U.S. FDA approves Inluriyo (imlunestrant) for adults with ER+, HER2-, ESR1-mutated advanced or metastatic breast cancer

September 25, 2025

An estimated 50% of patients with ER+, HER2– metastatic breast cancer will develop an ESR1 *mutation during or after exposure to an aromatase inhibitor*

In the Phase 3 EMBER-3 trial, Inluriyo monotherapy reduced the risk of progression or death by 38% versus endocrine therapy among patients with ESR1*-mutated MBC*

INDIANAPOLIS, Sept. 25, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the U.S. Food and Drug Administration (FDA) has approved Inluriyo (imlunestrant, 200 mg tablets), an oral estrogen receptor antagonist, for the treatment of adults with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2–), *ESR1*-mutated advanced or metastatic breast cancer (MBC) whose disease progressed after at least one line of endocrine therapy (ET). In the Phase 3 EMBER-3 trial, Inluriyo reduced the risk of progression or death by 38% versus ET. Among patients with *ESR1*-mutated MBC, Inluriyo significantly improved progression-free survival (PFS) versus fulvestrant or exemestane, with a median PFS of 5.5 months vs 3.8 months (HR=0.62 [95% CI: 0.46-0.82]); p-value=0.0008.

Inluriyo is a treatment for ER+, HER2–, *ESR1*-mutated MBC. Some breast cancers develop *ESR1* mutations that can cause estrogen receptors to become overactive and drive cancer growth. Inluriyo binds, blocks, and facilitates the degradation of these receptors, helping to slow disease progression. Its once-daily dosing provides patients with an oral treatment option.

"This therapy reflects our commitment to developing treatments that improve outcomes for people with breast cancer and represents an important step toward advancing innovative, all-oral treatment approaches," said Jacob Van Naarden, executive vice president and president of Lilly Oncology. "We are deeply grateful to the patients, investigators, Lilly team members and clinical care teams who made this advancement possible. This therapy has the potential to make the treatment journey more manageable for those living with breast cancer."

The Inluriyo label contains a warning and precaution for embryo-fetal toxicity. See Important Safety Information below and full Prescribing Information for additional information.

The FDA approval is based on the results of the EMBER-3 trial in the patient population harboring *ESR1*-mutated MBC (n=256). Patients received Inluriyo or ET as first-line treatment for MBC following recurrence on adjuvant aromatase inhibitor (AI), +/- prior CDK4/6 inhibitor (21%), or as second-line treatment for MBC following progression on AI, +/- prior CDK4/6 inhibitor (79%).

"This represents an important advancement for patients with *ESR1*-mutated MBC, a mutation found in nearly half of patients who have taken hormone therapies, often contributing to treatment resistance," said Komal Jhaveri, M.D., FACP, FASCO, section head of Endocrine Therapy Research and clinical director of Early Drug Development at Memorial Sloan Kettering Cancer Center, and a principal investigator of EMBER-3. "With its demonstrated efficacy, tolerability profile and oral administration, this therapy provides a meaningful alternative treatment option for this patient population."

In EMBER-3, the majority of adverse events (AEs) with Inluriyo were low grade (Grade 1-2) and the most common adverse reactions (≥10%), including laboratory abnormalities, were hemoglobin decreased, musculoskeletal pain, calcium decreased, neutrophils decreased, AST increased, fatigue, diarrhea, ALT increased, triglycerides increased, nausea, platelets decreased, constipation, cholesterol increased, and abdominal pain. In the study, 4.6% of patients permanently discontinued treatment due to AEs. Dose reductions and dose interruptions occurred in 2.4% and 10% of patients, respectively.

"The approval of Inluriyo expands the metastatic breast cancer treatment landscape for patients who test positive for the *ESR1* mutation," said Jean Sachs, CEO, Living Beyond Breast Cancer. "Eligible patients will now have access to an additional treatment option, offering them the potential for flexibility in their daily lives and disease management, and—above all—renewed hope for the future.'

Inluriyo is also being studied in the ongoing Phase 3 EMBER-4 trial in the adjuvant setting for people with ER+, HER2– early breast cancer (EBC) at increased risk of recurrence, which is enrolling approximately 8,000 patients worldwide.

Inluriyo is expected to be available in the United States in the coming weeks.

See Important Safety Information below and full Prescribing Information for additional information.

About EMBER-3
EMBER-3 is a Phase 3, randomized, open-label study of Inluriyo, investigator's choice of endocrine therapy, and Inluriyo in combination with abemaciclib in patients with ER+, HER2– locally advanced or metastatic breast cancer whose disease has recurred or progressed during or following an aromatase inhibitor (AI) therapy with or without a CDK 4/6 inhibitor. The trial enrolled 874 adult patients, 32% of which enrolled from the adjuvant setting into first-line treatment of MBC and 64% as second-line treatment following progression on initial therapy for MBC. Enrolled trial participants were randomized between Inluriyo, investigator's choice of fulvestrant or exemestane, or Inluriyo plus abemaciclib. More information on the EMBER-3 study can be found on clinicaltrials.gov.

About Inluriyo (imlunestrant)
Inluriyo (imlunestrant) (pronounced en-loo-ree-yoh) is an oral estrogen receptor antagonist that delivers continuous ER inhibition, including in

ESR1-mutant cancers. The estrogen receptor (ER) is the key therapeutic target for patients with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2–) breast cancer. Inluriyo is a U.S. FDA approved oral prescription medicine, 200 mg tablets taken as a once-daily dose of 400 mg taken on an empty stomach, at least 2 hours before food or 1 hour after food. Inluriyo is also currently being studied in combination with abemaciclib for advanced breast cancer and as an adjuvant treatment in early breast cancer, including: NCT04975308, NCT05514054 and NCT04188548.

Important Safety Information for Inluriyo (imlunestrant)

Warnings and Precautions — Embryo-Fetal Toxicity

Based on findings in animals and its mechanism of action, Inluriyo can cause fetal harm when administered to a pregnant woman. In an animal reproduction study, oral administration of imlunestrant to pregnant rats during the period of organogenesis led to embryo-fetal mortality and structural abnormalities at maternal exposures that were below the human exposure at the recommended dose based on area under the curve (AUC). Avoid the use of imlunestrant in pregnant women. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Inluriyo and for 1 week after the last dose.

Serious and Fatal Adverse Reactions

Serious adverse reactions occurred in 10% of patients who received Inluriyo. Serious adverse reactions in >1% of patients included pleural effusion (1.2%). **Fatal adverse reactions** occurred in 1.8% of patients who received Inluriyo, including cardiac arrest, acute myocardial infarction, right ventricular failure, hypovolemic shock, and upper gastrointestinal hemorrhage (each 0.3%).

Most Common Adverse Reactions

The **most common adverse reactions** (incidence ≥10%), including laboratory abnormalities, in patients who received Inluriyo were: hemoglobin decreased (30%), musculoskeletal pain (30%), calcium decreased (26%), neutrophils decreased (26%), AST increased (25%), fatigue (23%), diarrhea (22%), ALT increased (21%), triglycerides increased (21%), nausea (17%), platelets decreased (16%), constipation (10%), cholesterol increased (10%), and abdominal pain (10%).

Drug Interactions

Imlunestrant is a CYP3A substrate. Avoid concomitant use of Inluriyo with **strong CYP3A inhibitors**. If concomitant use cannot be avoided, reduce the dosage of Inluriyo. Avoid concomitant use of Inluriyo with **strong CYP3A inducers**. If concomitant use cannot be avoided, increase the dosage of Inluriyo.

Imlunestrant inhibits both **P-gp** and **BCRP**. Avoid concomitant use unless otherwise recommended in the Prescribing Information for P-gp or BCRP substrates where minimal concentration changes may lead to serious adverse reactions.

Use in Specific Populations — Lactation

Because of the potential for serious adverse reactions in the breastfed child, **advise lactating women to not breastfeed during treatment with Inluriyo and for 1 week after the last dose**.

Use in Specific Populations — Hepatic Impairment

Reduce the dose of Inluriyo for patients with moderate (**Child-Pugh B**) or severe (**Child-Pugh C**) hepatic impairment. No dosage adjustment is recommended for patients with mild hepatic impairment (**Child-Pugh A**).

Inluriyo (imlunestrant) is available as 200 mg tablets.

Please click to access Prescribing Information for Inluriyo.

IN HCP ISI M APP

About Metastatic/Advanced Breast Cancer
Metastatic/advanced breast cancer (MBC) is a cancer that has spread from the breast tissue to other parts of the body. Locally advanced breast cancer means the cancer has grown outside the organ where it started but has not yet spread to other parts of the body.[1] Of all high risk early-stage breast cancer cases diagnosed in the U.S., approximately 30% will become metastatic[2] and an estimated 6-10% of all new breast cancer cases are initially diagnosed as being metastatic.[3] Survival is lower among women with a more advanced stage of disease at diagnosis: five-year relative survival is 99% for localized disease, 86% for regional/locally advanced disease, and 30% for metastatic/advanced disease.[4] Other factors, such as tumor size, also impact five-year survival estimates.[4]

About Breast Cancer
Breast cancer is the second most commonly diagnosed cancer worldwide (following lung cancer), according to GLOBOCAN. The estimated 2.3 million new cases indicate that close to 1 in every 4 cancers diagnosed in 2022 is breast cancer. With approximately 666,000 deaths in 2022, breast cancer is the fourth-leading cause of cancer death worldwide.[5] In the U.S., it is estimated that there will be more than 310,000 new cases of breast cancer diagnosed in 2024. Breast cancer is the second leading cause of cancer death in women in the U.S.[6]

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable

diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram, and LinkedIn. P-LLY

PP-IN-US-0139 09/2025

MSK Disclosure: Dr. Jhaveri has financial interests related to Eli Lilly and Company.

Trademarks and Trade Names
All trademarks or trade names referred to in this press release are the property of the company, or, to the extent trademarks or trade names belonging to other companies are referenced in this press release, the property of their respective owners. Solely for convenience, the trademarks and trade names in this press release are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that the company or, to the extent applicable, their respective owners will not assert, to the fullest extent under applicable law, the company's or their rights thereto. We do not intend the use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Inluriyo as a treatment for people with certain types of breast cancer and other conditions and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that Inluriyo will receive additional regulatory approvals, or that Inluriyo will be commercially successful. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

Endnotes & References
1. André F, et al. Ann Oncol. 2021;32(2):208-217.

2. O'Shaughnessy J. Extending survival with chemotherapy in metastatic breast cancer. Oncologist. 2005;10 Suppl 3:20-9. PMID: 16368868 DOI: 10.1634/theoncologist.10-90003-20.

3. Metastatic Breast Cancer Network. 13 Facts about Metastatic Breast Cancer. http://www.mbcn.org/13-facts-about-metastatic-breast-cancer/. Accessed July 9, 2024.

4. American Cancer Society. Breast Cancer Facts & Figures 2022-2024. Atlanta: American Cancer Society, Inc. 2022. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2022-2024-breast-cancer-fact-figures-acs.pdf. Accessed July 9, 2024.

5. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263.

6. American Cancer Society. Cancer Statistics Center. http://cancerstatisticscenter.cancer.org. Accessed July 9, 2024.

Refer to: Michelle Webb; michelle.webb@lilly.com; 463-206-4463 (Media)
Michael Czapar; czapar_michael_c_@lilly.com; 317-617-0983 (Investors)

View original content to download multimedia:https://www.prnewswire.com/news-releases/us-fda-approves-inluriyo-imlunestrant-for-adults-with-er-her2-esr1-mutated-advanced-or-metastatic-breast-cancer-302567490.html

SOURCE Eli Lilly and Company