

January 30th, 2023



Stemline Therapeutics, a subsidiary of Menarini Group, Receives U.S. FDA Approval for ORSERDU™ (elacestrant) as the First and Only Treatment Specifically Indicated for Patients with *ESR1* Mutations in ER+, HER2- Advanced or Metastatic Breast Cancer

- *ESR1 mutations are present in up to 40% of ER+, HER2- advanced or metastatic breast cancers.*
- *ESR1 mutations are a known driver of resistance to standard endocrine therapy, and so far, have been difficult to treat.*
- *ORSERDU is the first endocrine innovation in more than 20 years, specifically addressing *ESR1* mutations, a major unmet need.*

FLORENCE (Italy) and New York City (U.S.) January 30th, 2023 – The Menarini Group (“Menarini”), a leading Italian pharmaceutical and diagnostics company, announced today that the U.S. Food and Drug Administration (FDA) has approved ORSERDU for the treatment of postmenopausal women or adult men, with ER+, HER2-, *ESR1*-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy. Stemline Therapeutics (“Stemline”), a wholly-owned subsidiary of the Menarini Group, headquartered in New York and focused on bringing transformational oncology treatments for cancer patients, will commercialize ORSERDU in the U.S.

“The FDA approval of ORSERDU marks the first ever therapy for ER+, HER2- advanced or metastatic breast cancer patients with *ESR1* mutations and we are very proud to offer a targeted therapy addressing this huge unmet need,” commented Elcin Barker Ergun, Chief Executive Officer of the Menarini Group. “We are grateful to the patients, investigators and administrators who participated in the clinical trials that led to this remarkable innovation.”

ORSERDU is approved under the FDA’s Priority Review and Fast Track designation based on the results of the registrational Phase III trial EMERALD, that demonstrated statistically significant progression-free survival (PFS) with elacestrant vs SOC endocrine monotherapy (fulvestrant, letrozole, anastrozole, exemestane), meeting both primary endpoints in all patients and in those patients whose tumors harbor *ESR1* mutations.

In the group of patients whose tumors had *ESR1* mutations, elacestrant reduced the risk of progression or death by 45% (PFS HR=0.55, 95% CI: 0.39, 0.77) vs SOC. A post-hoc analysis of the PFS results based on the duration of prior CDK4/6i inhibitors (CDK4/6i) usage was presented at San Antonio Breast Cancer Symposium (SABCS) in December 2022. The median PFS was 8.6 months on elacestrant vs 1.9 months for SOC, in those patients whose tumors harbored *ESR1* mutations and had been treated with a CDK4/6i for at least 12 months.

Safety data is consistent with the other endocrine therapies. Most of the adverse events (AEs), including nausea and musculoskeletal pain were grade 1 and 2. No hematological

safety signal was observed and none of the patients in either of the two treatment arms had sinus bradycardia.

“Advanced or metastatic ER+, HER2- breast cancer pre-treated with endocrine-based therapy remains an area of unmet medical need. The last endocrine therapy approved was about 20 years ago, and effective endocrine options for this patient population are needed,” said Dr. Aditya Bardia, MD, MPH, Director of Breast Cancer Research at Mass General Cancer Center, Associate Professor at the Medicine Department at Harvard Medical School, and Principal Investigator for the EMERALD trial. “*ESR1* mutations are a known driver of resistance to standard endocrine therapy, and so far, have been difficult to treat. The approval of elacestrant is welcomed as it offers a novel option for patients with ER+, HER2- metastatic breast cancer. This therapy targets the *ESR1* mutations in metastatic breast cancer and provides patients with a convenient oral once-daily dose.”

“Each year 300,000 Americans are diagnosed with breast cancer and metastatic breast cancer causes the vast majority of deaths from the disease: more than 43,000 annually. We urgently need new and better treatment options to extend and improve the lives of people with metastatic breast cancer,” said Sonya Negley, Executive Director, Metavivor. “We are thrilled to see the approval of ORSERDU, a new oral endocrine therapy, for patients who have tumors that harbor *ESR1* mutations, which are present in up to 40% of ER+, HER2- advanced or metastatic breast cancer. We advise patients to get tested for *ESR1* mutations at progression in their metastatic treatment, so that their healthcare team can identify the right treatment options for their disease.”

ORSERDU will soon be available in the United States. Stemline is committed to helping patients access ORSERDU and will be offering services to overcome access barriers. Stemline ARC, a patient support program is available to help guide eligible patients through the various aspects of getting started on treatment, from providing educational information to helping them understand their insurance coverage and identify potential financial assistance options. For more information, patients and healthcare professionals can call 1-833-4-STEMLINE (1-833-478-3654)

The Menarini Group obtained global licensing rights for elacestrant in July 2020 from Radius Health, Inc., who conducted the EMERALD study. With this approval, Radius will receive milestone payments and royalties from commercial sales. The Menarini Group is now fully responsible for global registration, commercialization, and further development activities for elacestrant.

About EMERALD Phase 3 Study (NCT03778931)

The EMERALD Phase 3 trial is a randomized, open label, active-controlled study evaluating elacestrant as second- or third-line monotherapy in ER+, HER2- advanced/metastatic breast cancer patients. The study enrolled 478 patients who had received prior treatment with one or two lines of endocrine therapy, including a CDK4/6 inhibitor. Patients in the study were randomized to receive either elacestrant or the investigator’s choice of an approved hormonal agent. The primary endpoints of the study were progression-free survival (PFS) in the overall patient population and in patients with estrogen receptor 1 gene (*ESR1*) mutations.

About ORSERDU (elacestrant)

The U.S. Food and Drug Administration (FDA) has approved ORSERDU for the treatment of postmenopausal women or adult men, with ER+, HER2-, ESR1-mutated, advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy. The Marketing Authorization Application (MAA) is currently under review by the European Medicines Agency (EMA).

Elacestrant is also being investigated in several clinical trials in metastatic breast cancer disease, alone or in combination with other therapies: ELEVATE ([NCT05563220](#)); ELECTRA ([NCT05386108](#)); ELONA ([NCT05618613](#)); ELCIN ([NCT05596409](#)). Elacestrant is also planned to be evaluated in early breast cancer disease.

Full prescribing information can be found at www.orserdu.com

Important Safety Information

Warning and Precautions

Dyslipidemia: Hypercholesterolemia and hypertriglyceridemia occurred in patients taking ORSERDU at an incidence of 30% and 27%, respectively. The incidence of Grade 3 and 4 hypercholesterolemia and hypertriglyceridemia were 0.9% and 2.2%, respectively. Monitor lipid profile prior to starting and periodically while taking ORSERDU.

Embryo-Fetal Toxicity: Based on findings in animals and its mechanism of action, ORSERDU can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ORSERDU and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ORSERDU and for 1 week after the final dose.

Adverse Reactions

Serious adverse reactions occurred in 12% of patients who received ORSERDU. Serious adverse reactions in >1% of patients who received ORSERDU were musculoskeletal pain (1.7%) and nausea (1.3%). Fatal adverse reactions occurred in 1.7% of patients who received ORSERDU, including cardiac arrest, septic shock, diverticulitis, and unknown cause (one patient each).

The most common adverse reactions ($\geq 10\%$), including laboratory abnormalities, of ORSERDU were musculoskeletal pain (41%), nausea (35%), increased cholesterol (30%), increased AST (29%), increased triglycerides (27%), fatigue (26%), decreased hemoglobin (26%), vomiting (19%), increased ALT (17%), decreased sodium (16%), increased creatinine (16%), decreased appetite (15%), diarrhea (13%), headache (12%), constipation (12%), abdominal pain (11%), hot flush (11%), and dyspepsia (10%).

Drug interactions

Concomitant use with CYP3A4 Inducers and/or inhibitors: Avoid concomitant use of strong or moderate CYP3A4 inhibitors with ORSERDU. Avoid concomitant use of strong or moderate CYP3A4 inducers with ORSERDU.

Use in specific populations

Lactation: Advise lactating women to not breastfeed during treatment with ORSERDU and for 1 week after the last dose.

Hepatic Impairment: Avoid use of ORSERDU in patients with severe hepatic impairment (Child-Pugh C). Reduce the dose of ORSERDU in patients with moderate hepatic impairment (Child-Pugh B).

The safety and effectiveness of ORSERDU in pediatric patients have not been established.

To report SUSPECTED ADVERSE REACTIONS, contact Stemline Therapeutics, Inc. at 1-877-332-7961 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Indication

ORSERDU (elacestrant), 345 mg tablets, is indicated 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.

For more information, please see the full Prescribing Information for ORSERDU [here](#)

About The Menarini Group

The Menarini Group is a leading international pharmaceutical and diagnostics company, with a turnover of over \$4 billion and over 17,000 employees. Menarini is focused on therapeutic areas with high unmet needs with products for cardiology, oncology, pneumology, gastroenterology, infectious diseases, diabetology, inflammation, and analgesia. With 18 production sites and 9 Research and Development centers, Menarini's products are available in 140 countries worldwide. For further information, please visit www.menarini.com.

About Stemline

Stemline Therapeutics, a wholly-owned subsidiary of the Menarini Group, is a commercial-stage biopharmaceutical company focused on the development and commercialization of novel oncology therapeutics. Stemline commercializes Elzonris[®], a novel targeted treatment directed to CD123 for patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), a rare hematologic cancer, in the United States and Europe, the only approved treatment for BPDCN in the US and EU to date. Stemline also commercializes Nexpovio[®] in Europe, an XPO1 inhibitor for multiple myeloma originating from a licensing deal with Karyopharm. Stemline has an extensive clinical pipeline of small molecules and biologics in various stages of development for a host of solid and hematologic cancers.

Media Relations:

The Menarini Group

Stemline Therapeutics, Inc.

Valeria Speroni Cardi
Email: pressoffice@menarini.com

Cheya Pope
Email: cpepe@stemline.com