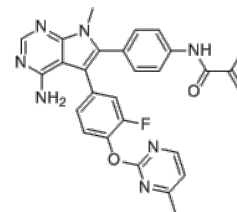


Product Name : RLY-4008
Cat. No. : PC-20046
CAS No. : 2549174-42-5
Molecular Formula : C₂₈H₂₄N₇O₂
Molecular Weight : 509.55
Target : FGFR
Solubility : 10 mM in DMSO



Biological Activity

Lirafugratinib (RLY-4008, RYL4008) is a potent, highly selective and irreversible **FGFR2** inhibitor with biochemical IC₅₀ of <100 nM, shows high cellular potency (IC₅₀=6 nM, pFGFR; pERK, IC₅₀=3 nM).

RLY-4008 demonstrates > 200-fold selectivity over FGFR1, and > 80-fold and > 5000-fold selectivity over FGFR3 and FGFR4, respectively, in biochemical assays.

RLY-4008 also demonstrates high kinome selectivity for FGFR2 against a panel of > 400 human kinases.

RLY-4008 has strong activity against primary and acquired FGFR2 resistance mutations in cellular assays, and potent antiproliferative effects on FGFR2-altered human tumor cell lines.

RLY-4008 demonstrates dose-dependent reduction of phosphorylation of FGFR2 signaling pathway nodes and induction of apoptosis.

RLY-4008 inhibits cellular proliferation with IC₅₀ < 14 nM in FGFR2 fusion-positive, FGFR2-amplified, and FGFR2-mutant cancer cell lines. RLY-4008 does not have strong inhibitory activity in FGFR1, FGFR3 or FGFR4-dependent cell lines, demonstrating the exquisite selectivity of RLY-4008 on FGFR2 in cellular assays.

RLY-4008, administered orally, twice daily from 1 to 30 mg/kg, exhibits dose-dependent antitumor activity and induces tumor regression in subcutaneous xenograft tumor models harboring FGFR2 alterations.

RLY-4008 induces regression in xenograft models expressing FGFR2V565F and FGFR2N549K, two common FGFR2 kinase domain mutations that drive clinical progression on current pan-FGFR inhibitors.

References

Jessica Casaletto, et al. RLY-4008, a novel precision therapy for FGFR2-driven cancers designed to potently and selectively inhibit FGFR2 and FGFR2 resistance mutations. *Cancer Res* (2021) 81 (13_Supplement): 1455.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

E-mail: tech@probechem.com