Lilly presents first clinical data for its investigational, next-generation FRα targeting ADC in platinum-resistant ovarian cancer at the 2025 ASCO Annual Meeting

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INDIANAPOLIS, June 2, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced new Phase 1 data showing that its folate receptor alpha (FRα) antibody-drug conjugate (ADC) (LY4170156) demonstrated an encouraging safety profile and anti-tumor activity across dose and FRα expression levels in women with heavily pre-treated platinum-resistant ovarian cancer, including patients previously treated with mirvetuximab soravtansine. A preliminary overall objective response rate (ORR) of 55% was observed at the potential recommended Phase 2 dose of 4 mg/kg. Lilly's FRα targeting ADC is composed of an Fc-silent, FRα specific humanized monoclonal antibody linked to exatecan, a topoisomerase I inhibitor, via a proprietary cleavable polysarcosine linker. These data will be presented today in a poster presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting.

"ADCs have begun to change the treatment paradigm for some women with ovarian cancer, but a large proportion of patients still have a significant need for new therapies that improve outcomes regardless of FRα expression level," said Isabelle Ray-Coquard, M.D., Ph.D., president of the ENGOT (European Network of Gynecological Oncology Trial) group, medical oncologist at the Centre Léon Bérard Lyon France and principal investigator for the trial. "These initial data show activity across all doses and levels of FRα expression, including in patients previously treated with a FRα targeting treatment. Taken together with the emerging safety and tolerability profile, these data demonstrate early potential to meaningfully improve outcomes for women living with advanced ovarian cancer."

As of the March 9, 2025 data cutoff, the study enrolled 95 participants with high-grade serous ovarian cancer across four dose levels (2 - 6 mg/kg). Patients received a median of five prior systemic regimens (range 1-10), and 15% were previously treated with mirvetuximab soravtansine. Among the 95 patients, 51% had tumors with FRα expression less than 75%, 34% had FRα expression of 75% or higher, and 16% had expression results pending. Key endpoints were safety, pharmacokinetics, and anti-tumor activity per RECIST v1.1.

Efficacy results demonstrate responses at all dose levels, across all FRα expression levels, including in patients who progressed on prior mirvetuximab soravtansine. In the 58 efficacy-evaluable patients (37 patients remain ongoing prior to first response assessment and were therefore not yet efficacy-evaluable at the time of the data cutoff), the ORR was 45% (26/58 patients), and the disease control rate was 74% (43/58). At the potential recommended Phase 2 dose of 4 mg/kg, the ORR was 55% (11/20 patients). The most common treatment-emergent adverse events across all dose levels included nausea (64%), anemia (40%), fatigue (32%), vomiting (32%), diarrhea (28%), and neutropenia (27%). Treatment-emergent neuropathy and ocular toxicity has not been observed to date. No maximum tolerated dose has been established.

"We are excited to share these first clinical data for our FRα targeting ADC, demonstrating a promising tolerability and efficacy profile across all FRα expression levels," said David Hyman, M.D., Chief Medical Officer, Lilly. "Based on these results, we believe there is the potential to significantly expand the number of ovarian cancer patients who could benefit from a FRα ADC. We are now focused on rapidly advancing this potential new medicine into registrational Phase 3 clinical trials."

For more information on Lilly's oncology pipeline click here.

About LY4170156
LY4170156 is an investigational, next-generation antibody-drug conjugate (ADC) targeting folate receptor alpha (FRα). FRα is a cell-surface glycoprotein encoded by the gene *FOLR1* that binds to the essential nutrients folic acid and reduced folates, bringing them into cells to facilitate cell division and growth.[1,2] FRα is overexpressed in many solid tumors such as ovarian, non-small cell lung, and colorectal cancers.[1,3,4]

LY4170156 was designed to target FRα across expression levels with an improved therapeutic index. LY4170156 is composed of an Fc-silent, FRα specific humanized monoclonal antibody linked to exatecan, a topoisomerase I inhibitor, via a proprietary cleavable polysarcosine linker (PSARlink™). PSARlink's unique structure "masks" the cytotoxic molecules enabling them to stay in the body longer, providing the potential to broaden the therapeutic index of ADCs. LY4170156 is currently being studied in patients with ovarian cancer as well as other FRα-expressing solid tumors, NCT06400472.

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

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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 preclinical data for an antibody-drug conjugate targeting folate receptor alpha 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 any of these therapies will prove to be a safe and effective treatment or receive regulatory approval, or that Lilly will execute its strategy as expected. 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.

1. Bax, Heather J et al. "Folate receptor alpha in ovarian cancer tissue and patient serum is associated with disease burden and treatment outcomes." *British journal of cancer* vol. 128,2 (2023): 342-353. doi:10.1038/s41416-022-02031-x Bax HJ, et al. *Br J Cancer*. 2023;128(2):342-353.
2. Scaranti, Mariana et al. "Exploiting the folate receptor α in oncology." *Nature reviews. Clinical oncology* vol. 17,6 (2020): 349-359. doi:10.1038/s41571-020-0339-5.
3. Kalli, Kimberly R et al. "Folate receptor alpha as a tumor target in epithelial ovarian cancer." *Gynecologic oncology* vol. 108,3 (2008): 619-26. doi:10.1016/j.ygyno.2007.11.020.
4. Viricel W, et al. *Cancer Res*. 2023;83(suppl 7):1544.

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