April 26, 2023

Robert Califf, MD, Commissioner, FDA
Peter Marks, MD, PhD, Director, CBER
Celia Witten, MD, PhD, Acting Director, OTP, CBER

Douglas S. Ingram, President and Chief Executive Officer, Sarepta Therapeutics
Louise R. Rodino-Klapac, PhD, Chief Scientific Officer, Sarepta Therapeutics

Dear Ladies and Gentlemen,

On behalf of the Duchenne Muscular Dystrophy Community, we are writing to urge the Food & Drug Administration (FDA) and Sarepta Therapeutics (Sarepta) to make every effort in the coming weeks to reach a decision to approve SRP-9001 (delandistrogene moxeparvovec) through the Accelerated Approval (AA) pathway. Since the 1986 discovery of the gene whose mutation causes Duchenne, many in our Community have collaborated to help reach a point where the fruits of our efforts are realized through a gene therapy that can change the course of this lethal disease. Assuming that the application has met the FDA's approval standard for AA, we cannot afford to delay this opportunity now that it is within reach for those living with Duchenne and for those diagnosed in the future.

Even considering the advances made with prior product approvals for Duchenne, the continuing profound unmet medical needs for people with Duchenne cannot be overstated. The threat to functionality and longevity are very real and unrelenting as the lack of dystrophin leads to muscle degeneration throughout the body. Notwithstanding a burden that increases markedly as the disease progresses, incremental advances in care have added nearly ten years to the average lifespan of effected individuals. A gene therapy that targets both skeletal muscle and the heart, delivering a smaller, but functional version of the protein should likely both improve longevity and quality of life across the later stages of disease and therefore further building upon, and extending, the positive impact of Duchenne product developments.

We also commend the FDA for its commitment to appropriate regulatory flexibility and innovation in confronting the devastation of Duchenne, as well as of other rare, progressive, and deadly disorders. Our experience with earlier therapy reviews in CDER's neurology division has vividly demonstrated how patient-focused drug development programs which capture patient expectations for benefit, as well as tolerance for risk, can encourage both timely advancement of individual products and expand the broader therapeutic ecosystem. This flywheel effect has helped the community advance from a treatment desert to a broadening array of options and the promise of profoundly disease-modifying treatments. The Duchenne community has partnered with the FDA and all stakeholders through groundbreaking guidance development, regulatory-grade patient preference studies, natural history studies, and a vast array of pre-competitive collaboration projects to ensure that the patient voice is clearly and scientifically characterized at the center of this complex process.

Finally, we recognize a central question in the review of SRP-9001 is whether the micro-dystrophin delivered via an AAV and quantified on biopsy with participants in the clinical study is reasonably likely to predict clinical benefit in Duchenne. The Dystrophin protein is fundamental to preservation of muscle stability. There is considerable evidence from asymptomatic individuals that smaller versions of the dystrophin protein are both stable and functional and it is from these data that the micro-dystrophin protein has been developed over the last thirty years We therefore urge the FDA to exert maximal regulatory flexibility to allow incremental innovations that encourage new research in order to extend such advances. In addition, it may be useful to the FDA to consider the AA criteria in gene therapy content developed by research, clinical, and

advocacy leaders set forth in the Community-led draft drug development guidance submitted to the Agency in October 2022.

Thank you for your careful consideration of these views. We stand ready to support the continuing progress on SRP-9001 and, once again, call on each and every one of us to stand behind a fair, timely, and flexible review of the benefits and risks of this critical source of hope for our community.

Sincerely,

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