Zoligratinib

Cat. No.: HY-19957

CAS No.: 1265229-25-1

Molecular Formula: $C_{20}H_{16}N_6O$

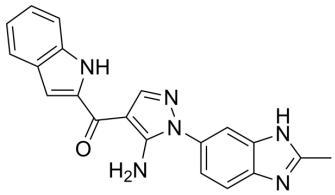
Molecular Weight: 356.38

Target: FGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (70.15 mM; ultrasonic and warming and heat to 50°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8060 mL	14.0300 mL	28.0599 mL
	5 mM	0.5612 mL	2.8060 mL	5.6120 mL
	10 mM	0.2806 mL	1.4030 mL	2.8060 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zoligratinib (Debio 1347) is an orally available and selective FGFR inhibitor with IC_{50}s of 9.3, 7.6, and 22 nM for FGFR1, FGFR2, FGFR3, and FGFR4, respectively.

IC_{50} & Target

FGFR1	FGFR2	FGFR3	FGFR4
9.3 nM (IC_{50})	7.6 nM (IC_{50})	22 nM (IC_{50})	290 nM (IC_{50})

In Vitro

Zoligratinib is well balanced in cellular antiproliferative activity against SNU-16 and stability in human liver microsome. The

	selectivity of 8 to inhibit FGFR over KDR is suggested to be caused by the difference in the interaction with M535 in FGFR1 and L889 in KDR[1]. The IC_{50} of Zoligratinib is 29 nM for FGF-dependent proliferation and 780 nM for VEGF-dependent proliferation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Zoligratinib treatment shows a dose-dependent tumor regression (tumor growth inhibition (TGI)=106% at 30 mg/kg and 147% at 100 mg/kg) without apparent body weight loss. Zoligratinib treatment also shows significant in vivo efficacy in xenograft mice models with FGFR genetic alterations, such as KG1 (leukemia, FGFR1OP-FGFR1 fusion), MFE280 (endometrial cancer, FGFR2 S252W mutation), UM-UC-14 (bladder cancer, FGFR3 S249C mutation), and RT112/84 (bladder cancer, FGFR3-TACC3 fusion)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The cell lines are added to the wells of 96-well plates containing 0.076−10,000 nM tested compounds (CH5183284) and incubated at 37°C. After 4 days' incubation, Cell Counting Kit-8 solution is added, and after incubation for several more hours, absorbance at 450 nm is measured. The antiproliferative activity is calculated using the formula (1-T/C) × 100 (%), where T and C represent absorbance at 450 nm of the cells treated with drugs (T) and that of untreated control cells (C)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][2]	Rats: Male Wistar rats (340-390 g) implanted with a telemetry transmitter are used for the assessment of effects on blood pressure (BP). Vehicle (0.5% carmellose sodium, 0.5% polysorbate 20, and 0.9% benzyl alcohol in purified water) or CH5183284/Debio 1347 (10 and 30 mg/kg) are administered by oral gavage once a day for 4 consecutive days. Data for blood pressure are automatically analyzed and continuously recorded at 5-minute intervals[2]. Mice: The in vivo efficacy is evaluated in mice bearing an SNU-16 xenograft. CH5183284 is orally administered once daily for 11 days, and the body weight of mice and the volume of the tumors are measured twice a week[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2022 Aug;608(7923):609-617.
- Oncotarget. 2020 Nov 3;11(44):3921-3932.

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REFERENCES

[1]. Nakanishi Y, et al. The fibroblast growth factor receptor genetic status as a potential predictor of the sensitivity to CH5183284/Debio 1347, a novel selective FGFR inhibitor. Mol Cancer Ther. 2014 Nov;13(11):2547-58.

[2]. Nakanishi Y, et al. Mechanism of Oncogenic Signal Activation by the Novel Fusion Kinase FGFR3-BAIAP2L1. Mol Cancer Ther. 2015 Mar;14(3):704-12.

[3]. Nakanishi Y, et al. ERK Signal Suppression and Sensitivity to CH5183284/Debio 1347, a Selective FGFR Inhibitor. Mol Cancer Ther. 2015 Dec;14(12):2831-9.

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

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