An Irreversible FGFR1-3 Inhibitor for the Treatment of Solid Tumors

With High Activity and Selectivity

Overview

Drug Name	BioLink2020
Description	BioLink2020 is an oral, irreversible, highly selective inhibitor targeting fibroblast growth factor receptor 1-3 (FGFR1-3). It is being developed for the treatment of gastric cancer and other solid tumors harboring FGFR aberrations. In the first-in-human study, treatment with BioLink2020 was well tolerated with a manageable safety profile and showed preliminary anti-tumor activity in patients with advanced solid tumors.
Target	FGFR1-3
Drug Modality	Small molecule
Indication	Advanced solid tumors
Product Category	Inhibitor
Mechanism of Action	Inhibiting FGFR1-3 phosphorylation and signaling
Status	Phase I
Patent	Granted

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for BioLink2020. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

Target

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FGFR 1-3

Fibroblast growth factor receptors (FGFRs) are transmembrane tyrosine kinase receptors with an extracellular domain composed of three immunoglobulin-like domains (Ig-I-III) and one intracellular tyrosine kinase domain. Ig-I is linked to Ig-II by a stretch of 30 acidic residues called the acid box. Ig-I and the acid box have a role in receptor autoinhibition, while the Ig-II and Ig-III domains form the ligand binding site to bind fibroblast growth factor (FGF) ligands and heparan sulfate proteoglycans (HSPGs). Ig-II contains the heparin/heparan sulfate binding region and FGF binding activity site, while the junction between Ig-II and Ig-III controls heparin and FGF affinity. Four different FGFRs (FGFR1-4) have been identified. The alternative splicing events of FGFR1-3 allow the generation of multiple isoforms that exhibit significantly varying FGF-binding specificity.
FGFs are secreted glycoproteins that are readily sequestered by the extracellular matrix and the cell surface by HPSG, which stabilize the FGF-FGFR interaction by protecting FGFs from protease-mediated degradation. FGFs that create signals by binding with FGFRs play a critical role in many physiologic processes, such as embryonic development, differentiation, proliferation, survival, migration, and angiogenesis. The aberrant FGF/FGFR signaling is involved in the pathogenesis of many malignancies, therefore FGFRs are attractive targets for the cancer treatment.

Drug Modality

Small Molecule

BioLink2020 is a potent, selective, small molecule inhibitor of FGFR 1, 2, and 3. Preclinical data showed that BioLink2020 had great potential in combination with other targeted drugs or chemotherapeutic agents. Oral BioLink2020 in the first-in-human study showed a manageable and well-tolerated safety profile.

Indication

Advanced Solid Tumors

Aberrant FGF/FGFR signaling is implicated in the cancer cell proliferation, survival, migration, invasion and

angiogenesis of malignant tumors. The oncogenic signaling is mainly caused by FGFR genetic alterations including amplification, overexpression, missense mutation, translocation, and loss of expression. Aberrant FGF/FGFR signaling has been characterized in almost all cancer types, and the forms of FGFR mutation may vary in different tumors.

Lung cancer is the malignancy of highest impact in the world, which is divided into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is further subdivided into adenocarcinoma, large cell carcinoma, small cell carcinoma and squamous cell carcinoma. FGFR1 gene amplification is preferentially occurs in squamous NSCLC. In addition, FGFR1 is frequently amplified and overexpressed in breast cancer, which is the most commonly diagnosed malignancy in women. Endometrial cancer is the sixth most common cancer in women worldwide, and continues to increase in both incidence and mortality. FGFR2 mutation is associated with endometrial cancer. FGFR2 amplification occur in gastric cancer that is the fifth most prevalent malignancy and there were more than one million new cases diagnosed in 2020 according to the international agency for research on cancer (IARC). FGFR2 amplification is significantly associated with lymphatic invasion and a poor prognosis. In addition, FGFR2 gene fusion is associated with hepatocellular carcinoma (HCC), and FGFR3 mutations are potent oncogenic drivers in bladder cancer. Given the impact of aberrant FGFR signaling in oncogenesis, FGFR inhibitors have emerged as potential targeted therapies.

Mechanism of Action

Inhibiting FGFR1-3 Phosphorylation and Signaling

Dysregulation of FGF/FGFR signaling leads to oncogenesis and progression, resistance to anticancer therapies, as well as immune escape and angiogenesis in the tumor microenvironment. BioLink2020 is an irreversible, highly selective FGFR1-3 inhibitor that binds to the cytoplasmic kinase domain to inhibit the catalytic activity or autophosphorylation of FGFRs, exerting anti-tumor effects.

Status

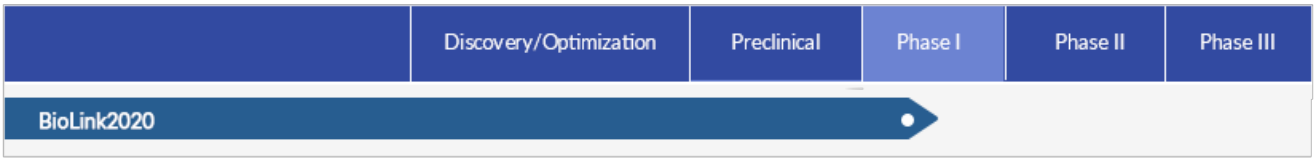
The Status of BioLink2020

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BioLink2020 is under early clinical development for the treatment of advanced solid tumors including bladder cancer, cholangiocarcinoma, endometrial cancer, and gastric cancer. Preliminary data showed that BioLink2020 was safe and well tolerated, and had positive efficacy against advanced solid tumors harboring FGFR aberrations.



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