Orserdu™ (elacestrant) – New drug approval

- On January 27, 2023, the FDA announced the approval of Menarini Group and Stemline Therapeutics' Orserdu (elacestrant), for the treatment of postmenopausal women or adult men with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, *ESR1*-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy.

- *ESR1* mutations are present in up to 40% of ER+, HER2- advanced or metastatic breast cancer cases.

- Orserdu is an estrogen receptor antagonist. Orserdu demonstrated *in vitro* and *in vivo* antitumor activity including in ER+ HER2- breast cancer models resistant to fulvestrant and cyclin-dependent kinase 4/6 inhibitors and those harboring *ESR1* mutations.

- The efficacy of Orserdu was established in EMERALD, a randomized, open-label, active-controlled study in 478 postmenopausal women and men with ER+/HER2- advanced or metastatic breast cancer of which 228 patients had *ESR1* mutations. Patients were randomized to receive Orserdu, or investigator's choice of endocrine therapy, which included fulvestrant, or an aromatase inhibitor (anastrozole, letrozole or exemestane). The major efficacy outcome was progression-free survival (PFS). An additional efficacy measure was overall survival (OS).

    - A statistically significant difference in PFS was observed in the intention to treat (ITT) population and in the subgroup of patients with *ESR1* mutations. An exploratory analysis of PFS in the patients without *ESR1* mutations showed a hazard ratio (HR) 0.86 (95% CI: 0.63, 1.19) indicating that the improvement in the ITT population was primarily attributed to the results seen in the *ESR1* mutated population.
    - In the *ESR1* mutated population, median PFS was 3.8 months for Orserdu vs. 1.9 months for investigator's choice of endocrine therapy (HR 0.55, 95% CI: 0.39, 0.77; p = 0.0005). There was not a statistically significant difference in OS between the two groups.

- Warnings and precautions for Orserdu include dyslipidemia and embryo-fetal toxicity.

- The most common adverse reactions (≥ 10%), including laboratory abnormalities, with Orserdu use were: musculoskeletal pain, nausea, increased cholesterol, increased aspartate aminotransferase (AST), increased triglycerides, fatigue, decreased hemoglobin, vomiting, increased alanine aminotransferase (ALT), decreased sodium, increased creatinine, decreased appetite, diarrhea, headache, constipation, abdominal pain, hot flush, and dyspepsia.

- The recommended dosage of Orserdu is 345 mg taken orally with food once daily until disease progression or unacceptable toxicity occurs.

    - Patients should be selected for treatment with Orserdu based on the presence of *ESR1* mutation(s) in plasma specimen using an FDA-approved test.
    - Information on FDA-approved tests for detection of *ESR1* mutations in breast cancer is available at: http://www.fda.gov/CompanionDiagnostics.

- Stemline Therapeutics plans to launch Orserdu soon. Orserdu will be available as an 86 mg and 345 mg tablet.