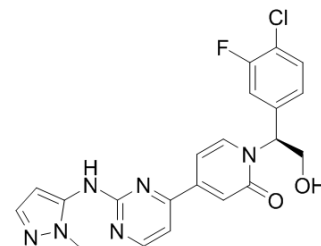


Ravoxertinib

Cat. No.:	HY-15947		
CAS No.:	1453848-26-4		
Molecular Formula:	C ₂₁ H ₁₈ ClFN ₆ O 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

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ravoxertinib (GDC-0994) is an orally bioavailable ERK kinase inhibitor with an IC₅₀ of 6.1 nM and 3.1 nM for ERK1 and ERK2, respectively.

IC₅₀ & Target

ERK2	ERK1	p-RSK
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	3.1 nM (IC ₅₀)	6.1 nM (IC ₅₀)	12 nM (IC ₅₀)
In Vitro	<p>Ravoxertinib (GDC-0994) also inhibits p90RSK with an IC₅₀ of 12 nM^[1].</p> <p>Ravoxertinib (GDC-0994) is highly selective for ERK1 and ERK2, with biochemical potency of 1.1 nM and 0.3 nM, respectively [2].</p> <p>Ravoxertinib (GDC0994; 50 nM, 0.5 μM, and 5 μM; 48 hours) decreases the viability of lung adenocarcinoma cell lines (A549, HCC827, HCC4006)^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		
In Vivo	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		

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 mm³. 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.
- Sci Transl Med. 2021 Jan 27;13(578):eaba7308.
- Environ Pollut. 2020 Sep 28;268(Pt B):115748.
- Mol Oncol. 2020 Oct 5.
- Cancer. 2020 Mar 15;126(6):1339-1350.

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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]. MICHAEL LAI. Opportunity for Pharmaceutical Intervention in Lung Cancer: Selective Inhibition of JAK1/2 to Eliminate EMT-Derived Mesenchymal Cells.

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

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