



Xcess Biosciences Inc.

7144 N Harlem Ave #169
Chicago, IL 60631 USA

<http://www.xcessbio.com>

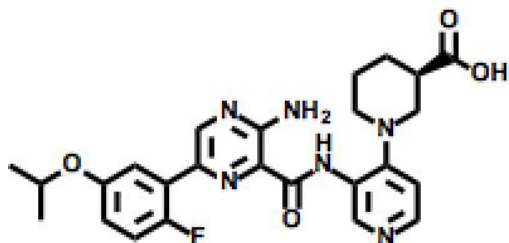
Toll free: 1-866-706-2330

Fax: 1-619- 810-0718

Email: info@xcessbio.com

β Cell Proliferation Inducer – GNF4877

Chemical Name: (R)-1-(3-(3-amino-6-(2-fluoro-5-isopropoxyphenyl)pyrazine-2-carboxamido)pyridin-4-yl)piperidine-3-carboxylic acid



Molecular Weight:	494.53
Formula:	C ₂₅ H ₂₇ FN ₆ O ₄
Purity:	≥ 98%
CAS#:	n/a
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

GNF4877 is a highly potent and selective small molecule that promotes pancreatic β cell proliferation in rodent (EC₅₀ ~0.66 μM) and human primary islets (EC₅₀ ~0.54 μM), better than its analog GNF7156. It acts most likely as a result of combined inhibition of DYRK1A and GSK3B. GNF4877-treated human islets retain functionality in vitro and after transplantation into diabetic mice. Oral dosing of GNF4877 in diabetic mice induces β-cell proliferation, increases β-cell mass and insulin content, and improves glycaemic control. Biochemical, genetic and cell biology data point to Dyrk1a as the key molecular target. GNF4877 and its analog GNF7156 are the good chemical tools to support the feasibility of treating diabetes with an oral therapy to restore β-cell mass, and highlights a tractable pathway for future drug discovery efforts.

How to Use:

In vitro: GNF4877 was used at 2 μM concentration in beta cell proliferation assays.

In vivo: GNF4877 was orally dosed to mice at 50 mg/kg twice a day for 14 days.

Reference:

1. Shen W, et al. Inhibition of DYRK1A and GSK3B induces human β-cell proliferation. (2015) Nat Commun. 6:8372.

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