Regorafenib

Cat. No.: HY-10331

CAS No.: 755037-03-7

Molecular Formula: $C_{21}H_{15}ClF_4N_4O_3$

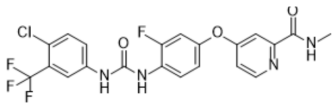
Molecular Weight: 482.82

Target: VEGFR; Autophagy; PDGFR; Raf; RET; c-Kit; FGFR; Tie

Pathway: Protein Tyrosine Kinase/RTK; Autophagy; MAPK/ERK Pathway

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 : 125 mg/mL (258.90 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0712 mL	10.3558 mL	20.7117 mL
5 mM	0.4142 mL	2.0712 mL	4.1423 mL
10 mM	0.2071 mL	1.0356 mL	2.0712 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 7.5 mg/mL (15.53 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.75 mg/mL (5.70 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.18 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Regorafenib (BAY 73-4506) is an orally active and potent multi-targeted receptor tyrosine kinase inhibitor, with IC_{50} values of 13/4.2/46, 22, 7, 1.5 and 2.5 nM for VEGFR1/2/3, PDGFRβ, Kit, RET and Raf-1, respectively. Regorafenib shows very robust antitumor and antiangiogenic activity[1].

IC_{50} & Target

Raf-1	Tie2	VEGFR2	VEGFR1
2.5 nM (IC_{50})	311 ± 46 nM (IC_{50})	4.2 nM (IC_{50})	13 nM (IC_{50})

	$BRaf^{V600E}$ 19 nM (IC_{50})	PDGFRβ 22 nM (IC_{50})	Braf 28 nM (IC_{50})	VEGFR3 46 nM (IC_{50})

In Vitro

Regorafenib (0-10 μM, 96 h) shows anti-proliferation activity in GIST 882, Thyroid TT, MDA-MB-231, HepG2, A375 and SW620 cells[1].

Regorafenib (0-3000 nM, 30 min) inhibits the autophosphorylation of VEGFR2, TIE2 and PDGFR-β, and inhibits FGFR and pERK1/2[1].

Regorafenib causes a concentration-dependent decrease in Hep3B cell growth, with an IC_{50} of 5 μM. Regorafenib subsequently increases the levels of phospho-c-Jun, a JNK target, but not total c-Jun in Hep3B cells[3].

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

Cell Proliferation Assay[1]

Cell Line:	GIST 882, Thyroid TT, MDA-MB-231, HepG2, A375 and SW620 cells
Concentration:	10 μM and 5 nM
Incubation Time:	96 h
Result:	Showed anti-proliferation activity in GIST 882, Thyroid TT, MDA-MB-231, HepG2, A375 and SW620 cells, with IC_{50} values of 45 ± 20, 34 ± 8, 401 ± 88, 560 ± 200, 900, 967 ± 287 nM. respectively.

Western Blot Analysis[1]

Cell Line:	NIH-3T3/VEGFR2 cells, (CHO)-TIE2 cells, HAoSMCs cells, MCF-7 cells
Concentration:	0, 10, 30, 100, 300, 1000, 3000 nM
Incubation Time:	30 min
Result:	Inhibited the autophosphorylation of VEGFR2, TIE2 and PDGFR-β, with IC_{50} values of 3, 31, and 90 nM, respectively, inhibited FGFR signaling in MCF-7 breast cancer (BC) cells stimulated with FGF10, and showed inhibition of phosphorylated FGFR substrate 2 (pFRS2) and the downstream signaling kinase pERK1/2.

In Vivo

Regorafenib (10 mg/kg, Orally, single dose or daily for 4 days) inhibits tumor vasculature and tumor growth in a rat GS9L glioblastoma model[1].

Regorafenib (0-100 mg/kg, Orally, qd × 9) exhibits antitumorigenic and antiangiogenic effects in the Colo-205, MDA-MB-231 and 786-O model[1].

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

Animal Model:	Rat GS9L glioblastoma xenograft[1]
Dosage:	10 mg/kg
Administration:	Orally, single dose or daily for 4 days
Result:	Inhibited tumor vasculature and tumor growth in a rat GS9L glioblastoma model.

Animal Model:	Female athymic NCr nu/nu mice, Multiple xenograft models, including models derived from CRC (Colo-205), BC (MDA-MB-231) and RCC (786-O) tumors[1]
Dosage:	0, 3, 10, 30, 100 mg/kg
Administration:	Orally, qd × 9

Result:	Effectively inhibited growth of the Colo-205, MDA-MB-231 and 786-O model. Significantly reduces tumor MVA, effectively inhibited the RAF/MEK/ERK signaling cascade, and drastically inhibited tumor cell proliferation.

CUSTOMER VALIDATION

- Cell Res. 2020 Sep;30(9):779-793.
- Cancer Discov. 2021 Jul;11(7):1716-1735.
- Cancer Discov. 2019 Dec;9(12):1686-1695.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Adv Sci (Weinh). 2023 Jun 17;e2206798.

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REFERENCES

[1]. Wilhelm SM, et al. Regorafenib (BAY 73-4506): a new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. Int J Cancer, 2011, 129(1), 245-255.

[2]. Heng DY, et al. Targeted therapy for metastatic renal cell carcinoma: current treatment and future directions. Ther Adv Med Oncol, 2010, 2(1), 39-49.

[3]. Carr BI, et al. Fluoro-Bay 43-9006 (Regorafenib) effects on hepatoma cells: growth inhibition, quiescence, and recovery. J Cell Physiol, 2013, 228(2), 292-297.

[4]. Wagner J, et al. Anti-tumor effects of ONC201 in combination with VEGF-inhibitors significantly impacts colorectal cancer growth and survival in vivo through complementary non-overlapping mechanisms. J Exp Clin Cancer Res. 2018 Jan 22;37(1):11.

[5]. Matsuoka K, et al. Effective Sequential Combined Chemotherapy with Tipiracil and Regorafenib in Human Colorectal Cancer Cells. Int J Mol Sci. 2018 Sep 25;19(10). pii: E2915.

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