Attachment — Additional Questions for the Record

The H. Morgan Griffith (R-VA)

1. Do you consider the list price of a drug the real price of the drug or a starting point for negotiation?

A medicine's list price typically refers to its wholesale acquisition cost (WAC). Set by the manufacturer, WAC is the price charged to wholesalers or other direct purchasers before any discounts, rebates, or other price concessions are applied. Public and private payers rarely, if ever, pay the list price for medicines. List prices typically serve as a starting point for negotiations with private payers, as the discounts and rebates pharmacy benefit managers (PBMs) and insurers obtain are customarily set in relation to WAC.

   a. Do you consider the true price of a drug the list price or net price?

The net price of a medicine reflects the final cost to a public or private payer after factoring in applicable manufacturer discounts, rebates, and other price concessions. Because payers rarely, if ever, pay the list price for medicines, analyses based on list prices can paint an inaccurate and misleading picture of drug pricing and spending trends. For example, rebates negotiated by private payers are often substantial and can reduce list prices by 50 percent or more for commonly used classes of medicines.[i]

Unfortunately, PBMs and insurers typically require patients with deductibles and coinsurance to pay their cost-sharing amounts based on the undiscounted list price of a medicine, rather than the lower net price the payer receives. This differs from other health care services, where insurers typically base patient out-of-pocket spending for care received from in-network doctors and hospitals on negotiated rates. If a PBM or insurer excludes a medicine from formulary or imposes utilization management criteria that delay or restrict access, patients may have to pay the full list price out of pocket to obtain the medicine they need.

The Honorable Frank Pallone, Jr. (D-NJ)

2. In your testimony, you stated, "$2.5 billion in revenue is needed to invent one new chemical entity".

   a. Can you please provide the average revenue a brand-name drug receives in the first five years following its approval by the FDA?

Revenues earned in the first five years after FDA approval should be viewed in the context of the high cost, long timelines, and substantial risk of failure associated with drug development. Peer-reviewed estimates of average development cost vary by

methodology, but all indicate that bringing a medicine to market requires very large up-front investment and that the costs of development failures and unsuccessful programs are an important part of the overall R&D equation.

DiMasi et al. estimated that it costs $2.6 billion on average (in 2013 dollars) to develop one new medicine, and only 12 percent of compounds that enter clinical testing ultimately achieve FDA approval.[ii] In that context, Tu et al. found that among newly marketed brand-name medicines first marketed between 2008 and 2016, median five-year net sales were $719 million for medicines with an initial orphan designation and $812 million for non-orphan medicines, in 2021 U.S. dollars.[iii] These revenue figures therefore should not be viewed in isolation: revenues from successful medicines must help offset the costs of the many development programs that do not result in approval and support continued investment in future R&D.

b. Can you please provide the average revenue that brand-name drugs that maintain market exclusivity receive on an annual basis?

Peer-reviewed literature indicates that the average time to generic entry for small-molecule brand-name medicines has been consistent since the passage of the Hatch-Waxman Act and is finite. In their most recent analysis, Grabowski et al. found that for new molecular entities (NMEs) experiencing first generic entry in 2017 to 2019, the average market exclusivity period (MEP) was 13.0 years for higher-sales medicines with more than $250 million in sales before generic entry.[iv] The authors found that the MEP of 13 years had changed relatively little since the previous decade and remained lower than for all NMEs (14.1 years).[v]

In the context of expected market exclusivity periods, the peer-reviewed literature does not provide a single estimate of the average annual revenue for all brand-name medicines that maintain market exclusivity, but it does provide a range of estimates. In a narrow study of 153 top-selling medicines eligible for price setting under the Inflation Reduction Act (IRA), Vogel et al. found that median discounted U.S. revenue by year nine was $2.4 billion for small molecules and $4.3 billion for biologics, rising by year 13 to $3.4 billion and $6.1 billion, respectively. These figures, taken together with the Tu et al. analysis discussed above, suggest that estimates of annual revenue during the market exclusivity period vary substantially depending on whether one is examining a broader cohort or a smaller group of top-selling products and what methodology is applied. Additionally, an analysis of 75+ small molecule medicines launched from 2005 to 2009 found that sales revenues in post-launch years 10 to 13 accounted for approximately one-third of gross and net sales. Lifetime sales revenues were even more backloaded for first-in-class medicines in the cohort, with 40 percent of gross and 38 percent of net total sales occurring between 10 to 13 years after launch.[vi]

3. Your written testimony states, "Early evidence shows that the IRA has reduced investment in small-molecule medicines by 68 percent, and by 74 percent for diseases mainly affecting Medicare patients, since the law was introduced." However, the citation to back up this claim is research that appears to have been conducted on behalf of drug manufacturers.

    a. Can you provide any independent assessments, devoid of any funding from drug manufacturers, that show that the IRA has decreased investment in small-molecule drugs?

To the best of our knowledge, no such studies have yet been conducted. However, that does not diminish the significance of the existing empirical evidence, which has undergone peer review and is subject to disclosure requirements and methodological transparency, safeguards that help mitigate potential bias by subjecting studies to external scrutiny, and enabling other researchers to evaluate and replicate the analyses. Furthermore, focusing solely on funding criteria misses the more salient point: multiple studies using different data sources, modeling approaches, and analytical frameworks have independently reached similar conclusions about the IRA's effects on small-molecule investment.

The strongest empirical evidence published to date points in a consistent direction. Schulthess et al. analyzed a longitudinal dataset of early-stage investments linked to lead assets in clinical development and reported that aggregate investment into small molecules in 2024 was 68 percent lower after IRA passage, with investment size declining as Medicare exposure increased.[vii] Zheng, Patterson, and Campbell used Citeline Trialtrove data and an interrupted time-series design to study post-approval trials and found that, after the IRA's passage, the average monthly number of industry-sponsored post-approval trials fell by 38.4 percent, with larger declines for small molecules (47.3 percent) than for large molecules.[viii] Genia Long likewise reported early evidence of reductions in clinical trial starts for small molecules before and after IRA passage, utilizing data from Citeline Trialtrove and Pharmaprojects databases, finding reductions in industry-sponsored pre-approval trials for new small molecule medicines of 25.2 percent and post-approval small molecule trials of 29.5 percent after IRA passage. In comparison, the model did not find significant declines for trials of biologic medicines.[ix] The best available early empirical evidence indicates emerging signs of reduced investment in and development of small-molecule medicines, even though the literature is still developing and longer-term effects will require additional study.

<u>The Honorable Raul Ruiz (D-CA)</u>

1. It is no secret that Secretary Kennedy is a long-time vaccine skeptic and this past year has worked to decimate U.S. vaccination policy, including by dropping recommendations for COVID-19 shots for pregnant women and children, directing

states to limit their vaccine administration and cutting funding for mRNA-based vaccine research. Pfizer's CEO, a member of PhRMA, even said that Kennedy's policies are "almost like a religion" and "anti- science." Ms. Reilly, from PhRMA's position, if changes continue to be made that fly in the face of well-established, rigorous and evidence-based research, what will happen to the progress we have made in protecting children and families from dangerous diseases?

PhRMA and our member companies share your commitment to protecting children and families from vaccine-preventable disease. Innovative biopharmaceutical companies are developing new ways of preventing and treating illnesses, with vaccines at the forefront. Today, there are nearly 300 vaccines in development by biopharmaceutical research companies for the treatment or prevention of disease.[x]

However, the advancements made in eradicating so many diseases are not guaranteed. Continued public health progress depends on a stable, evidence-based policy environment that supports research, development, and protections for vaccine access and coverage. When that environment becomes uncertain, vaccination rates decline and diseases re-emerge[xi,xii] and the innovation pipeline that delivered decades of advances is jeopardized. In today's uncertain vaccine policy environment, access can be compromised in two reinforcing ways:

- **Shifting CDC recommendations can create confusion for parents, heath care providers, and payers about which vaccines must be covered and when they should be administered. Any changes in recommendations could disrupt coverage and vaccine uptake. Those who rely on coverage protections and public programs (such as Vaccines for Children)[xiii] could be left less protected from vaccine-preventable disease.[xiv]**

- **Regulatory unpredictability and changing evidentiary standards[xv] can deter or delay vaccine research and development manufacturing investment, weakening the pipeline.[xvi]**

The vaccine pipeline promises a brighter future, with new technologies that could treat or prevent disease in ways once not possible. To sustain that progress, vaccine policies should be transparent and grounded in evidence, with immunization recommendations developed by clinicians and infectious disease experts. This will reduce avoidable confusion for payers and providers, protect access to recommended vaccines, and preserve the innovation ecosystem that delivers lifesaving vaccines.

The Honorable Jake Auchincloss (D-MA)

1. I am concerned that the staff at FDA have been eviscerated and demoralized. Last year, there were reports that the Administration laid off 3,500 employees from across the agency. We still cannot get answers on where these staff were taken from, how many may have been brought back, or how many may be conflicted out of their jobs in reviewing product application because they are rightfully fed up with how they have been treated by the Administration and have decided to leave the agency. What

we do know is that data from FDA, which we only have because it is mandated by statute that they report it, posted on their website shows that the drug and biologics centers continued to lose staff through the first quarter of FY 2026. Part of the user fees that FDA and industry negotiate and that Congress has authorized are designated to go toward hiring efforts. To me it looks like they are having trouble doing that because of the turmoil under this administration.

a. What is the importance of maintaining staffing levels at FDA?

Maintaining robust, stable staffing at the FDA is foundational to both public health and the continued strength of the U.S. biopharmaceutical industry. FDA scientific and medical reviewers, project managers, statisticians, inspectors, and other staff are the backbone of the drug review and approval process and work tirelessly to ensure patient access to safe and effective life-saving medicines. When staffing levels decline or turnover rises, review timelines can slow, meetings may be delayed, feedback may become less predictable or less thorough, and scientific questions can go unresolved. That directly translates into delayed access for patients, particularly those with serious or rare diseases who depend on efficient review of innovative therapies. Through programs like the Prescription Drug User Fee Act, FDA is provided significant funding specifically to support hiring and retention. If FDA is unable to recruit, retain, and effectively deploy staff, it undermines the intent of those agreements and the performance goals negotiated with Congress.

Adequate staffing is not just about speed; it is also about maintaining the high-quality, science-based review process that helps ensure safe and effective medicines can reach patients. Overburdened or inexperienced teams increase the risk of errors, inconsistent application of standards, and lack of familiarity with regulatory standards, directly impacting patient safety. FDA has long been the global gold standard for regulatory review because of its scientific rigor and reliability – there is no substitute for sound scientific principles to protect public health.

Additionally, drug and biologics review, especially for complex modalities like cell and gene therapies, require highly specialized expertise. Loss of experienced staff erodes institutional knowledge, increases the burden on remaining reviewers, and raises the risk of inconsistent or less predictable decision-making. It can also lead to less regulatory flexibility as it takes significant review experience to apply innovative regulatory thinking effectively; newer reviewers are often more comfortable relying on a conservative interpretation of statutes and regulations. Rebuilding that expertise is neither quick nor easy. Ongoing attrition raises serious concerns about morale and retention. If sponsors begin to experience delays, unclear guidance, or inconsistent engagement due to staffing gaps, it risks driving even more early development or first-in-human trials to other jurisdictions. This poses a real risk for the competitiveness of the U.S. biotech industry as countries like China and Australia actively streamline clinical trial pathways. This can also stall or delay drug development programs and related regulatory review.

Finally, a fully staffed inspectorate within the FDA is critical to ensuring the integrity of the global pharmaceutical supply chain. Staffing shortages can lead to inspection backlogs, reduced foreign surveillance, and delays in product approvals related to facility inspections. Maintaining staffing levels at FDA is essential to protecting public health and facilitating innovation. Instability in the workforce risks slower reviews, reduced scientific capacity, decreased ability for external engagement, quality and patient safety issues, and diminished global leadership at a time when the complexity of drug development is increasing and international competition is intensifying.

The Honorable Jennifer D. McClellan (D-VA)

1. One of the best-selling drugs in the world, Keytruda, is manufactured by one of your member companies, Merck. Keytruda is an effective cancer medication that can cost upwards of $100,000 per course of treatment. This drug has been on the market since 2014, and as one of the witnesses at the hearing noted, Merck's revenue on Keytruda on was $31.7 billion in 2025 alone. As part of the Republican reconciliation legislation, Keytruda received an exemption from price negotiations required by the Inflation Reduction Act – an exemption that the Congressional Budget Office estimated will cost taxpayers billions of dollars.

    a. Can you detail how much CBO estimated this provision will cost? And how much of that cost is attributed to Keytruda?

Keytruda was not exempted from price setting under the IRA; its eligibility for selection was delayed due to the enactment of the Orphan Cures Act (OCA), which reduces some of the disincentives to developing orphan drugs created by the IRA and CMS's approach to the original statute. Just 5 percent of the 7,000 known rare diseases have an available treatment option, each of which affect fewer than 200,000 people.[xvii,xviii] In the absence of incentives to encourage the development of medicines to treat rare diseases, where there is limited ability to earn a return on investment and enormous development challenges, there would be very few treatments to meet this enormous unmet need. Cancer medicines in particular are often initially researched and approved in rare cancer types, in patients with more advanced stages of disease, and in those who have exhausted other treatment options. Over time, additional research may demonstrate that the medicine is beneficial, for example, before trying other treatments or in earlier disease stages. While the IRA provided a specific exclusion from price setting for medicines approved for certain orphan drugs, this exclusion was far too narrow to preserve incentives for orphan drug development, including in rare cancers. Products with multiple orphan designations or approved for additional indications outside of a sole orphan designation, for either a rare or non-rare condition, could be subject to price setting.

The OCA corrects the narrow orphan drug exclusion by excluding medicines approved solely for rare diseases or with multiple orphan designations from Medicare price setting. It also addresses CMS's overreach by setting the eligibility clock to begin only once an orphan drug is approved for a non-orphan use, supporting essential incentives for orphan drug development and post-

approval R&D. As Keytruda was initially approved for an orphan designated use, its eligibility clock for price setting was delayed to the date of approval of Keytruda's first non-orphan indication.

We are unaware of Keytruda's specific contribution to the score of the OCA. However, it is important to note that claims that delaying selection of medicines that treat rare diseases will increase costs misrepresent the broader context of how Medicare price setting works. First, when the selection of a medicine is delayed, CMS still selects another medicine for price setting in its place. Second, medicines with delayed selection may still be selected in a future year once they are eligible, allowing price setting to go into effect later in the budget window. Some medicines may never end up becoming newly eligible for selection due to the arrival of a biosimilar or generic competitor, and the Medicare program benefits from savings in this scenario. Indeed, Medicare payment rates for originator biologics covered under Medicare Part B have fallen by up to 95 percent since the introduction of biosimilars.[xix] And Medicare spending on both originator biologics and their biosimilars fell by 24 percent between 2022 and 2023.[xx]

b. How does this exemption align with PhRMA's stated positions on affordability and competition?

As noted above, while the OCA may affect the timing of eligibility of certain orphan drugs for price setting, CMS can still select the requisite number of medicines for price setting each year. Moreover, shorter timelines to conduct post-approval R&D for all medicines under the IRA will continue to impact the development of orphan drugs regardless of the OCA's fix.

The U.S. market-based system is designed to balance innovation, access, and cost containment by promoting robust competition among brand medicines, generics, and biosimilars—driving down prices, and often reducing costs by 50 percent or more.[xxi] Competition among brand medicines alone has generated billions in savings, with one study showing that launches of new brand medicines between 2013 and 2017 led to over $10 billion in price reductions across 12 therapeutic classes.[xxii] Over time, this system delivers long-term savings as branded medicines are followed by generics and biosimilars, which now account for 90 percent of prescriptions and have saved $3.4 trillion over the past decade.[xxiii]

Despite this success, the IRA and CMS' implementation of its price setting program threaten to dismantle these incentives by allowing the government to impose prices so low that generic and biosimilar manufacturers may no longer find it viable to enter the market. Ultimately, by substituting price setting for competition, the IRA risks unraveling the very system that has delivered innovation, competition, and affordability to patients. It also does not help patients afford their medicines – 90% of Medicare fee-for-service beneficiaries have supplemental insurance that covers their Medicare Part B out-of-pocket drug costs, meaning price setting will not lower these beneficiary costs.

[i] MedPAC (July 2025). A Data Book: Health Care Spending and the Medicare Program. Available here.
[ii] DiMasi JA, Grabowski HG, Hansen RW. (2016) Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ*. Available here.
[iii] Tu SS, Nagar S, Kesselheim AS, et al. (2023) Five-year sales for newly marketed prescription drugs with and without initial orphan drug act designation. *JAMA*. Available here.
[iv] Grabowski, Henry, Long G, Mortimer, R, et al. (2021). Continuing trends in US brand-name and generic drug competition. *Journal of Medical Economics* 24.1 Available here.
[v] *Ibid.*
[vi] Ehrenberg R. (December 2016). Medicare's drug price negotiation program: the disproportionate impact on small molecules. IQVIA. Available here
[vii] Schulthess, Duane G., et al. (2025) The Inflation Reduction Act's impact upon early-stage venture capital investments. *Therapeutic Innovation & Regulatory Science*. Available here.
[viii] Zheng H, Patterson JA, Campbell, JD. (2025) The Inflation Reduction Act and drug development: potential early signals of impact on post-approval clinical trials. *Therapeutic Innovation & Regulatory Science*. Available here.
[ix] Long, Genia. (2026). Trends in industry-sponsored clinical trial activity since passage of the Inflation Reduction Act. *Journal of Medical Economics*. Available here.
[x] PhRMA. (July 2024). Vaccines in Development. Analysis based on Number of vaccines obtained through public government, and industry sources, and the Adis "R&D Insight" database. Available here.
[xi] Seither R, Yusuf OB, Dramann D, et al. (2024). Coverage with Selected Vaccines and Exemption Rates Among Children in Kindergarten — United States, 2023–24 School Year. *CDC Morbidity and Mortality Weekly Report.* Available here.
[xii] Hill HA, Yankey D, Elam-Evans LD, et al. Decline in Vaccination Coverage by Age 24 Months and Vaccination Inequities Among Children Born in 2020 and 2021 — National Immunization Survey-Child, United States, 2021–2023. (2024). *CDC Morbidity and Mortality Weekly Report.* Available here.
[xiii] Kolb K. (November 2025). Lower-Income Kids Are at Higher Risk of Going Unvaccinated. The Commonwealth Fund. Available here.
[xiv] Crays A, Farrell C, Musumeci M. (January 2026). Kids Lose When Vaccine Coverage Rules Are Unclear. The Commonwealth Fund. Available here.
[xv] Prasad V, Makary MA. (2025). An Evidence-Based Approach to Covid-19 Vaccination. *New England Journal of Medicine*. Available here.
[xvi] Califf, Robert M, von Eschenbach AC, Friedman MA, et al. (2025). A Threat to Evidence-Based Vaccine Policy and Public Health Security at the FDA." *New England Journal of Medicine.* Available here.
[xvii] Fermaglich, L, Miller, K. (2023). A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. *Orphanet Journal of Rare Diseases*. Available here.
[xviii] FDA. Rare Diseases Accelerator. Available here.
[xix] MedPAC (July 2025). A Data Book: Health Care Spending and the Medicare Program. Available here.
[xx] *Ibid*.
[xxi] *Ibid*.
[xxii] Dickson S, Gabriel N, Hernandez I. (2023). Changes in Net Prices and Spending for Pharmaceuticals After The Introduction Of New Therapeutic Competition. *Health Affairs.* Available here.
[xxiii] Association for Accessible Medicines. (2025) The U.S. Generic & Biosimilar Medicines Savings Report. Available here.