Citizen Petition

Date: June 2, 2024

The undersigned submits this petition pursuant to the authority of 21 CFR §10.20 and 21 CFR §10.30 as well as Section 351 of the Public Health Service Act (and other related relevant statutory authority) to request the Commissioner of Food and Drugs to refrain from expanding the label of SRP-9001(also known as delandistrogene moxeparvovec-rokl, or Elvidys) until further conclusive benefit is established.

A. Action Requested

This petition requests the Commissioner refrain from authorizing an expanded label for SRP-9001 (Elvidys) and consider re-evaluating the limited benefit relative to the risks of treatment.

B. Statement of Grounds

The FDA granted SRP-9001 (delandistrogene moxeparvovec-rokl, Elvydis) accelerated approval in June 2023. According to Sarepta, the Phase 2, randomized, double-blind, placebo-controlled clinical trial evaluating the safety and efficacy of delandistrogene moxeparvovec-rokl, Study 9001-102 "SRP-9001-treated participants showed an increase in NSAA total score compared to placebo at 48 weeks; however, the study did not achieve statistical significance on the primary functional endpoint of improvement in NSAA total score compared to placebo at 48 weeks post-treatment." Per the trial data, change in NSAA score of 1.7 vs 0.9; difference, 0.8 [95% CI, −1.0 to 2.7].

As noted by David Rind, MD, Director of the Institute for Clinical and Economic Review in the recent JAMA publication, "Compared with patients receiving placebo, those receiving the intended dose had the worst numeric change in NSAA score (−1.5), those receiving a two-thirds dose had the best change (2.6), and those receiving a half dose had an intermediate change (0.7). As such, no dose-response effect was seen with SRP-9001."

He also noted,"SRP-9001 can cause harm. Among 85 patients across 3 studies, 5 patients had serious liver injury requiring hospitalization, though all recovered. Two patients developed myocarditis. One of these patients required intensive care unit admission, but ultimately symptoms resolved. The other patient developed a chronic cardiomyopathy requiring ongoing treatment with medications. One additional patient developed a life-threatening immune-mediated myositis that appeared 1 month after receiving SRP-9001. Symptoms included muscle weakness, dysphagia, dysphonia, and

difficulty sitting and walking that only partially resolved after treatment with plasmapheresis and corticosteroids."

The Phase 3 EMBARK trial comparing SRP-9001 to placebo similarly failed to achieve its primary endpoint in 125 boys based on change in NSAA score over 52 weeks (2.6 vs 1.9; P = .24). Unfavorable data for this petition is the company's argument that secondary endpoints of time to rise (P=0.0025) and 10-meter walk test (p = 0.0048) are clinically meaningful. However, the NSAA primary endpoint was not achieved. As discussed in Dr. Hind's JAMA article, "It seems clear that the evidence for net benefit with SRP-9001 is weak. It also appears that if benefits with SRP-9001 are real, they are not large, although it may be that longer trials could show greater effects."

Given these outcomes, expanding the label of Elvidys will obstruct the developmental path and availability for disease-stricken patients to obtain treatment with developing therapies that actually show potential for disease modification and physiologic improvement. As a corollary, the FDA approved Aducanumab but the drug was withdrawn by the sponsors because there were serious concerns about safety and efficacy. Premature expansion of the Elvidys label may similarly impede scientific development, resulting in derailment of alternate therapeutic opportunities. At present, several promising alternative therapies show minimal to no significant safety signals but also demonstrate statistically significant efficacy. The obstruction or delay of the development of these therapies could be devastating to patients. Patients need a safe and effective treatment now. It is imperative that FDA focuses its limited resources and expedite review on other candidates to help find a cure.

Further, expanding the label of SRP-9001(Elvidys) in its present form with successive failed primary endpoints would have the potential of irreparably damaging the credibility of the FDA and undermine its mandate to provide medicines that are both safe and efficacious. This drug has demonstrated serious harm and without compelling benefit to show for it.

Additional studies and perhaps next generation gene and cell therapies are sorely needed to demonstrate a real and significant benefit for the children suffering from Duchenne's. The FDA should seek to expedite therapies in development that meet their primary endpoints and make a true difference for these patients.

C. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.30 and § 25.31, as the relief requested in this Citizen Petition will have no environmental impact and therefore an environmental assessment or environmental impact statement is not required.

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), economic impact information will be submitted by the Petitioner only upon request of the Commissioner following review of this Petition.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

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