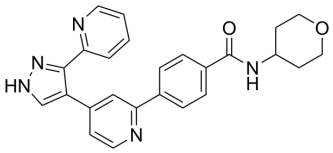
GW788388

Cat. No.:	HY-10326
CAS No.:	452342-67-5
Molecular Formula:	$C_{25}H_{23}N_5O_2$
Molecular Weight:	425.48
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
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 : 25 mg/mL (58.76 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3503 mL	11.7514 mL	23.5029 mL
	5 mM	0.4701 mL	2.3503 mL	4.7006 mL
	10 mM	0.2350 mL	1.1751 mL	2.3503 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: ≥ 2.5 mg/mL (5.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW788388 is a potent and selective inhibitor of ALK5 with IC_{50} of 18 nM, and also inhibits TGF-β type II receptor and activin type II receptor activities, without inhibiting BMP type II receptor.

IC_{50} & Target

IC50: 18 nM (ALK5)

In Vivo

GW788388 given orally for 5 weeks significantly reduces renal fibrosis and decreased the mRNA levels of key mediators of extracellular matrix deposition in kidneys in db/db mice[1]. GW788388 (50 mg/kg/day, p.o.) significantly attenuates systolic

dysfunction in the MI animals, together with the attenuation of the activated (phosphorylated) Smad2 ($P < 0.01$), α-smooth muscle actin ($P < 0.001$), and collagen I ($P < 0.05$) in the noninfarct zone of MI rats[2]. GW788388 reduces the expression of collagen IA1 by 80% at a dose of 1 mg/kg twice a day (b.i.d.). GW788388 significantly reduces the expression of collagen IA1 mRNA when administered orally at 10 mg/kg once a day (u.i.d.) in a model of puromycin aminonucleoside-induced renal fibrosis[3].

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

PROTOCOL

Animal Administration [2]

One week postsurgery, sham-operated (N=6) and infarcted animals (N=10) are randomized to treatment with the ALK5 inhibitor GW788388 (GSK) at a dosage of 50 mg/kg/day by gavage, which has been shown to significantly attenuate collagen overexpression in a rodent model of dimethylnitrosamine-induced liver disease. Untreated rats, that is, sham-operated (N=9) and MI animals (N=15), are gavaged with vehicle (1% carboxymethyl cellulose solution). Four animals with < 25% infarct size as determined postmortem by histology are excluded from further analyses.

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

CUSTOMER VALIDATION

- Cell Prolif. 2021 Jan;54(1):e12933.
- Int J Mol Sci. 2022, 23(20), 12219.
- J Funct Foods. December 2021, 104758.
- Org Lett. 2020 Aug 7;22(15):5726-5730.
- Org Lett. 2017 Jan 6;19(1):286-289.

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REFERENCES

[1]. Petersen M, et al. Oral administration of GW788388, an inhibitor of TGF-beta type I and II receptor kinases, decreases renal fibrosis. Kidney Int, 2008, 73(6), 705-715.

[2]. Tan SM, et al. Targeted inhibition of activin receptor-like kinase 5 signaling attenuates cardiac dysfunction following myocardial infarction. Am J Physiol Heart Circ Physiol, 2010, 298(5), H1415-1425.

[3]. Gellibert F, et al. Discovery of 4-{4-[3-(pyridin-2-yl)-1H-pyrazol-4-yl]pyridin-2-yl}-N-(tetrahydro-2H- pyran-4-yl)benzamide (GW788388): a potent, selective, and orally active transforming growth factor-beta type I receptor inhibitor. J Med Chem. 2006, 49

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