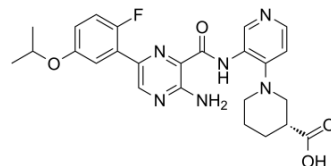


## GNF4877

<b>Cat. No.:</b>	HY-129492		
<b>CAS No.:</b>	2041073-22-5		
<b>Molecular Formula:</b>	C <sub>25</sub> H <sub>27</sub> FN <sub>6</sub> O <sub>4</sub>		
<b>Molecular Weight:</b>	494.52		
<b>Target:</b>	DYRK; GSK-3		
<b>Pathway:</b>	Protein Tyrosine Kinase/RTK; PI3K/Akt/mTOR; Stem Cell/Wnt		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 4.17 mg/mL (8.43 mM; Need ultrasonic and warming)

Concentration	Mass		
	1 mg	5 mg	10 mg
1 mM	2.0222 mL	10.1108 mL	20.2216 mL
5 mM	0.4044 mL	2.0222 mL	4.0443 mL
10 mM	---	---	---

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

### BIOLOGICAL ACTIVITY

#### Description

GNF4877 is a potent DYRK1A and GSK3β inhibitor with IC<sub>50</sub>s of 6 nM and 16 nM, respectively, which leads to blockade of nuclear factor of activated T-cells (NFATc) nuclear export and increased β-cell proliferation (EC<sub>50</sub> of 0.66 μM for mouse β (R7T1) cells)<sup>[1]</sup>.

#### IC<sub>50</sub> & Target

GSK3β	DYRK1A
16 nM (IC <sub>50</sub> )	6 nM (IC <sub>50</sub> )

#### In Vitro

High glucose concentrations and glucokinase activators (GKAs) increase Ca<sup>2+</sup> signalling in β-cells, and increase intracellular Ca<sup>2+</sup> leads to activation of calcineurin and nuclear translocation of NFATc proteins. Indeed, concentrations of GNF4877 ((0.1 μM, 0.3 μM) well below the EC<sub>50</sub> for β-cell proliferation are able to induce proliferation in the presence of high glucose or pharmacological activators of glucokinase. Finally, increasing intracellular Ca<sup>2+</sup> with glibenclamide (a sulfonylurea receptor 1 inhibitor) or Bay K8644 (an L-type Ca<sup>2+</sup> channel activator) show additive activity with GNF4877<sup>[1]</sup>.

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

#### In Vivo

GNF4877 (50 mg/kg; oral gavage; twice a day; for 15 days; double transgenic RIP-DTA male mice) treatment induces β-cell

proliferation, increases  $\beta$ -cell mass and insulin content, and improves glycaemic control<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Double transgenic RIP-DTA male mice (Tg (Ins 2-rtTA) 2 Efr Tg (teto-DTA) 1 Gfi/J) with Doxycycline (28.8 $\pm$ 2.4 g; 82 $\pm$ 2 days) <sup>[1]</sup>
Dosage:	50 mg/kg
Administration:	Oral gavage; twice a day; for 15 days
Result:	Induced $\beta$ -cell proliferation, increased $\beta$ -cell mass and insulin content, and improved glycaemic control.

## REFERENCES

[1]. Shen W, et al. Inhibition of DYRK1A and GSK3 $\beta$  induces human  $\beta$ -cell proliferation. Nat Commun. 2015 Oct 26;6:8372.

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

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