May 17, 2022

The Honorable Frank Pallone
Chair
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Cathy McMorris Rodgers
Ranking Member
House Committee on Energy and Commerce
2322 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Anna Eshoo
Chair
House Committee on Energy and Commerce
Subcommittee on Health
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Brett Guthrie
Ranking Member
House Committee on Energy and Commerce
Subcommittee on Health
2322-A Rayburn House Office Building
Washington, D.C. 20515

Dear Chair Pallone, Ranking Member McMorris Rodgers, Chair Eshoo, and Ranking Member Guthrie:

We respectfully write to offer feedback on the draft of the Food and Drug Amendments of 2022.

The National Brain Tumor Society (NBTS) unrelentingly invests in, mobilizes, and unites the brain tumor community to discover a cure, deliver effective treatments, and advocate for patients and caregivers. Building on over 30 years of experience, we are the largest patient advocacy organization in the United States committed to curing brain tumors and improving the lives of patients and families. With thousands beside us, our collective voices and actions are a powerful force for progress.

Improving Diversity in Clinical Trials

The National Brain Tumor Society is pleased to see the Committee advance the laudable and appropriate objective of increasing diversity in clinical trials. Embracing and leveraging diversity in its many forms is consistent with our organizational values including efforts to include traditionally underrepresented patients. We are also pleased with the flexible framework provided in the draft that would have the FDA consider disease prevalence in the FDA's

requirement to complete diversity plans. There are many types of brain tumors and with their molecular subtypes, prevalence may be extremely small.

We urge the Committee, as it considers ways to include historically underrepresented people in clinical trials, to go a step further and authorize the creation of novel public-private partnerships to provide funding, including travel, childcare, meals, and ancillary medical benefits, to significantly reduce out-of-pocket costs for patients who generously enroll in clinical trials. Clinical trials should not only be possible for the affluent who have the means to travel.

Decentralized Clinical Trials

NBTS encourages the use of appropriately designed decentralized clinical trials as a means of improving access to and enrollment in clinical research. We applauded the FDA's guidance to industry for operating clinical trials during COVID-19. In section 506 of the new guidance document, we ask that the Committee call for the FDA to include "tumor type and neurological conditions" in considerations for decentralized trials, as these factors have direct impact upon trial design and implementation and take into account additional diversity factors.

In addition, we urge that the Committee review barriers to patients interacting with clinician-researchers due to medical licensure rules limiting out of state medical practice. Removal of barriers without compromising standards is an important way to increase clinical trial enrollment, particularly by rural populations and those at significant geographic distance from trial sites. Patients should be able to be seen by the doctors and in the clinical trials that are most appropriate to their disease — not just doctors in their own state.

Research, Development, and Supply Chain Improvements

Emerging technology program

NBTS supports the intent of this section to foster innovative approaches to drug design and manufacturing. We are especially encouraged about the potential for supporting medicinal chemistry approaches to repurposing drugs and developing novel drugs for brain tumors that cross the blood brain barrier. We urge the Committee to broaden the scope of this section to include medical devices because there are opportunities to realize the potential of drug-device combinations to treat a variety of cancers. In brain tumors in particular, one standard of care medical device is called tumor treating fields and may be delivered concurrently with drug and/or radiation.

Improving the treatment of rare diseases and conditions
NBTS supports the intent in this section and offers to be a resource to Congress and the FDA as it implements this section.

Reauthorization of orphan drug grants
NBTS supports the Committee's intent to support the FDA's orphan drug grants program. It is an important source of financial support for innovation in clinical trial design. In the spirit of diversity, innovation, and help for rare disease, we encourage the Committee to consider authorizing two new aspects of the orphan drug grants program.

First, we ask the Committee to authorize a grants program whereby eligible companies can apply for support to start new expanded access programs. This new grant initiative would help improve access to investigational drugs by patients facing life threatening rare diseases including many types of brain tumors. The program could be designed further to incentivize companies to collect real world data that may be additive to their clinical trials.

Second, we ask the Committee to authorize and support for the Orphan Drug Grants program to aid companies and medical academic researchers who are eligible and seeking to develop fit to purpose external control arms with the use of historical or contemporaneous patient data sets. The cancer world has seen recent innovation in clinical trial design through the use of adaptive designs. The GBM AGILE clinical trial is one example. In adults, survival from glioblastoma is less than twenty months from time of diagnosis; in the most aggressive pediatric brain tumors, such as DIPG and ATRT, children may have less than a school year of survival time. Thus, it is critical that patients are able to go on to the investigational drug or device "arm" of the trial. Given the need to conduct randomized control trials to have adequate comparisons and to maintain equipoise, we urge the Committee to help the FDA continue to work with researchers to develop appropriate external or "synthetic" control arms.

Postapproval studies and program integrity for accelerated approval drugs
NBTS appreciates the Committee's intent to provide clear rules for the withdrawal of accelerated approval as an expedited approval pathway. We agree that sponsors should have the ability to rebut and appeal the FDA's decision and for patients and patient advocacy organizations to be able to provide input. We support the Committee's intent in the draft to develop clear guidance and process regarding the development of surrogate endpoints that are appropriate proxies for clinical benefit. NBTS offers to share our experience in working with industry, FDA, patients, and the neuro-oncology field to develop novel surrogate endpoints using imaging and clinical outcomes assessments.

As the Committee advances the PDUFA legislation, we urge that the Accelerated Approval process continue to require that drugs seeking accelerated approval demonstrate a "meaningful advantage over available therapies" and surrogate endpoints are "reasonably likely to predict clinical benefit" for the intended patient population. Additionally, we discourage the Committee from allowing a weakening of the standards for approval using the Accelerated Approval pathway. We support the role of Accelerated Approval in the FDA process and hope it can bring forward more effective treatments while maintaining approval standards.

Facilitating the Use of Real-World Evidence (RWE)

NBTS supports the Committee's intent to facilitate the use of real-world evidence in the development of new treatments. We encourage the Committee to further support the development of RWE by providing direction to the National Institutes of Health and FDA to fund the development of natural history studies and to collect and annotate RWE that may be used with appropriate clinical trial data. The National Cancer Institute's Childhood Cancer Data Initiative is headed in this general direction.

Thank you for the opportunity to provide feedback on the PDUFA draft. We respect the great challenge faced by Congress, the FDA, and the greater disease community to bring forward potential cures today and set standards for approval so that the next generation of therapies is better than the last. We offer ourselves as a resource as the Committee considers the implications of policy changes to the brain tumor community.

Sincerely,

David Arons JD
Chief Executive Officer

Danielle Leach, MPA
Chief of Community and Government Relations