July 6, 2022

Mr. Gene Dodaro
Comptroller General
Government Accountability Office
441 G St, NW
Washington, DC 20548

Dear Mr. Dodaro:

As the GAO evaluates the Research To Accelerate Cures and Equity (RACE) For Children Act ("RACE Act"), we wish to provide feedback on its implementation.

Background

The Children's Cancer Cause (CCC), established in 1999, was founded to ensure the needs and perspectives of children with cancer, survivors and their families are integrated into federal health care, research, and cancer policy. For more than twenty years, CCC has worked to accelerate anti-cancer drug development so that children can achieve access to less toxic and more effective therapies for children with cancer.

Working with the childhood cancer community, CCC helped lead the charge to pass legislation that would ensure that potentially promising new oncology drugs in development for adults would be evaluated for their potential to treat children. The RACE Act, passed in 2017 as part of the FDA Reauthorization Act (**FDARA**), went into effect in August 2020. Under the RACE Act provisions, new adult cancer drugs and biologics whose molecular targets are substantially relevant to pediatric cancers must be evaluated for pediatric use.

Children affected by cancer face unique needs and challenges. Modern therapies are needed to increase survival rates among children with diseases resistant or refractory to current therapies and to decrease lifelong health impairments experienced by children treated with older standard chemotherapy agents.

With over 200 types of childhood cancer, survival rates for many remain cancers remain unacceptably low. The biopharmaceutical industry is necessarily market-driven with a focus on developing cancer drugs for large enough patient populations to generate substantial revenue. Childhood cancers are rare diseases and offer little market incentive for companies to develop agents specifically to treat pediatric malignancies. Clinical investigators have treated children

with chemotherapy agents developed for adults over the past 40 years leaving children who survivor with multiple often dire late health impairments.

With recent burgeoning insights in the biology of cancer, pediatric oncologists, parents and patients desire early access to modern targeted therapies as critical to improving outcomes for children whose cancers.

Implementation of The RACE For Children Act

The RACE for Children Act was developed to address the need for early and better availability of therapeutics. It requires that children have access to modern therapies by mandating the evaluation of new molecularly targeted drugs and biologics, intended to treat adult cancers, which are directed at a molecular target that is substantially relevant to the growth or progression of a pediatric cancer. It is too early in the implementation of the law to know definitively what impact it has on early access and ultimately on improving outcomes for children with cancers. However, below are some of our initial observations since its inception:

Company Engagement

- We have observed in reports by FDA representatives in meetings that indicate that companies have responded to the Race Act by actively engaging the Agency in planning pediatric studies to meet the law's requirements. Academic pediatric oncology researchers report that companies are now approaching them to help design and implement pediatric trials, requests which are unlike the past when sponsors were typically reluctant to have their drugs evaluated in children.

- In meetings in which we participate with other stakeholders, it is clear that the law has increased companies' attention to the pediatric potential of their cancer drug pipeline. Until now, sponsors' attention to pediatric cancer applications of their drugs focused on the six-month marketing exclusivity incentive, which can occur at the end of a drug patent's life rather than an inclination to allow their agents to be evaluated earlier in a development program.

- We also know from meetings in which we participate that the law is generating competing pediatric studies from different sponsors for drugs in the same therapeutic class. Because childhood cancers are rare and research is revealing that there are many biological subtypes, there may be too few patients to answer questions reliably about the safety and efficacy of any one compound. An international strategy has emerged that is lending insights on this conundrum. ACCELERATE, a European nonprofit organization, conducts Pediatric Strategy Forums that partially address questions of prioritization for pediatric evaluation among sponsors' agents in the same class.

Enforcement

- Once an adult oncology drug is approved, sponsors are required to conduct pediatric studies agreed upon in Pediatric Study Plans. Delays in implementing pediatric studies can result from sponsors requesting multiple deferrals. While deferrals may legitimately be needed in some cases, in other cases deferrals or other postponements may delay access to critical information necessary for further pediatric therapy investigations and to children's treatment with potentially life-saving medicines.

- When sponsors do not complete required studies by the deadline specified in the deferral or deferral extension, FDA's existing authorities to enforce these deadlines have proven insufficient. Because the Race Act is an amendment to Pediatric Research Equity Act, we are concerned that sponsors' patterns of delay of pediatric studies required by the PREA amendment of 2012 may set a precedent for delays in their compliance with the RACE Act. The PREA amendment required FDA to issue and publicly post non-compliance letters to companies that have failed to submit their assessments on time. The law was also changed to allow FDA to extend deferral deadlines for good cause, meaning that sponsors with reasonable delays are not included among those that receive non-compliance letters. The issuance of non-compliance letters has unfortunately not resulted in the completion of delinquent PREA studies, and many required studies are still outstanding after being years overdue.

- It is too early in the implementation of the RACE Act provisions to know if it will be necessary for FDA to issue non-compliance letters. However, we continue to advocate for the FDA to enforce the PREA requirement for companies to complete post-marketing pediatric cancer studies and issue noncompliance letters as appropriate. Related to this point, FDA is allowed to assess civil monetary penalties for late post-market study requirements for adults, but the law currently forbids FDA from doing the same for children. This is an inequity that needs to be addressed.

Future Challenges

Implementation of the RACE Act requires a determined response from Congress, regulators, clinicians and advocates to implement its promise of access to new more targeted cancer agents to treat children. For this reason, we remain focused on additional Congressional action in this arena.

First, we recommend increasing resources for the FDA to meet the increased workload necessary to fulfill the law's requirements. Examples include an increase in the number of

oncology agents requiring multiple meetings to assess evolving pediatric plans; an increase in the number of oncology agents in sponsors' pipelines that require pediatric discussion and planning in Early Advice Meetings and later initial Pediatric Study Plans (PSPs); an increase in the potentially multiple pediatric cancer evaluations for a single product; and the growing number of Cluster Calls and Common Commentaries, FDA's mechanisms critical for coordinating global pediatric oncology clinical trials.

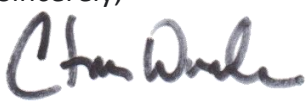
Second, it is important to note that the RACE Act does not address the question of developing drugs when there is no agent that is molecularly relevant to a cancer in children. For malignancies that are unique to children, there is no legal or regulatory mechanism to develop drugs for these rare cancers, an ongoing problem that we should seek to address. Many rare pediatric cancers have molecular and genetic characteristics that are unique to children, such as tumors with gene fusions, embryonic tumors, germline tumors and many brain tumors – cancers that the Race Act does not cover

We recommend that a new entity be created to meet this need. The formation of a new public-private partnership (PPP) could drive and catalyze scattered resources in academia, the nonprofit sector and industry to assume responsibility for conducting pediatric oncology drug development programs when agents may have no associated adult indications. A January 2020 GAO report on pediatric vouchers made this specific recommendation: "A collaborative agreement to share development risk and reward between a public or quasi-public organization and one or more private developers." Subsequent to the GAO report, the COVID-19 pandemic demonstrated the potential of public-private partnerships as in Operation Warp Speed's rapid deployment of vaccine options.

With its focus on cancer, the Advanced Research Projects Agency (ARPA-H) could serve as a powerful mechanism through which a public private partnership could be created. By including such a public-private partnership in its authorizing section, the partnership could rapidly advance the development of emerging pediatric oncology therapies.

Thank you for your efforts to evaluate the effectiveness of the RACE Act and its importance in advancing life-saving therapies for children with cancer. We are happy to discuss further and answer any questions.

Sincerely,



Steve Wosahla
Chief Executive Officer