Testimony of Alexis Borisy
Partner, Third Rock Ventures
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Energy and Commerce Subcommittee on Health Hearing

"21st Century Cures: Examining the Role of Incentives in Advancing Treatments and Cures for Patients"

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Chairman Pitts, Ranking Member Pallone, and Members of the Subcommittee, my name is Alexis Borisy, and I am a partner at Third Rock Ventures. Our firm's mission is to launch and grow exceptional healthcare companies. Our work focuses on forming and building innovative companies in areas of disruptive sciences and medicines. We work to advance pipelines to the clinic and develop new products that will make a meaningful difference for patients, physicians, and our healthcare system overall. I personally have over 20 years of experience in building and operating innovative science-based companies. In addition to my role as a Partner with Third Rock, I am Chairman of the Board and co-founder of NASDAQ-listed Foundation Medicine, Chairman of Warp Drive Bio, CEO for Blueprint Medicines, and serve on the Boards of the National Venture Capital Association and the Biotechnology Industry Organization.

I applaud this Committee for initiating the 21st Century Cures Call to Action and its commitment to finding solutions that will ensure the United States biopharmaceutical industry is best equipped to maintain global leadership and empowered to deliver the next generation of medicines. Our understanding of diseases and how we develop medicines has advanced tremendously over the last 20 years. With over 3,400 medicines in development and over 2,000 public and private companies in the U.S., the promise of this industry is great.[1,2] We have the potential to transform how we treat patients with life-threatening and chronic diseases, a goal that not only would improve the lives of patients and their families but create new solutions to our nation's most pressing health care needs.

This hearing is focused on a critical component of ensuring a forward-leaning and robust biopharmaceutical industry – what incentives are needed to advance treatment and cures? Before I discuss specific policies and offer ideas for consideration, it is important to understand that successful development of new medicines is dependent on policies that support the entire life science ecosystem – beginning with basic research and ending with providing treatments and therapies to patients. Disruption or weakening of policies that negatively impact any part of this ecosystem weakens the entire enterprise.

Assuming that a strong foundation of societal investment in basic research exits, then developing modern medicines from that point onward is a capital- and time-intensive

[1] http://www.phrma.org/pipeline
[2] Copley, Caroline. With biotech hot on Wall Street, VCs look to Europe for promising companies. *MedCity News*. August 7, 2013.

endeavor taking an average of 10 years and $1 billion to deliver a single new drug.[3] It is also a high-risk endeavor involving finding solutions to complex scientific and medical problems. However, when successful there can be no question of the reward. Over the last 20 years we have provided medicines that have vastly improved the quality and longevity of lives for patients dealing with diseases such as HIV/AIDS, cancer, and heart disease.

The U.S. Must Commit to Funding Discovery

A keystone to ensuring a robust life science industry is a national commitment to support basic research. Our nation's historical commitment to life sciences basic research is viewed as a precious jewel among nations. However, funding for the National Institutes of Health has been directly or effectively declining for the past several years with decreased or flat budgets that have not recognized inflation.[4] Basic research is the key to unlocking the mysteries of diseases and providing foundational discoveries that enable the biopharmaceutical industry to continue to research and ultimately develop new medicines for patients. Diminished support for basic research will lead to a smaller pipeline of next-generation medicines and impede our country's potential to transform how we treat diseases.

Research dollars provided by the National Institutes of Health to universities and colleges throughout the country also serve to train future scientists for 21st century jobs. Currently, the U.S. biomedical research sector supports over 5 million high-paying jobs in the United States and has tremendous potential for growth.[5] However, we must understand that our position as the global leader in medical science is constantly being challenged, and without a sustained commitment for scientific discovery, this is not a position that will be maintained.

Enabling Adoption of Modern Approaches to Drug Development & Approval Will Incentivize Investment

This Committee has heard and received written testimony regarding the enormous increase in requirements and duration of clinical trials.[6,7,8,9] These increases are especially acute for drugs designed to treat chronic diseases with larger patient populations. As a consequence, the cost of developing drugs has likewise been increasing. The Committee is right to ask whether these trends could be minimized by more effectively incorporating modern tools and approaches.

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[3] Adams CP and Bratner VV (2006) Spending on New Drug Development. *Health Economics.* 19, 13-141.
[4] Federation of American Societies for Experimental Biology. "Budget Cuts Reduce Biomedical Research." http://222.faseb.org/portals/2/PDFs/opa/5.16.13%20Funding%20Cuts%202-pager.pdf.
[5] Battelle Technology Partnership Practice. "Battelle/BIO State Bioscience Industry Development 2012". June 2012. http://ww.bio.org/sites/default/files/vebattelle-bio_2012_industry_development.pdf.
[6] Scannell JW, Blanckley A, Boldon H, and Warrington B (2012) Diagnosing the decline in pharmaceutical R&D efficiency. *Nature Reviews: Drug Discovery* 11, 191-200.
[7] Avik R (2012) The Stifling Cost of Lengthy Clinical Drug Trials. *Manhattan Institute*. http://www.manhattan-institute.org/pdf/fda_05.pdf.
[8] Tufts Center for the Study of Drug Development (12 April 2010) *PDUFA V Meeting*.
[9] Allison M (2012) Reinventing clinical trials. *Nature Biotechnology* 30 (1): 41-49

Venture funding is the life-blood of the small biotechnology companies working on disruptive science, and these venture-backed small biotechnology companies are the life-blood of innovative new medicines. In fact, a study published in 2010 found that in the United States a majority of scientifically innovative drugs were discovered or developed by biotechnology companies.[10] Large pharmaceutical companies may take over late-stage development and commercialization of many small biotech drug development programs. However, without innovative small biotech companies, many of today's innovative medicines would not exist, which in turn would not exist without the early-stage venture capital funding.

Venture capitalists invested $4.5 billion into private biotechnology companies in 2013, exactly equal to the prior 10-year average but down more than $1 billion from the pre-fiscal crisis 2007 peak. However, venture capital investment in early-stage life sciences companies has been under significant pressure over the last seven years. In fact, first-time financings in 2013 were down 35% from 2008 and in 2012 the number of early-stage financings dropped to a 15 year low.[11] A primary reason for this decline is the increased time and cost of developing new drugs and devices.

The decision to deploy capital is directly impacted by regulatory decisions and behaviors. Better enabling and encouraging FDA to utilize flexible approaches reflective of our understanding of the disease and patient being treated, as well as incorporation of modern approaches to development and approval, would have a positive impact on venture funding. For example, since the implementation of the Accelerated Approval pathway in 1992 over 80 drugs have been approved utilizing this pathway, including 29 to treat cancer and 32 to treat HIV.[12] This pathway allows for approval based on surrogate endpoints such as shrinking tumors or decreasing viral loads indicative of clinical benefits to patients with a commitment by the company to conduct confirmatory trials post-market to confirm the benefit. This has allowed oncology and HIV drugs to enter the public market in a significantly more effective manner. It is no coincidence that oncology has been and is projected to be one of the most active and innovative therapeutic markets.[13]

Likewise, in recent years FDA has shown an increased willingness to work with companies to develop more effective clinical development programs for rare diseases. This, along with added exclusivity for orphan drugs, has led to a significant increase in venture investment in rare diseases. The results are clear. In 2012, FDA reported that from 2007 to 2012 approximately one-third of the NMEs approved were drugs for rare diseases.[14] This trend continued in 2013, when 33% of NMEs approved were drugs to

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[10] Kneller, Robert. "The importance of new companies for drug discovery: origins of a decade of new drugs" *Nature Reviews Drug Discovery* 9, 867-882 (2010)
[11] PricewaterhouseCoopers, National Venture Capital Association. "MoneyTree Report." https://www.pwcmoneytree.com/MTPublic/ns/index.jsp

[12] FDA. FY 2012 Innovative Drug Approvals. December, 2012
[13] JP Morgan. 2014 Global Biotech Outlook. January 6, 2014.
[14] FDA FY 2013 Innovative Drug Approvals. December, 2012

treat rare diseases.[15] Again, we see that investment in early-stage, potentially breakthrough innovation in life sciences follows these signals, as venture investment in rare genetic diseases has significantly increased over the past few years.[16]

In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) created a new Breakthrough Therapy designation that will provide increased interactions with FDA to ensure the most effective development and approval processes for promising new treatments. As of June 2, 2014 there have been 52 breakthrough designations granted by FDA.[17] Similar to statistics for Accelerated Approval, a majority of these designations have been given to oncology and rare disease treatments and therapies.[18]

The benefit of these programs has clearly been mostly realized in the oncology and rare disease space. As a society, while we celebrate these incredible successes, and indeed we *should* celebrate these successes, we have to ask ourselves what we want to do to improve how we treat the most egregious diseases affecting the greatest numbers our citizenry and long-term health costs, such as obesity, diabetes, and Alzheimer's, among others. As we examine the successes of these programs in terms of number of approvals for cancer and rare genetic diseases, we should endeavor to learn from the flexible and modern approaches utilized under these programs and work to apply them more broadly across therapeutic areas.

The fact is that while there are several examples where FDA has allowed for the utilization of novel endpoints, advanced tools such as biomarkers, and non-traditional clinical trial designs, the basis for such decisions is still poorly understood and inconsistent across review divisions. Without a more transparent and consistent approach as to what criteria such decisions are based on, the private sector will be hesitant to develop or utilize advanced approaches.

When it comes to chronic diseases with varying stages of progression and severity, there seems to be an actual reticence to employ modern tools and approaches. Recent ideas such as Special Medical Use and Europe's adaptive licensing pilot could serve to modernize our current system. Currently, our regulatory system is based on a philosophy that more information before approval is better. We must advance to a system that critically examines information required and determine whether it is actually informative as to the potential success of the drug in the real world. Creating approval pathways that enable the development of drugs for subpopulations of patients in areas like Alzheimer's and diabetes could be a game-changer. These approaches could serve to ensure the right drugs are getting to right patients in a much more effective manner.

From early-stage life sciences venture investment perspective, we know that when we start a company with breakthrough innovations in new areas of science and medicine it

[15] FDA. Approved Drugs 2013
[16] Jarvis, Lisa M. Orphans Find a Home. C&EN Volume 91 Issue 19 | pp. 10-12. May 13, 2013.
[17] FDA
[18] Aggarwal, Saurabh (Rob). A Survey of Breakthrough Designations. *Nature Biotechnology* 32, 323–330 (2014)

will take a long time to turn that innovation into a drug that will reach patients and physicians and improve public health. The reality is the time required to put a drug on the market is, more often than not, longer than the length of our investment funds. Thus, when we create a new innovative company in a new area of science and medicine we are counting on the new medicine being developed being seen as important and valuable when it is still in the early stages of development. This is often referred to as the "proof of concept in the clinic," or Phase IIA. At that point, we are counting on the company and the product being sufficient to either take the company public on the NASDAQ or to have the company and/or product acquired by a pharmaceutical or larger biotech company.

The modern approach to regulation that exists now for cancer and rare genetic diseases allows this to work very well for three reasons. First, the regulatory process is more interactive, flexible, and reflective of the disease and patient being treated. Second, the amount, of time, and size of investment required to fund a company through 'proof of concept' is better understood. And, third, the next steps in our innovation ecosystem, larger companies and public investors, value the early-stage proof of concept data because they feel more confident about the development and approval process for these drugs. However, the same cannot be said for diseases such as obesity, diabetes, and Alzheimer's, where the time, amount of funds, and regulatory requirements are greater and there is less understanding about how to utilize modern tools and approaches. Without improving these processes, it is very difficult to imagine how early-stage investment can occur in such important areas.

In addition to the need for understanding the criteria which FDA will allow for utilization of modern tools, such as biomarkers and personalized medicine diagnostically defined subsets of a disease, there is also a need to provide incentives for the development of such tools. This is particularly important for the development of new diagnostics. It is imperative that regulatory processes for personalized medicine encourage early collaboration for the approval of therapeutics and companion diagnostics, as well as the development of advanced diagnostics in general.

Another, perhaps more critical, barrier to the advancement of diagnostic development is the fact that there are no consistent reimbursement policies for diagnostics. Congress recently passed the Protecting Access to Medicare Act of 2014 which included the Improving Medicare Policies for Clinical Diagnostic Laboratory Tests provision. This provision is an important and positive step forward. How transformative depends on whether the potential benefits are realized and implemented in the regulations. There remains substantial uncertainty in the private and public world of reimbursement for molecular diagnostics. This uncertainty continues to hold back investment in breakthrough personalized medicine innovation that could significantly advance how we develop drugs and treat patients with critically important diseases such as Alzheimer's, diabetes, and others.

I would like to recommend that the Committee consider a process whereby the Centers for Medicare and Medicaid create a program for diseases important to the public health

with high unmet diagnostic needs. This would be particularly useful in advancing how we develop treatments for Alzheimer's and diabetes. Diagnostics has the potential to play a much more significant role in helping to identify subsets of patients suffering from either advanced stages of disease progression or with different benefit/risk profiles based on genetics. By identifying these subsets of patients we will be able to develop treatments for these diseases and patients in a much more effective manner. However, in order to fully realize these benefits we must provide clear reimbursement policies for these diagnostics that reflect the value the diagnostic provides to patients, providers, and our nation's health care system overall. One approach would be to look at disease areas critical to our nation's health care system such as Alzheimer's or diabetes. Establishing a payment policy for diagnostics in these disease areas for some meaningful determined period of time would serve to incentivize development of such products. Clear payment polices of personalized medicine tools combined with modern regulatory approaches would advance personalized medicine by leaps and bounds.

Utilization of Real-World Data: A Life-Cycle Approach to Drug Development

We currently have a system that requires a life-cycle approach to drug development with increasing abilities to monitor the safety and efficacy of drugs in the real world. However, we have not turned any of these new abilities to collect and share information into tools to advance drug development and improve how we treat patients. As we think about how we can accelerate drug development in chronic diseases such as diabetes, obesity, and Alzheimer's, and as we consider what is the evidence required for approval in such areas, we should keep in mind that real world data post-approval may be a very effective tool in understanding the scope of such drugs and may allow us to get to approval of these important new medicines more quickly. We should be actively working to integrate real-world data into the drug development and review process, and to achieve the right balance of what data we are requiring before and after approval. These approaches would help ensure patients have access to new medicines more expeditiously and could serve to support expanded indications in a more effective manner.

To ensure the promise of such real world data is realized, we must incorporate it as scientifically appropriate in the drug development process and make sure such data is available for use. As such, we must advance our healthcare system to one that has inter-operability capabilities that would enable more efficient use of electronic medical records with the real-world data required. We must also ensure that our systems have the ability to exchange such information in a privacy-protected manner. A balkanized set of such data would be missing an opportunity to support tremendous innovation in our health care ecosystem.

Conclusion

These are just a few incentives that could serve to advance how we develop medicines and treat patients. There are other critical policy areas that have the ability to impact or weaken the life science ecosystem not mentioned in this statement, but I would be happy to discuss these areas further with this Committee. For example, we must ensure that intellectual property is protected. There is no investment if the primary asset of an industry is not protected in a manner that allows for returns on investments. Data

exclusivity of sufficient lengths of time can also be a powerful incentive, and we could consider aligning small molecule data exclusivity to the 12 years for biologic drugs, as the current 5 years of exclusivity for small molecules does not provide incentive from a venture capital perspective. We must work to ensure we encourage investment in small, innovative pre-revenue life science companies.[19] Lastly, we must ensure that reimbursement policies are determined in the context of the disease and patient being treated and the impact of a drug is evaluated over appropriate time lines. We must not create a system that will severely diminish investment in the next generation of cures and treatments. Thank you for the opportunity to share my thoughts and I would be happy to answer any questions.

[19] CSBI. http://www.smallbusinessinnovators.org/