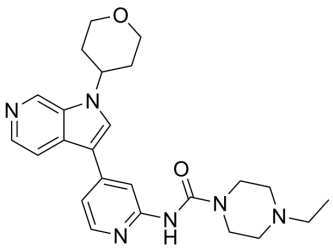
GNF2133

Cat. No.:	HY-142295
CAS No.:	2561414-56-8
Molecular Formula:	$C_{24}H_{30}N_6O_2$
Molecular Weight:	434.53
Target:	DYRK
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 4 mg/mL (9.21 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3013 mL	11.5067 mL	23.0134 mL
	5 mM	0.4603 mL	2.3013 mL	4.6027 mL
	10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

GNF2133 is a potent, selective and orally active DYRK1A inhibitor with IC_{50}s of 0.0062, >50 μM for DYRK1A and GSK3β, respectively. GNF2133 shows good proliferation potency and efficacy on rat and human primary β-cell. GNF2133 significantly improves glucose disposal capacity and increases insulin secretion. GNF2133 has the potential for the research of type 1 diabetes[1].

IC_{50} & Target	DYRK1A	GSK3β
	0.0062 μM (IC_{50})	>50 μM (IC_{50})

In Vivo

GNF2133 (30 mg/kg; p.o.) shows good oral absorption with oral bioavailability of 22.3%[1].

GNF2133 (30 mg/kg; p.o.; once a day for 5 days) shows the ability to proliferate β-cells in vivo[1].

GNF2133 (3, 10, 30 mg/kg) significantly improves glucose disposal capacity and increased insulin secretion in RIP-DTA mice [1].

Pharmacokinetic Parameters of GNF2133 in CD-1 mice[1].

	plasma (iv)	plasma (po)	pancreas (po)
CL (mL/min/kg)	23.5	/	/
$V_{ss\ (L/kg)}$	11	/	/
AUC (h·nM)	3268	10974	144420
C_{max}(nM)	1977	1675	13319
t_{max}<(h)	0.03	3.0	3.0
C_{last}(nM)	36.6	19	1324
$t_{1/2}$<(h)	6.6	3.4	6.6
F (%)	/	22.3	/

CD-1 mice; 30 mg/kg; p.o.[1].

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

Animal Model:	CD-1 mice[1]
Dosage:	30 mg/kg
Administration:	P.o.
Result:	Showed good oral absorption and moderate plasma exposure with oral bioavailability of 22.3%.

Animal Model:	Wistar Han rat[1]
Dosage:	30 mg/kg (0.5% methylcellulose + Tween-80)
Administration:	P.o.; once a day for 5 days
Result:	Increased cyclin D1 levels and overall cell density, and increased in cell proliferation marker Ki67 and insulin.

Animal Model:	Diphtheria toxin A (RIP-DTA) mice[1]
Dosage:	3, 10, 30 mg/kg (20 mg/kg doxycycline (Dox) for 5 days)
Administration:	P.o., once a day for 35 days
Result:	Significantly improves glucose disposal capacity and increased insulin secretion.

REFERENCES

[1]. Liu YA, et al. Selective DYRK1A Inhibitor for the Treatment of Type 1 Diabetes: Discovery of 6-Azaindole Derivative GNF2133. J Med Chem. 2020 Mar 26;63(6):2958-2973.

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