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 that is reasonably likely to predict clinical benefit in ambulatory patients with DMD.

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, the NSAA at Week 48.

   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, for 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 DMD.

4. If the investigational product were to be approved under Accelerated Approval provisions, Sarepta proposes that Part 1 of Study 301, the Phase 3 randomized, double-blind, placebo-controlled 52-week, may serve as the required post-marketing confirmatory trial to verify and describe clinical benefit. Note that the 52-week analysis timepoint is expected to be completed by the end of September 2023.

   Please discuss the impact of marketing approval on completion of Part 1 of the study.

Voting Question

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, for the treatment of ambulatory patients with DMD with a confirmed mutation in the *DMD* gene?
   a. Yes
   b. No
   c. Abstain