December 31, 2018

By Electronic Delivery

Seema Verma, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Blvd
Baltimore, MD 21244

Cc: Alex Azar, Secretary, Department of Health and Human Services
Adam Boehler, Deputy Administrator for Innovation and Policy, Director, Center for Medicare & Medicaid Innovation

RE: Advance Notice of Proposed Rulemaking: International Pricing Index Model for Medicare Part B Drugs [CMS-5528-ANPRM]

Dear Administrator Verma,

The Biotechnology Innovation Organization (BIO) writes to express our strong opposition to the Centers for Medicare & Medicaid Services' (CMS') Advance Notice of Proposed Rulemaking on the International Pricing Index (IPI) Model for Medicare Part B Drugs (the ANPRM).[1]

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes, but also have reduced healthcare expenditures due to fewer physician office visits, hospitalizations, and surgical interventions. BIO membership includes drug, biologics and vaccine manufacturers and developers who have worked closely with stakeholders across the spectrum, including the public health and advocacy communities, to support policies that help ensure access to innovative and life-saving medicines and vaccines for all individuals.

BIO strongly opposes the potential proposal detailed in the ANPRM and calls for withdrawal of the IPI model in its entirety, as:

I. The IPI model is inconsistent with the charge of CMS' Innovation Center, and does not appropriately consider benefit to the patient;

[1] 83 Fed. Reg., October 30, 2018.

II. **The IPI model imports foreign price controls on American innovation, jeopardizing access to new medicines for Medicare's vulnerable beneficiaries;**
III. **The IPI model introduces new middlemen and complexity into providers' delivery of critical medicines, potentially jeopardizing care to patients without reducing beneficiary costs; and**
IV. **The IPI model is part of broader Agency efforts that are eroding the value of the Medicare benefit for seniors and putting patient access to care at risk.**

These concerns are described further in the balance of this comment letter.

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Introduction

BIO members represent the entire biotechnology innovation ecosystem devoted to the discovery of new treatments – from universities and research institutes, to start-up biotechnology companies, to the private investors that risk massive amounts of capital to fund these companies, to the larger, established companies that play a critical role in bringing these life-changing innovations through the development and approval process and into the marketplace. Of our approximately 1,000 members, the vast majority are small companies engaged in some of the most challenging, cutting-edge research in the world. They typically have no marketed products and no profits, and thus are heavily reliant on private capital to fund their work. They take enormous risks every day to develop the next generation of biomedical breakthroughs for the millions of patients suffering from diseases for which there currently are no effective cures or treatments.

To that end, BIO closely monitors policy changes across the healthcare spectrum to confirm that proposals:

1. Promote patient access through lower out-of-pocket (OOP) costs and the choice of clinically appropriate therapy;
2. Promote holistic, market-driven solutions; and
3. Sustain investment in biopharmaceutical innovation.

We were therefore extremely concerned to see CMS issue a potential proposal that does the exact opposite – moving Part B from a market-based payment formula, to one based on artificially low and government-controlled foreign prices that largely ignore impacts on patient access and the development of new cures. As stated, we urge CMS to immediately reverse course before it does serious damage to America's global leadership in biomedical innovation and access to these critically important treatments for patients.

More than 330 stakeholder organizations, including patient and provider representatives, have registered their significant concerns with the unprecedented, mandatory "experiment" being contemplated that would negatively impact all beneficiaries who take Part B covered drugs.[2] Additionally, more than 50 prominent public policy thought leaders and

[2] See: Part B Access for Seniors and Physicians Coalition Letter, December 10, 2018.

organizations have called for withdrawal of this proposed model.[3] Instead of advancing an experiment with such potential to harm provider and patient access, CMS should continue a broad stakeholder dialogue that focuses on real policy solutions that prioritize American patients' access and reduce their OOP costs, while maintaining incentives for future biomedical innovation.

To accomplish this shared goal, we must harness – not abandon – the free market system within the United States that has made us the global leader in both delivering amazing innovations in treatment for patients and maintaining a robust competitive marketplace for drugs. Further, rather than focusing on just one sector of the healthcare system, the Agency should evaluate services and cost trends across the healthcare continuum so that any policy proposals appropriately focus on the key drivers of negative cost trends, address utilization of high-cost/low-value care, and do not disincentivize the development of new medicines – which often lead to decreased costs elsewhere in the healthcare system.

In this vein, we remind the Agency that spending for Part B drugs only represents approximately 4% of overall Medicare spending.[4] Across all national healthcare spending, non-retail drugs like those covered by Part B are projected to continue to represent under 5% of overall healthcare spending through 2026.[5] By contrast, spending for hospital and physician services is projected to grow at a rate that is 3.5 times higher than that for Part B and D drugs over the next 10 years.[6] It is thus perplexing and troubling that the Agency would seek to achieve minimal governmental cost savings on the backs of the most vulnerable population of seniors in the Medicare program.

BIO and our members recognize that too many patients – even those with insurance – cannot afford their appropriate care and treatment, and therefore we must work collectively to ensure the sustainability of the healthcare system. We support efforts aimed at improving the value of overall healthcare spending, but believe that the IPI model would do nothing to further this objective, or to foster a marketplace of enhanced choice, quality, and competition, which includes both generic and biosimilar options for beneficiaries. Unfortunately, the proposed IPI model threatens these objectives. To that end, we strongly urge the Agency to withdraw the proposal and re-engage with the broader stakeholder community on solutions where patient access and value play a central role, and the promise of future innovation is maintained.

Yet, inexplicably, CMS now seems to be embracing approaches that run counter to similar ideals outlined in the Administration's Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs released earlier this year:[7]

> *"The United States is first in the world in biopharmaceutical investment and innovation. Combining our free market system and generous public investment made America home to the first chemotherapy treatments for*

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[3] See: 57 Conservative Groups & Activists Oppose HHS Advanced Notice of Proposed Rule Making: International Pricing Index Model for Medicare Part B Drugs [CMS-5528]. November 28, 2017.
[4] See: MedPAC June 2016 Data Book; 2016 Annual Medicare Trustees Report, $279 billion total Part B spending.
[5] Projections of the Prescription Drug Share of National Health Expenditures Including Non-Retail. Altarum, May 2018.
[6] Moran Company Analysis of 2016 National Health Expenditures Data.
[7] American Patients First: The Trump Administration Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs, May 2018.

> *cancer, the first effective treatments for HIV, the first cure for Hepatitis C, and now, the first therapies that turn our own immune systems against cancer…The American pharmaceutical marketplace is built on innovation and competition."*

Before addressing our specific concerns with the ANPRM, it is necessary to first dispel some of the erroneous or misleading assertions made throughout the ANPRM. First, importing foreign prices is a formula for importing systems that free-ride on, and systematically undervalue, American innovation and intellectual property, and which restrict patient access to innovative treatments. It is simply untrue that companies offer "voluntary discounts" in European and other developed economies or that these prices reflect market pricing. The reality is that companies typically are facing a single-payor system run by the government, often using external price referencing, that basically establishes a "take or leave it" price for access to that market. This places manufacturers in a situation where patients in that market will not get access to the medication if the demanded price is not agreed upon. Unfortunately, these restrictions often result in fewer new drugs entering such markets, or at least significant delays in their availability.[8]

Second, biopharmaceutical companies are not able to charge the Medicare program "whatever they want," as has been alleged. The statutory Average Sales Price (ASP) calculation includes discounts and rebates provided in the commercial market, and thus by design leverages market competition to determine Medicare payment rates. Further, the current ASP system has proven to temper price increases for therapies subject to this payment methodology. We note that, in fact, weighted average ASPs for all Part B medicines have grown slower than the consumer price index for medical services over the last 10 years.[9] CMS has recognized the impact of market competition as well, noting in 2018 that "payment amounts for the top 50 Part B drugs decreased by 0.8 percent" on average and "among the top drugs with a decrease, there are a number of competitive market factors at work – multiple manufacturers, alternative therapies or market shifts to lower priced products."

Third, the impact on R&D spending will be far greater than the 1% assumed by HHS. At a recent presentation at the Brookings Institute, Secretary Azar said:

> *"Over the next five years . . . we will go from paying 180 percent of what other countries pay for these drugs to 126 percent of what they pay. . . The pharmaceutical industry reports they spend an average of 21 percent of revenue on R&D. So at most this model could pull around $700 million out of the entire pharmaceutical industry's annual R&D budget, which they boost is more than $70 billion a year right now. These savings, while very substantial for American patients and American taxpayers, cannot, therefore, possibly pull out more than 1 percent of R&D."*

According to a recent analysis,[10] this assumed impact on R&D is far from reality because it ignores the fact that the proposed reference pricing policy is a mandatory price ceiling that

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[8] See: New Medicines Are Launched First in the US, PhRMA analysis of IQVIA Analytics Link and FDA, EMA and PMDA data.

[9] Trends in Weighted Average Sales Prices for Prescription Drugs in Medicare Part B, 2007-2017. The Moran Company, December 2017.

[10] See: Don't Believe the Hype – International Reference Pricing Will Cost Far More than 1% of R&D Budgets.

will affect a subset of drugs that are often the most successful and effective new therapies in their classes. Accordingly,:

> *"[T]the impact on R&D and innovation globally will be devastating. The most successful drugs a company sells are those products which fund R&D and future acquisitions; i.e. the future products a company needs to make in order to stay in business are built upon the revenues of their currently successful products. This is the entire point of innovation in biopharma; 92% of all new innovations fail, success is rare, it takes a long time to make a product, and truly novel products are expensive."*

In just one example, the analysis demonstrates that the reduction in revenue due to the proposed reference pricing policy for a single novel Part B drug would result in a 30% reduction in that particular company's total R&D budget, not 1%, and emphasizes that:

> *"Targeting only the most new, successful, and cutting-edge technologies for arbitrary price ceilings will have a debilitating impact on U.S. innovation and likely drive biotech firms to move to other markets."*

Below we outline in further detail our significant concerns with the proposed model detailed in the ANPRM and its potential serious consequences for patient access and innovation of new treatments for American patients.

* * *

I. The IPI model fails to meet the charge of CMS' Innovation Center, and does not appropriately consider benefit to the patient.

First and foremost, BIO believes that this widespread, mandatory model is an inappropriate application of the Center for Medicare and Medicaid Innovation's (CMMI) authority. Just as with the 2016 Medicare Part B demonstration project that proposed changes to reimbursement for half of all Medicare Part B providers - and was widely opposed by patients, providers, and industry stakeholders – the IPI model falls outside the spirit and charge of the authorizing statute. Instead, we believe that it is critical for the Agency to work closely with stakeholders to develop models that are market-driven and patient-centric, using strong data elements in model design and assessment, and continuing to collect stakeholder feedback to ensure models are meeting stated goals.

With this ANPRM, CMS is putting forward a model that fails to address a defined population for which there are identified deficits in care leading to poor clinical outcomes or potentially avoidable expenditures. The IPI is focused on the use of a widespread, mandatory demonstration impacting half of the population using Medicare Part B drugs. The outcomes of the model are predetermined and have a nationwide impact, placing downward pressures on the existing ASP system. Thus reducing reimbursement for all Medicare Part B providers, and potentially jeopardizing patient care.

Additionally, it is unclear how the model will preserve or enhance the quality of care for patients served by the model. CMS states in the ANPRM that, "the IPI Model aims to drive better quality for Medicare beneficiaries and reduce Medicare drug spending by offering comparable pricing relative to other countries and addressing flawed incentives in the

current payment system." This model instead undermines patient access to treatment innovations, as demonstrated below by the experience in other countries using price controls. Further, as explored, the model adds significant complexity into a drug delivery system where there are other ongoing models that are more appropriately aimed at improving patient quality of care. BIO has previously stated significant concern with this "layering" approach to CMMI demonstrations.[11]

II. The IPI model imports foreign price controls on American innovation, jeopardizing access to new medicines for Medicare's vulnerable patient population.

BIO opposes CMS' adoption of foreign price controls on American biopharmaceutical innovation. By benchmarking U.S. prices to prices in other countries, the Agency will impede the development of and patient access to novel treatment options. The United States is responsible for the development of more biopharmaceuticals than all other countries combined.[12] Economists have estimated that had European-style price controls been adopted in the U.S. from 1986-2004, 117 fewer new medicines would have been produced for worldwide use.[13] Similarly, a 50 percent drop in drug prices could lead to a 14-24 percent drop in the number of drugs in the development pipeline.[14] Sweeping changes to the market-based reimbursement system in the U.S. can have serious impacts for development of new medicines. It is critical that policies implemented in the U.S. foster an environment that enhances and sustains innovation.

As noted above, the Administration's emphasis on impacts to overall R&D spending understate the particularly pronounced effects of the foreign price controls suggested in the IPI model for investment in small, clinical stage development companies.[15] Further, the impacts on innovations of new treatments will be exacerbated in diseases impacting America's seniors – Alzheimer's, cancer, autoimmune diseases, and rare diseases – if the IPI is adopted in the Medicare Part B program.[16] These potential impacts are incredibly concerning given the extraordinary and unprecedented activity currently taking place in biopharmaceutical development. BIO and our members are making discoveries that were unimaginable decades ago. The therapies in development and coming to the market represent a new era of medicine and ever more personalized options for patients. Innovation is giving way to the development of entirely new ways to treat and ultimately cure disease for targeted patient populations using living organisms, including a patient's own cells.

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[11] See BIO Comments RE: Centers for Medicare & Medicaid Services: Innovation Center New Direction, November 20, 2017.
[12] Milken Institute; Xconomy, "Which Countries Excel in Creating New Drugs? It's Complicated" 2014; Kneller, Nature Biotechnology, 2012.
[13] Government Price Controls on Drugs Will Reduce Innovation and Cost Lives, December 2008.
[14] Civan, A The U.S. Has Been the World's Medicine Cabinet for Too Long. Forbes, February 23, 2016.
[15] Note: Seventy percent of innovative clinical programs are being led by small companies, which rely heavily on venture capitalists, angel investors, or partnerships to provide the enormous amounts of private capital required to fund these challenging and incredibly risky endeavors (see: Emerging Therapeutic Company Investment and Deal Trends 2007–2016, BIO Industry Analysis, 2017).
[16] Note: Ninety percent of clinical programs ultimately fail to lead to a Food and Drug Administration approval, these success rates can be even less, particularly in areas such as Alzheimer's and cancer (see: Clinical Development Success Rates 2006–2015, BIO Industry Analysis, 2016; for example, since 1998, 123 medicines in development for Alzheimer's have not made it through clinical trials, while only 4 have been approved — resulting in a 97% failure rate. See PhRMA, Researching Alzheimer's Medicines: Setbacks and Stepping Stones, Summer 2015.)

The U.S. healthcare system is market-based, and prices are accordingly determined by the market. The adoption of foreign price controls counters the Administration's own statements around maintaining this competitive, free-market system. When the American Patients First Drug Pricing Blueprint was released in May, the Department of Health and Human Services (HHS) referenced a 2013 World Health Organization paper on the growing use of external reference pricing, stating:[17]

> *"Such price controls, combined with the threat of market lockout or intellectual property infringement, prevent drug companies from charging market rates for their products, while delaying the availability of new cures to patients living in countries implementing these policies."*

The adoption of foreign price controls jeopardizes patient access to the newest treatment options and violates the free market system. For instance, of 74 cancer drugs launched between 2011 and 2018, 95% are available in the United States, compared with 74% in the United Kingdom, 49% in Japan, and 8% in Greece.[18] Given the potential to undermine patient access to new innovations in the Part B program, BIO strongly urges the Agency against importing foreign price controls.

Further, most of the countries under consideration for benchmarking of prices under the IPI policy are using external price referencing to determine the cost of pharmaceuticals, including prices in the U.S. If the U.S. is in turn referencing lower foreign prices, this will cause a downward spiral – U.S. prices will go down, forcing foreign prices down further, etc. Ultimately, this will choke incentives to develop new medicines and reduce their availability to patients. A 2015 European Commission detailed the limitations associated with reference pricing, including the barriers to access such policies can create.[19]

Moreover, government agencies in these countries set the conditions under which doctors can prescribe new medicines, routinely imposing regulations that limit the use of new medicines, often narrower than those included in the drug's approved uses. Some foreign governments also determine whether they will use a drug based on a threshold price per "unit of health" (called a Quality-Adjusted Life Year or QALY) it is estimated to provide. In short, they set a price on human health and life that governs the whole country, which is based on the *average* efficacy of the medicine, ignoring whether there are patients who may benefit more than others.

It is critically important that the U.S. continue to foster an environment that sustains and enhances innovation, ensuring the continued discovery and development of treatments that revolutionize patient care, quality of life, and reduce overall healthcare expenditures. The changes included in the IPI model place direct pressures on the development of critical new treatment options, and as such, this model should not move forward.

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[17] American Patients First: The Trump Administration Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs, May 2018.
[18] New Medicines Are Launched First in the US, PhRMA analysis of IQVIA Analytics Link and FDA, EMA and PMDA data.
[19] European Commission, Study on enhanced cross-country coordination in the area of pharmaceutical product pricing: Final report. 2015.

III. The IPI model introduces new middlemen and complexity into providers' delivery of critical medicines, potentially jeopardizing care to patients without reducing beneficiary costs.

The IPI model layers in the use of private vendors for the delivery of Medicare Part B drugs subject to foreign price indexed reimbursement under the authority for the Competitive Acquisition Program (CAP). BIO believes that the combination of sweeping changes to the reimbursement structure alongside the use of private vendors could cause disruptions to drug delivery and patient and provider access to critical specialty medications.

BIO has previously stated our concern with the reinvigoration of the CAP,[20] given its inability to work for providers, vendors, and patients; or produce the desired savings and outcomes during its original iteration.[21] We previously cautioned the Agency against moving forward on the development of innovation models that leverage the CAP authority without ensuring that the model was voluntary, limited in scope, workable for physicians, and did not create access barriers for patients.[22]

In comments submitted in response to the CY 2019 Hospital Outpatient Prospective Payment System Proposed Rule, we outlined that CMS must take a thoughtful, measured approach in testing voluntary alternatives to the existing structure of buy-and-bill, using design elements that support a competitive, market-driven approach. We encouraged the Agency to address the following key elements in the development of any potential model:

- Adequate protections for patient access to clinically appropriate care and lowering costs to beneficiaries;
- Not creating interference that erodes the existing coverage and reimbursement structure;
- Encouraging robust competition and avoiding misaligned incentives;
- Ensuring workability for physicians who may choose to participate;
- Considering appropriate exemptions for certain drugs and biologicals from such models; and
- Transparency in model design, development, and assessment processes.

As currently detailed in the ANPRM, it is unclear how the Agency intends to adhere to critical design elements that should be incorporated into new delivery mechanisms for Part B drugs as outlined by BIO and other stakeholders. The focus of such a program should be on providing voluntary, alternative pathways for delivery for providers who no longer want to take on the risk of purchasing Part B drugs, while maintaining timely and appropriate access

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[20] See: BIO Comments RE: HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs, July 13, 2018; BIO Comments RE: Medicare Program: Proposed Changes to Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Requests for Information on Promoting Interoperability and Electronic Health Care Information, Price Transparency, and Leveraging Authority for the Competitive Acquisition Program for Part B Drugs and Biologicals for a Potential CMS Innovation Center Model, September 24, 2018.

[21] Centers for Medicare and Medicaid Services, Office of Research, Development, and Information. Evaluation of the Competitive Acquisition Program for Part B Drugs: Final Report. December 2009.

[22] See: BIO Comments RE: Medicare Program: Proposed Changes to Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Requests for Information on Promoting Interoperability and Electronic Health Care Information, Price Transparency, and Leveraging Authority for the Competitive Acquisition Program for Part B Drugs and Biologicals for a Potential CMS Innovation Center Model, September 24, 2018.

for patients; not on how to import price controls for these complex medicines through the use of additional middlemen.

Further, the ANPRM purports that the model would reduce OOP costs for seniors taking Medicare Part B drugs. However, the vast majority of seniors – over 80 percent - receiving Medicare Part B drugs have supplemental coverage either through enrollment in Medicare Advantage (MA) with maximum OOP limits or Medigap plans that cover these costs. [23] Rather than implementing sweeping changes to Medicare Part B reimbursement and drug delivery, BIO urges the Administration to work with stakeholders, particularly in the physician and patient community in developing small scale delivery reforms that can truly test their impacts on quality of care and have real impacts for patient cost of care.

IV. The IPI model is part of broader Agency efforts that are eroding the value of the Medicare benefit for seniors and placing patient access at risk.

This proposed model is part of a concerning and unfortunate trend that places the care of vulnerable seniors in the Medicare program at risk. Earlier this year, CMS authorized the use of step therapy in MA plans for Part B drugs and followed on with increasing plan flexibility to manage drugs in Part D through indication-based formularies and proposing to increase utilization management tools for the six protected classes. BIO believes that the Agency's efforts are misplaced, inappropriately targeting access for vulnerable patient populations, by giving wide latitude to plans and pharmacy benefit managers to deny patient access to medicines prescribed by their physician.

Utilization management policies such as step therapy present barriers to accessing timely and appropriate treatment for vulnerable patient populations, particularly when applied to the drugs delivered in the Medicare Part B program. These medicines are intended for treatment of some of the most serious health conditions, such as cancer, autoimmune disorders, end stage renal disease, and hemophilia. Further, many of these treatments interact dynamically with patients' immune systems or vary based on their individual genetic profiles, which means that an individual patient can fare better or worse on a treatment (in terms of efficacy and side effect profile). In other words, one size does not fit all.

BIO has registered our serious opposition to this policy,[24] and the need for significant patient protections to ensure beneficiary care is not harmed, and the patient-provider decision-making process is not compromised. While the recently released proposed rule governing MA and Part D did incorporate some positive changes relative to the appeals process timeline and internal review of step therapy for Part B through plans' P&T committees, BIO is still extremely concerned by the use of step therapy for Part B drugs.[25] We believe that if the Agency is insistent on maintaining such a policy, further CMS oversight is needed, as well as increased education for beneficiaries about the potential impact of such policies on their care.

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[23] Sources of Supplemental Coverage Among Medicare Beneficiaries in 2016. Kaiser Family Foundation, November 28, 2018.
[24] See BIO Comments RE: Step Therapy for Part B Drugs in Medicare Advantage, September 10, 2018.
[25] 83 Fed. Reg., November 30, 2018.

Additionally, in the Part D program, CMS will be allowing plans to develop indication-based formularies, as announced in August, and is proposing additional use of utilization management for Part D's protected classes as detailed in the recent proposed rule. Such policies could restrict patient access to necessary medicines for patients with serious diseases that already have been stable on a therapy that works well for their given condition. BIO's continued concerns will be detailed further in BIO's comments on the Part D and MA proposed rule.

The interaction of these various utilization management tools have the combined effect of limiting access and creating confusion for beneficiaries. Additionally, the entities that would likely have interest in filling the role of vendors under the IPI model, have been on record calling for the increased ability to employ utilization management tools. BIO is extremely concerned that the collection of these policies has the effect of putting patient's last, interfering with the sanctity of the patient-provider decision-making process and impeding access to new innovations in treatment.

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Conclusion

BIO reiterates our serious concern with the International Pricing Index model and calls for withdrawal of the model in its entirety. As detailed, we believe reforms to the drug delivery system should prioritize ensuring patient access, delivering value, and lowering patient OOP costs. Policy solutions to achieve these aims must be holistic and market-driven and sustain biopharmaceutical innovation. The IPI model fails to meet these goals and outcomes, and we urge CMS to work with stakeholders on solutions that address the issues facing patients, including healthcare costs, without placing access to critical medical innovations at risk. Should you have any questions, please do not hesitate to contact Crystal Kuntz, BIO's Vice President for Health Policy & Research, at 202-962-9220.

Sincerely,

/S/

Thomas DiLenge
President, Advocacy, Law & Public Policy
Biotechnology Innovation Organization