

Product Data Sheet

Product Name: GW788388

Cat. No.: GC11878

Chemical Properties

Cas. No. 452342-67-5

Chemical Name N-(oxan-4-yl)-4-[4-(5-pyridin-2-yl-1H-pyrazol-4-yl)pyridin-2-yl]benzamide

SMILES C1COCCC1NC(=O)C2=CC=C(C=C2)C3=NC=CC(=C3)C4=C(NN=C4)C5=CC=CC=N5

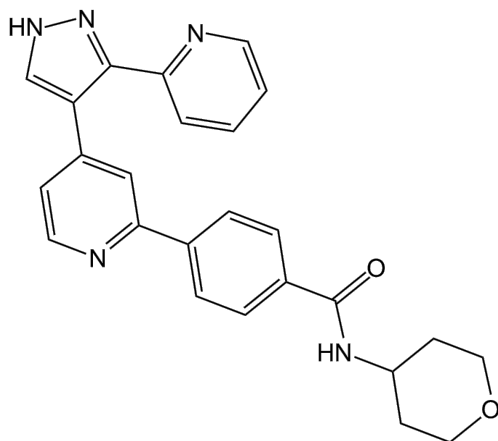
Formula $C_{25}H_{23}N_5O_2$ M.Wt 425.49

Solubility $\geq 21.25\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines C2C12 skeletal muscle myoblasts (murine myoblast cell line)

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

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Preparation Method C2C12 cells were plated on gelatin-coated coverslips and maintained in growth medium (DMEM with 10% FBS). For differentiation, cells were switched to differentiation medium (DMEM with 2% horse serum) and treated with GW788388 (1–10 μ M) for up to 6 days.

Reaction Conditions 1–10 μ M; 2–6days

Applications GW788388 significantly enhanced myogenic differentiation, increasing the fusion index and mean nuclei count. GW788388 also suppressed TGF- β -induced epithelial-mesenchymal transition (EMT) by restoring E-cadherin expression and reducing fibrotic markers in renal epithelial cells.

Animal experiment [2]:

Animal models db/db mice (model of type 2 diabetic nephropathy)

Preparation Method Six-month-old male db/db mice with established diabetic nephropathy were orally administered GW788388 (2mg/kg/day) mixed with powdered chow for 5 weeks. Urine was collected via metabolic cages, and kidneys were harvested for analysis.

Dosage form 2mg/kg/day; p.o.

Applications GW788388 significantly reduced renal fibrosis (collagen deposition) and glomerulopathy, and decreased mRNA levels of fibrotic markers in kidney tissue.

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References:

- [1] Levolger S, Wiemer EAC, van Vugt JLA, et al. Inhibition of activin-like kinase 4/5 attenuates cancer cachexia associated muscle wasting. *Sci Rep*. 2019 Jul 8;9(1):9826.
- [2] Petersen M, Thorikay M, Deckers M, et al. Oral administration of GW788388, an inhibitor of TGF-beta type I and II receptor kinases, decreases renal fibrosis. *Kidney Int*. 2008 Mar;73(6):705-15.

Background

GW788388 is a potent and selective ALK5 inhibitor ($IC_{50}=18nM$) [1]. GW788388 also inhibits TGF- β type II receptor ($IC_{50}=93nM$) and activin type II receptor activity, but does not inhibit BMP type II receptors[2]. GW788388 can inhibit epithelial-mesenchymal transition in cells [3], and attenuate left ventricular remodeling and cardiac dysfunction[4].

In vitro, treatment of dengue virus type 2 (DENV-2)-infected macrophages with GW788388 (0.5–2 μM) for 48 hours significantly reduced Smad2 protein phosphorylation levels and decreased TGF- β 1 secretion by inhibiting TGF- β type I/II receptors. This enhanced the macrophages' ability to clear the virus, resulting in a dose-dependent reduction in viral load[5]. Treatment of C2C12 skeletal muscle cells with GW788388 (1–10 μM) for 6 days significantly increased the myotube differentiation index and mean nuclear number, enhancing myogenesis[6].

In vivo, pretreatment of male C57BL/6J mice with GW788388 (1mg/kg, intraperitoneal injection) 1 hour before acetaminophen (600mg/kg) injection significantly alleviated acetaminophen-induced liver necrosis and reduced serum ALT and AST levels. GW788388 also decreased the expression of pro-inflammatory cytokines IL-1 β and TNF α , reduced phosphorylated JNK levels and DNA fragmentation in the liver, and promoted hepatocyte proliferation[7]. Oral administration of GW788388 (2mg/kg/day) for 5 weeks to 6-month-old db/db mice significantly ameliorated diabetic nephropathy-related glomerulosclerosis and renal fibrosis[8].

References:

- [1] Ferreira RR, Abreu RDS, Vilar-Pereira G, et al. TGF- β inhibitor therapy decreases fibrosis and stimulates cardiac improvement in a pre-clinical study of chronic Chagas' heart disease. *PLoS Negl Trop Dis*. 2019 Jul 31;13(7):e0007602.
- [2] Gellibert F, de Gouville AC, Woolven J, et al. Discovery of 4-{4-[3-(pyridin-2-yl)-1H-pyrazol-4-

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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 Apr 6;49(7):2210-21.

[3] Lho Y, Do JY, Heo JY, et al. Effects of TGF- β 1 Receptor Inhibitor GW788388 on the Epithelial to Mesenchymal Transition of Peritoneal Mesothelial Cells. Int J Mol Sci. 2021 Apr 29;22(9):4739.

[4] Tan SM, Zhang Y, Connelly KA, et al. Targeted inhibition of activin receptor-like kinase 5 signaling attenuates cardiac dysfunction following myocardial infarction. Am J Physiol Heart Circ Physiol. 2010 May;298(5):H1415-25.

[5] Teixeira GS, Andrade AA, Torres LR, et al. Suppression of TGF- β /Smad2 signaling by GW788388 enhances DENV-2 clearance in macrophages. J Med Virol. 2022 Sep;94(9):4359-4368.

[6] Levolger S, Wiemer EAC, van Vugt JLA, et al. Inhibition of activin-like kinase 4/5 attenuates cancer cachexia associated muscle wasting. Sci Rep. 2019 Jul 8;9(1):9826.

[7] McMillin M, Grant S, Frampton G, et al. The TGF β 1 Receptor Antagonist GW788388 Reduces JNK Activation and Protects Against Acetaminophen Hepatotoxicity in Mice. Toxicol Sci. 2019 May 1;170(2):549-561.

[8] Petersen M, Thorikay M, Deckers M, et al. Oral administration of GW788388, an inhibitor of TGF-beta type I and II receptor kinases, decreases renal fibrosis. Kidney Int. 2008 Mar;73(6):705-15.

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