Biocom California

December 22, 2022

Dockets Management
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Re: Rare Disease Endpoint Advancement Pilot Meeting Program (FDA-2022-N-2480)

Submitted electronically

Dear Sir/Madam:

Biocom California appreciates the opportunity to offer comments on the Food & Drug Administration (FDA) Rare Disease Endpoint Advancement (RDEA) Pilot Meeting Program[1].

Biocom California is the largest, most experienced leader and advocate for California's life science sector, which includes biotechnology, pharmaceutical, medical device, genomics and diagnostics companies of all sizes, as well as research universities and institutes, clinical research organizations, investors and service providers. With more than 1,700 members dedicated to improving health and quality of life, Biocom California drives public policy initiatives to positively influence the state's life science community in the research, development, and delivery of innovative products. California's life sciences industry generates over $375 billion in annual economic activity, supports 435,000 jobs, and increases labor income by $115 billion per year[2].

We commend the agency's efforts to advance and facilitate the development of drugs and biological products for rare diseases. With hundreds of members in the rare disease and orphan drug sector, Biocom California is committed to engaging with the agency to provide feedback on this pilot program and future initiatives supporting rare disease research and drug development.

As part of the Prescription Drug User Fee Amendments (PDUFA) VII, the FDA and industry agreed upon various initiatives to advance drug development for rare diseases[3]. With 30 million people in the United States affected by more than 7,000 different rare diseases, of which less than 10 percent have an FDA-approved treatment, there is a profound unmet need to develop therapies for these conditions, many of which are serious or life threatening[4,5]. Rare disease drug development faces unique challenges including

[1] Federal Register, 87 FR 65085, pp. 65085-65088, October 27, 2022.
[2] Biocom California 2022 Economic Impact Report Databook. https://www.biocom.org/eir/
[3] https://www.fda.gov/media/151712/download
[4] https://www.fda.gov/patients/rare-diseases-fda
[5] https://www.fda.gov/drugs/regulatory-science-research-and-education/rare-disease-cures-accelerator

small, heterogeneous trial populations, minimal understanding of a disease's natural history, and limited regulatory precedent.

Biocom California is aware of and supports multiple efforts across the FDA to advance rare disease drug development, including the Center for Drug Evaluation and Research's Accelerating Rare disease Cures (ARC) program, FDA's Rare Disease Cures Accelerator (RDCA), and the various commitments from the FDA made during the User Fee reauthorization process. We encourage robust collaboration across these efforts to ensure consistency from FDA, clarity to sponsors, and limit potential duplication of efforts.

The RDEA Pilot Program will offer additional engagement opportunities and interactions between the agency and sponsors to support the development of efficacy endpoints for rare disease drug treatments. **In general, Biocom California supports the RDEA Pilot Program and its opportunities for sponsors of rare disease drug development programs to interact with the agency through early meetings. We offer comments in the following areas:**

Rare Disease Cures Accelerator

In 2019, the FDA established the RDCA to further support innovation in rare disease drug development by facilitating "a cooperative approach and common standardized platforms to better characterize rare disease[6]." The Accelerator's Data Analytics Platform, in partnership with the Critical Path Institute, receives rare disease data from a variety of sources to inform disease characterization, clinical trial design (including endpoint selection) and other challenges in drug development. The RDCA is also home to an effort to develop standard core sets of clinical outcome assessments (COAs) and endpoints for specific disease indications. While many of those efforts are still ongoing, it is unclear whether COAs and endpoints developed through the RDCA may impact how FDA considers and selects programs for the RDEA pilot.

Biocom California asks that the FDA clarify the relationship, if any, between the RDCA and RDEA Pilot Program, and specifically whether the agency will give preference to sponsor applications that utilize RDCA-developed endpoints. Additionally, we encourage the agency to facilitate collaboration between these two initiatives in order to utilize all available resources towards advancing rare disease drug development and limit duplicative efforts.

Selection Criteria

In section II.B. Eligibility and Selection Information, the FDA describes eligibility for the RDEA Pilot Program[7]. The criteria include development programs with an active investigational new drug application (IND) or pre-IND, sponsors performing natural history studies, or novel proposed efficacy endpoints intended to establish evidence of effectiveness for a rare disease treatment. While we appreciate the agency's effort to be inclusive of a wide range of participants, the lack of clearly defined selection criteria may create confusion and deter sponsors from applying.

[6] https://www.fda.gov/drugs/regulatory-science-research-and-education/rare-disease-cures-accelerator
[7] Federal Register, 87 FR 65085, pp. 65085-65088, October 27, 2022.

Biocom California urges the agency to provide more specific eligibility and selection criteria to the industry in its final guidance. We encourage, where possible, FDA to indicate broadly which novel endpoints may be ripe for RDEA consideration. **Additionally, we would like the FDA to clarify whether a sponsor can participate in both the RDCA and the RDEA Pilot Program simultaneously and if there are overlapping eligibility criteria for these programs.**

Accelerated Approval Pathway

The FDA also states that preference will be given to proposals "that have novel approaches for collecting additional clinical data in the premarket stage to advance validation of the endpoint for a surrogate endpoint proposal." **However, it is unclear if sponsors using surrogate endpoints as part of the accelerated approval pathway will also be considered for the RDEA Pilot Program. Biocom California asks that the FDA clarify whether a sponsor seeking accelerated approval with a surrogate endpoint would be eligible for the RDEA Pilot Program.**

FY 2024-2027 Applications

The Federal Register notice explains that "for FY [fiscal year] 2023, sponsors may submit RDEA proposals beginning in the fourth quarter, and FDA will accept a maximum of one proposal. For FYs 2024 through 2027, FDA will accept up to one RDEA proposal per quarter with a maximum of three proposals per year." While the agency has noted the pilot's proposal acceptance timeline, the FDA has not provided specific information on whether the meeting timeline and eligibility criteria may be altered for sponsors who choose to apply to the program in its later years. **We ask the agency to clarify how the program eligibility criteria and meeting timeline may differ, if at all, if a sponsor chooses to apply to the program during fiscal years 2024-2027.**

Biocom California supports the RDEA Pilot Program and believes it will provide a more streamlined collaboration between the FDA and industry on the development of novel efficacy endpoints for rare disease drug development. We respectfully suggest that there may be increased industry participation in the pilot, leading to more robust endpoint data, if the agency's feedback during the program translated into long-term developments. Understanding how the Agency views endpoints that might be successfully developed via the RDEA program within their context of use, would be beneficial to sponsors. Lastly, we ask the agency to allow sponsors a continued opportunity to provide feedback on the program throughout the duration of the pilot.

We appreciate the opportunity to provide feedback on behalf of our members and thank you for your time and diligence in examining our comments. Please contact Biocom California's Associate Manager of Regulatory Policy, Zoe Bilis, at zbilis@biocom.org for additional information or questions. We look forward to continuing to work with you on this critical matter.

Sincerely,

Joe Panetta
President and CEO
Biocom California