with more data and a new lead drug candidate (PRT-201) and got a borderline score. The program director Dr. Marva Moxey-Mims contacted me and indicated that if I formed a partnership with the University of Kansas and converted the grant into an STTR she might be able to get it funded. Within days, the grant was rewritten as an STTR and we got the $157,000. This allowed Proteon to hire our first real employee and helped build out a small laboratory at a local biotechnology incubator mostly with used equipment, some purchased off eBay. I went part-time as a physician in order to devote more time to the Company. That grant really made a difference for Proteon.

While raising subsequent rounds of capital from angel investors, it became clear to me that many of the individuals that we were talking with had difficulty assessing the technology and the likelihood for success. For a $50 - 100K investment, it did not make sense for them to spend too much time or money trying to figure this out either. In this setting, angel investors look for external signs to guide them. Being able to say that Proteon had submitted a grant application to a panel of experts at the NIH, had received a good score, and that the SBA had decided to fund the Company was a big help. I went so far as to show potential investors the actual grant reviews, which indicated that the problems were we addressing were big and important, and that the technology was novel and had a reasonable chance of making a difference. The partnership with the University of Kansas helped a lot as well, giving us access to some of the resources there. The grant and partnership was invaluable in attracting the additional capital that helped us through the "valley of death" that Doug described in his remarks.

In 2005 we were awarded a second SBIR grant by the NHLBI to study the use of our drug for patients with blocked arteries in their legs who are at risk for amputation. The work in both grants has ended successfully, and both drug development

programs continue to advance toward clinical testing. In the spring of 2006, Proteon was able to raise a $19M round of capital from a group of four venture capitalists from Boston, San Francisco, Durham, and Munich, Germany. It was the biggest biotech venture capital financing in Kansas City history. With that money, Proteon has continued the development of our lead drug candidate, which we expect will undergo testing in our first human clinical trials this year. In many regards, Proteon is an SBIR success story. Without those two grants, I think Proteon very well might have failed in 2005 and the development of our drug would have been halted. Given that, I would encourage the committee to renew the program and raise funding levels. I believe that the statement by the National Research Council that "U.S. technological performance is challenged less in the creation of new technologies than in their commercialization and adoption" is as true today as it was when they made it.

If this were a movie, the story would stop here, to make for a nice ending. However, there is another chapter. The Small Business Administration (SBA) Office of Hearings and Appeals (OHA) has ruled that once a company is owned more than 50% by venture capitalists, the employees of those venture capital companies and the employees of all of the other companies they have invested in count toward the 500 employee limit, effectively disenfranchising most biotechnology companies from the program, including a post-2006 Proteon. In my opinion, this will have a profoundly negative effect on the pace and quality of new technology development in the United States and will slow our economic growth. It will also slow the development of life saving medicines. As I sit here today, I have an idea for a new drug to treat aortic aneurysms, a life threatening condition where the main blood vessel coming from the heart bulges and is at risk for rupture, bleeding, and death. The problem is that Proteon's capital was raised to develop PRT-201, a necessary focus given that it may take an additional $50M or more to bring this drug to market. In prior years, I could have submitted an SBIR grant to start work on this new treatment and use the grant support to generate the data that could be used to get the project going internally. Today, however, this idea sits on the shelf, in limbo. Not moving forward, but not forgotten. Who knows if it will work? We will probably never know.

Sincerely,

F. Nicholas Franano, M.D.
Founder and Chief Scientific Officer
Proteon Therapeutics, Inc
4420 Madison Ave, Suite 180
Kansas City, Missouri, 64113
816-531-0028
nfranano@proteontherapeutics.com

HEARING TESTIMONY
DOUGLAS A. DOERFLER
PRESIDENT AND CHIEF EXECUTIVE OFFICER
MAXCYTE, INC.

ON BEHALF OF
THE BIOTECHNOLOGY INDUSTRY ORGANIZATION (BIO)

BEFORE THE HOUSE OF REPRESENTATIVES COMMITTEE ON SMALL BUSINESS

"SBIR: AMERICA'S NATIONAL TECHNOLOGY DEVELOPMENT INCUBATOR."

JANUARY 29, 2008

Chairwoman Velázquez , Ranking Member Chabot, and Members of the Committee:

Thank you for providing the opportunity to testify before you today regarding the reauthorization of the Small Business Innovation Research Program (SBIR).

My name is Doug Doerfler and I have been President and Chief Executive Officer of Maxcyte, Inc. in Gaithersburg, MD since 1999. Currently, I serve on the Biotechnology Industry Organization's (BIO's) Board of Directors, the Executive Committee of the Emerging Company Section Board of Governors and am co-chair of the Capital Formation Committee.

I have led the development of global biotechnology companies and products for more than 25 years. MaxCyte currently has approximately 20 employees who are developing novel therapeutics using cells that have been modified by our process to treat serious diseases. We have one product in Phase I/II clinical human testing for the treatment of patients with Leukemia, a product in Phase IIa human clinical trials for the treatment of Pulmonary Arterial Hypertension and additional products in pre-clinical development for the treatment of cardiovascular disease, cancers and infectious disease. These programs are partnered with commercial partners and major Universities, including Baylor, the University of Pennsylvania, Duke University and Stanford University. MaxCyte was the proud recipient of Phase I SBIR grants in 2003.

Today I am testifying on behalf of BIO, an organization representing more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in 50 U.S. states and 31 other nations. BIO members are involved in the

research and development of health care, agricultural, industrial, and environmental biotechnology products. The overwhelming majority of BIO member companies are small, early stage research and development oriented companies pursuing innovations that have the potential to improve human health, expand our food supply, and provide new sources of energy.

SBIR'S CRITICAL ROLE IN COMMERCIALIZATION OF BIOTECHNOLOGY INNOVATIONS

Biotechnology Company Profile and Path to Product Development

Before discussing the critical role of the Small Business Investment Research (SBIR) program in the commercialization of biotechnology innovations, I would first like to provide a description of a typical biotechnology company and the capital required for research and development. BIO has over 600 emerging companies in its membership. In a recent survey conducted by BIO, 80 % of respondents had fewer than 50 employees.

Promising biotechnology research by these companies has a long, arduous road from preclinical research, through Phase I-safety, Phase II-efficacy, and Phase III-broader population clinical trials, and ultimately, to FDA approval of a therapy. It is estimated it takes between 8 and 12 years to bring a biotechnology therapy to market and costs between $800 million and $1.2 billion.[1] In the absence of product revenue biotechnology companies are almost entirely reliant on capital markets or other sources of financing to fund research and development. This is particularly challenging at the earliest, highest-risk stages of research and development. The majority of biotechnology companies are without any product revenue for a decade or more. As a result, significant capital requirements to advance a new therapy to the market necessitate fundraising through a combination of angel investors, venture capital firms and occasionally other investors. The role and importance of venture capital fundraising cannot be understated. In 2006 alone, venture capital investment in the life sciences and medical devices industry totaled $7.2 billion in 2006, up from $2.8 billion in 1998.

Biotechnology companies are generally a collection of research projects with one lead product and an average of 5 other therapies or candidates in early stage/pre-clinical research.[2] Typically, a biotechnology company will begin fundraising for its lead product in development. Companies generally raise between $5 million and $15 million in their first round of venture financing, an amount that usually results in multiple venture capital companies owning more than 50 percent of the company. This is especially the case with very young companies whose valuation may reflect their high-risk, early stage nature. However, it is typically the case that no single venture capital company will own more than 15 to 20 percent of the equity.

---

[1] Tufts Center for the Study of Drug Development
http://csdd.tufts.edu/NewsEvents/NewsArticle.asp?newsid=69

[2] BIO sponsored, third-party administered, survey of 144 BIO emerging companies' Chief Executive Officers and Chief Financial Officers, March-April 2007

Despite the extensive fundraising a biotechnology company undertakes for the lead product, these funds are not interchangeable, that is they are tied to very specific milestones to support the lead product's development. As such, in order to develop secondary or tertiary candidates/therapies a company has to find secondary sources of fundraising capital. At the very earliest stages of development other sources of financing, like Small Business Investment Research (SBIR) grants, have been instrumental in advancing research and development in biotechnology.

Mission of SBIR: Bringing Innovation to the Public

Congress created the SBIR grant program in order to utilize the capabilities of small, innovative, domestic companies to fulfill federal research and development needs. In the early 1980's there was growing concern the United States federal research and development spending was not improving the health and well being of the citizenry through the development and commercialization of new products and therapies. Furthermore, it was recognized that some early stage, promising scientific research failed to be funded through the markets because it was viewed as too high risk. This failure of the markets is often referred to as the "valley of death." In biotechnology, the "valley of death" delays potential therapies for HIV, cancer, and infectious diseases from reaching patients, who often lack other comparable alternatives.

For these reasons, in 1983, Congress authorized the SBIR program. When the program approached reauthorization in the early 90's a report by the National Research Council discussed continued concerns that *"U.S. technological performance is challenged less in the creation of new technologies than in their commercialization and adoption."*.[3] Currently, these grants set aside 2.5% of certain departments and agencies extramural research budgets for innovative research grants with an aim towards commercialization.

Historical Success of SBIR Program

For twenty years small, domestic biotechnology companies competed for SBIR grants. In addition to providing critical funding, these grants were a powerful signal to the private sector that company's research was compelling and possessed scientific and technical merit. In biotechnology, the SBIR program has played a role in advancing the science and research of companies that have ultimately brought a product to market. For example, there are 163 companies and affiliates involved in the development of the 252 FDA approved biologics, 32% of those companies and affiliates have received at least one SBIR/STTR award. These grants have helped make the U.S. the world's leader in biotechnology by providing critical early-stage funding for innovative research.

[3] (National Research Council, *The Government Role in Civilian Technology: Building a New Alliance*, Washington, D.C.: National Academy Press, 1992, pp. 29).

IMPACT OF RECENT CHANGES TO SBIR PROGRAM

Unintended Consequences of the SBA's Domestic Company Proxy

On April 7, 2003, the Small Business Administration (SBA) Office of Hearings and Appeals (OHA) arbitrarily ruled that a biotechnology firm, Cognetix, did not meet the SBIR size standard because it had venture capital investment in excess of 50%. This ruling is base upon SBA regulations, not underlying statute, by which a small business concern (SBC) for the SBIR program is defined as having fewer than 500 employees, including affiliates, and is at least 51% owned by U.S. citizens.

SBA has stated the ownership rule is meant to be a proxy for determining that a company is domestic.[4] However, the use of capital structure as proxy for determining domesticity and the subsequent OHA ruling has had the unintentional consequence of excluding a sizeable portion of the biotechnology industry that would otherwise be eligible to participate in the program. These are companies that have participated in the SBIR program for 20 years prior to this ruling and were a fundamental part of the aforementioned success of the SBIR program. These are companies solely based in the United States and are majority funded through a combination of U.S. based venture capital companies and citizens. The result is that many emerging biotechnology companies are ineligible to compete for SBIR grants.[5] Perhaps more importantly, this ruling has the potential of negatively impacting the competitive pool of SBIR applicants and the program's ability to award projects with the highest scientific merit and commercialization potential.

My own company, MaxCyte was in the fundraising process in 2003, when we submitted a proposal to NIH to do basic research in our technology and expand its capability so one day it may be used for biodefense or pandemic influenza vaccine development. Venture funds were not interested in this project as it was too early and risky but were clearly motivated by our team's ability to obtain attractive scores for our program through the NIH study section process. We received $95,000 in funding for our Phase I and subsequently closed on a $20.0 million venture round. We were able to satisfy the rigorous milestones of our project including breakthrough science to prove general concept-although we are currently eligible for follow on SBIR funding our eligibility may change with another needed financing.

There are numerous examples of promising discoveries that have been shelved or delayed as a result of the recent interpretation of ownership. I will mention just a couple of examples.

1. Intronn Inc. (Gaithersburg, MD) won SBIR grant for Phase I and II study to advance research in treatment for Cystic Fibosis. They were awarded a second

[4] (54 Fed. Reg. 5264 (Dec. 21, 1989) Interim Final Rule on defining a business concern for the purposes of the SBIR program.)
[5] BIO sponsored, third-party administered, survey of 144 BIO emerging companies' Chief Executive Officers and Chief Financial Officers, March-April 2007

Phase II grant in 2003 but the award was rescinded due to the new rule on venture capital investment. The project was shelved.

2. Paratek Pharmaceuticals (Boston, MA) won a Phase I SBIR grant in 2001 to research antibiotic therapies for things such as malaria and anthrax. In 2003, due to changes in SBIR rules, Paratek was forced to turn down a Phase II grant and their antibiotic therapy research program was shut down.

3. Xcyte Therapies (Seattle, WA) received a Phase I SBIR grant in 2002 to develop new treatments for cancerous tumors in the kidney and prostate. In early 2004 Xcyte Therapies received a Phase II SBIR grant to help fund clinical testing but was unable to use the funds as they were deemed ineligible.

These are ironic outcomes considering that venture capital is a necessary part of the ability to achieve SBIR's mission of supporting commercialization. It is unfortunate that venture capital invested with the goal of bringing new therapies to the market has, in many instances, caused SBIR funding to be pulled and research projects to shelved. This is exactly the opposite of what Congress had in mind when they created SBIR.

OPPORTUNITY TO STRENGTHEN/RESTORE SBIR PROGRAM

I appreciate the opportunity to discuss changes to the SBIR program that I believe would strengthen the program and make it more effective in the years to come. My recommendations can be grouped under four general goals for SBIR Reauthorization. First, increasing competition for SBIR grants and, as such, improving science and fostering innovation and commercialization by small companies. Second, clarifying SBIR eligibility rules to make them easier to understand and increasing transparency regarding the program's operation. Third, maintaining agency flexibility so as to make certain the SBIR program continues to serve the needs of individual agencies. And fourth, making certain that the SBIR guidelines appropriately safeguard taxpayer funds.

I will touch briefly on each of these important goals.

Increase Competition and Foster Innovation and Commercialization

SBA's 2003 ruling that excludes majority venture-backed companies inhibits the SBIR program from receiving the most competitive pool of applicants possible and stifles the ability of SBIR to carry out its mission to fund projects that will improve public health and have the most commercial potential. It is vital to the American public to ensure they realize the benefits not just of products with commercial potential but the benefits of projects funded based on scientific merit and deemed to be of value to promoting our citizens public health.

The current SBA interpretation would deem eligible a public company with 300 employees, as well as, a private company with 400 employees, $200 million in venture

capital from multiple venture capital firms that equal 49% of equity with additional angel investment dollars. However, a private company with 20 employees, $50,000 in annual revenue and $8 million in venture capital by multiple venture capital funds equaling 56% of equity – even though no one venture capital firm has more than 30% of total equity – is ineligible. Among BIO emerging companies, a significant amount are ineligible, the majority of which would apply to SBIR if able. These companies are working on breakthroughs for the treatment of diseases such as Alzheimer's, lupus, and leukemia.

The National Institutes of Health (NIH) have documented disturbing trends since the 2003 ruling. Applications for SBIR grants at NIH have declined by 11.9 percent in 2005 and by 14.6 percent in 2006.[6] Additionally, the number of new small businesses participating in the program has decreased to the lowest proportion in a decade.[7] The Director of the National Institutes of Health, Dr. Elias Zerhourni, wrote in a letter to SBA Administrator Barreto dated June 28, 2005: *"NIH believes that the current rule undermines the statutory purposes of the SBIR program.... It undermines NIH's ability to award SBIR funds to those applicants whom we believe are most likely to improve human health."* (emphasis added). I would like to submit this letter for the record.

Some critics have recommended that biotech companies look for other grants to fund their research. However, this is easier said than done. For instance, only 0.4% of non-SBIR/STTR grants at NIH went to biotech companies. SBIR supports small business concerns to conduct high-risk, early-stage, innovative research that has a focus toward commercialization of a product or service. Unlike other NIH grant mechanisms, SBIR grants are not hypothesis-driven research. Hypothesis driven research is scientific research solely for the purpose of advancing knowledge in the subject area and is not concerned with commercialization. SBIR is the only program that bridges the two.

BIO respectfully requests the Committee recognize the necessary and complex involvement of venture capital in small biotechnology companies. As stated previously, small biotechnology companies have high and intense capital needs (up to $1 billion) and an unusually long development time of 5-12 years. The vast majority of biotechnology companies raise between $5 million and $15 million in their first round of venture financing for their lead product(s), an amount that usually results in the venture capital firms collectively owning more than 50% of the company. However, the investment group usually consists of several firms, none of which owns more than 15-20% of the company. SBIR plays a critical role in aiding small biotechnology companies in their early stage research to navigate through the "valley of death" where the concept is too high-risk for private market support.

BIO respectfully asks the Committee to reinstate the eligibility of small biotechnology firms into the SBIR program. This will ensure the most competitive pool of applicants

---

[6] The National Institutes of Health

[7] Testimony from Jo Anne Goodnight, SBIR/STTR Program Coordinator for NIH to the House Subcommittee on Technology and Innovation, Committee on Science and Technology: *The SBIR and STTR Programs at the National Institutes of Health – How are Programs Managed Today;* June, 26, 2007).

and that grants awarded will be based on projects that show the most promise in bringing breakthrough therapies to the public.

Clarify SBIR eligibility rules to make the application process more straightforward and user-friendly

It is equally important the reauthorization clarify SBA affiliation regulations. Under current SBA regulations, when determining the size of a business, the SBA considers the number of direct employees at the business as well as affiliated businesses' employees. Businesses are affiliates of each other if the SBA determines that another business has either affirmative or negative control. Current regulations state that a venture capital company that holds a minority share in another business can be considered an affiliate of that business. If the SBA determines a venture capital company is affiliated with the business, not only are the employees of the venture capital company included in the size determination but so are the employees of all other businesses in which the venture capital firm is invested.

As a result of these affiliation rules, a small company with 50 employees could be deemed to be affiliated with hundreds of other employees of companies with which the small company has no relationship whatsoever, just because the companies share a common investor. It is important to note that this can be the case where the VC investor owns a minority stake in the small business applying for SBIR.

Not only are these affiliation rules non-sensical, the manner in which they are applied is often a mystery to the small business applying for the SBIR grant. As a result, a small company may certify in good faith that it is eligible for an SBIR grant, only to later find out that the SBA has affiliated it with a large number of employees at other unrelated companies, thus making the small business ineligible. BIO recommends the reauthorization bill provide language to clarify that investment by a venture capital operating company does not make that company an affiliate of another company for the purposes of determining size. This is a common-sense measure that will provide clarity and peace of mind for small business entrepreneurs looking to participate in the SBIR program.

Maintain Agency Flexibility

BIO also supports maintaining agency flexibility in the SBIR program. One of the great strengths of the SBIR program is that Congress provided the affected departments and agencies with flexibility in establishing the program. Maintaining flexibility in the program is also supported by a National Research Council 2007 report which states, *"...flexibility is a positive attribute in that it permits each agency to adapt its SBIR program to the agency's particular mission, scale and working culture."* [8]

[8] National Research Council, *An Assessment of the Small Business Innovation Research Program at the National Science Foundation*: Washington, D.C.: National Academy Press, 2007. pp 21 (www.nap.edu/catalog/11929.html)

The reality is that various government agencies may structure their SBIR program in different ways to meet differing agency needs. This is a good thing, so long as the original goals of the SBIR program are preserved. Certain agencies, for example, may need the flexibility to award larger grants, if the project they are funding is in an area where research is typically more expensive. This is sometimes the case for biotechnology companies researching therapies that are especially novel or cutting-edge. For this reason, BIO does not believe that a hard cap should be applied to the SBIR grant amounts. Agencies should be the best judge of how to use their SBIR funds to advance science and commercialize new innovations.

Additionally, any caps on SBIR grants, if imposed, should apply to particular SBIR phases and should not apply to the entire amount that the agency spends on a particular project. The NIH, for example, has chosen to implement a commercialization assistance program for those companies who may need extra funding before they can attract private dollars. A hard dollar cap in the SBIR program could threaten such a program and this would be, in BIO's opinion, very unfortunate.

Appropriately safeguard taxpayer dollars

As with any government program, Congress has the obligation to ensure that taxpayer funds are being used in an efficient and effective manner. The SBIR program is not a basic research program, it is about developing new products for the benefit of society. There have been concerns expressed over the number of grants an individual company may receive from the SBIR program. While BIO supports some agency flexibility in these decisions, we would support reasonable limitations, such as capping the number of awards per company to 5 -10 awards per year/per company

No company should make SBIR grants the basis of its business model. SBIR exists to fill the funding void for companies that are raising private capital to do their research and development. SBIR plays the very important role of funding early-stage research, research that might not otherwise be funded or whose development would otherwise be significantly delayed. Any company that receives excessively large numbers of SBIR grants year after year, without commercializing technology, is probably not the type of company into which the federal government should be investing taxpayer resources. BIO believes it is appropriate to include safeguards in the SBIR reauthorization bill to ensure that firms are applying for SBIR grants as a supplement to the private capital they have raised and are not trying to "game" the program.

CLOSING REMARKS

Congress can continue to support the United States biotechnology community by allowing the government to partner with small biotechnology companies that have promising science but need additional resources at key stages of development not readily available in the private capital markets. SBIR should be an aggressively competitive program that fulfills federal research and development goals of bringing breakthrough public health discoveries to the public.

Again, thank you for providing me the opportunity to testify today before the Committee.

○