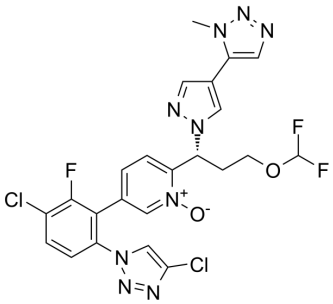
FXIa-IN-10

Cat. No.:	HY-151196
CAS No.:	2816108-08-2
Molecular Formula:	$C_{23}H_{18}Cl_2F_3N_9O_2$
Molecular Weight:	580.35
Target:	Others
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	FXIa-IN-10 (Compound 3f) is a potent activated factor XI (FXIa) inhibitor with an K_i of 0.17 nM. FXIa-IN-10 has good oral bioavailability[1].
IC_{50} & Target	K_i: 0.17 nM (FXIa)[1]

In Vivo

FXIa-IN-10 (Compound 3f) (1.7+2.0 and 8.5+10.0 (bolus + infusion) mg/kg; i.v.; twice) shows antithrombotic efficacy in a rabbit AV shunt thrombosis model[1].

FXIa-IN-10 (0-10 mg/kg; p.o.; once) demonstrates oral bioavailability in preclinical species (rat 36.4%, dog 80.5%, and monkey 43.0%)[1].

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

Animal Model:	Male New Zealand White (NZW) rabbits, AV shunt thrombosis model[1]
Dosage:	1.7+2.0 and 8.5+10.0 (bolus + infusion) mg/kg
Administration:	Intravenous injection, 20 min prior to and 40 min during the AV shunt
Result:	Reduced thrombus weights in a dose-dependent manner.

Animal Model:	Sprague-Dawley rats, Beagle dogs, Cynomolgus monkeys[1]
Dosage:	1, 2, 5 or 10 mg/kg
Administration:	Intravenous or oral administration (Pharmacokinetic Analysis)
Result:	Pharmacokinetic Profile of FXIa-IN-10 (Compound 3f) in Preclinical Species[a][1]

animal species	clearance (mL/min/kg)	$T_{1/2}$ (h)	V_{dss} (L/kg)	F%	AUC (iv) (μM•h)	AUC (po) (μM•h)	Dose iv/po (mpk)

rat	10.7 ± 1.8	1.4 ± 0.0	0.8 ± 0.1	36.4	5.5 ± 1.0	10.0 ± 2.4	2/10
monkey	25.6 ± 4.0	1.0 ± 0.4	1.5 ± 0.4	43.0	1.1 ± 0.2	2.5 ± 0.3	1/5

[a]Compound was dosed as a free base, vehicle for iv: 20% HPbCD and po: 10% ethanol; 70% PEG-400; 20% water. Data were derived from three animals per study.

REFERENCES

[1]. Xu G, et al. Discovery of Potent and Orally Bioavailable Pyridine N-Oxide-Based Factor XIa Inhibitors through Exploiting Nonclassical Interactions. J Med Chem. 2022 Aug 11;65(15):10419-10440.

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