LY4170156

FRα ANTIBODY-DRUG CONJUGATE

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyloxooncologypipeline.com.

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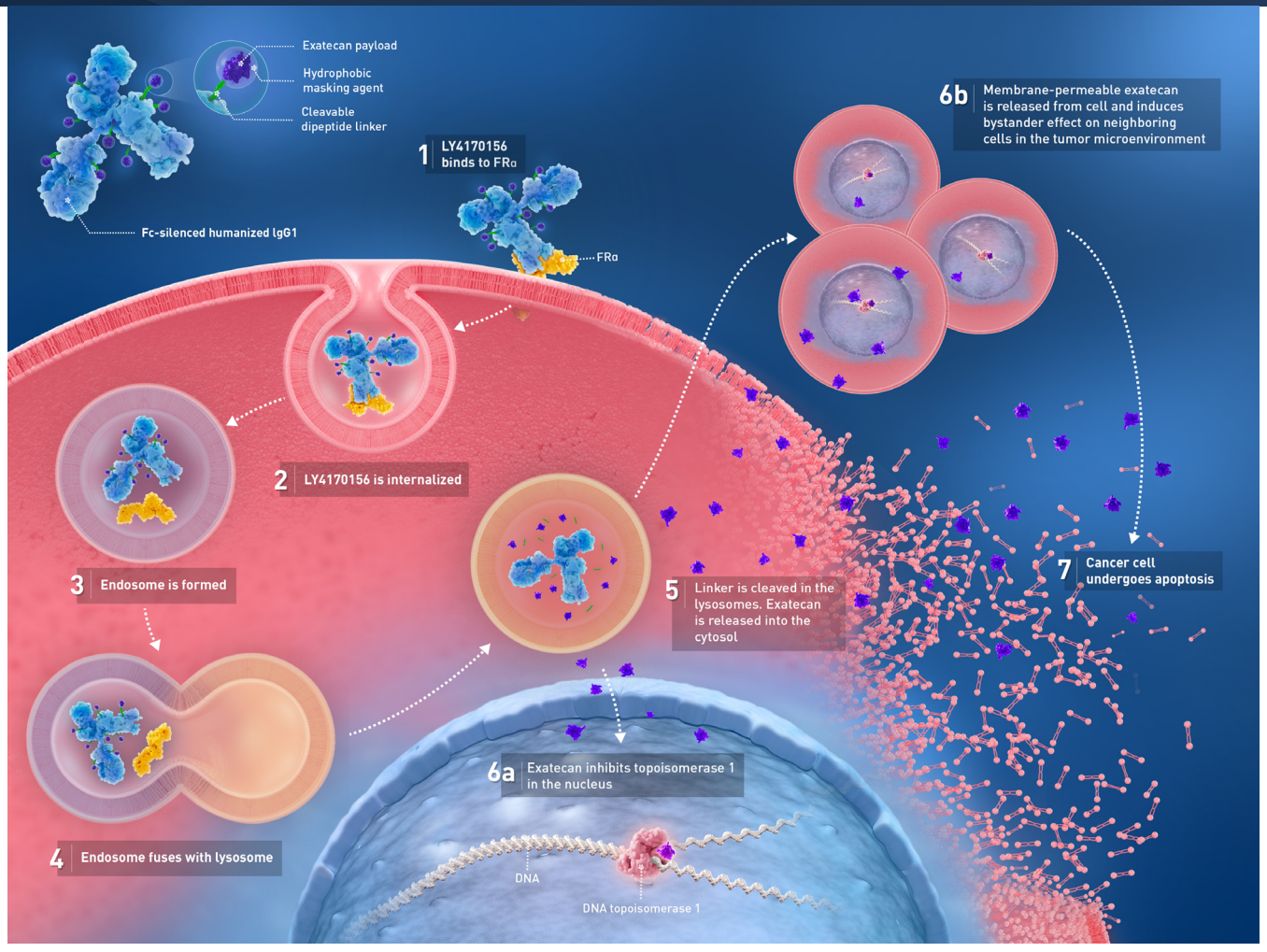
LY4170156 | MECHANISM OF ACTION[1-4]



References: 1. Bax HJ, et al. *Br J Cancer*. 2023 Jan;128(2):342-353. **2.** Scaranti M, et al. *Nat Rev Clin Oncol*. 2020 Jun;17(6):349-359. **3.** Kalli KR, et al. *Gynecol Oncol*. 2008 Mar;108(3):619-26. **4.** Viricel W, et al. *Cancer Res*. 2023 Apr; 83(7_Supplement):1544.

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TARGET

Folate receptor alpha (FRα) is a cell-surface glycoprotein encoded by the gene *FOLR1*. It binds to folic acid and reduced folates with high affinity.[1,2] Upon binding, the receptor-ligand complex is internalized via potocytosis and fused with a lysosome, releasing the folate for use in reactions.[2] The expression of FRα in non-malignant tissues is limited, whereas it is overexpressed in many solid tumors such as ovarian, non-small-cell lung, and colorectal cancers, making the receptor an attractive therapeutic target for these indications.[1,3]

MOLECULE

LY4170156 is an FRα-targeting antibody-drug conjugate (ADC) composed of an Fc-silenced, humanized IgG1 monoclonal antibody, a polysarcosine hydrophobicity masking agent with a dipeptide cleavable linker, and the topoisomerase I inhibitor payload exatecan. It has a drug-antibody ratio (DAR) of 8. In pre-clinical models, LY4170156 has shown activity against a range of FRα-expressing tumors including low and moderate FRα-expressing ovarian tumors, as well as other solid tumors.[3]

CLINICAL DEVELOPMENT

LY4170156 is being studied in ovarian and endometrial cancers, as well as other FRα-expressing solid tumors, in a Phase 1 study.[4]

References: 1. Bax HJ, et al. *Br J Cancer*. 2023 Jan;128(2):342-353. **2.** Scaranti M, et al. *Nat Rev Clin Oncol*. 2020 Jun;17(6):349-359. **3.** Viricel W, et al. Poster presented at: *AACR 2023*. Abstract 1544. **4.** https://www.clinicaltrials.gov/study/NCT06400472 (Accessed May 09, 2024).

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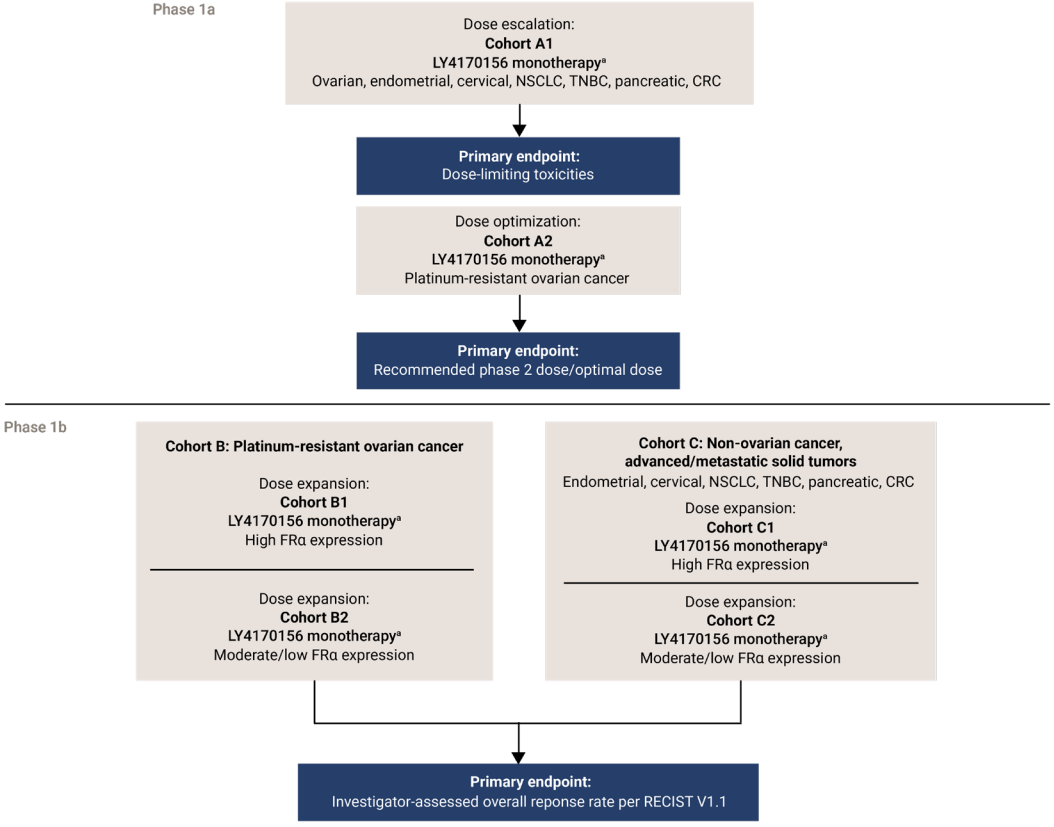
NCT06400472

A First-in-Human, Phase 1a/1b Trial to Assess the Safety, Tolerability, and Preliminary Efficacy of LY4170156, an Antibody-Drug Conjugate Targeting Folate Receptor α-Expressing Tumor Cells, in Participants with Selected Advanced Solid Tumors



[a]LY4170156 is administered IV.

Abbreviations: CRC=Colorectal Cancer; FRα=Folate Receptor Alpha; IV=Intravenous Infusion; NSCLC=Non-small-Cell Lung Cancer; RECIST V1.1=Response Evaluation Criteria in Solid Tumors Version 1.1; TNBC=Triple-Negative Breast Cancer.

Please visit clinicaltrials.gov for more information on this clinical trial [NCT06400472].

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KEY INCLUSION CRITERIA

- Participants aged ≥18 years with historic diagnosis of locally advanced or metastatic solid tumor malignancy as defined below for each cohort:
  - Cohort A1 (Dose Escalation): Ovarian cancer[a], endometrial cancer, cervical cancer, non-small-cell lung cancer (NSCLC), triple-negative breast cancer (TNBC), pancreatic cancer, or colorectal cancer (CRC)
  - Cohort A2 (Dose Optimization), Cohort B1 and B2 (Dose Expansion): Ovarian cancer[a] that is resistant to prior platinum treatment.[b] Individuals with platinum-refractory disease[c] are not eligible
  - Cohort C1 and C2 (Dose Expansion): Endometrial cancer, cervical cancer, NSCLC, TNBC, pancreatic cancer or CRC

[a]Includes epithelial ovarian, primary peritoneal, and fallopian tube; [b]Recurrence or progression within 6 months of last platinum dose; [c]Progression on front-line platinum-based chemotherapy or within 3 months of completing front-line treatment.

KEY EXCLUSION CRITERIA

- Known or suspected uncontrolled central nervous system (CNS) metastases
- History of carcinomatous meningitis
- Any serious unresolved toxicities from prior therapy
- History of pneumonitis/ interstitial lung disease
- Has significant cardiovascular disease
- Has prolongation of the corrected QT interval by Fridericia (QTcF) >470 ms
- Has an active uncontrolled systemic bacterial, viral, fungal, or parasitic infection
- Evidence of corneal keratopathy or history of corneal transplant
- Individuals who are pregnant, breastfeeding or plan to breastfeed during study or within 30 days of last dose of study intervention

Please visit clinicaltrials.gov for more information on this clinical trial [NCT06400472].

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Pipeline information is current through May 15, 2024.

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