74th Cellular, Tissue, and Gene Therapies Advisory Committee (CTGTAC) Meeting
May 12, 2023

Discussion Topics

1. Please discuss the strengths and limitations of the available evidence supporting the use of measurement of Sarepta's micro-dystrophin, expressed through the administration of SRP-9001, as a surrogate endpoint "reasonably likely to predict clinical benefit" in ambulatory patients with Duchenne muscular dystrophy with a confirmed mutation in the *DMD* gene.

2. Part 1 of Study 102 was the only randomized, double-blind, placebo-controlled clinical study for which data currently are available. The study failed to demonstrate a statistically significant effect of treatment with SRP-9001 versus placebo on the primary clinical outcome measure, change in the North Star Ambulatory Assessment (NSAA) Total Score from baseline to Year 1.

   Exploratory subgroup analyses suggest that the SRP-9001 group may have had a better NSAA outcome compared to the placebo group among ambulatory patients between 4 to 5 years of age; however, among ambulatory patients between 6 to 7 years of age, there appeared to be no difference between the SRP-9001 group and the placebo group, and the SRP-9001 group showed no improvement from baseline.

   Please discuss the clinical significance of these findings.

3. Please discuss the potential benefits, risks, and uncertainties that may be associated with administration of SRP-9001 for treatment of ambulatory patients with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene.

4. If SRP-9001 were to be approved under Accelerated Approval provisions, the Applicant proposes that Part 1 of Study 301 (the Phase 3 randomized, double-blind, placebo-controlled 52-week crossover clinical study) may serve as the required postmarketing confirmatory trial to verify and describe clinical benefit. Please note that the last patient last clinical visit for the 52-week primary endpoint is expected to be completed by the end of September 2023.

   Please discuss the potential impact of marketing approval on completion of Part 1 of Study 301.

Discussion Question, Then Voting

1. Do the overall considerations of benefit and risk, taking into account the existing uncertainties, support Accelerated Approval of SRP-9001 — using as a surrogate endpoint, expression of Sarepta's micro-dystrophin at Week 12 after administration of SRP-9001 — for the treatment of ambulatory patients with Duchenne muscular dystrophy with a confirmed mutation in the *DMD* gene?
   a. Yes
   b. No
   c. Abstain