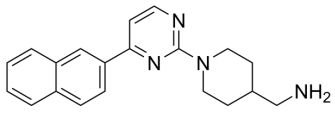
WAY-262611

Cat. No.:	HY-11035
CAS No.:	1123231-07-1
Molecular Formula:	$C_{20}H_{22}N_4$
Molecular Weight:	318.42
Target:	β-catenin
Pathway:	Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 42 mg/mL (131.90 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1405 mL	15.7025 mL	31.4051 mL
	5 mM	0.6281 mL	3.1405 mL	6.2810 mL
	10 mM	0.3141 mL	1.5703 mL	3.1405 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (5.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (5.24 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (5.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

WAY-262611 is a wingless β-Catenin agonist that increases bone formation rate with an EC_{50} of 0.63 μM in TCF-Luciferase assay. WAY-262611 is also a Dkk1 inhibitor.

IC_{50} & Target

EC50: 0.63 μM (β-Catenin)[1]

In Vitro

WAY-262611 has the most potent activity in the primary assay, low kinase inhibition potential, and high solubility[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	WAY-262611 has excellent pharmacokinetic properties and shows a dose dependent increase in the trabecular bone formation rate in ovariectomized rats following oral administration. Calvariae from wt mice treated with WAY-262611 shows statistically increased BFR, while similarly treated KO animals are no different from control. This indicates that WAY-262611 is acting via the Wnt β-catenin pathway and most likely through inhibition of Dkk-1[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats: WAY-262611 is dissolved in DMSO and diluted with saline for iv (Rats). WAY-262611 is prepared in 0.5% methylcellulose/2% Tween-80 for po OVX rats14 are treated orally with 5 (po, vehicle=0.5% methylcellulose/2% Tween-80, qd, 28 days) at four doses. Trabecular bone formation rate (BFR) in the tibia is established in all dose groups at the end of the in-life portion of the study. A clear dose response and activity as low as 0.3 mg/kg/day are observed[1]. Mice: To confirm activity via the Wnt pathway, the calvariae of wild type (wt) and Dkk-1 knockout (KO) mice are treated with 5 once a day for 7 days (DMSO solution, sc injection). The KO animals are not expected to respond because of the inherent inability to inhibit a missing target protein, while wild type animals with fully expressed Dkk-1 are expected to show a pharmacological response [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Biotechnol. 2020 Sep;38(9):1087-1096.
- Glia. 2023 Jan 8.
- Bone. 2022 Jun 7;116456.
- Int J Biochem Cell Biol. 2020 Apr;121:105703.
- J Cell Sci. 2019 May 16;132(10):jcs228478.

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REFERENCES

[1]. Pelletier JC, et al. (1-(4-(Naphthalen-2-yl)pyrimidin-2-yl)piperidin-4-yl)methanamine: a wingless beta-catenin agonist that increases bone formation rate. J Med Chem. 2009 Nov 26;52(22):6962-5.

[2]. L Enochson, et al. GDF5 reduces MMP13 expression in human chondrocytes via DKK1 mediated canonical Wnt signaling inhibition. Osteoarthritis Cartilage. 2014 Apr;22(4):566-77.

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