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House Small Business Committee
Stifling Innovation: Examining the Impacts of Regulatory Burdens on Small Businesses in Healthcare
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Chairman Williams, Ranking Member Velázquez, thank you for the opportunity to appear before this Committee to discuss the drug development ecosystem and the challenges small biotechnology companies face. My name is Bill Newell and I am the CEO of Sutro Biopharma, Inc. I have been at Sutro since January 2009 and working in small company biotech since 1998. I also serve on the Board of the Biotechnology Innovation Organization and chair BIO's Capital Formation Work Group.

The Sutro Story

Sutro Biopharma focuses on research & development and manufacturing for next generation cancer medicines, primarily antibody-drug conjugates (ADCs). Our company is 21 years old, founded in 2003 with patent-protected technology licensed from Stanford University. I was employee number 19 and today we have over 300 employees and a market cap of approximately $300 million. Like many U.S.-based biotechs, Sutro has seen substantial domestic job creation, with about 40% of our work force in or supporting our US-based cGMP manufacturing facility. We built and operate the world's only manufacturing facility utilizing cell-free protein synthesis technology at scale and producing clinical trial materials for Sutro and our partners. We have begun two pivotal Phase 3 trials for our most advanced therapeutic candidate luveltamab tazevibulin – for patients with late-stage ovarian cancer and patients with an ultra-rare pediatric acute myeloid leukemia (AML) – with read outs not expected for a few more years. We have multiple additional potential medicines in research and early clinical development.

In many ways, Sutro's corporate journey is a microcosm of the small biotech experience. We were initially financed by private investors, including venture capitalists and big pharma/biotech venture investors. We raised Series A through E venture rounds totaling approximately $190 million. We went public in 2018, benefiting from the JOBS Act of 2012 that made it easier for small companies to go public. So far, we have raised approximately $535 million in public market offerings. In addition, collaborations with larger industry players have been essential to our growth. We have received approximately $720 million in funding and reimbursements for R&D collaborations and/or licensing of product candidates from large and midsized biopharma companies. In addition, at various points in time, we have borrowed from venture lenders. I am proud to say that we are debt-free as of earlier this year. All told, Sutro has raised almost $1.6 billion in the company's history, and we are still several years from the possibility of a commercial product. That eyebrow-raising figure and our over 20-year company journey is, unfortunately, very typical of the small biotech experience in bringing a product to market.

Also, like many biotechs, we have had our share of failures along the way. Three potential medicines have made it to the clinic, but development was halted by us or our partners as they did not meet criteria for continued advancement. This is not unusual in our industry; only approximately 12% of products reaching clinical development stage are ever approved and just half of products reaching Phase 3 (pivotal trial stage) ever get FDA approval.

Given these high costs and low success rates, small biotech companies and their investors are particularly sensitive to the U.S. policy environment in which we operate. Ensuring a robust domestic biotechnology industry is rightfully recognized as a critical national security issue. In addition, it is also an economic juggernaut, with high growth potential and high wages across the country. Thus, it is critical that we

implement and support policies that encourage our development and reexamine policies that deter investment and delay treatments. Accordingly, I'd like to devote the rest of my testimony to outlining some of the critical policy factors impacting the biotech ecosystem and what policies should be considered for our industry to survive.

Access to Capital

It is a truism that capital is the lifeblood of small biotechs. In our continuing quest for sufficient investment to fund our mission, federal policies that encourage investment and capital formation are essential. Congress should:

- Restore the R&D deduction is extremely important for companies like mine that are being hit with a multi-million dollar tax liability as a result of the switch to 5-year amortization, even though we have no product on the market. Our tax liability reduces our funds that were, and should be, going to research and development to bring new medicines to patients.
- Right-size SEC reporting requirements for small public companies would save small companies millions in reporting costs that provide information our investors don't want or need.
- Reauthorize the SBIR/STTR government grant programs would help the very early-stage companies and provides a critical lifeline that should be reauthorized and expanded.
- Allow for pre-revenue companies with less than 500 employees to monetize their Net Operating Losses (NOLs) today to provide a much-needed cash infusion by forgoing this existing tax benefit in the future.

In the ongoing search for investment, policies like these can make the difference between a promising company succeeding in bringing a new medicine to patients or running out of runway and ending research and development on potential new medicines.

Importance of Strong Protections for Intellectual Property

Very few sectors of the nation's economy are as dependent on predictable, enforceable patent rights as the biotechnology industry. Robust patents that cannot be easily circumvented or invalidated, and that can be predictably enforced against infringers, enable biotechnology companies to secure the enormous financial resources needed to advance biotechnology products to the marketplace. Further, they allow biotechs to engage in the partnering and technology transfer that is necessary to translate basic scientific discoveries into real-world solutions that treat disease, address climate and other environmental challenges, and produce abundant, healthy food for the world. These financing pathways include venture financing, IPOs, follow-on offerings, and licensing partnerships, and are all predicated on the existence of stable and enforceable intellectual property rights. Anyone who has ever watched Shark Tank knows that without a dependable patent system, capital for the cures of the future will not be available.

These financing pathways have been critical to the success of our companies like Sutro. Without strong and reliable patents, we would not have been able to secure the investments or partnerships over the years as we seek to prove the safety and efficacy of our leading therapeutic drugs. If patents can be invalidated under overly broad criteria, if the ability to enforce them becomes limited, or if limits on patent eligibility call into question the ability to obtain patent protection for innovative cures, third parties would be less likely to invest in or license the technology and major sources of R&D funding would move elsewhere. The result – patients waiting for the next new cure or treatment will have to wait longer or may not ever get it at all. Because investment-intensive businesses can tolerate only so much risk, even moderate additional uncertainty can cause business decisions to tip against developing a high-risk, but potentially highly beneficial, therapeutic medicine.

Unfortunately, changes to our patent laws through legislation, agency actions, and court decisions, have severely weakened our patent system. Although the U.S. patent system was once considered the gold standard for the rest of the world, in the latest global survey conducted by the U.S. Chamber of Commerce, our patent system was rated behind Singapore, Japan, and South Korea.[1]

There are several reasons why the US patent system is no longer the international gold standard. As the Chamber of Commerce report notes, "the patenting environment in the United States continues to be held back by uncertainty over what constitutes patent-eligible subject matter and patent nullity proceedings through the inter parties review, which occurs before the specialized Patent Trial and Appeals Board within the U.S. Patent and Trademark Office (PTO). Since the Supreme Court decisions in the Bilski, Myriad, Mayo, and Alice cases, there has been a high and sustained level of uncertainty about which inventions are patentable in the United States."[2] These continuing threats merit the attention of Congress.

It has become clear that the PTO's Inter Partes Review (IPR) system of administrative patent challenges in the Patent Trial and Appeal Board (PTAB) is having a game-changing effect on the reliability of patents as a basis of investment in the biotechnology industry. Patents that are involved in district court litigation are now routinely subjected to concurrent administrative litigation in the PTO, where they are being invalidated at rates so high that the basic procedural fairness of these proceedings is increasingly being questioned. This creates a great risk of duplicative proceedings and inconsistent outcomes, as alleged infringers seek to gain advantages or leverage over patent owners that would not exist under district court litigation alone. For example, the way claims are interpreted, and other procedural protections are less favorable to patent owners in the PTO administrative setting.

In addition, third parties with no commercial interest in the patent or field to which the patent pertains have figured out that they can extort settlements or otherwise gain financially from bringing, or even threatening to bring, patent challenges against critical patents owned or licensed by biotech companies. Biotech companies can be particularly vulnerable to such extortion because – in contrast to most high-tech companies – biotech companies often rely on just a handful of highly valuable patents to protect their products and massive investment therein.

Such abuses of the PTO administrative review system are attractive and growing because, as is quite clear to those following the evidence to date, the rules governing these proceedings are unfairly stacked against patent owners in many ways. In particular, the PTO uses a claim construction standard that is much broader than that used in district court and has limited the ability of patent owners to file narrowing amendments to preserve their patent claims.

Bipartisan legislation to address the most glaring problems with the PTAB system has been introduced in both Chambers: the "Promoting and Respecting Economically Vital American Innovation Leadership Act" or the "PREVAIL Act" introduced by Senators Chris Coons (D-DE) and Thom Tills (R-NC) and Representatives Ken Buck (R-CO) and Deborah Ross (D-NC).[3]

Continued uncertainty remains with respect to patent eligible material under section 101 of the Patent Act.[4] It is important that our patent system keeps pace with advancements in science. Our foreign competitors in Europe and China now extend patent protection to significant innovations that are not

[1] US Chamber of Commerce, Global Innovation Policy Center, International IP Indelx, 12th ed. at 45 (2024).
[2] Id. at 46.
[3] S. 2220/H.R. 4370.
[4] 35 USC §101.

patent eligible in this country. That places us at an unacceptable competitive disadvantage in emerging technologies.[5] It is legislation like the PREVAIL Act, and others such as S. 2140, the Patent Eligibility Restoration Act of 2023, introduced by Senators Tills and Coons, that would bring predictability to our patent system and place U.S. innovators such as Sutro on an even footing with our competitors around the world.

I am also concerned about calls to expropriate patents. The Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights[6] would reverse more than 40 years of successful federal policy under administrations of both parties by using the Bayh-Dole Act as a price control mechanism. The threat of government seizure of patents would place a cloud over every patent developed with federal funding. It would ensure that federally funded research remained on the shelf rather than attracting startups prepared to make the substantial investments to further invent and develop life changing therapeutics.

Modernize the FDA to Ensure a Predictable Regulatory Environment

Industry routinely invests in innovative tools and approaches to develop better medicines that meet the needs of patients, such as decentralized clinical trials, model-informed drug development, drug development tools, complex innovative trial design, patient-focused drug development, and leveraging real-world data. In general, there remains a degree of hesitation among drug developers regarding the adoption of such innovative approaches for clinical trials which is largely attributed to a lack of clarity, consistency and dedicated Agency resources. While the FDA encourages industry to explore new methodologies, such as new study designs and approaches, industry still finds these methodologies risky to implement due to continued uncertainty regarding the regulatory outcome. For the industry to effectively design and conduct innovative clinical trials, the FDA's timely, substantive, and interactive scientific input is needed to help reduce regulatory uncertainty.

Preserve and Protect the Accelerated Approval Program

The FDA's traditional approval pathway measures how drugs improve patients' symptoms, functioning, or survival. But it can take years to verify this "clinical benefit." For patients whose disease can't wait that long, the Accelerated Approval Program evaluates drugs based on "surrogate endpoints" or "intermediate clinical endpoints" likely to predict clinical benefit. These endpoints might include X-rays, reduction in tumor size, or blood tests. Policy discussions about the evaluation of the Accelerated Approval Program cannot be complete without assessing its impact on its most important target outcome: patient survival. A recent analysis shows[7] that that from 2006-2022, more than 900,000 patients with cancer gained approximately 263,000 life years as a result of earlier access to medicines through accelerated approval. For this reason, the Accelerated Approval Program needs to be protected from detractors who question its benefit.

Unfortunately, in the past few years the FDA has tightened, to the point of constricting, the utilization of the Accelerated Approval Program. For example, small companies with new cancer medicines previously

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[5] Adam Mossoff, Kevin Madigan, Turning Gold to Lead: How Patent Eligibility Doctrine Is Undermining U.S. Leadership in Innovation, 24 Geo. Mason L.Rev. 939 (2017).
[6] 88 FR 85593 (Dec. 8, 2023).

[7] *From <https://jnccn.org/view/journals/jnccn/aop/article-10.6004-jnccn.2024.7010/article-10.6004-jnccn.2024.7010.xml?sp_sn=linkedin&spclid=128E9C41-D359-4165-BC81-BFBC1C18BB60&ArticleBodyColorStyles=abstract%20%2F%20extract>*

could seek to take advantage of the Accelerated Approval Program by first pursuing a single arm pivotal trial in one hundred or so late-stage cancer patients using surrogate end points and then further demonstrating patient benefit with a much larger confirmatory trial to demonstrate prolonged disease control and ultimately a survival benefit. Achieving a successful outcome and accelerated approval, the small company would raise additional funding and start a much larger (hundreds of patients) confirmatory trial. The data underpinning the accelerated approval provides the confidence to the company and its investors to make the substantial additional investment in the confirmatory trial.

Recently, the FDA has required that companies have completed or substantially completed enrollment in their confirmatory trial by the time the FDA takes action on a request for accelerated approval. Sutro has recently been held to this newly changed regulatory standard. This forces companies like Sutro to commit additional resources (hundred of millions of dollars) much earlier than would have been previously required. This additional accelerated expense can prove extremely challenging for small companies and threatens the promise of rapidly bringing new life-extending medicines to patients who desperately need them.

User Fees in PDUFA VII

The biotechnology industry supports the FDA's ability to pursue its mission through user fees. Indeed, industry now pays approximately 75% of FDA's drug review program costs. Of great concern, in 2023, FDA increased user fees by 25%, meaning that a New Drug Application or Biologics License Application is $4 million. To continue to develop innovative new medicines for the American people, the biotechnology industry needs user fees that are predictable, stable and affordable.

Reauthorize the Pediatric Priority Review Voucher Program

The Pediatric Priority Review Voucher (PPRV) program provides critical incentives to promote R&D for drugs to treat rare diseases impacting children across the country. Rare diseases, by definition, impact a small percentage of the patient population. The costs of drug development paired with the risk involved of bringing a successful drug to market can often discourage investment in the rare disease space. This is especially true for rare diseases unique to children.[8] The current program expires Sept. 30, 2024, and Sutro and our industry partners strongly support the *Creating Hope Reauthorization Act of 2024*. This bipartisan bill would reauthorize the Pediatric Rare Disease Priority Voucher Program. As I testified earlier today, Sutro is pursuing a pivotal trial for an ultra-rare pediatric acute myeloid leukemia (AML). This type of AML affects globally approximately 50 infants and toddlers a year. While our medicine shows encouraging efficacy in this very aggressive form of AML, as well as good tolerability, and while the pivotal study is for a small number of these children, the economics of pursuing this indication would clearly dictate that we not do so. The key economic rationale for us to pursue this ultra-rare indication for regulatory approval is the value to Sutro of a Pediatric Priority Review Voucher. It is cases like this one that make it imperative that this program be reauthorized.

Fix the Disincentives in the Inflation Reduction Act

The Inflation Reduction Act (IRA) authorizes the Secretary of Health and Human Services to “negotiate” the price Medicare pays for certain medicines. With stiff penalties for drug companies that don't comply, there is little room for negotiation and so, it is simply a price control. The IRA’s impact drives companies to make difficult choices on therapy class, population size, which indications to pursue first and whether to invest in new indications. Companies and investors now factor in more limited economics in their decision making, not the science. I believe that fewer medicines will be developed as a result.

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[8] https://bio.news/federal-policy/reauthorize-pprv-pediatric-rare-disease-priority-review-voucher-vaccine-safety-systems/

Continue Investment in Rare Disease Drug Development and Pass the ORPHAN Cures Act
As discussed, developing new drugs is an incredibly risky and capital-intensive endeavor-- only 12% of drugs entering clinical trials ultimately receive FDA approval.[9] [10] [11] Now consider rare diseases-- which in some cases afflict just a few hundred people.[12] [13] Such a small patient population makes it extraordinarily difficult for biotech companies to justify the massive R&D costs required to develop a new treatment.

Congress sought to help alleviate the lack of investment in rare diseases in 1983 when it passed the Orphan Drug Act. The law gives tax credits to companies who develop novel rare disease treatments, also known as "orphan drugs."[14] The legislation has been a resounding success-- FDA-approved treatments for rare conditions have increased over 2,000% since its passage.[15] In fact, Sutro has received orphan drug designation, as well as rare pediatric disease designation for our treatment of this ultra-rare AML.

But instead of building on the successes of the Orphan Drug Act, the Inflation Reduction Act (IRA) punishes companies trying to find novel treatments for rare diseases. The law permits the federal government to impose severe price caps on prescription drugs covered under Medicare. The IRA exempted orphan drugs from the price controls if they treat a *single* rare disease.[16] But medicines that treat *multiple* rare diseases don't qualify for the exemption.

This limited exception from negotiation is a significant problem. Drug makers routinely investigate whether a drug already approved to treat one rare condition could possibly treat another.[17] Historically, this "follow-on" research has provided transformational cures to patient groups who don't have access to effective treatments. The IRA is already forcing some drug companies to freeze efforts to find additional applications for existing rare disease drugs.[18] In short, the IRA's negative treatment of orphan products is a direct contradiction of the positive, and life-changing, work done by Congress in passing the Orphan Drug Act itself many years ago.

Ensure Critical Research for Small Molecule Drugs
Certain areas of research will feel the devastating impact of the IRA even more than others because IRA price controls apply differently to different kinds of medicine. "Small molecule" (oral) drugs can be subject to price controls just nine years after earning FDA approval. By contrast, biologics – typically infused or injected medicines – are not subject to price controls for 13 years.

Most pharmaceuticals on the market today, including at least 89 anti-tumor drugs for treating cancer, are small-molecule drugs. But the new IRA rules disincentivize research into this critical area of medicine. Consider that much research on oncology medicines happens after they earn FDA approval and patient

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[9] https://www.m2gen.com/company-news/industry-insights/how-long-do-new-cancer-drug-therapies-take-to-go-to-market#:~:text=On%20average%2C%20it%20takes%2010,the%20Study%20of%20Drug%20Development

[10] https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf p. 3

[11] https://www.cbo.gov/publication/57126#:~:text=Only%20about%2012%20percent%20of,for%20introduction%20by%20the%20FDA.

[12] https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf p. 1

[13] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4543882/

[14] https://oig.hhs.gov/oei/reports/oei-09-00-00380.pdf p. 1

[15] https://pkdcure.org/saving-the-orphan-drug-tax-credit/ (MATH: 650-30/30 = 20.667 x 100 = 2067%)

[16] https://www.kff.org/medicare/issue-brief/explaining-the-prescription-drug-provisions-in-the-inflation-reduction-act/

[17] https://www.cahc.net/newsroom/2023/3/1/how-the-inflation-reduction-act-is-impacting-rare-disease-patients#:~:text=In%20the%20rare,in%20later%20years.

[18] https://www.bloomberg.com/news/articles/2022-10-27/alnylam-halts-work-on-eye-drug--citing-new-us-law-over-pricing?sref=C4viNJ4s

benefit in one indication has been established. That's when scientists can perform additional tests to discover new uses for a drug, sometimes over the course of a decade or more. It's not uncommon for a medicine developed to treat one cancer to prove highly effective at treating other forms of the disease. But the threat of near-term price controls makes companies much less likely to invest in additional post-approval research.

Given the choice between a nine-year and a 13-year window until price controls kick in, many will choose to prioritize research and development efforts on biologics. An industry colleague who leads a small private biotech company working on small molecule medicines for the most important undrugged targets across human disease told me that he is feeling the discriminatory effects of this "pill penalty". He shared with me that venture investors, who previously funded companies like his, have pulled back from funding such early stage small molecule discovery platforms citing the IRA. But by disincentivizing work on small-molecule drugs, the IRA is robbing patients of life-changing new treatments. Cancer isn't the only research area that will suffer. For example, for neurological diseases like Alzheimer's or the disease that took my mother's life Progressive Supranuclear Palsy, small-molecule medicines may offer some of our best prospects for breakthroughs.

There seems to be a misguided notion that small molecules are cheaper to develop and less risky. This is not the case – the calculus for funding their development is essentially the similar as that for biologics and they merit the same treatment. Extremely effective and cutting-edge medicines exist in both classes – and both avenues of development are complex, expensive, and fraught with failure. One is not "better" than the other. And of course, such distinctions mean little to patients, who just want the best medicine available. Congress should protect innovation and patient access to needed medicines by revising the new rules for Medicare "negotiation" and apply the same 13-year window to both small-molecule drugs and biologics.

Congress should pass two bipartisan pieces of legislation that would mitigate these market distortions.

- The Ensuring Pathways to Innovative Cures (EPIC) Act (H.R. 7174), sponsored by Reps. Greg Murphy, M.D. (R-NC) and Don Davis (D-NC) would fix the small molecule "pill penalty" to ensure continued R&D investments into small molecule medicines.
- The Maintaining Investments in New Innovation (MINI) Act (H.R. 5547/S.476), sponsored by Reps. Wiley Nickel (D-NC) and John Joyce, M.D. (R-PA), and Senators Bob Menendez (D-NJ) and Marsha Blackburn (R-TN), would extend the negotiation of genetically targeted therapies (small complex molecules) to 13 years.

IRA Implementation

Beyond the problems inherent in the IRA statute itself is CMS's implementation of the IRA. Congress should increase its oversight of the Centers for Medicare & Medicaid Services (CMS) as the Agency moves forward in implementing the IRA's price negotiation program. Unfortunately, a critical policy that CMS finalized was its decision that, in determining which drugs are eligible for negotiation, it would not treat drugs approved under unique New Drug Applications (NDAs) or Biologics License Applications (BLAs) as distinct drugs but, rather, would combine NDAs and BLAs with the same active moiety/active ingredient together for negotiation purposes. CMS must reverse this policy as it is bad for innovation, bad for patients, and not supported by the statute. CMS's approach leaves no incentive for therapeutic advancement in additional indications and will have significant, negative impacts on treatments for patients for decades.

CMS must also clarify how its review of the evidence will inform its setting of the maximum fair price ("MFP") for a drug selected for negotiation. CMS's approach remains unclear and presents untenable levels of uncertainty. Essentially, CMS has said it will use the net price of the "therapeutic alternatives" of drugs selected for negotiation as a starting point and then adjust this starting point based on its review of the clinical evidence. In addition, CMS has said it may make further adjustments based on other data manufacturers are required to submit, such as "recoupment" of research and development costs. But CMS has not provided a framework for how it will review all this evidence. Nor has the agency indicated how certain evidence or factors will be weighed. This lack of clarity and uncertainty is of great concern. CMS should clarify its standards for evidence review and be transparent and accountable about what evidence drove its decisions in setting the MFP and why. Further, CMS's review of the evidence should focus on factors that are critical for patients, specifically factors related to clinical benefit and unmet medical need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

Other CMS Policies Impacting Small Biotech Companies

Last year, under the guise of "technical changes", CMS proposed to upend more than 30 years of historical precedent under the Medicaid Drug Rebate Program (MDRP). CMS's proposed changes present significant access threats to a vulnerable group of patients and are without any solid legal grounding.

Of particular concern is the proposed rule's new definition of "best price." Current law defines this as the lowest or "best" price available to any entity in the drug supply chain, be it a wholesaler, insurer, nonprofit, or government entity. The proposed rule would fundamentally change how this best price is determined-- and in a way that makes it vastly more difficult for small- and medium-sized firms like ours to serve Medicaid patients. Specifically, the proposed rule mandates that companies aggregate or "stack" any discounts or rebates provided to various entities who encounter the drug unit in the drug supply chain to calculate the best price. This task is not only daunting but is impossible to implement.

In addition to operational impediments, the rule's overall cost to our companies would be significant and could make ongoing participation untenable. It could thus dramatically reduce the number of drugs available to vulnerable patients and seniors. In so doing, it further could create perverse incentives, decreasing the potential that companies would offer rebates beyond the statutory minimum Medicaid Drug Rebate for fear of not being able to track such discounts and report them accurately under the new rule. This could lead to further market consolidation and higher ultimate costs for entities like providers and hospitals.

By increasing both the costs and risks involved in serving underprivileged patients through the Medicaid Rebate Program, the rule would discourage investment in medicines from which these vulnerable populations are most likely to benefit. This decreased investment will affect not only small and mid-size companies but also companies that are seeking to bring their first product to market, as the increased liabilities and uncertainties introduced by these changes will make ongoing investment in treatments for the Medicaid population untenable. The result would be less innovation, fewer new cures, and worse health outcomes for disadvantaged groups.

The policies I laid out are of the greatest impact to emerging biotech companies like Sutro, but there are more to consider as the Federal Government seeks to promote and protect the biotechnology industry's complex ecosystem. Thank you for inviting me to testify today. I look forward to your questions.