Ogsiveo™ (nirogacestat) – New orphan drug approval

- On November 27, 2023, the FDA announced the approval of SpringWorks Therapeutics' Ogsiveo (nirogacestat), for adult patients with progressing desmoid tumors who require systemic treatment.

- Desmoid tumors are rare, aggressive, locally invasive tumors of the soft tissues. In rare cases when vital structures are impacted, these tumors can be life-threatening.

    — It is estimated that there are 1,000 - 1,650 new cases diagnosed per year in the U.S.

- Ogsiveo is a gamma secretase inhibitor that blocks proteolytic activation of the Notch receptor. When dysregulated, Notch can activate pathways that contribute to tumor growth.

    — Ogsiveo is the first FDA approved treatment for desmoid tumors.

- The efficacy of Ogsiveo was established in DeFi, a randomized, double-blind, placebo-controlled study in 142 adult patients with progressing desmoid tumors not amenable to surgery. Patients were randomized to receive Ogsiveo or placebo until disease progression or unacceptable toxicity. The major efficacy outcome was progression-free survival (PFS). Objective response rate (ORR) was an additional efficacy outcome measure.

    — Median PFS was not reached in the Ogsiveo-treated patients vs. 15.1 months in the placebo-treated patients (Hazard ratio 0.29; 95% CI: 0.15, 0.55; $p < 0.001$).
    — The ORR was 41% (95% CI: 29.8, 53.8) in the Ogsiveo-treated patients vs. 8% (95% CI: 3.1, 17.3) in the placebo-treated patients ($p < 0.001$).

- Warnings and precautions for Ogsiveo include diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancer, electrolyte abnormalities, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 15%) with Ogsiveo use were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection and dyspnea.

- The most common laboratory abnormalities (≥ 15%) with Ogsiveo use were decreased phosphate, increased urine glucose, increased urine protein, increased aspartate aminotransferase, increased alanine transaminase, and decreased potassium.

- The recommended dose of Ogsiveo is 150 mg administered orally twice daily until disease progression or unacceptable toxicity.

- SpringWorks Therapeutics plans to launch Ogsiveo through a specialty pharmacy in five to ten business days. Ogsiveo will be available as a 50 mg tablet.