Amvuttra™ (vutrisiran) – New orphan drug approval

- On June 13, 2022, Alnylam announced the FDA approval of Amvuttra (vutrisiran), for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults.

- hATTR amyloidosis is an inherited, progressively debilitating, and fatal disease caused by mutations in the TTR gene. TTR protein is primarily produced in the liver and is normally a carrier of vitamin A. Variants in the TTR gene cause abnormal amyloid proteins to accumulate and damage body organs and tissue, such as the peripheral nerves and heart, resulting in intractable peripheral sensory-motor neuropathy, autonomic neuropathy, and/or cardiomyopathy, as well as other disease manifestations.

    - hATTR amyloidosis affects approximately 50,000 people worldwide.
    - The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients presenting with cardiomyopathy.

- Amvuttra is a small interfering RNA (siRNA) therapeutic that targets mutant and wild-type TTR messenger RNA (mRNA). By silencing mRNA, Amvuttra prevents disease-causing protein (TTR) from being made.

    - Amvuttra is similar to Alnylam's other siRNA product, Onpattro® (patisiran), which shares the same indication. However, Amvuttra is administered subcutaneously (SC) once every 3 months while Onpattro is administered via intravenous infusion once every 3 weeks.

- The efficacy of Amvuttra was established in a randomized, open-label study in adult patients with polyneuropathy caused by hATTR amyloidosis. Patients were randomized to receive Amvuttra or Onpattro (reference group). Efficacy assessments were based on a comparison of the Amvuttra with an external placebo group in another study composed of a comparable population of adult patients with polyneuropathy caused by hATTR amyloidosis. The primary endpoint was the change from baseline to month 9 in modified Neuropathy Impairment Score +7 (mNIS+7). The mNIS+7 has a total score range from 0 to 304 points, with higher scores representing a greater severity of disease.

    - The least squares mean change from baseline for the mNIS+7 score was -2.2 for Amvuttra vs. +14.8 for placebo (difference of -17.0, 95% CI: -21.8, -12.2; $p < 0.001$).

- A warning and precaution for Amvuttra is reduced serum vitamin A levels and recommended supplementation.

- The most common adverse reactions (≥ 5%) with Amvuttra use were arthralgia, dyspnea, and decreased vitamin A.

- The recommended dose of Amvuttra is 25 mg administered by SC injection once every 3 months. Amvuttra should be administered by a healthcare professional.

- Alnylam plans to launch Amvuttra in early July. Amvuttra will be available as a 25 mg/0.5 mL single-dose prefilled syringe.