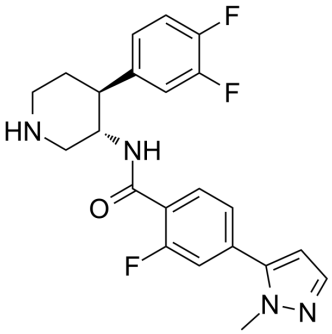
Hu7691 free base

Cat. No.:	HY-132302A
CAS No.:	2241232-43-7
Molecular Formula:	$C_{22}H_{21}F_3N_4O$
Molecular Weight:	414.42
Target:	Akt; PKA; PKC; ROCK; Ribosomal S6 Kinase (RSK); SGK
Pathway:	PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Epigenetics; TGF-beta/Smad; Cell Cycle/DNA Damage; Cytoskeleton; MAPK/ERK Pathway; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Hu7691 free base is an orally active, selective Akt inhibitor with IC_{50}s of 4.0 nM, 97.5 nM, 28 nM for Akt1, Akt2 and Akt3, respectively. Hu7691 free base inhibits tumor growth and enables decrease of cutaneous toxicity in mice[1].

IC_{50} & Target

Akt1 4.0 nM (IC_{50})	Akt2 97.5 nM (IC_{50})	Akt3 28 nM (IC_{50})	PKA 11 nM (IC_{50})
PKCη 629 nM (IC_{50})	ROCK1 354 nM (IC_{50})	RSK1 756 nM (IC_{50})	p70S6K 229 nM (IC_{50})

In Vitro

Hu7691 free base displays low inhibitions against most of the kinases in the four families (AGC, TK, TKL, Lipid/Atypical; PKA, IC_{50}=11 nM; PKCη, IC_{50}=629 nM; ROCK1, IC_{50}=354 nM; RSK1, IC_{50}=756 nM; P70S6K, IC_{50}=229 nM; SGK, IC_{50}=1009 nM)[1].
Hu7691 free base (2.25-36 μM; 24 hours) induces effective decrease of the phosphorylation level of Akt (S473)[1].
Hu7691 free base (10, 20, 30, 40 μM; for 72 h) exhibits low toxicity against HaCaT cells with an IC_{50} value of 15.2 μM[1].
Hu7691 free base has a significant inhibitory effect on the growth of 18 kinds of human tumor cells (U87-MG, U251, A549, HepG2, HT-29, KHOS, MDA-MB-231, PC3, SKOV3 and so on) derived from different tissues, with the IC_{50} range of 0.6-27 μM.
Hu7691 free base shows low antiproliferation activities against the HL7702 and HPDE6-C7 normal cells, exhibiting IC_{50} values of 5.4 and 16.1 μM, respectively[1].

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

Western Blot Analysis[1]

Cell Line:	HaCaT cells
Concentration:	2.25, 4.5, 9, 18, 36 μM
Incubation Time:	24 hours
Result:	Induced effective decrease of the phosphorylation level of Akt (S473).

In Vivo

Hu7691 free base (12.5-50 mg/kg/day; i.g.; for 22 days) shows dose-dependent tumor growth inhibition[1].
Hu7691 free base (15 mg/kg; oral) has a $T_{1/2}$ of 8.68 hours, a C_{max} of 171.17 ng/mL and an AUC of 2820.64 ng/mL•h in rats[1].
Hu7691 free base (2 mg/kg; iv) has a $T_{1/2}$ of 6.24 hours, a C_{max} of 207.52 ng/mL and an AUC of 532.87 ng/mL•h in rats[1].
Hu7691 free base (20 mg/kg; oral) has a $T_{1/2}$ of 16.7 hours, a C_{max} of 905.65 ng/mL and an AUC of 36303 ng/mL•h in beagle

dog (male, 40 weeks old, 8–10 kg)[1].

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

Animal Model:	Balb/c mice (nu/nu, female, 3-4 weeks old, 20-25 g) with 786-O and KHOS xenograft[1]
Dosage:	12.5, 25, 50 mg/kg
Administration:	Oral; once daily for 22 days
Result:	Showed dose-dependent tumor growth inhibition.

Animal Model:	SD rats (male, 8 weeks old, 250-300 g)[1]
Dosage:	15 mg/kg (Pharmacokinetic Analysis)
Administration:	Oral
Result:	Had a $T_{1/2}$ of 8.68 hours, a C_{max} of 171.17 ng/mL and an AUC of 2820.64 ng/mL•h.

REFERENCES

[1]. Jinxin Che, et al. Discovery of N-((3 S,4 S)-4-(3,4-Difluorophenyl)piperidin-3-yl)-2-fluoro-4-(1-methyl-1 H-pyrazol-5-yl)benzamide (Hu7691), a Potent and Selective Akt Inhibitor That Enables Decrease of Cutaneous Toxicity. J Med Chem. 2021 Aug 26;64(16):12163-12180.

Caution: Product has not been fully validated for medical applications. For research use only.

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