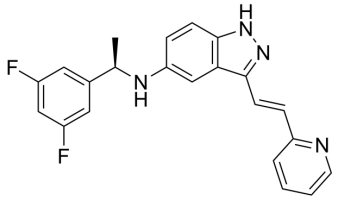
Trk-IN-20

Cat. No.:	HY-150561
CAS No.:	2460924-63-2
Molecular Formula:	$C_{22}H_{18}F_2N_4$
Molecular Weight:	376.4
Target:	Trk Receptor
Pathway:	Neuronal Signaling; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Trk-IN-20 is a kind of 3-vinylindazole derivatives. Trk-IN-20 suppresses Trk kinases functions by phosphorylation inhibition of TrkA/B/C with IC_{50} values of 1.6 nM, 2.9 nM and 2.0 nM, respectively[1].

IC_{50} & Target

TrkA	TrkB	TrkC
1.6 nM (IC_{50})	2.9 nM (IC_{50})	2.0 nM (IC_{50})

In Vitro

NTRK1 is a proto-oncogene in colon cancer, Trk inhibitors have been detected to against a variety of human cancers[1].
Trk-IN-20 (compound 7mb) (0.031, or 0.018 μM, respectively; 72 h) exhibits strong inhibition against the Larotrectinib-resistant cells with NTRK1-G667C or NTRK3-G696A mutations with IC_{50}s of 0.031 and 0.018 μM, respectively[1].
Trk-IN-20 (compound 7mb) (9-22 nM; 72 h) inhibits BaF3 murine cells stably transformed with NTRK oncogenic fusions including CD74-NTRK1, ETV6-NTRK2 and ETV6-NTRK3 with IC_{50}s of 15, 22, and 9 nM, respectively[1].
Trk-IN-20 (compound 7mb) (0.32, 1.6, 8, 40, 200; 6 h) inhibits activation of Trk and its downstream proteins in BaF3-CD74-NTRK1, BaF3-ETV6-NTRK2, BaF3-ETV6-NTRK3 cells[1].
Trk-IN-20 (compound 7mb) tightly bound to ATP-binding site of TrkA, TrkB, and TrkC with binding constant (K_d) values of 1.6, 3.1 and 4.9 nM, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	BaF3-CD74-NTRK1, BaF3-ETV6-NTRK2, BaF3-ETV6-NTRK3 cells
Concentration:	0, 0.32, 1.6, 8, 40, 200 nM
Incubation Time:	6 hours
Result:	Inhibited the phosphorylation of TrkA/B/C and their downstream signaling molecules ERK, AKT, and PLC-γ1. And also induced partial degradation of Trk protein in BaF3-ETV6-NTRK2, BaF3-ETV6-NTRK3 cells.

In Vivo

Trk-IN-20 (compound 7mb) (p.o.; 10 mg/kg) shows short half-life of 1.39 hours and a low oral bioavailability of 8.79% in rats [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Pharmacokinetic Profile of Trk-IN-20 (Compound 7mb) in Rats[1]
Dosage:	
Administration:	
Result:	

Route	Dose (mg/kg)	$AUC_{0-\infty}$ (μM.h)	C_{max} (μM)	$T_{1/2}$ (h)	***CL*** (L/h/kg)	BA (%)
i.v.	2	3.69	6.77	1.39	1.44	/
p.o.	10	1.62	0.36	1.13	-	8.79

REFERENCES

[1]. Duan Y, et al. Design, synthesis, and Structure-Activity Relationships (SAR) of 3-vinylindazole derivatives as new selective tropomyosin receptor kinases (Trk) inhibitors. Eur J Med Chem. 2020 Oct 1. 203:112552.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA