

**Testimony of Alexis Borisy
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Before the United States Senate
Health, Education, Labor and Pensions Committee**

***Continuing America's Leadership:
Advancing Research and Development for Patients***

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Chairman Alexander, Ranking Member Murray, and Members of the Committee, my name is Alexis Borisy, and I am a partner at Third Rock Ventures. Our firm's mission is to build great companies that discover and develop products that make a difference for the patients we serve. Our work focuses on forming, launching, and building innovative companies in areas of disruptive science and medicine, and matching that to the right business and strategy. We work to advance pipelines of discovery projects 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 and currently am Chairman of the Board and co-founder of NASDAQ-listed Foundation Medicine, Chairman of Warp Drive Bio, Director for Blueprint Medicines, which I co-founded, and Director for Editas Medicines and Revolution Medicine. I also serve on the Board of the National Venture Capital Association and was formerly on the Board of the Biotechnology Industry Organization.

I applaud this Committee for its commitment to advancing research and development for patients. 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 for our society is great.ⁱⁱⁱ 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. We must work together to ensure the United States' biopharmaceutical and medical device and diagnostic industries are best equipped to maintain global leadership and empowered to deliver the next generation of medicines and therapies.

This hearing is focused on the critical components of fostering continued investments in research and development and advancing therapies for patients. America's leadership in this space historically has led to translation of cutting edge science, medicine, and technology into products that manage or treat medical conditions that otherwise would decrease quality of life and productivity for Americans. There is much that has been done right in the past few years to encourage this investment into companies focused on breakthrough science and its application to products. Yet there are also areas of significant opportunities to improve, and the patients are waiting.

It is important to understand that successful development of new medicines, devices, and diagnostics 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. Part of what makes life sciences innovation so

successful here in America is the functioning of this entire ecosystem, from basic research, to venture and industry investment in early discovery, through extensive investment in development, and then to commercialization.

Assuming that a strong foundation of societal investment in basic research exists, the development of modern medicines and technologies from that point onward is a capital- and time-intensive endeavor taking an average of 10 years and \$1 billion to deliver a single new drug.ⁱⁱⁱ 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 current conditions for private investments into life sciences are strong in some areas but difficult in others, and I will attempt to exemplify in my comments how policy conditions have strengthened investment into some of these areas, such as therapeutics for oncology and rare genetic diseases, while conditions have challenged other areas such as devices and diagnostics.

In general terms of first-time financings, industries that captured the highest total of venture capital dollars and deals in 2014 were software, media and entertainment, and biotechnology. Overall, investments in 2014 in the life sciences sector, both Biotechnology and Medical Devices combined, rose to the highest level since 2008 with \$8.6 billion invested into 789 deals. While there was a 29 percent increase in dollars there was also a 3 percent drop in deals compared 2013. Dollars invested into life sciences companies accounted for 18 percent of total venture capital investments in 2014. Venture capitalists alone invested \$6 billion into private biotechnology companies.

These private investments trends are a result of a positive regulatory and policymaking environment for the biotechnology and pharmaceutical arenas, with one particular example being the success of FDA's Breakthrough Therapy Designation. Medical device and diagnostics did not fare as well, as venture capitalists invested \$2.6 billion in private medical device companies in 2014, down more than 27% from the 2008 peak of \$3.6 billion. Of even greater concern, first-time investments into medical device companies tell an even starker story. In 2014, there were only 58 medical device companies that raised their first round of venture capital financing, the lowest number of companies since 1995. A primary reason for this decline is the increased time and cost of developing new devices coupled with an increased uncertainty about reimbursement once on the market.

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.^{iv} 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. It is a long, expensive, and risky road from basic research to a breakthrough medical product, and investors and industry are willing to make those investments and take on those risks, but the investments and risks cannot be made without the substratum in basic research to start from. 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 jobs of the future. Currently, the U.S. biomedical research sector supports over 5 million high-paying jobs in the United States and has tremendous potential for growth.^v 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, Device and Diagnostic Development & Approval Will Incentivize Investment

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.^{vi} 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.

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, 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.^{vii} 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.^{viii}

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 (New Molecular Entities) approved were drugs for rare diseases.^{ix} This trend continued in 2013, when 33% of NMEs approved were drugs to

treat rare diseases.^x 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.^{xi}

We have seen continued commitment from FDA and policy makers to work on ensuring an effective development and review process. In fact, in 2014, the FDA approved 41 novel new drugs the highest number of novel drugs approved in the past 10 years. In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) created a new Breakthrough Therapy designation that provides increased interactions with FDA to ensure the most effective development and approval processes for promising new treatments. As of February, 2015 there have been 80 breakthrough designations granted by FDA.^{xii} Similar to statistics for Accelerated Approval, many of these designations have been given to oncology and rare disease treatments and therapies.^{xiii}

It is important to note the positive effect that steady leadership over these past recent years has had at the FDA, and I cannot underscore enough the importance to the venture community of having stable, long term leadership at the agency. It is also important to note the positive effect of policy initiatives such as Breakthrough Therapy, and its successful implementation in some areas. Currently, FDA is in the process of implementing these improvements. Ensuring FDA can hire, retain, recruit and has tools to ensure the organization is best able to carry out its mission is also critically important.

The benefit of these programs has clearly been mostly realized in the oncology and rare disease space. Much has been written regarding the enormous increase in requirements, duration, and expense of clinical trials.^{xiv xv xvi xvii} These increases are especially acute for drugs designed to treat chronic diseases with larger patient populations. As a consequence, the cost and regulatory uncertainty of developing drugs for these populations has been increasing, and we must ask if there is more we could do to get these potential therapies to patients.

As a society, while we celebrate the incredible successes, and indeed we *should* celebrate these successes, we have to ask ourselves what we want to do to improve how we treat some of the other egregious diseases affecting great numbers of our citizenry and long-term health costs, such as obesity, diabetes, Alzheimer's, and depression among others, as well as pressing issues such as antibiotic resistance. 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. Guidance from and involvement of FDA are critical to creating processes for data collection to support the utilization and adoption of novel endpoints and modern drug development tools and approaches would incentivize investment and enable a modern and effective approach to drug development and review.

However, while there is a lot to be excited about when it comes to the number of FDA approvals and programs discussed above, 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 approval based on identified subpopulations, and Europe's adaptive licensing pilot could serve to modernize our current system. Limited population approvals could make a significant difference, not only for antibiotic resistance, but for many subpopulations of disease. Currently, our regulatory system is based on a philosophy that more information before approval is better. We must always support the highest standard of safety, but 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, diabetes, and antibiotic resistance could be a game-changer. We need to incorporate the perspective of the patients closely, and make sure that we are examining the right benefit and risk trade-offs. 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 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 understanding the criteria needed for FDA to allow for utilization of modern tools, such as biomarkers and diagnostics — which are key to advancing personalized medicine by enabling the ability to diagnostically define subsets of patients suffering from

a disease — there is also a need to provide incentives and clarity 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. Furthermore, the lack of clarity around approval of advanced molecular diagnostics, coupled with an enormous lack of clarity on reimbursement for them once approved, has been making investment into this necessary space to recognize the vision of precision medicine quite challenging.

A key barrier to the advancement of diagnostic development is the fact that there are no consistent reimbursement policies for diagnostics. Last year, Congress 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 of this provision 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. Lack of regulatory clarity coupled with lack of clarity on reimbursement also limits investment in medical devices. For both diagnostics and devices, it may take 2 -5 years after the product is approved to secure reimbursement. This uncertainty is a significant factor in limiting investment. A recent NVCA survey found that regulatory concerns were cited as the number one reason investors were moving away from putting funds into medical technology companies.

There are two more areas critical to modernizing our approach to developing medicines and ensuring continued investment in new solutions that will benefit patients. We must strengthen the ability to integrate patient perspectives in the drug development and review process. The ability to provide information about patients' perspectives about their diseases and what they believe to be benefits or acceptable risks would help ensure that the medicines being developed are seen as helpful to the patients they are being designed to treat.

Protection of intellectual property and patents is also paramount. Patents are the only asset a small company has to attract investment. If patents are weakened, the already high-risk proposition becomes one that is too much and investment in this industry will be decimated. We must ensure that the patent system protects the patent owners, abuses of the system for sheer monetary gain and not the advancement of science and discovery should not be supported.

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. With regard to devices and diagnostics we must make the same policy strides as we have in other medical spaces. Appropriate federal investments and a robust and transparent and predictable process for approvals will allow for increased private investments. 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 provide my testimony on this important topic. 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.

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^{iv} 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>.

^v Battelle Technology Partnership Practice. "Battelle/BIO State Bioscience Industry Development 2012". June 2012. http://www.bio.org/sites/default/files/vebattelle-bio_2012_industry_development.pdf.

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^{vii} FDA. FY 2012 Innovative Drug Approvals. December, 2012.

^{viii} JP Morgan. 2014 Global Biotech Outlook. January 6, 2014.

^{ix} FDA FY 2013 Innovative Drug Approvals. December, 2012.

^x FDA. Approved Drugs 2013.

^{xi} Jarvis, Lisa M. Orphans Find a Home. C&EN Volume 91 Issue 19 | pp. 10-12. May 13, 2013.

^{xii} FDA.

^{xiii} Aggarwal, Saurabh (Rob). A Survey of Breakthrough Designations. Nature Biotechnology 32, 323–330 (2014).

^{xiv} 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.

^{xv} Avik R (2012) The Stifling Cost of Lengthy Clinical Drug Trials. Manhattan Institute. http://www.manhattan-institute.org/pdf/fda_05.pdf.

^{xvi} Tufts Center for the Study of Drug Development (12 April 2010) *PDUFA V Meeting*.

^{xvii} Allison M (2012) Reinventing clinical trials. Nature Biotechnology 30 (1): 41-49.