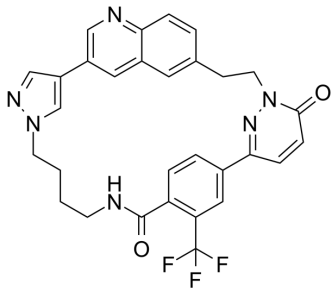
D6808

Cat. No.:	HY-151905
CAS No.:	3029240-84-1
Molecular Formula:	$C_{30}H_{25}F_3N_6O_2$
Molecular Weight:	558.55
Target:	c-Met/HGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	D6808 is a highly selective and potent c□Met inhibitor with an IC_{50} value of 2.9 nM. D6808 induces cell apoptosis and cell cycle arrest. D6808 can be used for the research of NSCLC and gastric cancers[1].
IC_{50} & Target	IC50: 2.9 nM (c□Met)[1]

In Vitro

D6808 shows c-Met biochemical kinase inhibitory activity with an IC_{50} value of 2.9 nM[1].

D6808 (0.0001-10 μM; 5 d) shows cellular antiproliferative potency to Hs746T cancer cells with an IC_{50} value of 0.7 nM[1].

D6808 displays extraordinary kinome selectivity with IC_{50} values of 401.3, 437.2, 1386 and 203.9 nM for Axl, TrkA, TrkB and TrkC kinase, respectively[1].

D6808 (0-10 μM; 72 h) show antiproliferative potency to Tpr-Met fusion protein-transformed Ba/F3 cells with IC_{50} values of 4.3, 4.2, 3.2, 1.0, 39.0 and 33.4 nM for Ba/F3-Tpr-Met, Ba/F3-Tpr-Met^{F1200L}, Ba/F3-Tpr-Met^{M1250T}, Ba/F3-Tpr-Met^{H1094Y}, Ba/F3-Tpr-Met^{F1200I}, Ba/F3-Tpr-Met^{L1195V}, respectively[1].

D6808 (0-30 nM; 12 h) affects activation of MET and dose-dependently decreases the protein levels of CDK2, CDK4, CDK6, cyclin D2, and cyclin E1 and the cleave activation of PARP and caspase-9 in Ba/F3-Tpr-Met cells[1].

D6808 (40 nM; 24 h) induces cell apoptosis and 87.37% G0/G1 phase arrest in Ba/F3-Tpr-Met cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	Hs746T cancer cell line
Concentration:	0.0001-10 μM
Incubation Time:	5 days
Result:	Inhibited the cell proliferation of Hs746T cancer cells.

Western Blot Analysis[1]

Cell Line:	Hs746T and Ba/F3-Tpr-Met cell lines
Concentration:	0, 0.37, 1.1, 3.3, 10 and 30 nM
Incubation Time:	12 hours
Result:	Suppressed the activation of MET in Hs746T and Ba/F3-Tpr-Met cells.

Apoptosis Analysis[1]

Cell Line:	Ba/F3-Tpr-Met cell line
Concentration:	40 nM
Incubation Time:	24 hours
Result:	Induced 50.89% apoptosis after 48 h treatment.

In Vivo

Pharmacokinetic Properties of D6808 in Rats[1].

	Rats IV 2.0 mg/kg	Rats PO 10.0 mg/kg	Rats IP 10.0 mg/kg
$T_{1/2}$ (h)	0.57	2.49	4.63
T_{max} (h)	0.08	0.25	0.25
C_{max} (ng/mL)	1071.23	60.98	282.12
AUC_{0-t} (h×ng/mL)	483.84	48.89	820.38
V_z (mL/kg)	3470.78		
CL (mL/h/kg)	4207.06		
MRT_{0-t} (h)	0.36	1.71	3.40
F (%)		2.02	33.91

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REFERENCES

[1]. Wang C, et al. Discovery of D6808, a Highly Selective and Potent Macrocyclic c-Met Inhibitor for Gastric Cancer Harboring MET Gene Alteration Treatment. J Med Chem. 2022 Nov 24;65(22):15140-15164.

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