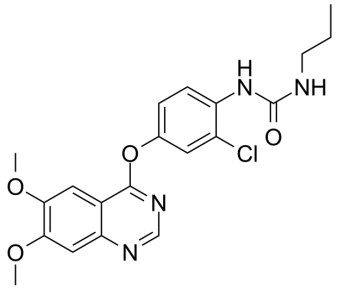
KRN-633

Cat. No.:	HY-12060
CAS No.:	286370-15-8
Molecular Formula:	$C_{20}H_{21}ClN_4O_4$
Molecular Weight:	416.86
Target:	VEGFR
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 (59.97 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3989 mL	11.9944 mL	23.9889 mL
	5 mM	0.4798 mL	2.3989 mL	4.7978 mL
	10 mM	0.2399 mL	1.1994 mL	2.3989 mL

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

BIOLOGICAL ACTIVITY

Description

KRN-633 is a potent VEGFR inhibitor with IC_{50}s of 170, 160 and 125 nM for VEGFR1, VEGFR2 and VEGFR3, respectively.

IC_{50} & Target

VEGFR1	VEGFR2	VEGFR3
170 nM (IC_{50})	160 nM (IC_{50})	125 nM (IC_{50})

In Vitro

KRN-633 inhibits tyrosine phosphorylation of VEGFR-1, VEGFR2, c-Kit, and PDGFR-β (IC_{50}=11.7, 1.16, 8.01, 130 nM) in human umbilical vein endothelial cells. KRN-633 also inhibits the VEGF-driven proliferation of HUVECs (IC_{50}=14.9 nM). KRN-633 suppresses capillary tube formation of endothelial cells[1].

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

In Vivo

KRN-633 inhibits tumor growth in several tumor xenograft models with diverse tissue origins, including lung, colon, and prostate, in athymic mice and rats. KRN-633 also causes the regression of some well-established tumors and those that have regrown after the cessation of treatment. KRN-633 is well tolerated and has no significant effects on body weight or the general health of the animals. Histologic analysis of tumor xenografts treated with KRN-633 reveals a reduction in the number of endothelial cells in non-necrotic areas and a decrease in vascular permeability[1].

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

PROTOCOL

Kinase Assay [1]	Cell-free kinase assays are done to obtain IC_{50} values against a variety of recombinant receptor and non-RTKs. KRN-633 is tested from 0.3 nM to 10 μM. All assays are done in quadruplicate with 1 μM ATP[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	A549, Ls174T, HT29, DU145, LNCap, and PC-3 cells cancer cells are cultured for 24 hours before adding KRN-633 (0.01 to 10 μM) or vehicle (0.1% DMSO in medium) and then grow for a further 96 hours. Cell viability is measured using WST-1 reagent. The percentage viability is determined relative to the untreated control[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: Human tumor xenografts are established in the hind flank of athymic rats (BALB/cA, Jcl-nu). Rats are randomized into groups of five at the point when the tumors reach the average size indicated (162 to 657 mm^3) and are then treated with KRN-633 or vehicle, either once (qd) or twice (bid) per day, at the dosages shown. The percentage of tumor growth inhibition compared with the vehicle-treated group is calculated on the day after the last treatment (day 14)[1]. Mice: The mice are randomized into groups of five at the point when the tumors reached the average sizes: 103 to 260 mm^3 or 500 to 667 mm^3. They are then treated with KRN-633 or vehicle, either once (qd) or twice (bid) per day, at the dosages of 10-100 mg/kg. The percentage of tumor growth inhibition (TGI) compared with the vehicle-treated group is calculated on the day after the last treatment[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Bone. 2015 Sep;78:102-13.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Nakamura K, et al. KRN633: A selective inhibitor of vascular endothelial growth factor receptor-2 tyrosine kinase that suppresses tumor angiogenesis and growth. Mol Cancer Ther. 2004 Dec;3(12):1639-49.

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