## Vyondys 53™ (golodirsen) – New orphan drug approval

- On December 12, 2019, the FDA announced the approval of Sarepta Therapeutics' Vyondys 53 (golodirsen), for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping.
    - This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.
- DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact. The first symptoms are usually seen between 3 and 5 years of age and worsen over time. The disease often occurs in people without a known family history of the condition and primarily affects boys, but in rare cases it can affect girls. DMD occurs in about 1 out of every 3,600 male infants worldwide.
    - People with DMD progressively lose the ability to perform activities independently and often require a wheelchair by their early teens. As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary.
- Vyondys 53 is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping.
- The efficacy of Vyondys 53 was established in a two-part study in DMD patients with a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Part 1 was a double-blind, placebo-controlled, dose-titration study in 12 DMD patients. Part 2 was a 168-week, open-label study assessing the efficacy and safety of Vyondys 53 in the 12 patients enrolled in Part 1, plus 13 additional treatment-naïve patients. Efficacy was assessed based on change from baseline in the dystrophin protein level (measured as a % of the dystrophin level in healthy subjects, ie, % of normal) at week 48 of Part 2.
    - Mean dystrophin levels increased from 0.10% of normal at baseline to 1.02% of normal by week 48, with a mean change in dystrophin of 0.92% of normal levels ($p < 0.001$); the median change from baseline was 0.88%.
- Warnings and precautions for Vyondys 53 include hypersensitivity reactions and renal toxicity.
- The most common adverse reactions (≥ 20% and higher than placebo) with Vyondys 53 use were headache, pyrexia, fall, abdominal pain, nasopharyngitis, cough, vomiting, and nausea.
- The recommended dose of Vyondys 53 is 30 milligrams per kilogram administered once weekly as a 35 to 60-minute intravenous infusion.
- Vyondys 53 is priced at parity to Sarepta's other DMD product, Exondys 51® (eteplirsen).
    - Exondys 51 is indicated for the treatment of DMD in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 51 skipping.

Continued . . .

- Sarepta plans to launch Vyondys 53 immediately. Vyondys 53 injection will be available in a 100 mg/2 mL single-dose vial.