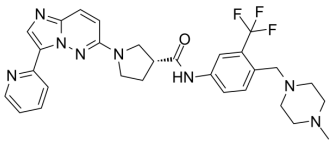
TRK II-IN-1

Cat. No.:	HY-151945
CAS No.:	2904690-41-9
Molecular Formula:	$C_{29}H_{31}F_3N_8O$
Molecular Weight:	564.6
Target:	Trk Receptor; FLT3; RET; VEGFR
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 II-IN-1 is a potent type II TRK inhibitor, with IC_{50}s of 3.3, 6.4, 4.3 and 9.4 nM, for TRKA/B/C and $TRKA^{G667C}$, respectively. TRK II-IN-1 also inhibits FLT3, RET, and VEGFR2 with IC_{50}s of 1.3, 9.9, and 71.1 nM, respectively. TRK II-IN-1 can be used for the research of TRK driven cancers[1].

IC_{50} & Target

TrkA 3.3 nM (IC_{50})	TrkB 6.4 nM (IC_{50})	TrkC 4.3 nM (IC_{50})	$TRKA^{G667C}$ 9.4 nM (IC_{50})
FLT3 1.3 nM (IC_{50})	RET 9.9 nM (IC_{50})	VEGFR2 71.1 nM (IC_{50})	

In Vitro

TRK II-IN-1 (compound 12d) (1 μM) demonstrates over 90% of kinase inhibition towards VEGFR2, RET, FLT3 and nearly 70% inhibition against Kit, CSF1R, DDR1 and DDR2[1].

TRK II-IN-1 (72 h) inhibits Ba/F3-CD74-TRKA, Ba/F3-ETV6-TRKB and Ba/F3-ETV6-TRKC cells, with IC_{50}s of 26.1, 44.7 and 15.7 nM, respectively[1].

TRK II-IN-1 (72 h) suppresses proliferation of a panel of Ba/F3 cells stably transformed with wild type, xDFG as well as solvent-front (SF) mutant TRK fusion proteins, with IC_{50}s ranging from 2.6 to 143.3 nM[1].

TRK II-IN-1 (0.4-500 nM; 48 h) induces apoptosis of Ba/F3-CD74-TRKA and Ba/F3-CD74-$TRKA^{G667C}$ cells[1].

TRK II-IN-1 (0.4-500 nM; 24 h) arrests cell cycle progression in the G0/G1 phase in Ba/F3-CD74-TRKA and Ba/F3-CD74-$TRKA^{G667C}$ cells[1].

TRK II-IN-1 (0.8-500 nM; 6 h) suppresses the phosphorylation of TRKA, $TRKA^{G667C}$ kinases, and their downstream AKT, ERK and PLCγ1 in a dose-dependent manner[1].

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

Apoptosis Analysis[1]

Cell Line:	Ba/ F3 stable cell lines expressing wild type and G667C mutant fusions
Concentration:	0.4, 2, 10, 50 nM for Ba/F3-CD74-TRKA cells; 4, 20, 100, 500 nM for Ba/F3-CD74-$TRKA^{G667C}$ cells
Incubation Time:	48 hours
Result:	Notable apoptotic cells (18.74% in 100 nM and 35.65% in 500 nM) were observed in Ba/F3-CD74-TRKA cells. Induced Ba/F3-CD74-$TRKA^{G667C}$ cell apoptosis with 11.22% and 56.25% at the

	concentration of 10 nM and 50 nM, respectively.

Cell Cycle Analysis[1]

Cell Line:	Ba/ F3 stable cell lines expressing wild type and G667C mutant fusions
Concentration:	0.4, 2, 10, 50 nM for Ba/F3-CD74-TRKA cells; 4, 20, 100, 500 nM for Ba/F3-CD74-TRKA^{G667C} cells
Incubation Time:	24 hours
Result:	Arrested cell cycle progression in the G0/G1 phase.

Western Blot Analysis[1]

Cell Line:	Ba/ F3 stable cell lines expressing wild type and G667C mutant fusions
Concentration:	0.8, 4, 20, 100, 500 nM
Incubation Time:	6 hours
Result:	Inhibited the activation of TRKA and downstream signaling.

REFERENCES

[1]. Xiang S, et, al. Switch type I to type II TRK inhibitors for combating clinical resistance induced by xDFG mutation for cancer therapy. Eur J Med Chem. 2023 Jan 5;245(Pt 1):114899.

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