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Highlights from the Stakeholder Sessions Organized by the Committee on Ensuring Patient Access to Affordable Drug Therapies

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As part of its work thus far, the committee has held 3 public sessions with sponsors and various stakeholders. Highlights from these public sessions are described below. Presentation materials from the sessions can also be found on the project website: www.nas.edu/affordabledrugs.

Session I: November 14, 2016, Washington, DC

The committee's first public session was centered on reviewing current trends in prescription drug prices and spending in the United States as well as abroad. The stakeholder presentations included a review of the recent report from a United Nations panel on the topic of affordable drugs (UN, 2016). Maria Freire, a member of the UN panel, discussed the report's salient points including the role of transparency, market incentives, and intellectual property rights.

Rashmi Agarwal of the Government Accountability Office discussed findings and conclusions from their recent report on generic drugs under Medicare. In the pool of 1,400 generic drugs reviewed by the GAO, Agarwal said, 351 of them had an "extraordinary price increase" from 2010 to 2015, where the increase was 100 percent or more in a one-year period. The report also found that in some cases, drug prices increased by 1000 percent in one year (GAO, 2016).

Jennifer Moore of the Institute for Medicaid Innovation said that the overall prescription drug spending increased by 12.2 percent in 2014, compared to a 4.6 percent increase for all other health expenditures (Martin et al., 2016). Moore said that the increase in spending as a whole can be attributed to both increases in drug volume and an increase in the average spending per claim, particularly for brand drugs.

Freda Lewis-Hall of Pfizer said that commonly reported list or invoice prices are higher than what payers ultimately pay for medicines. She added that the invoice price growth of branded medicines slowed in 2015, declining from 14.3 percent in 2014 to 12.4 percent as discounts, rebates and other price concessions rose sharply (IMS, 2016). She said that the increase in spending in 2015 was driven by new brands and protected brand price increases, which was partially offset by the impact of patent expiries. She noted that generic drugs account for nearly 90 percent of all U.S. prescriptions, the remainder being new and more expensive medicines for conditions including cancer, heart disease and rare diseases. She said that "medicines save money by improving health", and with new advances in science, these innovative medicines are also more targeted and more effective in treating a condition and delaying or reducing other health care costs, such as surgery and hospital stays (Zalesak et al., 2014).

Aaron Kesselheim of Brigham and Women's Hospital said that drug price escalations have become a major concern for patients, prescribers, payers, and policy makers. Among some potential actions that could make drugs more affordable, he suggested that the most promising approaches include drug importation from other countries, providing opportunities for price negotiation by the government, expediting the drug approval process, and reducing unjustified granting and extension of patent exclusivity (Kesselheim et al, 2016).

Ernst Berndt of MIT discussed recent trends in mergers and acquisitions of pharmacy benefit managers (PBMs), insurers, and wholesalers, and their impact on drug prices. For example, the list prices of brand-name drug manufacturers have been increasing along with negotiated rebates (Aitken et al., 2016). He noted how heterogeneity exists in the size of these rebates, both across firms and across products within firms, and how they tend to grow over the life cycle of brand drugs, peaking several years before loss of exclusivity, but generally ceasing after loss of exclusivity and generic entry. He stated that some PBMs have even negotiated inflation-protected provisions that incorporate automatic rebate increases whenever the manufacturer raises the list price, leaving the net price unchanged. Berndt said that the simultaneous increase of list prices and rebates is due to the growth in PBMs, calling this a "pharms race" between manufacturers and PBMs. "The three largest PBMs have increased their share of total commercial prescription volume from 42 percent in 2005 to 68 percent in 2015," Berndt noted. "This has increased their aggregated purchasing power and ability to extract rebates and discounts from manufacturers." As an example, Berndt pointed out that in an earnings call to investors, Gilead announced that average discounts off list prices in 2013 on its hepatitis C drugs were about 22 percent, but by 2014, after market entry of several more competitors, the average discounts off list prices increased to 46 percent. He noted that, due to provisions in the Affordable Care Act, more people now have health insurance, which has increased the demand for prescription drugs, but at the same time, cost-sharing policies such as tiering and high deductibles have become more common in insurance benefits designs.

Frank Lichtenberg of Columbia University observed that in the past 10 years there have been 66 new cancer drugs whereas there were only eight between 1975 and 1985, indicating an eight fold increase in the amount of pharmaceutical innovation for cancer. He noted that each generation of pharmaceutical innovation is better overall than the previous one, resulting in increased life expectancy and quality of life (Lichtenberg, 2014a). He discussed his analysis that suggested that pharmaceutical innovation has reduced non-drug medical expenditures (such as hospital expenses) more than it has increased drug expenditures (Lichtenberg, 2014b).

Session II: December 13, 2016, Washington, DC

The committee's second public session explored many factors that influence drug costs for patients, including: the high cost of R&D, regulatory factors, the role of PBMs and specialty pharmacy, out of pocket patient costs due to cost sharing policies and insurance benefit design.

Robert Galvin of the Blackstone Group noted that in 2015 spending on prescription drugs grew faster than spending on any other health care service (HCCI, 2016). He highlighted five commonly reiterated concepts that dominate the drug pricing debate: "today's drug costs are justified by the overall improvement in health; lower drug prices will stifle innovation; using comparative effectiveness to link price to value will lead to rationing and harm patients; PBM practices are the major source of the problem; the drug cost problem will be solved if the Food

and Drug Administration (FDA) can speed approval and the Centers for Medicare & Medicaid Services (CMS) can negotiate discounts.” Galvin urged the committee to recommend actionable directions to create reforms that will be meaningful to both employers and private payers. He stated that “transparency is necessary but not sufficient” to address the drug cost problem.

Peter Bach of Memorial Sloan Kettering Center said that the current patterns of drug spending and prices will keep rising and out of pocket costs and premiums will continue to increase. He said that payments toward deductibles by consumers who have insurance through large employers rose 256 percent from 2004 to 2014, and over the same period, wages increased 32 percent (KFF, 2016). He added that the inflation rate on drug spending has exceeded every other major sector of healthcare for the past three years, and will lead to increased financial harms and reduced access. On “value”-based approaches, Bach commented that “the term ‘value’ is hard to define and that means different things to different people”. He pointed out that over the past 20 years, new drug prices have been linked to gains in cancer survival.

While reviewing recent trends, Steve Miller of Express Scripts noted that the rising cost of prescription drugs is “unsustainable” and managing prescription drug cost requires a holistic approach that improves both care and value. Ron Cohen of Acorda and BIO attributed the increases in prescription drugs to the high cost of R&D. He said that people do not eagerly invest in the biopharmaceutical industry because of the inherent risks in the nature of product development. Harold Paz of Aetna reiterated that drug spending is rising sharply and he said that specialty pharmacy is driving this spending. For example, in 2014, 27 of the 51 drugs approved by the FDA were high-cost specialty drugs (Express Scripts, 2015). He suggested that payers could be part of the solution by supporting individualized treatment based on clear evidence, encouraging adherence, moving to value-based arrangements that reward good outcomes, and driving appropriate use through utilization management.

Andrew Lo of MIT Sloan School of Management emphasized that there “is a difference between medicines and other kinds of products and services.” He pointed out that health care decisions are not purely economic, but economics can usefully inform decisions. He proposed an alternative financing model: amortize the cost of cures over many years, thereby increasing access to expensive curative therapies (Montazerhodjat et. al, 2016). “Drug ‘mortgages’,” Lo said, in the “very long run” would require the government to assume the amortized debt, and in the “long run”, insurance companies should pay for it. These approaches would require new regulation or legislation to address disincentives for insurers to cover expensive but curative therapies, he added. In the “short run” Lo argued, patients, families, and foundations could pay for curative therapies through a special purpose entity to fund expensive drug purchases from which patients can borrow to pay for drug costs, and the loan is amortized over a repayment period as with other consumer loans such as mortgages, credit card debt, and auto and student loans, he concluded.

Christopher Viehbacher, executive chairman and co-founder of Boston Pharmaceuticals (formerly CEO of Sanofi), detailed the challenges the biopharmaceutical industry faces in generating returns from its R&D investments due to high costs and stringent regulatory pathways. He noted that the prolonged time it takes for product development, along with the high failure rate, significantly affects the total R&D costs.

Breakout discussions focused on state level initiatives (such as the State Medicaid Alternative Reimbursement and Purchasing Test for High-Cost Drugs or SMART-D), drug rebate programs, challenges with transparency in drug pricing, and the approaches used by other

countries in providing access to expensive curative treatments for conditions like Hepatitis C to improve public health.

Susan Stuard of Oregon Health Sciences University noted that Medicaid “best price” provisions for bulk drug purchasing do not necessarily benefit Medicaid programs. “Best price is a lever in commercial negotiations” she added. On pricing transparency, Mason Tenaglia of QuintilesIMS Institute noted that “manufacturer subsidies in the form of rebates and patient savings programs and their beneficiaries vary so significantly by therapeutic area, product life cycle, and patient population that transparency will have limited value to the general public.” Bruce Rector of Doctors for America described Australian approaches that are being implemented with the goal of eliminating hepatitis C (government viewing it as a public health problem) and how that differs from the U.S. approach, which is restricted by Medicaid budget limits and cost control strategies by public and private payers. Kevin Schulman of Duke University School of Medicine discussed his research results on the impact of increasing total specialty drug costs on overall health care costs, and insurance premiums for patients (Schulman et al., 2015).

Other discussions explored the importance of the generic and off-patent prescription drugs, comparative effectiveness frameworks, and examples from other regulated industries (such as finance) to guide governance strategies. Jeremy Greene of Johns Hopkins School of Medicine discussed how generic pharmaceuticals have historically lowered overall healthcare costs. For example in 2014, generic drugs were responsible for an estimated \$254 billion in health system savings (Generic Pharmaceutical Association, 2015). Steven Pearson of the Institute for Clinical and Economic Review noted that the current drug pricing system does not provide sustainable access to high value care for all patients, and is decoupled from market forces that would align prices with the added value to patients. Joseph Dimasi of Tufts Center for the Study of Drug Development explained their analyses suggesting that the average cost to develop and gain marketing approval for a new drug is \$2.5 billion, including opportunity cost and the cost of development failures (DiMasi et al., 2016). Haime Workie of Financial Industry Regulatory Authority offered insights from the realm of financial regulation and how it might relate to the biopharmaceutical industry.

Session III: January 23, 2017, Stanford, CA

George Poste of Arizona State University (formerly, SmithKline Beechem R&D), gave a comprehensive overview of systemic factors that influence drug pricing. Among the many factors, Poste emphasized, are rising clinical trial costs, market distortion and market failure, the roles of PBMs and the health insurance benefit plans. Discussing the drug market trends, Poste pointed out that spending for specialty drugs has been growing at a faster rate than spending for traditional small molecule drugs (Kirchhoff, 2015). He noted that in 2012, specialty drug spending in the United States reached \$87 billion, and current trends suggest that specialty drug spending will total \$400 billion by 2020 (UnitedHealth 2014). He discussed the challenges and concerns faced by the biopharmaceutical industry, and noted the decline in annual projected pharma R&D returns (Deloitte Centre for Health Solutions, 2015). Commenting on the “vicious cycle in the pharmaceutical pricing,” Poste noted that apart from the multidimensionality, the other key characteristic is opacity. “There is no transparency in the pricing structure”, and there are complexities in the gross to net pricing of branded pharmaceuticals, he said. On rebates and

subsidies, Poste said that there are different prices for different payer channels (e.g. Department of Defense, Medicare Part D, Medicaid); different therapeutic classes (e.g. Hepatitis C, insulin, immunotherapies for cancer); and different disease categories (e.g. acute or chronic), among others. “There is no uniformity here, the only constant is opacity”, Poste said. He also discussed the different value-based pricing models and noted that there is no consensus about the evaluation criteria and definitions of value. He discussed the potential value of companion diagnostics to improve patient outcomes, reduce R&D spending, and increase drug approval rates, and but also noted the lack of incentives to develop and validate such diagnostics. His suggested actions to make drugs more affordable for patients included: allowing Medicare to negotiate improved pricing on brand-name drugs, requiring transparency on prices and margins for multiple stakeholder transactions, denying tax breaks for direct-to-consumer prescription drug advertising, and speeding up FDA oversight processes for generic drugs.

Gail Cassel of Infectious Disease Research Institute (formerly, Eli Lilly) discussed the importance of precision medicine in relation to drug pricing. She focused on tuberculosis drugs and noted other factors (beyond just the prices of the medications) that affect access and affordability. Discussing the global burden of TB, Cassel added that an estimated 480, 000 people developed multidrug-resistant TB in 2015, and some of these cases require 10 antibiotics to effectively treat them. She noted that the development of new TB drugs has been extremely slow, and R&D funding for better TB prevention, diagnosis, and treatment dropped by \$53.4 million to \$620.6 million in 2015, the lowest level of funding since 2008.

David Parkinson of Essa Pharmaceuticals echoed the concerns and complexities about the current business model for drug development. He noted that the current pharma business model is “drugs as products”, with little direct relationship to actual value returned at the personal and societal levels. He noted that much of the drug discovery process has migrated from large pharmaceutical companies to smaller companies but the smaller companies still rely on the larger companies for resources and commercialization. He said that although there are many stakeholders involved in the drug discovery and commercialization process, they are not well aligned. He suggested that any solution to address the affordability of drugs to patients requires a holistic approach that extends beyond pricing.

Kevin Grimes of Stanford Medical School gave an overview of how repurposing existing drugs for novel conditions may offer the potential benefit of saving time and money. He said that drug repurposing has the potential to reduce by half the costs and time associated with bringing a new drug to market since repurposing relies on previously approved studies that have already assessed multiple toxicity endpoints (Ashburn and Thor, 2004).

David Beire of Bay City Capital provided information on factors that affect the pricing of drugs including R&D costs, sales costs, marketing and advertising costs, the strength of the value proposition, the competitive landscape, intellectual property situation, and the role of shareholders. He pointed out that the biopharmaceutical sector accounts for the single largest share of all US business R&D, representing 21 percent of all domestic R&D funded by US businesses. He also expressed the opinion that transparency is not as beneficial as commonly touted and may actually lead to increases in drug prices.

Roy Vagelos, former CEO of Merck and present chair of the board of Regeneron Pharmaceuticals highlighted the various accomplishments by biopharmaceutical companies, ranging from successes in infectious diseases to immuno-oncology. Vagelos said that the prices paid for innovations are high in the U.S. so the incentives for success are very strong and it is not

an accident that most of the innovations in the past forty years have also come from the U.S. He shared his personal experiences in capping drug price increases as CEO of Merck. In particular, he described his efforts in the 1990s to link drug price increases to consumer price index—plus or minus one percent (also discussed in Vagelos, 1991). Vagelos noted that within about a year of announcing this approach at Merck, all the other large companies followed the example and that put a lid on the annual price increases. “That has gotten out of line obviously,” he said in regard to recent industry practices. He maintained that pharmaceutical products have to be priced with consideration of the value being delivered to the people being treated. He mentioned that there needs to be a robust and transparent discussion in the industry on how to measure value, so that people can understand exactly how they are setting their prices. Secondly, companies should reconsider the concept of limiting price increases. “Unless we can handle the total launch price and stifle the enormous annual increases - there are no ways to defend those - then we are in for trouble,” he added. Vagelos stressed that this can be done because it has been done before and it has to be done within the industry.

Steven Galson of Amgen noted that despite the higher drug spending, medication adherence by patients with chronic vascular disease provides substantial medical savings, as a result of reductions in hospitalization and emergency department use (Roebuck et al., 2011). Galson said that patients deserve more appropriate methods for value assessment, and suggested that a holistic view of the value of medicines has to be considered when setting drug prices. He underscored the importance of understanding the role of the drug supply chain in the price of medicines.

Autumn Ehnou of Medicines360 introduced her organization’s mission: “to expand access to quality medicines for all women regardless of their socioeconomic status, insurance coverage or geographic location.” For example, she said that in 2013, Medicines360 and Allergan partnered to support Medicines360’s mission to reduce cost as a barrier to women’s access to birth control. She noted that the partnership made the LNG20 Intrauterine Device (IUD) commercially available in the U.S., with a very low price in U.S. public sector clinics.

Sharon Levine of Kaiser Permanente Medical Group said that biopharmaceutical market is different from traditional markets in that there is no “free” market. She explained that in a healthy free market, prices are determined through a process of negotiation and competition but in the biopharmaceutical market, laws provide monopoly protection for sellers, both in terms of patents and other forms of market exclusivity. Likewise, buyers have had their bargaining power systematically undermined by coverage policies, essentially turning many buyers into price-takers who must accept whatever price the pharmaceutical companies set. Levine suggested possible ways to make drugs affordable to patients, including legislation at the state and federal level requiring transparency in pharmaceutical pricing, balance among public health, health of individuals and a fair return on investment that does not bankrupt society, and re-examining current patent law and exclusivity parameters. She added that Congressional action may be necessary to create meaningful reform in drug pricing. Like many other speakers, Levine called for multi-stakeholder agreement on defining the term “value” (as in value-based pricing).

Ronald Hansen of University of Rochester Simon Business School described analyses of FDA approvals and R&D spending for new drugs and biologics (DiMasi, Grabowski, and Hansen, 2003; 2016). Hansen noted that the R&D process is lengthy and entails substantial financial risks, with expenditures incurred for many development projects that fail to result in a marketed product. He noted that the approach used in these analyses links the costs of

unsuccessful projects to those that are successful in obtaining marketing approval from regulatory authorities. Hansen explained the challenges in disaggregating the overall R&D costs and the caveats in using aggregate data in these analyses.

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