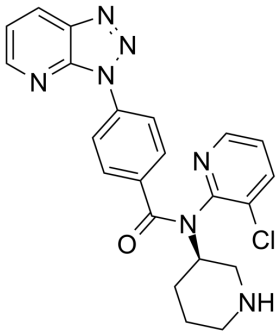
PF-06446846

Cat. No.:	HY-120088
CAS No.:	1632250-49-7
Molecular Formula:	$C_{22}H_{20}ClN_7O$
Molecular Weight:	433.89
Target:	Ser/Thr Protease
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

PF-06446846 is an orally active proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor. PF-06446846 directly and selectively inhibits translation of PCSK9 by stalling the 80S ribosome in the proximity of codon region[1].

In Vitro

PF-06446846 inhibits the secretion of PCSK9 by Huh7 cells with an IC_{50} of 0.3 μM[1].PF-06446846 inhibits PCSK9(1–35)-luciferase expression with an IC_{50} of 2 μM[1].PF-06446846 (Compound 7f) shows rat bone marrow and human $CD34^+$ toxicity [2].

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

Cell Cytotoxicity Assay[2]

Cell Line:	Rat bone marrow lineage (−) cell and $CD34^+$ cell
Concentration:	0-20 μM
Incubation Time:	72 h
Result:	Showed cytotoxicity with IC_{50} values of 2.9 μM and 2.7 μM against rat Lin(−) and human $CD34^+$, respectively.

In Vivo

PF-06446846 reduces circulating PCSK9 and total plasma cholesterol levels in vivo without obvious toxicity[1].

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

Animal Model:	Male Sprague-Dawley (Crl:CD [SD] rats, five per group; 6–8 wk old at initiation of dosing)[1]
Dosage:	5, 15, and 50 mg/kg
Administration:	Oral administration, daily, 14 days
Result:	Reduced plasma PCSK9, total plasma cholesterol, and LDL-C (low-density lipoprotein cholesterol) in a dose-dependent manner without obvious toxicity.

CUSTOMER VALIDATION

- Protein Cell. 2021 Apr;12(4):240-260.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Nathanael G Lintner, et al. Selective stalling of human translation through small-molecule engagement of the ribosome nascent chain. PLoS Biol. 2018 Apr 17;16(4):e1002628.

[2]. Allyn T. Londregan, et al. Small Molecule Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors: Hit to Lead Optimization of Systemic Agents. J Med Chem. 2018 Jul 12;61(13):5704-5718.

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