July 22, 2021

The Honorable Diana DeGette
2111 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, D.C. 20515

Dear Representative DeGette and Representative Upton,

The Biotechnology Innovation Organization (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. Our mission is to advance biotechnology innovation by promoting sound public policy and fostering collaboration, both locally and globally. Our members range from entrepreneurial companies developing a first product to Fortune 500 multinationals. BIO and our members appreciate the opportunity to provide comments to the 21st Century Cures 2.0 proposal discussion draft.

TITLE I: Public Health

SECTION 101. Further Understanding of Implications of Long COVID

BIO supports this effort to further understand the implications of long COVID; however, we believe that collecting, analyzing, and reporting this data may take longer than six months. We also suggest that such a survey could be added as an addendum to an existing national survey (e.g., NHANES), since the infrastructure and population-based sampling methods for such surveys are already well established. This would be beneficial as it also could provide follow-up data and associated biomarker information.

SECTION 102. National Testing and Response Strategy for Future Pandemic

As investments are made in vaccines and countermeasures, the ancillary products and API needed to facilitate their development and deployment need investment and prioritization in pandemic planning as well.

- Recommend expanding the language to include the development of and access to supplies, reagents, syringes, manufacturing components, etc.

BIO is supportive of the Medical Countermeasure Priority Review Voucher (PRV) program created by the 21st Century Cures Act and sees the program as an important incentive for the research and development of medical countermeasures. A sunset on the program will likely offset any incentive that the program offers.

- Recommend repealing MCM PRV sunset date.

SECTION 104. Vaccine and Immunization Programs

BIO supports the authorization of funding included in Section 104. Recognizing the importance of sustained investment in these efforts to protect against future pandemics, we urge you to consider modifying the clauses in these provisions regarding spending authority. As drafted, the authorization of appropriations would require the Appropriations Committee to build these increases into annual budget authority. We believe Congress should continue to direct spending for these activities.

- *ADDITIONAL FUNDING FOR VACCINE AWARENESS*

  BIO supports the authorization for funding for a public campaign about the safety and importance of vaccines. The COVID-19 pandemic has raised the issue of vaccination for the American public, and we must leverage the strides made for COVID-19 vaccines for raising public awareness of all recommended immunizations. This is especially critical for awareness of adolescent and adult vaccines, which already lag behind childhood vaccination rates. Additionally, as a result of the pandemic, we have seen immunization rates drop across the life course as people delayed primary preventive care. High immunization rates are needed to avert outbreaks of preventable diseases such as measles, pertussis, and influenza as we continue to beat back COVID-19.

  A lesson learned through COVID-19 vaccine campaigns is the power of community-based organizations. Community-based organizations, including faith-based organizations, were critical in spreading evidence-based information about the safety and efficacy of vaccines using trusted voices. Partnerships built during the pandemic to promote COVID-19 vaccination should be leveraged and funding provided for vaccination campaigns should include an element specific to community-based partnerships. HHS leaders should be empowered to find more direct mechanisms for funding community and faith-based organizations' educational vaccine activities directly as well as through state health partners. This will allow for more tailored outreach programs built upon the knowledge and experience of community leaders

- *STRENGTHENING THE IMMUNIZATION INFORMATION SYSTEM*

BIO supports the authorization of funding for strengthening immunization information systems (IIS). Our everyday public health and immunization infrastructure forms the backbone of pandemic response. Investments made in infrastructure improvements to systems like state-based IIS during the pandemic must be continued and built upon in order to strengthen our routine immunization data and to ensure that these systems are ready to respond to the next public health emergency. It is critical that these systems capture all ACIP-recommended vaccines for all populations.

- *ADDITIONAL RECOMMENDATIONS*

  First dollar coverage for vaccines: While most Americans have access to vaccines without cost-sharing, this is not the case for all populations. Vaccines are currently the only source of primary prevention, meaning they prevent a person from getting sick and also keep them from making others sick. This is why they generate such high societal benefits in terms of productivity and healthcare cost reductions. Yet two key populations still face copayments for vaccines: Medicare and Medicaid beneficiaries.

  H.R. 1978, the Protecting Seniors Through Immunization Act of 2021, would eliminate cost-sharing in Medicare Part D for all CDC-recommended vaccines. Currently seniors pay copayments only on those vaccines covered under Medicare Part D (tetanus-diphtheria-acellular pertussis (Tdap) and varicella zoster (shingles) and these co-pays vary widely across plans. This significant legislation would bring much needed parity to the out-of-pocket payment required of Medicare beneficiaries for vaccines covered under Part D, making it the same as those vaccines covered under Part B. Immunizations should be available with no cost to the beneficiary in the same way vaccines are covered under Part B (Covid-19, influenza, pneumococcal) and under private insurance through the Affordable Care Act (ACA). Removing this barrier would provide a direct financial and health benefit for people aged 65 and over and help to improve access and equity among the Medicare population.

  H.R. 2170, the "Helping Adults Protect Immunity Act" (HAPI Act), also addresses cost-sharing for another population that suffers from access and equity issues, adults in state Medicaid programs. Infectious diseases often exacerbate underlying conditions making recovery longer and resulting in enduring negative health outcomes. COVID-19 made this point extremely clear. The worst outcomes from this highly transmissible respiratory infection hit communities of color, those with long-term underlying health conditions and those in occupations that could not be done at home. Many of the individuals in these populations are uninsured, underinsured, or are covered by Medicaid. The intersection of these populations highlighted the inequities in our healthcare system which must be addressed through many different

policies. For vaccines, removing financial barriers is the first step to improving access and increasing uptake for at-risk adults. In addition, not all states cover all ACIP-recommended vaccines and those that do might have copayment requirements that discourage access to this important preventive service. Passage of the HAPI Act would provide equitable vaccines coverage and help reach more Americans who benefit the most from vaccination.

Finally, current law requires that insurers provide coverage without cost-sharing for vaccines that are recommended by CDC (Section 2713 of the Public Health Service Act). However, HHS regulations limit mandatory coverage without cost-sharing to vaccines considered "routine" and listed on a CDC Immunization Schedule. Tying coverage without cost-sharing to the CDC Immunization Schedules results in inconsistent coverage of CDC-recommended vaccines, by excluding some vaccines recommended by CDC in the usual course of preventive care. Examples of non-routine vaccines, such as occupation-related and travel vaccines, include those for several infectious diseases such as cholera, Japanese encephalitis, rabies, typhoid, and yellow fever. This lack of regulatory clarity allows payers to impose cost-sharing on policyholders for non-routine vaccines, creating a disincentive to vaccination. Given the clear benefits of preventive vaccination for infectious diseases and a desire to eliminate barriers and ensure equitable access to all populations, Congress should direct HHS to ensure that its regulations are aligned with the Public Health Service Act requiring insurance coverage without cost-sharing of all CDC-recommended vaccines, including those recommended to prevent travel or occupational risks.

SECTION 105. Developing Antimicrobial Innovations

This section reinforces the importance of the Pioneering Antimicrobial Subscriptions To End Up Surging Resistance (PASTEUR) Act. BIO supports the goal of this provision to bring innovative new antibiotic medicines to patients who need them. The use of antimicrobials to prevent and treat infections underpins modern medical innovation today, including organ transplantation, cancer chemotherapy, major surgery, and care of preterm infants and immunocompromised patients. Resistance to antimicrobials threatens these medical innovations, undermines traditional care for respiratory, skin, and other common infections, and already impacts at least three million Americans annually, killing between 48,000 and 162,000 annually. If unchecked, AMR could kill as many as 10 million annually worldwide by 2050.

Ensuring we have a robust pipeline of new medicines and vaccines to meet both current and emerging resistance threats will be critical to addressing AMR. Unfortunately, the AMR product pipeline is in grave danger of collapse, as the small companies currently responsible for the majority of antibiotic innovation struggle to stay in business. Additional failures would be catastrophic to a pipeline that is already inadequate to meet the current AMR threats facing our patients.

Urgent action is needed to implement a package of incentive policies that address the unique market challenges of AMR products. Any legislative package should include policies that address the reimbursement challenges for antimicrobials that are impacting patient access to these medicines, such as those proposed within the DISARM Act, or other outcome-based innovative policies that include new approaches to reimbursement. These policies should also establish a pull incentive that rewards the successful approval of innovative antimicrobials that treat unmet medical needs, such as the one included in the PASTEUR Act.

TITLE II: Patients and Caregivers

SECTION 201. Educational programs and training for caregivers

Provisions that would seek to increase health literacy for patients and provide additional support for caregivers is extremely important. BIO is supportive of this provision and recommends the following:

- Ensure that the programs and training covered are multi-language to promote patient and caregiver's awareness and understanding.
- Ensure inclusion of educational content for caregivers about taking care of their own health (including mental health).
- In the definition section, expand the term 'care-giver' to include parent/guardian and those caring for pediatric population as well.
- Guidance on ensuring access to these educational programs to patients and caregivers

SECTION. 202. Increasing Health Literacy to Promote Better Outcomes for Patients

This provision requires the Centers for Medicaid and Medicare Services (CMS) to solicit input on how the agency can work with federally subsidized health care program stakeholders to encourage and promote greater health literacy. BIO supports this provision.

SECTION 203. Increasing Diversity in Clinical Trials

Clinical trial representation for underrepresented populations has long been a public health priority. This section would direct FDA to submit an updated report to Congress on its effort to increase representation in clinical trials, as originally required under Section 907 of the FDA Safety and Innovation Act (FDASIA), and to update its FDASIA-mandate action plan on inclusion of underrepresented demographic subgroups. Over the past year, FDA has issued several guidance documents that are intended to help sponsors include historically excluded patients as clinical trial participants, but there is more progress to be made.

Currently there is a regulatory requirement that New Drug Applications include analyses of safety and effectiveness by demographic subgroups. While BIO is supportive of the intent of the provisions in Cures 2.0 that direct FDA to update the report and action plan mandated under FDASIA, and have GAO analyze barriers to participation, BIO is also developing additional proposals we think would help improve representation and diversity in clinical trials. We are examining modern approaches to clinical development that enable more diverse participation across races, genders and geographies. We look forward to sharing these proposals with the Committee in the near future.

BIO recommends that FDA take a more rigorous and proactive approach in identifying barriers to subgroup enrollment in clinical trials and employs strategies to enable and encourage greater participation in clinical trials, including improving the completeness and quality of overall demographic data collection, disease demographic data collection, reporting and analysis. BIO recommends that this approach have the goal of encouraging and facilitating the inclusion of all populations who may be impacted by a disease targeted in the clinical trials.

BIO is generally supportive of requiring the Department of HHS to conduct a public awareness campaign to increase awareness and understanding, particularly in minority communities and establishing a taskforce on making clinicaltrials.gov more user- and patient-friendly. We recommend additional clarity and details on how ongoing disparate activities and initiatives related to diversity in clinical trials will be coordinated as part of the Administration's goal, and how this task force aligns with the ongoing NIH clinicaltrials.gov modernization efforts. We also recommend including industry, medical professionals and community leader's representation on the Diversity Task Force. As the primary submitters of clinical trial information, biopharmaceutical companies are a key stakeholder and have a strong interest in making the database more user-friendly.

SECTION 204. Patient Experience Data

Patient experience data as part of clinical development programs is an area of interest for both regulators and industry, as these types of data are used to inform the benefit risk profile of a product. Over the last few years, FDA's activities on patient experience data have focused on encouraging the use of Patient-Reported Outcomes (PROs), qualifying Clinical Outcomes Assessments (COAs), and conducting externally led public Patient Focused Drug Development (PFDD) meetings to understand what is meaningful to patients.

BIO has long recognized the importance of patient experience data in current and future drug development; however, we believe that making this a requirement is premature at this time. BIO supports these efforts but believes that the FDA should take certain steps prior to the implementation of such a requirement.

For example, FDA should finalize and publish two important PFDD guidance: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments; and Incorporating Clinical Outcomes Assessments into Endpoints for Regulatory

Decision Making. Furthermore, policymakers should work to address the challenges laid out in the recently-released Eastern Research Group (ERG) report, for example: the lack of transparency on how the Agency uses PED in its regulatory decision making; the lack of clarity and specificity in FDA expectations for PED; the challenges sponsors face in scheduling timely meetings with FDA to discuss PED during drug/biologic development; and the endpoints that FDA staff and some sponsors focus on (*e.g*. endpoints that are easily measured or of primary interest to clinicians) are not of most importance to patients (who prefer greater focus on psychosocial, quality of life and measures of ability to function).

Further, even with additional guidance from the Agency regarding these points, we caution against the push for "standardized" patient experience data as most PED is qualitative in nature and the methods for collections are still emerging. While general agreement on practice and process for PED collection would be valuable, not all PED will be collected in the same manner or be able to be standardized. Any effort to overly standardize may inhibit the ability of Sponsors to gain important insights into patient and caregiver preferences and how to incorporate that information into in trial designs and development of medicines.

BIO is supportive of FDA being directed to "consider patient experience data and related information" as part of the review process and would like to add that patient experience data might also be collected outside of a specific trial. BIO recommends amending the language as follows "require FDA to fully consider all patient experience data collected as part of a development program in benefit-risk decisions and advance inclusion of patient experience data outcomes in the in the labeling of medicine'. It is also important for FDA to provide report on how key patient experience data was utilized and any impact that data had on its regulatory decision-making or a rationale as to why the data submitted by the applicant was not considered as part of the review process.

TITLE III: Food and Drug Administration

SECTION 301. Report on Collaboration and Alignment in Regulating Digital Health Technologies

Digital health technologies provide a more holistic view of a patient's health through access to data and giving patients more control over their health. These tools offer real opportunities to improve medical outcomes and enhance efficiency. However, Digital Health Technologies are not a single regulated product, and hence none of the FDA's medical product centers (CBER, CDER and CDRH) have full regulatory authority over all digital health technologies. In late 2020, FDA launched the Digital Health Center of Excellence (DHCoE) which focuses on providing technological advice across FDA in the area of digital health devices and creating a network of digital health experts to share digital health technology expertise across FDA medical product Centers.

Digital Health Technologies was a priority area for both industry and the FDA during the PDUFA VII negotiations[1], and as noted in the PDUFA VII reauthorization public meeting minutes, FDA and industry discussed areas of alignment and resources needed to implement use of Digital Health Technologies in drug development and review. Both FDA and Industry have the mutual desire to apply consistency of practice across the human drugs and biologics program across the Agency. BIO suggests that any new legislation on this topic take into account any existing commitments and efforts between the Agency and industry to promote the use of Digital Health Technologies in drug development. Additionally, it would be beneficial if new legislation presented a clear (measurable) desired outcome justifying its implementation, for example, a benchmark describing to what degree the FDA should strive to improve its "acceptance" and use of digital technologies and validated tools within investigational drug/product development over the course of the next year.

On the use of digital health technologies in decentralized clinical trials: decentralized clinical trials are already "accepted" by the FDA; however, further guidance is needed by the FDA to ensure successful implementation of decentralized clinical trials and identification of barriers with potential solution and approaches. We suggest that the term, "acceptance" be better defined with a metric to report to Congress such as the proportion of accepted clinical development plans for BLA, PMAs, or NDAs or submissions that utilized decentralized trials within one year of the bill, compared to same period prior to this bill. Further stratification of acceptance should be performed not just by each center, but by review division *within each center* as wide discrepancies exist on acceptance by review divisions and centers.

Lastly, BIO believes it is critical that FDA coordinates with foreign regulators to ensure harmonization on the regulation and use of digital health technologies. FDA should identify opportunities for mutual recognition and reliance with the foreign regulators.

SECTION 302. Grants for Novel Trial Designs and Other Innovation in Drug Development

Innovative and novel trial designs help increase flexibility and agility for sponsors of drug development program; however, they are complex to launch and administer appropriately. Policies and resources towards complex innovative trial design was a priority for both the FDA and industry during PDUFA VII negotiations[2]. There is already significant interest amongst industry to develop new ways of conducting trials, and increased grant funding for industry to develop these programs would likely be beneficial. We concur with prioritizing use of digital technologies and real-

[1] PDUFA VII Industry Discussion on Reauthorization public meeting minutes https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027

[2] [4] PDUFA VII Industry Discussion on Reauthorization public meeting minutes https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027

world evidence and would recommend including decentralized trial approaches as a priority.

BIO recommends providing additional clarity on who would receive these grants, and how "novel" would be interpreted (as the definition of "novel" may differ per therapeutic area). BIO suggests that this funding could be best utilized if applied to toward actual clinical development programs for investigational new products, as well as expanded indications for existing products. Focusing appropriations of funds to meet these ends would minimize unsystematic spending on part of the FDA and would ensure that funds spent would be applied to directly address the objective of this section of the bill. A report after 2 years of the funding outlining the use of the funds and describing the degree to which these novel designs were used in specific development plans is warranted.

SECTION 303. FDA Cell and Gene Therapy

In recent years, FDA has seen a substantial workload increase in submissions for cell and gene therapies. From a regulatory perspective, FDA needs to hire additional resources to develop regulatory framework to accommodate the emerging science and assist in the review process. The increased workload has forced FDA to limit sponsor and external interactions. Dedicated resources were a priority for FDA and Industry during the PDUFA VII negotiations[3] for cell and gene therapy program due to the rapid growth in drug development. The improvement to the program in PDUFA VII may include increased time spent on cell and gene therapy submissions, increased engagement with industry and stakeholders, and further policy and guidance development. The provisions provided in the legislation with a ten-year lookahead report may be helpful; however, the information requested in the provision is generally already available.

The discussion of foreseeable challenges and how FDA will address these challenges in the report should include topics such as (but not limited to) international harmonization of data requirements and other development challenges, incorporation of novel trial designs to meet the specific needs of cell and gene therapy development, and differing data requirements based on stakeholder need (*e.g.,* regulatory approval vs. coverage decisions). It is worth noting that the rapid pace of drug development maybe be difficult to predict the number of applications, the timing of the submission and the number of staff needed by FDA to employ during the next ten years.

SECTION 304. Increasing use of Real-World Evidence

Real world evidence can be generated from many sources and can be used in drug or medical device applications to the FDA. FDA uses a totality of evidence approach to evaluate the entire submission, and regardless of the source, the data must meet FDA's evidentiary standards. The 2018 Framework for FDA's Real-World

Evidence Program[3] specifies a three-part approach to evaluating the potential use of Real-World Evidence to support changes to labeling about drug product effectiveness:

1. Whether the Real-World Data are fit for use
2. Whether the trial or study design used to generate Real-World Evidence can provide adequate scientific evidence to answer or help answer the regulatory question, and
3. Whether the study conduct meeting FDA regulatory requirements (e.g., for study monitoring and data collection)

This approach highlights the regulatory considerations in leveraging real-world data to support regulatory decision making. FDA's 2021 guidance agenda indicates for release of three guidances on the use of Real-World Evidence/Data to address challenges and bring clarity to leveraging the use of such data in regulatory decision making. It would be helpful to have a better understanding on how the guidance listed in the Cures 2.0 provision would differentiate from guidance expected to issue by FDA this year. As the above-mentioned three guidances are not expected to be limited to product development under expedited pathways, is the Cures 2.0 guidance intended to demonstrate/encourage more willingness from FDA towards use of Real-World Data/Evidence under those pathways and provide more clarification on how sponsors would communicate with FDA under those pathways regarding the use of such data and evidence?

BIO is generally supportive of building on FDA's effort by requiring HHS to outline approaches to maximize and expand the use of Real-World Data/Evidence (RWD/RWE) and would recommend including clear mandate and Key Performance Indicators that demonstrate FDA is using Real-World Evidence in regulatory decision making. BIO is also generally supportive of establishment of a permanent task force to coordinate programs and activities with regards to the collection and use of Real-World Data and Evidence.

There are several outstanding questions related to Real-World Data (*e.g.*, unified data standards and how to address data gap) that could benefit from a cross-agency task force. Having HHS harmonize how RWD/RWE would be evaluated and utilized across the Department could potentially streamline processes. This task force should also include the perspectives from both the biopharmaceutical industry and real-world data information technology sector. BIO further recommends that the task force include as a permanent member, at least one expert (*e.g.*, academic pharmacoepidemiologist) on the conduct of Real-World Evidence studies. We posit that this Task Force could be set up not only to identify opportunities for the use of Real-World Data and Evidence in clinical trials, but also to assess the use of Real-World Evidence in the non-interventional or minimally interventional setting. BIO also recognizes the need for collaboration between industry and regulators to

[3] 2018 Framework for FDA's Real-World Evidence Program https://www.fda.gov/media/120060/download

determine the best approach to ensure transparency and data privacy on the use of patient data (*i.e.,* RWD).

Lastly, we see a connection between this section and Section 203 on increasing diversity in clinical trials. We encourage the development of provisions for these sections to be crafted in a way that is complementary to both goals.

SECTION 305. Improving FDA-CMS Communication Regarding Transformative New Therapies

BIO notes that this language is much more expansive and concerning compared to the language that was in the concept paper from last year which stated, "This provision would establish an automatic communication requirement between FDA and CMS for products granted Breakthrough Therapy designations. The communication requirement would commence upon the grant of the designation and would continue through the collection of any RWE post-FDA approval."

Importantly, the respective agency mandates for both the FDA and CMS vary: the FDA reviews a product for safety and efficacy, while CMS determines Medicare coverage and reimbursement for a product. The language in the Cures 2.0 provision is problematic, particularly in regard to each agency's decision-making authorities. Specifically, the language states that the agencies shall "share such information with each other as may be appropriate to inform and ***coordinate such decisions***" (emphasis added). This language contradicts the clear and distinct remits of each agency and would make FDA's regulatory approval and CMS' coverage decisions more challenging.

FDA should **not** be granted any authority to make, modify, or condition any Medicare coverage decisions and CMS should **not** have the authority to alter any previous decision by the FDA. Further, BIO rejects any notion that FDA designation as breakthrough, fast track, priority review, or accelerated approval would imply a level of value or condition of coverage any different than products approved under FDA's standard approval timelines. Rather, CMS should be focused on ensuring timely access to, and sustainable reimbursement for, approved therapies for the Medicare program.

Rather, the provision should solely focus on concrete ways to facilitate communication without changing respective agency authorities on approval and coverage. We suggest the following revision on page 65 lines 1-6:

> *(1) maintain communication with each other regarding **FDA** approval and **CMS** coverage decisions with respect to such product; and (2) share such information with each other as may be appropriate*

Additionally, we would note that CMS and health insurance providers should not characterize drugs, devices, and biologics that are approved by the FDA via any of the expedited approval pathways as experimental and investigational. Finally, any FDA-CMS interaction on transformative new therapies should continue to protect existing intellectual property protections and rules under the Uniform Trade Secrets Act.

SECTION 306. Establishment of Additional Intercenter Institutes at the Food and Drug Administration

Currently, the FDA has a small number of "Center of Excellence" which serve as coordinating, policy-focused entities. The provision directs the Secretary of HHS to establish two additional FDA Centers of Excellence. The language in this provision would benefit from more clarity. The current language suggests that the first center would be charged with focusing on "a group of diseases" with some specific criteria such as eligible diseases that negatively affect one major body system, represent a major disease burden, affect more than 50 million Americans each year, are a leading cause of mortality and a major contributor to health costs, and for which the coronavirus exacerbates symptoms. This likely would include diseases of the heart and lungs, as well as obesity.

The second proposed center would focus on rare diseases, defined as diseases affecting fewer than 200,000 persons in the U.S. In other words: These centers would not represent Centers of Disease Excellence, but rather Centers of *Diseases* Excellence. A center of excellence first needs a strong scientific framework, resources, and appropriate structure to be effective. Without these elements, the Center for Excellence will not help accelerate drug development and may potentially serve as a barrier to efficient drug development and review. In the case of these two centers of excellence, the lack of focus and clarity of each center – essentially very common diseases and rare diseases – may add bureaucracy, but not necessarily clarity. We recommend changing the language to state the Secretary should "explore value of" instead of "establish" at least two additional Institutes.

SECTION 307. IND Application Not needed to Initiate Accelerated Approval

The Breakthrough Therapy Designation is eligible for medical products intended to treat a serious condition, with evidence indicating the product may result in substantial improvement to a clinically significant endpoint relative to already approved therapies. Under the current legislation, the sponsor of an Investigational New Drug Application (IND) may apply for breakthrough designation concurrently with, or at any time after the submission of an IND. However, under the current provision of Cures 2.0, sponsors would be able to request breakthrough designation at any point before or after submission of an application for approval of the drug. The provision indicates that a sponsor would be able to request for the Regenerative Medicine Advanced Therapy (RMAT) designation in the same way.

At present, the FDA recommends that a Breakthrough Therapy Designation should be received by FDA no later than the end-of-phase 2 meeting if any of the features of the designation are to be obtained. This is primarily because the primary intent of the designation is two-fold: 1) encourage scientific dialogue between FDA and sponsors and 2) best ensure the development of evidence needed to support approval as efficiently as possible. The benefits of which would be limited if the designation was obtained after the submission of an application for approval. While sponsors would now be permitted to apply for Breakthrough Therapy Designation at

any point during the IND phase and after the submission of application for approval, it is likely to have little or no effect on the program if the request is filed too late. Therefore, the current draft provision has limited value.

Additionally, the title of the section in this provision does not match the content of the section – the title section refers to Accelerated Approval; whereas, the content of the section is focused on Breakthrough Therapy Designations. We recommend a revision to the title section to match the content of the section.

SECTION 308. Guidance regarding development and submission of Chemistry, Manufacturing, and Controls (CMC) Information for Expedited Approval

FDA has several expedited programs intended to expedite the review of medicines intended to treat serious or life-threatening conditions. However, much of the focus of these expedited programs is on clinical efficacy and safety of the drug, and in reality, one of the biggest barriers to the expedited approval of these drugs is related to the CMC data and information of the drug product. Exploring ways to accelerate CMC review and clarification on the content expected to be in a regulatory application was a priority topic for Industry during the PDUFA VII negotiations[4]. BIO is supportive of the draft provision language for FDA to release a "draft revised guidance to provide clarity regarding the development and submission of chemistry, manufacturing and controls information" related to the submission of expedited programs. Such guidance on FDA's expectation relating to CMC content in expedited programs would allow for more efficient planning and process for sponsors.

SECTION 309. Post-approval Study Requirements for Accelerated Approval

Accelerated approval is a regulatory pathway that allows FDA to approve drugs for serious or life-threatening illnesses based on intermediate or surrogate clinical endpoints that are reasonably likely to predict the clinical benefit of the drug. The current provision calls for the Federal Food, Drug and Cosmetic Act to be amended to allow for the submission of "clinical evidence, patient registries, or other sources of Real-World Evidence" to satisfy post-marketing commitments. BIO is supportive of this provision and recommends FDA to issue a guidance articulating FDA's expectation of the sponsor.

TITLE IV: CMS

SECTION 403. Extension of Medicare's Telehealth Capabilities

Section 403 extends Medicare's telehealth flexibilities – the bill would permanently remove Medicare's geographic and originating site restrictions which require a patient to live in a rural area and be physically in a doctor's office or clinic to use telehealth services. It would also allow the Secretary of HHS to permanently

[4] PDUFA VII Industry Discussion on Reauthorization public meeting minutes https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027

expand the types of health care providers that can offer telehealth services and the types of services that can be reimbursed under Medicare. BIO supports this provision and encourages policymakers to strike an appropriate balance between the importance of telehealth as a tool for expanded patient access and the implications to inappropriately expand the 340B program.

SECTION 407. Expanding Access to Genetic Testing

This provision is working to include policy provisions to increase access to genetic diagnostics. This policy would provide federal support for the use of genetic and genomic testing for pediatric patients with rare diseases. BIO supports this provision.

BIO Comments on Addressing Ongoing Concerns with Access and Reimbursement

Ensure patient access to transformative therapies

BIO's members are rapidly advancing a new wave of innovative, transformative therapies that provide a significant, durable benefit and value for patient health outcomes, delivery of care, and overall healthcare spending. These therapies, such as cell and gene therapies, are aimed at serious and rare diseases where patients often have limited treatment options today.

BIO is committed to working with Congress and other stakeholders to develop innovative payment models and financing approaches to ensure patient access to these novel, transformative therapies for which current reimbursement paradigms do not work particularly well.

Outdated reimbursement pathways – particularly in Medicare and Medicaid – must catch up to the fast pace of biomedical innovation and ensure patient access once a therapy is approved by the FDA. Payment systems should provide timely and sufficient reimbursement for not only the transformative therapy itself but for associated services as well.

Medicare's payment systems should anticipate and plan for innovation so robust reimbursement is available upon FDA approval which will help ensure patient access. Unfortunately, today, it can take years for Medicare's reimbursement systems to adapt to new therapies, which is particularly acute in the Inpatient Prospective Payment System.

To this end, policymakers should consider several new proposals:

With respect to the National Technology Add-on Payment (NTAP), Congress should direct CMS to:

- Increase the frequency of awarding New Technology Add-on Payments (NTAP) which will facilitate more timely updates for provider reimbursement. CMS could align NTAP eligibility with ICD-10-PCS coding updates, which are proposed to occur bi-annually. This change would decrease the potential lag

time from 15 months down to 9 months. CMS could build on the OPPS Pass-Through Status frequency of quarterly updates, which would further decrease the lag time to 6 months.

- Rely on RMAT and Breakthrough designations granted by FDA as sufficient evidence to meeting the "significant clinical improvement" criterion. CMS already relies on similar designations for breakthrough devices and should extend this pathway to drugs and biologics. This change would offset any increased administrative burden of more frequent NTAP awards.
- Extend the length of time that an NTAP is available to 4 years to allow for additional data collection to inform DRG assignments.
- Increase the payment amount of NTAP to 80% to align with the current outlier payment level.
- Create more flexibilities for innovators to be eligible and apply for NTAP regardless of their FDA approval date.
- Allow innovations that are subject to a lag between FDA approval/introduction to the market to receive the NTAP for 2-3 years after receiving NTAP designation.
- Consider alignment of timing around the around the various payment rules and cycles.
- Consider alternative mechanisms to NTAP for ensuring patient access to innovations such as a separate add on payment based on therapy cost or paying the drug cost outright.

With respect to MS-DRG assignments, Congress should direct CMS to:

- Minimize the variability within a given DRG to create payment stability for providers, including creating new MS-DRGs with smaller case volume, particularly in rare or orphan diseases.

Pay for Value.

Much of our health care system operates on a legacy construct where payments are based on volume rather than value. However, because many transformative therapies are administered only once, with their effects expected to last a lifetime, there is no easy way to tie payment at the time of administration to measures of ongoing effectiveness, as under a value-based paradigm. The current paradigm places payers at financial risk and can create negative short-term budgetary impacts. More importantly, these considerations can lead to access restrictions and negative patient outcomes.

Policymakers should ensure that tools aimed at sharing information on cost and value with patients are maximizing their utility and being appropriately utilized, for

instance, in the case of hospital cost information reporting, or the information the is contained in Medicare Plan Finder.

Address Barriers to Value-Based Purchasing Arrangements (VBPs).

- Value-based purchasing arrangements, where payments are tied to the value the therapy provides to patients and the healthcare system, can address specific access issues that transformative therapies face today. But barriers to the adoption of VBAs for both commercial and public payers must be addressed first.
- In December 2020, CMS altered the Medicaid Best Price provisions to better enable VBPs, but hurdles still remain. CMS has delayed the implementation date to continue working out operational issues. However, while BIO believes CMS should continue working toward implementation with no more delays, we believe legislation is necessary on other issues that must be addressed in order to more fully advance full adoption of VBPs. Policymakers should support the necessary legislative and regulatory changes that would more easily allow the formation of such contracts.
- Additionally, the Anti-Kickback Statute (AKS) continues to present another barrier to innovative approaches. Value-based arrangements tied to the performance of a drug can only be effective if patient adherence can be managed and ensured. Nevertheless, adherence programs could be interpreted as a "kickback" under the broadly worded statute. We have urged the Office of Inspector General (OIG) to create AKS safe harbors to allow for flexibility to enter into these types of arrangements both with states and private payers.

BIO supports innovative negotiation between pharmaceutical manufacturers and all payers, which will, in turn, help ensure patient access to necessary transformative therapies. We forward to working with policymakers and other stakeholders to modernize our health care system and support innovative payment models that reward the value a medicine provides rather than the volume that is prescribed.

Ensure beneficiary access to all Medicare Part B drugs.

We have long advocated for policies that will ensure timely coverage and coding, as well as sufficient reimbursement, so that Medicare beneficiaries can have access to necessary therapies administered by physicians under Medicare Part B. These complex biological products address some of the most challenging health conditions for America's sickest and most vulnerable populations.

- **Ensure Access to Part B Drugs During the Current and Future National Health Emergencies.** Responding to the current COVID pandemic, a recent CMS Interim Final Rule permits hospitals to send staff to alternative locations (such as parking lot tents, converted hotels or a patients' home) and provides payment as hospital outpatient services,

including Part B drug administration. While these new flexibilities during the pandemic represent important initial steps towards addressing the significant access issues beneficiaries are facing, without additional changes too many Medicare beneficiaries might remain without access to needed Part B therapies during the emergency.

- **Improve Packaging Policies.** Access issues occur when patients do not receive the most clinically appropriate drug, biological, or service that could be provided as one component of a larger package of services, because providers and practitioners could be incentivized under packaging policies to stint—that is, to make choices that prioritize minimizing costs relative to their expected payment over clinically appropriate care personalized to the patient. These potential access issues are ever more important as the healthcare system continues to move toward the delivery of more personalized medicines.
- **Ensure Patient Access and Sufficient Reimbursement Bundled Payments.** Medicare is actively exploring the extent to which the basic principles of bundled payments (e.g., per-beneficiary payments for multiple services or condition-specific episodes of care) apply in the Physician Fee Schedule. Part B drugs are required, under the Medicare statute, to be separately reimbursed under the Medicare physician fee schedule at ASP+6% (which equates to ASP+4.3% due to the effects of sequestration).
- **Clarify Certain Coverage Policies.** Determinations of which drugs are covered in conjunction with an office visit under Medicare Part B as "not usually self-administered," has created areas of confusion and potential access problems for patients who may require assistance in administering drugs and biologics that other Medicare beneficiaries can safely self-administer.
- **Patient Protection Guardrails on CMMI.** Supporting scientific research and medical breakthroughs are paramount to a strong healthcare system and for the general health and wellness of the public. CMMI plays a critical role in our healthcare system but oversight and accountability of CMMI are necessary for protecting patients, ensuring low costs and improving care. We need to support innovation and progress while also having sensible oversight and transparency. The current CMMI framework allows the executive branch to waive certain Medicare and Medicaid rules to test controversial approaches to deliver care without assurance that these changes will not have a negative effect on health care delivery outcomes. To address these concerns, policymakers should establish guardrails, increase overall transparency, and incorporate greater opportunity for public input.

Ensure beneficiary access to innovative diagnostic technologies that improve outcomes for small patient populations

Just as coverage, coding, and reimbursement are key to patient treatment, diagnostics are an essential tool in the healthcare toolbox to diagnose, detect and

intervene in conditions that, if left untreated, can cause disabilities, developmental delays, illness or even death. A robust innovation environment for diagnostics is particularly beneficial for rare disease patients who commonly endure a diagnostic odyssey over multiple years before their disease is accurately diagnosed. This diagnostics odyssey means that patients—along with their families—must endure an extensive time period in which they consult several medical specialists and numerous bouts of testing to eventually learn the underlying disease that's causing their symptoms.

To address these concerns, Congress should direct CMS to:

- Reimagine the reimbursement and coverage paradigm for CDx across all therapeutic areas, including oncology and beyond;
- Consider coverage decisions that provide broad access to multiple NGS tests for the same diagnosis;
- Avoid placing a lifetime limit on the coverage for the use of the same NGS-based test on a particular patient;
- Provide latitude to physicians who have determined retests, confirmatory tests or repeat testing is needed—when reasonable and necessary—for the same diagnosis;
- Provide continued flexibility for MACs to analyze and cover NGS tests in local coverage determinations in the absence of an adequate national coverage determination; and
- Permit expedited LCD expansion without requiring full notices and comment process.

Improve body of clinical evidence for sequencing technologies

BIO recognizes that limited clinical evidence for sequencing technologies provides a challenge for CMS and other payers. It may be helpful for a non-partisan, independent organization like the National Academy of Medicine to conduct a landmark study on the use of genetic and genomic testing to address how clinical evidence for such products can improve patient outcomes. To address these concerns, Congress should provide funding for a landmark study to evaluate the clinical utility of sequencing technologies.

Part D Beneficiary Access Improvements

BIO believes a number of targeting improvements to the Medicare Part D program could enhance access for beneficiaries and improve their experience in the benefit. These include:

- An annual out-of-pocket spending cap for Part D enrollees.
- Smoothing of high-cost sharing obligations that enrollees would encounter under a Part D OOP cap.
- Ensuring timely, seamless access to needed medications through the appeals and exceptions process, such as allowing cost-sharing at a lower or preferred level for successful appeals.

- Increasing the Medicare Part D specialty tier threshold.

Medicaid Best Practices

The coverage requirements of Section 1927 of the *Social Security Act* are included in the federal statute to ensure Medicaid patients, who are among the most vulnerable, have an efficient and expeditious means of obtaining medically necessary drugs. The statute permits states to conduct appropriate utilization management under the established guidelines. Unfortunately, not all states and their MCOs are covering drugs according to federal statute. In addition, their coverage criteria policies are too often developed in non-transparent processes, without seeking the valuable input from experts or patients. As a result, there can be differing drug coverage and reimbursement policies even within the same state amongst Medicaid patients. Further, these policies are often not aligned with a drug's medically accepted indication, the *FDA-approved indication*.

Reimbursement policies can vastly impact access to new products. Some reimbursement policies could be standardized amongst states. For example,

- Ensure Medicaid has established mechanisms for incorporating new HCPCS codes and has means to approve claims with miscellaneous J-codes
    - Require automatic updates
    - Require state agencies to add reimbursement policies no later than 30-days following the releases of HCPCS update file, or NDC to the HCPCS crosswalk file, with coverage effective date aligned with the drug's FDA approval date.
- Require state fee schedules be updated quarterly to keep pace with government price reporting updates (e.g., ASP).
- Require states to provide timely updates to bundled payment rates, no less than once every two years, and prioritize reimbursement methodologies that base hospital payment rates on the actual acquisition cost of items and services to the extent that such invoice costs are available (e.g., provided on the claims form submitted to the State Medicaid Agency).

TITLE V: Research

SECTION 501. Advanced Research Projects Agency for Health

The draft provision indicated establishment of a new agency, The Advanced Research Project for Health (ARPA-H). The text in the draft provision is limited about how the new agency would engage with other agencies or operational activities. BIO is including responses to the RFI for ARPA-H to provide our thinking and thoughts on establishment of this new agency.

Sincerely,

Dr. Michelle McMurry-Heath, Ph.D.
President & CEO