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Hearing entitled "Treatments for an Ailing Economy: Protecting Health Care Coverage and Investing in Biomedical Research."

My name is Joachim Kohn and I am pleased to be able to address this committee about the economic value to the nation of investment in the National Institutes of Health.

At Rutgers, the State University of New Jersey, I hold the title of Board of Governors Professor of Chemistry and Chemical Biology. I am also the Director of the New Jersey Center for Biomaterials, and an Adjunct Associate Professor of Orthopedics at the University of Medicine and Dentistry of New Jersey. One of my most significant current activities is my leadership in the Armed Forces Institute of Regenerative Medicine (AFIRM) - a DoD-funded national effort to advance medical research rapidly into the clinic to benefit severely injured military service members.

Over the course of my studies, I have not only published more than 200 scientific manuscripts, but also have made numerous inventions which have resulted in a portfolio of about 40 issued US patents (and a commensurate number of related international patents and patent applications). As part of my entrepreneurial activities, I have founded three spin-off companies (Vectramed, TyRx Pharma, and Renova) and participated in the successful negotiations for a total of eight technology transfer licenses (Integra, Vectramed, Surmodics, Osteotech, TyRx Pharma, Lux Biosciences, REVA Medical, and Renova). I have received the prestigious Thomas Alva Edison Award for Best Patent in New Jersey twice, and have been inducted into the New Jersey Biotechnology Hall of Fame. I have had the honor of being an invited speaker on several occasions both in Europe and at home, on the topic of the technology transfer process in the US and the commercialization of University inventions. Since joining the faculty at Rutgers in 1986, I have received NIH awards continuously through a variety of funding mechanism ("First

Award", "Career Development Award", multiple R01 awards, SBIR awards, and a P41 Award). Thus, through my work as an NIH funded academic researcher and a successful entrepreneur, I have significant personal experience relating to the impact of NIH funding on our economy.

In my testimony today, I would like to make two key points:

First key point: Immediate economic impact of NIH funding

NIH funding directly contributes to economic activity. In my experience, each dollar of grant or contract funding awarded by the NIH to an academic laboratory buys about 70 cents of salary support for students, postdoctoral researchers and faculty, and about 30 cents worth of supplies and equipment which are purchased predominantly from US-based suppliers. I have read the June 2008 report by Families USA entitled "In your own backyard: How NIH funding helps your State's economy". To the best of my knowledge, this report accurately describes the immediate economic impact of increased NIH funding. Families USA describes this impact in terms of "real, direct economic benefits at the local level, including increased employment; growth opportunities for universities, medical centers, and local companies".

The findings of the Families USA report include a description of the "multiplier effect" - successive rounds of spending emanating from the original stimulus like successive ripples in the surface of a pond after a stone has been thrown into the water. The immediate economic impact, together with the substantial "multiplier effect" described in the Families USA report, provide, in my opinion, strong justification for the inclusion of NIH funding in any new economic stimulus package. However, I also believe that the Families USA report underestimates the full impact of NIH on the economy. In addition to the "multiplier effect", there is a second, longer-term benefit to the economy. I would like to describe this longer-term benefit as "economic leverage" of the original government investment in the NIH as well as the "indirect health dividend" derived from the scientific discoveries made as part of NIH-funded research programs. These longer-term benefits of NIH funding are the focus of the second key point of my testimony.

Second key point: Longer-term benefits to the economy: "Economic Leverage" and "Indirect Health Dividend"

NIH funding has a measurable and significant secondary effect on the economy, which I refer to as the "economic leverage". Simply stated, the scientific knowledge gained by NIH-funded researchers and the inventions made in the course of their studies are the basis of a substantial amount of economic activity relating to the translation of NIH inventions into medically useful products, services and new therapies. Furthermore, these new products, services, and therapies can reduce our nation's health care costs significantly. This is the "Indirect Health Dividend".

In my personal experience, the "economic leverage" has been tremendous: About $4.5 million in direct NIH support for my research activities at Rutgers resulted in technology commercialization efforts in four start-up companies (REVA Medical, TyRx Pharma, Lux Biosciences, and Renova) which, over the last three years alone, have attracted almost $120 million in private equity funding (Table 1). As a consequence of these investments, these companies have created over 100 high-salary jobs. Additional outcomes from these high-tech private equity investments include:

1) TyRx Pharma has obtained FDA market clearance for two products (hernia repair devices and antimicrobial protective sleeves for coronary implants)

2) REVA Medical is testing a revolutionary coronary stent in clinical trials in Germany and Brazil (with the expectation to start clinical trials in the USA sometime in 2009)

3) Lux Biosciences is completing Phase 3 Clinical Trials of Voclosporin, a new derivative of Cyclosporin A, for the treatment of major diseases of the eye, such as "dry eye syndrome", uveitis, and (age related) macular degeneration.

Table 1 – Private Leveraging Investments Raised by Companies Licensing Technology Developed with NIH funding in the Kohn Laboratory at Rutgers

Company and Location	**Private Investment Raised**
TyRx Pharma Inc., *Monmouth Junction, NJ*	about $40M (5/1998 to 2/2008)
REVA Medical Inc., *San Diego, CA*	$42M (12/2007)
Lux Biosciences Inc., *Jersey City, NJ*	$49M (7/2006)
Renova Biomaterials Inc., *Bridgewater, NJ*	$1.2M (10/2008)

Let me describe the "economic leveraging effect" in more detail. I will also explain how my collaborations have produced this significant leveraging of the government's investment in the NIH by private capital.

When I was a newly-appointed assistant professor in 1986, I was fortunate to receive grants from the NIH that enabled me to establish my laboratory and develop a program of research about synthetic biomaterials. My NIH-funded research studies led to the invention of several classes of new polymers. With the help of the Rutgers technology transfer office, I was able to apply for patents to protect that intellectual property. Some of my seminal inventions were made in the period of 1990 to 1996 - almost exclusively based on research supported by the NIH awards listed in Table 2. In terms of a time line, funding received in the early 1990s is the foundation for much of the significant economic leveraging in the early 2000s - with the full value of NIH's investment in my laboratory becoming apparent only over the next five years, e.g., about 15 years AFTER the original grants were awarded.

Table 2 – NIH Awards to the Kohn Laboratory at Rutgers (exclusive of center and training grants)

NIH Funding Received	Date	Total amount awarded
First award - Structurally new biopolymers derived from alpha-L-amino acid	1/88 to 12/92	$350,000
New biopolymers dervied from alpha-L-amino acids	1/90 to 6/95	$267,840
Polymers designed for biomedical applications	8/93 to 7/97	$624,904
Structurally new biopolymers derived from alpha-L-amino acids	4/97 to 3/02	$934,367
Combinatorial approach to biomaterial design	7/98 to 6/04	$960,919
Radio opaque resorbable polymers for vascular application	9/03 to 7/09	$1,313,537
Total grant amount awarded		**$4,451,567.00**

In terms of the total benefit to society, I can see one additional economic incentive for the government's investment in the NIH which I refer to as the "indirect health dividend": the significant improvement in the overall health of the nation. Often, advances in medical technology can lead to increases in health care costs. However, in the field of biomedical engineering, I believe that many of the NIH-funded research projects have

the potential to reduce the overall health care costs. A personal experience relates to the problem of macular degeneration that threatens my aging mother with blindness. Twice every day, a nurse has to come by my mother's home to administer her prescription eye drops. My mother, at age 84 is too frail to administer these drops herself. In response to this need, shared by millions of disabled and elderly Americans, I am collaborating with Lux Biosciences to develop a new, fully bioresorbable, drug delivery system that can be inserted into the eye and that will deliver a variety of ophthalmic drugs for 6 to 12 month - eliminating the need for daily administration of eye drops (Figure 1). The polymers we are using to develop this drug delivery system were invented as part of an NIH-funded research project. In addition, I believe that many of the scientific advances needed to conceptualize such drug delivery systems can be traced back to NIH supported research in numerous laboratories throughout the nation. While I lack the expertise to estimate the total value of the "indirect health dividend", I believe that it is very substantial.

Figure 1: Prototype of a new drug delivery system, designed to be inserted under the eye. This device will deliver ophthalmic drugs for 6 to 12 months continuously while slowly degrading. The elimination of the need to administer eye drops several times daily will not only increase patient compliance and improve clinical outcomes, but will also reduce the health care costs for millions of disabled or elderly patients who require assistance with the administration of conventional eye drops.

During the remainder of my testimony, I shall describe the "economic leveraging effect" and the "indirect health dividend" in more detail using TyRx Pharma and their antimicrobial sleeve as a specific example. In addition, I will highlight the way NIH funding as contributed to the creation and success of three additional companies: REVA Medical, Lux Biosciences and Renova.

A detailed example for economic leverage and indirect health dividends derived from the funding of single NIH grant

People are excited about the potential capabilities of synthetic biodegradable polymers and the effect they will have on the design and function of implanted devices. Whether

they are used to enable an implanted controlled drug delivery system or to regenerate lost tissue, these materials are crucial to the development of a wide range of new medical applications.

TyRx Pharma, Inc., based in Monmouth Junction, New Jersey, is a 10-year old company that came into existence when a venture capital fund agreed to underwrite the effort to commercialize a class of new biomaterials called "tyrosine-derived polyarylates". These materials were invented by me and one of my students as part of an NIH funded research project in my laboratory. I received the Thomas Alva Edison award for best patent in New Jersey for this invention. TyRx Pharma focuses on the development of new drug-eluting medical devices. In January last year, FDA cleared for marketing TyRx's new hernia repair device (Figure 2a), incorporating one of our new biodegradable tyrosine-derived polyarylates.

For the next generation of this product line, TyRx Pharma added antibiotics that elute into the body as the polymer degrades over time. This new device addresses an important medical need: In the US alone, about 700,000 patients annually need a hernia repair device, about 5% of which tend to fail due to infection. An infected hernia repair device is painful and potentially life-threatening for the patient and very costly to replace. By reducing the number of patients suffering from infected hernia repairs, the TyRx device has the potential to reduce hospital and health care costs.

Figure 2a: The TyRx hernia repair device (Pivit™). Photograph from http://www.tyrxpharma.com

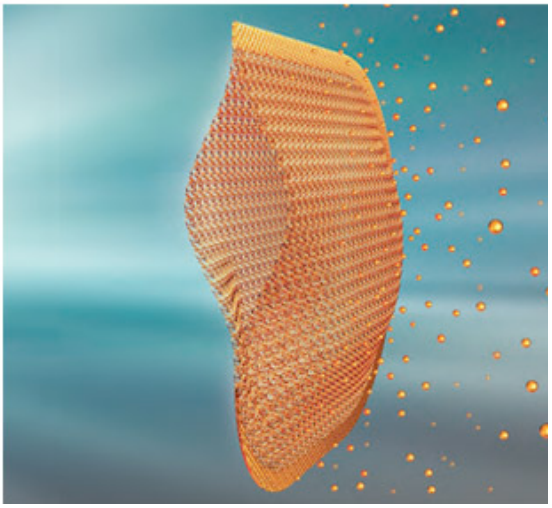

Figure 2b: The TyRx antimicrobial sleeve for prevention of infection of cardiac devices (AIGIS™). Photograph from http://www.tyrxpharma.com

A second line of TyRx products (Figure 2b) targets the problem of infected cardiac rhythm management devices. In a public press release (February 27, 2008), TyRx Pharma announced that

> "more than 400,000 cardiac rhythm management devices (CRMDs) are implanted each year in the U.S. According to a recent study presented during the Heart Rhythm Society (*Heart Rhythm 2006 Scientific Sessions, Boston*), the University of Pittsburgh Medical Center noted that the 2003 national incidence of CRMD implant infection was estimated to be 5.8% for pacemakers and 3.7% for implantable cardioverter defibrillators (ICDs). Furthermore, according to Infection Control Today (8/2003), the average cost of each infection related to invasive medical devices varies from $34,000 to $56,000."

If every CRMD patient would use the TyRx product[1], the extra cost of the devices would be about $400 MM annually, compared to the potential savings of over $640 MM annually in health care costs due to the prevention of infection. To the best of my knowledge, I believe that the TyRx AIGIS product alone has the potential to result in a $240 MM annual "indirect health dividend"[2]- brought about by the government's investment of only $624,904 in NIH funding for the grant entitled: "Polymers designed for biomedical applications", which was awarded in August 1993. This grant supported the invention of the tyrosine-derived polyarylates which are at the foundation of the TyRx Pharma products.

In the same press release, TyRx Pharma also announced a new $25 MM private equity investment that further leverages the original NIH investment made in August 1993. Over its 10-year history, TyRx has raised about $40 million to commercialize products using "tyrosine-derived polyarylates". In this example, the specific NIH grant mentioned above, resulted in a 64-fold leveraging of the government's investment by private equity funding. I am unable to calculate the substantial economic impact of this single NIH grant, but I believe that the sum of the "direct economic impact", the "multiplier" as described by Families USA, the "economic leveraging effect", and the "indirect health dividend" must be staggering - making this grant probably one of the very successful government investments.

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[1] I have heard that each antimicrobial sleeve will cost about $1000

[2] This calculation is based on hospital care costs only and does not take into account the costs to the economy due the patient's lost productivity.

Highlights promising additional high-impact economic benefits from NIH investment

I will briefly touch on three other companies that are licensing technology developed in my laboratory. They each have products in clinical trials or in development.

REVA Medical Inc.

The San Diego based company REVA Medical, Inc. came to our laboratory with a new structural design for a cardiovascular stent – the small tubular device used to keep coronary arteries open after transcutaneous balloon angioplasty. To fabricate the REVA stent, the company was looking for a biodegradable material that would have the proper mechanical and chemical properties. We offered them a license to another invention made in our laboratory, the "tyrosine-derived polycarbonates". I believed at that time that the mechanical and chemical properties of our "tyrosine-derived polycarbonates" would be a particularly good match for REVA's design needs.

In this case history, NIH funding had multiple, beneficial effects: First, the original invention of our "tyrosine-derived polycarbonates" can be traced back to NIH funding provided between 1990 and 1995 in the amount of $267,840 under a research grant entitled: "New biopolymers derived from alpha-L-amino acids". Later on, NIH support in the amount of $1,313,537 (from 9/03 to 7/09) allowed us to further refine this family of new biomaterials for use in the cardiovascular system. Finally, REVA Medical received an NIH SBIR grant that allowed them to establish the feasibility of using our polycarbonates as part of their stent design.

The development of a fully resorbable stent is not only a challenging research project but also a high-risk commercial R&D effort. I credit the support provided by the NIH for making this entire effort possible. I believe that the availability of timely NIH support allowed REVA to establish the feasibility of a polycarbonate-based, resorbable stent. Only at that point, did private investors agree to provide about $42 MM which enabled REVA to advance the polycarbonate stent into clinical trials in Germany and Brazil.

In terms of the "economic leveraging effect", about $1.7MM in NIH support was leveraged by $42 million in private equity funding so far, corresponding to a 24:1 ratio of

government funding to private funding. Because of this leveraging effect, REVA is a thriving company with 40 employees who contribute to the overall economic activity in the San Diego area. REVA is currently raising additional private funding to conduct clinical trials in the USA. Thus, the economic leveraging effect will certainly increase over time.

The future "indirect health dividend" is exceptionally high. In the US, about 2.4 million patients annually are diagnosed with cardiovascular disease, requiring some medical treatment. Increasingly, that treatment has involved angioplasty followed by the placement of a permanent metal stent. By contrast, the REVA stent is intended to act as a temporary scaffold to support the vessel during the healing process. Once the vessel has healed, the stent will resorb, leaving the patient free of a permanent metal implant. Because of the large number of patients with coronary disease, I believe that the economic impact of any improved treatment option will be staggering.

Lux Biosciences

This example brings me back to my mother, who I mentioned earlier. A Jersey City startup called Lux Biosciences focuses on ophthalmic diseases such as uveitis (eye inflammation), macular degeneration, and dry eye. Like TyRx, they are creating combination products that bring a biomaterial together with an active pharmaceutical agent. The pharmaceuticals they are using are already marketed for non-ophthalmic conditions.

To assemble a unique package of technologies, Lux has licensed the use of a number of advanced drug molecules from pharmaceutical companies, a controlled release technology that was developed by intramural NIH scientists, and the "tyrosine-derived polycarbonates" that were invented in my laboratory. Thus, Lux is leveraging both NIH's intramural research program as well as NIH's extramural research support.

Based on press releases published by Lux Biosciences, uveitis is an inflammatory condition in the eye that affects about 300,000 people in the US. Typically treated with corticosteroids, which produce numerous adverse effects, uveitis is responsible, according to some experts, for 10% of new cases of blindness. Financially, the market is small but could grow with a truly effective therapy. A much larger market exists with

age-related macular degeneration which affects 25 million patients in the US and Europe. Lux's hypothesis is that 90% of these cases result from the accumulation of inflammatory insults. Treatment of age-related macular degeneration could become a major application of Lux' approach to anti-inflammatory ophthalmic therapy. Dry eye is a common condition that can result from numerous causes. It is so common that it is responsible for about 40% of all visits to the ophthalmologist. Lux is exploring both topical and long-term drug delivery systems for dry eye disorders.

The company has so far raised $49 million since 2006 when it started.

RENOVA

Last, I mention Renova Biomaterials, Inc., the third and most recent company I have founded. Renova was incorporated in New Jersey in the summer of 2008. It has so far raised $1.2MM in private equity funding from a group of angel investors, further leveraging the investment made by the NIH in supporting our research on "tyrosine-derived polycarbonates". Renova's technology portfolio is entirely based on inventions made with NIH research support. While it is too early for Renova to have had significant economic impact, it is an example of the entrepreneurial activities that can grow out of NIH funding. I believe that a majority of biomedical start-ups coming out of academic research laboratories can trace the creation of their technology portfolios to NIH funded research programs. For that reason, I believe, that a significant portion of the national pipeline of medical technology innovation and entrepreneurship is tightly linked to the level of NIH support available to underwrite research through grants and contracts.

Conclusion

I want to leave you with the message that government investment in the NIH stimulates our economy by four different mechanisms: In the short term, NIH funding has a direct stimulatory effect, just like any other cash infusion into the economy that results in the consumption of services and products. However, in addition to this direct stimulatory effect, NIH funding has a significant "multiplier" or "ripple effect" that is felt throughout the nation. This was described comprehensively in the Families USA report cited earlier in my testimony. In the long term, I believe that the grants and contracts provided by the NIH have a disproportionately large impact on our economy through "economic leverage" and the "indirect health dividend". I hope that I was able to show you that NIH

support for research can create large multipliers in private investment in biomedical enterprises, enterprises that transform our university research into clinical products that improve the health of our population. On a personal level, I, like many other scientists and clinicians, have received from NIH the resources to pursue interesting biomedical science. Entrepreneurial companies take the next step of commercializing the technologies emerging from our science toward a broad variety of biomedical targets. On the way, both levels of investment – research and commercialization – impact the local economies of their regions. **I am firmly convinced that increasing the NIH budget, whether in a near-term stimulus package or as part of future funding bills will pay off both now and in the long run. I encourage you to take this comprehensive view.**

Thank you for your attention.