21st Century Cures: The President's Council of Advisors on Science and Technology (PCAST) Report on Drug Innovation

Testimony Before
Committee on Energy and Commerce
Subcommittee on Health
United States House of Representatives

Jeff Allen, PhD
Executive Director
Friends of Cancer Research

May 20, 2014

21st Century Cures: The President's Council of Advisors on Science and Technology (PCAST) Report on Drug Innovation

Testimony of Jeff Allen, PhD, Executive Director, Friends of Cancer Research

Good morning, Chairman Upton, Ranking Member Waxman, Subcommittee Chairman Pitts, Ranking Member Pallone, and Members of the sub-committee. I am Dr. Jeff Allen, Executive Director of Friends of Cancer Research, a cancer research think tank and advocacy organization dedicated to accelerating science & technology from bench to bedside. I would like to thank all Members and the staff of this committee for putting together this important hearing. It is an honor to testify before you today and provide our perspective as you embark on this important 21st Century Cures initiative, and I'd like to especially thank Chairman Upton and Congresswoman DeGette for undertaking this endeavor. Along with my colleagues here, I also had the pleasure of serving on the working group that contributed to the September 2012 ***Report to the President of the United States on Propelling Innovation in Drug Discovery, Development and Evaluation.***

While compelling progress has been made within the field of oncology, there is much more to be done to alleviate the current cancer epidemic and profound suffering it causes. It is estimated that, in 2014, over 1.66 million Americans will be newly diagnosed with cancer. If something is not done, cancer will claim the lives of 585,720 mothers, fathers, grandparents, sisters, brothers, and friends, this year.[1] This, Mr. Chairman, is roughly the equivalent of every citizen in your home county of Lancaster, Pennsylvania. This profound human toll also comes with a staggering cost to our health care system of an additional $226 billion dollars.[2,3]

[1] The American Cancer Society Facts & Figures: http://www.cancer.org/acs/groups/content/@research/documents/webcontent/acspc-042151.pdf Accessed 5/19/14

[2] The American Cancer Society: http://www.cancer.org/Cancer/CancerBasics/economic-impact-of-cancer Accessed 5/19/14

Improved ways to combat cancer are urgently needed. Advancements in basic science have never been more profound, but unfortunately they do not always translate into new treatment as rapidly as patients deserve. Recent estimates indicate that it currently could take upwards of 12 years and over $1 billion to develop a new cancer drug.[4] With all of this personal and economic loss, and the hurdles new therapies face, there is still great hope and resilience by patients and there is incredible work being done across all sectors to battle this and many other life-threatening diseases. The remarkable advancements being made at the National Institutes of Health (NIH), at academic medical centers all across the country and within private sector industry is rapidly changing how we look at disease, and how we are able to treat patients. The drugs and biologics being developed today to treat many different diseases are far more effective, but also more complex than their predecessors. I, and millions of people across this country, hope that the work of this committee will be a catalyst to accelerate getting the right medicines to the right patients at the right time.

Much like this Committee is examining the current state of developing new medicines though 21st Century Cures, the Working Group that developed the report to the President was charged to identify key barriers to optimal new drug development and make recommendations on how they might be addressed. I would like to focus on a few of the key areas identified within the report, describing both areas in which there has been significant progress and areas to which the committee might turn its attention and resources to further enhance.

Improving Drug Regulation – Breakthrough Therapy Designation

One key challenge that the working group explored was *Improving Drug Regulation.* The role of the FDA is to protect and promote the health of the American public by ensuring the safety, effectiveness,

---

[3] http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-041782.pdf Accessed 5/19/14

[4] Adams, C. P. and Brantner, V. V. Health Economics, 19 (2010), 130–141. doi: 10.1002/hec.1454

and security of medical products, devices, food, and cosmetics.[5] The authority and tools to fulfill this monumental responsibility continues to evolve to keep pace with the current state of science. I'd like to provide you with a few examples that demonstrate this.

With the expansion of knowledge about the biological basis of complex disease, new therapies are being developed that are targeted to unique molecular changes known to "drive" a disease. These new, "targeted therapies" allow selection of patients highly likely to respond to the new treatment. For these new treatments (or combinations) that show the promise of dramatic clinical activity and significant improvement over currently-available treatment early in the new drug's development, the traditional multi-phase, sequential development approach is not be appropriate, particularly if existing treatment options have limited efficacy.

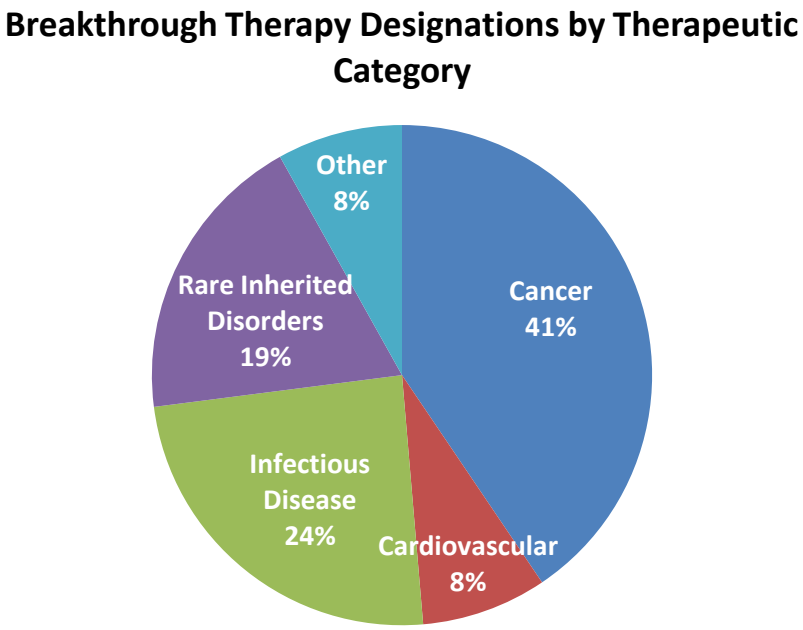
In collaboration with our expert colleagues from FDA, NIH, patient advocacy, industry, and academia, we at Friends of Cancer Research proposed a series of approaches of how clinical testing could be modified to expedite the development of these new "breakthrough therapies." With the leadership of this committee, and your colleagues in the Senate, the creation of a new FDA program called the "Breakthrough Therapies Designation" was codified into law as part of the Food and Drug Administration Safety and Innovation Act (FDASIA).[6]

FDA has rapidly implemented this new regulatory tool. It is important to note that the Breakthrough designation preserves the standards of safety and efficacy that have been in place for over 50 years, but when a new drug shows such and unprecedented effect, like current science is allowing, a new approach is needed. [7] Once a breakthrough therapy designation is granted, different divisions of FDA and the drug sponsor begin an intensive collaboration to plan the future research with the drug. Through this

[5] About FDA: http://www.fda.gov/AboutFDA/Transparency/Basics/ucm192695.htm Accessed 5/16/14
[6] FDASIA Sec. 902 Breakthrough Therapies. Public Law 112-144
[7] Kefauver-Harris amendments to the 1938 Food, Drug, and Cosmetic (FD&C) Act [PL 87-781; 76 Stat. 788-89]

collaboration an expedited, and optimally efficient, development program of the Breakthrough drug is designed and executed.

Mr. Chairman, I am happy to report that in just two years, 178 requests for Breakthrough Designation have been submitted, and 44 designations have been granted.[8] While the basis for developing this new tool may have utilized cancer as a case study, it was not envisioned that this program should be applied only to cancer drugs, and as shown below, FDA has been rapidly implementing the program in many serious disease settings.



Since its passage into law, there have been 6 breakthrough therapies that have successfully completed testing and are now FDA approved drugs. It has been estimated by some of the sponsors of the drugs that the Breakthrough Therapy program accelerated the development process by several years. The "all hands on deck" approach demonstrates the importance of the public-private collaboration that the

[8] FDA CDER and CBER Breakthrough Requests: http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/fdasia/ucm341027.htm Accessed 5/16/14

Breakthrough designation brings to enhancing science-based regulation; translating to reduced development times, increased investment in the biotech sector, and improve the health of the patients that previously had few treatment options. This designation and the process to create it is an incredible example of congress putting partisan politics aside and acting deliberately to address one of our country's most pressing health issues. For that, I want thank this Committee and the Congress for enacting this new law.

Improving Drug Discovery and Development – Lung-MAP

Another key component of the report to the President explored ways of addressing inefficiencies in clinical trial conduct. The report describes clinical trials as, "the largest single component of the R&D budget of the biopharmaceutical industry, at approximately $31.3, representing nearly 40 percent of the R&D budget of major companies."[9] There is no doubt that our antiquated, patch-work clinical trial system makes developing new treatments a cumbersome, expensive and protracted process. In order to truly realize the promise of evolving science, new models and tools, ones that capitalize on the rapid scientific discovery including modern informatics, are needed. However, innovative paradigms to evaluate potentially promising drugs will only be successful through multi-sector collaboration.

To begin to address this issue directly, and truly change the course of how trials are done, Friends of Cancer Research is spearheading a project which in many ways originated at the FDA itself. We are currently working with a large, diverse set of partners from academia, industry, government and advocacy to develop a modern day clinical trial as innovative as the therapies it seeks to test. In this project, called Lung-MAP, a "master" protocol will govern how multiple drugs, each targeting a different biomarker, will be tested as potential treatments for lung cancer. Each arm of the study will test a different drug that has been determined to target a unique genetic alteration. The use of cutting-edge

[9] Report to the President on Propelling Innovation in Drug Discovery, Development and Evaluation. Sept 2012; p.20

screening technology will help identify which patient is a molecular match to each arm. This will create a rapidly evolving infrastructure that can simultaneously examine the safety and efficacy of multiple new drugs. This approach will have the ability to improve enrollment, enhance consistency, increase efficiency, reduce costs, and most importantly - improve patients' lives.

Much like advancements in regulation should be driven by cutting-edge science, so too should be the approach to designing new research paradigms. Lung-MAP has the ability to reinvigorate the research enterprise and rapidly facilitate the development of molecularly targeted medicine. It is our hope that this can serve as a template for the future of clinical research. As the project moves forward, each of our partners has committed to do business differently. Mr. Chairman, this project has begun to change culture. We have five of the largest pharmaceutical companies working together, and willing to do what it takes to make sure patients have therapies available that can improve and save lives. This is crucial - the patients that we are striving to help simply do not have time to wait.

There are other public-private efforts that strive to enhance different components of the biomedical research enterprise. For example, the Foundation for the NIH (FNIH) supports the scientific mission of the NIH by uniting experts and resources around specific projects identified by the Institutes' directors. In addition to playing a critical role in Lung-MAP, the FNIH supports project ranging from biomarker discovery, advancement of Alzheimer's research, improvement of global health and NIV/AIDS vaccine discovery. Similarly, the Reagan-Udall Foundation was established by the Congress in 2007 to facilitate research in support of the mission of the FDA and the advancement of regulatory science. Their work includes the Observation Medical Outcomes Partnership to support drug safety research methodology, efforts to develop tuberculosis treatment regimens, and improve understanding of the mechanisms of toxicology. Other specific efforts include the Clinical Trial Transformation Initiative, whose specific mission is to identify and promote practices that will increase the quality and efficiency of clinical trials.

Each of these initiatives, and many others, represent public-private efforts to enhance medical research at different points along the continuum. The report to the President also acknowledged their potential. With appropriate resources, these on-going collaborations have the ability to help address the challenges to discovering and developing new medicine and ultimately improve human health.

Improving Scientific Communication – Guidance Development

One way that the FDA communicates to researchers and developers about new approaches or changes to current policies is through the use of Guidance Documents. These documents provide FDA's view on current challenges, provide clarity and often times recommendations to industry and prompting vibrant discussion and debate among those involved in drug development – an interchange that is vital to modernizing the enterprise.

These documents communicate best practices internally within FDA as well as to external stakeholders. However, developing them is resource intensive. Given the breadth and continuously growing responsibilities of FDA staff, contributing to a scientific activity such as the development of a Guidance document often becomes secondary to their primary job. Critical activities such as providing scientific communication to external stakeholders is just one of the many functions of FDA that can suffer as a result of insufficient resources. The duties of the agency is often increased without matching appropriated dollars in tandem, and user fees are infrequently able to be applied to the many Guidance documents that FDA works to develop. This is one of many specific examples of how additional resources could benefit the FDA it its mission to help patients.

The report, and the working group's deliberations, did include the importance of new FDA Guidance documents. The report suggested that external partnerships could be beneficial in providing input on

scientific subjects that would be fit for FDA Guidance. [10] FDA is often constrained on how they can receive input from external stakeholders, but scientific exchange between all stakeholders involved in biomedical research is critical to its success. Neutral, public venues that can facilitate the exchange of ideas can greatly inform the topics and approaches that FDA may take when considering best practices and guidance development. Without such preliminary discussions, and input from thought leaders in the field of science and medicine, the agency is left to develop Guidance documents and only receive public input once they are complete as part of the routine comment period.

We have seen the benefits of early interactions firsthand, and have developed a model to bolster the access to expertise that the FDA has as they deliberate guidance. Noting the promise that combinations of new drugs have shown to combat diseases like HIV and cancer, we convened an expert group to provide specific ideas on how novel combinations could optimally be developed. FDA was part of that working group and was open and wiling to be a part of these expert discussions and recommendations. The FDA completed their own internal process to develop guidance on this topic but the rapidity with which the guidance was released suggests that the broad, thoughtful scientific discussion, of which FDA was privy, appears to have accelerated the process.

The same is true with the development of important Guidance documents issued last year regarding the development of companion diagnostics to support drug development[11] and the recently issued draft guidance proposing a program for expedited access to medical devices to treat serious diseases.[12]

---

[10] Report to the President on Propelling Innovation in Drug Discovery, Development and Evaluation. Sept 2012; p.55

[11] Co-Development of Two or More Investigational Drugs for Use in Combination: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM236669.pdf June 2013. Accessed 5/16/14

[12] Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf. April 2014. Accessed 5/16/14

Much like FDA policies benefit from hearing the challenges faced by the research community, the external community gains from hearing from FDA. Processes and funding streams need to be established to increase FDA's ability to gain external input and develop new Guidance documents. Guidance documents like these and many others have the ability to greatly enhance the success of research endeavors and encourage the types of innovative collaborations like Lung-MAP and can inform vital legislation like Breakthrough.

Improving Drug Discovery and Development – Companion Diagnostics

The PCAST report was specifically focused on propelling new drug development, and while the working group focused their deliberations on this specific topic, I believe that considerations should also be given to opportunities in the development of companion diagnostics. In the prior examples of successful, science-based initiatives in research and regulation, Lung-MAP is based on advanced screening technology that can detect different genetic alterations for which a drug may target. For Breakthrough Therapies, over half of the currently designated drugs utilize some sort of tool to identify the subset of patients most likely to benefit from the drug.

The use of a companion diagnostic to guide the use of new therapies has become increasingly important. The FDA recently took proactive steps to issue important Guidance documents last year regarding the development of companion diagnostics to support drug development[13] and recently issued draft guidance proposing a program for expedited access to medical devices to treat serious diseases.[14] These Guidance documents provide new pathways and important advice to the research

[13] Co-Development of Two or More Investigational Drugs for Use in Combination: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM236669.pdf June 2013. Accessed 5/16/14

[14] Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf. April 2014. Accessed 5/16/14

community. Building on the foundation that FDA has provided, this Committee could facilitate new policies to advancement of how novel technologies can inform the use of new drugs to ensure that the right patients have access to the right treatments at the right time.

Conclusion

The state of science and medicine has never been as promising as it is today. The 21st Century Cures initiative is an important way of examining new policies to ensure that new discoveries are rapidly translated to life improving treatments for patients. The examples that I have provided today are case studies that can be learned from, and are stepping stones upon which more work can be done. Innovation is incremental, but with continually improved understanding of disease processes, these incremental steps toward improving health can and will be transformational. This, however, is only made possible with adequate support, including increased funding, for critical health agencies like NIH and FDA. The regulatory framework has been put into place to accelerate the development of medical breakthroughs. Enhanced collaborations, like Lung-MAP, will be needed to uncover such breakthrough and alleviate current inefficiencies. Aligning policies with the current state of science has the ability to accelerate the development of safe and effective therapies to improve the state of biomedical research and improve the lives of patients. The 21st Century Cures initiative can be the next step toward that goal.

###

About Friends of Cancer Research

Friends of Cancer Research is our country's leading voice in advocating for policies and solutions that will get treatments to patients in the safest and quickest way possible. Friends of Cancer Research (Friends) develops groundbreaking partnerships and creates a more open dialogue among both public and private sectors and tears down the barriers that stand in the way of conquering cancer. By collaborating with premier academic research centers, professional societies, and other advocacy organizations, Friends is able to accelerate innovation. www.focr.org

For more information please contact: Ryan Hohman, JD, Managing Director, Policy & Public Affairs, Friends of Cancer Research at rhohman@focr.org or 202.944.6708