Congress of the United States
Washington, DC 20510

May 2, 2023

The Honorable Robert M. Califf, M.D.
Commissioner
Food and Drug Administration
Department of Health and Human Services
White Oak Building One
10903 New Hampshire Avenue
Room 2217
Silver Spring, MD 20993

Dear Commissioner Califf:

As leaders of the bipartisan, bicameral Rare Disease Congressional Caucus, joined with Members of Congress interested in rare disease policy, we write to urge the Food and Drug Administration to improve policy and uniformity across the agency for the review of rare disease therapy and product applications. Specifically, we ask the FDA to establish an agency task force to, first, identify areas of strength and areas that challenge the efficient but appropriate review of therapies and products developed for patients living with a rare disease and, second, for that task force to publicly issue specific recommendations to achieve greater alignment across the FDA.

The FDA has approved more than 1,100 orphan designations over the last four decades. Still, the vast majority of the more than 10,000 rare diseases that collectively impact more than 30 million Americans have no FDA-approved treatment.

We recognize and appreciate the actions FDA has taken over the years to address the challenges associated with developing treatments for orphan diseases and conditions, including through the Office of Orphan Products Development and the recent establishment of the Accelerating Rare disease Cures (ARC) program. However, across the agency there remains significant uneven application of rare disease policies, guidance, and expertise, even, at times, for the same product application. As the FDA moves toward implementing the recently-finalized Prescription Drug User Fee Act (PDUFA) VII performance goals, particularly those connected to rare disease, a thorough assessment by an FDA task force of the agency's rare disease policies and processes across divisions and centers to identify shortcomings, promote best practices, share learnings, and clarify the basis for FDA decision-making would be helpful for patients, FDA reviewers, and product applicants alike.

We urge the convening of an FDA task force including leaders from all divisions, offices, and centers which process rare disease therapy applications to fully examine areas of policy and procedural inconsistency and shortcomings, as well as best practices, and provide concrete

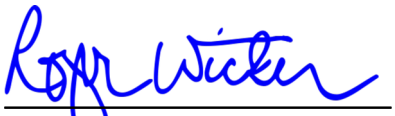
recommendations to the administration and Congress for improvement. Specifically, we request the task force promulgate a public report by December 2024 that does the following:

- Identify specific areas of both concordance and discordance involving rare disease policies across review divisions, offices, and centers through a timely and objective assessment of these disparities, including root cause analysis;
- Offer specific recommendations to address instances of discordance and promote policies and practices that will strengthen the agency's overall commitment to rare disease;
- Provide tracking metrics to assure implementation of corrective measures across time;
- Promulgate shared learning communication programs with stakeholders inside and outside the FDA;
- Review how FDA advisory committees have addressed rare disease applications and identify examples of inconsistent processes and policies;
- Review the implementation of the Accelerated Approval pathway for rare disease therapeutic products across medical product centers, including when novel surrogate endpoints were proposed and what the outcome was;
- Review gaps in guidance specific to small population development ("ultra-rare diseases") and offer recommendations for how the agency can address the unique challenges in these populations with new guidance and where new authorities would be required;
- Provide a status update to ongoing internal and external FDA-supported initiatives to modernize their approach to data for regulatory decision-making as well as any barriers encountered and how stakeholders can help address them;
- Provide increased clarity for how real-world evidence can be used in regulatory approvals to support post-approval study requirements and post-approval labeling changes;
- Evaluate and update new reviewer training materials to improve the review of therapies for rare diseases, including increased awareness and use of the inter-center consult process;
- Recommend a standard operating procedure for departing agency employees to adhere to ensure continuity of an in-process application review;
- Evaluate practices for consulting external rare disease experts and offer specific recommendations to enable useful, efficient, and timely engagement; and
- Provide examples of statutory changes or new authority that would support the FDA in its efforts to streamline and standardize rare disease treatment development across the agency.

Thank you for your commitment to meeting the needs of the millions of Americans and their families affected by rare diseases and for your prompt attention to this request.

Sincerely,

Amy Klobuchar
United States Senator



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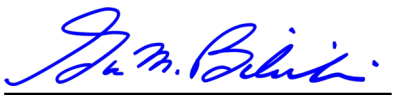
United States Senator



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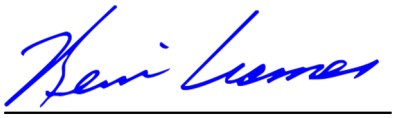

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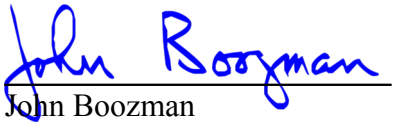

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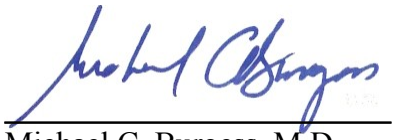

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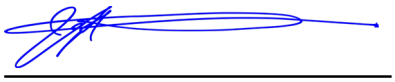

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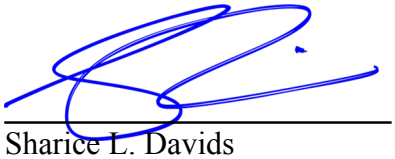

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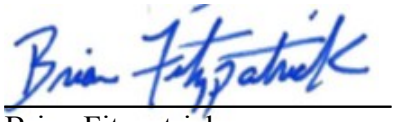

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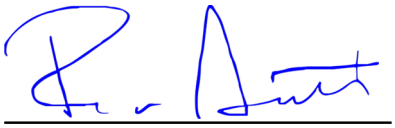

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