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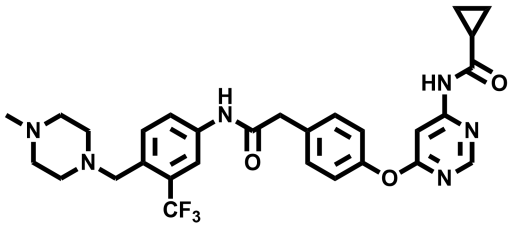
β Cell Proliferation Inducer – WS6

Chemical Name: N-(6-(4-(2-((4-((4-methylpiperazin-1-yl)methyl)-3-(trifluoromethyl)phenyl)amino)-2-oxoethyl)phenoxy)pyrimidin-4-yl)cyclopropanecarboxamide



Molecular Weight:	568.59
Formula:	$C_{29}H_{31}F_3N_6O_3$
Purity:	≥ 98%
CAS#:	1421227-53-3
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

WS6 is a highly potent and selective small molecule that promotes pancreatic β cell proliferation in rodent and human primary islets, identified by a high-throughput, cell-based screening using rodent pancreatic β cells. It can induce proliferation of mouse R7T1 cells with an EC_{50} ~0.28 μM, and induce up to 4% of rat β cells and 3% of human β cells to proliferate, with a similar EC_{50} of 0.4 μM. WS6 induces proliferation of primary rat and human β cells in intact islet format at 0.2-1.0 μM concentration. In the RIP-DTA mouse model of β cell ablation, WS6 demonstrated excellent in vivo effect on normalizing blood glucose and inducing concomitant increases in β cell proliferation and β cell number. Affinity pulldown and kinase profiling studies implicate Erb3 binding protein-1 and the IκB kinase pathway in the mechanism of action of WS6.

How to Use:

In vitro: WS6 was used at 0.5-1 μM concentration in beta cell proliferation assays.

In vivo: WS6 was intraperitoneally (IP) dosed to mice 5 mg/kg every other day.

Reference:

1. Shen W, et al. Small-Molecule Inducer of β Cell Proliferation Identified by High-Throughput Screening. (2013) J Am Chem Soc. In press.