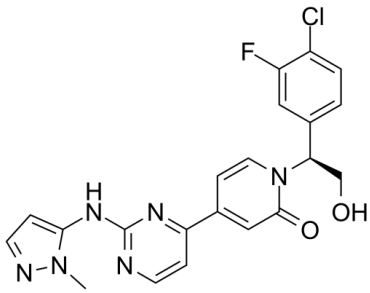
Data Sheet

Product Name:	Ravoxertinib
Cat. No.:	CS-3704
CAS No.:	1453848-26-4
Molecular Formula:	C21H18ClFN6O2
Molecular Weight:	440.86
Target:	ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
Solubility:	DMSO : ≥ 35 mg/mL (79.39 mM)



BIOLOGICAL ACTIVITY:

Ravoxertinib (GDC-0994) is an orally bioavailable **ERK** kinase inhibitor with an **IC_{50}** of 6.1 nM and 3.1 nM for **ERK1** and **ERK2**, respectively. IC50 & Target: IC50: 6.1 nM (ERK1), 3.1 nM (ERK2), 12 nM (p90RSK)[1] **In Vitro:** Ravoxertinib (GDC-0994) also inhibits p90RSK with an IC_{50} of 12 nM[1]. Ravoxertinib (GDC-0994) is highly selective for ERK1 and ERK2, with biochemical potency of 1.1 nM and 0.3 nM, respectively[2]. **In Vivo:** In CD-1 mice, a 10 mg/kg oral dose of Ravoxertinib (GDC-0994) is sufficient to achieve the desired target coverage for at least 8 h[1]. Daily, oral dosing of Ravoxertinib results in significant single-agent activity in multiple in vivo cancer models, including KRAS-mutant and BRAF-mutant human xenograft tumors in mice[2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: Ravoxertinib (GDC-0994) is prepared in 40% PEG400/60% (10% HPβCD) (Mice)[1].[1]Mice[1]
PK/PD data for Ravoxertinib (GDC-0994) in the HCT116 mouse xenograft model. HCT116 tumors are established in nude mice to a tumor volume of 400-600 mm^3. Mice are treated with a single oral dose of 22 at 15, 30, or 100 mg/kg versus vehicle control alone (40% PEG400/60% (10% HPβCD)) follow by tumor and plasma collection at 2, 8, 16, and 24 h postdose. Tumor levels of phosphorylated p90RSK (pRSK) relative total p90RSK (tRSK) are measured by quantitative Western blot and are normalized to vehicle control at 2 h postdose (set to 100%). Plasma and tumor concentrations are measured by LC−MS.

References:

[1]. Blake JF, et al. Discovery of (S)-1-(1-(4-Chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one (GDC-0994), an Extracellular Signal-Regulated Kinase 1/2 (ERK1/2) Inhibitor in Early Clinical Developme

[2]. Kirk Robarge, et al. Abstract DDT02-03: Discovery of GDC-0994, a potent and selective ERK1/2 inhibitor in early clinical development. Proceedings: AACR Annual Meeting 2014; April 5-9, 2014.

[3]. Huang X, et al. Targeting Epigenetic Crosstalk as a Therapeutic Strategy for EZH2-Aberrant Solid Tumors. Cell. 2018 Sep 20;175(1):186-199.e19.

CAIndexNames:

2(1H)-Pyridinone, 1-[(1S)-1-(4-chloro-3-fluorophenyl)-2-hydroxyethyl]-4-[2-[(1-methyl-1H-pyrazol-5-yl)amino]-4-pyrimidinyl]-

SMILES:

O=C1C=C(C2=NC(NC3=CC=NN3C)=NC=C2)C=CN1[C@@H](C4=CC=C(Cl)C(F)=C4)CO

Caution: Product has not been fully validated for medical applications. For research use only.

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