Biotechnology Innovation Organization

June 25, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2018-D-1328: Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals; Draft Guidance For Industry

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA or Agency) for the opportunity to submit comments on FDA's Draft Guidance for Industry "Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals" (Draft Guidance).

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. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products.

BIO believes this Draft Guidance is a positive step forward in articulating a streamlined, science-based approach for nonclinical development of pharmaceuticals. We applaud FDA for continuing to assess and accept science-based approaches that will help to get important, needed biopharmaceuticals to patients in a timely manner. We greatly support FDA's goal of getting safe and effective products to patients and avoiding the unnecessary use of animals. While we understand that this Draft Guidance is specific to severely debilitating or life-threatening hematologic disorders (SDLTHDs), BIO believes it could be used as a model for other disease areas. On the whole, BIO supports this Draft Guidance and believes it is helpful for Sponsors working in this space. We offer the following high-level and overarching comments to help strengthen and clarify some areas.

Examples of Severely Debilitating or Life-Threatening Hematologic Disorders

The Draft Guidance references the regulatory definitions of "life threatening" and "severely debilitating" and then goes on to give some examples of severely debility or life-threatening hematologic disorders, specifically listing "hemophagocytic lymphohistiocytosis, cold agglutinin, severe aplastic anemia, paroxysmal nocturnal hemoglobinuria, and severe idiopathic thrombocytopenic purpura."[1] While the Draft Guidance states that these are *some* examples of SDLHTDs, BIO believes that a more comprehensive list of disease areas that FDA would consider for this approach would be beneficial. By providing a more comprehensive list of qualifying disease areas, FDA would give Sponsors confidence that their indication could use the streamlined approach. Without this confidence, Sponsors will need to continue to ask FDA for pre-IND meetings to discuss whether their hematology indication is an SDLT or not. Providing a more

[1] FDA Draft Guidance "Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals" April 2018 lines 53-55.

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comprehensive list of qualifying diseases would ease the burden on both FDA and Sponsors. Specifically, we note that diseases such as sickle cell anemia and beta-thalessemia are not mentioned.

Additionally, most of the conditions cited in the Draft Guidance are SDLTHDs *and* rare diseases. It would be helpful to include additional examples of more common SDLTHDs in the list of examples to alleviate the potential concern that this approach is only relevant to disorders that are severely debilitating or life-threatening *and* meet the definition of a rare disease.

Incorporation of ICH S9 Guideline

ICH S9 and its specific concepts are extensively referenced throughout the Draft Guidance. BIO believes that in general, more fully incorporating the specific language from S9 into the Draft Guidance would be helpful to Sponsors, especially as there are areas of the Draft Guidance that differ slightly from the specific guidance discussed in S9. Fully articulating which concepts and specific language from S9 is applicable to SDLTHDs will help to alleviate any confusion and ensure Sponsors are providing the Agency with the appropriate study designs and information.

Nonclinical Studies vs. Nonclinical Assessments

The Draft Guidance nicely outlines in table format the expectations for appropriate nonclinical support. While the table has a column header indicating "nonclinical studies", the flexible approach detailed in prior sections is more consistent with these being "assessments" rather than "studies". For example, when integrated safety pharmacology assessments are included in a general toxicology study, or when safety endpoints are included in a disease model, the toxicology program might not align well with the specific studies listed in the table. For this reason, BIO believes that the term "assessments" rather than "studies" would provide more clear guidance, and is more consistent with the content overall. As such, BIO asks FDA to use the term "nonclinical assessments" rather than "nonclinical studies".

Conclusion

BIO appreciates the opportunity to provide comments on FDA's Draft Guidance for Industry "Severely Debilitating or Life-Threatening Hematologic Disorders: Nonclinical Development of Pharmaceuticals". We appreciate FDA's continued assessment and acceptance of science-based approaches in order to facilitate getting safe and effective treatments and cures to patients in a timely manner. As mentioned, we believe this Draft Guidance is a good step forward and could be used as a model for a streamlined nonclinical approach for other disease areas. We would be happy to provide additional information or clarification on our comments as necessary.

Sincerely,

/S/

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/S/

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