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21ST CENTURY CURES: EXAMINING THE ROLE OF INCENTIVES IN ADVANCING TREATMENTS AND CURES FOR PATIENTS

WEDNESDAY, JUNE 11, 2014

House of Representatives,

Subcommittee on Health

Committee on Energy and Commerce

Washington, D.C.

The Subcommittee met, pursuant to call, at 10 a.m., in Room 2322 of the Rayburn House Office Building, Hon. Joe Pitts [Chairman of the Subcommittee] presiding.

Present: Representatives Pitts, Burgess, Shimkus, Murphy, Blackburn, Gingrey, McMorris Rodgers, Lance, Cassidy, Guthrie, Griffith, Bilirakis, Ellmers, Upton (ex

officio), Pallone, Engel, Schakowsky, Matheson, Green, Barrow, Christensen, Castor, DeGette and Waxman (ex officio).

Staff present: Clay Alspach, Chief Counsel, Health; Gary Andres, Staff Director; Matt Bravo, Professional Staff Member; Noelle Clemente, Press Secretary; Paul Edattel, Professional Staff Member, Health; Brad Grantz, Policy Coordinator, Oversight and Investigations; Sydne Harwick, Legislative Clerk; Robert Horne, Professional Staff Member, Health; Carly McWilliams, Professional Staff Member, Health; Krista Rosenthall, Counsel to Chairman Emeritus; Chris Sarley, Policy Coordinator, Environment and Economy; Heidi Stirrup, Health Policy Coordinator; John Stone, Counsel, Health; Tom Wilbur, Digital Media Advisor; Ziky Ababiya, Democratic Staff Assistant; Eric Flamm, Democratic FDA Detailee; Karen Nelson, Democratic Deputy Committee Staff Director for Health; and Rachel Sher, Democratic Senior Counsel.

Mr. {Pitts.} The subcommittee will come to order. The chair will recognizes himself for an opening statement.

Today's hearing provides us with an opportunity to examine an important aspect of the 21st Century Cures Initiative: whether current economic and regulatory incentives are sufficient to encourage robust investment in the research and development of innovative new drugs and medical technologies.

I am particularly interested in better understanding what we can do to make it more attractive for companies and venture capitalists to invest in the development of therapies that would provide hope to patients without adequate treatment options. After all, as we have learned, there are only effective treatments for 500 of the 7,000 known diseases impacting patients today.

To help close this innovation gap, as part of 21st Century Cures Initiative, we must take a fresh look at the challenges facing innovative companies and make certain the right incentives are in place so America is home to the next generation of cures.

The Hatch-Waxman Act created the modern generic drug industry as we know it and has brought great benefits to our Nation's patients and health care system. Nonetheless, as Senator Hatch recently explained, since the early 1980s, ``the cost of developing a drug has doubled, as has the number of clinical trials necessary to file a new drug application. Further, the number of participants required for those trials has tripled.''

We continue to hear about the many unique challenges of developing and testing therapies for patients with rare diseases and certain types of cancer. However, we cannot lose sight of the fact that new products targeting diseases that impact large patient populations such as diabetes and Alzheimer's take much longer to get to market and are therefore becoming less attractive for investors and companies to pursue. Innovative trial designs with surrogate endpoints are almost unheard of in some of these areas, despite the fact that patients and our health care system would greatly benefit from new treatments. If and when they ultimately get to the market, these products are often left with the least amount of patent life and are granted the

shortest exclusivity periods. We must reexamine the incentive structure, particularly for small-molecule drugs, before we are left wondering who will be developing the next generation of treatments and in which country.

Finally, for a variety of what are oftentimes different reasons, investment in new medical technology companies is at startlingly low levels. There are only 11 venture capital firms remaining in this space, down from almost 40 in in 2007. In 2013, we witnessed the lowest level of initial funding activity in more than two decades. This is not only a cures issues; this is a jobs issue and one we must address head on.

I want to welcome our witnesses today and look forward to learning more about the incentives necessary to encourage vital investment in biomedical innovation across the board.

[The prepared statement of Mr. Pitts follows:]

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Mr. {Pitts.} Thank you, and I yield the remainder of my time to the vice chairman of the subcommittee, Dr. Burgess.

Dr. {Burgess.} Thank you, Mr. Chairman, and I want to join you in welcoming our panel of witnesses. I certainly look forward to hearing your testimony today.

Once again, we are examining the role of various market incentives on the development of new drugs, biologics and devices. From bench to bedside, the timeline right now is about 12 years, and that is a long time. Of all the drugs that enter pre-clinical testing, only five of 5,000 will make it to human testing. Balancing the importance of facilitating innovation and expediting patient access has been a priority of this committee. Many of these incentives have been actually quite successful over the years. Hatch-Waxman--we have a robust market. The Orphan Drug Act--we have encouraged manufacturers to develop and test existing products for the treatment of rare diseases. The bottom line in each instance, patients have benefited.

The greatest market incentive is a developer knowing that there is a market for their product and that it will be

covered. Whether the payer is the Federal Government or the private insurance, payers need to know what is coming down the road so that they are prepared to integrate the new treatments into their coverage because really, what difference does it make to the patient that a product was developed if they have got no access to it.

Really, the headline in all of this should be, we have the ability to develop cures that no generation of doctors has been able to deliver to patients ever, and we can't let the regulatory side get in the way. We want to be facilitators. We want to be catalysts.

And again, we thank you for being here. We welcome your testimony this morning, and I yield back.

[The prepared statement of Dr. Burgess follows:]

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Mr. {Pitts.} The chair thanks the gentleman and now recognize the ranking member of the subcommittee, Mr. Pallone, for 5 minutes for an opening statement.

Mr. {Pallone.} Thank you, Chairman Pitts.

When we talk about medicines and disease, there is a natural emotion that comes from the personal stories we hear from our constituents as well as from our own lives, and many of us know all too well about the pain and suffering families face when battling an illness and losing those we love.

As Members of Congress, we typically speak about treating disease in sound bites. Innovation, cures, discovery, incentives and, of course, access are some of the key words that we use. In today's hearing, we will hear about the thousands of diseases with little or no treatments and we will examine whether additional steps need to be taken to accelerate biomedical discoveries in this country.

Innovative new drugs for decades have made major contributions to our lives. In many instances, they have allowed us to watch our loved ones get better and live longer, sometimes even healthier lives, and now we are even

seeing some new drugs curing diseases outright, discoveries certainly worthy of praise.

But we must be careful in this debate. We can't look at these issues filled with emotion and we certainly can't look at these issues in a vacuum. It is complicated with far-reaching effects, and we continue to battle thousands of rare diseases affecting small populations for which there are no known causes or cures. We need to address this problem. The Orphan Drug Act, which includes tax incentives and market exclusivity, has been successful, leading to a number of medical treatments, and many of these treatments, while they can be expensive, serve a fairly small number of patients.

When we think about diseases like Alzheimer's or chronic conditions like diabetes, we may be talking about treating millions of people for decades, and what is more, baby boomers are aging into Medicare at a pace of thousands a day, so we absolutely need to encourage innovation and help to ensure that new treatments emerge but we also need to make sure that patients have access to affordable treatments. Otherwise we will bankrupt families for which new medicines may be the difference between life and death. And we will

strain our federal health care system. Cures and cutting-edge medicines are of no value if their high costs put them out of reach of the patients who need them.

Thirty years ago, Congress sought to address the high costs and access to medicine, and as a result, the Hatch-Waxman Act was negotiated to strike an important balance between providing incentives to innovative new and better medicines and access to lower-cost medicines. Since then, there has been a tremendous public health and economic benefit. Today, generic drugs account for 84 percent of all prescriptions in the United States with savings amounting to $217 billion annually. But Hatch-Waxman isn't just about lower-cost drugs. Fundamentally, I believe its existence has resulted in competition, innovation and great discoveries. Without the threat of generic alternatives, brand companies would have little reason to engage in research on new drugs to outpace their competitors. Furthermore, there are real examples of brand companies spurring innovation amongst other brands.

So as we move forward, it is important that we do not alter the central construct of Hatch-Waxman. However, that

doesn't mean there aren't additional ways to find further balance in our development ecosystem. In 2012, the committee worked to pass the FDA Safety and Innovation Act, or FDASIA, which included a number of additional economic incentives. One example was the GAIN Act for antibiotics for serious or life-threatening infections. In that provision, we carefully constructed narrowly focused incentives for companies to advance in the antibiotic space. At only 2 years old, there is promise with nearly 17 applications in the pipeline and one approval so far.

So Mr. Chairman, I believe that there are many factors to encouraging and ensuring robust investment in medicines. Federal funding is one notable example. It is the foundation of our biomedical ecosystem and is one of the best investments we can make to spur economic prosperity, drug and device development and cures for the 21st century.

And I would like to yield the remainder of my time, Mr. Chairman, to Ms. DeGette, a member of the full committee who joins us today.

[The prepared statement of Mr. Pallone follows:]

This is a preliminary, unedited transcript. The statements within may be inaccurate, incomplete, or misattributed to the speaker. A link to the final, official transcript will be posted on the Committee's website as soon as it is available.

209 ********** COMMITTEE INSERT **********

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Ms. {DeGette.} Thank you very much. I appreciate you yielding, and I am very proud to be co-chairing the 21st Cures Initiative with Chairman Upton.

This is our second hearing focused on the initiative. The first hearing broadly touched on the eight recommendations provided in the President's Council of Advisors on Science and Technology report on propelling innovation and drug discovery development and education. The hearing today focuses on one of those recommendations, studying current and potential economic incentives to promote drug innovation.

We know there are many types of incentives in place right now--some of the other members have mentioned them--to help spur research and development in both the drug and device space. These range from funding for research and public-private partnerships to tax credits and various exclusivity periods.

I look forward to hearing form the witnesses talking about some of these incentives. For example, the recently implemented exclusivity provided under the GAIN Act seems to

be spurring investment in antimicrobial and antifungal drugs. And so there are other initiatives too.

I want to thank you, Mr. Chairman, for having this hearing and I look forward to this continuing discussion that we are having.

[The prepared statement of Ms. DeGette follows:]

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Mr. {Pitts.} The chair thanks the gentlelady and now recognizes the chairman of the full committee, Mr. Upton, for 5 minutes for an opening statement.

The {Chairman.} Thank you, Mr. Chairman.

We did launch the 21st Century Cures Initiative with the goal of accelerating the discovery, development and delivery of innovative new treatments and cures to patients, ensuring that the United States remains the biomedical innovation capital of the world. 21st Century Cures aims to close any gaps between the science of cures and how we regulate those therapies, and this must be an ongoing conversation.

Today we are going to hear testimony about whether our current legislative and regulatory framework encourages innovators to pursue the development of drugs and devices that are crucial to helping our Nation's patients. I am so proud of the fact that this committee recently came together on a bipartisan basis to address this innovation gap in the context of antibiotics, but it is clear that our work is far from over.

We lack effective treatments for almost 95 percent of

the known diseases affecting patients today and over 95 percent of drugs in development do not make it to market. In addition to working with the FDA and others to decrease the time and cost it takes to bring new products to patients, we have got to heed the advice of the President's Council of Advisors and take a fresh look at current and potential economic incentives to promote innovation. As we have seen in the context of orphan diseases and most recently for antibiotics, periods of market exclusivity are powerful tools for us to consider in ushering in the next generation of treatments and cures. This is certainly a balancing act, and I am committed to pursuing any such changes only after engaging in a thorough and thoughtful dialogue with all interested stakeholders, which is precisely why we are here today.

The Hatch-Waxman Act is an enduring piece of legislation that will undoubtedly form the basis for any such conversation. I agree with Senator Hatch, who recently said, ``The foundation laid by Hatch-Waxman Act 30 years ago will continue to be the mechanism by which the management incentives development of lifesaving drugs but we do have an

obligation to periodically reevaluate how the balance can be adjusted to account for the sweeping changes in the broader health care sector.''

The time and cost of bringing an innovative product to market today is much different than it was in 1984, and yet under Hatch-Waxman, the same baseline exclusivity period is still granted to new drugs. We have an opportunity today to assess whether we still have the right balance in place, particularly for products meeting unmet medical needs.

We also have an opportunity to hear about incentives for new devices. This committee has worked with FDA and stakeholders to help make the regulation of devices more predictable and consistent, but it is clear that we have to continue that collaboration to not only improve FDA but also coverage and reimbursement.

So I want to thank everyone that is here. Please continue to share your ideas with cures@mail.house.gov. Working together, we are going to make a difference.

I yield the balance of my time to the vice chair of the committee, Ms. Blackburn.

[The prepared statement of Mr. Upton follows:]

This is a preliminary, unedited transcript. The statements within may be inaccurate, incomplete, or misattributed to the speaker. A link to the final, official transcript will be posted on the Committee's website as soon as it is available.

299 ********** INSERT 2 **********

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Mrs. {Blackburn.} Thank you, and I appreciate that we are having this hearing today and focusing on 21st century cures.

The United States has done so much to advance health and wellness in the country. Just looking back over some of the recent accomplishments, in children, 90 percent of all leukemia is cured. You have survival rates for melanoma post 5 years that have doubled. Kalydeco for cystic fibrosis. Diabetes--they have done away with the twice-daily shots. You have got the pump. Now they are working on the artificial pancreas. The list could go on and on talking about different vaccines, but I have to tell you, I am very concerned because when you look at the investment that has taken place in medical devices from 2007 to 2013, it is down 40 percent. This isn't good for us and we want to make sure that the incentive is there to come back into that marketplace just as the chairman and Ms. DeGette have both mentioned. We have got to reverse that trend for 21st century cures.

Some of the incentives, the protection of intellectual

property, the use of new pathways in order to move through the maze of FDA regulation and of course FDASIA has the breakthrough therapy designation, clarity around reimbursement issues that focuses on the value of treatment. These incentives provide an investment in our Nation's fiscal future as well.

Alzheimer's disease is a great example of this. It is one where I have a particular interest and focus. It is something that costs our Nation $215 billion a year. That is about $50,000 per patient, or the median household income, to care for an Alzheimer's patient.

So to focus on these cures is an imperative. It is the proper use of our time. I welcome you and I yield back the balance of my time.

[The prepared statement of Mrs. Blackburn follows:]

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Mr. {Pitts.} The chair thanks the gentlelady and now recognizes the ranking member of the full committee, Mr. Waxman, 5 minutes for an opening statement.

Mr. {Waxman.} Thank you very much, Mr. Chairman.

This hearing today has very real implications for patients everywhere. How do we ensure that drug and device companies have the right incentives to discover important new treatments for disease? We cannot legislate scientific advances. In some areas, the lack of new treatments is attributable to a lack of scientific knowledge, not the lack of incentives. To tackle these problems, we will need more investment in research.

That is why our country has been so far ahead of the rest of the world. Our taxpayers want basic research to be funded through the National Institutes of Health, and I would assume everybody that cares about this problem is outraged when we see cuts at the NIH budget. But in other areas, incentives can play a key role in sparking and sustaining innovation. That is why it is important for us to consider how the incentives that exist today are working and whether

they can be improved.

The good news is that innovation in this country is flourishing. More important new drugs are launched here than any place else in the world. A key reason is that our system recognizes that both competition and market exclusivity can spur innovation. We have led the world in developing new treatments because we have sought to get the balance right.

There are a variety of types of incentives: tax credits, monetary prizes, and public funding of basic scientific research, to name a few. I hope we will focus today on this wide range of incentives. I suspect, however, that much of our time will be spent on patents and marketing exclusivities.

Let me say a few words about these tools because I don't think anyone in Congress has worked longer or harder on getting their use right than I have. I authored the Orphan Drug Act, which provides 7 years' exclusivity to incentivize development of drugs for rare diseases. The 7 years was justified because the small populations in need of these drugs did not provide an adequate market. The Act has been a resounding success. Prior to enactment, only ten drugs for

rare diseases had been developed. In the 30-plus years since enactment, over 400 have been approved and many are in the development stage and are being used without the final approval.

I was the co-author of the Hatch-Waxman law, which established our generic drug system. The Act struck a balance between generic competition and maintaining adequate incentives for brand companies to continue to innovate. We allowed generics to rely on the brands' safety and effectiveness data in order to avoid wasteful duplicative clinical trials. In exchange, we gave the brands 5 years of exclusivity to store some of the patent time lost during the FDA review process. The law has been an enormous success. Today, over 86 percent of prescriptions are generics, yet spending on generics accounts for only 29 percent of total drug spending, and at the same time, the brand industry is booming.

Most people understand that the introduction of generic competition has drastically lowered our national drug bill. But generic competition also has another critical effect that may seem counterintuitive: it also spurs innovation. An

innovator company that knows generic competition is just around the bend needs to develop new products. In contrast, excessive periods of exclusivity allow innovators to sit back and relax. Why spend a lot of money on discovering the next groundbreaking product, if it can continue to charge monopoly prices for 10, 12, or even 15 years on a drug that has already been approved? Too much exclusivity is as bad as too little, if not worse. Innovation is stifled by the lack of competition, and American patients foot the bill by paying higher prices for their drugs.

When our committee considers these issues, the first question should be whether new or additional incentives are really needed in any particular area and what is an appropriate incentive. We should insist on getting the answers that are supported with data demonstrating this need. If new marketing protections are warranted, they should be narrowly focused to achieve a targeted aim. Otherwise we run the risk of allowing companies to reap huge windfall profits, windfalls that are paid for by American patients and the government and insurance companies in this Nation.

So I urge caution when considering patents and

exclusivity as incentives. These are not the only tools, and in many cases, they are not the best ones for ensuring the development of new cures.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Waxman follows:]

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Mr. {Pitts.} The chair thanks the gentleman. The written opening statements of all members will be made a part of the record.

That concludes our opening statements by the members. We will now go to our witnesses. We have one panel with seven witnesses. I will introduce them in the order of their speaking.

First is Mr. Marc Boutin, Executive Vice President and Chief Operating Officer of National Health Council. Then Dr. Sam Gandy, Chair, Mount Sinai Alzheimer's Disease Research Center on behalf of Dr. Ken Davis, the President and CEO of Mount Sinai Health System. Then Mr. Alexis Borisy, Partner, Third Rock Ventures; Mr. Mike Carusi, General Partner, Advance Technology Ventures on behalf of National Venture Capital Association; Dr. Steven Miller, Vice President and Chief Medical Officer, Express Scripts Holding Company; Dr. Fred Ledley, Professor, National and Applied Sciences, Management Director, Center for Integration of Science and University, Bentley University; and finally, Mr. Scott Hemphill, Professor of Law, Columbia Law School.

Thank you all for coming. You will each have 5 minutes to summarize your testimony. Your written testimony will be made a part of the record. There is a little system of lights on your desk so you have 5 minutes when the green light will be on. When the red light goes on, we ask that you wrap up your opening statement.

So at this time, Mr. Boutin, we will start with you. You are recognized for 5 minutes for an opening statement.

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^STATEMENTS OF MARC BOUTIN, EXECUTIVE VICE PRESIDENT AND CHIEF OPERATING OFFICER, NATIONAL HEALTH COUNCIL; DR. SAM GANDY, CHAIR, MOUNT SINAI ALZHEIMER'S RESEARCH CENTER, ON BEHALF OF DR. KENNETH DAVIS, PRESIDENT AND CEO, MOUNT SINAI HEALTH SYSTEM; ALEXIS BORISY, PARTNER, THIRD ROCK VENTURES; MIKE CARUSI, GENERAL PARTNER, ADVANCED TECHNOLOGY VENTURES, ON BEHALF OF THE NATIONAL VENTURE CAPITAL ASSOCIATION; DR. STEVEN MILLER, SENIOR VICE PRESIDENT AND CHIEF MEDICAL OFFICER, EXPRESS SCRIPTS HOLDING COMPANY; DR. FRED LEDLEY, PROFESSOR, NATURAL AND APPLIED SCIENCES, AND MANAGEMENT DIRECTOR, CENTER FOR INTEGRATION OF SCIENCE AND INDUSTRY, BENTLEY UNIVERSITY; AND C. SCOTT HEMPHILL, PROFESSOR OF LAW, COLUMBIA LAW SCHOOL

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^STATEMENT OF MARC BOUTIN

} Mr. {Boutin.} Good morning, Chairman Pitts, Ranking Member Pallone, Ms. DeGette, members of this subcommittee.

There are more than 133 million people living with one or more chronic conditions. That is more than 40 percent of

the population. Effective treatments are available for some but for many patients, all they have is hope.

My name is Marc Boutin. I am the Executive Vice President and Chief Operating Officer at the National Health Council. We provide a united voice for people with chronic disease and disabilities.

As a child, I remember growing up in a tiny town in northern Maine. Every surface of my home was covered in floral wallpaper, including the light switches. You actually had to rub the wall to find the switch. The wallpaper, the rugs, the furniture, everything was covered in flowers, and when my mom sat perfectly still in her floral dress, you couldn't see her. In my 30s, I remember sitting in the doctor's office when my father was told he had incurable cancer. My mom became his primary caregiver even though she had multiple chronic conditions herself. I held my father's hand when he took his final breath. My mom soon died on my birthday. Dismantling our family home was difficult. All the memories, all that wallpaper. Getting the house ready to sell was not easy but it had to be done.

Nearly every person in this room has been touched by the

burden of disease. Michael Gollin sitting behind me is an intellectual-property lawyer. He is also living with ALS, or Lou Gehrig's disease, which progressively robs you of your ability to walk, talk, swallow and even breathe.

Thirty years ago, Representative Waxman coauthored the Hatch-Waxman Act, which updated our innovation ecosystem and made medications affordable for millions of Americans. But as Senator Hatch recently wrote, ``We cannot rest on our laurels. We have an obligation to periodically reevaluate and adjust to account for the sweeping changes in the health sector.''

Our current innovation ecosystem was built decades ago, long before we mapped the human genome, had supercomputers or advanced diagnostics. Much like my family home, the ecosystem has not kept pace with time. No one is to blame for this. It just happens. You get used to the wallpaper.

The 21st Century Cures Call to Action provides an opportunity to update, to modernize. While we may not all yet agree on the specific solutions, consensus is emerging on some of our most pressing challenges. Let me address two.

First, we all know that you need a patent to develop a

new medicine but just because you cure Parkinson's or lupus doesn't mean you get a patent. Some of the best science is not translated into treatments simply because they don't meet the technical requirements of the law. From a patient perspective, this makes no sense, and Congress can fix it.

Second, our current system encourages the fastest, least expensive innovation, not necessarily the treatments that are most important to society or individual patients. As you know, patents run concurrently with clinical and regulatory review. As a result, the best and most promising medicines sometimes receive the shortest protection from general competition. For example, conditions which progress slowly like Alzheimer's can come to the market with the shortest periods of protection. This also encourages the development of treatments for late-stage illness rather than early-stage illness despite the huge social and economic value of addressing and preventing disease early. From a patient perspective, this makes no sense, and Congress can address it.

The MODDERN Cures Act, introduced by Representative Lance with bipartisan support, is the first legislative

attempt to address these two challenges. It promotes the best science, not the best patent, but only for drugs that address an unmet medical need.

On behalf of my dad, my mom, Mr. Gollin and nearly everyone in this room affected by disease, thank you for including the patient community in this multi-stakeholder approach. We stand willing, ready and able to help you solve this and other complex challenges. It is time to take down the wallpaper. It is time to modernize our innovation ecosystem. Thank you.

[The prepared statement of Mr. Boutin follows:]

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Mr. {Pitts.} The chair thanks the gentleman and now recognizes Dr. Gandy 5 minutes for an opening statement.

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^STATEMENT OF SAM GANDY

} Dr. {Gandy.} Chairman Pitts, Ranking Member Pallone, distinguished members of the Subcommittee on Health, thank you for inviting me here today. I am Dr. Sam Gandy. I am Professor and Chair of Alzheimer's Disease Research at Mount Sinai Medical Center and Director of the Center for Cognitive Health Care. Dr. Ken Davis was meant to be here addressing you but he became ill at the last minute and was unable to come. Thank you for allowing me to present in his stead.

In the 1970s, as a young researcher, Dr. Davis was the first to show that Alzheimer's symptoms could be improved by restoring levels of a brain chemical called acetylcholine as required for memory function. His work eventually lead to FDA approval of three of the four drugs currently on the U.S. market for Alzheimer's disease but that was decades ago, and incredibly, in terms of caring for Alzheimer's patients, almost nothing has changed.

The need for breakthrough medications for Alzheimer's is greater than ever, and the public health impact and the

economic impact of Alzheimer's are both escalating.

Alzheimer's affects more than 5 million American seniors today, and by 2050, that number will rise to 15 million. Fully one-half of everyone over age 85 is demented. That means that everyone across the country and everyone in this room who lives past age 85 will be either a patient or a caregiver.

The financial implications are staggering. This year, Medicare and Medicaid are expected to pay $150 billion in acute, chronic and hospice care for individuals with Alzheimer's. The Medicare cost of caring for Alzheimer's will increase more than 600 percent over the next 35 years, rising to $627 billion.

Alzheimer's symptoms begin when people are in their 70s, so if we were able to slow the progression of the disease by half, most of these individuals would not develop symptoms until their 90s, and indeed, many would not live long enough to develop the disease at all. If we could simply delay the onset of Alzheimer's by 5 years, that would cut costs to all payers by half a trillion dollars by 2050.

Scientific opportunities for breakthrough oral

medications, in other words, pills, have never been more promising. An extraordinary series of recent studies have found that most people who will eventually develop Alzheimer's accumulate in their brains clumps of a material known as beta amyloid, and this begins two decades or more before symptoms. My own research career began in the 1980s when my team identified the first model drugs that reduce amyloid buildup.

The FDA appropriately requires that safety and efficacy of new drugs must be demonstrated in two independent and most commonly sequential trials. Developing a drug for Alzheimer's is a slow process. Unlike antibiotic medications, for example, that can be tested over a few weeks, Alzheimer's trials require 3 to 5 years. When that is added to, say, 2 years to recruit patients and another year to analyze the results, virtually all the drug's patent life will have lapsed. Because of this, many drug companies, I would say most, are reducing their emphasis on Alzheimer's.

As you well know, Congress has stepped in before to provide market incentives for research. We now need an exclusivity policy for orally administered compounds--pills--

that slow Alzheimer's. Why do I stress the need for a pill? Because infused biologics can cost as much as 20 times the cost of ordinary medication. For Alzheimer's, that kind of cost would provide no fiscal advantage.

In conclusion, Alzheimer's science is poised to accelerate but business incentives must be realigned in order to provide for the public's best interest. By providing market exclusivity for pills, we would allow innovators to receive a return on their expenditure of resources. In exchange, we would bend the dementia cost curve and reduce the number of individuals suffering from Alzheimer's disease.

I would like to thank the subcommittee for inviting me here today and for shining a spotlight on this important issue. Thank you.

[The prepared statement of Dr. Gandy follows:]

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Mr. {Pitts.} The chair thanks the gentleman and now recognizes Mr. Borisy 5 minutes for an opening statement.

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^STATEMENT OF ALEXIS BORISY

} Mr. {Borisy.} Good morning, Chairman Pitts, Ranking Member Pallone and members of the subcommittee. My name is Alexis Borisy, and I am a Partner at Third Rock Ventures. At Third Rock, our mission is to create, launch and grow innovative companies that will make a meaningful difference for patients, for physicians, for our health care system overall. I applaud this committee for initiating the 21st Century Cures Call to Action to ensure that U.S. biopharmaceutical and life sciences industry is best equipped to maintain global leadership and deliver lifesaving medicines.

Successful development of new medicines is dependent on policies that support the entire life sciences ecosystem from the lab to the patient. Disrupting any part of the ecosystem weakens the entire enterprise. This endeavor is high risk, taking over a decade and more than a billion dollars to deliver a single new drug. But there can be no question of the reward. Over the last 20 years, we have provided

medicines that have changed and saved the lives of patients with diseases such as cancer, heart disease, HIV/AIDS.

This hearing is focused on a critical component of ensuring a forward-learning biopharmaceutical industry, life sciences industry. What incentives are needed to advance treatments and cures? One key to a robust life sciences industry is a national commitment to support basic research. The United States has long been a world leader in basic research but funding for NIH has been flat or declining for the past several years. Diminished support for basic research will lead to a smaller pipeline of next-generation medicines and impede our country's innovation potential.

Building from that base, venture funding is the lifeblood of small biotech companies. However, early-stage venture investment is under significant pressure in the life sciences. A primary reason for its decline is the increased time and cost of developing new treatments. These struggles are especially acute for drugs designed to treat chronic diseases with larger patient populations. The decision to deploy capital is directly impacted by regulatory and reimbursement behaviors. Better enabling and encouraging FDA

to utilize flexible approaches and modern tools would have a positive impact on venture funding.

For example, since the implementation of the accelerated approval pathway, over 80 drugs have been approved, most in cancer and HIV. Likewise, in recent years, FDA has shown an increased willingness to work with companies to develop more effective clinical development programs for rare diseases. The majority of designations under the new breakthrough therapy program are also for cancer and for rare diseases. The time required to put a drug on the market is usually longer than the length of time of a typical venture capital investment fund.

The modern approach to regulation that exists now for cancer and rare diseases attracts investment for three important reasons. First, the regulatory process is more interactive, flexible and reflective of the disease and patient being treated. Second, the amount of investment required to fund a company through proof of concept is better understood, and third, the next step in the innovation ecosystem, be that a larger company or public investors, feel more confident about the development and approval process

688 going form that step further.

689 The results are clear. Over a third of recent drugs
690 approved have been drugs for rare diseases, and oncology
691 remains one of the hottest investment areas. However, the
692 same cannot be said for chronic diseases where the regulatory
693 requirements are greater. Without improving these processes,
694 early-stage investment in those areas will continue to
695 struggle. We must ask ourselves how we can learn from rare
696 disease and oncology and work to improve how we treat
697 conditions like obesity, diabetes and Alzheimer's, which have
698 a dramatic impact on our long-term health care costs. We
699 must advance to a system that critically determines whether
700 the information required is actually informative as to the
701 potential use of the drug in the real world. Creating
702 approval pathways that enable the development of drugs for
703 subpopulations of patients in these chronic diseases could be
704 a game changer.

705 There is also a need to provide incentives for the
706 development of new diagnostics. I applaud Congress for
707 passing PAMA, which includes a provision designed to
708 significantly improve reimbursement for diagnostics but its

ultimate impact will be determined by the rule writing process. I would like to recommend that we consider a program for diseases important to the public health with high unmet dg needs where we could identify these diseases critical to the Nation's health and establish a payment policy for these desired diagnostics. Clear reimbursement policies for personalized-medicine tools combined with modern regulatory approaches would advance personalized medicine by leaps and bounds.

Congress has the opportunity to support a policy environment that fosters the search for the next generation of cures and treatments, and I applaud the committee for taking steps to improve this process.

Thank you for the opportunity to share my thoughts.

[The prepared statement of Mr. Borisy follows:]

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Mr. {Pitts.} The chair thanks the gentleman and now recognizes Mr. Carusi 5 minutes for an opening statement.

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^STATEMENT OF MIKE CARUSI

} Mr. {Carusi.} Chairman Pitts, Representative Pallone, members of the subcommittee, thank you for the opportunity to testify today on behalf of the National Venture Capital Association. Chairman Upton, Representative DeGette, thank you for spearheading the 21st Century Cures Initiative. It is important work.

My name is Mike Carusi. I have been in the venture capital business for over 16 years. Over the course of my career, I have had the privilege of helping innovative companies develop therapies for some of the most daunting diseases of our time including heart disease, diabetes and cancer.

I am here today to share my perspective on what is happening with medical technology innovation. Simply put, we are facing a crisis, and the continued leadership of this committee is needed more than ever. Without changes in public policy, the United States will no longer lead the world in developing lifesaving treatments, and American

patients face a grave risk of losing access to these innovative cures.

The promise and importance of innovation has never been greater. Our understanding of the origins of disease and human physiology are growing. We see dramatic advancements in engineering, material science, information technology. As the population ages, new and improved medical technologies can play a critical role in not only helping to improve patient care but also in reducing long-term costs as well. But despite our patients' needs and our ability to meet them, funding for innovative medical technologies has declined substantially in recent years. As Congresswoman Blackburn noted, between 2007 and 2013, medical device venture investments fell by a total of 40 percent. In 2013, we witnessed the lowest level of medical device initial funding activity in more than two decades with just 44 companies receiving first-time funding--44 companies.

Poor investment returns have resulted in institutional investors such as universities, pension funds and foundations fleeing the device sector. It is important to note that these are the very groups that we get our money from. As a

result, an estimated 70 percent of all medical device venture investors have or will exit the business over the next 5 years, and most of these departures are not by choice.

Another equally troubling fact is that for those with capital, we are shifting more and more of our resources overseas. In my firm's case in particular, 25 percent of our future investment will focus out of the United States. This is a big change from the way we have done business in the past.

So why is this shift occurring? First, access to capital. Countries like Ireland and Singapore are offering powerful economic incentives to groups like Lightstone to invest. Second and more importantly, the regulatory path in these markets is simply faster and more predictable. It is now commonplace for our companies to seek regulatory approval and commercialize new products in other markets ahead of the United States.

We have talked at length about the path to FDA approval, about the challenges in this path, about the delays in the unpredictability, and I am happy to say that progress has been made to begin reducing these regulatory barriers. The

2012 FDASIA bill included a number of important provisions which are beginning to have a positive effect. The veterinarian community and medical device incubators also has enjoyed a productive dialog with CDRH Director Shuren and other members of his leadership team in working to further improve the medical device regulatory process. We are by no means done and we have more work to do to continue to build on this progress, but FDA has no longer become the greatest obstacle to innovation. That obstacle is now reimbursement.

Obtaining coverage and reimbursement for innovative products has become an increasingly difficult process that can add another 3 to 5 years to the development of a new product. It is a process that lacks transparency, predictability and consistency. I have experienced this firsthand--changing standards for data, no clear benchmarks, an ever-moving bar. It is an extraordinarily frustrating process that you simply need to go through once to clearly see that the system is broken.

In my written testimony, I have included several specific recommendations on how we can improve on the system. At its core, I would bring us back to transparency,

predictability and consistently, similar themes that we echoed in our discussion on FDA. These are the three hallmarks that we need as investors to have confidence in moving ahead.

Again, it is important to underscore that none of these steps alone will ensure a reinvigorated medical technology ecosystem. There is no silver bullet. But I believe a renewed focus on drastically improving the coverage and reimbursement situation is sorely needed.

Again, thank you for the opportunity to testify today. I love what I do, I love the process of innovation, I love developing treatments for patients. That is why the work of this committee is so important and so necessary. We look forward to working with you, and I am happy to answer any questions you might have.

[The prepared statement of Mr. Carusi follows:]

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Mr. {Pitts.} The chair thanks the gentleman and now recognizes Dr. Miller 5 minutes for an opening statement.

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^STATEMENT OF STEVEN MILLER

} Dr. {Miller.} Thank you, Chairman Pitts, Ranking Member Pallone and members of the committee.

Mr. {Pitts.} Can you push the mike?

Dr. {Miller.} I appreciate the opportunity to testify today. I am the Chief Medical Officer for Express Scripts but a former transplant nephrologist and former Vice President and Chief Medical Officer for Washington University and Barnes Jewish Hospital. I started my career in primary drug discovery and hold many patents and have been with Express Scripts for the last 9 years. Express Scripts is the largest pharmacy benefits manager, administering the benefits for 85 million Americans on behalf of clients including health plans, large and small businesses, and the Department of Defense. Each day we work to make the use of prescription drugs safer and more affordable.

The current system works very well to drive innovation. There is more than 5,000 drugs in human testing in the United States today, more than any time in my 30-year career. But

for payers, this is concerning. Whether highly or mildly innovative, these advances come at enormous cost to patients and payers. These new therapies cost tens of thousands of dollars per patient, and the challenge is made clear by one recent approval, Solvadi. Solvadi is a new treatment for hepatitis C. In the first quarter of 2014, its sales exceeded $2 billion. Cost of Solvadi varies by nation, but in the United States, it is $84,000, or $1,000 per pill. You compare that to Canada or Europe where it is $55,000, and in Egypt, $900, which is less than a single dose in the United States.

Solvadi is a breakthrough with a high cure rate but varied analysis suggests that Solvadi may not be worth the price. A study from the California Technology Assessment Forum found that even over a 20-year horizon, the cost-benefit is only two-third of the original $84,000.

Solvadi is valuable to patients worldwide but should it be the United States' role to pay the lion's share where Solvadi manufacturers have the most incentives available to promote innovation. Americans will pay more for the medicine than anywhere else. Incentives available for Solvadi or

other include, one, market exclusivity. In addition to the usual patent protection afforded to high-tech products, brand drug manufacturers receive a period of exclusivity under Hatch-Waxman where they are protected for competition. Two is they get breakthrough approval designations. Since 2012, drug makers have had the ability to see a breakthrough therapy designation by the FDA to expedite the review of new drug applications that demonstrate substantial improvements over existing therapies. Three, we have a free market to sell medicines. Unlike other nations, the new drug approval process doesn't include cost-effectiveness comparisons. Manufacturers are free to sell their medications at prices they determine without government intervention, validation or approval. And four, NIH support. The NIH supports drug makers with bench science, basic research and support for clinical trials.

The price of Solvadi should be disappointing to lawmakers, who have worked to foster innovation and encourage a marketplace in the United States for brand drugs. Any action that Congress considers should explore the need for an environment where America doesn't pay the lion's share for

research and development that is benefited worldwide. Congress should consider the proven ideas. One: Support NIH with additional funding. Drug discovery begins with excellent work by the team at the NIH. Two: Support the FDA. Given the success of Fast Track, accelerated approval, priority review programs, without compromising safety and effectiveness of drugs, these hastened timelines can become the norm of new drug approval if additional funding is provided. And three: Reserve marketplace incentives for true innovations. Market exclusivity is invaluable to drug makers and it should only be granted to new drug applications that substantially improve upon existing therapies. What better way to promote innovation than to more carefully grant monopolies to drug manufacturers?

In conclusion, existing incentives for innovation are working. Today we have more companies doing drug discovery than ever. The industry is healthy and profitable. Express Scripts is concerned by the idea that rewarding certain types of drug development with additional market exclusivity will pervert the commercial market for prescription drugs. It will inhibit innovation. It artificially restrictions

competition and it affords the same reward to breakthrough therapy as to less innovative product improvements. Most importantly, it places the burden for funding this additional incentive solely on the back of payers of health care rather than socialized equally by society through the tax code. Proposals that seek to expand market exclusivity in any situation need to be approached very carefully, very narrowly to ensure the right solution to the underlying problem.

Thank you very much for this opportunity.

[The prepared statement of Dr. Miller follows:]

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Mr. {Pitts.} The chair thanks the gentleman. Dr. Ledley, you are recognized for 5 minutes for an opening statement.

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^STATEMENT OF FRED LEDLEY

} Dr. {Ledley.} Good morning, Chairman Pitts, Ranking Member Pallone, members of the committee. My name is Fred Ledley. I am Director of the Center for Integration of Science and Industry at Bentley University, where we focus on studies aimed at accelerating the translation of scientific discoveries for public benefit. I have been an investigator of the Howard Hughes Medical Institute, the founder of an early company in the field of gene therapy, gene medicine, the president and CEO of another startup, which was a pioneer of personalized medicine, and I am the holder of 10 U.S. patents.

My takeaway message today is very simple, that the role of incentives should be exclusively to promote 21st century cures based on 21st century science. This requires sustained support for translational science from the early stages of basic research that comes out of the NIH through drug discovery and drug development. It requires patent rights that protect the inventor's priority to novel art. It

requires predictable pricing, and it can be inhibited by statutory exclusives granted to older products, which draw resources away from the discovery of new cures and innovations that could reduce the cost of health care.

While testimony before this committee has celebrated the many advances scientific advances of recent decades, our research suggests that few of these advances are being translated into cures. Let me give you an example. Monoclonal antibodies are one of the most important classes of new medicines now covering the market but the basic science that enabled that dates to 1975. My colleague, Laura McNamee, has recently studied 100 new medicines approved by the FDA since 2010 and found that these products arose from basic science that was on average 40 years old. Thus, in the second decade of the 21st century, the pharmaceutical pipeline is not providing 21st century cures but rather cures based on 20th century science.

One reason the pharmaceutical industry is facing the dwindling pipeline and a patent cliff is that it is depended for too long on the products of old science--``me too'' drugs, product extensions and the eternal hope that there

will be a blockbuster around the corner. I urge the committee to focus on incentives that will move the pharmaceutical industry forward, forward from reliance on old science towards these 21st century cures.

Now, patent rights are essential for this innovation. Patents transform scientific discoveries into economic capital that can be monetized through technology transfer, capital investments by our venture colleagues, licensing fees or royalties. Innovation can be incentivized by more efficient and timely patenting of these discoveries.

Statutory exclusives can have the opposite effect. Extended exclusivity makes companies less likely to commit resources to the always risky business of translational science. Such companies are less likely to discover and develop modern cures, less likely to enter into alliances with startup companies and less likely to acquire those companies. Extended exclusivity granted to products that are late in their lifecycle or dormant are particularly problematic since they explicitly favor the products of old science over modern science. Statutory exclusivity can promote science, as we have seen in Hatch-Waxman, in the

Orphan Drug Act and in the Best practices Pharmaceuticals for Children Act, which I remind you achieved this goal with 6 months of extended exclusivity.

Even with market incentives, the path to 21st century cures needs to be nurtured. I started a gene therapy company 25 years ago. I have been working in the field for 30 years. There are no gene therapy products on the market. One of the reasons is that while more than $4 billion has been invested in gene therapy companies, all this money went to technologies that were immature and not likely to develop drugs. This is a long process that requires sustained, continuous investment. Incentives that engage stakeholders in the long-term success of innovation can promote innovation. These could include accounting standards that assign value to R&D spending, valuation models that consider the intermediate products of innovation or differential tax rates or even shareholder rights that favor long-term over short-term investments.

The reason we are here today is that the treatments and cures that were developed from 20th century science are just not good enough. There are critical unmet needs and

incurable diseases and the ever-increasing cost of health care. Incremental improvements are not what we are after. I urge the committee to focus on the mission of advancing 21st century cures that move the industry forward to using 21st century science.

Thank you very much for the time.

[The prepared statement of Dr. Ledley follows:]

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Mr. {Pitts.} The chair thanks the gentleman and now recognizes Mr. Hemphill 5 minutes for an opening statement.

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^STATEMENT OF C. SCOTT HEMPHILL

} Mr. {Hemphill.} Thank you. Mr. Chairman, Ranking Member, members of the subcommittee, my name is Scott Hemphill, and I am a Professor at Columbia Law School. I write and teach about innovation and competition. My research examines the incentives for drug innovation and affordable drug access provided by patents and regulation. Thank you for the opportunity to testify today about these important issues.

I think we can all agree that innovative drugs have made an enormous contribution to longer and healthier lives. Patents and regulation are the key to that success by supplying incentive to innovate, thereby justifying large investments in research and clinical testing. Patents and regulation also serve a second goal, which is to ensure low-priced access to lifesaving drugs. This is the balancing act discussed by Chairman Upton and others.

As an engine of drug innovation, of course, the patent system is not perfectly tuned. Sometimes a patent can't be

secured, for example, or a drug development takes too long and the patent expires too soon.

Now, this issue is not a new problem but rather a longstanding focus of drug regulation. For example, as you have heard, the Waxman-Hatch Act fills in the gaps in patent protection by giving drugs special non-patent protection from competition, and to help make up for long development time, the Act extends the term of existing drug patents, and the Orphan Drug Act serves a similar purpose.

Now, to the extent that there is a problem even after these extra protections, the question arises, what should we do about it, and we have heard a few options. One option is to rethink and speed up clinical trials. Another is targeted public support where appropriate. A third option is to expand existing legal exclusivity. Now, the key here, I think, is to limit the expansion and target it to situations where it is truly needed, and one possibility here is Dr. Gandy's suggestion of narrower protection to help address Alzheimer's disease.

The MODDERN Cures Act also expands exclusivity but not in a way that is narrow or targeted. It would grant a large

increase in protection for essentially all novel drugs. The Act gives 15 years of protection for so-called dormant therapies. Now, when I first heard the term ``dormant therapy, '' I figured this would be a limited, targeted expansion along the lines of the Orphan Drug Act but I think that conclusion is incorrect. The key point is that a drug must address a so-called unmet medical need but unmet medical need is defined quite broadly. It is not just a drug for a disease that has no treatment but any sort of improved outcome. So even a drug that merely improved patient compliance or increased convenience would count under the Act.

Now, in effect, the Act grants 15 years of protection to any drug with a novel active ingredient, and 15 years is a long time. It is about 3 years longer on average than even novel drugs get today, 3 years longer than biologics, and is 4 or 5 years longer than protection in Europe. The result, I fear, is a large windfall through longer exclusivity for many drugs that would have been developed anyway. Billions of dollars will be transferred from drug purchasers to drug makers, and worse, where patients pay in whole or in part for

the drugs, this would also reduce access to drugs.

How big is this problem? Well, we can consider just the novel drugs that experienced generic entry over the decade between 2001 and 2010 and imagine that all of these drugs had gotten a 15-year term instead of the average 12 or so that they do today. That roughly 3-year extension would suggest an overpayment for these drugs of more than $120 billion. In other words, purchasers are likely to pay a lot more for drugs that would have been produced even without the extra protection. Beyond the windfall problem, the Act seems quite vulnerable to evergreening strategies that would extend protection beyond the 15 years, and as we have already heard, risks placing a disproportionate burden on U.S. purchasers, and I am happy to discuss these issues during the question-and-answer period.

To conclude, claims that larger drug maker rewards would increase innovation are easy to make but hard to pin down. The right next step here is careful study to determine the scope of the lost innovation problem in practice, and if warranted, a solution narrowly targeted at that problem.

Thank you again for the opportunity to discuss these

1098 important issues with the subcommittee.

1099 [The prepared statement of Mr. Hemphill follows:]

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Mr. {Pitts.} The chair thanks the gentleman, and that concludes the opening statements of our panel.

I would like to ask unanimous consent to submit for the record a statement submitted by the Premier Health Care Alliance and a submitted by the Generic Pharmaceutical Association. Without objection, so ordered.

[The information follows:]

********** COMMITTEE INSERT **********

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Mr. {Pitts.} We will now begin questioning, and I will recognize myself 5 minutes for that purpose.

In a statement issued by the California Public Employees Retirement System related to this hearing, they state that ``Despite historic breakthroughs in scientific research, clinical trials and new lifesaving therapies, many common diseases remain incurable. Heart disease and stroke continue to be leading causes of mortality. Psychiatric diseases are serious burden on patients, their families and society as a whole, and infectious disease presents new critical challenges in terms of drug resistance.''

I will note that the committee acted in an overwhelmingly bipartisan manner to pass the GAIN Act as part of FDASIA, which was a needed first step towards addressing this innovation gap by granting an additional 5 years of exclusivity to new qualified infectious-disease products. We must build on this momentum in the antibiotic space as well as in other areas of unmet medical need and where public health demands innovation.

We will start with you, Mr. Borisy. Have there been

breakthroughs in clinical trial designs for chronic diseases that impact large patient populations?

Mr. {Borisy.} So we have seen--if the goal is ultimately to get medicines to patients and to our society that needs them, we have seen through breakthrough therapy, through accelerated approvals in multiple different disease areas an adoption of approaches that have helped to speed those therapies to the patients that need them. So it becomes a question of, what is the information that is necessary to understand how a drug will be in the real world setting and are we applying the current best understanding of biomarkers, of personalized medicine subsets of patients in some of these other disease settings, could we move things more quickly.

Mr. {Pitts.} How long does it typically take to conduct a clinical trial for a new therapy targeting a chronic condition such as heart disease or stroke?

Mr. {Borisy.} The total time in clinical development for those types of chronic diseases are usually longer than 10-plus years.

Mr. {Pitts.} Are venture capitalists investing in the

development of new products targeting chronic diseases?

Mr. {Borisy.} It is very difficult to do so. If our focus is on patients and bringing through those innovative breakthrough medicines, if the time in clinical development is going to be on the order of 10-plus years, building from wonderful basic research that has been done, there still is usually additional years before you ever get to the clinic to create that drug that can then go be in the clinic for another 10 years of development. So as a venture capitalist, if you are considering deployment into an area that is going to take 15-plus years before it may get to the market, that is very challenging. It is challenging in that time period is longer than the length of our investment funds, which means that we will be dependent on other entities, recognizing that that is an important product for patients, but other entities, if they have uncertainty about how long it will take them to continue developing it or what risks may be involved, we will not recognize the value that we have created early on. So that long period of time and uncertainty makes those very conditions which as a society and as a Nation we need to be some of the most challenging to

invest in from a venture-capital perspective.

Mr. {Pitts.} Thank you.

Dr. Gandy, in your testimony you note that the lack of therapeutics for chronic conditions such as Alzheimer's places an enormous strain on our country's finances and that without novel therapies, costs will only escalate. At this rate, will the next generation of Americans that develop Alzheimer's be taking the same medications that were approved over a decade ago, and what would this mean to health system costs?

Dr. {Gandy.} At this point, the medications that are used to treat Alzheimer's disease are the same that were developed in the 1970s, so we have nothing new on the horizon. Those medications don't change the progression of a disease. They relieve symptoms briefly. They always wear off. So we have--we continue in the current cycle of having no way to slow the progression of the disease.

Mr. {Pitts.} And Mr. Boutin, the California Public Employees Retirement System asserts in their testimony that the market exclusivity period of 5 years for brand drugs is ``appropriate to properly incent innovation.'' Can you

comment on whether 5 years of exclusivity is appropriate to properly incent innovation for chronic diseases?

Mr. {Boutin.} It is clear when you look at the number of conditions that lack treatments that it is not. It has worked in some cases but we now have approximately 7,500 conditions without treatments, and I hear Representative Waxman's comment of ``the science is not always there'' but the incentives are clearly not there to drive the innovation we need for many of the conditions. We hear from NIH-funded researchers that they develop treatments or potential treatments that could come to market but lack patent protection and therefore they don't. We hear repeatedly from our patient organizations and the organizations they work with on developing treatments that the timeline is taking too long to bring many of these products to market. We have a huge opportunity to incentivize them.

Now, I think the question is, what is the right balance point of incentivizing them. I think we agree that the need is there, and I want to just take issue with the notion of unmet medical need. Unmet medical need is really important to people with chronic conditions. Alzheimer's is clearly an

unmet medical need but so is ALS, so are countless other conditions without effective treatments. Our challenge is to incentivize those highly innovative, highly valued products to address those needs. We can quibble over what that balance is but this Congress has an opportunity to do the hard work, figure that out and incentivize treatments for people who are dying now waiting for them.

Mr. {Pitts.} The chair thanks the gentleman. My time is expired. The chair recognizes the ranking member, Mr. Pallone, 5 minutes for questions.

Mr. {Pallone.} Thank you, Mr. Chairman.

I wanted to ask some questions of Dr. Gandy and Dr. Miller. Let us start with Dr. Gandy.

In reading your testimony, it is apparent that you share my concern about the seemingly ever increasing cost of drugs and its impact on both patients and on the health care system as a whole. You mentioned the Affordable Care Act and the biosimilars provision, which provided for 12 years of exclusivity for innovator biologics, and as you point out, biologics are extremely expensive, 22 times the cost of ordinary drugs, so if a biologic at that price were to be

discovered for Alzheimer's, it would cost as much, if not more, than it currently costs to treat and care for patients with the disease. It would also not alter the unsustainable trajectory for Medicare as your testimony explains.

You mention an Alzheimer's Association report that concluded that if there were an effective Alzheimer's treatment that could delay the onset for 5 years, American taxpayers would save $447 billion in the year 2050 and the human suffering brought by Alzheimer's of course heartbreaking and obviously the projections for how much of our health care system will be spending on the care of those with Alzheimer's are dire. So it would be a tremendous public health advance if we could get this treatment and see that kind of savings, and I share your goal in trying to bring this treatment to market. Your recommendation to the committee is that we would consider extending the current 5-year term of exclusivity for drugs to treat Alzheimer's but I seriously question whether a lengthy exclusivity will achieve the kind of savings we all hope to see or whether it would necessarily give patients access to treatments they can afford, and your testimony seems to assume that if we extend

exclusivity for traditional or small-molecule Alzheimer's drugs, the price of these drugs would be lower than we are seeing in the biosimilars area. I think we have seen recently that is not a safe assumption to make, and your testimony points out that ideally a novel Alzheimer's treatment would start to be given to people in their 50s before they develop symptoms in order to slow the development of plaques.

So Dr. Gandy, if we are talking about giving a drug that could actually prevent Alzheimer's, how many people do you estimate would need to take it? Obviously the dosage might take different forms. If it is an oral solid, I would guess that it might need to be taken daily, maybe even more than once a day, and that potentially means taking a drug every day for decades. So I guess I wanted to ask, if we were talking about that kind of drug, how many people do you estimate would need to take it? I just have to ask a series of questions, if you could.

Dr. {Gandy.} Sure. The number of people who would have to take the medication would be in the tens of millions.

Mr. {Pallone.} And what if the cost of this new

Alzheimer's treatment was $1,000 per pill, and if we extended the term of exclusivity for that treatment beyond the current 5 years to, say, 12 years, as you suggest, or even 15 as some of my colleagues suggest, what would that look like for an individual patient and what would it look like for the health care system overall?

Dr. {Gandy.} I think the details of how to focus the exclusivity and target it narrowly are sort of a second-generation problem. I mean, I think we are really trying to find ways to deal with what we clearly observe as the retreat of the pharmaceutical industry from Alzheimer's both at the venture level and at the large pharmaceutical level, and this is at least a way to begin to do that, but I share your concern about the expense, and it is difficult to know exactly which business model to use to get started. But think of the financial savings from the polio vaccine, think of having people who would be on iron lungs for their entire lives. There clearly needs to be some balance between the exclusivity and the cost savings.

Mr. {Pallone.} Well, let me ask Dr. Miller. Would you comment on it? Would you care to comment?

Dr. {Miller.} Yes. I am very familiar with Alzheimer's. I am on the board of an Alzheimer's cure at the University of California San Francisco and so have studied this quite a bit. It turns out these models of savings often are never seen in reality so it doesn't matter if you are looking at drugs, devices, imaging or even robotic surgery, they often have these models when they try to get to the marketplace but their savings are rarely appreciated when they get to the market, therefore, the health crisis we have today.

If you look at this drug, though, and you were to take your scenario, you just make it the price of a traditional oral solid branded product, you would quickly actually mitigate if not swamp any potential savings that are there, especially when you consider drug price inflation. That model that you are speaking to prices the new therapy at zero. It is free. And so the savings of a half a trillion dollars or when the drug is free. If you have to truly treat the tens of millions that you are talking about, you would never have any savings.

Mr. {Pallone.} And the problem I have is if we grant

exclusivity, we are essentially giving the pharmaceutical free rein to charge whatever it wants during that time period, and we are removing the effect of market competition forces, and I don't think we have any guarantees that a company developing a new groundbreaking drug treatment would do the same thing and, you know, I mean, obviously that is my concern.

Dr. {Miller.} Well, it has been our experience that they don't because they do have the ability to freely price in the United States, and if you are going to treat Alzheimer's, there is a lot of reasons to treat Alzheimer's. This is not about an economic argument. This is because it is the right thing to do for patients, but the likelihood of us seeing savings downstream are much less likely, especially if you extend exclusivity.

Mr. {Pallone.} Thank you very much. Thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentleman and now recognize the chairman of the full committee, Mr. Upton, 5 minutes for questions.

The {Chairman.} Well, again, we appreciate all your

testimony this morning.

Mr. Carusi, the fact that the number of venture capital firms investing in medical technology has dropped from 39 in 2007 to just about 11 or 12 today is certainly concerning to a lot of folks. Who is going to provide the necessary startup capital for innovative new medical technology companies? How can we grow that number back to where it was before?

Mr. {Carusi.} Well, I think that is exactly the challenge right now. I think at its core, venture capitalists raise money from institutional investors, so we raise capital from universities, endowments, pension funds. As a part of that process, we also have a fiduciary duty to generate returns. That is the agreement that we are entering into. We can get that number back to 20, 25, 30, 35 if we can fix the math problem that we have, which is that it is very difficult right now to generate the kind of returns that our investors need to see when you look at the delays of FDA, you look at the delays of reimbursement. So I think this Congress and we as a device community, if we can find ways to get back to streamlining that innovation process, the math

starts to work better and that starts to bring these investors back into the fold. Until then, we have been forced to go elsewhere, and as we like to say, we have been looking for a new set of best friends. That is in part why I am spending a lot of time my time overseas, and so we have seen other countries that are very interested in building their own life sciences ecosystem invest in venture capital funds directly in return for us locating our companies in those local geographies. So there are ways to access capital but it does come with strings and some of those strings are that we need to start to conduct business outside of the United States, and we are doing that right now to fill the gap.

The {Chairman.} So are those venture capital companies that are helping companies overseas, are they located overseas themselves or are they U.S. firms that are encouraging--that are investing and then encouraging those companies to in fact develop those products overseas?

Mr. {Carusi.} So will speak for my own firm. Our new fund, Lightstone Ventures, it is a U.S.-based fund but we are--in fact, we just announced that we are opening an office

in Dublin. We are moving one of our partners to Dublin, and a part of what we will do, not all, but a part of what we will do will be to look for innovative ideas and innovative technologies but to reside those companies overseas and to build those companies overseas. And so they are U.S. funds that are locating elsewhere.

The {Chairman.} Is any part of that equation that decision making part of the tax code consequences? I know we lost a company in my district to Ireland--Perrigo--in terms of their headquarters, in large part because of the tax rate of 35 versus 10-1/2.

Mr. {Carusi.} So that has certainly been in the press and certainly tax rates and lower tax rates and more attractive tax rates play a role but recognizing--recognize the fact that our companies are very far from revenues and very far from profits and so the bigger driver for our companies is really around, A, the access to capital, and B, the regulatory environment in those markets, and it comes back to the fact that we can get a device product approved in Europe 3 to 4 to 5 years ahead of what we can get that product approved in the United States. The fact that product

is approved 3 to 4 to 5 years ahead of time then allows us to start to do the studies that the payers want to see to start to try to generate some of the cost data. In the United States, we are behind in that cadence and so consequently given the fact that we are now running these trials in Europe and seeking European approval, we like to be close to our companies. We don't just invest and so we are naturally moving overseas to be closer.

The {Chairman.} Mr. Borisy, you referenced the expected patent life and market exclusivity of a drug in development does impact the investment decisions, and you also indicated earlier that the size and cost of clinical trials is an impediment to investment and innovation. What are other thoughts that you might have in advancements and technology that can help make up the difference for those?

Mr. {Borisy.} So for any drug that is being brought forward, as a society we are putting a level to say what is the information that we need to have that drug will be useful in the real world population and make a difference for patients and have the requisite safety information associated with it. We have in areas as has been discussed here in the

committee in cancer and rare genetic diseases been willing to adopt the use of biomarkers, surrogate endpoints and a recognition that the full understanding of the use of that drug will come post approval with experience in the real world.

For some of these areas that are outside of cancer and rare genetic disease, there are likewise opportunities to take some of those modern approaches, and we can be doing that both pre approval as well as post approval. I think an important point to recognize is to the comment of we are in the 21st century now and not the 20th century with electronic medical records, with information technology, we are able to know an enormous amount about what is actually happening with a drug in the real world. So when we are dealing with the question of how do we develop drugs for some of these chronic diseases, some of these things affecting such large swaths of our population and we are dealing with the question of how do we make sure that innovation invests in those areas. We should ask, can we use some of these modern technologies to make that process more doable, more stable, more predictable.

Mr. {Pitts.} The chair thanks the gentleman and now

recognize the ranking member of the full committee, Mr. Waxman, 5 minutes for questions.

Mr. {Waxman.} Thank you very much, Mr. Chairman. I appreciate all the testimony. I am sorry, I had to go to another subcommittee and didn't hear all of your oral presentations. The chairman has often said to me, I ought to clone myself, but we don't know how to do that, and it probably wouldn't be allowed anyway, and nobody would want it.

Mr. Hemphill, I want to ask you some questions about this MODDERN Cures Act, because that is a legislative proposal that has been put forward. In your testimony, you said it is likely that some drugs are not developed because the exclusivity rewards are not large enough, but it is unclear how large a problem this is, and I would like to explore that with you. Certainly we ought to be willing to use patent term extensions and exclusivities as an incentive to spur the research and development of new drugs. That was the basis of some of the laws that we are all praising like the Orphan Drug Act. In that law, we gave 7 years of market exclusivity for drugs to treat rare disease. That meant that

these were rare and didn't offer a huge profit potential because they weren't a lot of people that were likely to buy the drug but this MODDERN Cures Act gives not 7 but 15 years of exclusivity and post-approval patent protection to so-called dormant therapies. Do you see a reason why we would need an even longer period for these drugs than we gave for orphan drugs? The Orphan Drug Act has been very successful. We have a lot of new drugs for people with these rare diseases.

Mr. {Hemphill.} So I would say no, not necessary under the MODDERN Cures Act as it is currently conceived, given the breadth of applications of unmet medical need and its applicability to essentially any new drug. I leave open the possibility that in principle, there could be therapies for which the lead time is so long that some kind of targeted additional protection would be worthwhile. I just think the MODDERN Cures Act goes way beyond that in its current breadth of application as well as its duration.

Mr. {Waxman.} In a biosimilars provision in the Affordable Care Act, we gave 12 years of exclusivity to biologics. That is 7 years longer than we gave in Hatch-

Waxman for small-molecule drugs. I have always believed that the 7 years was too long. However, the argument was made that a lengthier time was needed because biologics were harder to develop and their patents were weaker. Do you see any reason why dormant therapies would need 3 years longer exclusivity than biologics?

Mr. {Hemphill.} Well, I think in principle, it is always possible that longer protection would elicit additional innovation, and then the question is, at what cost to the therapies that we would get either way, which is why I think it is so important for us to do careful study to figure out where those gaps are, if anywhere.

Mr. {Waxman.} Well, you mentioned the evergreening provision in your testimony. Now, that is not just a one-time event, that could go on forever wherever a small change can produce another 15 years of exclusivity. There was an interesting statement. Mr. Boutin in his testimony claims that MODDERN Cures has the strongest anti-evergreening language ever included in legislation. Do you agree with that? Do you think that that law prevents evergreening or could companies get multiple 15 years exclusivity?

Mr. {Hemphill.} I don't agree. I am very concerned about evergreening in this bill. There may be a difference in what we mean by ``evergreening. '' One particular issue that I am very concerned about is product hopping where you get close to the end of the exclusivity and then the drug maker switches the patients over to a new version of the same drug. We have been talking about Alzheimer's, and Namenda is a nice example. The existing Namenda treatment is going away this summer and all the customers are being--all the patients are being shifted to a once-a-day version, and this extends the exclusivity, and I don't see how the MODDERN Cures Act is going to get around that.

Mr. {Waxman.} This MODDERN Cures proposal, the sponsors point out it is only for therapies that address an unmet medical need for serious or life-threatening diseases. On the surface, that sounds reasonable. Do you think it is appropriately targeted to only those drugs whose development would warrant and be appropriately stimulated by such extraordinarily long periods of exclusivity and patent protection?

Mr. {Hemphill.} It looks like it would apply to roughly

any drug that currently gets new chemical entity protection. Maybe there are small exceptions to that but I think it extends quite a bit further than what would you normally think of by unmet medical needs.

Mr. {Waxman.} And that could be a huge windfall?

Mr. {Hemphill.} Correct.

Mr. {Waxman.} Mr. Boutin, I know you met with our staff on several occasions, and I understand you are trying to get them data and information to show whether there are significant numbers of dormant therapies out there waiting to be developed. Have you had any success in collecting this data? And I would also appreciate data justifying why 15 years of exclusivity and patent protection are necessary for these therapies.

Mr. {Boutin.} So with respect to the data question, there is data that is available but it is very limited. It is very challenging to collect that information because the incentives are not there to exist, and when we speak with companies, they routinely tell us that when they had a good product that they shelve because it has gone dormant because there is not enough time to develop it, they routinely shred

the data. What we have seen with the filing of MODDERN Cures is, companies now are starting to keep that data in-house. So they are starting to look at how they might potentially recapture these lost opportunities.

Mr. {Waxman.} Well, it is important that we insist on receiving more information as we look at this law because this is a huge windfall in some cases, and we want to know if it is necessary. If it is necessary, we certainly want to do what will help spur innovation.

Mr. {Boutin.} Well, in--

Mr. {Waxman.} But we know, Mr. Chairman, in conclusion, that there have been many laws where we have just overpaid. We have overpaid the drug companies to do research on dosages for kids and we look at how much money that costs them to do it and that exclusivity was so much more valuable. We have overpaid for even some of the orphan drug laws, and we are overpaying at the expense of patients going without drugs or the payers for drugs not being able to afford it or the Medicare system and the Affordable Care Act not being able to sustain these kinds of costs. So we have got to get the balance right and we need the data to make sure that we are

doing that. Thank you.

Mr. {Pitts.} The gentleman's time is expired. The chair now recognizes the vice chair of the committee, Ms. Blackburn, 5 minutes for questions.

Mrs. {Blackburn.} Thank you, Mr. Chairman, and I want to thank everybody for being here and, you know, we have a hearing downstairs as well as here so we are kind of back and forth.

Mr. Carusi, I want to come to you. I would like to talk with you a little bit about your due diligence process as you look at funding a startup with a concept, and being from the Nashville area where a lot of health IT is taking place and Health Box is active there, the Entrepreneur Center, when I go over there and I talk to some of these innovators and you look at what is taking place from concept to commercialization to distribution, it is a pretty long timeline. In preparing for the hearing and reading through your testimony, I want you to just talk to me about that due diligence process, what you are looking at, how the FDA approval process affects that, how that window has changed in the past 10 to 15 years.

Mr. {Carusi.} I would be happy to. I think it is important to note that at my firm, so at Lightstone, we are involved from the very early stages. In fact, about a third of our companies have been created either in-house or in coordination with incubators that we work with. So this means that we are literally sitting down with an entrepreneur, a physician, an inventor looking at a market and inventing. So we are involved at that early stage. We then have to take a look at that starting process. We have to look at the technical risks, the development risks, the risks in the clinical trials, what kind of a study can we run. If we run that study, will we get FDA approval. How long will that take. We then have to make a determination as to whether or not we will have created enough value that we can then find another player, be it at the public market or one of the major players take on that project or if we have to keep going. If we have to keep going, then we have to look at the whole reimbursement process, what is involved in getting coding, coverage, payment. At the end of the day, we have to get the product from the ideation phase all the way through to the point where we are generating revenues and we

are generating profits. That is what we do. If you look at that timeline, and Mr. Borisy has already mentioned this, that timeline is now pushing anywhere in devices up to 8 to 10 to 12 years with a great deal of uncertainty along the way, and one of the things that we as venture investors hate the absolute most is seeing our companies fail late. We would rather introduce experiments where we can have these companies fail early and move on. But what is happening is, these companies are either failing at the point where they get in front of panel for FDA approval, even if we have met the appropriate endpoint, or they are failing when they get into the morass of reimbursement, and then they become restarts. Nobody wants to fund a restart. It is easier to give birth than resurrect, and the reality is, if these companies then die and we have to move on and it is dragging won the returns of our industry and it is dragging down innovation, and that is the process that we are facing right now.

Mrs. {Blackburn.} You mentioned the challenges with the IDE process. Do you want to add anything more to that?

Mr. {Carusi.} Yes. So I mean, again, on the IDE

process, that is the process to actually initiate our clinical studies to then demonstrate the safety and the efficacy of the device. What happened over the years is the data requirements to start those studies, it was as if we were actually going for approval. We are not going for approval; we are going for the approval to start the trial. And again, some of these are going to fail. They are not going to work. If you start to layer on additional preclinical requirements, additional bench requirements that aren't necessarily adding to the safety of these products, then again you are adding to the cost of time before we actually get to the experiment where we can run the clinical trial and see if the product is safe, more effective and good for patients, and if it costs too much, you know, capital is fungible. We will go somewhere else.

There was just a discussion around Alzheimer's. We are not funding Alzheimer's drugs. We can't. We can't bring them to market. And so the math won't work, and so it is simply a matter of making sure that the right incentives are in place so that we don't kill innovation. At the same time, we are in the game of disrupting things. That is what we do

for a living. So we don't want to see incumbents sitting on drugs and new devices down the road but we need enough incentive to make sure that the math works so that we can fund them to begin with, and right now in a lot of spaces, we are not able to do that.

Mrs. {Blackburn.} Thank you, and I will yield back my time, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentlelady and now recognizes the gentleman, Mr. Matheson, 5 minutes for questions.

Mr. {Matheson.} Thank you, Mr. Chairman.

I want to talk a little bit about the issue with medical devices, small manufacturers in particular. They are the ones in the marketplace who are really creating some of the groundbreaking technologies. They rely heavily on venture capital, as we just heard in the last answer. And I think that as should be expected, venture capitalists are going to only take on a certain amount of risk both in terms of product performance and uncertainty and regulatory uncertainty as well because uncertainty in business is a cost. I think that sounds pretty basic but I think that is

something Members of Congress need to be reminded of.

One area in which I believe venture capital firms consider when deciding whether to make an investment in medical device is the likelihood of adequate and predictable reimbursement from Medicare because once you get FDA approval, that doesn't mean Medicare is going to give you reimbursement.

Over the past several years, I have heard from device manufacturers and venture capital firms that Medicare is requiring more data to obtain appropriate coverage of payment, and I appreciate that CMS wants to put forth an effort to spend taxpayers' dollars in an efficient and responsible manner, but this change in standards, if you will, and the lack of clarity surrounding what the standards are from what I understand has made it increasingly difficult for VC firms to make an educated and informed decision about the viability of a device once it gets through the FDA approval process. So if an FDA-approved device is not approved by Medicare, its viability in the marketplace and the ability for patients to access the technology obviously is greatly reduced.

In order to help alleviate some of this uncertainty, I have cosponsored legislation authored by my friend and colleague, Congressman Paulson, the Accelerating Innovation in Medicine, or AIM Act, which would give device manufacturers the opportunity to make an FDA-approved product available on a self-pay basis for an initial 3-year period before approaching CMS about Medicare coverage on reimbursement. This program would be entirely voluntary. It would allow manufacturers the time to collect needed data to justify reasonable and adequate coverage and payment for Medicare down the road, reducing some of the uncertainty associated with the Medicare coverage process and hopefully providing the venture capital community with a measure of certainty in the device and more broadly in the market in general.

So Mr. Carusi, I wanted to ask you if you had heard of this or were aware of this proposal and do you feel it would assist both the venture capital community and the small device manufacturers in reducing some of the uncertainty in the process and bringing products to the market on a more expedited basis?

Mr. {Carusi.} Yes, I am familiar with the AIM Act, and I think it very much goes to the heart of one of the challenges that we are facing, which is to your point. We now have FDA approval but we are now in a process where we have to generate more data. As we are generating that data, we are not profitable entities. We are burning $500,000 to $2 million a month, and in fact, that number tends to go up because we now have to start marketing these products. So the question comes down to, we can't as small companies continue to fund these products through that next phase of development. So I think what the AIM Act does or could potentially do is help to provide a source of funding during this period of time so that we can continue to generate the data that payers, that Medicare would want to see.

Look, the world has changed. We recognize that data is everything. Clinical data is our sole focus, so generating that data is necessary, it is important, but if we are going to have to add more years, more uncertainty and more disruption, then we need policies like the AIM Act, and I would say that is one of several potential approaches. That is not going to do it. We need more things and more creative

ways to try and think about how we can as an ecosystem help the ecosystem generate this data. It is not simply about device companies or biotech companies. It benefits hospitals, payers, patients. So what is the right mechanism to fund this additional data-gathering exercise?

And then the other thing I would add is, and then what is the data that is required. Don't move the bar. Tell us-- and we have had this conversation with FDA. If it is X, we hit X, then you are going to get paid, and right now that bar is constantly moving so we don't even know if we generate that data if we are going to get payment and coverage.

Mr. {Matheson.} I appreciate that.

Mr. Chairman, I will yield back.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the vice chair of the subcommittee, Dr. Burgess, 5 minutes for questions.

Dr. {Burgess.} Thank you, Mr. Chairman, and Mr. Carusi, just briefly before we leave that point, it was the intention or the desire of this committee 2 years ago when the reauthorization of the Food and Drug Administration came to our committee that many of these problems would be, if not

solved, at least managed or mitigated, and that has not been the case?

Mr. {Carusi.} No. On FDA, that is having an impact, and so I think we are starting to see benefits from FDASIA, and certainly with FDA and improved dialog with Commissioner Shuren and his leadership, we are seeing improvements. So that is why in my testimony I moved from FDA, we still want to continue to improve it, but to the reimbursement side of the equation because parallel to the discussions we had several years ago around FDA and a lack of transparency and predictability and consistency, that is what we are now facing in reimbursement.

Dr. {Burgess.} Let me ask you a question because it came up yesterday in a Rules Committee hearing over the appropriation for the United States Department of Agriculture, which for reasons that escape most of us includes the FDA. But the whole issue of special protocol assessments came up and the fact that the rules might be changed late in the game in that environment. Can you speak to that just briefly?

Mr. {Carusi.} Yeah, I can. Again, I think that has

been utilized more on the drug side, which is frankly less where I play. It is probably more where you play. Again, I think the intention of SPAs is terrific. I think the intention is to provide again a bar where if you hit a certain data requirement, you have certainty that you will get approval. That is the right intent. Where it runs into problems if that doesn't prove to be the case. So in other words, if you are now three-fourths down the process, you are in the middle of your clinical trial and the bar has changed, the bar has moved, you have to start that clinical trial all over. You have just taken a step of 3 to 4 years back. In many ways you may have flushed $50 million to $100 million down the drain. So I think the intent is right but we can't monkey with the SPA, unless there is some meaningful new clinical piece of data that has emerged one that has been established.

Dr. {Burgess.} I thought it was telling, your comment, fail early, avoid the rush, you certainly get why that concept is there.

Dr. Gandy, I really appreciate you being here and appreciate the work you are doing in Alzheimer's. It must

have been as startling for you to hear as it was for me that Mr. Carusi is no longer funding Alzheimer's research. But let us talk about that for a minute because one of the first things after I was elected to Congress in 2003, I asked for a meeting with Dr. Zarounian out at the NIH and we talked about things on the horizon, things in the future, and he related that statistic that you gave us, that 5 years delay in the onset of symptoms, big savings on the other side. So if I have done the math calculation correctly where I am now into my third of those 5-year intervals but as you relate, it hasn't really happened, has it?

Dr. {Gandy.} No, that is right. We currently don't have anything on the horizon that will make an impact on the course of Alzheimer's, on the progress of Alzheimer's disease.

Dr. {Burgess.} Well, what about actions like establishing clinical trial networks in the study of Alzheimer's?

Dr. {Gandy.} The NIA has established a nationwide network of Alzheimer's centers, and that is the mechanism by which it uses to recruit and test new drugs--recruit patients

and test new drugs, and that system, that network often partners with industry to test new industry drugs as well.

Dr. {Burgess.} And that in turn then spur new investment, perhaps get Mr. Carusi again involved and invested in our research?

Dr. {Gandy.} I think what we need is a success, and I think that would attract more investors. I mean, we have relationships and actually a number of public-private fora for discussion but I think the thing that would really build the enthusiasm is some success.

Dr. {Burgess.} And would things like standardizing biomarkers, would that help?

Dr. {Gandy.} That certainly is the--the NIH has established what is called the Alzheimer's disease Neuroimaging Initiative, which has been really a landmark study, ongoing study, in defining a number of biomarkers of the natural aging process, of the conversion from aging to mild cognitive impairment and then conversion from mild cognitive impairment to Alzheimer's disease.

Dr. {Burgess.} Thank you.

Dr. Ledley, you brought up a gene therapy, and I can

remember reading in the newspapers in the mid-1990s, late 1990s about some promising gene therapies and then unfortunately there were a series of unsuccessful problems, and then it kind of went away. Can you kind of give us an idea of what is on the horizon with gene therapies?

Dr. {Ledley.} So the short answer, gene therapy works. The last couple of years have been incredibly exciting. It has seen some very high-profile IPOs in the past couple years. So people are happy about it again. I think it is a classic story where a lot of--there is a real disconnect between the good support for therapy for NIH, venture capitalists who made a lot of profit early in the field and found a lack of sustained support for the innovations required to take immature technologies and make them mature, and we believe the field has slowed by that. It was a difficult process. There are very important pricing issues for that field to work out in the next couple of years but it is a great example of where the basic science is now ready for investments that can take advantage of discovery and the type of review process which is put in place at the FDA.

Dr. {Burgess.} All right. I have more questions, Mr.

Chairman, if we have time for a second round, but I will yield back.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentleman from Texas, Mr. Green, 5 minutes for questions.

Mr. {Green.} Thank you, Chairman, and both you and the ranking member for asking our witnesses to testify.

First of all, it is frustrating that what my mother-in-law went through with Alzheimer's in the 1990s. There is no drug today different from that than Aricept. It wasn't really useful then, slow delay of the illness but we are just not there. And Dr. Gandy, I appreciate all your efforts, and I even appreciate your purple tie, Mr. Carusi, from working with our local Alzheimer's group in Houston.

But let me get to my other issue. The need for greater antibiotic drug development is something I along with Congressmen Gingrey, Shimkus, DeGette and others have long championed. We have successfully started getting the ball rolling with GAIN Act last Congress and we are already seeing positive signs. However, as much as it pains me to say, it has not done enough to fully set our country back on a path

of investment and development in new antibiotics. We need to combat ever-emerging and deadly diseases. The health of our soldiers and veterans is particularly at risk. An article that ran in The Hill yesterday titled Fighting Superbugs by Developing Targeted Weapons in which the author was Rear Admiral James Kerry stating that many soldiers and civilians have lost their lives because we do not have the drugs we need. It is time to mount an urgent defense against superbugs and use all the tools at our disposal to put new weapons on the field.

Mr. Borisy, I know that knowing that you know about the antibiotic space today, the risk-reward profile, would you advise your clients or colleagues to invest in antibiotic development today, and why or why not?

Mr. {Borisy.} Investment from a venture perspective in new antibiotic development is very challenging. As an optimist from the science and the medicine perspective, I actually believe we have the tools and the technologies today that if we applied it and focused the capital around it, we could come up with the tremendous innovations that we need against some of these superbugs and areas of very important

need to our society in infectious disease.

Mr. {Green.} Okay. I only have 5 minutes. But if Congress were to create additional incentives on antibiotic development, do you believe that it might help move the needle with investors such as yourself?

Mr. {Borisy.} Yes.

Mr. {Green.} If so, what types of reforms or incentives would be needed to improve your outlook on investment in this area?

Mr. {Borisy.} So one of the most important would be again drawing the analogy from cancer and from rare genetic diseases, which is if we accept it for these antibiotic infections, allowing to develop for those specific populations to show that if we could show that a drug works in those specific populations, that would have a tremendous impact.

Mr. {Green.} I along with my colleague, Congressman Gingrey, have introduced the ADAPT Act, which is a follow-up on the GAIN law from last Congress. It would create a special designation for critically important antibiotics with a goal of improving FDA process around them. If we could

demonstrate to industry leaders such a process would shorten approval times for safe and effective products, would that help increase the worth of antibiotic products on the market?

Mr. {Borisy.} Yes, it would. It would have a direct impact.

Mr. {Green.} Thank you. Without new antibiotics, medical advances and new cures to treat other diseases will largely be moot since treatments like chemotherapy, even a miracle future therapy could be too dangerous to patients because of the risk of infection and no antibiotics to protect them, and I urge my colleagues to take swift action and aggressive action because we do not have a moment to waste, and again, hopefully our subcommittee will look at the ADAPT Act as a follow-up to the success we are seeing with GAIN. I know just recently there was one of the pharmaceuticals approved.

Mr. Chairman, I will yield back my time.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentleman from Illinois, Mr. Shimkus, 5 minutes for questions.

Mr. {Shimkus.} Thank you, Mr. Chairman. It is great to

be here. I am way down on this side. And it is great--I too am in the other subcommittee so I am bouncing back and forth, but it is really important to hear the plethora of the panel because it really just gets your mind going. It drives staff crazy because they want us to direct our questions, but you start thinking. So I am going off script for a second.

Mr. Hemphill, Alzheimer's, everyone has been touched by it. So you hear the testimony. Obviously the capital community is not here. There is no return on investment, can't make the case. It is an epidemic. It is going to--so this whole brand exclusivity stuff, I mean, doesn't that not make a case for creating a market condition where capital will flow so they can get a return so we can solve this disease?;

Mr. {Hemphill.} So--

Mr. {Shimkus.} I have got to be quick so--

Mr. {Hemphill.} I am off script.

Mr. {Shimkus.} I am off script too. That is right.

Mr. {Hemphill.} I completely agree that in principle if you have a situation where you otherwise would not have a drug--

Mr. {Shimkus.} Like this, I mean right now, we got it.

Mr. {Hemphill.} Well, I am not sure the case is proved from the fact of long development.

Mr. {Shimkus.} But I will just say, there is no money going right now so the market is making the case now.

Mr. {Hemphill.} The absence of investment doesn't necessarily tell us that a different legal regime would yield a different result.

Mr. {Shimkus.} Okay. Let me move forward. That is part of the challenge, this debate that we have to get to.

I also want to just highlight--Mr. Matheson did a great job. I am a cosponsor of the AIM Act for all the reasons that--I am not going to go into it in detail, but I would encourage my colleagues to look at that and get on it.

Mr. Chairman, I would encourage you to--I don't know if we want to wait, you know, on this 21st century cures thing or you may want to consider trying to at least get it through the process so we can see where we are because I don't see a downside to it. I just don't. It helps bring capital in the early formation. It is outside the Medicare morass, coding issue. It brings more certainty than less at a time when you

are looking for capital flow.

So now I will get on script, Chris. But we are trying to focus in--and a lot of this debate has been on obviously the lifesaving drug that will emerge and the cost, but I think as important in this debate is the diagnostic portion because the way the world is changing and the science behind this, you can target specific drugs to specific conditions based upon markers and the like.

So Mr. Borisy, starting with the premarket approval process, what types of incentives do you believe might spur development in this space? Were you thinking it might be constructed similar to a drug-like postmarket incentive structure or something different?

Mr. {Borisy.} So for diagnostics, a clear and predictable understanding of reimbursement, which does not exist today, would have a direct connection to capital formation for innovative new diagnostics that we mean and that clear and predictable reimbursement in diagnostics, whether that was in some form of postmarket exclusivity, whether that was just in clear Medicare rules and understanding that clarity and transparency would make a

tremendous difference.

Mr. {Shimkus.} In your testimony, you recommend the committee consider a process whereby CMS create a program for diseases important for public health with high unmet diagnostic needs. Can you tell us more about how such a program might work and for instance, could it help cut down the time between FDA approval and the CMS coverage?

Mr. {Borisy.} So if we take an example that we have been talking about at the hearing today such as Alzheimer's and if we said from the work that Dr. Gandy and others are doing that we had a diagnostic imaging biomarker that we felt was meaningful and predictive, understanding how that would be paid for, just simply having that clarity and stability would allow then the development and proof of that diagnostic. That diagnostic would then enable the development of therapeutics to Alzheimer's that we have been bemoaning here today as lacking.

Mr. {Shimkus.} Yeah, and I just want to throw--Mr. Miller is here and in part of his testimony he said on Alzheimer's, it is just the right thing to do. So we have got to change our programs and processes to address this, and

hopefully we can get there working together. This is a very exciting time but there are unmet needs that we should be about meeting, and with that, Mr. Chairman, thank you and I yield back my time.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentlelady from Florida, Ms. Castor, 5 minutes for questions.

Ms. {Castor.} Thank you, Mr. Chairman. I want to thank the panel for your expert advice today and also commend my colleagues for focusing on this important issue for American families.

We have today about the MODDERN Cures Act, which would extend the period of exclusivity for essentially any new drug to 15 years. That is 3 years longer than any other term of exclusivity currently in the law, and the intent of the bill is very good, but I have been listening closely and I haven't heard today that a case has been made for why there would be a need to extend exclusivity for such a lengthy term, and a number of you have testified to that today and to some of the negative effects of lengthy periods of exclusivity.

Dr. Ledley, could you explain in greater detail how in

your view greater exclusivities would discourage uptake by hands of smaller biotech companies?

Dr. {Ledley.} Sure. Fifteen years is a very long time in the progress of science. We don't use 15-year-old computers anymore, and by the time a drug has been on the market for a certain length of time, science is able to come up with something better and should, and the public needs it. So there needs to be a return on the investment in the original drug and there needs to be an immediate turnaround to invest in the next drug that is that much better, and 15 years is just out of proportion to the space of scientific progress.

Ms. {Castor.} And I am also extremely concerned about the price tag for providing extended exclusivities. Dr. Miller, your testimony mentions the Solvadi situation, the hepatitis C drug that is now about $1,000 per pill. It is an extraordinary price but coupled with the fact that we have over 3 million Americans that could have their hepatitis C cured, they would benefit greatly. So that has raised these difficult questions for public and private payers especially. Could you describe for us the tradeoffs and compromises that

payers are having to make as a result, and could you tell us why Solvadi is unique or could it be part of a trend or are there other similarly priced drugs on the market?

Dr. {Ledley.} That is a great point. So what you see is that for manufacturers, the only--they don't have just exclusivity as a lever to pull, they have pricing. So in this country we allow them to freely price, and that is what has happened with Solvadi. If you treat all 3 million patients in the United States, you will spend over $300 billion, which is equal to the entire drug spend for the United States, and when you look at the pipeline, of that 5,400 drugs that are in human testing, there are many that are going to be breakthrough products that also will be at prices that we can't afford. And so it is no good having drugs that people can't afford and so access has to be considered in your policies when you consider extending exclusivity because you are guaranteeing higher prices for longer periods of time.

Ms. {Castor.} And one of the issues that confronts us as the population ages and the call on Medicare will be greater is the fact that we don't allow negotiation of drug

prices in America. It is kind of un-American that we don't negotiate by law. This means that drug companies can charge almost any price that they would like, particularly for lifesaving drugs that are the only treatments or cures for a particular disease. In such cases, it is hard to imagine the need for extending the length of time for which they are shielded from price competition by generics.

Professor Hemphill, is America, in having that policy against negotiating drug prices, do we subsidize drug use in other countries?

Ms. {Castor.} Well, certainly, U.S. payers and patients pay a disproportionate part of the research and development that ultimately has a global benefit.

Ms. {Castor.} Well, I thank you for your testimony, and I want to end on the note of even though we might have differences of opinion on the panel on the Cures Act, I think everyone that I heard today was united in the fact that we need to make sure we are committed to basic research, and the fact that the budget battles, sequester, government shutdowns of the past few years has taken a bite out of NIH and sent scientists possibly looking at careers in other countries, is

really something that this committee has got to focus on. Dr. Collins said NIH has lost 25 percent of its purchasing power. We are throwing away half of the innovated, talented research proposals. This really should be the committee's primary point, and maybe moving medical research from a discretionary category to something we have a long, sustained commitment.

Thank you, and I will yield back.

Mr. {Pitts.} The gentlelady's time is expired. The chair recognizes the gentleman from Georgia, Dr. Gingrey, 5 minutes for questions.

Dr. {Gingrey.} Thank you, Mr. Chairman, Ranking Member Pallone, and to the witnesses for testifying today.

You know, the GAIN Act of course was an important first step in addressing a lack of new antibiotic drug development and we have already seen the first successes of the GAIN Act. I am real happy to have worked with Mr. Green, Ms. DeGette, MR. Shimkus and others on the committee in a bipartisan way to develop the GAIN Act. Obviously--and Mr. Green talked about this a little bit earlier about the ADAPT Act, which of course is follow-on to GAIN and the work that we need to do

in regard to that.

I wanted to direct my questions mainly to Mr. Borisy. When making investment recommendations, Mr. Borisy, can you explain how not just potential economic returns but clinical trials and the approval process impact the likelihood that you would recommend to your team investing in a particular drug?

Mr. {Borisy.} So me and my partners at Third Rock focus fundamentally on early-stage investments in areas of science and medicine where we can make a breakthrough, make a big difference for patients. So if we talk about infectious diseases as an example, coming up with therapies that would work for something where, you know, it is a superbug and nothing works and it is a critical need, that is the type of thing that we would like to do.

When we are considering an area to invest, when we are in the process of translating those out of the basic research that has been done, a lot of work, multiple years before it can even get to the clinic to refine it into being a drug has to be done. This takes tens of millions of dollars. Then we go into the clinical development period of time, and the

questions focusing us are two, which is how much money and how long is it going to take until we can get that proof of concept that we have created something that really makes a difference for patients, not the final bar of approval perhaps but that smart people looking at it say that is important, and the second is, does other parts of the ecosystem that we have talked about recognize that as important. That could be public investors so we could take the company as an IPO. It could be a larger pharmaceutical company that is going to take it across the finish line. Things such as ADAPT where we know that the clinical study can be faster, quicker in a specific targeted population that we can really show it works and makes a difference, if that is more doable, then that is what enables our capital formation to invest in that.

Dr. {Gingrey.} Well, cutting right to the chase, let me ask you this follow-on. And I think Mr. Green asked you this question but maybe I would like for you to elaborate a little bit more.

Knowing what you know about the antibiotic space today, the risk-reward profile, would you advise your clients or

colleagues to invest in antibiotic development today, and why or why not?

Mr. {Borisy.} And this is not an academic question to us. Actually yesterday morning before flying down here to Washington, D.C., I was looking at an innovative technology in infectious diseases that could do exactly what we all here talking about want it to do, and it is a very difficult question for us right now because it is that question of regulatory uncertainty in the area, and so it is something that we want to be able to do but as we have talked about, the question of if we can do what we have done in areas of cancer and rare genetic diseases with breakthrough therapies, accelerated approvals, it could make it very doable.

Dr. {Gingrey.} And the last question in my remaining minute, again, Mr. Borisy, my colleague, Gene Green, and I introduced, as you know, the ADAPT Act, which 23 other members of this committee have cosponsored. The legislation allows the FDA to approve antibiotics that treat serious and life-threatening infections for specific patients based on smaller and then more rapid clinical trials. Do you believe if Congress could streamline the approval process for such

products without lowering the FDA's safety and effectiveness standards the climate for investing in new antibiotics wou8ld improve?

Mr. {Borisy.} Yes, it would.

Dr. {Gingrey.} Well, I thank you very much, and I don't have time to address the other members of the panel--it is a large panel--but again, I am grateful that you all are here.

Without new antibiotics, advancements in new cures to treat other diseases would largely be moot since treatments like chemotherapy, even a miracle future treatment, would be too dangerous to patients if you didn't have these antibiotics because you wipe out the bone marrow, you lower their resistance to infection, and as you well know, in many cases the patient doesn't get the cure because they get wiped out and get overwhelmed with an infection and die before the bone marrow has a chance to recover. So all of this is interrelated very closely.

Thank you very much, Mr. Chairman. I yield back.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentlelady from Virgin Islands, Dr. Christensen, 5 minutes for questions.

Dr. {Christensen.} Thank you, Mr. Chairman, and I thank the panelists for being here this morning.

I am going to direct my questions to Mr. Hemphill. Your testimony describes various types of market protections that are granted to brand drugs in current law and you assert that those protections are, for the most part, functioning quite well. So I am correct in interpreting that in your testimony, that they are functioning quite well?

Mr. {Hemphill.} So my testimony is that they have been effective in providing strong incentive for drug makers to innovate.

Dr. {Christensen.} Okay. Obviously there are many diseases for which no effective treatments exist. You mentioned the possibility that some drugs are not developed because pharmaceutical companies do not view current protections are providing an adequate reward but you state that the scope of the problem is unclear, and I would assume it is also unclear whether weak market protections, if they exist, are actually the cause of failures by companies to develop new treatments. Can you say more about the impact of so-called weak market protections?

Mr. {Hemphill.} Sure. So two brief points on this. One, I think we just don't know a lot about the innovation that doesn't happen. We have anecdotes but we don't have hard data so the data collection effort that was mentioned earlier seems really important.

Second, even though limited protection, the limited non-patent protection that is provided, for example, by the Hatch-Waxman Act, has a big effect. We have therapies on the market that have no patent protection. An Alzheimer's drug, if it a great Alzheimer's drug, suppose they only get 5 years of new chemical entity protection but 20 million people are taking it, and each are a $1,000-a-year business for the brand, not an unreasonable amount judged from what other chronic diseases have as a pay. A thousand times, you know, 20 million people, 10 million people times 5 years, and that is a $50 billion business which I think would focus the mind if you have the kind of excellent drug that we are talking about. Now, that is not going to answer every question but I think for some drugs, a lot of times the existing protections are going to be adequate.

Dr. {Christensen.} Are there other factors that might

be causing delays in the emergence of new lifesaving treatments that we haven't discussed?

Mr. {Hemphill.} Well, sure. I mean, we have talked a bit about just the nature of scientific inquiry and the uncertainties in solving really tough problems like Alzheimer's and cancer.

Dr. {Christensen.} It is clear we have a lot to learn about how much a problem this even is but we are hearing a lot of conclusions from some of our witnesses today about insufficient patent protections being the cause of pharmaceutical development failures. Mr. Hemphill, have you heard anything in the other testimony today that convinces you that others on this panel have new facts and new data to substantiate this problem?

Mr. {Hemphill.} So I think we certainly have new anecdotes, and it is quite possible that in principle that as we get better at science, the remaining problems are harder and therefore require new solutions. I think the question is nailing down what that other world would look like were we to engage in the kind of changes that are being proposed.

Dr. {Christensen.} And finally, we have heard a lot

today about the need for new incentives. A major focus has been on marketing protections like exclusivity and patent extensions. Mr. Hemphill, your testimony briefly described some other incentives that you indicate could be affected such as providing government funding for certain research and development itself. Can you maybe give us some more ideas about what other incentives are out there and whether you think they hold potential to spur innovation?

Mr. {Hemphill.} Sure. Just briefly, we hear about extremely lengthy trials sometimes being a problem vis-à-vis patent protection because if the patent runs out before you can get your drug to market because of the long trial, the Hatch-Waxman renewal or extension of patents might not be enough. But in those situations where we feel some confidence that this is a worthwhile project to pursue, you could readily imagine, you know, it is a subsidy, it is a government outlay to support those trials. We see this sometimes in cancer, and I think that has been effective, and that is the kind of targeted solution that I think we should really be paying a lot of attention to.

Dr. {Christensen.} Thank you. Thank you, Mr. Chairman.

I yield back.

Mr. {Pitts.} The chair thanks the gentlelady and now recognizes the gentleman from New Jersey, Mr. Lance, 5 minutes for questions.

Mr. {Lance.} Thank you very much, Mr. Chairman.

I am the Republican chair of the Rare Disease Caucus, and in that capacity, I frequently meet with patients and families where there are no medicines, and I am the sponsor of MODDERN Cures. MODDERN Cures is completely bipartisan in its sponsorship, and I want to thank all of my colleagues who have become cosponsors including, for example, Mrs. Eshoo, Mr. Butterfield, Mr. Tonko, distinguished members of this committee on the Democratic side, as well as Republican cosponsors I see, Mrs. Ellmers and Mr. Bilirakis right in front of me.

Mr. Boutin, can you give your perspective on the incentives in the Orphan Drug Act, which is an improvement in orphan-drug therapies from the original Hatch-Waxman Act, a monumental piece of legislation, whether regarding the Orphan Drug Act and whether you think it is sufficient to incentive rare-disease research or should we be doing more?

Mr. {Boutin.} Thank you for the opportunity.

Mr. {Lance.} Certainly.

Mr. {Boutin.} Orphan Drug Act is a monumental piece of legislation. I think everybody in the room recognizes that. But at the same time, we have approximately 8,000 rare diseases.

Mr. {Lance.} Yes.

Mr. {Boutin.} We have 500 treatments.

Mr. {Lance.} Yes.

Mr. {Boutin.} Clearly, we need to do more.

Mr. {Lance.} Yes. And regarding Alzheimer's and the moving questioning of my colleague, Congressman Green, would it be fair and is this the consensus of the panel that we need to do a much better job regarding Alzheimer's and somehow have to reach a solution to bring that to a better situation for the hundreds of thousands, indeed millions of patients who will suffer from Alzheimer's? Is that the consensus of the panel?

Mr. {Boutin.} Without question.

Mr. {Lance.} Is there anyone who dissents from that? Thank you.

Professor Hemphill, in responding to Congressman Shimkus's questioning, I believe you said--and I am paraphrasing and I certainly want to give you the opportunity to respond fully--I believe you said that the absence of new drug therapy doesn't necessarily mean that we need a new legal regime. Is that what you said? And I certainly want to give you every opportunity to express your point.

Mr. {Hemphill.} Yes.

Mr. {Lance.} You did say that?

Mr. {Hemphill.} Yes. Do you want me to explain?

Mr. {Lance.} OF course.

Mr. {Hemphill.} So the idea here is simply that we don't know simply by the fact of increased legal protection that we will thereby have new cures.

Mr. {Lance.} Yes, I am an attorney, and we do not know. It seems to me we need some progress in these terrible rare diseases and not so rare diseases like Alzheimer's, and of course, we cannot be conclusive that a new legal regime would bring that about. Is it possible that modification of the current legal regime would bring that about?

Mr. {Hemphill.} As I said, in principle, it is

possible. What is tricky here is that we know a lot about the costs from length and exclusivity vis-à-vis drugs that are going to be elicited either way and we know almost nothing about the theoretical improvement that we would get from a longer period of--

Mr. {Lance.} That is why we need a healthy discussion to reach a balance.

Mr. {Hemphill.} Agreed about a balance.

Mr. {Lance.} And at the moment, the balance--and there is the balance in Hatch-Waxman and then there is the balance in the Orphan Drug Act and we are trying to move forward in rare diseases, I as the Republican chair of the Rare Disease Caucus. We need a healthy balance, and that is what this committee in particular is trying to strike, and I would encourage all on the panel to determine what that healthy balance should be, and Mr. Boutin, you believe we need to update or at least modify orphan drugs regarding rare diseases?

Mr. {Boutin.} Without question, we need to update the balance, strike it better, and two quick points. The anti-evergreening issue that was raised applies to every

medication--

Mr. {Lance.} That is precisely accurate.

Mr. {Boutin.} --not what would be on MODDERN Cures. The issue around costing currently applies to every medication, not what would come out of MODDERN, just to be very clear.

Mr. {Lance.} Thank you.

And finally, Professor Hemphill, I don't think we have ever met before. You are welcome to come into my office at any time to discuss my legislation, MODDERN Cures. I understand you teach in Upper Manhattan and live in Manhattan, and I assure you, the Lincoln Tunnel, the Holland Tunnel and even the George Washington Bridge are all open, and I welcome healthy discussion on my completely bipartisan legislation, MODDERN Cures Act.

Thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentleman from New York, Mr. Engel, 5 minutes for questions.

Mr. {Engel.} Well, thank you very much, Mr. Chairman. I live on the other side of the George Washington Bridge, the

side that people couldn't get to when it was blocked, so I want to thank all of you for your testimony and especially give a call out to the New Yorkers, Dr. Gandy and Mr. Hemphill. Always good to see New Yorkers down here in Washington.

The 21st Century Cures Initiative creates an important bipartisan opportunity for us to consider creative new approaches to incentivize getting new treatments into the hands of patients as quickly and safely as possible. I am the coauthor of the Paul Wellstone Muscular Dystrophy Community Assistance Research and Education Amendments of 2008 and 2013 along with my colleague on this committee, Dr. Burgess. I have seen how new research models have produced great advances in our understanding of the various forms of muscular dystrophies. So I raise this now because I think we can use the Wellstone Muscular Dystrophy Research Centers' model to incentivize other forms of research. Much like the National Pediatric Research Network, the Wellstone Centers use a network approach that is designed to ensure that research is not conducted in silos, and I believe this network approach fosters collaboration and allows government

funding to be supplemented by nonprofits and patient advocacy dollars and by private biotech and pharmaceutical funding.

Let me ask you, Dr. Gandy, given your experience with Alzheimer's research at Mount Sinai, could you comment on how a network approach to research can serve as a force multiplier to incentivize treatments and cures for patients?

Dr. {Gandy.} I think the network approach is essential. For one thing, the network standardizes the approach to medication, the approach to diagnosis across all centers, and by disbursing the person power across the country enables the rapid recruitment of new subjects for trials. I think in terms of operations, there is really no other way to do it.

Mr. {Engel.} Are there any other models of public-private partnerships that you think would be constructive to consider in addition to the Wellstone Center approach?

Dr. {Gandy.} No, I think that is a reasonable place to start.

Mr. {Engel.} Okay. Thank you.

I would also like to ask about the development of treatment and cures for patients with rare diseases. Within our rare-disease research communities, more and more

personalized approaches to therapeutic development are becoming possible but these lifesaving personalized drug therapies have small consumer markets and are among the most expensive therapeutics ever created. So let me ask Mr. Borisy and Dr. Miller, could you comment on how we can continue to attract biotech and pharmaceutical industry partners into this space and how we can support industries' work with payer groups to ensure access once therapies are approved?

Mr. {Borisy.} So on the investing in new potential companies that are focused on rare genetic disease, if we believe the science and medicine is there to really make a tremendous different for the lives of those patients, my partners and I are one by one working through those opportunities and forming multiple companies to do exactly that. Part of that is based on the understanding as we have talked about here today on the path through regulatory approval. A second part is understanding the reimbursement as being there, and when we are talking about diseases that might have a couple thousand patients, a couple hundred, or some that are even as few as 100 patients that are involved,

that necessarily means a high price associated with those, and we know those are challenging issues. There are potential therapies that could make a huge difference for patients. If we have stable reimbursement, even at those high prices, then innovation in those rare diseases will continue.

Mr. {Engel.} Thank you.

Dr. Miller?

Dr. {Miller.} Yes. What has been proven that makes a difference for these diseases is, one, NIH funding, so having basic science to support it. So even when look at Alzheimer's, it is rarely about the basic science that is going to drive the industry development. Second, it is actually the FDA. You have heard from everyone, it's regulatory and reimbursement certainty. That is actually their bigger risk than looking for added incentives, and so if you are really going to concentrate on the things that help everything from antibiotics to Alzheimer's to rare diseases, it is really about regulatory and reimbursement certainly.

Mr. {Engel.} Thank you. I see my time is up.

I was wondering if I could just ask one more. Many of you have mentioned that funding basic science through funding the NIH is critical to the goal of creating incentives for innovation, and I certainly agree.

So let me ask Dr. Miller and Dr. Ledley, if either of you could tell us more about how basic science gets translated into cures that can then be capitalized upon by drug makers and what effect have recent cuts to NIH's budget had on this process?

Dr. {Miller.} So I started as an NIH investigator. My wife is the Chairman of Medicine at Washington University. The NIH budget cuts have been devastating to basic science research at universities. The great thing about the NIH is they allow the investigators to actually spin these products off and work with the venture capitalists to start new companies. When you stop that process, when you choke off at NIH the basic science level, the rest of the process doesn't work and so it is crucial that we restore and even improve funding for basic science.

Dr. {Ledley.} I think we have heard big numbers about how many rare diseases and how many unmet needs there are,

and there are enormous numbers. I think it is useful to look at the number of grants the NIH puts out every year relative to that number and ask how many investigators do we think should be taking independent new initiatives for these diseases, each one of which harbors the potential for the new cure that can then be developed.

Mr. {Engel.} Thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentleman from Louisiana, Dr. Cassidy, 5 minutes.

Dr. {Cassidy.} Thank you, Mr. Chair. I really enjoy the panel.

Now, Mr. Hemphill, I have to say when I read your testimony, your spoken testimony had something different. I say this not to challenge, merely to understand. You said listen, you don't think extending exclusivity is necessarily important but when you spoke you said except maybe as Dr. Gandy suggested. Now, clearly you left a door open there. Do you see that there is circumstances in which this extension of patent protection exclusivity for something particularly like I think you used the example of an oral

therapy for neuromuscular disease or neurologic disease would indeed be helpful?

Mr. {Hemphill.} So I certainly didn't intend any inconsistency between my written testimony and my oral. I feel strongly that if we have clear evidence that a targeted increase in exclusivity would work, we should take that really seriously.

Dr. {Cassidy.} Now, hang on, and again, this is a great conversation, so I am not saying this to challenge but there is a certain existentialism about this, right?

Mr. {Hemphill.} Right.

Dr. {Cassidy.} Now, we cannot know the future, and so we are always going to have the anxiety that oh, my gosh, I made the wrong decision.

Mr. {Hemphill.} Right.

Dr. {Cassidy.} I do that whenever I, you know, buy a stock. So that said, we know Gandy. He is an incredible investigator, which by the way, the NIH 20 years ago was advised to redirect their funding to things which have more importance to modern disease. They have not done it in 20 years. So as we speak of the NIH, let us note that the IOM

has suggested that they redirect funding and they have not done so, and in a period of constrained resources, we have to call upon them perhaps to be a little bit more directing towards your diseases.

Now, that said, I go back to my point. Is there a kind of situation in which indeed these sorts of incentives would be important?

Mr. {Hemphill.} Yes. Certainly that is possible, and I also don't mean to suggest that certainty has to be our standard. As you say, we are investing, we are gambling, but we are gambling with the public's money to the extent that--

Dr. {Cassidy.} I agree.

Mr. {Hemphill.} --existing drugs get this extension, which is why I say narrowing our view not to every single drug and probably not every single--

Dr. {Cassidy.} So let me challenge you. Are you ready, man?

Mr. {Hemphill.} Yes.

Dr. {Cassidy.} You are a bright guy. Figure out that metric and give it to Lance. That would have an incredibly important--because I look at Alzheimer's, and there is few

models I think outside of Down's kids of where you know they are going to develop disease.

Now, as the son of a man who died of Alzheimer's, this is so incredibly important. If you could figure out that metric talking to Gandy across town, that would be fantastic for our country. So I say that just to kind of put the plug in.

Mr. {Hemphill.} I appreciate that.

Dr. {Cassidy.} Yeah, thanks.

Dr. Miller, good to see you, man. Listen, I have some problems with your California study. I am a hepatologist. And so if you look at the intention to treat, I do think they underestimate the impact of Solvadi upon outcomes. Every time I still see patients mentally ill and such who are not candidates for interferon, wouldn't be included in a clinical trial so the 47 percent cure rate that that paper posits, it doesn't happen among my patients with addiction disorders or mental illness. That said, I am struck that you suggest that we need to have a mechanism by which we would limit what a company could charge but you don't mention that mechanism. And I say that because your company is incredibly disruptive.

I mean, you all are good. So you think about how markets work. Do you have a suggestion how the Federal Government could limit what companies charge without squelching the innovative drive that has given us a drug which is truly a breakthrough drug?

Dr. {Miller.} If you interpret what I said as the government should be price-setting, the answer is absolutely not. We do not believe the government--

Dr. {Cassidy.} And you didn't say that but I didn't know where you would go with it.

Dr. {Miller.} No, we actually believe it is a free market solution that has to be required, and so we look at it the exact opposite. We think that they have taken advantage of it, which is just a warning to you all that when you talk about extending the period of exclusivity, remember that that is not the only lever that these people have. They have pricing as a lever and they clearly have exercised it, and Solvadi is a great example of it, but we believe that the pushback to Solvadi has to come from the marketplace, not from the government.

Dr. {Cassidy.} So if we are talking about patent

protection, it seems like there is limited levers to push back form the marketplace. Is that a fair statement?

Dr. {Miller.} So you know--

Dr. {Cassidy.} And again, we are kind of guessing what their true cost is to develop a drug, which is an incredible drug.

Dr. {Miller.} So we actually know in this particular case their true cost of developing it because they didn't develop it, they bought it for $11 billion and they will make that back in the first year alone. The trouble is, is that you also need the pharmaceutical manufacturers to act responsibly in their pricing, but even in that absence, there is going to be competitors to the marketplace and they will have to pay a consequence if the competitors can create a product that is equally good because, as you said, we will shift our market share to someone that is willing to give us a better price.

Dr. {Cassidy.} Well, I am out of time. You all have been--I really enjoyed the written testimony and I wish I had more time to ask questions, and thank you each for your good work. I mean, I thank you each for your good work. Thank

you.

Mr. {Pitts.} The chair thanks the gentleman and now recognizes the gentlelady from North Carolina, Ms. Ellmers, 5 minutes for questions.

Mrs. {Ellmers.} Thank you, Mr. Chairman, and thank you to our panel for being here today.

You know, the 21st Century Cures is certainly something that I have considerable amount of passion for, and I think it is certainly the right approach for us to take here in government when unfortunately many times we are always reactive rather than proactive.

My first question is for Mr. Borisy. You know, we have all discussed the challenges of the costly cures to come up with for diseases. Again, Alzheimer's is a devastating disease. Certainly I know many of us have been touched by this personally. My mother died of Alzheimer's. And we all want a cure, and I hear this from my constituents all the time--you know, I don't understand, you spend so much money in Washington on so many different things, why can't you come up with a cure for Alzheimer's, why can't you come up with a cure for diabetes, and you know, we know how much this

affects the American people.

I think I have a better understanding from listening to the testimony that you are all giving today that the cost and the benefit are not necessarily adding up and that that forces some of the innovations and the research and the development outside of our own country. What can we do here in Washington right now today as part of this 21st Century Cures, what changes in policy can we make and what specifically--I know a lot of it is the length of time, it is the FDA. If you had one thing that you could say would change this dramatically, what would it be?

Mr. {Borisy.} So we want to bring these innovations to patients, as you just very eloquently said. Of course, the science and the medicine, the basic science and medicine has to be there, but with it there, what we can do is if we can apply the tools that we have learned from accelerated approval, from breakthrough therapies with FDA to say as a society that we want to apply those for these chronic diseases like diabetes, like Alzheimer's, that simple act alone will change the consideration of the game. It doesn't guarantee we will successfully create--

Mrs. {Ellmers.} Right. No guarantees. That is never--

Mr. {Borisy.} But it totally would change the game that if there are ideas and sparks out there, it makes it something that is investable in to go take that risk.

Mrs. {Ellmers.} So again, it is getting back to that uncertainty that is out there and the unfortunate--you know, we are talking about dollars. I mean, we are talking about investment. We are talking about folks putting their hard-earned money behind these initiatives, and there has to be a payoff, and you know, sometimes that is hard for us because again, we are passionate about the issues and it is a very emotional and personal issue.

Mr. Carusi, one of the things--again, it gets back to, you know, the availability to be developing drugs and things. I have a business company in my district, Entera Health, which is a medical foods company. Basically, you know, this is one of the innovations that we are seeing moving forward, you know, for patients, medical foods, you know, helping patients who are taking many of these medications for HIV, Parkinson's, Alzheimer's, rheumatoid arthritis, irritable bowel syndrome, helping the patient to respond better to

drugs. How can we help this process when we are talking about reimbursement? How can we do a better job to make sure that there again we are making this advancement? What changes at the FDA level would you say would streamline this process for something that is kind of on the edge here when we are talking about medical foods?

Mr. {Carusi.} Yes. Medical foods is not an area where I have been heavily focused or invested, but again, I think the theme that you have heard is one of consistency, transparency and predictability, and when you start to have, as you defined it, devices, drugs, therapeutics that are on the fringe, the pathways start to become less defined, less certain, and so as a result, any of these approaches, we need to know with clarity starting with FDA what the path is and then with reimbursement if these were indeed reimbursed products what that looks like, what the bar is and will they be reimbursed. Alternatively, some of these may be self-pay opportunities and that has its own set of discussions. But all of these testimonies and all these discussions, it comes back to transparency, certainty and predictability.

Mrs. {Ellmers.} Thank you. I have just one quick

question. Does CMS now have the authority to create codes? Because I know this is a conversation we have had in the past where we have reached that level and then we have to unfortunately see another level realized. Do they have that authority right now?

Mr. {Carusi.} To create codes?

Mrs. {Ellmers.} To create codes.

Mr. {Carusi.} My understanding is--around medical foods specifically or more--

Mrs. {Ellmers.} Well, not necessarily around medical foods.

Mr. {Carusi.} My understanding is yes, but again, this is starting to get to the--there are others that are more knowledgeable in that area than me.

Ms. {Ellmers.} Thank you, Mr. Carusi, and I have overstepped my time, so thank you, Mr. Chairman.

Mr. {Pitts.} The chair thanks the gentlelady and now recognizes the gentleman from Florida, Mr. Bilirakis, 5 minutes for questions.

Mr. {Bilirakis.} Dr. Gandy and Mr. Borisy and also Mr. Carusi, let us talking about increasing incentives. I know

that it was mentioned earlier. We want companies to continue to invest in new and innovative treatments but it seems to be because of so many diseases that currently go without treatment options. In your testimony, you all touched on extending exclusivity and patent life. Can you elaborate on how market exclusivity, data exclusivity and patent life play a part on driving innovation for treating neurological diseases such as Alzheimer's or perhaps Parkinson's and how if we do nothing this could hurt the development of new innovative therapies? Why don't we start with Dr. Gandy?

Dr. {Gandy.} I would say in my experience over the past 30 years, I have watched the pharma and VC investment in Alzheimer's research dwindle and the single reason that is most frequently cited is the regulatory path, the challenge for getting approval and then having sufficient patent life left to recoup any of the investment. Alzheimer's disease moves very slowly. The clinical trials require hundreds of patients. They take years to complete, and it is a monumental task, and we don't have yet any templates. We are trying to do something in biology we have never done before.

Mr. {Bilirakis.} Thank you. Mr. Borisy, please.

Mr. {Borisy.} Two weeks or so ago, I was talking with a senior pharmaceutical executive who is running a program in Alzheimer's, literally spending billions of dollars over many years. If we are to try to create and invest in a company that is going to pursue Alzheimer's therapeutics, given that type of scale of time and money that is required, we need to have confidence that if we get to some early stage of proof of concept in the clinic that a future partner, be that a pharmaceutical company or be that public market investors, will believe or be willing to take on the risk from there, we need to be able to hand the ball off to the next stage in the ecosystem for it to have been a viable place to put our money in the beginning. If for the next step in the ecosystem they literally are spending billions of dollars and an indefinite period of time, then they will say you have created that innovation but there is no protection left for that product and therefore even if we show that proof of concept, they will say but that has no value to us. That is a fundamental impediment to us investing in companies in the area.

Mr. {Bilirakis.} Thank you. Mr. Carusi, please.

Mr. {Carusi.} Yeah, I think it comes back to time, and

so I want to give an example. In my portfolio of companies, we have a company GI Dynamics, and GI Dynamics is developing a device-based approach to treat type 2 diabetes and obesity, two of the biggest chronic-disease issues we have in this country. We first started that company in 2004. It is now 2014. We are still in the midst of running our clinical trial for FDA approval and we are starting to commercialize the product outside of the United States. If you had asked me today, okay, you know, 10 years back, would you invest in this company knowing you weren't going to have approval until 2015, 2016, I wouldn't have made the investment despite the fact that what they are doing is tremendously valuable. So it comes back to the incentives and whether or not if it is going to take this much time and this much money that again we can make a reasonable return on that investment, and to me, it is a math problem and that is what this comes down to, and I do think there are certain areas, and I think they are in the chronic-disease field, where there are big studies a lot of times huge potential but we are going to need help, and I think that is what we are asking for.

Mr. {Bilirakis.} Very good. Thank you.

Can anybody on the panel give me a rundown on Parkinson's disease, if there are any promising therapies, breakthroughs, maybe delaying the onset of Parkinson's disease? Is there anybody on the panel that would like to discuss that?

Dr. {Gandy.} The Parkinson's disease field is now following in the template of the Alzheimer's field in terms of generating these networks that are nationwide looking for biomarkers. I think that they have the advantage of having a little more in terms of impact using transmitter replacement and manipulation than has happened with Alzheimer's, so there are some new medications there targeting some new receptors for symptomatic relief, but they haven't yet changed the progression of the disease, and that is really what the key is, to slow the progression.

Mr. {Bilirakis.} Anyone else?

Dr. {Ledley.} A lot of good work on gene therapy. This came up earlier, but this is one that is a challenging target but clearly a feasible and difficult one, but a lot of good work. Some of the companies that have raised money lately are doing it aimed at Parkinson's.

Mr. {Bilirakis.} Very good. Thank you.

Thank you, Mr. Chairman. I appreciate it. I yield back.

Mr. {Pitts.} The chair thanks the gentleman. I hate to cut this off, but this has been the best interaction we have had with members and witnesses, and frankly, this has been one of the most informative, helpful, exciting hearings that we have had. So I want to thank each of the witnesses for your testimony. We have a UC request?

Mr. {Pallone.} Thank you, Mr. Chairman.

Let me echo what you said about the hearing and the value of it. I totally agree.

I just would ask unanimous consent to enter into the record the statement of Ann Boynton, Deputy Executive Officer for the California Public Employees Retirement System.

[The information follows:]

********** COMMITTEE INSERT **********

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Mr. {Pitts.} Without objection, so ordered.

There will be follow-up questions. We have members at other hearings on the Floor. Dr. Burgess is having to manage time on the Floor. We have follow-up questions. We will submit those to you in writing. We ask that you please respond promptly. I remind members that they should submit their questions by the close of business on Wednesday, June 25th.

Again, thank you so much, a very good hearing. Without objection, the subcommittee is adjourned.

[Whereupon, at 12:38 p.m., the subcommittee was adjourned.]