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**HIGH DRUG PRICES IN THE US:**  
**WHAT WE CAN LEARN FROM OTHER COUNTRIES (AND SOME US STATES)**

Testimony of:

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**United States Senate**  
**Committee on Health, Education, Labor, and Pensions**  
**Tuesday, March 23, 2021**  
**Washington, D.C.**

### Summary of major points

- The US spends far more on prescription drug prices per capita than any other industrialized nation – about double that of many wealthy countries. Overall prescription drug spending jumped from \$427 billion in 2015 to \$511 billion in 2019. Even though brand-name drugs account for only 10% of prescriptions, they are responsible for about 75% of drug spending.
- US prices for the same drugs, made by the same companies, are far higher in the US than in other comparable countries. For example, some drugs covered by the Medicare program cost 40-60% less than the prices paid for those same drugs in 4 other high-income countries.
- Government-granted monopolies in the form of patents allow companies to freely set prices at any level they wish – a situation not seen in any other countries.
- Reforming the US drug pricing system should be based on a three-pronged approach:
  1. The government should engage in direct price negotiation with manufacturers over the medications it purchases (e.g., in the Medicare program), based on the additional clinical benefit that a new drug provides to patients. Other countries evaluate how much additional benefit a new drug offers above existing alternatives; products that provide little or no additional benefit are reimbursed at the same price as the existing therapeutics. Several states are implementing review boards to evaluate evidence to inform such negotiation, but this should be carried out by a centralized body to leverage the market power of the US. Experience in other countries shows that successful, evidence-based negotiations can be conducted by the government or non-governmental bodies representing private payors.
  2. In the US, manufacturers often raise the list prices of brand-name drugs each year well beyond inflation, placing new financial strains on patients and insurers in the public and private sectors. The federal government should prevent price increases well beyond inflation that are not justified by new clinical evidence of improved effectiveness by limiting such increases to the rate of inflation, as is already done in Medicaid. Again, the US is an outlier in allowing these increases, and in most countries they are either prohibited by law or tightly limited.
  3. It will be vital to ensure a competitive market once a drug's basic period of patent-provided exclusivity ends. Drug companies often obtain numerous extra patents to extend their monopoly powers for years longer than originally expected, often for clinically trivial changes. This allows them to move market share to their newer product formulations even if these offer limited or no clinical advantages but can be sold at a high prices. The US Patent and Trademark Office has been undermined in its ability to ensure that all patents issued are legitimate, resulting in lengthy legal battles and delays to the availability of more affordable generic versions as patents are challenged in court.
- The pharmaceutical lobby is large and well-funded and will argue that any reduction in revenues will harm innovation. But most drugs approved each year are not truly innovative and in a review of 2017 new approvals, only a minority of those reviewed by independent expert bodies offered more than minimal clinical advantages over available treatments. In addition, only 10-20% of large pharmaceutical manufacturer revenues go to research and development of new drugs, and public funding often plays a key role in financing research that leads to the most innovative new drugs.
- By contrast, these 3 proposals will actually increase innovation by providing greater incentive to discover truly important medications, an improvement over the current system that incentivizes manufacturers to profit by extending patent life beyond its original duration and developing drugs that offer little clinical benefits but can be priced freely. Negotiations based on additional patient benefit, limited price increases, and stronger patent scrutiny incentivizes what matters most: the development of drugs providing important new benefits to patients and addressing unmet need.

## **Chairman Sanders, Ranking Member Collins, and Members of the Committee:**

My name is Aaron Kesselheim. I am an internal medicine physician, lawyer, and health policy researcher and a Professor of Medicine at Harvard Medical School in the Division of Pharmacoepidemiology and Pharmacoeconomics of the Department of Medicine at Brigham and Women's Hospital in Boston, one of the main Harvard teaching hospitals. I lead its Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research group that studies the intersections between prescription drug affordability and use, laws and regulations related to medications, and the development and cost of drugs. PORTAL is one of the largest and most prolific non-industry funded research centers in the country that focuses on pharmaceutical law, use, and economics. I am honored to have been invited today to talk to you about brand-name drug prices in the US: both why they are so high and you can actually do about it.

I will start by reviewing the problem of high drug prices, touching on why prices are so high in the US and what the implications are of high drug prices for patients and the health care system. I will then describe a three-pronged approach to ensuring that US patients pay fair prices for new therapeutics: negotiating with brand-name drug manufacturers, ensuring that prices cannot rise excessively over time, and ensuring a timely and efficient transition to generic competition at the end of the market exclusivity period. For each of these major categories, I will compare the US approach to other industrialized countries (and some cutting-edge US states) to provide points of contrast and pathways forward for policymaking by Congress. Finally, I will address some important counter-arguments that are sometimes made in opposing plans to address high US drug prices. I will conclude by explaining the problems with these arguments, and suggest how they can be addressed in any policy changes that are made.

### **I. The Problem of High Drug Prices**

The US spends far more on prescription drug prices per capita than any other industrialized nation. Total prescription drug spending here jumped from \$427 billion in 2015 to \$511 billion in 2019.<sup>1</sup> According to the World Health Organization, the US spent \$1,011 per capita on retail pharmaceuticals in 2015, which increased to \$1,229 in 2018, far outpacing all other OECD countries: the next highest, Switzerland, came in at \$894, and the OECD average was far lower, at \$562.<sup>2</sup> One government report estimated that about 17% of the US health care spending goes to prescription drugs, although some payors have reported that pharmaceuticals account for closer to 25% of spending overall.

High US drug prices are primarily driven by spending on brand-name drugs, which make up only about 10% of prescriptions, but account for about 75% of spending. Most of this spending is not for the newest drugs approved in the last year or two, but from brand-name drugs that have been on the market for many years, during which time they have been subject to substantial promotion to physicians and direct-to-consumer advertising. Many of them have been subjected to astonishing price increases from year to year, even with no changes in the drug itself. For example, in 2019, Medicare Part D—the federal government's outpatient prescription drug insurance program for patients over age 65—topped its list of greatest spending with three drugs: the anticoagulants apixaban (Eliquis), which has been on the market for 8 years, and rivaroxaban (Xarelto), on the market for 10 years, and the cancer treatment lenalidomide (Revlimid), which has been on the market for 15 years. These three drugs accounted for about \$16 billion in gross spending for Medicare Part D alone just in 2019 (or approximately \$10 billion in net spending). In Medicare Part B—which covers hospital- or physician-administered drugs for older patients—top-spending drugs in 2019 included the ophthalmologic drugs aflibercept (Eylea, \$2.9 billion total spending, 9 years on market) the anticancer drug rituximab (Rituxan, \$1.7 billion, 23 years), and the pegfilgrastim (Neulasta, \$1.2 billion,

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<sup>1</sup> Tichy EM, Schumock GT, Hoffman JM, et al. National trends in prescription drug expenditures and projections for 2020. *American journal of health-system pharmacy.* 2020;77(15):1213-1230.

<sup>2</sup> Kesselheim AS, Hwang TJ, Avorn J. Paying for Prescription Drugs in the New Administration. *JAMA* 2021;325(9):819-820.

19 years). High spending and prices are not indicators of innovation reaching patients but of a system that allows manufacturers to freely set and raise prices while preventing effective competition.

Among the most concerning examples of high drug prices relate to drugs that have been available for multiple decades, including products like insulin, the opioid reversal agent naloxone, and epinephrine for potentially fatal allergic reactions. In a study led by Dr. William Feldman in our group, we studied data on Medicare Part D drug spending to examine injectable insulin products. We found that in 2017, Medicare Part D spent about \$7.8 billion (even after assuming large rebates) on 31 different insulin products.<sup>3</sup> Unfortunately, the availability of multiple brand-name products does not consistently lead to substantial reductions in prices, as might be expected, because they are not interchangeable, reducing the possibility of price competition.<sup>4</sup>

The prices paid for these same brand-name drugs are much lower in other industrialized countries than they are in the US. In one study led by Thomas Hwang in our group, we evaluated the prices of 75 brand-name drugs that accounted for the highest Part B expenditures in fee-for-service Medicare beneficiaries in 2016, compared to the prices for the same drugs in four comparator high-income countries: Japan, Germany, Switzerland, and the UK. In virtually all cases, the US paid more for these drugs than the median of prices in comparator high-income countries. Overall, drug prices in high-income countries were 46-60% lower than those in Part B, taking rebates into account.<sup>5</sup>

Brand-name prescription drug prices are so high in the US, and much higher than in other comparable countries, because in the US we allow brand-name pharmaceutical manufacturers to charge whatever they want during their periods of government-granted market exclusivity—a condition not seen in any other developed nation. At the same time, numerous laws and rules require coverage of many high-priced drugs by government or private payors. As a result, brand-name manufacturers set drug prices in the US at levels far exceeding prices for the same drugs made by the same companies for use in other high-income countries around the world, because they can, and then raise those prices each year at rates much higher than the rate of inflation.<sup>6</sup> As a final step, manufacturers also take numerous steps to extend their market exclusivity periods as long as possible by building a “thicket” of patents designed to delay generic entry.<sup>7</sup>

These high prices have important implications for patients. Americans struggle to afford their prescriptions, and three in ten report not taking a medication as prescribed by their doctor because of the cost.<sup>8</sup> Non-adherence to important medications can lead to increased patient mortality.<sup>9</sup> Drug costs passed

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<sup>3</sup> Feldman WB, Rome BN, Lehman LS, Kesselheim AS. Estimation of Medicare Part D spending on insulin for patients with diabetes using negotiated prices and a defined formulary. *JAMA Internal Medicine* 2020;180(4):597-601.

<sup>4</sup> Sarpatwari A, DiBello J, Zakarian M, Najafzadeh M, Kesselheim AS. Competition and price among brand-name drugs in the same class: a systematic review of the evidence. *PLoS Medicine* 2019;16(7): e1002872. See also Luo J, Avorn J, Kesselheim AS. Trends in Medicaid Reimbursements for Insulin From 1991 through 2014. *JAMA Internal Medicine* 2015;175 (10):1681-1686.

<sup>5</sup> Hwang TJ, Jain N, Lauffenburger JC, Vokinger KN, Kesselheim AS. Analysis of proposed Medicare Part B to Part D shift with associated changes in total spending and patient cost-sharing for prescription drugs. *JAMA Internal Medicine* 2019;179(3):374-380.

<sup>6</sup> Kesselheim AS, Avorn J, Sarpatwari A. The high cost of prescription drugs in the United States: origins and prospects for reform. *JAMA* 2016;316(8):858-871; Ways and Means Committee Staff. *A Painful Pill to Swallow: U.S. vs. International Prescription Drug Prices*. Washington, DC September 2019.

<sup>7</sup> Vokinger KN, Kesselheim AS, Avorn J, Sarpatwari A. Strategies that delay market entry of generic drugs. *JAMA Internal Medicine* 2017;177(11):1665-1669.

<sup>8</sup> “Three in ten of all adults (29 percent) also report not taking their medicines as prescribed at some point in the past year because of the cost.” Kirzinger A, Munana C, Wu B, Brodie M. Data Note: Americans’ Challenges with Health Care Costs. KFF. 2019. <https://www.kff.org/health-costs/issue-brief/data-note-americans-challenges-health-care-costs/>. 11 June 2020.

on to consumers and patients through insurance premium increases make such insurance less affordable, and can force people off of their insurance plans. High drug prices have spillover implications for other aspects of health care and social spending, since public and private spending on prescription drugs is not available to meet other needs. Medicaid programs, for example, have had to respond to expanding drug budgets by cutting coverage for other services and limiting access to drugs.<sup>10</sup>

I am optimistic that this hearing, among the first held by the HELP Committee, indicates a new commitment by the new leadership in the Senate to make progress on the issue of unaffordable drug prices and their harmful effect on patients and the US economy. Progress on excessive drug prices in the US has been stymied before by the pharmaceutical industry and its well-funded and powerful lobbying clout. In the past, both Republicans and Democrats have responded to that pressure by staying away from taking evidence-based and enforceable steps to bring pharmaceutical spending in line with other industrialized nations. In the last 4 years, the Trump Administration continued this tradition by doing little to address drug prices in a meaningful way. However, I believe bold action now will be rewarded at the polls. There is clear evidence that most Americans favor action to help them with the high drug prices faced by them and their family. In a national survey leading up to the 2020 election, the second-ranked domestic priority for Democrats and Republicans alike was lowering the cost of prescription drugs, following just behind access to affordable health care.<sup>11</sup>

Below, I describe a three-pronged practical approach that Congress could implement to address high drug prices, drawing on lessons from other countries—and from a few states that have begun to enact such thoughtful reforms.

## **II. A Three-Pronged Solution to Ensure Fair Prices in the US**

A comprehensive approach to address high US brand-name drug prices must account for the several major components of the US market that sustain those high prices: (1) brand-name manufacturers can freely set prices for new drugs at the time of FDA approval at any level they wish, unlike what is seen in other countries, and important payors such as Medicare are required to accept those prices and to cover nearly all such products, whether they represent an increase in patient benefit or not; (2) brand-name manufacturers are permitted to freely raise prices to any level they choose during government-protected market exclusivity periods; and (3) these companies can use patents and other government-enforced tools to delay effective generic or biosimilar competition as long as possible.

A multi-pronged solution to ensure fair prices is therefore grounded in negotiating fair prices for brand-name drugs, ensuring that brand-name manufacturers cannot raise prices over time beyond inflation unless they make meaningful improvements to their drugs, and providing an efficient transition to a competitive generic market after exclusivity periods ends. Most other industrialized nations already have strategies that address each of these components.

### **A. Negotiating Prices of Brand-Name Drugs**

While other countries have implemented a variety of effective price negotiation and review tools, US legislators have not directly addressed drug prices and instead allow manufacturers to freely set prices

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<sup>9</sup> Gagne JJ, Choudhry NK, Kesselheim AS, Polinski JM, Hutchins D, Matlin OS, Brennan TA, Avorn J, Shrank WH. Comparative effectiveness of generic and brand-name statins on patient outcomes. *Annals of Internal Medicine* 2014;161:400-407.

<sup>10</sup> Galewitz P. States Cut Medicaid Drug Benefits to Save Money. *Kaiser Health News* July 24 2012. <https://khn.org/news/medicaid-cuts-sidebar/>

<sup>11</sup> Harvard T.H. Chan School of Public Health & Politico, Americans' Domestic Priorities for President Trump and Congress in the Months Leading Up to the 2020 Election (Feb. 2020), <https://cdn1.sph.harvard.edu/wp-content/uploads/sites/94/2020/02/PoliticoFeb2020.pdf>.

while enforcing purchases by public sector programs and allowing for prolonged extension of government-granted monopolies. This situation is different from the purchase of nearly all other goods and services in our free-enterprise marketplace economy. The markets for prescription drugs are served by a patchwork of public and private payors that are unable in many cases to negotiate effectively, and/or are prohibited from declining to cover drugs that do not add anything meaningful to available treatment options. Medicare is forbidden by law from negotiating prices with drug manufacturers, despite the fact that it negotiates or sets the price for every other medical service it covers. Medicare Part B pays for all drugs at their average sales price (plus an additional percentage that acts as a dispensing fee), while the individual plans that offer coverage through Medicare Part D are forced to buy all drugs in several “protected” classes and cannot exclude any from their formularies, whether or not they add benefit or are severely overpriced. This situation – uniquely different from nearly all other federal procurements – limits their ability to negotiate effectively. Medicaid programs receive a guarantee that they will get the best price being offered in the commercial market, but generally cannot negotiate any further since they are required to list virtually all FDA-approved drugs on their formularies.

In the private sector free from Medicare restrictions, commercial insurers can refuse to pay for particular costly drugs that have equivalent less expensive alternatives; they may also impose high co-payments to discourage patient demand for such lower-value medications. Unfortunately, such negotiation may not necessarily be based on the clinical benefit of the drug but on the extent of rebates, the financial goals of the pharmaceutical benefit manager (PBM) that often controls the negotiation, and other arrangements the PBM may have with it. Manufacturers, through PBMs, do negotiate prices but these other issues are central to the negotiation, rather than the extent of clinical benefit. The approach is also counteracted by manufacturer coupons to patients and patient assistance programs, as well as state laws that require coverage of certain drug products.

One most direct way to address excessive drug prices would be for the government to negotiate the price of drugs for taxpayer-supported drug benefit programs, just as the Defense Department negotiates the prices of armaments it purchases. The prevailing approach to negotiating brand-name drug prices in other industrialized countries begins after regulatory approval with a process known as Health Technology Assessment (HTA). Numerous other countries have health technology assessment organizations that assess a newly-approved drug’s actual clinical benefit and help determine a fair price based on how well the new drug is expected to perform against other available treatments. These publicly-funded organizations conduct assessments of the effectiveness, safety, and cost of new drugs compared with other interventions to evaluate what price the payor should agree to reimburse.

Germany, for example, launched a major drug pricing reform law in 2011 (Arzneimittelmarktneuordnungsgesetz, or AMNOG) to align prices and reimbursement more closely with expected treatment benefits. Under this law, called AMNOG, the manufacturer sets prices freely during a drug’s first year on the market. During this time, the Institute for Quality and Efficiency in Health Care (IQWiG), a nonprofit, nongovernmental research organization, assesses its possible additional therapeutic benefits relative to existing standards of care (rating drugs as having: major, considerable, minor, or no or not quantified benefit). For drugs without sufficient clinical evidence of therapeutic benefit that surpasses the standard of care, payors will not reimburse prices higher than the existing standard of care. A 2018 analysis showed that of 139 drugs reviewed in the clinical benefit pricing procedure, only 22 were later withdrawn by the manufacturer from the market, and of those 22 all but one had received a rating of no additional clinical benefit; the remaining drug had a non-quantifiable benefit and was withdrawn from all European markets.<sup>12</sup>

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<sup>12</sup> Spuleucel-T (Provence) received a benefit rating of “not quantifiable” and was scheduled to be re-reviewed but was withdrawn from European markets before then. Staab TR, Walter M, Mariotti Nesurini S, et al. “Market withdrawals” of medicines in

In France, the Economic Committee for Health Products (CEPS) primarily judges the value of a new prescription drug based on the added clinical benefit that a drug provides to patients in comparison to available alternatives. This added benefit is classified as major (I), substantial (II), moderate (III), mild (IV), or absent (V). CEPS is composed of representatives from the health and finance ministries, the country's national health insurer, and private insurers. It negotiates drug prices with manufacturers on that basis. Drugs with major, substantial, or moderate added benefit are guaranteed to have a list price similar to those in the United Kingdom, Germany, Spain, and Italy.<sup>13</sup>

As these examples show, in Germany and France—as well as in other countries like Australia, Japan, and Canada—the primary tool for leveraging lower drug prices is to rigorously assess the clinical benefit of new drugs against pre-existing therapies or comparators. If a new drug does not have clinical evidence to show it is more effective than other drugs already available to treat a condition, then payors should not pay more for it than they do for those pre-existing drugs, a mainstay of all market-based transactions.<sup>14</sup> The basic logic is that if a drug costs more than other options, it should provide more benefit to patients. Benefit is usually evaluated with patient-relevant outcomes, including evidence of effectiveness on life-extension, improvements in quality of life, and/or other clinical outcomes. Additional benefit can be translated into health economic terms and cost-effectiveness to determine whether a proposed price is defensible. Alternatively, clinical benefit can be plotted as an “efficiency frontier” to determine whether a price is in line with the degree of benefit, an approach which does not any set values of cost-effectiveness.<sup>15</sup> These evaluations inform an anchor price for negotiations with manufacturers.<sup>16</sup> Other countries have either a government or independent agency that reviews the manufacturer's evidence of clinical effectiveness and

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Germany after AMNOG: a comparison of HTA ratings and clinical guideline recommendations. *Health Economic Review* 2018;8(1):23.

<sup>13</sup> Rodwin MA. Pharmaceutical Price and Spending Controls in France: Lessons for the United States. *International Journal of Health Sciences*. 2020;50(2):156-165.

<sup>14</sup> Pharmaceutical Benefits Advisory Committee. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee. September 2016; IQWiG. General Methods. Köln 10 July 2017. <https://www.iqwig.de/en/about-us/methods/methods-paper/>; Shiroiwa T, Fukuda T, Ikeda S, Takura T. New decision-making processes for the pricing of health technologies in Japan: The FY 2016/2017 pilot phase for the introduction of economic evaluations. *Health Policy*. 2017;121(8):836-841; <https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Guidelines2020-en.pdf>. The French Haute Autorité de Santé, its national health authority, rates drugs on two scales: first, whether the new drug provides clinical benefit, which determines whether it will be reimbursed. The second, is whether the new drug provides additional benefit compared to available therapies, and the amount or degree of additional benefit determines the extent to which its price may be higher than comparator therapies. Haute Autorité de Santé. Pricing & Reimbursement of drugs and HTA policies in France. Haute Autorité de Santé. [https://www.has-sante.fr/jcms/c\\_1729421/en/transparency-committee](https://www.has-sante.fr/jcms/c_1729421/en/transparency-committee). Published 2015. Updated 29 January 2021.

<sup>15</sup> For example, the Australian and Canadian health technology assessment bodies (PBAC and CADTH, respectively) translate clinical benefit into health economic measures of cost-effectiveness. By contrast, the German health technology assessment body (IQWiG) plots an efficiency frontier using the most significant clinical outcome or a combination of net health benefits and extrapolates an appropriate price from this. Pharmaceutical Benefits Advisory Committee. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee, version 5.0; CADTH. Guidelines for the Economic Evaluation of Health Technologies: Canada. Ottawa March 2017. IQWiG. General Methods. Köln 10 July 2017. <https://www.iqwig.de/en/about-us/methods/methods-paper/>

<sup>16</sup> See e.g., Patented Medicines Prices Review Board <https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Guidelines2020-en.pdf>; Pharmaceutical Reimbursement and Pricing in Germany. June 2018. <https://www.oecd.org/health/health-systems/Pharmaceutical-Reimbursement-and-Pricing-in-Germany.pdf>; Transparency Committee. Principles of medicinal product assessments and appraisal for reimbursement purposes. 2 December 2020.

the proposed list price.<sup>17</sup> This process does not occur in the US, making it difficult for value-based assessments to drive medication use and cost. Currently, several smaller public and private entities, like the Institute for Clinical and Economic Review, take on this role on a voluntary basis.

Thus, my first recommendation is for the US to establish similar publicly-funded body that would determine a verifiable, evidence-based price for a drug based primarily on the clinical benefits it would provide. This effort should start with some of the brand-name or single-source drugs that account for the greatest spending or have the highest prices. Eventually, this body would be charged with reviewing all new drugs within the first year after approval; until then, manufacturers could be permitted to charge the price they believe is appropriate. This approach is analogous to the Drug Efficacy Study Implementation (DESI), a program that Congress mandated in the 1960s through the 1980s, to assess existing drugs for evidence of efficacy once that became a requirement for marketing. In determining a rational price, this body could also consider information about the cost of development, cost of failure, overall health care budget, extent of government funding in its development, and other relevant factors. Drugs that do not show benefits over other products would be offered the same price as the pre-existing alternatives. The advantages of such a reference pricing system are two-fold: first, at market entry, the prices for new drugs will be more consistent with their clinical benefits, and second, it incentivizes manufacturers to invest in research and development that will bring new drugs to market that meaningfully improve upon pre-existing therapeutics or address unmet needs. Manufacturers would also be incentivized to conduct the research needed to demonstrate comparative effectiveness. This system does provide extra rewards to drugs that offer no or minimal improvements on pre-existing therapies.

Past legislative efforts to establish such a body in the US to review drugs' clinical benefits and determine their cost-effectiveness have been derailed by the political process. At different points, the Office of Technology Assessment, the Agency for Healthcare Research and Quality, and the Patient-Centered Outcomes Research Institute have all been proposed as the centers of such an effort. More recently, a few states have successfully initiated such review boards. For example, the New York legislature delegated the new authority for drug assessments and negotiation to an existing agency within the state Department of Health to review the cost-effectiveness and clinical benefit of prescription drugs that the state's Medicaid program purchases.<sup>18</sup> The board primarily relies on third-party organizations, such as the Institute for Clinical and Economic Review, and evaluates the following factors: publicly-available pricing information, information supplied by the state Department of Health, value-based pricing analyses provided by third parties, the severity and prevalence of the treated condition, utilization data, the effectiveness of the drug, the extent to which the drug improves patient health or quality of life, the likelihood that use of the drug will reduce patients' utilization of other medical services, the post-rebate cost of the drug to Medicaid, the availability of therapeutic alternatives, the number of manufacturers that produce the drug (in the case of generics), and information supplied confidentially by the manufacturer to the board. After the board agrees on a fair, value-based price for the drug, New York's Medicaid program uses this price as a benchmark in negotiations with the drug's manufacturer for additional supplemental rebates. The board has completed three full reviews to date and successfully exacted additional discounts for at least two reviewed drugs. Such an effort would not be excessively costly. Though a New York-specific fiscal analysis is not available, the Maryland prescription drug affordability board is expected to fully fund its activities by assessing \$1,000 fees on the approximately 1,400

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<sup>17</sup> Emanuel EJ, Zhang C, Glickman A, Gudbranson E, DiMagno SSP, Urwin JW. Drug Reimbursement Regulation in 6 Peer Countries. *JAMA Internal Medicine* 2020; See also Rand LZ, Kesselheim AS. An International Review of Health Technology Assessment Approaches to Prescription Drugs and Their Ethical Principles. *Journal of Law Medicine, and Ethics* 2020;48(3):583-594.

<sup>18</sup> For a full description of the New York process, as well as processes created in Massachusetts and other states, see Bendicksen L, Rome BN, Avorn J, Kesselheim AS. Pursuing value-based prices for drugs: a comprehensive comparison of state prescription drug pricing boards. *Milbank Quarterly* 2021 [in press].



corporations in the prescription drug supply chain in Maryland (generating a yearly operating budget of \$1.4 million).

Such value-based price negotiations can be effective at reducing prices. In France, the government takes clinical benefit into account in pricing negotiations and additional factors, such as the price of alternatives that treat the same or similar conditions, and the number of people eligible to use the drug: products that treat conditions that affect more people are priced lower because manufacturers can make the same profits with lower margins given increased volume. The French system has been very effective; in the 1970s and 1980s, the US and France were among the OECD countries with the highest spending on pharmaceuticals, but in France, the rate of spending began to slow with implementation of new regulations, and was only \$638 per capita in 2018—half the amount the US spent per person (\$1,229).<sup>19</sup> The House’s Elijah E. Cummings Lower Drug Costs Now Act (H.R. 3), introduced in 2019, included a provision for direct negotiation of drug prices in Medicare and was expected to save \$448 billion in direct Medicare spending.<sup>20</sup>

It is important that the price identified and negotiated through this process be offered to the private market too. The US has a fragmented health system with many different payors, each of whom is responsible for securing drugs. By contrast, in other countries, a single entity is responsible for negotiating the list price for the country. This leverages the full market power of the country’s payors. In some countries, such as the UK, France, and Japan, a government department of health carries out negotiations with manufacturers to secure a price for a national health insurance system. Within this framework in Europe, drug price negotiations can be centralized and involve both public and private insurance plans: in Germany, centralized negotiations are carried out by a body called the Federal Joint Committee and representing more than 100 insurance plans.<sup>21</sup> Prescription drug pricing defaults to reference pricing to comparators, but if there is evidence of additional benefit, then the Federal Joint Committee negotiates with drug manufacturers to determine a list price that will be paid by all the insurers.<sup>22</sup> If negotiations fail in Germany, a price is set by arbitration. In a study we conducted with Prof. Ariel Stern at Harvard Business School using data on 57 anticancer drugs launched in Germany from 2002 to 2017, we found that implementation of these negotiations was associated with drug prices being more closely aligned with clinical benefit and a 24.5% decrease in negotiated prices relative to launch prices.<sup>23</sup> Another study found that prior to the introduction of these centralized negotiations, US prices in Medicare Part B were 29% higher than German prices for the same drugs. Following the introduction of the centralized negotiations and assessment of clinical benefit in Germany, German prices became lower than US prices by a further 29%.<sup>24</sup>

An alternative approach is to implement price limits and allow public and private plans to each negotiate their own prices with manufacturers. In Canada, the Patented Medicine Prices Review Board (PMPRB) is a quasi-judicial, independent body that was created in 1987 to protect consumers from

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<sup>19</sup> Raimond VC, Feldman WB, Rome BN, Kesselheim AS. Why France spends less than the United States on drugs: a comparative study of drug pricing and pricing regulation. *Milbank Quarterly* 2021 [in press]

<sup>20</sup> Congressional Budget Office. 2019. Budgetary Effects of H.R. 3, the Elijah E. Cummings Lower Drug Costs Now Act. Washington, DC: Congressional Budget Office.

<sup>21</sup> Gemeinsamer Bundesausschuss (G-Ba), or Federal Joint Committee <https://www.g-ba.de/english/>

<sup>22</sup> <https://www.g-ba.de/english/benefitassessment/>

<sup>23</sup> Lauenroth VD, Kesselheim AS, Sarpatwari A, Stern AD, Lessons from the impact of price regulation on the pricing of anticancer drugs in Germany. *Health Affairs* 2020;39(7):1185-1193.

<sup>24</sup> For new drugs authorized between 2004-2018, the average price ratio between US, Medicare Part B and German prices before 2011 was 29.2%. After the introduction of the German AMNOG law, which established the Federal Joint Committee and introduced clinical benefit as the basis for price negotiation, the difference between Medicare Part B and German prices rose another 28.9%. Berkemeier F, Whaley C, Robinson JC. Increasing Divergence in Drug Prices Between the United States and Germany After Implementation of Comparative Effectiveness Analysis and Collective Price Negotiations. *J Manag Care Spec Pharm.* 2019;25(12):1310-1317.

excessive prices during brand-name drug exclusivity periods. When a patent-holder applies to sell a drug in Canada, it must submit information on the labeling of the drug, price, information from benefit analyses undertaken, and estimated use by the population to the PMPRB. The PMPRB then reviews the proposed price, taking into account information that includes reference pricing to comparator therapies, market size for the drug, consumer price index, and prices charged in other countries. Through this process, the Board first establishes an “Interim Maximum List Price”, which is followed by a “Maximum List Price” as more information about the drug becomes available. If a manufacturer is found to have excessively priced a drug, the Board can require that the drug price be lowered and introduce clawbacks.<sup>25</sup> In the Canadian example, an independent body protects patients and plans from excessive pricing, and payors then have the option to negotiate discounts with manufacturers.<sup>26</sup>

In summary, experience from other countries (and a few US states) shows that brand-name drug prices can effectively be lowered by first assessing the clinical benefits of a drug and then engaging in effective negotiation on that basis, without the artificial limits currently placed on US public and private payors. For drugs that offer substantial clinical value to patients, this system may lead to paying high prices commensurate with the benefit the drug provides. But most drugs do not have such high value; in fact, one review we conducted of drugs the FDA approved in 2017 found that of those reviewed by international health technology assessment organizations only one-third were rated as offering more than minor benefit over currently available treatments.<sup>27</sup> Another recent review found that of 122 “ultra-expensive” drugs in Medicare, those with annual spending greater than GDP per capita or \$63,000, up to 85% were rated as having no or low additional value by international health technology assessment organizations.<sup>28</sup> In the US, we will be able to better afford paying high prices for truly meaningful improvements because we will pay far less for drugs that do not offer clear clinical benefits.

Importantly, the US is already implementing an approach with some of these features in the Veterans Affairs Health System. Unlike Medicare and Medicaid, the VA is allowed to determine which drugs it will cover, and can negotiate process with manufacturers on this basis. Because of this, prices paid by the VA are substantially lower than those in all other US government-financed systems. We have already developed this approach to a large extent, and it is working very well, so it should not be seen as some kind of exotic “foreign import.”

## B. Addressing Price Increases During Market Exclusivity

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<sup>25</sup> <https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/2020/PMPRB-Guidelines2020-en.pdf> The PMPRB is currently updating its guidelines. Following a court challenge, the new guidelines, which are cited here, took effect on January 1, 2021.

<sup>26</sup> Prescription drugs administered in hospitals are at no cost to patients, but for outpatient drugs, plans are responsible. Provincial and territorial governments have their own public plans, while many Canadians are covered through private plans, such as employer-based coverage. (<https://www.canada.ca/en/health-canada/services/health-care-system/pharmaceuticals/access-insurance-coverage-prescription-medicines.html>) Public and federal plans in Canada formed the pan-Canadian Pharmaceutical Alliance (as it is now called) in 2010 with the objective of combining negotiating powers to achieve greater value for publicly funded drug programs and patients. The pCPA takes into account health technology assessment (HTA) reports from the two Canadian HTA organizations, budget impact analysis and affordability, the therapeutic landscape and gaps, and other considerations when negotiating with manufacturers. <https://www.pcpacanada.ca/negotiation-process>

<sup>27</sup> Frank RG, Avorn J, Kesselheim AS. What do high drug prices buy us? Health Affairs Blog. April 29, 2020.

<sup>28</sup> Prices based on 2018 GDP per capita. Average annual spending per beneficiary was \$174,699 and of these drugs, Germany rated 29% as having no additional value and France rated 31% as having no additional value. Overall a majority of drugs were rated as having low or no additional value: 85% in France, 74% in Germany, and 73% in Canada. DiStefano MJ, Kang SY, Yehia F, Morales C, Anderson GF. Assessing the Added Therapeutic Benefit of Ultra-Expensive Drugs. *Value in Health* 2021;24(3):397-403.

In the US, drug manufacturers are free to raise the price of a drug each year, and often do so, far beyond the cost of inflation. Imatinib (Gleevec), a treatment for numerous rare cancers, was introduced in 2001 for a list price of \$26,400 per year, a price which increased to more than \$120,000 by 2016.<sup>29</sup> One study found that price inflation of existing brand-name oral drugs rather than market entry of new drugs accounts for 87.3% of average weighted costs.<sup>30</sup> Many brand-name drugs provide rebates to commercial payors and Medicare Part D plans that offset some of the list price increases, and while drug-level rebates are confidential, estimates of those rebates indicate that they do not keep pace with list price increases. One review of list and estimated rebates from 2007-2018 on branded pharmaceutical products found that list prices increased by 159%—or 9.1% per year—but net prices increased by 60% overall, with discounts offsetting only 62% of increases in list prices for drugs.<sup>31</sup>

Excessive annual price increases are reflected in higher prices to patients. Over 10% of people in the US have no drug insurance, and often must pay the full list price. One recent study found that list prices for the 14 top-selling drugs doubled from 2010 to 2016 while median patients' out-of-pocket costs increased by 53%.<sup>32</sup> A recent review led by Dr. Benjamin Rome in our group found that patients with insurance who pay deductibles or co-insurance are particularly at risk and are likely to experience substantial increases in out-of-pocket spending when drug list prices rise.<sup>33</sup>

By contrast, in other countries, agreements between the government or payors and manufacturers keep price increases in check. In France and the UK, manufacturers agree to spending caps, essentially growth caps on drug sales, which if exceeded require a portion of excess profit to be rebated.<sup>34</sup> As a result, drug prices in France do not increase routinely over time. If France's Transparency Committee lowers a drug's effectiveness rating, the price for that drug decreases. For example, the rating for insulin glargine was changed from "moderate improvement" to "minor improvement" and then to "no improvement" as new safety data were documented and market competitors emerged.<sup>35</sup> In one study comparing the 6 highest spending drugs in Medicare between the US and France, we found that the spending per unit for lenalidomide in the US increased from 2010 to 2018 from about \$400 per unit to nearly \$700 per unit, while during that same period the price of the drug in France decreased from \$239 to \$202 per unit.<sup>36</sup>

Other countries, including Australia, even require statutory price decreases. On the Australian formulary, brand-name drugs that have no comparator therapies take a 5% price cut after 5 years. This arrangement is part of a five-year agreement made with the drug trade group Medicines Australia.<sup>37</sup> Like

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<sup>29</sup> Johnson CY. This drug is defying a rare form of leukemia — and it keeps getting pricier. Washington Post. March 9 2016.

<sup>30</sup> Hernandez I, Good CB, Cutler DM, Gellad WF, Parekh N, Shrank WH. The Contribution of New Product Entry Versus Existing Product Inflation in the Rising Costs of Drugs. *Health Affairs* 2019;38(1):76-83.

<sup>31</sup> Hernandez I, San-Juan-Rodriguez A, Good CB, Gellad WF. Changes in list prices, net prices, and discounts for branded drugs in the US, 2007-2018. *JAMA* 2020;323(9):854-862.

<sup>32</sup> Yang EJ, Galan E, Thombly R, et al. Changes in Drug List Prices and Amounts Paid by Patients and Insurers. *JAMA Network Open* 2020;3(12):e2028510.

<sup>33</sup> Rome BN, Feldman WB, Desai RJ, Kesselheim AS. Correlation between Changes in Select Brand-Name Drug Prices and Patient Out-of-Pocket Costs, 2015-2017. *JAMA Network Open* 2021 [in press]

<sup>34</sup> Rodwin MA. Pharmaceutical Price and Spending Controls in France: Lessons for the United States. *International Journal of Health Services* 2020;50(2):156-165; The 2019 Voluntary Scheme for Branded Medicines Pricing and Access (2018)

<https://www.gov.uk/government/publications/voluntary-scheme-for-branded-medicines-pricing-and-access>.

<sup>35</sup> Raimond VC, Feldman WB, Rome BN, Kesselheim AS. Why France spends less than the United States on drugs: a comparative study of drug pricing and pricing regulation. *Milbank Quarterly* 2021 [in press]

<sup>36</sup> Id.

<sup>37</sup> "PBS medicines are divided into two categories for pricing purposes. Formulary 1 (F1) is for single brand (generally patented) medicines and Formulary 2 (F2) is for medicines (generally off-patent) that have multiple brands listed on the PBS. Medicines on F1 currently take a five per cent cut in the price paid by the Government after five years on the PBS. When a second brand of a medicine is listed on the PBS, the medicine moves to F2 and takes a 16 per cent price cut. Under this budget measure, F1 medicines will continue to take a five per cent price cut after five years on the PBS (extended to 2022), but will also take

using clinical benefit as the basis of price negotiations, the Australian plan is intended to incentivize the development of new drugs that offer improvements or address areas of unmet need. Japan uses a different approach and reviews list prices every two years, decreasing them if the actual market price paid is lower than the list price.<sup>38</sup>

In each of these countries, the government secures agreement between payors and manufacturers: once a price has been negotiated between payors and manufacturer, it cannot be raised without re-reviewing the clinical and economic evidence. By contrast, the US government grants drug manufacturers a monopoly through patents and FDA exclusivity periods, during which time they can freely set prices, including raising list prices. Therefore, my second major recommendation is to limit the rate of drug price increases, so that the government-granted monopoly does not exploit the patients who rely on these medicines. One model for how this would work would be to implement the drug price inflation rebate penalty currently in place for Medicaid, which contains exorbitant annual increases by requiring a higher rebate if drug price increases exceed inflation. Bills were introduced in the prior Congress with bipartisan support for extending the Medicaid inflation penalty to Medicare Part D: a version of this policy was included in the House Elijah E. Cummings Lower Drug Costs Now Act (H.R. 3) and the Senate Prescription Drug Pricing Reduction Act (S. 2543). According to the Congressional Budget Office, for drugs covered under Medicare Parts B and D, limiting annual price increases to the rate of inflation is expected to save \$36 billion over ten years.<sup>39</sup>

### C. Ensuring Effective Transition to a Competitive Market

A final approach to move toward fairer drug pricing is to arrange for an efficient transition to a competitive market at the end of a brand-name drug's period of market exclusivity. The government provides about 6-7 years of guaranteed generic-free marketing periods for new brand-name drugs via the Hatch-Waxman Act of 1984. (This has been expanded to about 12 years for qualified antibiotics or biologic drugs.) Additionally, a drug is usually protected by numerous patents, each lasting up to 20 years, that have started accumulating since the drug was originally synthesized or discovered. A study led by Dr. Rome in our research group found that patents actually provide 13-17 years of market exclusivity for new brand-name small-molecule drugs, and even more for biologic products, keeping generic manufacturers from the market long after the exclusivity period ends.<sup>40</sup>

Patents perform a very important role in enabling innovators to profit from their discoveries for a finite amount of time, and rewarding that creativity. But this system has become subject to many abuses, with two distinct patent-related problems contributing to unjustifiably high drug prices. First, pharmaceutical manufacturers can obtain multiple patents—occasionally even hundreds—covering their drugs, even for attributes that reflect no meaningful innovation. The legal and scientific complexity of drug patent applications, combined with the heavy demands on patent assessors who are often not expert in the issues at stake, means that personnel in the U.S. Patent and Trademark Office (USPTO) sometimes issue patents in error. The fact that a patent was improperly granted

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further price cuts of 10 per cent after 10 years and five per cent after 15 years. When a medicine moves to F2, the price cut will increase from 16 to 25 per cent. Legislation will be required to implement the price cuts." Grove A. Pharmaceutical Benefits Scheme. Parliament of Australia.

[https://www.apf.gov.au/About\\_Parliament/Parliamentary\\_Departments/Parliamentary\\_Library/pubs/rp/BudgetReview201718/PBS](https://www.apf.gov.au/About_Parliament/Parliamentary_Departments/Parliamentary_Library/pubs/rp/BudgetReview201718/PBS).

<sup>38</sup> Shiroiwa T, Fukuda T, Ikeda S, Takura T. New decision-making processes for the pricing of health technologies in Japan: The FY 2016/2017 pilot phase for the introduction of economic evaluations. *Health Policy* 2017;121(8):836-841.

<sup>39</sup> Congressional Budget Office. 2019. Budgetary Effects of H.R. 3, the Elijah E. Cummings Lower Drug Costs Now Act. Washington, DC: Congressional Budget Office.

<sup>40</sup> Rome BN, Lee CC, Kesselheim AS. Market exclusivity length for drugs with new generic or biosimilar competition, 2012-2018. *Clinical Pharmacology and Therapeutics* 2020 July 12.

generally becomes evident only following litigation, long after the patent has issued, when far greater resources are devoted to their evaluation.<sup>41</sup> By this time, however, the delay in generic competition caused by patents that should never have issued can contribute to substantial excess expenditures on brand-name drugs by public and private sector payors, and by patients.<sup>42</sup> This “thicket” of additional patents makes it possible for brand-name manufacturers to introduce new versions of their products that provide longer exclusivity with little or no clinical benefit for patients.<sup>43</sup> In one study of drugs approved in 2002, we found that 9 (53%) were introduced in patentable new formulations in the subsequent 15 years, with many of these changes clinically trivial.<sup>44</sup> In another study, we found that the proportion of patents listed with the FDA that cover drug-related devices tripled between 2000 and 2016 (from 3% to 9% of all drug-related patents).<sup>45</sup> These device patents extend exclusivity periods even though the patent on the drug itself has lapsed. It is important to ensure that such invalid patents are not mistakenly issued, because manufacturers can extract substantial revenues from patented changes. In a recent study, we found that a manufacturer introduced a version of the multiple sclerosis drug glatiramer (Copaxone) that could be taken 3 times per week instead of daily, providing benefits that were tiny in comparison to the \$6.5 billion in the resulting additional drug expenditures that the US spent on the new formulation instead of generics.<sup>46</sup> A federal appeals court ultimately held that the patents protecting the new version of glatiramer were invalid, but the payments had already occurred.

Here again, lessons on how to improve experience in the US can come from analyzing how other countries handle patents. Results from foreign patent offices suggest the USPTO could reduce the number of erroneously-issued patents by allocating greater resources to ensure patent quality. The European Patent Office (EPO) and Japan Patent Office (JPO) issue fewer, higher-quality patents despite applying a similar legal standard as the USPTO.<sup>47</sup> The EPO and JPO do this in part by spending more time and resources scrutinizing patents, retaining high-quality examiners, and having their employees work in teams.<sup>48</sup> In one study, a 50% increase in examination time was associated with a 10% decrease in invalid patents.<sup>49</sup> As Doni Bloomfield and I recounted in a recent Washington Post article, “The problem of weak drug patents has worsened under the Trump administration. In the past two years, the PTO has made it even more difficult for examiners to reject patent applications. The office issued directives that increase the amount of work examiners must do to reject certain applications, such as those that seek to patent a process found in nature.

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<sup>41</sup> Hemphill CS, Sampat B. Drug patents at the Supreme Court. *Science* 2013;339:1386-1387.

<sup>42</sup> Dave C, Sinha MS, Beall RF, Kesselheim AS. Estimating the cost of delayed generic entry to Medicaid. *Health Affairs* 2020;39(6):1011-1017.

<sup>43</sup> Amin T, Kesselheim AS. Secondary patenting of branded pharmaceuticals: a case study of how patents on two HIV drugs could be extended for decades. *Health Affairs*. 2012;31(10):2286-2294. doi:10.1377/hlthaff.2012.0107

<sup>44</sup> Beall RF, Kesselheim AS, Sarpatwari A. New drug formulations and their respective generic entry dates. *Journal of Managed Care and Specialty Pharmacy* 2019;25(2):218-224.

<sup>45</sup> Beall RF, Kesselheim AS. Tertiary patenting on drug-device combination products in the United States. *Nature Biotechnology* 2018;36:142-144.

<sup>46</sup> Rome BN, Tessema FA, Kesselheim AS. US spending associated with transition from daily to three-times-weekly glatiramer acetate. *JAMA Internal Medicine* 2020;180(9):1165-1172.

<sup>47</sup> Picard PM, Bruno VPDLP. Patent office governance and patent examination quality. *Journal of Public Economics* 2013;104:14-25; Chien CV. Comparative Patent Quality. *Arizona State Law Journal*; 2018; 50:71-140; Lemley MA, Sampat B. Examiner Characteristics and Patent Office Outcomes. *Review of Economics and Statistics* 2012;94:817-827; Lei Z, Brian DW. Why Weak Patents? Testing the Examiner Ignorance Hypothesis. *Journal of Public Economics* 2017;148:43-56.

<sup>48</sup> Id.

<sup>49</sup> Frakes MD, Wasserman MF. Investing in ex ante regulation: evidence from pharmaceutical patent examination. Cambridge, MA: National Bureau of Economic Research; July 2020 (<https://www.nber.org/papers/w27579>).

Predictably, these directives decreased examiners' rejections for such ineligibility by more than 25 percent."<sup>50</sup>

Thus, my third major recommendation is to closely scrutinize the process for issuing drug patents and enforcing them against generic manufacturers. This can be accomplished at a number of different levels. Without even requiring legislation, the USPTO would benefit from greater resources; better agency regulation can give examiners more time and administrative leeway to reject ineligible applications, reflecting current practices in some patent offices around the world. In addition, we could better leverage the US Patent Trial and Appeals Board (PTAB), set up by the 2011 America Invents Act. The PTAB could help weed out invalid patents before they get caught up in litigation if it had the authority to review all patents as soon as they are listed with the FDA by a manufacturer. If steps cannot be taken to clear out the thicket of patents that threatens transitions to an effective competitive market, then we might need to consider automatic price reductions for brand-name drugs after a reasonable period of time on the market;<sup>51</sup> one recent analysis of applying this concept to biologic drugs predicted potential cost-savings over the next 5 years of \$265 billion when compared to the current model of biosimilar competition.<sup>52</sup> At the level of the pharmacy, we could allow closely similar drugs to be more easily substituted with each other by pharmacists even if they have patentable differences, if the FDA judges those drugs to be therapeutically interchangeable. Such a move would broaden competitive markets and require manufacturers seeking to introduce a slightly changed version of a product to ensure that the product really offers important benefits to patients.

### III. Common Counter-Arguments and Responses

The greatest challenge in enacting these changes will be the political strength of the pharmaceutical industry lobby, one of the largest in Washington, which will charge that any drug pricing reform will reduce innovation. This is a false assertion; much evidence indicates that meaningful innovation need not decline. Large pharmaceutical manufacturers invest only about 10-20% of their revenues in research and development, so providing exceedingly high profit margins to such manufacturers does not directly translate to substantial investment in innovation. A substantial amount of work from our research group has documented how transformative drug innovation often emerges in large part from publicly funded research and development, even though this is rarely reflected in the pricing of the resulting drugs, or in commensurate "payback" to the funding agencies that made them possible.<sup>53</sup> As long as Congress continues funding for the National Institutes of Health, then we can be assured that the next generation of important new therapeutics will be in the pipeline. This view is bolstered by experiences in other countries. In recent work focused on Germany led by my colleague Ariel Stern, we found that for drugs found to provide important new patient benefits, none of them left the German market, despite price negotiations.<sup>54</sup> If concern arises about insufficient support to bring certain types or classes products through clinical testing and regulatory approval—the roles dominated in the current system by venture capital and private

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<sup>50</sup> Bloomfield B and Kesselheim AS. Biden can lower drug prices without Congress doing anything. *Washington Post* Jan 5 2021.

<sup>51</sup> Dudzinski DM and Kesselheim AS. Scientific and legal viability of follow-on protein drugs. *New England Journal of Medicine* 2008;358:843-849.

<sup>52</sup> Bach PB and Trusheim MR. The drugs at the heart of our pricing crisis. *NY Times*. March 15 2021.

<sup>53</sup> See e.g., Kesselheim AS, Tan YT, Avorn J. The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs. *Health Affairs* 2015;34:286-294; Nayak RK, Avorn J, Kesselheim AS. Public support for late-stage new drug discovery; cohort study. *BMJ* 2019;367:l5766

<sup>54</sup> Stern AD, Pietrulla F, Herr A, Kesselheim AS, Sarpatwari A. The impact of price regulation on the availability of new drugs in Germany. *Health Affairs* 2019;38(7):1182-1187. The oncology drug regorafenib (Stivarga) was withdrawn from the market; it received an early positive assessment, but was later reassessed by the Federal Joint Committee, which failed to confirm its prior positive benefit assessment.

industry funding—the recent evolution of Covid-19 treatments and vaccines has shown that public funding and partnerships can help advance highly promising new treatments.

These changes are likely to actually improve meaningful innovation. The current system in which brand-name manufacturers are rewarded with high US prices for new drugs that have limited clinical advantages may even reduce the pressure for them to develop medications that truly add clinical value. It is notable that less than one-third of new drugs approved in the past decade were rated as providing high clinical value compared to existing alternatives, although this has not led to lower prices.<sup>55</sup> If drug prices more adequately reflected the clinical benefits they offer to patients, this would incentivize more meaningful pharmaceutical innovation, and there would be less investment in making trivial changes to existing products and more investment in meeting unmet medical needs. If reference pricing and clinical benefit assessment formed the basis for price negotiations, new drugs that offer improved outcomes to patients would be rewarded with higher prices than available options, creating a powerful incentive for manufacturers to invest their resources in bringing to market drugs that will achieve this price premium rather than products that can be priced high but will not offer patients more health.<sup>56</sup>

Finally, as described above, more data-driven policies on drug pricing need not reduce prices equally across the board; pricing based on a product's actual clinical benefits could still lead to substantial manufacturer revenue and thus offer a strong incentive for private investment in research and development.<sup>57</sup> Payor drug budgets would better be able to account for these situations without being burdened by payments for non-innovative expensive drugs and high-priced drugs for which competitive generic or biosimilar entry is delayed. Particular attention may need to be provided for the rare but clinically ideal scenario of an extremely effective drug with tremendous long-term clinical benefits, similar to the direct-acting antiviral hepatitis C virus drugs when they were introduced in 2015. In that case, the high price set by the manufacturer was ultimately cost-effective, but too expensive for many payors, particularly Medicaid programs, in the short-term. In these situations, Congress could support Medicaid with support for payments over time assuming ongoing clinical benefits, or create a special high-risk pool of federal dollars separate from a patient's insurance, similar to the way in which Medicare pays for the medical expenditures of all dialysis patients.

#### **IV. Conclusion**

The high drug prices faced by US patients directly result from existing federal policies that have helped shape the organization of the pharmaceutical market in the US, in which brand-name manufacturers are given years-long government-granted market exclusivity periods and near-total freedom to establish prices – with nearly half of that expenditure paid by government programs such as Medicare and Medicaid. Compounding this situation, the lattice of public and private payors in the US are limited by their inability to negotiate (as for Medicare Part B) or restrictions that require them to cover any FDA-approved drug no matter how useful it is (as for Medicaid and Medicare Part D “protected drug classes”).

To effectively lower prices, policymakers can adopt three important principles currently in place in other industrialized countries to better ensure that we are paying prices commensurate with the utility offered by new drugs. First, the US needs to set up a system to evaluate the clinical benefits of brand-name drugs and help determine the basis for reasonable pricing given those benefits. Health technology

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<sup>55</sup> Hwang TJ, Vokinger KN, Ross JS, Kesselheim AS. Association between FDA and EMA expedited approval programs and therapeutic value of new medicines. *BMJ* 2020;371:m3434.

<sup>56</sup> Fojo T, Mailankody S, Lo A. Unintended Consequences of Expensive Cancer Therapeutics—The Pursuit of Marginal Indications and a Me-Too Mentality that Stifles Innovation and Creativity: The John Conley Lecture. *JAMA Otolaryngology–Head & Neck Surgery*. 2014;140(12):1225-1236.

<sup>57</sup> Kesselheim AS, Hwang TJ, Avorn J. Paying for prescription drugs in the new administration. *JAMA* 2021;325(9):819-820.

assessment organizations that conduct this work are operating effectively in many other countries. The US then needs to empower negotiation of prices based on that clinical evaluation process and offer negotiated prices to the private market. Second, the US must ensure, as other countries do, that brand-name drug prices are not increased exorbitantly beyond inflation during a drug's market exclusivity period unless the manufacturer makes clinically meaningful improvements to the drug. Third, the US needs to provide a rapid, efficient transition to a competitive generic market after a product's government-enforced monopoly expires. Currently, brand-name manufacturers can delay generic entry by obtaining numerous patents, many of them for trivial changes, and then leverage them to introduce new formulations with only minor clinical effects that can forestall direct competition. If the USPTO adopted approaches similar to those used by its counterparts in Europe or Japan, protecting drugs with invalid or otherwise problematic patents would happen less often.

Congress can take up this model secure in the knowledge that the drug industry's charges that their effects on innovation are overblown. Enhanced investment in public funding for research will continue to provide the insights needed to develop transformative products, as it has done for numerous important drugs and Covid19 vaccines. Fair and even generous rewards would still be provided to drugmakers who create important new medications – just not for those that add little or nothing to what we can offer patients. With the changes proposed above, policymakers can rest reassured that more patients will be able to access these vital products at an affordable price that accords with a drug's value and cost of development. In fact, better aligning US drug prices with their clinical benefits will reward and promote innovation because it will better incentivize manufacturers to invest in helping develop new treatments that meet unmet medical needs or offer meaningful clinical benefits to US patients.