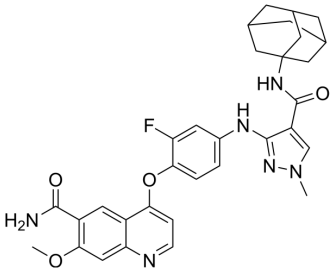
RET-IN-20

Cat. No.:	HY-151987
Molecular Formula:	$C_{32}H_{33}FN_6O_4$
Molecular Weight:	584.64
Target:	RET; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

RET-IN-20 is a potent RET inhibitor with an IC_{50} value of 13.7 nM. RET-IN-20 decreases the expression of p-Ret, p-Shc protein. RET-IN-20 induces apoptosis. RET-IN-20 shows antiproliferative and anti-tumor activity[1].

IC_{50} & Target

IC_{50}: 3.7 nM (RET)[1]

In Vitro

RET-IN-20 (compound 8q) (0, 1.2, 3.7, 11.1, 33.3, 100 nM; 4 h) decreases the expression of p-Ret, p-Shc protein in a dose dependent manner[1].

RET-IN-20 (0, 33.3, 100, 300 nM; 48 h) induces apoptosis in a dose dependent manner[1].

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

Cell Proliferation Assay[1]

Cell Line:	Ba/F3 RET^{WT}, Ba/F3 RET^{V804M}, Ba/F3 RET^{G810C}, Ba/F3 RET^{G810R}, Ba/F3 parental cells
Concentration:	0-10000 nM
Incubation Time:	72 h
Result:	Showed antiproliferative activities with IC_{50}s of 5.6, 24.4, 15.4, 53.2, >10000 nM for Ba/F3 RET^{WT}, Ba/F3 RET^{V804M}, Ba/F3 RET^{G810C}, Ba/F3 RET^{G810R}, Ba/F3 parental, respectively.

Apoptosis Analysis[1]

Cell Line:	CCDC6-RET-WT, CCDC6-RET-V804M, CCDC6-RET-G810C, CCDC6-RET-G810R cells
Concentration:	0, 1.2, 3.7, 11.1, 33.3, 100 nM
Incubation Time:	4 h
Result:	Inhibited the expression of p-Ret, p-Shc protein in a dose dependent manner.

Western Blot Analysis[1]

Cell Line:	Ba/F3-CCDC6-$RET^{G810\ C/R}$ cells
Concentration:	0, 33.3, 100, 300 nM

Incubation Time:	48 h
Result:	Induced approximately 53.40% and 32.67% of cells undergoing apoptosis at a concentration of 300 nM in Ba/F3-CCDC6-RET^{G810C} and Ba/F3-CCDC6-RET^{G810R} cells, respectively.

In Vivo

RET-IN-20 (10, 30 mg/kg; i.p.; once a day for 13 continuous days) shows anti-tumor activity in mouse[1].

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

Animal Model:	CB17-SCID mice (Ba/F3-CCDC6-RETG810C tumor)[1]
Dosage:	10, 30 mg/kg
Administration:	I.p.; once a day for 13 continuous days
Result:	Suppressed tumor growth in a dose-dependent manner with tumor growth inhibition values (TGI) of 17.1% and 66.9%, respectively.

REFERENCES

[1]. Zhang Y, et al. 1-Methyl-3-((4-(quinolin-4-yloxy)phenyl)amino)-1H-pyrazole-4-carboxamide derivatives as new rearranged during Transfection (RET) kinase inhibitors capable of suppressing resistant mutants in solvent-front regions. Eur J Med Chem. 2022 Dec 15;244:114862.

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