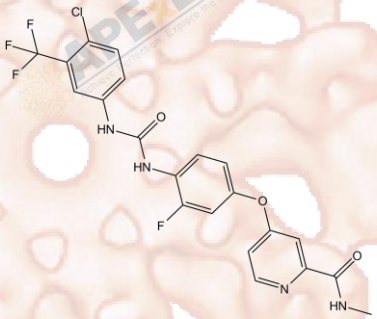
Product Data Sheet

Regorafenib



Cat. No.:	A8236
CAS No.:	755037-03-7
Formula:	C21H15ClF4N4O3
M.Wt:	482.82
Synonyms:	BAY 73-4506
Target:	Tyrosine Kinase
Pathway:	c-RET
Storage:	Desiccate at -20°C

Solvent & Solubility

In Vitro

⩾25.04 mg/mL in DMSO; insoluble in H2O; ⩾6.25 mg/mL in EtOH with ultrasonic

Preparing Stock Solutions

Mass / Solvent / Concentration	1mg	5mg	10mg
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.

Biological Activity

Shortsummary	Inhibitor of VEGFR/PDGFR/FGFR/mutant kit/RET/Raf-1
IC_{50} & Target	13 nM/4.2 nM/46 nM (VEGFR1/2/3), 22 nM (PDGFRβ), 7 nM (Kit), 1.5 nM (RET), 2.5 nM (Raf-1)

In Vitro

Cell Viability Assay

Cell Line:	PLC/PRF/5 cells
Preparation method：	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.
Reacting conditions:	1 μM, 72 hours for migration assay5 μM, 24 hours for invasion assay

	Applications:	For the migration assay, PLC/PRF/5 cells were treated with the drugs and microscopically analyzed at the time of the scratch (T0) and after 48 and 72 hours. For the invasion assay, invading PLC/PRF/5 cells were treated with different drug concentrations (0.5, 1, 2.5 and 5 μM). Invasion was calculated as a percentage of the invading drug-treated cells compared to drug-untreated control cells. Regorafenib inhibited HCC cell migration in both AFP-positive and AFP-negative cells at the same low concentration range as inhibited AFP levels. Similar results were found in a cell invasion assay, at almost identical drug concentrations.
In Vivo	**Animal experiment**	
	Animal models:	Female athymic NCr nu/nu mice injected with Colo-205, MDA-MB-231 or 786-O xenografts
	Dosage form:	Oral administration; 100, 30, 10, and 3 mg/kg
	Applications:	Regorafenib dosed qd orally inhibited tumor growth in a dose-dependent manner in multiple xenograft models, including models derived from CRC (Colo-205), BC (MDA-MB-231) and RCC (786-O) tumors. Regorafenib effectively inhibited growth of the Colo-205 xenografts in the dose range of 10-100 mg/kg, reaching a TGI of about 75% at day 14 at the 10 mg/kg dose. A slow regrowth was observed at all doses when treatment was terminated after 9 days. In the MDA-MB-231 model, regorafenib was highly efficacious at a dose as low as 3 mg/kg, resulting in a significant TGI of 81%, which increased to ~ 93% at doses of 10 and 30 mg/kg, where tumor stasis was reached. Regorafenib also very efficiently inhibited the growth of the 786-O RCC model. TGI >90% was observed at the end of a 21-day dosing period with regorafenib 10 and 30 mg/kg.
	Other notes:	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Product Citations

1. Barot S, Abo-Ali EM, et al. "Inhibition of glycogen catabolism induces intrinsic apoptosis and augments multikinase inhibitors in hepatocellular carcinoma cells." Exp Cell Res. 2019 Aug 15;381(2):288-300.PMID:31128107

2. Wu LW, Zhou DM, et al. "Suppression of LSD1 enhances the cytotoxic and apoptotic effects of regorafenib in hepatocellular carcinoma cells." Biochem Biophys Res Commun. 2019 May 14;512(4):852-858.PMID:30929918

3. Hu X, Wu LW, et al. "The anti-tumor effect of regorafenib in lung squamous cell carcinoma in vitro." Biochem Biophys Res Commun. 2018 Sep 5;503(2):1123-1129.PMID:29944884

4. Yang Q, Guo X, et al. "Metformin Enhances the Effect of Regorafenib and Inhibits Recurrence and Metastasis of Hepatic

Carcinoma After Liver Resection via Regulating Expression of Hypoxia Inducible Factors 2α (HIF-2α) and 30 kDa HIV Tat-Interacting Protein (TIP30)." Med Sci Monit. 2018 Apr 14;24:2225-2234.PMID:29654226

5. Zhang WJ, Li Y, et al. "Synergistic antitumor activity of regorafenib and lapatinib in preclinical models of human colorectal cancer." Cancer Lett. 2017 Feb 1;386:100-109.PMID:27864115

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References

[1] Carr B I, D'Alessandro R, Refolo M G, et al. Effects of low concentrations of regorafenib and sorafenib on human HCC cell AFP, migration, invasion, and growth in vitro. Journal of cellular physiology, 2013, 228(6): 1344-1350.

[2] Wilhelm S M, Dumas J, Adnane L, et al. Regorafenib (BAY 73‐4506): A new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. International Journal of Cancer, 2011, 129(1): 245-255.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

APExBIO Technology

www.apexbt.com

7505 Fannin street, Suite 410, Houston, TX 77054.

Tel: +1-832-696-8203 | Fax: +1-832-641-3177 | Email: info@apexbt.com