National Brain Tumor Society

DATE: March 16, 2022

TO: The Honorable Anna Eshoo, Chairwoman
The Honorable Brett Guthrie, Ranking Member
U.S. House Energy and Commerce Committee Subcommittee on Health

FROM: David Arons, Chief Executive Officer
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The National Brain Tumor Society

National Brain Tumor Society submits the following statement for the March 17, 2022, U.S. House Energy and Commerce Committee Subcommittee on Health hearing, "*The Future of Medicine: Legislation to Encourage Innovation and Improve Oversight.*" We respectfully request that this statement be entered into the hearing record.

The National Brain Tumor Society (NBTS) is the largest patient advocacy organization in the United States committed to curing brain tumors and improving the lives of brain tumor patients and their families. Our vision of conquering and curing brain tumors is powered by our partnerships across science, health care, policy, and the business, nonprofit, and governmental sectors. We fund treatment-focused research and convene those most critical to curing brain tumors once and for all.

We support the Committee's work to bring attention to the proposed legislation in the hearing and are pleased that H.R. 5585, the *Advanced Research Project Agency-Health Act* and H.R. 6000, the *Cures 2.0 Act* will be two of the main focuses. NBTS is supportive of both H.R. 5585, the *Advanced Research Project Agency-Health Act* and H.R. 6000, the *Cures 2.0 Act* and hopes that they will be passed expeditiously in order to create the cures and quality of life improvements our brain tumor community urgently needs.

Why brain tumor patients and loved ones need breakthroughs now

Today, an estimated 700,000 people in the United States live with a primary brain tumor. More than 88,000 new diagnoses are expected in 2022, and as many as 170,000 additional cases of metastatic brain cancer are further anticipated. A diagnosis comes with a severe impact to patients and loved ones, and certain brain tumors are among the most life-threatening forms of cancer. Brain tumor patients and loved ones need breakthroughs now.

- **For those with cancerous brain tumors, few treatment options are available.** In addition to surgery and radiation, only five drugs and one medical device have been approved for malignant brain tumors since the 1980s. None of these are curative or extend survival more than two years on average. Survival rates for adult and pediatric brain tumor patients have not changed significantly over the past 30 years despite major

breakthroughs made in the treatment of other cancers.

- **For malignant brain tumors, incidence and survival rates have remained stagnant for 45 years**, with five-year relative survival rate of 35.6% and only 6.8% for glioblastoma.

- **Tragically, pediatric brain tumors are the leading cause of cancer-related death among children and young adults ages 19 and younger**. There is currently no standard of care for treating some of the most aggressive pediatric brain tumors, and there has never been a drug developed and approved uniquely for these patients.

ARPA-H Principles

We believe ARPA-H holds the potential to confront specific challenges that, if solved, can substantially increase the likelihood of realizing transformative new treatments for brain tumor patients. We hope that ARPA-H has the following principles:

1. **Transformation** - All projects funded should aim to enable clear change in disease from that which is recalcitrant to manageable and curable.
2. **Convergence** - We encourage ARPA-H to foster greater opportunities and conditions for the disciplines of biology, engineering, physics, data mining and management, mathematics, psychology, and others to come together in new and robust ways.
3. **Risk-taking** - We urge that ARPA-H create the conditions for projects to be daring while still using strong scientific methods.
4. **Inclusive** - We know firsthand how critical the patient and caregiver experience can be to improving the quality of research. We urge ARPA-H to build in the role of patients, caregivers, and patient advocates from day one and leverage growing knowledge of race, ethnicity, sex, and economic status in research projects.
5. **Results-oriented** - Failure of experiments and projects is inevitable and expected in science. We urge ARPA-H to choose initiatives (including those we propose below) and see them through to completion, engaging parallel and sequential projects as needed to accomplish the end result in service of the "lasting revolutionary change" that is stated in DARPA's mission.
6. **Collaborative** - It is critical that strong federal cross-departmental collaboration and coordination occurs to ensure the success of this program. Cross-agency collaboration is critical to foster new initiatives and leverage existing projects and research to ensure smart investments of ARPA-H.

Why brain tumors are a perfect focal point for the new ARPA-H

Brain tumors offer a strategically advantageous place to start new initiatives in the following areas, as they also have the potential to yield significant progress for other disease areas.

Blood-brain barrier penetration - The blood-brain barrier's protective network has thwarted

many successful drug development and delivery attempts in neuro-oncology and other neurological indications over the years, yet the last five years have seen some innovation in this area. A coordinated, focused initiative is now needed to harness the powers of biology, engineering, and other technologies to develop novel platforms that enhance the delivery of targeted agents into the central nervous system.

Imaging and companion diagnostics - Brain tumor patients live from MRI to MRI constantly wondering if their imaging is telling them the truth about the status of their cancer. Yet, neuro-oncologists and neuro-radiologists remain frustrated about the ability to interpret MR images of brain tumors across scans as they try to decipher pseudo- progression from actual tumor growth. Advanced imaging, including metabolic imaging, remains fantastically expensive and is also hampered by its own unresolved issues such as distinguishing true tumor progress from an inflammatory response when immunotherapy is being administered. ARPA-H could make a transformative difference for brain tumor and patients with other diseases if it could bring together the best of medical academic imaging, industry, and the NCI's Cancer Imaging Program to solve these challenges with clear objectives to develop new imaging endpoints and companion diagnostics that can be used in drug and device clinical trials.

Innovation in biopsy - It is more important than ever for brain tumors and other brain diseases that novel biopsy approaches be developed, validated, and brought to scale, as repeat surgical biopsies of brain tumors is often not feasible. Emerging liquid biopsy approaches, including using cerebral spinal fluid, blood, and plasma are emerging, but there needs to be a concerted, focused, and coordinated effort to validate accurate, repeatable, and affordable liquid biopsies for patients with brain-related diseases.

Leverage the power of patient experience through technology - The rise of Real World Evidence as a potential source of data in prospective FDA-regulated clinical trials is also creating new opportunities for remote monitoring of patients through the use of wearable and other mobile technology. ARPA-H, based on experience from technology innovation from DARPA, could propel this field forward through a focused initiative on producing affordable, regulatory-grade, standardized patient- and caregiver-reported (symptom, sign, function) assessment tools. Validation and adoption of patient-reported outcomes measures would significantly improve the patient-centeredness of drug development and also help reveal clinical benefit in addition to survival.

Tumor heterogeneity - Glioblastoma and many additional adult and pediatric gliomas, as well as embryonal tumors like medulloblastoma, represent some of most cellularly heterogeneous cancers. To elucidate commonalities that can serve as actionable treatment targets amidst this inter- and intra-tumoral heterogeneity, research will benefit greatly from efforts that combine such emerging technologies and techniques as single- cell RNA sequencing and computational modeling powered by AI and machine-learning. Convergence with existing NCI-funded efforts like Project HOPE and GBM CARE offer immediate possibilities. Given the heterogeneity of glioblastoma and other brain tumors, if this level of biological diversity can be confronted and turned into biomarkers and treatment development pathways, it may provide significant benefits

for less complex cancers.

Other Cures 2.0 provisions that will help to create cures and quality of life for brain tumor patients

Clinical trials education and diversity in clinical trials: Cures 2.0 includes a number of provisions designed to increase diversity in clinical trials, which are one of the best ways for brain tumor patients to receive potentially impactful new treatments during the course of their care. In Section 203: Increasing Diversity in Clinical Trials under (c), we encourage that you expand the role of the CDC's comprehensive cancer control program to add public education about clinical trials on an on-going basis in addition to the campaign called for in (c) (1). We applaud the inclusion of the GAO Study on barriers to improving diversity and reducing barriers to under represented groups in clinical trials and the authorization of funding for public awareness campaigns related to clinical trials. Our brain tumor community can have unique disability and accessibility issues that we propose any educational efforts to include as the programs are designed. In the taskforce proposed for making Clinicaltrials.gov more patient friendly, we strongly encourage the inclusion of patient advocacy organizations, in addition to patients and caregivers, for membership on the taskforce, since these organizations are often the frontline providers of patient education and information. We also urge the Committee to provide clarity on how these task forces will be constructed to sustain transparency.

Telehealth and decentralization of clinical trials: Expanded telehealth eligibility has improved access to care for brain tumor patients by making it easier to manage the myriad medical appointments they have to attend during their care experience, and may help improve patient outcomes and lower health care costs. In addition, telehealth eligibility has helped create accessibility to clinical trials and ensured retention in trials, which are critical to quality care for brain tumor patients. In Section 310, the incentives for decentralized clinical trials, again, we strongly encourage patient advocacy organization participation in the taskforce, since they not only educate and support patients during their treatment experience, but also often fund trials. This collaborative approach to provide incentives for decentralization for both public and private funding is crucial to the success of any effort.

Novel Trial Designs and Other Innovations in Drug Development: Clinical trial design in oncology and in particular, neuro-oncology has innovated to include adaptive designs using Bayesian statistics. We encourage the Committee's direction to foster use of this and other designs to expand opportunities for biomarker driven clinical trials that improve the potential to evaluate promising treatments in molecularly defined cohorts. In addition, we urge the Committee to in turn require the Food and Drug Administration to provide clarity regarding the use of historical data, real world data and other sources as it finds appropriate in the design of clinical trials. Specifically we ask that the Committee encourage the FDA to issue guidance related to the construction of external or synthetic control arms in oncology clinical trials.

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Patient Experience Data/RWE: We ask that under 304(a)(2) Considerations, that the guidance considers patient benefit risk assessment and in particular the needs of recalcitrant cancer patients.

Education for Caregivers: Caregivers are a crucial partner in the care of brain tumor patients. In Section 201: Educational Programs and Training for Caregivers under (b), we ask that you include emotional health and psychosocial among the types of programs and training funded by HHS.

We look forward to working together, and if you have any questions or would like additional information, please contact Danielle Leach, Chief of Community and Government Relations, at dleach@braintumor.org.