Executive Summary

Testimony Before the Committee on Energy and Commerce

Health Subcommittee Hearing

21st Century Cures: The PCAST Report on Drug Innovation

Garry A. Neil, MD

May 20, 2014

The American biomedical research and development ecosystem remains the envy of the world. It's value to the US and the world is immense with respect to jobs, export and new therapies. It is imperative that we continue to invest to maintain our global lead in biomedical research.

The 2012 PCAST report, "Propelling Innovation in Drug Discovery, Development and Evaluation" identified a series of challenges and obstacles that raise costs, lengthen timelines and increase risk. These include difficulties in "translating" basic scientific discoveries into developable therapies, inefficient clinical trials, the need to streamline the regulatory process and the need to ensure that appropriate incentives are in place to encourage investment in US biomedical research.

Since its release there are encouraging signs of improvement but much more needs to be done if we are going to reach the ambitious goals set in PCAST report.

Areas for Congress to target are:

- Facilitation the creation of clinical trial networks
- Investment in new biomarkers and clinical trials endpoints
- Increasing and sustaining funding for both FDA and NIH including new programs to expand scientific expertise in translation and clinical trials and staff development
- Expansion of Public Private Partnerships to support the scientific mission of both FDA and NIH
- Ensuring FDA has the increased flexibility to accelerate development programs for life saving medicines
- Examination of existing incentives for capital investment

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Chairman Pitts, Ranking Member Pallone and members of the Committee thank you for the opportunity to testify before you this morning. My name is Garry Neil. I am privileged to head Research and Development in Medgenics, a small biotechnology company headquartered in Wayne, Pennsylvania with operations in the US and in Israel. My colleagues and I are working to bring novel ex-vivo gene therapies to patients with serious rare and orphan diseases. I am a physician and have spent the past 30 years in biomedical research in academia and industry, where I have worked in both large and small companies. I have also spent time in venture capital. I have also been engaged with a number of non-profit organizations in support of the missions of FDA, NIH and industrial R&D. These include membership on the Boards of Directors of the Foundation for the NIH, the Reagan-Udall Foundation for the FDA, the Science Management Review Board of the NIH, the Biomarkers Consortium and Transcelerate Biomedical, an industry collaboration I helped found in 2012 to address inefficiencies in industry sponsored clinical trials. I also provided expert input into the 2012 PCAST report, "Propelling Innovation in Drug Discovery, Development and Evaluation."

I am here today representing myself.

The American biomedical research and development ecosystem remains the envy of the world. Its value to the US and the world is immense. Biomedical innovation employs nearly one million people and exports from the biopharmaceutical industry reached nearly $47 billion in 2010[1]. Beyond economic impact it provides increasingly effective treatments and hope for patients everywhere.

The PCAST report comprehensively documented the state of the biomedical research and development "ecosystem" and identified a series of challenges and obstacles that raise costs, lengthen timelines and increase risk including the difficulties in "translating" basic scientific discoveries into developable therapies, inefficient clinical trials, the need to streamline the regulatory process and the need to ensure that appropriate incentives are in place to encourage investment in US biomedical research[1].

Since the release of the report a number of important developments have occurred demonstrating the resilience of the ecosystem.

The Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 expanded the use of accelerated approval and introduced a new "breakthrough" designation[2]. As of April 2014 the agency had received 178 requests for breakthrough designation[3]. Forty-four have been granted, and six drugs have been

approved for use under this pathway[3]. Under Commissioner Hamburg's leadership the FDA has continued to be the world's leading regulatory agency with 74% of new drugs globally being approved first in the USA[4]. Many of the 37 new drugs and biologics approved in 2012 and 27 in 2013 are first in class, targeted medications[4].

Transcelerate Biomedical was launched as an industry collaboration to improve the efficiency of clinical trials[5]. It currently has 16 member companies and has embarked on a number of projects aimed at reducing operational bottlenecks faced by all sponsors. Early results are extremely encouraging[6].
The National Center for Advancing Translational Sciences (NCATS) of the NIH has now been operationalized[7].

The Accelerating Medicines partnership, a public private partnership between NIH, the pharmaceutical industry and patient advocacy groups was established and will address a number of important diseases including Alzheimer's disease, diabetes, rheumatoid arthritis and lupus[8].

Another public private partnership, the lung cancer master protocol, a molecular biomarker-driven, multi-drug, phase 2/3 registration trial in lung cancer has been activated. The participants include The Friends of Cancer Research, NCI, FDA, FNIH and 5 pharmaceutical companies[9].

At the Reagan-Udall Foundation, a public private partnership created by Congress to support regulatory science, post-marketing safety surveillance is being advanced via the Innovation in Medical Evidence Development and Surveillance project. Among other projects, a new predictive toxicology project designed to identify women at risk for adverse events during breast cancer therapy is being rolled out[10].

Venture capital investment in biomedical research has started to increase. PWC reported that biotechnology investment dollars rose 8 percent in 2013 to $4.5 billion going into 470 deals. However the percentage of all VC dollars invested in the life sciences sector fell from 25 to 23% in 2013 compared with 2012[11]. There has also been a recent boom in biotechnology IPO with 37 in 2013 and 24 in the first quarter of 2014[12].

These are encouraging signs but much more needs to be done if we are going to reach the ambitious goals set in PCAST report[1], maintain our global leadership position in life sciences and address the healthcare challenges that we now confront. I expect that all members of the ecosystem will continue to rise to these challenges but additional help and leadership from Congress could be tremendously beneficial.

Some specific areas for Congress to target are:

1) Clinical trials are the greatest cost driver of biologic and drug development. Today each clinical trial essentially requires establishing a new

infrastructure facilitating the creation of clinical trial networks involving academic investigators, patient advocacy groups and industry sponsors in close collaboration with FDA to increase cost efficiency, shorten time lines and allow more "plug and play" clinical studies. Examples to consider are the Clinical Trials Transformation Initiative/NIH Collaboratory project that has been established to support the design and rapid execution of several "Pragmatic Clinical Trial Demonstration Projects" including performing randomized trials using electronic health records[13, 14] and the Cystic Fibrosis Foundation's Therapeutic Development Network (TDN), the largest cystic fibrosis clinical trials network in the world[15] and the Lung Cancer Master Protocol established under FNIH[9]. Training of additional investigators Likewise establishment of national IRB's and Safety Monitoring Boards staffed with professional staff who are experts and have the time to dedicate to these critical endeavors may further reduce cost and time. More industry collaborations such as Transcelerate Biomedical[6] should also be encouraged so that industry can find ways to share data and reduce cost in development infrastructure and cost in noncompetitive areas. FDA's involvement in all these initiatives is critical.

2) Ensuring that FDA has adequate resources to do their job. Scientific advances are driving an explosion of new molecular and targeted "precision" therapies. Many of these will likely be used in novel combinations and along with new diagnostics and require sophisticated biomarkers to assess their

efficacy as early in the course of therapy as possible. Likewise we are on the threshold of new gene and regenerative medicine therapies. New trial designs and clinical endpoints designed to allow assessment of efficacy in smaller more targeted populations is also urgently needed to make it feasible to perform appropriate clinical studies. This will require collaborative efforts with academics and patient advocacy groups.

3) Likewise FDA must expand its science base accordingly, by recruiting scientists trained in the new disciplines, providing training for its current work force, expanding intramural Fellowship programs to ensure a continuous influx of contemporary expertise, not just for FDA but for the ecosystem at large. Intramural regulatory science programs should also be expanded to ensure that FDA scientists could continue to advance emerging field of regulatory science. Congress should ensure that FDA has appropriate recruiting resources and staff development programs in place, such as sabbaticals, the ability to attend scientific meetings and protected time for original research and scholarship for scientific staff.

4) An increasing share of biomedical innovation is originating in small companies. Often these companies have spectacular science but may lack the requisite knowledge of the regulatory pathway to advance their products expeditiously. Experience has taught me that a frequent interaction with FDA along the development path is a factor for success. FDA should be

funded to expand staff in every division so that more frequent and productive meetings can be supported. FDA should also be funded to create an outreach program to facilitate training of small companies on complex development pathways and guidances.

5) We must rely upon FDA's expertise benefit/risk assessment and clinical trials. Congress should therefore examine the statutes to ensure that FDA has the statutory flexibility and latitude to work with sponsors to design scientifically rigorous programs based on contemporary research methods to more rapidly and cost efficiently. The Breakthrough designation and the recently introduced ADAPT act (H.R. 3742) creating a targeted accelerated approval path for anti-infective drugs are excellent examples of regulatory enhancements that could speed life saving therapies to market. FDA should have the flexibility to be able to work with sponsors liberally in any therapeutic area of high need to undertake similar programs that will result in accelerated access. Use of Special Medical Use (SMU) approvals for appropriate products and indications could allow accelerated approval of medicines that might ultimately have broader use with restricted distribution. An analysis should be undertaken to assess whether FDA has sufficient statutory authority to allow this flexibility.

6) Examine policies that limit how genomic data can be used to inform drug safety assessment and clinical trials. Additional emphasis should be placed

on interpretation of mechanistic "evidence" to guide approval and treatment decisions when numbers are very small or n=1.

7) The NIH is the ultimate engine of innovation for the biomedical ecosystem. Congress must provide sustainable funding for the NIH that includes a steady year over year increase to increase the investigator pool, including better funding young investigators. Additional targeted funding to allow expanded collaboration between NIH and FDA as well as NIH and industry should also be appropriated.

8) Increased and sustainable funding for highly valuable public private partnerships, notable Reagan Udall Foundation should be appropriated to allow FDA to cost leverage and acquire access to external expertise as needed to support its scientific mission. Like FNIH the RUF can provide a cost efficient organizational infrastructure and neutral convening organization to manage projects and help provide tools valuable to FDA, without impinging on FDA's regulatory function. Adequate structural funding provided by Congress would allow RUF to work with FDA to identify and find funders for such projects.

9) Examine existing incentives for investment in biomedical research and new drug/biologic development. Innovative R&D requires substantial capital investment over a long period of time. There will always be more innovative

ideas than capital to fund it. Competition for resources is thus healthy for the ecosystem. However, targeted tax reform designed to encourage investment pre-revenue companies would be enormously beneficial to innovative early stage companies like Medgenics. It would also be useful to examine tax incentives designed to encourage R&D and commercialization of patent-based products in the US. A number of European countries, most recently the UK have introduced such plans[16]

Our company, like hundreds of other small, innovative companies, faces many of these challenges every day. Our scientists – like virtually all industry scientists I have had the honor to lead or know – are incredibly dedicated, driven and focused on curing disease and alleviating suffering. Their ingenuity and problem solving ability amazes me every day. We are making rapid progress in understanding the diseases we target and advancing therapies. We rely heavily upon collaboration with academic scientists who advise us and also upon the regulators who seek to understand and help us to find the path forward. We also rely heavily upon our investors, including our Board Chairman, Dr. Sol Barer, the founder and ex-CEO of Celgene. They risk their capital because they believe we will succeed.

Clearly there is no time or resource to spare. We weigh every decision and every experiment with the utmost care. We understand the implications for our people, our investors, the country – but most importantly, for the patients and their parents who are desperately waiting for cures.

I applaud the Committee for undertaking this effort in the sincere belief that it can result in positive change. Enlightened, science-driven policy will allow companies like Medgenics to succeed, put the next generation of transformational therapies in the hands of caregivers around the world and increase the competiveness and prosperity of our country.

Citations

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