AMERICAN SOCIETY OF HEMATOLOGY
2021 L Street, NW, Suite 900, Washington, DC 20036-4929 ph 202.776.0544 fax 202.776.0545 e-mail ASH@hematology.org

May 25, 2023

Robert M. Califf, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: *Methods and Approaches for Capturing Post-Approval Safety and Efficacy Data on Cell and Gene Therapy Products (Docket No. FDA-2023-N-0398)*

Dear Commissioner Califf:

The American Society of Hematology (ASH) appreciates the opportunity to respond to the U.S. Food and Drug Administration's (FDA) solicitation on *Methods and Approaches for Capturing Post-Approval Safety and Efficacy Data on Cell and Gene Therapy Products.*

ASH represents more than 18,000 clinicians and scientists worldwide committed to studying and treating blood and blood-related diseases. These disorders encompass malignant hematologic disorders such as leukemia, lymphoma, and multiple myeloma, as well as non-malignant conditions such as sickle cell disease (SCD), thalassemia, bone marrow failure, venous thromboembolism, and hemophilia. In addition, hematologists are pioneers in demonstrating the potential of treating various hematologic diseases and continue to be innovators in the field of stem cell biology, regenerative medicine, transfusion medicine, and gene therapy. ASH membership is comprised of basic, translational, and clinical scientists, as well as physicians providing care to patients.

In 2018, ASH founded the ASH Research Collaborative (ASH RC) to accelerate change by making it more efficient to conduct research, from increasing access to high-quality clinical data to making it easier for individuals with hematologic conditions to participate in studies. Current ASH RC initiatives focus on multiple myeloma and SCD clinical research. The foundation of the ASH RC is its Data Hub, a technology platform that facilitates the exchange of information by aggregating research-grade data on hematologic diseases. The SCD Clinical Trials Network optimizes clinical trials research in SCD and leverages the Data Hub to collect key information and identify gaps to advance SCD research and treatment.

ASH is excited to see the rapid advances in gene editing and cellular therapies and the promising new therapeutic options that are poised to change care for individuals with hematologic conditions. The long-term follow-up of individuals who undergo these treatments will be critical to ensure the best outcomes for those patients and to help inform the research and use of these therapies over time. The Society has a significant interest in the safety and efficacy of cell and gene therapy products and commends the FDA for soliciting input on methods and approaches for capturing post approval data for these products. We appreciated the opportunity to have Dr. William Wood, Senior Medical Advisor to the ASH RC, provide oral comments on behalf of the Society at FDA's April 27, 2023, public listening meeting where he highlighted the ASH and ASH RC's efforts to address these issues. In addition to Dr. Wood's remarks, we are pleased to provide more details about ASH and ASH RC's work to support the advancement and long-term follow-up of these therapies. We encourage the FDA to leverage the ASH and ASH RC resources and expertise as the Agency considers data collection in the post-approval setting for these transformative therapies.

- **ASH RC Data Hub** – As noted earlier, it is imperative to track comprehensive long-term data on patients who receive gene and cell therapies. The ASH RC Data Hub, a shared data resource for the global hematology community, is a resource for industry, FDA, and others to efficiently collect post-approval cell and gene therapy product data, especially in multiple myeloma and SCD. Clinical care sites, such as health care systems, hospitals, and outpatient practices, participate in the Data Hub and establish electronic health record (EHR) data integration that facilitates clinical data submission. Participating clinical care sites review their data and make corrections to ensure patient health data are complete and accurate. At this time, the Data Hub is collecting EHR data, case report form-based electronic data from clinical information maintained outside structured EHR fields and conducting a feasibility study to capture -patient reported outcomes (PROs) from patient-facing portals and apps. Future data projects include ingestion of patient-generated health data (PGHD) from connected digital sensors, genomic and molecular data, and population data from a variety of sources. This real-world data can generate actionable insights for research, regulatory needs, and quality improvement. More information about the Data Hub and its capabilities as a real-world data infrastructure is available in the *Blood Advances* article: *ASH Research Collaborative: a real-world data infrastructure to support real-world evidence development and learning healthcare systems in hematology*.

- **Accelerating Genomic Therapies with Real-World Evidence** – As we prepare for broader use of gene and cell therapies, we must be ready to meet the need for continued monitoring when these approaches are applied in real-world treatment settings. We know that reaching consensus on standards for real-world data collection and sharing will help FDA, industry, and clinicians who must track the safety and effectiveness of these therapies over time. To prepare for this future, the ASH RC partnered with the Innovative Genomics Institute (IGI) on the "Accelerating Innovations for SCD with Real-World Evidence" initiative to recommend data to collect and methods to coordinate clinically relevant and reliable longitudinal real-world data for genomic therapies for genetic blood disorders, particularly SCD. We were pleased to engage representatives from FDA and other stakeholders throughout the effort. This initiative led to the following two reports that outline a future for regulatory science and for genomic therapies.

  - Coordinated Registry Network Work Group's Report
  - Genomic Therapies Work Group's Report

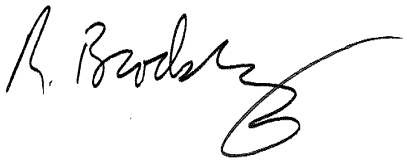
  The recommendations of this initiative are expected to be applicable to all hematologic diseases that will eventually be represented in the ASH RC Data Hub. The ASH RC Data Hub is also able to directly incorporate the data points referenced in the Reports into its data collection strategy in order to meet regulatory evidence generation needs. ASH encourages the FDA to utilize these recommendations as a resource as you consider the Agency's future work related to these innovative therapies.

- **ASH Focus on Emerging Gene and Cell Therapies** – Expanding approaches and applications of gene and cell therapies for hematologic diseases is one of ASH's research priorities listed in the *ASH Research Agenda for Hematological Research*. Towards that goal, ASH has a Subcommittee on Emerging Gene and Cell Therapies charged with advancing the use of immune-based therapies and identifying barriers in their application in both malignant and non-malignant hematologic diseases. In addition to identifying barriers, the Subcommittee investigates ways ASH could play a role in overcoming barriers to treatment, and if appropriate, makes recommendations to the Society. The Subcommittee is leading several efforts to advance this innovative field. For example, the subcommittee recently published a series of "How I Treat" research articles in *Blood,* ASH's flagship journal*,* focused on the management

of emerging and unusual Chimeric antigen receptor (CAR) T-cell related complications beyond cytokine release syndrome (CRS) and immune effector cell associated neurologic syndrome (ICANS). The ASH Subcommittee on Emerging Gene and Cell Therapies would be pleased to serve as a resource as the Agency seeks additional expertise on issues related to these innovative therapies.

ASH appreciates the opportunity to provide these comments. Please consider ASH a resource; we would be pleased to provide additional information. If you have any questions, please use ASH Deputy Director of Government Relations and Public Health Stephanie Kaplan (*skaplan@hematology.org* or 202-776-0544) as your point of contact.

Sincerely,



Robert A. Brodsky, MD
President