

TUKYSA Added to First-Line Maintenance Therapy Extends Median Progression-Free Survival by Over 8 Months in Patients with HER2+ Metastatic Breast Cancer

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- *TUKYSA, trastuzumab, and pertuzumab reduced the risk of disease progression or death by 36% compared to trastuzumab and pertuzumab alone in Phase 3 HER2CLIMB-05 study*
- *The combination demonstrated a manageable safety profile as a first-line maintenance therapy*

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced detailed results from the Phase 3 HER2CLIMB-05 trial of the tyrosine kinase inhibitor TUKYSA[®] (tucatinib) as part of an investigational first-line maintenance treatment combination, following chemotherapy-based induction, in patients with human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (MBC). The primary endpoint analysis showed a 35.9% reduction in the risk of disease progression or death among patients treated with TUKYSA, trastuzumab, and pertuzumab compared to those treated with placebo, trastuzumab, and pertuzumab, as assessed by the investigator (hazard ratio [HR] of 0.641, 95% confidence interval (CI): 0.514-0.799; 2-sided $p < 0.0001$). These findings were published today in the *Journal of Clinical Oncology*, shared in an oral presentation at the 48th San Antonio Breast Cancer Symposium (SABCS), and highlighted in the SABCS official press program.

In HER2CLIMB-05, the median progression-free survival (PFS) was 24.9 months (95% CI: 21.3-not reached) in the TUKYSA arm and 16.3 months (95% CI: 12.6-18.7) in the placebo arm, representing an extension in median PFS of 8.6 months. A PFS benefit was observed across all prespecified patient subgroups, including de novo or recurrent diagnosis, hormone receptor (HR)-positive or HR-negative disease, and with or without the presence or history of brain metastases at baseline. The key secondary endpoint of overall survival was not mature at the time of the analysis (20% of the required events have occurred to date) but showed a numerical trend for improvement with TUKYSA.

“Most patients with HER2-positive metastatic breast cancer face disease progression within two years of starting first-line treatment, often requiring a transition to chemotherapy,” said Erika Hamilton, M.D., principal investigator of HER2CLIMB-05 and Director of Breast Cancer Research for Sarah Cannon Research Institute (SCRI). “These results demonstrate that adding tucatinib to first-line maintenance therapy extends the time patients live without their disease progressing, while maintaining a manageable safety profile, suggesting a promising new potential approach that could advance the current standard of care for HER2-positive disease.”

TUKYSA in combination with trastuzumab and pertuzumab demonstrated a safety profile generally consistent with the established safety profiles of each individual therapy, except for a higher rate of asymptomatic Grade 3 liver transaminases, which were typically manageable and reversible with TUKYSA dose modifications and/or discontinuations. The most common adverse events observed in the TUKYSA combination arm were diarrhea,

hepatic events, and nausea.

“TUKYSA has become a trusted standard of care for patients with later-line HER2-positive metastatic breast cancer, and the results from HER2CLIMB-05 support its potential use as part of a chemotherapy-free, front-line maintenance strategy,” said Jeff Legos, Chief Oncology Officer, Pfizer. “At Pfizer, we are committed to advancing treatment options that meaningfully improve the lives of people with metastatic breast cancer, and we are proud to share these promising results for patients and their families.”

TUKYSA is not currently approved for first-line treatment. The results from HER2CLIMB-05 will be discussed with regulatory authorities. Since its initial approval in 2020, TUKYSA in combination with trastuzumab and capecitabine has become a standard of care for HER2+ MBC patients in the third-line setting. TUKYSA is currently approved in more than 50 countries; in the United States, TUKYSA is approved for use in combination with trastuzumab and capecitabine for adult patients with advanced unresectable or metastatic HER2+ breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.

About HER2-Positive Metastatic Breast Cancer (MBC)

HER2 is overexpressed in up to 15-20% of breast cancers and is associated with poor prognosis, with an estimated five-year survival rate for HER2+ MBC of 41-47%, depending on HR status.¹⁻³ First-line standard-of-care maintenance treatment has remained unchanged since 2012, and the majority of patients with HER2+ MBC face disease progression within two years of initiating therapy.⁴ Until recently, there have been limited advancements for these patients.

About the HER2CLIMB-05 Trial

HER2CLIMB-05 is a randomized, double blind, placebo-controlled, pivotal Phase 3 study evaluating the efficacy and safety of TUKYSA® (tucatinib) compared to placebo, both in combination with trastuzumab and pertuzumab, as maintenance therapy for patients with HER2+ MBC following induction therapy in the first-line setting.

Trial participants who completed induction therapy of trastuzumab, pertuzumab, and a taxane, with no evidence of progression were randomized to receive TUKYSA in combination with trastuzumab plus pertuzumab (n=326), or placebo in combination with trastuzumab plus pertuzumab (n=328). The primary endpoint is progression-free survival (PFS) as assessed by the investigator. Key secondary endpoints include overall survival.

About TUKYSA® (tucatinib)

TUKYSA (tucatinib) is an orally administered tyrosine kinase inhibitor of HER2. TUKYSA is approved in combination with trastuzumab and capecitabine to treat adults with HER2-positive advanced unresectable or metastatic breast cancer, including patients with brain metastases who have received one or more prior anti-HER2 breast cancer treatments in the metastatic setting.

The full U.S. Prescribing Information for TUKYSA can be found [here](#).

IMPORTANT TUKYSA® (tucatinib) SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

Warning and Precautions:

- **Diarrhea:** TUKYSA can cause severe diarrhea including dehydration, hypotension, acute kidney injury, and death. If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic

tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, then dose reduce or permanently discontinue TUKYSA.

In HER2CLIMB, 81% of patients who received TUKYSA experienced diarrhea, including 0.5% with Grade 4 diarrhea and 12% with Grade 3 diarrhea. The median time to onset of the first episode of diarrhea was 12 days and the median time to resolution was 8 days. Diarrhea led to dose reductions of TUKYSA in 6% of patients and discontinuation of TUKYSA in 1% of patients. Prophylactic use of antidiarrheal treatment was not required on HER2CLIMB.

- **Hepatotoxicity:** TUKYSA can cause severe hepatotoxicity. Monitor ALT, AST, and bilirubin prior to starting TUKYSA, every 3 weeks during treatment, and as clinically indicated. Based on the severity of hepatotoxicity, interrupt dose, then dose reduce or permanently discontinue TUKYSA.

In HER2CLIMB, 8% of patients who received TUKYSA had an ALT increase $> 5 \times \text{ULN}$, 6% had an AST increase $> 5 \times \text{ULN}$, and 1.5% had a bilirubin increase $> 3 \times \text{ULN}$ (Grade ?3). Hepatotoxicity led to dose reduction of TUKYSA in 8% of patients and discontinuation of TUKYSA in 1.5% of patients.

- **Embryo-fetal Toxicity:** TUKYSA can cause fetal harm. 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 TUKYSA and for 1 week after the last dose.

Adverse Reactions:

In HER2CLIMB, serious adverse reactions occurred in 26% of patients who received TUKYSA. Serious adverse reactions in ? 2% of patients who received TUKYSA were diarrhea (4%), vomiting (2.5%), nausea (2%), abdominal pain (2%), and seizure (2%). Fatal adverse reactions occurred in 2% of patients who received TUKYSA including sudden death, sepsis, dehydration, and cardiogenic shock. Adverse reactions leading to treatment discontinuation occurred in 6% of patients who received TUKYSA. Adverse reactions leading to treatment discontinuation of TUKYSA in ?1% of patients were hepatotoxicity (1.5%) and diarrhea (1%). Adverse reactions leading to dose reduction occurred in 21% of patients who received TUKYSA. Adverse reactions leading to dose reduction of TUKYSA in ?2% of patients were hepatotoxicity (8%) and diarrhea (6%). The most common adverse reactions in patients who received TUKYSA (?20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, hepatotoxicity, vomiting, stomatitis, decreased appetite, anemia, and rash.

Laboratory Abnormalities:

In HER2CLIMB, Grade ?3 laboratory abnormalities reported in ?5% of patients who received TUKYSA were decreased phosphate, increased ALT, decreased potassium, and increased AST. The mean increase in serum creatinine was 32% within the first 21 days of treatment with TUKYSA. The serum creatinine increases persisted throughout treatment and were reversible upon treatment completion. Consider alternative markers of renal function if persistent elevations in serum creatinine are observed.

About Pfizer Oncology

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and multispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues

work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on X at [@Pfizer](https://twitter.com/Pfizer) and [@Pfizer News](https://twitter.com/PfizerNews), [LinkedIn](https://www.linkedin.com/company/pfizer), [YouTube](https://www.youtube.com/channel/UCv3p00Dz3033333333333333) and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

Disclosure Notice

The information contained in this release is as of December 10, 2025. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer Oncology, TUKYSA® (tucatinib) and results from the Phase 3 HER2CLIMB-05 trial of TUKYSA as part of an investigational first-line maintenance combination therapy in patients with human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (MBC), including their potential benefits and plans to discuss the HER2CLIMB-05 results with regulatory authorities, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of TUKYSA; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; whether the HER2CLIMB-05 trial will meet the secondary endpoint of overall survival; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from the clinical studies; whether and when drug applications for TUKYSA may be filed in particular jurisdictions for any potential indications; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be pending or filed for TUKYSA, which will depend on a myriad of factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether TUKYSA for any potential indication will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety, and/or other matters that could affect the availability or commercial potential of TUKYSA; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

References:

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