Pepaxto® (melphalan flufenamide) – New orphan drug approval

- On February 26, 2021, Oncopeptides announced the FDA approval of Pepaxto (melphalan flufenamide), in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody.

    - This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).
    - Pepaxto is not indicated and is not recommended for use as a conditioning regimen for transplant outside of controlled clinical trials.

- Multiple myeloma is a cancer that impacts plasma cells. Approximately 7 per 100,000 Americans are each year diagnosed with multiple myeloma. A growing subset of this population is becoming triple-class refractory. This means that their disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody.

- Pepaxto is the first anticancer peptide-drug conjugate for patients with relapsed or refractory multiple myeloma. Pepaxto links a peptide carrier to a cytotoxic agent, resulting in a lipophilic compound. Due to its lipophilicity, Pepaxto is distributed into cells.

- Th efficacy of Pepaxto was established in HORIZON, a single-arm study in 97 patients with relapsed or refractory multiple myeloma. Patients received Pepaxto on day 1 and dexamethasone on day 1, 8, 15 and 22 of each 28-day cycle until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall response rate (ORR) and duration of response (DOR).

    - The ORR was 23.7% (95% CI: 15.7, 33.4).
    - The DOR was 4.2 months (95% CI: 3.2, 7.6).

- Warnings and precautions for Pepaxto include thrombocytopenia, neutropenia, anemia, infections, increased risk of mortality with Pepaxto at dosages higher than the recommended dosage, secondary malignancies, and embryo-fetal toxicity.

- The most common adverse reactions (> 20%) with Pepaxto use were fatigue, nausea, diarrhea, pyrexia and respiratory tract infection. The most common laboratory abnormalities (≥ 50%) were decreased leukocytes, decreased platelets, decreased lymphocytes, decreased neutrophils, decreased hemoglobin, and increased creatinine.

- The recommended dosage of Pepaxto is 40 mg administered intravenously (IV) over 30 minutes on day 1 of each 28-day cycle until disease progression or until unacceptable toxicity. Dexamethasone 40 mg orally or IV should be administered on days 1, 8, 15 and 22 of each cycle. For patients 75 years of age or older, reduce the dose of dexamethasone to 20 mg.

    - A serotonin-3 (5-HT3) receptor antagonist or other antiemetics should be considered prior to and during the treatment with Pepaxto.
    - Refer to the dexamethasone drug label for additional dosing information.

Continued . . .

- Oncopeptides plans to launch Pepaxto within approximately 2 weeks. Pepaxto will be available as a 20 mg lyophilized powder in a single-dose vial for reconstitution and dilution.