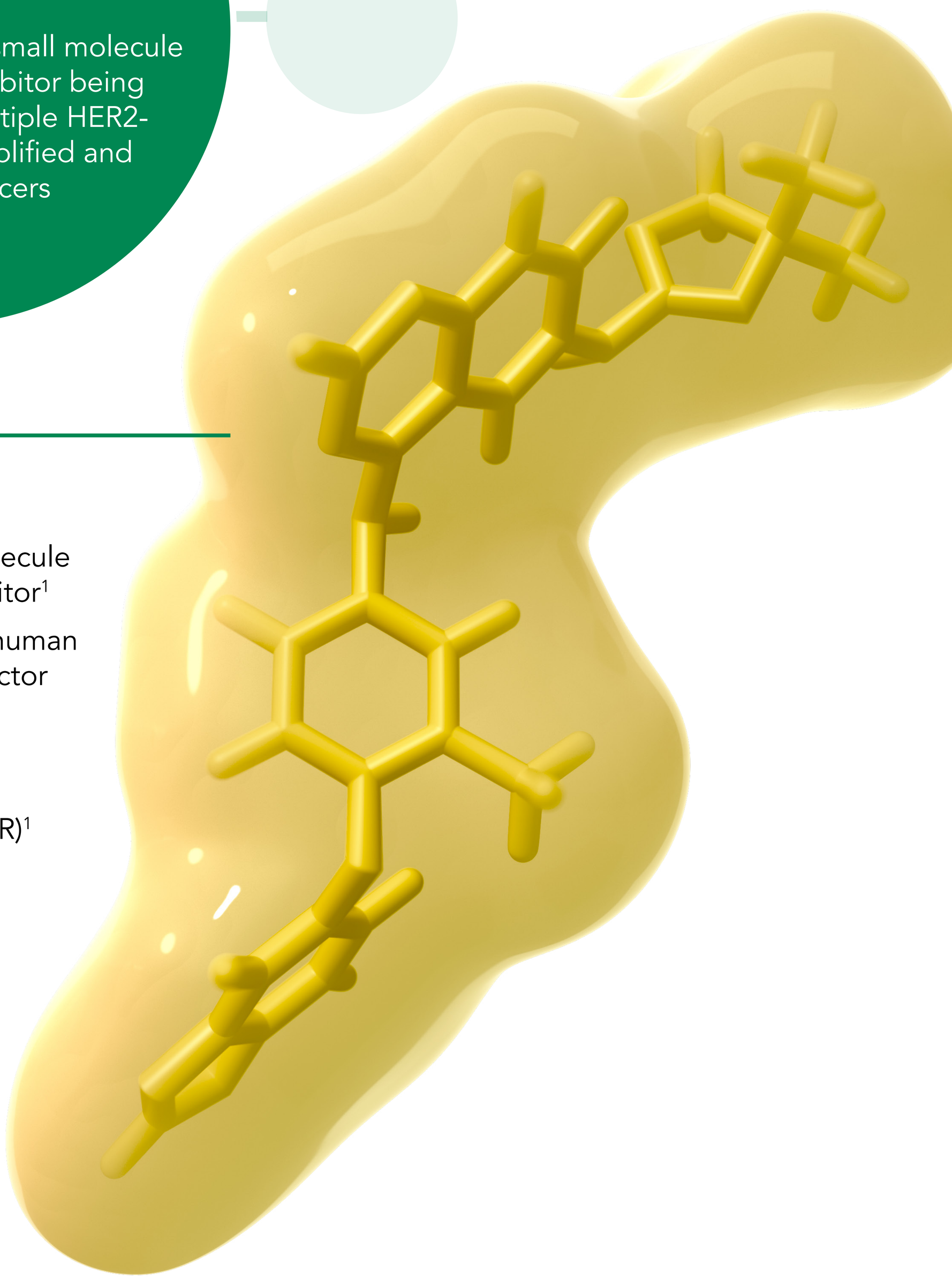
TUCATINIB

A highly selective small molecule tyrosine kinase inhibitor being investigated in multiple HER2-overexpressed/amplified and HER2-mutated cancers



Key Features

- Orally bioavailable, reversible, small-molecule tyrosine kinase inhibitor[1]
- Highly selective for human epidermal growth factor receptor 2 (HER2)[1]
- Minimal inhibition of epidermal growth factor receptor (EGFR)[1]

Target: HER2

- A tyrosine kinase receptor[2]
- Overexpressed or mutated in multiple cancers (breast, colorectal, ovarian, lung, gastroesophageal, and bladder)[3]

Proposed Mechanism of Action[1,4-7,a]

- Binds to kinase domain of HER2
- Inhibits activation of MAPK and PI3K signaling pathways
- Decreases tumor cell proliferation, survival, and metastasis

MAPK: mitogen-activated protein kinase; **PI3K**: phosphoinositide 3-kinase

[a]Based on preclinical data

1. Kulukian A. Mol Cancer Ther. 2020: 976-87. 2. Olayioye MA. Breast Cancer Res. 2001: 385-9. 3. Scholl S. Ann Oncol. 2001: S81-7. 4. Pheneger T. Cancer Res. 2009: Abstract 1795. 5. Segovia-Mendoza M. Am J Cancer Res. 2015: 2531-61. 6. Broekman F. World J Clin Oncol. 2011: 80-93. 7. Schlessinger J. Cell. 2000: 211-25.

The safety and efficacy of this agent(s), or use in this setting, has not been established or is subject to confirmation. For an agent(s) whose safety and efficacy has not been established or confirmed, future regulatory approval or commercial availability is not guaranteed.

TUCATINIB

Seagen®

Scan to learn more about the proposed mechanism of action of tucatinib

Clinical Trials

Phase 1 Phase 2 Phase 3

RECRUITING	**CompassHER2 RD[a]: High-risk adjuvant HER2+ breast cancer** (NCT04457596) Tucatinib or placebo + T-DM1
RECRUITING	**HER2CLIMB-02: HER2+ metastatic breast cancer** (NCT03975647) Tucatinib or placebo + T-DM1
RECRUITING	**HER2CLIMB-05[b]: HER2+ metastatic breast cancer maintenance therapy** (NCT05132582) Tucatinib or placebo + trastuzumab + pertuzumab
RECRUITING	**MOUNTAINEER-03[b]: HER2+ metastatic colorectal cancer** (NCT05253651) Tucatinib + trastuzumab + mFOLFOX6 vs mFOLFOX6 ± cetuximab or bevacizumab
ACTIVE, NOT RECRUITING	**HER2CLIMB-04: HER2+ metastatic breast cancer** (NCT04539938) Tucatinib + T-DXd
ACTIVE, NOT RECRUITING	**SGNTUC-019: Metastatic solid tumors with HER2 alterations** (NCT04579380) Tucatinib + trastuzumab
RECRUITING	**SGNTUC-024[c]: HER2+ metastatic gastrointestinal cancers** (NCT04430738) Tucatinib + trastuzumab ± pembrolizumab ± FOLFOX or CAPOX

HER2: human epidermal growth factor receptor 2; **T-DM1**: ado-trastuzumab emtansine; **T-DXd**: trastuzumab deruxtecan

[a]Trial being conducted by the Alliance for Clinical Trials in Oncology
[b]Trial being co-developed with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD)
[c]Phase 1b/2

Clinical trial information retrieved from clinicaltrials.gov, accessed Oct 2023.

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