Qalsody™ (tofersen) – New orphan drug approval

- On April 25, 2023, the FDA announced the approval of Biogen's Qalsody (tofersen), for the treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene.
    - This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with Qalsody.
    - Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

- ALS, also known as Lou Gehrig's disease, is a rare, progressive, and fatal disease that attacks neurons that control voluntary movement, resulting in the gradual loss of muscle movement, speech, swallowing, and eventually breathing. Most patients with ALS die from respiratory failure, usually within three to five years of diagnosis.

- The CDC estimates that approximately 16,000 to 32,000 Americans have ALS. Approximately 2% of ALS cases are associated with mutations in the SOD1 gene. The FDA estimates there are fewer than 500 patients with SOD1-ALS in the U.S.

- Tofersen is an antisense oligonucleotide that causes degradation of SOD1 mRNA through binding to SOD1 mRNA, which results in a reduction of SOD1 protein synthesis.

- The efficacy of Qalsody was established in a randomized, double-blind, placebo-controlled study in 147 patients with weakness attributable to ALS and a confirmed SOD1 mutation. Patients were randomized to receive treatment with either Qalsody or placebo for 24 weeks (three loading doses followed by five maintenance doses). The primary efficacy analysis was the change from baseline to week 28 in the ALS Functional Rating Scale-Revised (ALSFRS-R) total score in the modified intent to treat (mITT) population. The key secondary endpoint was change from baseline at week 28 in plasma NfL, a blood-based biomarker of axonal injury and neurodegeneration.
    - Patients treated with Qalsody experienced less decline from baseline in the ALSFRS-R compared to placebo, but the results were not statistically significant (Qalsody-placebo adjusted mean difference: 1.2; 95% CI: -3.2, 5.5).
    - Patients receiving Qalsody had nominally significant reductions in plasma NfL and cerebrospinal spinal fluid SOD1 protein at week 28 compared to placebo.
    - Other clinical secondary outcomes did not reach statistical significance.

- Warnings and precautions for Qalsody include myelitis and/or radiculitis, papilledema and elevated intracranial pressure, and aseptic meningitis.

- The most common adverse reactions (≥ 10% and greater than placebo) with Qalsody use were pain, fatigue, arthralgia, cerebrospinal fluid white blood cell increased, and myalgia.

- The recommended dose of Qalsody is 100 mg (15 mL) per intrathecal administration.
    - Patients receive three initial doses administered at 14-day intervals, followed by a maintenance dose every 28 days.
    - Refer to the Qalsody drug label for complete administration instructions.

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- Qalsody is expected to be priced within a range comparable to other recently launched ALS treatments (approximately $158,000 annually).

- Biogen plans to launch Qalsody in approximately one week. Qalsody will be available as a 100 mg/15 mL (6.7 mg/mL) solution in a single-dose vial.

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