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FROM JOINT PAIN TO POCKET PAIN: COST AND COMPETITION AMONG RHEUMATOID ARTHRITIS THERAPIES

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WEDNESDAY, FEBRUARY 7, 2018

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 9:31 a.m., in room SD–562, Dirksen Senate Office Building, Hon. Susan M. Collins (Chairman of the Committee) presiding.

Present: Senators Collins, Tillis, Fischer, Casey, Nelson, Gillibrand, Blumenthal, Donnelly, and Cortez Masto.

OPENING STATEMENT OF SENATOR SUSAN M. COLLINS, CHAIRMAN

The CHAIRMAN. The hearing will come to order.

Good morning. Prescription drugs are vital to the health and well-being of Americans, especially our Nation's seniors, 90 percent of whom take at least one prescription drug in any given month. For many Americans, access to affordable prescription drugs is not only critical for health, but also can be literally a matter of life or death.

Developing these medicines is a lengthy, expensive, and uncertain process. It often takes more than a decade to bring a new drug from the laboratory to the market. The process is often very costly, and most drugs fail during testing.

If we want new medicines to reach consumers who need them, the companies that invest in the research and take the risks necessary to develop these drugs must see a fair return on their investment.

At the same time, we cannot be blind to the costs of these drugs, nor to cases where patent laws are manipulated to preserve monopolies. Americans are expected to spend more than $387 billion on prescription drugs this year alone. Of this amount, individuals will pay about $48 billion out-of-pocket. The Federal Government is a major payer and will pick up another $172 billion in payments through Medicare, Medicaid, Veterans Affairs, and other programs. And, of course, the cost of prescription drugs affects what we pay for private health insurance as well.

While we understand that research and development are expensive, consumers are also familiar with reports of prescription drugs that have undergone significant and unwarranted price increases. Last Congress, this Committee conducted a bipartisan investigation

into the sudden, dramatic price increases of certain decades-old prescription drugs.

At the end of our investigation, we published a report documenting cases in which companies that had not invested a single dollar in the research and development of a drug, nevertheless bought it, hiked its price to an unconscionable level.

Today the Committee will examine why prices have soared for drugs used to treat a disease affecting 1.3 million Americans—rheumatoid arthritis, a chronic autoimmune and inflammatory condition that attacks the linings of joints. Untreated, RA can lead to permanent joint damage and is associated with significant morbidity. While it can begin at any age, the likelihood of onset increases with age and is highest among women in their 60's.

Biologic medicines have proven life-changing for many patients, halting the progression of symptoms and allowing them to remain actively engaged at work, at home, and in life. Derived from living organisms, biologics are much more complex than their chemical counterparts. They may require special handling and are often administered by injection or infusion. Sometimes referred to as "specialty drugs," these medicines can have astonishingly high price tags that are continuing to increase every year.

For example, the price of Humira, a self-administered biologic approved at the end of 2002 to treat RA, has risen from about $19,000 per year in 2012 to more than $38,000 per year today. Enbrel, another biologic that was first approved for treatment of RA in 1998, costs about the same. Sales of Humira reached $16.1 billion in 2016. It is the world's best-selling pharmaceutical drug, and Enbrel is No. 3.

The FDA approved biosimilars for both Humira and Enbrel in 2016, but neither has come to market. That is disturbing since we know that competition tends to drive down prices or at least curb increases. In the case of Remicade, a less expensive biologic approved for treatment of RA, two biosimilars did come to market at discounts of 15 and 35 percent. That raises the important question: Why haven't the biosimilar competitors of Humira and Enbrel become available to consumers? According to reports, Humira is covered by more than 100 patents, many of which were added as the expiration date of the drug's main patent approached in 2016.

Similarly, Enbrel's main patent has expired, yet the drug remains protected by at least two other so-called submarine patents nearly 20 years after it was first approved by the FDA. According to a CRS report from 2017, five of the seven biosimilars that had been approved by the FDA "have been delayed, or alleged to be adversely impacted, by actions of the brand-name manufacturers."

Treating rheumatoid arthritis costs the U.S. health care system an estimated $19 billion a year. As a result of the increasing costs of these vital drugs, we hear of the struggles of older Americans who face not only the pain of the disease, but also the financial pain associated with maintaining treatments.

One of these patients is my constituent, Patty Bernard. She is among the more than 8,000 people in Maine who live with rheumatoid arthritis. Mrs. Bernard is 80 years old—I hope you do not mind that we told your age at this hearing—and she was diagnosed with rheumatoid arthritis at age 55. In the early years of her diag-

nosis, she tried many different drugs, but her symptoms continued to get worse.

In 1998, when Enbrel came to market, she was one of the first in Maine to try the drug. She calls the medicine "God-given." Joint by joint, she felt her life come back. When Mrs. Bernard retired last year, she learned that on Medicare she would have to pay $3,800 per month for the medication, an unaffordable cost.

We look forward to hearing from all of our witnesses today and to better understanding what can be done to moderate the price of prescription drugs without discouraging the innovation that helps us live healthier lives.

I look forward to hearing from our witnesses, and I now turn to our Ranking Member, Senator Casey, for his opening statement.

OPENING STATEMENT OF SENATOR ROBERT P. CASEY, JR., RANKING MEMBER

Senator CASEY. Thank you, Chairman Collins, for holding this hearing today. We want to thank our witnesses for your presence here and your testimony.

Over 54 million Americans are living with arthritis, including 3 million just in the State of Pennsylvania alone. The prevalence of arthritis increases with age. Half of Americans age 65 and older are diagnosed with arthritis, and women are at a greater risk of arthritis than men. Three times more women than men are living with rheumatoid arthritis, as the Chairman noted. As she also noted, this is one of the more severe types of this disease.

The sheer number of people who may be diagnosed with arthritis gives us good reason to examine this illness and its treatments. We must promote pathways to foster innovation and promote access to life-changing medications. Indeed, with the emergence of novel treatments for rheumatoid arthritis over the last two decades, people are living longer, fuller lives. But these treatments are not always affordable. One of our witnesses here today, Dr. Harvey, will tell us about the impact this has had on patients.

Americans living with arthritis—just like any other disease or condition—must be able to access and afford the treatments they need. No baby boomer or senior should go without care simply because the price tag is too high or the out-of-pocket cost is too great. No one should live in fear that one day they will not be able to afford the medicine that allows them to live and work in their community.

It is for this reason that I was pleased to help close the Medicare prescription drug coverage gap—known by that benign phrase, "donut hole"—as part of the Affordable Care Act. Already since that time, over 275,000 Pennsylvanians with Medicare saved almost $1.6 million on their prescription medications because of this change. Now, that is the good news.

But as we will hear today, there is much more that can be done to ensure that seniors and people with disabilities can afford life-sustaining and life-saving treatments. These are issues that span research and innovation, regulatory approvals, market forces, and coverage. Our witnesses will shed light onto these different factors and more. I look forward to the Committee's discussion, and, Madam Chair, I would note for the record that two of our witnesses

have roots in Pennsylvania, but once they move out, I cannot claim them—Dr. Hoadley as well as Dr. Harvey. But we are grateful they are here with us.

Thank you.

The CHAIRMAN. Thank you very much. And I also want to welcome Senator Cortez Masto and Senator Fischer to our hearing today. We will now move to the introductions of our witnesses.

Our first witness is Patricia Bernard from Falmouth, Maine. Mrs. Bernard, as I explained in my opening statement, lives with rheumatoid arthritis. Her condition was debilitating, but with the advent of biologic therapy, she has gained control over her condition and her life. She was stable with Enbrel for nearly two decades until she retired at 79 and could no longer receive the drug once she transitioned to Medicare. She will describe her journey with rheumatoid arthritis and the impact of the skyrocketing cost of treatment.

Dr. William Harvey is the director of the Division of Rheumatology at Tufts University School of Medicine. He is also a longstanding member of the American College of Rheumatology, and he will share his experiences as a physician not only diagnosing and treating seniors, but also serving as an advocate to help his patients obtain and maintain the treatment they need in the face of soaring costs.

Also joining us today is Dr. Jack Hoadley. Dr. Hoadley has 30 years of experience in the health policy field and currently conducts research on health care financing at Georgetown University's Health Policy Institute. He is a member of the Medicare Payment Advisory Commission, better known as MedPAC.

We also welcome Terry Mahn, a distinguished attorney and managing principal of Fish & Richardson's Washington, DC, office. He is also group leader for the firm's Regulatory and Governmental Affairs Practice and an adviser for Bloomberg BNA Pharmaceutical Law and Industry Report.

We look forward to hearing from all of you and appreciate your joining us and hope that you all can get back home after the hearing.

Mrs. Bernard, we will start with you. Thank you.

STATEMENT OF PATRICIA BERNARD, RHEUMATOID ARTHRITIS PATIENT, FALMOUTH, MAINE

Mrs. BERNARD. Good morning. Thank you, Chairman Collins, Ranking Member Casey, and distinguished members of the Committee for inviting me to testify before you today.

My name is Patty Bernard. I will turn 81 in July, and I have rheumatoid arthritis. I have lived with diagnosed RA since I was 55. Before the diagnosis and treatment, I experienced excruciating pain—day in and day out. Every bone in my body ached. The pain made ordinary tasks difficult, often impossible. I would come home from work and take hot, hot showers. It was the only thing that relieved my pain—even just temporarily.

I finally visited a rheumatologist and learned that I had RA. In fact, at that time my doctor informed me that 79 percent of my body was inflamed. It was very difficult to hear the doctor tell me I had RA. My cousin had the disease, and I saw what it did to her

body. She was in a wheelchair, and her hands were like clubs. That night, I went home and cried.

My doctor tried many drugs, but they did not help. As I entered my 60's, my symptoms grew worse. My doctor discussed adding gold injections. Just as I was ready to try that, something new came on the horizon—a drug called Enbrel. I was one of the first in Maine to try this therapy. I got my first shot of Enbrel at the doctor's office. The doctor warned me not to expect it to work right away. But that day, as I was driving back to work, I could feel something going through my body. That afternoon, I felt much better. It was incredible. I just could not believe it.

Enbrel gave me my life back. I no longer woke up in the morning with excruciating pain or came home in the evening aching in agony. Because I had insurance through my job, I paid anywhere from $10 to $30 each month depending on my company's insurance plan. Every other week, I was able to give myself injections. Besides that, I was finally able to live an ordinary life. I went to work. I walked, I swam, and I took the stairs because I could.

For 19 years, I depended on Enbrel. My employer-sponsored insurance switched several times over the years. But every time, my employer went out of his way to find an insurer that would cover my Enbrel.

Although I did not really want to stop working, I retired in December 2016 at the age of 79. I would no longer have insurance through work. In the transition to Medicare, I was devastated to learn that I would have to pay $3,800 a month if I were to remain on Enbrel. $3,800 a month! I do not have that type of money. I feared I might have to sell my house. I was afraid that if I went without this medication I would end up back in so much pain and even in a wheelchair. The anxiety started causing heart palpitations that put me into the hospital on more than one occasion, one time over Christmas.

My rheumatologist proactively helped to find me an affordable option. He suggested a treatment called Remicade. It was not self-administered like Enbrel. Instead, I would have to go into the doctor's office to receive the infusion. Worse, there was no way to know whether or not it would work. I was scared. I knew that Enbrel had worked well for nearly two decades, and stopping it felt like going backward. I even called Medicare, and told them, "I don't understand. I am actually saving you money by administering the Enbrel myself." They said that is the way it is.

I was nervous the day I went to the doctor's office for my first injection of Remicade. Thankfully, after a year on this treatment, it has worked. It is not convenient compared to administering the drug myself. I have to go into the doctor's office in Portland once a month, and each infusion takes about 2½ hours.

I do not understand why I need to pay nearly $4,000 in a single month for a drug that for years I had for no more than $30 a month. I am grateful that I do have something that works so that I can be productive for my family, my church, and other friends who are not as fortunate as I am. But I feel very strongly that people should be able to access the treatment they need at an affordable cost.

Thank you for the opportunity to testify, and I am happy to answer your questions.

The CHAIRMAN. Thank you very much, Mrs. Bernard, for such compelling testimony. We really appreciate your sharing your story with the Committee.

Mrs. BERNARD. You are welcome.

The CHAIRMAN. Dr. Harvey.

STATEMENT OF WILLIAM F. HARVEY, M.D., RHEUMATOLOGIST, ASSOCIATE PROFESSOR OF MEDICINE, CLINICAL DIRECTOR, DIVISION OF RHEUMATOLOGY, TUFTS MEDICAL CENTER, BOSTON, MA

Dr. HARVEY. Thank you, Chairman Collins, Ranking Member Casey, and distinguished members of the Committee, for allowing me to speak with you today. I am here representing thousands of rheumatologists and our millions of patients who struggle to manage their disease in large part due to the high cost of treatment. I wear on my lapel a bent fork, which is a symbol from the American College of Rheumatology, to remind folks that when you have arthritis, even simple tasks like using a fork can be difficult.

Rheumatoid arthritis is the most common of more than 100 autoimmune diseases affecting the joints and afflicting over 1.3 million Americans. It is more common in women and is a lifelong illness, so there are many seniors today living with rheumatoid arthritis.

Untreated, rheumatoid arthritis leads to significant joint damage, disability, and pain. Fortunately, today we have many effective treatments.

For a long time, the only treatments available were highly toxic medications like gold salts that Ms. Bernard mentioned and steroids which cause a lot of comorbidities. But these really only work in about half the patients. The rest will require more potent medication, and more recently, a new class of therapies called biologics have emerged to treat these conditions. These medications have highly complex manufacturing processes, as has been alluded to, and thus have a very high cost. Copays for the oral therapies may be less than $50 a month, but for the biologics the copay is often several hundred or even thousands of dollars.

Choosing the right therapy for a patient is a complex decision that considers other conditions and medications a patient may have, balancing the risk of side effects and many patient-specific factors. Most physicians believe in the importance of shared decision-making, where the treatment goals and concerns of the patient are incorporated into the medical decision-making. Most rheumatologists would start treatment with the oral therapies, as you heard, but, again, only half of the patients will respond to these therapies.

Factors to consider when choosing the right biologic therapy include medications already tried, history of infections and malignancy, and the ability to administer the medication to themselves. But, overwhelmingly, the primary factor for the decision is which one is best covered by insurance. Because of their high cost, every one of these therapies requires prior authorization before use from the payer, and that is a process that can take days to weeks to complete before a patient can start treatment. A 1-to 3-month trial

and error may be necessary, as we do not have enough scientific evidence to determine which therapies may be best. The result may be that it takes months to get the patient's disease under control.

I mentioned the prior authorizations. Each insurance company has a different set of forms requiring different kinds of information. Most require that the patient have their medication provided by a specific pharmacy, called a specialty pharmacy. And that is because insurance companies, usually through pharmacy benefit managers, negotiate price discounts in exchange for preferred placement on the insurance formulary. If a provider or a patient wishes to have a medication that is not preferred, the prior authorization will be denied, and the provider must go through escalating steps of appeals, usually to the tune of more than a hour of that provider's time, in order to successfully procure the medication for the patient.

Many practices have begun to employ at significant expense other kinds of providers such as nurse practitioners, physician assistants, or pharmacists to navigate this process. Without my pharmacist, Jinkyu Lee, our resident "insurance wizard," we would drown in the administrative burden of getting medications for patients.

So to address this issue, I strongly endorse regulation requiring insurance companies to at least follow a standard, transparent process for documenting, evaluating, and approving prior authorization requests. Every minute spent away from a patient is a waste of time and limits access for other patients.

I also mentioned the trend of pharmacy benefit managers to address the rising costs of therapies. At face value, the concept makes intuitive sense, allowing companies to negotiate the best possible prices for treatments. While well intended, the use of pharmacy benefit managers has led to a very opaque process that favors maximizing payers' profits over the shared decision-making which utilizes that sacred bond between a doctor and their patient. Pharmacy benefit managers are for-profit companies that make the most profit when the list prices of drugs are higher because there is then a greater margin for them to make their profit.

I strongly endorse requirements to increase transparency for pharmacy benefit managers—starting with properly defining terms like what is a rebate and what is permitted—and for passing savings directly on to consumers, which most insurance companies do not do even when they negotiate a lower price.

Out-of-pocket expenses, as I noted, are substantial, and certainly Mrs. Bernard has given poignant testimony to that effect. Asking patients to pay their "fair share" is immoral and indefensible when it leads to medical bankruptcy. These copays were designed to incentivize people to choose the cheaper therapy, but in these cases there is no cheaper alternative. For these beneficiaries, the only option is to avoid the self-injectable treatments and get the infusion treatments, as you just heard.

Last, I want to focus on the importance of biosimilars. These are treatments which are similar to but not exact copies of biologics, and a safe and vibrant biosimilar marketplace is essential to the future of rheumatologic care. In Europe, where biosimilars have been introduced into the market earlier, they have seen an approxi-

mately 30-percent reduction in the total cost of treatment. However, this level was not achieved until there were three to four competitor medications on the market. The FDA does have a process for approving biosimilars, and two biosimilars to Remicade are on the market. I encourage the Committee to support adequate funding for the FDA to approve these therapies and to address the issue of extended patent litigation which prevents other competitors from reaching market.

I have discussed a number of these important issues, but the most important thing is that we continue to work together and continue to discuss these important issues so that the story that you just heard like Mrs. Bernard's never happens.

Thank you again for allowing me to be with you today.

The CHAIRMAN. Thank you, Dr. Harvey.

Dr. Hoadley.

STATEMENT OF JACK HOADLEY, PH.D., RESEARCH PROFESSOR EMERITUS, HEALTH POLICY INSTITUTE, McCOURT SCHOOL OF PUBLIC POLICY, GEORGETOWN UNIVERSITY

Dr. HOADLEY. Thank you, Senator Collins, Senator Casey, and members of the Committee. I am a research professor emeritus at Georgetown University. I also serve, as the Chair mentioned, on the Medicare Payment Advisory Commission, MedPAC. I will emphasize I do not speak on behalf of the Commission, but I am representing the views of myself as an individual. And I do appreciate this opportunity to share my perspectives about the cost of rheumatoid arthritis drugs.

Today several drugs are available to treat rheumatoid arthritis, as you have heard. This should offer us the benefits of robust market competition and, thus, lower prices. The reality is otherwise. From a Medicare perspective, three drugs dominate the RA drug market. Each is used by 50,000 to 60,000 beneficiaries every year, and each cost the Medicare program $1 billion to $1.5 billion in 2015. They are among the costliest drugs in the Medicare program.

One of them, Remicade, as you have heard, is covered under Medicare Part B because it must be administered by a clinician. Beneficiaries who take this drug must pay 20 percent coinsurance, although that cost for many may be covered by supplemental insurance or Medicaid and, thus, ends up being less expensive. In 2015, the average beneficiary taking Remicade incurred $4,280 in cost sharing. Again, that may be picked up by supplemental insurance. Spending on Remicade has been rising at a rate of 8 percent per year.

The other two, Humira and Enbrel, are covered under Medicare Part D because they can be self-injected. Beneficiary cost sharing varies across the year in the different Part D benefit phases. In 2015, beneficiary out-of-pocket costs for these drugs averaged about $1,600, but would be much higher for someone taking a full dose for the entire year. Beneficiary costs would also have been even higher if Congress had not phased out the coverage gap, or "donut hole," as Senator Casey mentioned. Total program spending on Humira more than tripled from 2011 to 2015, in just 4 years, and it more than doubled for Enbrel. Each experienced a 4-year price increase of 80 percent, nearly 20 percent each year.

What can we do to stem these rising costs? The most important step is to increase the role of biosimilars, as you heard from Dr. Harvey. The FDA has approved biosimilars for all three of these common RA drugs, but as of today, the biosimilars for Enbrel and Humira are not on the market because of patent litigation. In fact, the biosimilar for Humira will not be launched until 2023 because of a legal settlement. That is 5 years away. Remicade's biosimilars are on the market, but early indicators have not shown a lot of impact on pricing, but that may change.

At MedPAC, we approved a set of recommendations which we thought would strengthen the ability of Medicare to stimulate market competition and to lower prices. One recommendation calls for a common Part B billing code for all of the biosimilars and the original biologic that they are comparable to. The idea is to increase price competition because all of the competing drugs would be paid based on the average price for all of them, and that is not true of the way the system works today.

The Commission also called for a new and voluntary Part B drug value program that would be a program to allow private vendors to negotiate lower prices and share the savings with providers, with beneficiaries, and the taxpayer.

Last month, the Commission also voted for a recommendation that would change the Part D manufacturer's coverage gap discount program so that biosimilar manufacturers pay the same 50 percent discount as that paid by the original biologics, the manufacturers for those. This step would level the competitive playing field between these drugs. Right now, the incentives are such that plans are less likely to use the biosimilars.

These important steps should strengthen the competitive impact of biosimilars, but their widespread use and savings will also depend on other factors: the establishment of interchangeability status by the FDA, resolving the patent litigation issues, state laws on biosimilars substitution at the pharmacy, general acceptance by clinicians and patients; and further research on what happens when patients do switch between different drugs and make sure there are no adverse effects.

Finally, let me take note of some additional MedPAC recommendations to bring more savings for beneficiaries who take expensive RA drugs.

As I mentioned before, the Commission made a set of Part B recommendations last June, and I mentioned a couple of items from that set. Another item in that set would require manufacturers to pay a rebate when the drug's average sales price rises faster than inflation. Beneficiary cost sharing would then be based on the inflation-adjusted price, so that would be a means of combating some of the price increases we have seen.

For Part D, the Commission made a set of recommendations in June 2016. I will highlight two of them.

One is a hard cap, a new hard cap on beneficiary out-of-pocket costs so that beneficiaries would pay nothing after they exceed the catastrophic threshold, which is about $5,000 out-of-pocket. Still a lot of money, but at least once you get to that threshold, under this proposal there would be no additional cost for the rest of the year.

Another is a reduction in the federal reinsurance from the current 80 percent in the catastrophic phase down to 20 percent. Right now the Federal Government reimburses the plans for 80 percent of costs of drugs for those people who exceed that catastrophic threshold, and the change is designed to create a stronger incentive for Part D plans to manage costs and negotiate the lowest possible prices while maintaining a 20-percent reinsurance to still accomplish the goals that reinsurance has provided.

Today the biologics used to treat rheumatoid arthritis are expensive, both for the beneficiary and for the taxpayer. Biosimilars bring the potential for a more competitive market and lower prices. But policy changes could lower the barriers to getting to that endpoint. Also, the Congress should consider other policies such as the ones I mentioned to lower cost for Medicare and its beneficiaries.

Thank you for the opportunity to testify. I appreciate it.

The CHAIRMAN. Thank you very much, Doctor.

Mr. Mahn.

STATEMENT OF TERRY G. MAHN, J.D., MANAGING PRINCIPAL, REGULATORY AND GOVERNMENT AFFAIRS PRACTICE GROUP LEADER, FISH & RICHARDSON, WASHINGTON, DC, AND ADVISORY BOARD MEMBER, BLOOMBERG BNA PHARMACEUTICAL LAW AND INDUSTRY REPORT, WASHINGTON, DC

Mr. MAHN. Thank you. Chairman Collins, Ranking Member Casey, and members of the Committee, thank you for this opportunity to appear before you today.

After listening to this wonderful testimony and moving testimony, I guess it is no surprise that the attorney talking about patents is at the end. I hope I do not bring this hearing down.

My testimony today will focus on intellectual property-—patents, to be more precise—and the important role that they play in driving the discovery and development of new drugs and medical therapies. I will try to relate how patent protection can impact the cost of drugs and health care generally, and I will try to offer some insights on how these forces can be kept in balance. And before I say anything further, please understand that these comments are mine alone and do not reflect the thoughts or views of my law firm or any of its clients.

Every spring, I co-teach a 3-day patent course on the Hatch-Waxman Act and the law of biosimilars. I always begin the course by pointing out two related statistics that frame the issues for the rest of the session: the first statistic underscores the low probability of success associated with new drug discoveries; and the second statistic highlights the extraordinarily high cost of bringing a new drug discovery to market.

First, the probabilities. According to the Pharmaceutical Research and Manufacturers Association, for every 5,000 to 10,000 new compounds, newly discovered compounds with therapeutic potential, only 250 actually make their way into pre-clinical testing, only 5 will qualify for clinical trials, and then only one results in an approved drug. So you start with 5,000 to 10,000 new discoveries to produce one drug.

Second, the costs. According to Tufts University, which has modeled the cost of developing new drugs for well over a decade, in 2015 the fully loaded cost of bringing a new drug to market exceeded $2.5 billion. Any way you look at this data, the facts are indisputable. Drug development is an enormously costly and risky business.

Because the pharmaceutical business is essential to our public health, however, our legal system must properly incentivize and appropriately reward its risk takers. This is where the patent system comes in. In exchange for publicly disclosing new drug discoveries, the law grants patent owners a monopoly on those discoveries or inventions for a limited time. Ideally, this should only be long enough for patent owners to recover their investment and return a reasonable profit. After that, these new drug developers should be willing to face market competition so that the public will benefit from lower cost medications.

In fact, this was one of the important goals of the 1984 Hatch-Waxman Act, and after 34 years of tinkering—Congress has amended the act about a dozen times—many would argue that Congress now has it just about right. Today 85 percent of all prescriptions are filled with generic drugs, 35 percent of all industry revenues go to generic manufacturers, yet brand investment in new drug research and development is at an all-time high, exceeding over $100 billion annually. More tellingly perhaps, in 2017 FDA approved more novel drugs than in any year over the previous decade. So, from the data, it looks like this legislation is working well for the American public.

Still, achieving that brand/generic balance has not been the smoothest of roads. At its core, Hatch-Waxman radically simplifies the drug approval process by allowing generic applicants to piggyback on the proprietary clinical data strictly required for brand drug approval. In return, the generic must await the expiry of brand patents, which are listed in the FDA's Orange Book, or it must challenge those patents for earlier market entry. If challenged, the Hatch-Waxman Act affords the brand an opportunity to litigate those patents prior to generic launch.

The math then becomes simple. The more patents obtained for a drug, the longer the litigation, the slower the entry of generic drugs. Even after a generic drug is approved for launch, if patent litigation is ongoing the potential damages for infringement can be enormous, such as lost profits. That is a risk that is too great for most generic companies to bear. Thus, under the original Hatch-Waxman scheme, brand manufacturers were incentivized to list as many patents as possible in the FDA's Orange Book and then litigate them aggressively as a business strategy to slow down competition and preserve their market share. This patent-gathering tactic has been pejoratively called "ever-greening."

Congress through legislation and FDA through various rulemakings over the years have taken deliberate steps to stop patent ever-greening. But those efforts have only been partially effective. A recent study by The Hastings College of Law examined the types of patents submitted for Orange Book listing between 2005 and 2015 and concluded that it is alive. For example, the study found that: 74 percent of patents listed over this period were for

previously approved drugs; 80 of the top 100 selling drugs listed a new patent at least once; and 50 listed a new patent more than once; and 40 percent of all drugs listed new patents, with 80 percent of those listing patents more than once and some as many as 20 times.

In addition, brands have ventured into other areas to assert their patents, including the patenting of REMS programs, entering into "pay for delay" settlement agreements, and implementing so-called product-hopping strategies. Nonetheless, and despite anecdotal evidence, to my belief from all the available data, the Hatch-Waxman balance is working as intended, as both the new drug and generic businesses appear to be thriving.

I do not want to run over my time too much, but I have a few things to say about the biologic space, so I will go quickly.

So what about the biologic drug side? Well, as we know, until 2010, the U.S. drug laws did not provide an abbreviated approval pathway for "me-too" biologics, known as biosimilars. The Affordable Care Act sought to change that with new rules for approving biologic drugs that were loosely modeled on the Hatch-Waxman scheme. Yet stark differences remain. Most biologic drugs are produced by living organisms and, thus, are very large molecules, very difficult to characterize, and almost impossible to duplicate, even from batch to batch. For this reason, biosimilars must be studied much more carefully than small-molecule generics to determine their therapeutic equivalence to the brand drug. Clinical trials and detailed scientific analyses are required for biosimilars resulting in an approval process that is slower and much more expensive than for generic drugs. Moreover, full substitutability of a biosimilar for the brand drug, which is automatic in the generic world, requires separate FDA licensing of the law, a process that has yet to be fully developed or understood. Accordingly, only the most financially well-heeled manufacturers can afford to enter the biosimilar space which, understandably, limits future competition. Still, the rewards are tantalizing. In 2015, for example, nine of the top ten best-selling drugs in the world were biologics that averaged over $8 billion in annual sales.

As one would expect, patents play an important part in the development of biologic drugs and the market entry of biosimilars—only more so as compared to small-molecule generics. First, due to the complexity of these molecules and the processes required to grow them, many more opportunities exist for securing patent protection. Take Humira, for example. In 2015, we counted 76 patents that protected this $16 billion franchise; by 2017, the number was over 100 and still growing. Second, the biosimilar legislation creates an elaborate scheme involving two potential waves of patent litigation prior to biosimilar launch. Although the Supreme Court ruled last year that the first wave is optional, that does not diminish the fact that a large portfolio of patents presents an equally large barrier to entry.

So, to summarize, as of this date, as we have heard from Chairman Collins and others, FDA has approved only a handful of biosimilar drugs, nine to be specific—five in 2017 alone, three of which are now on the market. Patent litigation is tying up 18 other biosimilar applicants who have approved or pending applications.

And early pricing shows only a 15-percent discount off of the brand biologic, 35 percent in the case of a second generic for Remicade that has entered the market. Several reasons for this small discount that you do not see on the generic side: much higher regulatory costs to market entry; fewer anticipated competitors; no assurances of automatic substitution, thus requiring much higher direct marketing to physicians and hospitals; and the significantly higher costs for manufacturing.

An example in Europe may tell a story, which is ahead of the U.S. in biosimilar approvals. Yet the discount from the brand—I am sorry. Three biosimilars are on the market for Remicade in Europe, yet the discount from the brand is only 45 percent. The comparable discount for a three-competitor generic drug would be in the vicinity of 85 percent.

I have attached to my testimony a year-end blog prepared by my firm that contains some relevant data on pricing that should be instructive to the Committee. Thank you again for this opportunity to appear. I would be happy to try to answer any questions.

The CHAIRMAN. Thank you very much for your testimony.

Mrs. Bernard, I cannot imagine how you must have felt when you learned that your copay was going to go from $10 to $30 a month when you were privately insured through your employer to an astounding $3,800 a month for a drug that you had been on, a biologic that you had been on for decades that had made such a difference to you. Could you first explain what your reaction was? And, second, if today your copay went back to the level that you had paid, the $10 to $30 a month, would you switch back to Enbrel or would you stay on Remicade?

Mrs. BERNARD. Well, some of these drugs, they do not know if you—when you switch back, if they will do, you know, what they did at the beginning. Enbrel, I cannot stress to anyone so much, it is such a wonderful, wonderful drug. And I was—first of all, I panicked because I am thinking, "What am I going to do?" Because myself, I am a widow, and I do not have the money. And, really, panic set in. It really did. And I am thinking, "How dare they take something away from us," meaning everybody that has rheumatoid arthritis, "and say you cannot have it anymore?" Because you cannot afford it. And that is what is sickening to me to know that they have that much power to take something like that away.

The CHAIRMAN. Thank you. This is something we are going to follow up on with Medicare, with CMS about, because you raised a really good point, that you used to be able to self-administer Enbrel. Now you have to go to a doctor's office for a 2½ hour infusion, which clearly adds cost to the system. And this is an issue that we will follow up on.

Dr. Harvey, the prices of these biologic treatments have increased year after year after year, and, in fact, the New York Times recently reported that the price of Humira had risen by 100 percent from 2012 to today, from $19,000 to $38,000 for a year of treatment. Just in January, we saw another price increase of nearly 10 percent.

So you have dealt with this drug for many years and prescribed it. Has there been a difference in the drug's formulation that was

significant over the years that would account for such an enormous price increase based on your knowledge?

Dr. HARVEY. Senator, that is a great question. I cannot speak to what these companies do inside their laboratories, but I can tell you at the point of care with patients, there is no difference whatsoever in the efficacy of these therapies over the course of that time period.

The CHAIRMAN. Thank you. That is often what we have found, that the drug has not changed, the biologic has not changed, and yet the price has gone through the roof. And these are wonderful medicines that really change lives and make a big difference, but it is hard to understand why there is such an increase.

Mr. Mahn, you mentioned a patient device that is used, which I am wondering why we just do not crack down on or why the FTC does not prevent, and that is pay for delay. Could you explain how that can prevent a biosimilar or a generic drug in the case of a chemical compound from coming to the market?

Mr. MAHN. Thank you for that question, Senator Collins. Pay for delay commonly refers to an agreement between a brand and generics, one or more generics, that keep the generic off the drug based on patent rights. In other words, the patent is asserted by the brand. The generic is at risk of infringing the patent, and so the brand pays the generic money to stay off the market until the patent expires. And they basically settle up front a litigation that could cost them a lot of money. The brand makes out. The generic makes out. The consumer does not make out.

When those pay-for-delay settlements are for a legitimate purpose, which is related to the patent and its fair licensing, they are acceptable under the law, as the Federal Trade Commission has said. But when they are anticompetitive or there are other ulterior purposes that the parties have in mind, it can be actionable, and the FTC has brought actions against some of these companies for pay for delay. There has been a Supreme Court decision on the matter, and there has been a cracking down on pay for delay, and it is much more difficult nowadays for those agreements to withstand muster.

The CHAIRMAN. My time has expired, but I appreciate that explanation. In another round I want to talk to you about patent thickets, because the fact that Humira has 100 patents, many of which were added late in the process, I think is another technique that is used.

Senator Casey?

Senator CASEY. Dr. Harvey, I will start with you. You mentioned in your testimony that treatment for rheumatoid arthritis can be out of reach for some patients and far too costly. In your testimony, you talk about an interaction you had with a particular patient who was scared to tell you that she could not afford her treatment. You indicated she was scared to tell you this even though the result was, in your words, "suboptimal disease control and disability."

Can you share additional information about what might happen to a patient's condition when they cannot afford their medication?

Dr. HARVEY. I am happy to do that. Thank you for the question. So there are less expensive medications that can be used. The most commonly used one would be prednisone. It is a steroid, and it has

a tremendous amount of side effects. It can cause diabetes. It can cause hypertension, weight gain, and obesity. It can cause osteoporosis. And so when patients cannot afford the more effective therapy, we often use low doses of this therapy to try and treat them.

Still, it is often suboptimal, and when that happens you begin to develop irreversible joint damage. Once the joint damage has occurred, there is no therapy in existence today that repairs those joints. And so you start a downward spiral that can lead to disability. It can lead to absenteeism from work. It can lead to presenteeism at work where you are at work but less effective in your job. And the impact from an economic perspective of this phenomenon is very difficult to capture.

I would also say that at the end of the day, when patients cannot afford their medication, they are at risk for permanent disability, which then oftentimes results in them being supported by our government through disability services. So, really, it is an investment in people's health and future that we need to be more confident in making.

Senator CASEY. Doctor, thank you.

I wanted to go to Dr. Hoadley. I mentioned in my opening comments the donut hole, the coverage gap. We actually should come up with a better phrase for that. It sounds far too benign when somebody gets hit with those kinds of costs.

The national numbers in terms of what has happened since the Affordable Care Act is about $26 billion in savings for 12 million people with Medicare. How has this policy change—this one policy change, I should say, addressed affordability for patients or improved treatment options for patients?

Dr. HOADLEY. Thank you. That is a great question. It has really made an enormous difference. Instead of paying the full cost of a drug like Enbrel or Humira, about $5,000 a month, the price in that coverage gap phase is now—this year, it was brought down to $1,700. So remember that the Part D benefit has an initial coverage period, and then it goes into that coverage gap or donut hole, where originally you paid the full price of the drug. But this year the cost sharing to the beneficiary is 35 percent, and by 2020, when it is completely phased out, it will drop to 25 percent, so that will be closer to $1,200 a month.

Now, that is still a lot of money, but it increases the ability of these patients to take their medications, get the treatment they need, and avoid some of the consequences that you just heard about.

Senator CASEY. I know we still have some time to go to try to reach that 2020 period.

Doctor, I also wanted to ask you about building upon both Medicare and prescription drug-related improvements that were set in motion by the Affordable Care Act. If you have just three, what three policy recommendations would you have for this Committee to further limit out-of-pocket spending for people that actually receive Medicare?

Dr. HOADLEY. Thank you again. I will mention three of the items that are part of the package of MedPAC recommendations. Again, I do not speak for the Commission, but speaking for myself, one is

to try to remove some of the obstacles to the broad availability of biosimilars. There are certain of those steps you can take within the Medicare program. Some of the patent issues obviously go outside of Medicare. But there are certain things like the way the coverage gap discount is structured that can make a big difference.

Another is the common billing code that I mentioned in Part B to really put the biosimilar and the original biologic into one coding category to really put them against each other. The idea is if you are paying an average price that cuts across all of those, then any time the price comes down for one, the incentive is for the provider who is providing these drugs to go for the less expensive alternative. They can make a little money on the cheaper drug. They are going to lose money on the more expensive drug. So throwing them into that common coding category instead of setting an average sales price for each product has the potential to create some savings.

The third is in the Part D side, you know, we just talked about the coverage gap. Once people leave that coverage gap phase of the benefit, they go into the catastrophic phase. Now, usually when we talk about catastrophic coverage, it means you do not pay anything more. But in the Medicare Part D program, you continue to pay 5 percent of the cost of the drug. And so for a $5,000 drug like Enbrel, you know, that is still a lot of money. That 5 percent is still going to add up to $250 a month. And if we put a hard out-of-pocket cap on the program, then once people reach that maximum number of dollars, then you would not have to pay anything more for the rest of the year.

I would emphasize that the recommendations we made at MedPAC were a package and I think they go together, but I am just pulling a few out to highlight.

Senator CASEY. Thank you, Doctor.

The CHAIRMAN. Thank you, Senator Casey.

Senator Tillis?

Senator TILLIS. Thank you, Chairman. And thank you all for being here.

I wanted to start, I think, with Dr. Hoadley. Dr. Hoadley, I worked in research and development in the high-tech sector, but in research and development back in the 1980's. And as a product manager, when a new idea would come to me to try and build a business case for an R&D investment, I had to take a look at what my timeline was going to be—you know, what was the market life of this invention? I worked at Wang Laboratories up in Boston—and what the timeline was going to be and whether or not it was viable. And I am kind of curious to see, you know, we have had some bad actors in the pharmaceutical industry. We had the hearing I think when the Turing subject was up. Those are bad actors. You just need to deal with them and hopefully put some of them in prison. But I still hold out the belief that the pharmaceutical industry and the research and development capability they have is a very important part of developing treatments and cures that can address some of the health problems in the country.

So I am trying to get an idea maybe from you in terms of what kind of things can we work on that both those advocating for changes, those who have legitimate concerns about patent lengths,

those sorts of things, but what kind of discussion can we get into that could bring the industry and people on both ends of the argument together in terms of any specific maybe quick hits or low-hanging fruit to really make progress, in your opinion or the opinion of anybody else on the panel?

Dr. HOADLEY. Yes, thank you. It is a good question. And I think, you know, again, to focus on the biosimilar, original biologic competitive field, this is an area where we are trying to get the market to work. You know, in the traditional drug field, generics come in and have been one of the reasons why drug costs leveled off for much of the period from, you know, 2005 or so to about 2015. We did not see a lot of growth in drugs because a lot of those popular drugs to treat blood pressure and cholesterol had new generics entering the market, and people were able to switch to those generics and accomplish savings that were often in the range of 80 to 90 percent discounts once you had multiple competitors in the market. And we need to harness those forces of competition in the biological arena. And when you have situations where a drug like Humira that has been on the market for, I think, about 15 years now and because of the patent settlement they got, they are going to stay on that market another 5 years, you are forgoing the opportunity really to have a robust competitive market and let the products compete and bring the prices down. And so I think, you know, there are a bunch of steps that you could take. It is hard to know exactly what the right—some of them I focused on in terms of making sure Medicare does not get in the way of competition once they are on the market. But I also mentioned things like—and Mr. Mahn mentioned things like the interchangeability standard at the FDA and for a drug like Enbrel or Humira, which are drugs that people inject themselves and pick up at the pharmacy, you know—when you get a prescription for Lipitor, the pharmacist automatically substitutes the generic version unless the doctor specifies otherwise. And should we be in a situation for substitution that works like that for some of these biosimilars? And some states have been writing laws on what are the right terms for doing that. I think those are just areas we need to look more into to make sure that once the products get on the market, they can really enter into a competition, as well as making sure they get on the market in a prompt fashion.

Senator TILLIS. And just back to the comment I made earlier, the key here is to make sure—I am concerned with making sure we get the policy right so that it does not have an effect on the risk that the industry and researchers can take on the drugs, because at a publicly traded or privately held company that is in this business, ultimately it has to make sense, and they have to have some reasonable time horizon to recoup whatever investment they have on the risk. But I think we have got more work to do.

Mrs. Bernard, to what extent does the cost of copays and cost of drugs affect your ability to actually do what your doctor asks you to do in terms of proper treatment? In other words, do you believe that there are people out there that are simply not complying with the doctor's orders because they just simply cannot afford it, a lot of them?

Mrs. BERNARD. Oh, absolutely.

Senator TILLIS. I mean, there are various reasons why people do not comply. Some of it is they do not like the physical therapy or they do not like the effects of the drug. But I think that we have got to realize that one of the biggest issues we have in Medicaid is a lack of compliance. Some of that is just behavior that we need to change, but some of it is because the costs are simply at a point where they cannot do it, and they are making a decision to harm their health, and that is why this hearing is so important.

Dr. Harvey, a last question for you. To what extent do financial factors weigh in to your decision about the drug regimen you are willing to give somebody? In other words, if you know you have got a compliance risk, you may be prescribing something that may be too costly. Do you make a decision about a lesser treatment just because you think it is more likely that they will comply with it?

Dr. HARVEY. Every day. And it is a tragedy, actually. The reality of the matter is it is easier for a patient to walk out of my office with a prescription for oxycodone than it is for a treatment that will actually treat their disease, and that is contributing to the problems we are seeing in all of our states.

If I may, in response to the question about what you could do to try to solve this tension between research and development and innovation and controlling costs, I think the answer is value. When I buy a screwdriver or a car, I do not generally question how much it costs, the manufacture of that thing, when I decide whether I want to buy it or not. I decide if it has value to me. And so our message to the industry has to be we will pay for value, but the difficulty here is we have to define it. Defining value is the hardest part of this equation, and I think if we work together to do that, then we can start having a conversation about what things are valuable to pay for.

Senator TILLIS. Thank you.

The CHAIRMAN. Thank you, Senator.

Senator Gillibrand?

Senator GILLIBRAND. Thank you, Madam Chairwoman.

As many of you are aware, one of the top treatments for RA—and this has been addressed by the panelists earlier—is Humira. Last month the New York Times reported that between 2012 and 2018 the price has increased by 100 percent, costing patients more than $38,000 a year.

Dr. Harvey, in your testimony you also describe instances where your patients have rationed or gone without treatment due to prescription high costs. Given the limited number of drugs available to patients for treatment of RA, do you believe that companies who significantly raise the price year to year should be held accountable? What types of sanctions should we be imposing on such companies? And how might such penalties help to deter drug manufacturers from engaging in this kind of price gouging?

Dr. HARVEY. Thank you for that question. It is a difficult one to answer because I am not a policy expert per se. But I will tell you that stories like Mrs. Bernard's and the issues that happen to patients every day—I just wrote in my testimony about a woman who called crying because she had spilled her medication. When I said, "How could you spill the medication?" she told me she tried to in-

ject half of it so that it would last longer. It is really just awful what people go through to try to extend their therapies.

So I cannot speak to how we should hold the industry responsible. I will just reiterate that we have to do something.

Senator GILLIBRAND. Drs. Hoadley and Harvey, in your testimonies you both described the importance of patient access to biosimilar products in order to ensure affordability and competition in the market. Under the current system, however, it appears that many brand-name biologics have the ability to delay expiration of their patents and enter into settlements with the competition, thereby ensuring continued control of the market, and both of you have talked about that already.

Should drug manufacturers that block market access to biosimilar or generic drugs that would compete with their products be fined or otherwise penalized? What sort of sanctions might be effective in deterring manufacturers from blocking competition? If Congress were to take up legislation to address this kind of prolonged market exclusivity, what factors should be considered in determining the optimum period for which a brand-name drug manufacturer should have regulatory exclusivity?

Dr. HOADLEY. You know, it is a great question, and I am not sure there are easy answers to it. The issues of what happens in these patent cases have a lot of complexities, and I think Mr. Mahn talked about there are some cases where there is probably legitimate reasons going on around the intellectual property. There are other cases that seem much more about pure delay tactics. And I think, you know, maybe we need to empower the FTC to take a stronger role. Maybe we need to look at sort of are there certain legitimate reasons, and then when reasons do not meet that test, whatever that test would be—I am not a lawyer. I am not going to try to get into the intellectual property issues. But then potentially there is either, you know, you do not allow that extension to go on, or you invalidate that settlement or something like that. I think it is something we really need to try to study better and get into and figure out how to deal with that.

Dr. HARVEY. And I might also raise a subtle issue that was mentioned before about caps on out-of-pocket expense. We talk about biosimilars or increased competition. The best that we have seen so far is that the price of these therapies with competition has decreased 30 to 40 percent. If these medicines cost $50,000, it does not matter to the patient who still has a copay that is unaffordable.

So the package that he referred to is really important. There has to be not only something that brings down the price of the drugs, but also something that limits the expense to the patient.

Senator GILLIBRAND. This is a very outside-the-box idea, but do you think there is any room or relevancy to trying to create not-for-profit drug manufacturers who do not have a profit motive so they are not focused on things such as price gouging and over-exclusivity whose goal is not just shareholder profit but perhaps well-being of patients in this country and in the world?

Dr. HARVEY. I think it is an interesting idea. I think I am going to get an MBA now. But people have talked about that. Recently Intermountain Health in the Midwest I think raised the possibility of forming a generic drug manufacturing process within their orga-

nization. So it is being talked about, and I think people smarter than me would have to understand the business aspects of that. But it is intriguing.

Dr. HOADLEY. I agree it is an intriguing idea. You know, one of the things that you find is that some of these drugs get developed by startups, sometimes with federal dollar support, sometimes with maybe a patient association putting some of the money into it, and yet they still end up with very high price tags and all the other issues.

So, you know, we are seeing some of that sort of public sector or nonprofit sector building into some of the investment. It does make a certain amount of sense to say, well, then figure out a way not to have this all be a profit motive at the other end of the line.

Senator GILLIBRAND. Thank you very much, Madam Chairwoman.

The CHAIRMAN. Thank you.

Senator Donnelly?

Senator DONNELLY. Thank you, Madam Chair. And to all of you, this is a particularly poignant hearing for me. I have a family member who has rheumatoid arthritis and who was actually in the trials for Enbrel. And, Mrs. Bernard, as you mentioned, before Enbrel came along, it was hot showers and trying to get going in the morning. And Enbrel changed my family member's life to the point where they thought, "This has worked so well. I do not feel any more symptoms. It must have gone away." And as college students often do in their infinite wisdom, decided that they had been cured and stopped taking it, and found out shortly after not so much. But it had changed lives, just like for you. And when you think of going back to where you were before that point, it is just not thinkable.

And the thing that has always haunted me, Madam Chair, was always that my family member who had juvenile rheumatoid arthritis, we were able to figure out a way to pay for it. But there was some young person with a single mom or single dad in the same situation who was still taking hot showers, still moving forward with disfigurement simply because they did not have the funds to do it.

And so we had a health system where your future was basically dependent on what you could pay and what you could not pay, and we had a system where your future of whether you were going to be in a wheelchair or not was based on almost what house you were born in. And that is just not right. It is just not right.

Dr. HARVEY. That is right.

Senator DONNELLY. And so I wanted to ask you, Dr. Harvey, you know how our ability to treat rheumatoid arthritis has gotten better. Can you talk about what you see in the future, what future treatments you are seeing, and where you think this is going?

Dr. HARVEY. Sure. Well, I think the most important point to emphasize is that when someone walks into my office today with a new diagnosis of rheumatoid arthritis, I can tell them with reasonable certainty that their hand will never look like my fork if they can access the treatments as you alluded to.

What is coming in the future is, I think, more——

Senator DONNELLY. Which is a dramatic improvement over where it was.

Dr. HARVEY. It is a dramatic improvement. In fact, I saw a remarkable picture from the Arthritis Foundation. They have Hill days—one from the 1980's where everyone was in a wheelchair, and one from the 2000's where everyone was standing. It is remarkable. It is remarkable.

What is coming is, I think, more biologic therapies. We are starting to learn how to target very specific parts of the immune system. Our treatments over time I believe will get more specific, more effective. And so I think the trend that we are seeing is only going to get larger.

There is also an interesting bit of research going on in the area of nanotherapy, so being able to take medications that are already existing today but create very small doses of them that get to the place where they are effective so that you do not have to give large doses that are toxic to the whole body. Again, a lot of research and development into those treatments means they are likely to be quite expensive when they do come to the market.

But the story is not over. We are finding new ways to treat these patients every day.

Senator DONNELLY. How important has the NIH been to that effort?

Dr. HARVEY. Essential. In fact, Enbrel and Remicade that Mrs. Bernard is taking were able to be marketed because of initial discoveries out of the National Institutes of Health, and the primary initial treatment for juvenile arthritis, which you referred to, was also based on an NIH discovery.

Senator DONNELLY. When you look at that, how important is it to keep the NIH fully funded and moving forward?

Dr. HARVEY. So the NIH plays an important role because they do the most basic essential research and development work, you know, laboratory work with petri dishes and mice and such, that the pharmaceutical companies do not do. They are not doing that very basic research. They are taking the discoveries that come from NIH and taking them to the next level where they proceed with the drug development process. So without that seeding, we will not have discoveries in the future, not to mention the fact that researchers, including myself and many others, get NIH funding in order to do clinical-based research to find out how these therapies work most effectively in patients. So it is an essential part of our future.

Senator DONNELLY. Thank you very much. And, Mrs. Bernard, my goal is that we cure this so that when you are 100 years old, you do not even have to worry about it anymore.

Thank you, Madam Chair.

The CHAIRMAN. Thank you.

Senator Blumenthal?

Senator BLUMENTHAL. And I hope we reach 100 years along with you.

[Laughter.]

Senator BLUMENTHAL. At least Senator Donnelly.

Thank you all for being here. This hearing has been enormously helpful and enlightening, and thanks to our Chair and Ranking Member for holding it.

Dr. Harvey, as a practicing rheumatologist, your voice is very, very important in this discussion. My understanding is that rheumatoid arthritis therapies typically come either in a self-injectable form or an intravenous form, and I am sure you are aware that nationwide there is a shortage of small-volume IV bags as a result of manufacturing facilities in Puerto Rico losing power during the recent hurricane. This issue is one of profound public health importance, as are shortages of other medical devices and other often workhorse medicines, shortages that affect the quality of care in Hartford Hospital and other hospitals in Connecticut and every hospital around the country.

I have led a bipartisan, bicameral letter to FDA Commissioner Gottlieb on the IV bag issue, and I was pleased to see that this letter was supported by Chairman Collins and Ranking Member Casey. I appreciate their help and support. This letter very simply urges the FDA to use all of the tools at its disposal to address these ongoing shortages, which have impacted patient health in Connecticut and across the country. More specifically, it asks what expanded authorities are needed to prevent these kinds of shortages from occurring, and often, unfortunately, reoccurring in our health care system, and what measures can be taken to assure that companies are creating contingency strategies to avoid chronic shortfalls.

This long-winded introduction to my question is to drive the point that with rheumatoid arthritis, as with other illnesses, the shortages of critical drugs and devices can be very impactful. So my question is: Has this IV bag shortage impacted your ability to administer rheumatoid arthritis therapies? And do you think that the FDA, in coordination with the manufacturers, should do more to establish contingency strategies?

Dr. HARVEY. So I am not aware of any instances of the IV bag situation specifically affecting our infusion therapies. Although they are reconstituted with saline, it is usually a small volume, and it is not so troublesome.

However, we have seen over the years many drug shortages in medicines that have been around for decades, like methotrexate or hydroxychloroquine, brand name Plaquenil, that happen because of manufacturing facility problems—and in some cases there is only one manufacturer or two manufacturers of these therapies—leading to national shortages of generic drugs.

And so the answer to your question is yes, absolutely, the FDA should do everything in its power and you should grant it the power to do whatever it can to address drug shortages as quickly as they can.

Senator BLUMENTHAL. Do you have thoughts about what it can or should do?

Dr. HARVEY. Again, a somewhat complicated question, but I can tell you that during some of these shortages—we are about a 5-hour drive from Montreal—I have had patients drive across the border to get their therapies. Our more wealthy patients can explore things like reimportation on their own. But, obviously, the

government can explore that opportunity as well. And ensuring that there is redundancy for these essential—especially the essential sort of safety net therapeutics like IV bags, but also drugs that treat rheumatoid arthritis, making sure that there are redundancies so that we are not as impacted when something happens.

Senator BLUMENTHAL. And would you agree that it is not the sort of—I do not know what layman's terminology might apply, not the advanced cancer drugs that cost hundreds of thousands of dollars. We are dealing here with workhorse generic medicines, saline solutions, IV bags, basic sort of workhorse, everyday drugs, correct?

Dr. HARVEY. Yes, sir.

Senator BLUMENTHAL. I appreciate the opportunity to ask you—I know others of you on the panel may have thoughts about it, and my time has expired. Thank you.

The CHAIRMAN. Thank you, Senator.

Dr. Hoadley, actually Senator Blumenthal's question is a good intro to my next question, because living in Maine I am very well aware of how much less expensive pharmaceuticals are on the other side of the border in Canada. We know that our country is the global leader in the research and development and innovation of pharmaceutical drugs that lead to therapies and cures around the world. And yet the prices that we pay here in this country are almost always, it seems, higher than what people in other countries pay. And the chart that we have handed out to you, as well as put on the screen, shows that the cost of Humira varies enormously for a 1-month supply from $552 in South Africa to $1,362 in the United Kingdom to nearly $2,700 in the United States.[A copy of the chart follows in the Prepared Statements]

Is the United States essentially subsidizing the cost of prescription drugs for the rest of the world?

Dr. HOADLEY. I think it is. You know, it is a really interesting question, and I have looked at some of these numbers from time to time, and, you know, if you would have drawn a picture of this 10 years ago, it would have looked very similar. So it is not something that has changed, maybe it has gotten worse.

You know, other countries are making certain decisions about how to handle pricing, so in the United Kingdom they have the group called NICE that evaluates the clinical and cost-effectiveness of drugs and helps to make decisions about which substitutes should be available and addresses it. Some of these countries have other methods for sort of addressing pricing. You know, I think we as a country need to look at that question and say should we be taking some of those steps here in the United States and what would be politically acceptable, what would be acceptable to the broad public.

But, you know, this notion that it has an impact on research and development that a lot of people worry about, well, these are international companies. I mean, it is not like we get our drugs from U.S. companies and the U.K. gets their drugs from U.K. companies or Switzerland gets their drugs from Swiss companies. We all get them from companies all over the globe. It is a true global industry. And if you are seeing price differentiations like this, it does seem like it is the logical conclusion to say we are subsidizing the world.

The CHAIRMAN. Thank you.

Dr. Harvey, prescription drug prices are the second fastest growing component in health care costs, and when I asked my staff, well, what is No. 1, I was really surprised to learn that it is administrative costs. And yet your testimony today made the light bulb go off because you described how it took an hour of a provider's time to get prior authorization from an insurer to prescribe a drug that is needed to provide the relief that your patients deserve.

Are there other examples that you—and, Dr. Hoadley, you mentioned the need for a common code, for example. So it seems like there are some administrative efficiencies that could be achieved. But, Dr. Harvey, are there other examples you could give us of why administrative costs are the fastest-growing component of health care expenditures?

Dr. HARVEY. Sure. So dealing with the step therapy, as I mentioned, is a big one. And, in fact, we are even seeing prior authorization requests for medications that have been around for a long time. I got one the other day for prednisone. I do not know why still.

The CHAIRMAN. That is amazing, truly.

Dr. HARVEY. Other things, you know, our reimbursement system for physicians is built on evaluation and management codes that have pages of instructions on what qualifies for various levels of payment. I spend a lot of time doing documentation to support revenue which pays for the pharmacist and other things because our billing and coding system is incredibly complex. ICD–10, for example, changed the number of billing codes for rheumatoid arthritis from about 50 to about 250. So I have to figure out which of those codes is most appropriate for billing for an individual patient.

There are also medical-legal aspects to this where there is a certain amount of documentation that has to happen in order to protect myself and my organization from the threat of future lawsuits. All of this sort of conspires together. Imaging, medical imaging, is another one. I have to get prior authorizations to get my patients CAT scans and MRIs. I even sometimes have to get prior authorization to get a blood test for my patient to make their diagnosis.

It has become a process which is out of control and absurd. I will just tell you one quick story about the absurdity. The other day I was on a prior authorization appeals process. I was assigned to speak with a peer reviewer. This is another physician, not a rheumatologist, who was assigned to review the case. I told them what I wanted to give for my patient, and I heard some keyboards clacking in the background. And after they were done clacking, they said to me, "Well, I just Googled this, and I do not see anything about what you were talking about for this case." You know, if it was that simple, we should all go back to Maine tonight and take care of the probably thousands of underserved patients there because, you know, it is just absurd.

I understand why these processes are in place. Costs are skyrocketing. But there has to be thought about the impact that we are doing, because every time I am filling out one of those papers, I am not taking care of someone like Mrs. Bernard.

The CHAIRMAN. Thank you. That is a terrible example that you just gave, and it is really troubling to me.

By the way, we are very underserved for rheumatologists in the State of Maine. There is only, to my knowledge, one in Bangor, Maine, where I live, which is the third largest city in Maine. And there are none north of Bangor. One rheumatologist in Maine just recently retired who used to do clinics in Aroostook County in northern Maine. So if you could send some our way——

Dr. HARVEY. In fact, I am, Senator Collins. The fellow who is graduating from our training program this year will be practicing in Lewiston starting in July.

The CHAIRMAN. I am very happy to hear that. Good work. Keep them coming, because, truly, given our population is an older population, we really do need more rheumatologists, so I am happy to hear that.

Mr. Mahn, I promised that I would come back to you, and this will be my final question. You suggested in your testimony that there are times when the brand name manufacturers file for a lot of additional patents, and we have noticed in our research this often happens when the initial patent is getting close to the expiration data, and that at times there are very minor changes that are made in packaging, for example, that are used to justify additional patents.

Could you talk to us generally about patent thickets and ever-greening? You mentioned ever-greening in your testimony, but could you help us better understand the role that plays?

Mr. MAHN. Thank you, Chairman Collins. So when you talk about a patent thicket or ever-greening, it just means really if you are a manufacturer assembling a portfolio that protects the franchise—Abbvie brags about it in their public statements. They brag that their portfolio is so formidable that they expect to have the market to themselves through 2022 or 2023.

Now, if you look at the two suits that Abbvie has filed to protect Humira—and this is the two waves of litigation I talked about under the BPCIA, the biosimilars laws. Under the first wave, they are litigating, I think, six or eight patents against both of the biosimilar entrants that have been approved. And they have stated that in the second wave they are going to assert another 60-some patents.

Well, that does not add up to 100, so there are 30 or 40 that do not apply. And that is a telling story, which is that a lot of these patent thickets are, you know, to just be formidable, to scare, to say, look, there is a lot that we can throw at you.

Now, you cannot throw, justifiably throw invalid patents. You cannot throw patents that do not reasonably—that are not reasonably infringed. So as a lawyer representing a client with a large portfolio, you cannot just assert it because it has been granted. There has to be some good-faith basis—Rule 11, we call it—in litigation before you can assert those things. So a lot of times the thicket has a lot of underbrush that really does not matter.

In other cases, a lot of these patents are perfectly good patents. They cover perfectly sound discoveries and inventions. But they are not going to stop competition. They just will not. An example, which actually, it is funny, it is anecdotal. I had some antihistamine issues, and so I was seeing a doctor, and he gave me a prescription after I had gone through some stuff. He said, "Here, try

this." And I went to the pharmacy, and they said, "Your insurance will not cover this because it is not generic." So I thought, "Oh, great. So I will have to pay out-of-pocket." So I went back to my doctor, and I said, "What is this about?" And he goes, "Oh, here, here is the other prescription." I said, "What is that?" He said, "It is the exact same drug only you take it twice a day rather than once a day." And my insurance company covered it completely.

Well, I thought that was pretty fair. I mean, if they said, "Do you want to pay more for once a day or nothing for twice a day?" Now, that was because a patent on the once-a-day application was issued, protected—it is also known as product copying where you take a product that you have built a market around and then you move it as the competition comes after you to some new use or some new convenience that the market then begins to accept quickly, and then nobody wants the old stuff. Well, in a perfect system, a lot of people would want the old stuff. They would say, "OK, look, you have got something that is more convenient. Somebody has to pay for that. You are entitled to recover the investment you made to make that more convenient. And I am not willing to pay for it. I am happy with the old stuff." But the market does not smoothly work that way.

So a lot of these patents add things on to drugs, but that does not mean a generic cannot come along or a biosimilar cannot come long and get approval for non-infringing features and aspects and uses and so forth to avoid those patents. And that is what happens in many cases.

The CHAIRMAN. Thank you.

Senator Casey?

Senator CASEY. I am all set.

The CHAIRMAN. You are all set? OK.

I want to thank our witnesses for your testimony today. It is a difficult challenge for Congress to come up with the right response to the issue of escalating costs of prescription drugs. It involves complicated patent issues, as we have just heard. It involves the prior authorization problems that insurers impose on providers. It involves policies of Medicare that are different than private insurers and can impose enormous costs on patients as they age into the Medicare program. And it involves our desire to make sure that we prevent these flagrant abuses of the system that have led to an escalation of costs without justification without dampening or discouraging the innovation that brings us these wonderful biologics and other drugs that make such a difference in the lives of people like Mrs. Bernard. And that is a hard balance to strike, and it is what we are going to continue to look into in this Committee.

Senator Tillis is right that there are some obvious bad actors out there, and we focused on them last year. I will never forget one of the CEOs, when we were interviewing him, and we asked why did you increase this drug which you had no involvement in developing overnight by an enormous percentage, and he said, "Because I can." I mean, it was just a case of pure, simple greed.

On the other hand, the statistics that we know of how few drugs make it from the laboratory to the market and the cost of developing a new drug which can be so expensive urges us to take a cautious approach and make sure that we know what we are doing

when we are dealing with legitimate pharmaceutical companies as opposed to what I call "hedge fund pharma"—a term they do not like, by the way, but it does seem appropriate in many ways.

So I want to thank our witnesses for helping us better understand exactly the complexity of these issues, and yet I am determined that we end the abuses and that we also make life easier for patients like Mrs. Bernard, whom I thank very much for coming from Maine and sharing your story, and providers like Dr. Harvey who want only the best for their patients. So I thank all of you for being here today, and I thank our staff for their hard work also.

Senator Casey?

Senator CASEY. Thank you, Chairman Collins, for this hearing, and also I want to thank our witnesses for your presence here, your testimony, for the time you took today, but also for helping us better understand a number of these issues.

We learned today that living—among other things we learned, we learned that living with arthritis is a common experience for so many Americans, especially rheumatoid arthritis. For people with arthritis, access to affordable and appropriate treatment is absolutely essential. We must promote pathways to foster innovation and promote access to life-changing medications. We must also ensure that baby boomers or older adults can afford the treatments that work best for them. We thank you for your time today, and we are grateful that you took the time to be with us.

Madam Chair, thank you for the hearing.

The CHAIRMAN. Thank you. Committee members will have until Friday, February 16th, to submit additional questions for the record, so there may be some coming your way.

This concludes our hearing. Again, my thanks to all of our witnesses.

[Whereupon, at 11:04 a.m., the Committee was adjourned.]

APPENDIX

Prepared Witness Statements

Prepared Statement of Patricia Bernard, Rheumatoid Arthritis Patient, Falmouth, Maine

Good morning. Thank you Chairman Collins, Ranking Member Casey, and distinguished Members of the Committee for inviting me to testify before you today.

My name is Patty Bernard. I will turn 81 in July, and I have rheumatoid arthritis. I have lived with diagnosed RA since I was 55. Before the diagnosis and treatment, I experienced excruciating pain—day-in and day-out. Every bone in my body ached. The pain made ordinary tasks difficult, often impossible. I would come home from work and take hot, hot showers. It was the only thing that relieved my pain—even just temporarily.

I finally visited a rheumatologist and learned that I had RA. In fact, at that time, my doctor informed me that 79-percent of my body was inflamed. It was very difficult to hear the doctor tell me I had RA. My cousin had the disease, and I saw what it did to her body. She was in a wheelchair, and her hands were like clubs. That night, I went home and cried.

My doctor tried many drugs, but they didn't help. As I entered my 60's, my symptoms grew worse. My doctor discussed adding gold injections. Just as I was ready to try that, something new came on the horizon—a drug called Enbrel. I was one of the first in Maine to try this therapy. I got my first shot of Enbrel at the doctor's office. The doctor warned me not to expect it to work right away. But that day, as I was driving back to work, I could feel something going through my body. That afternoon, I felt so much better. It was incredible. I just couldn't believe it.

Enbrel gave me my life back. I no longer woke up in the morning with excruciating pain or came home in the evening aching in agony. Because I had insurance through my job, I paid anywhere from $10 to $30 each month depending on my company's insurance plan. Every other week, I was able to give myself injections. Besides that, I was finally able to live an ordinary life. I went to work. I walked, I swam, and I took the stairs because I could.

For 19 years, I depended on Enbrel. My employer-sponsored insurance switched several times over the years. But, every time, my employer went out of his way to find an insurer that would cover my Enbrel.

Although I didn't really want to stop working, I retired in December 2016 at the age of 79. I would no longer have insurance through work. In the transition to Medicare, I was devastated to learn that I would have to pay $3,800 a month if I were to remain on Enbrel; $3,800 a month! I do not have that type of money. I would wake up in the middle of the night panicked. I feared I might have to sell my house. I was afraid that if I went without this medication I would end up back in so much pain and even in a wheelchair. The anxiety started causing heart palpitations that put me into the hospital on more than one occasion, one time over Christmas.

My rheumatologist proactively helped to find me an affordable option. He suggested a treatment called Remicade. It was not self-administered like Enbrel. Instead, I would have to go into the doctor's office to receive the infusion. Worse, there was no way to know whether or not it would work. I was scared. I knew that Enbrel had worked well for nearly two decades, and stopping it felt like going backwards. I even called Medicare, and told them, "I don't understand. I am actually saving you money by administering the Enbrel myself." They said that's the way it is.

I was nervous the day I went to the doctor's office for my first injection of Remicade. Thankfully, after a year on this treatment, it has worked. It is not convenient compared to administering the drug myself. I have to go into the doctor's office in Portland once a month, and each infusion takes about two and a half hours.

I do not understand why I would need to pay nearly $4,000 in a single month for a drug that for years I had for no more than $30 a month. I am grateful that I do have something that works so that I can be productive for my family, church, and other friends who aren't as fortunate as I am. But, I feel very strongly that people should be able to access the treatment they need at an affordable cost.

Thank you for the opportunity to testify and I am happy to answer your questions.

Prepared Statement of William F. Harvey, M.D.
Rheumatologist, Associate Professor of Medicine,
Clinical Director, Division of Rheumatology, Tufts Medical Center, Boston, MA

Chairman Collins, Ranking Member Casey and distinguished members of the Committee on Aging, thank you for allowing me to speak before you today. My name is Dr. William F. Harvey and I am a practicing rheumatologist at Tufts Medical Center in Boston, MA. In addition to my daily duties caring for patients with rheumatic and musculoskeletal disease, I participate in research into treatments for these diseases and work to develop information technology to better care for patients. I am also privileged to hold a volunteer position on the Board of Directors of the American College of Rheumatology (ACR), which represents approximately 9,500 rheumatologists and rheumatology health professionals. The ACR advocates for, among other things, affordable access to treatments for chronic conditions including Rheumatoid Arthritis (RA), Psoriatic Arthritis, Lupus, and many more. I wear on my lapel a bent fork, created by the ACR as a symbol to remind everyone that when you have arthritis, even simple tasks, like using a fork, can be difficult.

Recent advances in the treatment of Rheumatoid Arthritis and other diseases have created a "new normal" for patients suffering from rheumatic diseases. With early diagnosis and treatment, the disability and disfigurement also symbolized by the bent tines may be prevented. A great tragedy emerging in our country is the increasing barriers to accessing these treatments, primarily related to their high cost. Before I discuss some of those barriers, I would like to share some background information.

Rheumatoid Arthritis is one of more than 100 auto-immune diseases. Auto-immune diseases are those in which the immune system attacks various parts of the body, instead of bacteria and viruses. In the case of rheumatoid arthritis, the immune system attacks the lining of the joints, most often in the hands and feet. Rheumatoid arthritis is the most common auto-immune disease targeting the joints, affecting over 1.3 million Americans. It afflicts women 2-3 times more frequently than men and has a peak incidence in middle age. However, it can be diagnosed at any age, and has a juvenile form. Because rheumatoid arthritis is a lifelong illness, there are many seniors today living with RA. Untreated, rheumatoid arthritis leads to significant joint damage, disability, and pain. Fortunately, today we have highly effective treatments for the condition.

Several decades ago, the mainstays of treatment were effective but highly toxic medications such as gold salts and steroids such as prednisone. While the latter is still used today, these medications do little to alter the progression of the disease and prevent disability. After advances in the 1980s, these medicines can effectively treat up to half of patients with RA. Examples of these disease-modifying anti-rheumatic drugs, or DMARDS, are hydroxychloroquine, leflunomide and methotrexate. These medications allow patients to get off the toxic steroids and prevent disability. Taken by mouth, they all currently have generic and brand name formulations and cost anywhere from a few dollars a month to several hundred. After application of insurance coverage, most patients pay co-pays less than 50 dollars each month for these medications. However, some patients will need additional medication to treat their disease.

After building on discoveries made initially by researchers funded by the NIH, pharmaceutical companies developed a new class of drugs called biologic DMARDs. They have the name "biologics" because they are proteins made from living organisms, and they are all administered via injection under the skin or by intravenous infusion. The ones available to inject under the skin may often be self-administered by the patient at home. Though designed in a laboratory, even today they are produced through a highly complex proprietary process involving using bacteria or other living organisms to produce copies of proteins that block parts of the immune system. Targets of these therapies include tumor necrosis factor alpha (TNF-α),

Interleukin 6, CD88, and CD-19, among others. These therapies are marketed by pharmaceutical companies under brand names, and there are currently 10 therapies in this class. Because of the complexity of production and the necessary quality control, these therapies are very expensive to study and produce. Consequently, their marketed are over $50,000 per year. Though highly effective, out-of-pocket costs to patients for these therapies can reach several hundred or even thousands of dollars per month. There are no generic versions of these treatments. Recently, biosimilars – which are not generics in the traditional sense because they are not exact copies of the original therapy – have begun to provide some alternatives.

Choosing the right therapy for a patient is a complex medical decision that considers other conditions and medications the patient may have, balancing the risk of side effects and many patient specific factors. Most physicians believe in the importance of shared decision making, which tailors treatment to the individual goals and concerns of the patient. Most rheumatologists start treatment with oral DMARDs and increase the dosage until the patient achieves remission or low disease state, which minimizes the risk of disability and pain. Using the lowest effective dose also limits potential toxicity of treatment, namely liver and other organ damage and infections. It may take 1-3 months, sometimes longer to find the effective dose for each medication tried. If the medication does not work, the patient will continue to have pain and disability, or require the use of toxic steroids until the right medication is found. If the oral DMARDs are ineffective, rheumatologists move on to the biologics. Factors to consider when choosing the right biologic therapy include medications already tried, history of infections and malignancy, and the ability to administer the medication to themselves. But overwhelmingly, the primary factor in the decision is which one is covered best by insurance. Because of their high cost, every one of these therapies requires prior authorization before use, a process that can take days to weeks to complete before the patient can start treatment. The same 1-3-month trial and error may be necessary, as we do not have scientific evidence to determine which treatment will work best for which patient; the result being that in may take months to get the disease under control. I will now provide some more detail about the difficulties in obtaining these treatments for patients.

I mentioned that each of these medications require a prior authorization. Each insurance company has a different set of forms requiring somewhat different types of information. Most require that the patient have their medication provided by a specific pharmacy. This is because the insurance companies negotiate; often through pharmacy benefit managers (PBMs), price discounts in exchange for preferred status on the insurance formulary. If a provider wishes to prescribe a medication that is not preferred, the prior authorization will be denied, and the provider must go through an escalating appeals process that may involve talking to a clerk, a pharmacist, a nurse, a "peer review" (another MD but typically not a rheumatologist), a same specialty review and, in the case of Medicare, an Administrative Law Judge. Each of these steps may take 10-30 minutes, during which time the provider is taken away from caring for other patients. Many practices have begun to employ at significant expense, other providers such as nurse practitioners, physician assistants and pharmacists to navigate this process. Without my pharmacist Jinkyu Lee, our resident "insurance wizard', we would drown in the administrative burden. To address this issue, I strongly endorse regulation requiring that insurance companies follow a standard, transparent process for documenting, evaluating and approving prior authorization requests. Every minute spent away from patients is a waste of providers' time and limits access for other patients. Policies requiring that a provider try therapies in a specific order are referred to as step therapy or fail first protocols. Since these are based primarily on cost rather than efficacy and shared decision-making, I strongly endorse regulation-requiring transparency of these policies and around the process by which providers may appeal to override them.

I mentioned the trend of using pharmacy benefit managers to address rising costs of therapies. At face value, this concept makes intuitive sense, allowing companies to negotiate the best possible prices for treatments. Some have advocated that Medicare exercise this same leverage. However, while well

intended the use of PBMs in this way has led to an opaque process that favors maximizing payers' profits over shared decision-making utilizing that sacred bond between doctor and patient. Pharmacy benefit managers are for-profit companies that make their margin based on the difference between the list price and negotiated price. They benefit when the list price of a treatment is increased, as it improves their ability to drive margin. Because of contract law, only the pharmacy benefit manager knows what the true difference between list price and negotiated price is. Perhaps most egregiously, pharmacy benefits managers and insurers are not required to pass negotiated savings on to their beneficiaries in the form of co-pay discounts, and in my experience in most cases, they do not. I strongly endorse requirements for increased transparency for pharmacy benefit managers – starting with properly defining terms like rebates – and for passing savings directly on to consumers.

Out-of-pocket expenses for patients are, as I have noted, substantial for these essential therapies. In addition to the issues noted above, I wanted to discuss co-pays specifically. They were originally conceived to require consumers, patients, to have some skin in the game. Medications that are more expensive carry larger co-pays, thereby incentivizing patients to request cheaper alternatives. This works well when considering typical, low-cost medications such as cholesterol, blood pressure and even oral DMARD medications. However, the system breaks down when applied to biologics for rheumatoid arthritis and other diseases. There are no generic alternatives and virtually all patients taking this medication have already tried and failed the cheaper oral therapies. Patients did not choose their disease, nor do they control the high cost of developing and marketing the only therapies left to treat their condition. Asking them to pay their 'fair share' is immoral and indefensible when it leads to medical bankruptcy. Further, these patients are more likely to leave the workforce, ending up on government-subsidized disability, which further burdens the federal government. I can say unequivocally that many patients with rheumatoid arthritis or its close cousin arthritis associated with psoriasis, that many patients have no skin left to give.

For patients on commercial insurance, most pharmaceutical companies offer co-pay assistance and other support on an income-adjusted basis. Medicare patients are prohibited by law from accessing this support. There are some private foundations that can support Medicare beneficiaries, but they are underfunded and not universally accessible. For these beneficiaries the only affordable option is to avoid self-injectable treatments, which fall under Part D pharmacy benefits and are therefore subject to copayments and the Medicare doughnut-hole phenomenon. The option in that case are those therapies which can be administered in a doctor's office or hospital by intravenous infusion and fall under the Part B benefit with lower out-of-pocket costs. This adds administrative and hospital costs to the drug costs, raising the total cost of treatment particularly in the hospital setting. But to me, and other rheumatologists, a patient who cannot afford to take their medication is an untreated patient, which we know will result in increased pain and disability. This puts providers in a very challenging position attempting to follow Medicare guidelines for appropriate use of Part B medication while making sure our patients have access to treatment. I can give many sad examples of patients under-dosing their medication to try to make their treatment more affordable, the result being suboptimal disease control and disability. For example, I have one patient who spread her injections out taking them every 3-4 weeks instead of every two. We were both frustrated with her lack of improvement and it was only when I recommended trying another medication that she tearfully let me know what she had been doing. In another case, a patient called my office upset because she had spilled her medication. I was puzzled because it came in a pre-filled syringe. It turns out she was trying to inject half the medication to make it last longer. I strongly endorse legislation such as the Patient Access to Treatment Act (H.R. 2999) or other efforts that limit or cap out of pocket expenses for patients, so that these sorts of stories never happen again.

Lastly, I wish to briefly comment on the importance of biosimilars. These are biologic treatments, which are similar to, but not exact copies of, existing biologics. A safe and vibrant biosimilar marketplace is essential to the future of rheumatologic care. In Europe, where biosimilars have been introduced into the

market earlier than in the U.S., they have seen an approximate 30 percent reduction in the total cost of the treatment. However, this level of reduction in cost did not occur until there were 3-4 competitor products in the market. The FDA has a process for approving biosimilars and two biosimilars to Remicade, a biologic DMARD are on the market. I encourage the committee to support adequate funding for the FDA to be able to rapidly but safely approve additional biosimilars. Unfortunately, other biosimilars approved by the FDA have been held up in patent litigation. Another panel member will address this issue, but I wish to reiterate generally that a vibrant biosimilar marketplace will lead to competition and reduced cost. As that happens, we must become vigilant about the drug distribution system and ensure that these savings are passed on to consumers, my patients.

I have covered many important issues with you and look forward to answering the committee's questions. I wish to thank the Chairman and Ranking Member for the opportunity to speak with you today. I have great faith in the institution of government and that its members will do everything in their power to protect the people of our nation who suffer from chronic disease such as rheumatoid arthritis and are burdened with the growing expense of treatment. These are not easy problems to solve. But the fact that we are gathered today to focus on this issue is a testament to the people of our country that it is a set of problems worthy of solving. Together we can continue the conversation and search for solutions. Compared to two decades ago, I can look at a person newly diagnosed with Rheumatoid Arthritis and tell them that their hands will never look like my fork. So long as they can access the revolutionary, therapies that we know can prevent this progression. Together, we can un-bend the tines of my fork for current and future generations, so that they may remain healthy productive members of our workforce, and more importantly our families. Mothers and fathers can pick up their kids without pain and go to work without taking too many days off. Our seniors, who have raised our nation and contributed so much, can be assured that they will be cared for without bankrupting themselves and their families. Scientific innovation has afforded our great nation so many opportunities, so long as they can access them. I look forward to working to solve those problems with you. Thank you again for accepting this testimony and I am happy to address any questions the Committee may have.

Drug Prices and Out-of-Pocket Costs for Rheumatoid Arthritis Drugs

Statement of
Jack Hoadley, Ph.D.

Research Professor Emeritus
Health Policy Institute, McCourt School of Public Policy
Georgetown University

Before the
Senate Special Committee on Aging

February 7, 2018

Good morning, Madame Chair, Ranking Member, and Members of the Committee. My name is Jack Hoadley, and I am a Research Professor Emeritus at Georgetown University's McCourt School of Public Policy. As a long-time analyst of prescription drug issues, I have published extensively on Medicare Part D and other drug issues. I also serve as a Commissioner on the Medicare Payment Advisory Commission (MedPAC). In today's testimony, I do not speak on behalf of the Commission but only for myself as an individual. I appreciate the opportunity to speak to the Committee on the issue of drug prices, specifically for drugs used to treat rheumatoid arthritis (RA), and the cost concerns experienced by Medicare beneficiaries who take these drugs.

Background

Medicare has covered outpatient drugs since the creation of Medicare Part D, which first offered coverage in 2006. However, certain drugs, particularly those that must be administered by a physician (usually by injection or infusion), have always been covered by Medicare Part B. Rheumatoid arthritis drugs include medications that fall on both sides of this program divide.

Payment for a Part B drug is made to the clinician who administers the drug. Medicare typically pays the clinician 106 percent of the average sales price (ASP) for the drug, an amount that reflects the average price collected by the manufacturer net of most rebates and discounts.[1] The cost to the beneficiary is set at 20 percent coinsurance, the usual Part B coinsurance amount. For many beneficiaries, their coinsurance is covered by supplemental coverage—either privately purchased Medigap insurance, employer-sponsored retiree benefits, or by Medicaid.

Under Part D, drugs are paid by the private Part D plan in which the beneficiary is enrolled.[2] In turn, the plan's costs (which vary across phases of the benefit) are covered by a combination of a federal premium subsidy, beneficiary premiums, and federal reinsurance once a beneficiary reaches the

[1] MedPAC, "Part B Drugs Payment Systems," October 2017. http://www.medpac.gov/docs/default-source/payment-basics/medpac_payment_basics_17_partb_final.pdf?sfvrsn=0.
[2] MedPAC, "Part D Payment System," October 2017. http://www.medpac.gov/docs/default-source/payment-basics/medpac_payment_basics_17_partd_final86a411adfa9c665e80adff00009edf9c.pdf?sfvrsn=0.

catastrophic phase of the benefit. Plans may negotiate the price of the drug with the manufacturer, often obtaining rebates (discounts) that are paid to the plan but are not reflected at the point of sale. Beneficiary cost sharing varies according to the phase of the Part D benefit. For a high-cost biological, cost sharing in the initial coverage period is typically 25 percent to 33 percent. Cost sharing rises to 35 percent in the coverage gap phase (which will drop to 25 percent in 2020, when the gap if fully phased out)[3] and then drops to 5 percent in the catastrophic coverage phase. Low-income Part D enrollees are eligible for subsidies that cover most of their cost sharing.

Competition for Rheumatoid Arthritis Drugs

The market for rheumatoid arthritis drugs consists of at least ten different biological medications as well as several older traditional medications. These drugs vary in terms of their mode of action and their method of administration, and some are much newer on the market than others. Some RA drugs are approved for other health conditions as well. The drugs in this class that require administration by a clinician are covered under Medicare Part B. Those which can be self-administered are covered under Part D. This coverage split in the RA drug class has implications for the method of payment used and the determination of out-of-pocket costs. It also affects the extent to which market forces work.

At present, three biological drugs dominate the RA market. Together Enbrel, Humira, and Remicade represent over two-thirds of the RA market. Enbrel and Humira are covered under Medicare Part D and Remicade by Part B. Between 50,000 and 60,000 beneficiaries use each of these drugs, based on the most recent CMS data.[4]

The presence of multiple competing drugs in this class might be expected to help keep prices from growing rapidly. But evidence suggests otherwise. For context on the trend in drug prices, we can refer to MedPAC's annual calculation of a Part D price index.[5]

MedPAC's index data show that overall Part D drug prices rose cumulatively by 57 percent from 2007 through 2014. However, MedPAC's separate index calculation for the same timespan taking generic substitution into account was only up by a cumulative 8 percent. The difference is explained because many traditional drugs have seen patent expirations that allowed brand drug users to switch to much cheaper generic alternatives.

Notably, prices for biological drugs have grown far more rapidly—up by a cumulative 119 percent over the same years (2007-2014), compared to the 57 percent growth for all Part D drugs. These high-cost drugs include the rheumatoid arthritis drugs that are covered under Part D.

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[3] As enacted in the Patient Protection and Affordable Care Act, beneficiary coinsurance is reduced gradually until reaching 25 percent in 2020.

[4] CMS, 2015 Medicare Drug Spending Dashboard. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs/2015Medicare.html.

[5] MedPAC, "Report to the Congress: Medicare Payment Policy," Chapter 14, Status Report on the Medicare prescription drug program (Part D), March 2017. http://www.medpac.gov/docs/default-source/reports/mar17_medpac_ch14.pdf?sfvrsn=0.

It should be noted that these price indexes exclude manufacturer rebates. CMS reports that rebates have increased generally over this same period (though data are not available for specific drugs or drug classes), so price increases net of rebates may be somewhat lower.

Cost to Medicare and the Beneficiary for Rheumatoid Arthritis Drugs

Looking specifically at the costs of the three most common RA drugs, they are expensive for both the Medicare program and the beneficiaries who take these drugs. In addition, the costs continue to rise.

In 2015, Remicade was one of the top five Part B drugs in terms of annual costs to Medicare—at $1.2 billion.[6] An average user of Remicade had $4,280 in out-of-pocket costs over the course of a year. As noted before, many beneficiaries have these costs are covered by supplemental coverage or Medicaid. Total spending on Remicade rose 34 percent between 2011 and 2015 or about 8 percent per year.

On the Part D side, Humira had the largest market share and a total cost for Medicare beneficiaries of $1.6 billion in 2015 (although Part D spending totals are calculated before the rebate discounts arranged between manufacturers and plans).[7] In terms of total dollar volume, it represented the 10th costliest Part D drug. An average user of Humira incurred $1,588 in out-of-pocket costs for the year. This amount is less than the average for Remicade because cost-sharing drops to 5 percent after a beneficiary exceeds the catastrophic spending threshold. Furthermore, a beneficiary taking a full dose of Humira for an entire year would incur almost $5,000 in out-of-pocket Part D costs for that drug.[8] Total spending for Humira has more than tripled—up 224 percent from 2011 to 2015. This reflects both a 79 percent increase in the unit price combined with a similar increase in volume.

The numbers for Enbrel are similar: $1.4 billion in total volume in 2015 and $1,590 in a year's out-of-pocket costs for the average user.[9] Total spending for Enbrel more than doubled—up 144 percent from 2011 to 2015. Like Humira, its price rose about 80 percent, but it experienced more modest volume growth.

It is worth noting that price increases have been more modest on the Part B side, in part because most rebates are incorporated into the Part B pricing system and in part, because the ASP system may be more effective in controlling price increases than the tools available to Part D plans.

Biosimilars: Potential for Savings and Barriers

Over the last decade, one of the largest checks on drug spending growth has been the emergence of generic alternatives for many of the most used traditional drugs, together with the absence of significant new medications to compete with these drugs. A key question is whether biosimilars can

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[6] CMS, 2015 Medicare Drug Spending Dashboard.
[7] CMS, 2015 Medicare Drug Spending Dashboard.
[8] J Hoadley, J Cubanski, and T Neuman, "It Pays to Shop: Variation in Out-of-Pocket Costs for Medicare Part D Enrollees in 2016," Kaiser Family Foundation, December 2015. https://www.kff.org/medicare/issue-brief/it-pays-to-shop-variation-in-out-of-pocket-costs-for-medicare-part-d-enrollees-in-2016/.
[9] CMS, 2015 Medicare Drug Spending Dashboard.

play the same role in bringing down prices for biologicals, such as those that treat RA. Many observers anticipate that prices should drop, perhaps in the range of 35 percent, as biosimilars penetrate the RA market.[10] Notably, even if prices drop, total spending on biologicals is likely to grow as more of these medications enter the market.

On the Part B side, two biosimilars for Remicade have entered the market. But their impact to date has been modest. When the first biosimilar (Inflectra) was launched in 2017, its price to Medicare was about 20 percent higher than the price of Remicade. The price of Remicade, meanwhile, rose by 4 percent between the first two quarters it had a competitor.[11] Public data are not available yet to determine whether the launch of a second competitor to Remicade has had a different effect.

In its report to Congress in June 2017, MedPAC made a set of recommendations with the goal of moderating Part B prices. One item in that set specifically focuses on biosimilars by modifying the ASP system to "require the Secretary to use a common billing code to pay for a reference biologic and its biosimilars."[12] Today the original biologic (the reference biologic) has one code and all biosimilars are combined into a second billing code. The idea behind consolidating to a single code is to increase price competition. Providers would be paid based on the average price (weighted by volume) across the competing drugs, providing a stronger incentive to use the lower-price competitor. CMS has proposed a move in the opposite direction—to create separate billing codes for each of the biosimilars that competes with a reference biologic. If this proposed policy is finalized, it could reduce the pressure among biosimilar manufacturers to compete for lower prices.

The MedPAC recommendations also calls on Congress to "create and phase in a voluntary Drug Value Program" designed to encourage lower prices by permitting private vendors to negotiate and share any savings with the participating providers.[13] Savings would be shared with beneficiaries in the form of lower cost sharing and with the Medicare program.

No biosimilars have reached the market yet for the two major Part D RA drugs. A biosimilar for Humira has been approved by the Food and Drug Administration (FDA), but entry into the U.S. market has been delayed until 2023 by a court settlement between the biosimilar manufacturer and the manufacturer of Humira. Similarly, a biosimilar for Enbrel has FDA approval, but patent litigation has delayed its market launch.

The future for RA and other biosimilars depends on the drugs reaching the market and gaining broad acceptance. Their timely launch on the market will rely on resolving patent cases and other legal issues. Once launched, the path to widespread acceptance and substantial market penetration will rely on several factors: (1) the establishment of interchangeability status by the FDA; (2) state laws that determine whether pharmacies can substitute biosimilars with the prescriber's approval—

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[10] A Mulcahy, Z Predmore, and S Mattke, "The Cost Savings Potential of Biosimilar Drugs in the United States," RAND Corporation, 2014. https://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND_PE127.pdf.
[11] MedPAC, "Report to the Congress: Medicare and the Health Care Delivery System," Chapter 2, Medicare Part B drug payment policy issues, June 2017, http://www.medpac.gov/docs/default-source/reports/jun17_ch2.pdf?sfvrsn=0.
[12] MedPAC, "Report to the Congress: Medicare and the Health Care Delivery System," Chapter 2, Medicare Part B drug payment policy issues, June 2017.
[13] MedPAC, "Report to the Congress: Medicare and the Health Care Delivery System," Chapter 2, Medicare Part B drug payment policy issues, June 2017.

as is done for traditional drugs; (3) general acceptance of the biosimilars by both clinicians and their patients; and (4) further research showing that patients who switch to biosimilars do so without problems. Several biosimilars for RA drugs are on the market in Europe, and some early evidence shows success in having most patients make the switch without any adverse consequences.[14]

Additional Ways to Protect Beneficiaries

The most important steps to achieving lower costs for biologicals, including expensive RA drugs, are likely to be those that increase the role of biosimilars in the market. But there are other measures that can also bring savings in both Part B and Part D for beneficiaries and the Medicare program.

The Part B ASP system that was put in place by the Medicare Modernization Act of 2003 has had some success in moderating price increases compared to the previous system. Nevertheless, prices for some drugs have gone up well beyond inflation. Earlier, I discussed the set of MedPAC recommendations addressing Part B drugs that were published in the Commission's June 2017 report to Congress.[15] In addition to calling for common billing codes for biosimilars and a reference biologic, the Commission recommended other modifications to the ASP system. They are (1) a requirement that all manufacturers submit ASP data with penalties for failure to report; (2) a reduction in wholesale acquisition cost (WAC)-based payment to WAC plus 3 percent; and (3) a requirement that manufacturers pay a rebate when ASP increases exceed an inflation benchmark (both beneficiary cost sharing and the ASP add-on would be based on the inflation-adjusted ASP). As noted above, the Commission linked these recommendations to creation of a new voluntary Drug Value Program to create more opportunities for achieving lower prices for Part B drugs.

According to the MedPAC report, these recommendations represent a balanced approach to improving the payment system for Part B drugs, including RA drugs like Remicade. If enacted and implemented, these measures could lower Part B drug prices in a way that should save money for both beneficiaries and the Medicare program.[16]

Just as in Part B, Part D presents opportunities for reducing costs. In June 2016, MedPAC approved a set of recommendations for Part D.[17] In January of this year, the Commission approved an additional recommendation that will be published in its upcoming March report to the Congress.

The recommendations in the June 2016 MedPAC report included multiple items that should be viewed together as a package. I highlight here the items that are most relevant to high-priced RA drugs. The first set of recommendations calls for reducing Medicare's individual federal reinsurance subsidy to create a stronger incentive for Part D plans to negotiate the best possible prices, especially

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[14] Center for Biosimilars, "4 Studies Address Successes, Failures, and Strategies in Non-Medical Biosimilar Switching," November 7, 2017. http://www.centerforbiosimilars.com/conferences/acr-2017/4-studies-address-successes-failures-and-strategies-in-nonmedical-biosimilar-switching.

[15] MedPAC, "Report to the Congress: Medicare and the Health Care Delivery System," Chapter 2, Medicare Part B drug payment policy issues, June 2017.

[16] MedPAC, "Report to the Congress: Medicare and the Health Care Delivery System," Chapter 2, Medicare Part B drug payment policy issues, June 2017.

[17] MedPAC, "Report to the Congress: Medicare and the Health Care Delivery System," Chapter 6, Improving Medicare Part D, June 2016. http://www.medpac.gov/docs/default-source/reports/chapter-6-improving-medicare-part-d-june-2016-report-.pdf?sfvrsn=0.

for high-priced drugs that typically drive costs into the catastrophic phase of the benefit. It also calls for eliminating enrollee cost sharing in the catastrophic phase while also excluding manufacturers' discounts in the coverage gap from the calculations of enrollees' true out-of-pocket spending. The latter measures have the potential to create significant savings for beneficiaries who take drugs like Enbrel or Humira. Another set of recommendations would modify the Part D Low-Income Subsidy to strengthen the incentive for subsidized beneficiaries to select generics and biosimilars. The final set includes several measures to provide Part D plans more tools to manage their formularies and thus reduce overall spending.

As noted above, the 2016 MedPAC recommendations were supplemented by an additional recommendation approved in January 2017. It states that "The Congress should change Part D's coverage gap discount program to require manufacturers of biosimilar products to pay the coverage gap discount by including biosimilars in the definition of applicable drugs; and exclude biosimilar manufacturers' discounts in the coverage gap from enrollees' true out-of-pocket spending." The idea of this change is to level the competitive playing field between biosimilars and reference biologics. Today only the original biologics have a required manufacturer discount in the coverage gap, which has the effect of making biosimilars noncompetitive.

The Commission's Part D recommendations address potential program improvements that go beyond the specific RA drugs under consideration in this hearing. If enacted, however, they should help lower costs for beneficiaries who take RA drugs.

The Bottom Line

Today, the biological medications used to treat rheumatoid arthritis are expensive for both the beneficiary and the taxpayer. Biosimilars bring the potential for a more competitive market and lower prices. But current policies create barriers to accomplishing these ends. In addition to considering actions that could lower those barriers, the Congress should consider other policy measures that could lower the cost of RA drugs for Medicare and its beneficiaries.

Prepared Statement of Terry G. Mahn, J.D.
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Chairman Collins, Ranking Member Casey and members of the Committee, thank you for the opportunity to appear before you today.

My testimony today will focus on intellectual property – patents to be more precise – and the important role that they play in driving the discovery and development of new drugs and medical therapies. I will try to relate how patent protection can impact the cost of drugs and health care generally, and I will offer some insights on how these forces are kept in balance.

A small caveat before I begin: all of my remarks today represent my views only and are not intended to represent the views of Fish & Richardson or any of its clients.

Every Spring, I co-teach a 3-day patent course on the Hatch-Waxman Act and the law of "biosimilars." I always begin by pointing out two related statistics that frame the issues for the course: the first statistic underscores the low probability of success associated with new drug discoveries; and the second statistic highlights the extraordinarily high cost of bringing a new drug discovery to market. First the probabilities – according to the Pharmaceutical Research and Manufacturers Association, for every 5K-10K newly discovered compounds with therapeutic potential, only 250 will make their way into pre-clinical testing, only 5 will qualify for clinical trials, and only one will result in an approved new drug. Second the costs – according the Tufts University, which has modeled the cost of developing new drugs for well over a decade, in 2015, the fully loaded cost of bringing a new drug to market exceeded $2.5 billion. Any way you look at this data, the facts are indisputable -- drug development is an enormously costly and risky business.

Because the pharmaceutical business is essential to our public health, however, our legal system must properly incentivize and appropriately reward its risk-takers. This is where patent system come in; in exchange for publicly disclosing new drug discoveries, the law grants patent owners a monopoly on those discoveries (or inventions) for a limited time. Ideally, this should only be long enough for patent owners to recover their investment and return a reasonable profit. After that, these new drug developers should be willing to face market competition so that the public will benefit from lower cost medications.

In fact, this was one of the important goals of the 1984 Hatch-Waxman Act, and after 34 years of tinkering – the Act has been amended about a dozen times – many would argue that Congress now has it just about right. Today, 85% of prescriptions are filled with generic drugs, 35% of industry revenues go to generic manufacturers, yet brand investment in new

drug R&D is at an all-time high exceeding more than $100 billion annually. More tellingly perhaps, in 2017 FDA approved more novel drugs than in any year over the previous decade. So, from the data, it looks like this legislation is working well for the American public.

Still, achieving that brand/generic balance has not been the smoothest of roads. At its core, Hatch-Waxman radically simplifies the drug approval process by allowing generic applicants to "piggyback" on proprietary clinical data strictly required for brand drug approval. In return, the generic must await the expiry of brand patents (which are listed in the FDA's Orange Book) or it must challenge those patents for earlier market entry. If challenged, however, Hatch-Waxman affords the brand an opportunity to litigate its patents prior to generic launch.

The math then, becomes simple – the more patents obtained for a drug, the longer the litigation and the slower the entry of generic drugs. Even after a generic drug is approved for launch, if patent litigation is ongoing the potential damages for infringement can be enormous (lost profits) – a risk that is too great for most generics to bear. Thus, under the original Hatch-Waxman scheme, brand manufacturers were incentivized to list as many patents as possible in the Orange Book and then litigate them aggressively as a business strategy to slow down competition and preserve market share. This patent gathering tactic was pejoratively known as "ever-greening."

Both Congress through legislation and FDA through various rulemakings have taken deliberate steps to stop patent ever-greening. But those efforts have only been partially effective. A recent study by The Hastings College of Law examined the types of patents submitted for Orange Book listing between 2005 and 2015 and concluded that ever-greening is still alive. For example, the study found that:

- 74% of the patents listed over this period were for previously-approved drugs;
- 80 of the 100 top selling drugs listed a new patent at least once; and 50 listed a new patent more than once; and
- 40% of all drugs listed new patents, with 80% of those listing patents more than once and some as many as 20 times.

In addition, brands have ventured to assert their patents in other ways to slow down generic competition, including the patenting of FDA-required REMS programs, entering into "pay for delay" settlement agreements and implementing so-called "product-hopping" strategies. Nonetheless, and despite anecdotal evidence to the contrary, all the available data seems to indicate that the Hatch-Waxman balance is working as intended, as both the new drug and generic businesses appear to be thriving.

But what about on the biologic drug side? Until 2010, the US drug laws did not provide an abbreviated approval pathway for "me-too" biologics, known as biosimilars. The Affordable Care Act sought to change that with new rules for the approval of biosimilar

drugs that were loosely modeled on the Hatch-Waxman scheme. Yet, stark differences remain. Most biologic drugs are produced by living organisms and thus, are very large molecules that are difficult to characterize and almost impossible to duplicate, even from batch to batch. For this reason, biosimilars must be studied more carefully than smaller molecule generics to determine their "therapeutic equivalence" to the brand. Clinical trials and detailed scientific analyses are required for biosimilars resulting in an approval process that is slower and much more expensive than for generic drugs. Moreover, full substitutability of a biosimilar for the brand biologic – automatic in generic world – requires separate FDA licensing, a process that has yet to be fully developed or understood. Accordingly, only the most financially well-healed manufacturers can afford to enter the biosimilar space which, understandably, severely limits future competition. Still, the rewards are tantalizing: in 2015, for example, nine of the top ten best-selling drugs in the world were biologics that averaged over $8 billion in annual sales.

As one would expect, patents also play an important part in the development of biologic drugs and the market entry of biosimilars – only more so when compared to small molecule generics. First, due to the complexity of these large molecules and the processes required to grow them, many more opportunities exist for securing patent protection. Take Humira for example. In 2015, we counted 76 patents protecting this $16 billion annual franchise; by 2017, the number was over 100 and still growing. Second, the biosimilar legislation created an elaborate scheme involving two potential "waves" of patent litigation prior to biosimilar launch. Although the Supreme Court ruled last year that the first litigation wave is optional, that does not diminish the fact that a large portfolio of patents presents can an equally large barrier to biosimilar entry.

As of this date, FDA has approved only nine biosimilar drugs (five in 2017 alone), three of which are now on the market. Patent litigation is tying up 18 other biosimilar applicants with approved or pending applications. Early pricing shows only a 15% discount off the price of the brand biologic with 35% discounting in the case of a second approved biosimilar to Remicade. Several reasons are given for these smaller discounts than what has been seen on the generic side: much higher regulatory costs to market entry; fewer anticipated competitors; no assurances of automatic substitution thus, requiring much higher direct marketing costs to physicians and hospitals; and significant higher manufacturing costs as compared to small molecule generics. The current situation in Europe, which is ahead of the US in biosimilar approvals, may be illustrative. There, three biosimilars to Remicade are competing on the market yet the discount from the brand is only 45%. The comparable discount for a three-competitor generic drug would be in the vicinity of 85%.

I have attached to my testimony a year-end blog prepared by my law firm that contains additional relevant information about biosimilar market entry and pricing which should be helpful to the Committee. Thank you again for this opportunity to appear before you and I will be happy to try to answer any questions that Committee members might have.

APPENDIX

Fish & Richardson P.C.
By Brianna Chamberlin, Tasha Francis, Ph.D. and Jenny Shmuel, Ph.D.

Biosimilars 2017 Year in Review

It was a busy year for biosimilar drug manufacturers, with 2017 being the most active year to date in the U.S. biosimilar space since the approval of the Biologics Price Competition and Innovation Act (BPCIA) in 2010. In 2017, five biosimilar drugs were approved, Renflexis® (a biosimilar of Remicade®) was launched, 11 new district court litigations were filed, and over 85 IPR petitions were submitted. This year also brought additional guidance on the bounds of the BPCIA, including from the Supreme Court and Federal Circuit. Moreover, in January 2017, the FDA provided much anticipated draft guidance on biosimilar interchangeability.

Increase in FDA Approval for Biologics and Biosimilars

Biologics and biosimilars are a growing industry in the U.S., as evidenced by the increasing number of applications approved by the FDA each year. For example, in 2017, the FDA approved more than 20 biologics license applications (BLAs), up from the 15 approved in 2016 and the 13 approved in 2015. Several of these recently approved applications were from the England-based Alba Bioscience. Roche, GlaxoSmithKline, Novartis and Merck also each a BLA approved.

Similarly, 2017 saw an increase in the number of FDA-approved abbreviated biologics license applications (aBLAs) for biosimilars. The FDA approved five new biosimilars this year: Cyltezo® (adalimumab-adbm), Mvasi® (bevacizumab-awwb), Ogivri® (trastuzumab-dkst), Renflexis® (infliximab-abda), and Ixifi® (infliximab-qbtx). Two of the five, Ogivri® and Mvasi®, biosimilars of Herceptin® and Avastin®, respectively, are the first biosimilars approved for cancer indications.

On January 17, 2017, the FDA released its long-awaited draft guidance on biosimilar interchangeability. The guidance recommends that interchangeable applicants perform switching studies to show that patients can alternate safely between the biologic and interchangeable. The comment period closed on May 19, with 53 filed comments by brand companies, biosimilar companies, healthcare providers, insurers, and other interested organizations. As of now, the FDA has not committed on when or if it will finalize this guidance, but has committed to provide draft guidance related to post-approval manufacturing changes by March 31, 2019 and to publish revised draft guidance applicable to biosimilars and interchangeables on "Good Review Management Principles and Practices for PDUFA Products" by the end of fiscal year 2018. Despite the FDA's draft guidance—and the fact that nine companies have publicly disclosed a total of 14 interchangeable applications—no interchangeable has yet been approved by the FDA.

The following charts summarize publicly available information regarding approved and pending aBLAs, and illustrate additional trends in the biosimilar space. For example, the data shows that the average time from aBLA acceptance to approval has been decreasing: 9.8 months in 2017 versus more than 12 months in previous years.

Table 1. Approved Biosimilars

Biosimilar Drug	Biologic Drug	Biosimilar Code Name	FDA Approval Date	Time from aBLA Acceptance to Approval	Commercial Launch Date	Price Discount
Ixifi® (Pfizer)	Remicade® (Johnson & Johnson)	Infliximab-qbtx	December 13, 2017	8 months	No U.S. launch intended	
Ogivri® (Mylan)	Herceptin® (Genentech & Roche)	Trastuzumab-dkst	December 1, 2017	11 months	Confidential under license agreement	
Mvasi ® (Amgen & Allergan)	Avastin® (Roche)	Bevacizumab-awwb	September 14, 2017	10 months		
Cyltezo® (Boehringer Ingelheim)	Humira® (AbbVie)	Adalimumab-adbm	August 25, 2017	7 months		
Renflexis® (Samsung Bioepis/ Merck)	Remicade® (Johnson & Johnson)	Infliximab-abda	April 21, 2017	13 months	July 2017	35%
Amjevita® (Amgen)	Humira® (AbbVie)	Adalimumab-atto	September 23, 2016	8 months or less	Will not launch until 2023 per settlement	
Erelzi® (Sandoz)	Enbrel® (Amgen)	Etanercept-szzs	August 30, 2016	13 months		
Inflectra® (Pfizer/ Celltrion)	Remicade® (Johnson & Johnson)	Infliximab-dyyb	April 5, 2016	20 months	November 2016	15%
Zarxio® (Sandoz)	Neupogen® (Amgen)	Filgrastim-sndz	March 6, 2015	10 months	September 2015	15%

Table 2. aBLA Applications Pending as of January 2018

Biosimilar Drug	Biologic Drug	Biosimilar Code Name	Date of FDA Acceptance	Notes
Retacrit® (Pfizer/ Hospira)	Epogen®/ Procrit® (Amgen/ Johnson & Johnson)	Epoetin alfa	January 2015	• Rejected in 2015 • Resubmitted in December 2016 • In June 2017, the FDA issued a complete response letter (CRL) regarding concerns about immunogenicity assays and the manufacturing process
LA-EP2006 (Sandoz)	Neulasta® (Amgen)	Pegfilgrastim	November 2015	• Rejected in 2016 • US resubmission planned for 2019
Adello Biologics	Neupogen® (Amgen)	Filgrastim	September 2017	
CHS-1701 (Coherus)	Neulasta® (Amgen)	Pegfilgrastim	October 2016	• CRL response letter issued in June 2017 that "request[ed] a reanalysis of a subset of subject samples with a revised immunogenicity assay and additional information on the manufacturing process."
Rixathon® (Sandoz)	Rituxan® (Genentech)	Rituximab	September 2017	
CT-P10 (Celltrion/ Teva)	Rituxan® (Genentech)	Rituximab	June 2017	
CT-P6 (Celltrion/ Teva)	Herceptin® (Genentech & Roche)	Trastuzumab	July 2017	
ABP 980 (Amgen/ Allergan)	Herceptin® (Genentech & Roche)	Trastuzumab	Pending acceptance	• aBLA submitted in July 2017
PF-05280014 (Pfizer)	Herceptin® (Genentech & Roche)	Trastuzumab	August 2017	
SB3 (Samsung Bioepis/ Merck)	Herceptin® (Genentech & Roche)	Trastuzumab	December 2017	
GP2017 (Sandoz)	Humira® (AbbVie)	Adalimumab	January 2018	• Sandoz announced that a 51-week clinical study confirms that its proposed biosimilar for adalimumab matches

				Humira®'s safety and efficacy profile
GP1111 (Sandoz)	Remicade® (Johnson & Johnson)	Infliximab	May 2017	
MYL-1401H (Mylan/ Biocon)	Neulasta® (Amgen)	Pegfilgrastim	February 2017	• CRL response letter issued in October 2017, but Biocon stated that it does not expect the CRL to affect commercial launch
Lapelga® (Apotex)	Neulasta® (Amgen)	Pegfilgrastim	December 2014	
Grastofil® (Apotex)	Neupogen® (Amgen)	Filgrastim	February 2015	

Increased Guidance From the Judiciary

In 2017, the judiciary was actively involved in interpreting and defining the contours of the BPCIA. For the first time, the Supreme Court weighed in on the BPCIA, deciding *Amgen v. Sandoz*, a case involving a biosimilar of Amgen's Neupogen® (filgrastim). The Supreme Court unanimously held that a biosimilar applicant could provide notice of commercial marketing to the reference product sponsors before the FDA's approval of the biosimilar. The court also held that biosimilar applicants cannot be forced through a federal injunction to participate in the BPCIA's "patent dance" disclosure provisions (requiring biosimilar applicants to provide copies of their aBLAs to reference product sponsors). The Court did not, however, decide whether the BPCIA pre-empted any state law remedies and remanded that issue back to the Federal Circuit. Six months later, the Federal Circuit held that the BPCIA preempted all state remedies when a biosimilar applicant opts out of the "patent dance."

This year, the Federal Circuit provided further guidance regarding the BPCIA. In *Amgen v. Hospira*, a case involving Hospira's biosimilar to Amgen's Epogen® (epoetin alfa), the Federal Circuit held that even if a biosimilar applicant fails to disclose information under the BPCIA, the biologic manufacturer still has a reasonable basis to list potentially infringed patents on its "patent dance" list and thereafter assert claims of patent infringement so long as it has a good-faith belief, which could be based on an applicant's withholding of information. In doing so, the court denied Amgen's motion to compel discovery to produce other manufacturing information—unrelated to the patents-in-suit—to identify other infringed patents.

Additionally, in *Amgen v. Apotex*, the Federal Circuit held that information in the pre-litigation letters exchanged under the BPCIA's disclosure provisions are party admissions and must be considered in an infringement analysis, but they are not binding and may be overcome by contrary evidence. In a suit involving Neulasta® (pegfilgrastim) and Neupogen® (filgrastim) biosimilars, Amgen argued that the district court below refused to give weight to pre-litigation admissions made by Apotex in its aBLAs and during the disclosures required under the BPCIA. Amgen further argued that Apotex's representations were party admissions and thus should have been considered in the court's infringement analysis. The Federal Circuit agreed with Amgen in holding that "statements in the pre-litigation letters are party admissions and have some

probative weight," but held that the court below properly considered the letters and did not err in finding the letters were outweighed by other evidence.

The federal district courts have also had a busy year, with 11 biosimilar cases filed, up from six filed in 2016. The new district court litigations are summarized in the chart below. A majority of the cases were filed in the District of Delaware. The most active biosimilar litigants in 2017 were Amgen and Genentech, each named as a party in five complaints.

Note that each new case does not correspond to a separate, new biosimilar. For example, four cases filed this year related to Amgen's Mvasi® biosimilar of Genentech's Avastin®. Further, the recently filed *Janssen v. Celltrion* case is the third in a series of cases ongoing since 2015 involving the same patent (US 7,598,083) and the same biosimilar of Remicade®.

Table 3. BPCIA Cases Filed in 2017

Case Name	Court	Filing Date	Drug at Issue	Number of Patents
Genentech, Inc. v. Amgen Inc. (1:17-cv-00165)	D. Del	2/15/2017	Avastin®/Mvasi® (bevacizumab)	0 (alleged violations of BPCIA)
Amgen Inc. et al v. Coherus Biosciences, Inc. (1:17-cv-00546)	D. Del.	5/10/2017	Neulasta®/CHS-1701 (pegfilgrastim)	1
Janssen Biotech, Inc. v. Samsung Bioepis Co., Ltd. (2:17-cv-03524)	D. N.J.	5/17/2017	Remicade®/ Renflexis® (infliximab)	3
Janssen Biotech, Inc. v. Celltrion Healthcare Co., Ltd. et al (1:17-cv-11008)	D. Mass.	5/31/2017	Remicade®/Inflectra® (infliximab)	1
AbbVie Inc. et al v. Boehringer Ingelheim Int'l GmbH et al (1:17-cv-01065)	D. Del.	8/2/2017	Humira®/Cyltezo® (adalimumab)	8

Amgen Inc. et al v. Mylan Inc. et al (2:17-cv-01235)	W.D. Pa.	9/22/2017	Neulasta®/MYL-140H (pegfilgrastim)	2
Amgen Inc. v. Genentech, Inc. et al (2:17-cv-07349)	C.D. Cal.	10/6/2017	Avastin®/Mvasi® (bevacizumab)	27
Genentech, Inc. et al v. Amgen Inc. (1:17-cv-01407)	D. Del.	10/6/2017	Avastin®/Mvasi® (bevacizumab)	25
Genentech, Inc. et al v. Amgen, Inc. (1:17-cv-01471)	D. Del.	10/18/2017	Avastin®/Mvasi® (bevacizumab)	25
Genentech, Inc. et al v. Pfizer, Inc. (1:17-cv-01672)	D. Del.	11/17/2017	Herceptin®/PF-05280014 (trastuzumab)	40
Genentech, Inc. et al v. Sandoz, Inc. et al (2:17-cv-13507)	D. N.J.	12/21/2017	Rituxan®/Rixathon® (rituximab)	24

As a preferred venue, it is not surprising that the District of Delaware saw the first damages award in BPCIA litigation. In September 2017, the jury in *Amgen v. Hospira* awarded $70 million in reasonable royalty damages to Amgen. This case concerned Pfizer's infringement of a now expired patent covering Amgen's biologic Epogen®. The jury found that some of Pfizer's biosimilar batches were not solely related to Hospira's aBLA application and thus were not exempted by the safe harbor of 35 U.S.C. § 271(e)(1). Further, the jury decided to award damages even though Hospira's aBLA had not yet been approved and no biosimilar sales had been made in the U.S.

Increase in Post-Grant Practice

Along with the increase in district court litigation, the total number of IPR petitions in the biologics space reached an all-time high this year, with 88 petitions filed. This is almost six times the number of petitions that were filed in 2016 (15 petitions total).

Of the 52 petitions that reached an institution decision, 28 were instituted. Of the 28 petitions instituted, two petitions were terminated following a settlement and only six final decisions were issued. Five of these final written decisions found three of AbbVie's Humira® patents unpatentable. The remaining final written decision upheld the validity of claims covering Orencia® (abatacept).

Pfizer was the most active entity challenging biologic patents in 2017, filing 23 petitions. The biosimilar manufacturers Celltrion and Sandoz were also active challengers, filing 13 and 10 petitions, respectively. Genentech's Herceptin® patent portfolio was the most challenged at the patent office, with 31 petitions. Biogen Idec / Genentech's Rituxan® came in second (with 19 petitions) and AbbVie's Humira® came in third (with 14 petitions). Method of treatment patents and formulation patents remained the most commonly challenged patents in the biologic space.

The large increase in IPR petitions in the biologics space may be attributed to a "freedom to operate" strategy aiming to clear patents in the early stages of biosimilar development so that they do not become impediments when a biosimilar application is filed. Additionally, IPRs may be useful for chipping away at a large biologic patent portfolio. Consistent with this, a majority of biologic petitions (56) have taken aim at three biologic drugs with large patent portfolios: Herceptin®, Humira® and Rituxan®.

Some petitioners have been fairly successful at the PTAB. For example, Coherus and Boehringer Ingelheim successfully petitioned to institute review of three of AbbVie's Humira® patents. The PTAB invalidated all claims in all three patents. On May 16, 2017, the PTAB invalidated all five claims of AbbVie's cornerstone method patent, US 8,889,135, marking the first time that any Humira® patent was invalidated in the U.S. On June 9, 2017, the PTAB also invalidated all claims of two other Humira® method of treatment patents—US 9,017,680 and US 9,073,987.

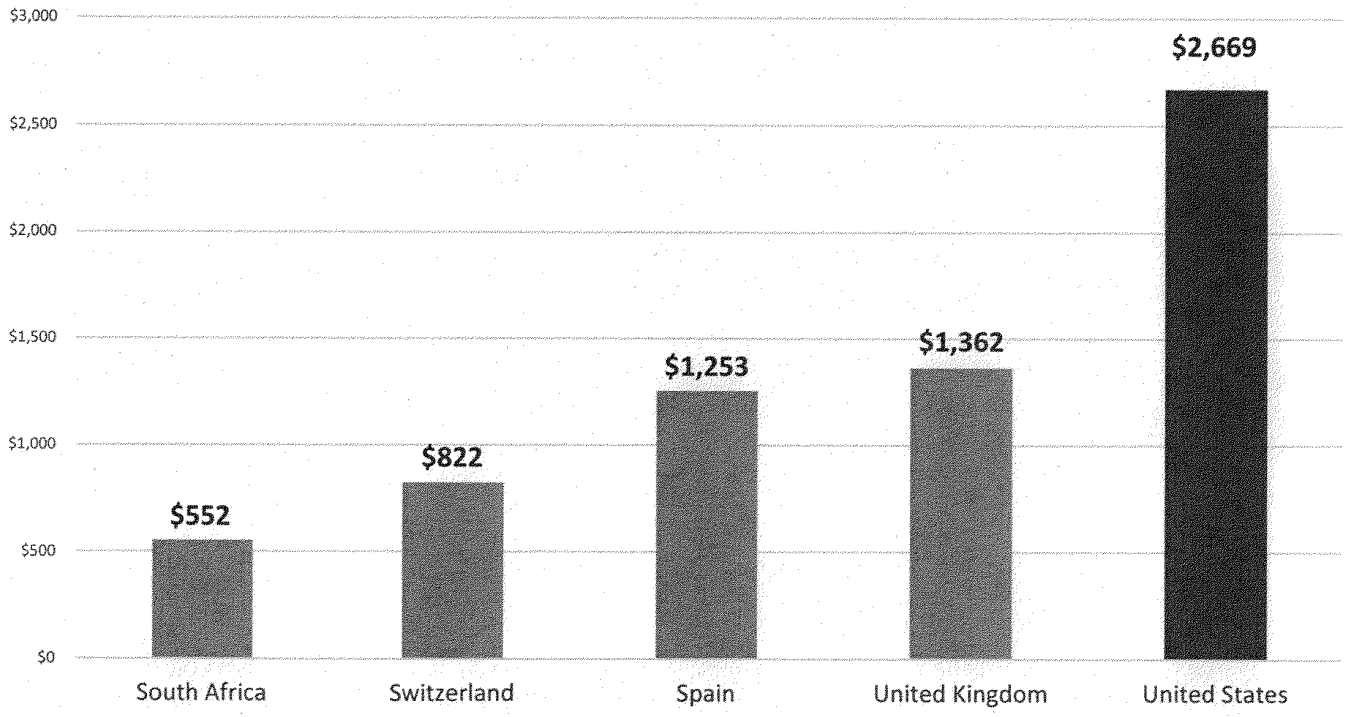
It is unclear if this uptick in biologics IPR petitions will continue in 2018. First, on November 20, 2017, the U.S. Patent and Trademark Office issued a rule adjusting IPR fees. The petitioning fee for challenging up to 20 claims will increase by $6,500, potentially dissuading some petitioners. IPR post-institution fees will also increase, but only by $1,000. Along with the rising costs, IPR lawyers and petitioners alike are awaiting the Supreme Court's decision in *Oil States*, which will decide whether post-grant patent practice, including the institution of IPRs, is unconstitutional. The Supreme Court's opinion is expected in early or mid-2018.

Conclusion

Seven years after the enactment of the BPCIA, the U.S. biosimilar market is continuing to grow, with three biosimilar drugs on the market, six others approved, and a pipeline of biosimilar applications under review at the FDA. Looking forward to 2018, we anticipate continued litigation in both the district court and at the PTAB, pending the outcome of *Oil States*. This year brought clarity in the form of Supreme Court and Federal Circuit decisions, and more is sure to come.

Additional Statements for the Record

Humira Global Costs for 28-day Supply



Source: International Federation of Health Plans 2015 Report