Exondys 51™ (eteplirsen) – New Orphan Drug Approval

- On September 19, 2016, the FDA announced the approval of Sarepta Therapeutics’ Exondys 51 (eteplirsen) for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.
  - This indication was approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51.
  - A clinical benefit of Exondys 51 has not been established. 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. It is the most common form of muscular dystrophy and is caused by an absence of dystrophin, a protein that helps keep muscle cells intact.
  - DMD occurs in about one out of every 3,600 male infants worldwide. It primarily affects boys, but in rare cases it can affect girls.
  - The first symptoms are usually seen between 3 and 5 years of age, and worsen over time. People with DMD progressively lose the ability to perform activities independently and often require use of 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.

- Exondys 51 contains eteplirsen and is the first FDA approved drug for DMD. Eteplirsen is designed to bind to exon 51 of dystrophin pre-messenger RNA (mRNA), resulting in exclusion of this exon during mRNA processing, which allows for the production of an internally truncated dystrophin protein.
  - Mutation of the dystrophin gene amenable to exon 51 skipping affects an estimated 13% of the DMD population.

- The approval of Exondys 51 is based on the surrogate endpoint of dystrophin increase in skeletal muscle observed in some Exondys 51-treated patients.
  - The FDA has concluded that the demonstrated increase in dystrophin production was reasonably likely to predict clinical benefit in some patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping.
  - However, a clinical benefit of Exondys 51, including improved motor function, has not been established.

- In making this decision, the FDA considered the potential risks associated with the drug, the life-threatening and debilitating nature of the disease for these children, and the lack of available therapy.
  - Under the accelerated approval provisions, the FDA is requiring Sarepta to conduct a clinical trial to confirm the drug’s clinical benefit.

- The most common adverse reactions (incidence ≥ 35% and higher than placebo) with Exondys 51 use were balance disorder and vomiting.

Continued . . .
The recommended dose of Exondys 51 is 30 mg/kg by intravenous infusion once weekly.

- Application of a topical anesthetic cream to the infusion site may be considered prior to administration of Exondys 51.

Sarepta plans to launch Exondys 51 immediately. Exondys 51 will be available as 100 mg/2 mL and 500 mg/10 mL single-dose vials.

- During a hosted conference call, Sarepta announced that the estimated average cost for Exondys 51 will be $300,000 per year. The specific cost of the drug will vary by patient as Exondys 51 is dosed based on individual body weight.
  - Exondys 51 will cost $1,600 and $8,000 for each 100 mg/2 mL and 500 mg/10 mL vial, respectively.