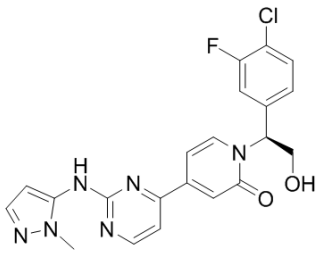
Ravoxertinib

Cat. No.:	HY-15947
CAS No.:	1453848-26-4
Molecular Formula:	$C_{21}H_{18}ClFN_6O_2$
Molecular Weight:	440.86
Target:	ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



Solvent & Solubility

In Vitro

DMSO : ≥ 35 mg/mL (79.39 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2683 mL	11.3415 mL	22.6829 mL
	5 mM	0.4537 mL	2.2683 mL	4.5366 mL
	10 mM	0.2268 mL	1.1341 mL	2.2683 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. GDC-0994 is prepared in vehicle (0.5% CMCNa+0.1% Tween80+ddH_2O)[3].

BIOLOGICAL ACTIVITY

Description

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.

IC_{50} & Target

ERK2	ERK1	p-RSK
3.1 nM (IC_{50})	6.1 nM (IC_{50})	12 nM (IC_{50})

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

Animal Administration [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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Cell**. 2018 Sep 20;175(1):186-199.e19.
- **Am J Physiol Heart Circ Physiol**. 2018 Mar 1;314(3):H580-H592.
- **Methods Mol Biol**. 2018;1711:351-398.
- **Harvard Medical School LINCS LIBRARY**

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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.

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