# Data Sheet

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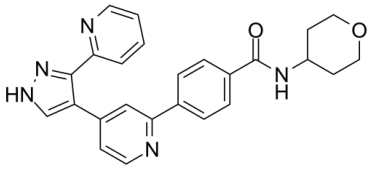
| **Product Name:** | GW788388 |
| **Cat. No.:** | CS-0254 |
| **CAS No.:** | 452342-67-5 |
| **Molecular Formula:** | C25H23N5O2 |
| **Molecular Weight:** | 425.48 |
| **Target:** | TGF-β Receptor |
| **Pathway:** | TGF-beta/Smad |
| **Solubility:** | DMSO : ≥ 48 mg/mL (112.81 mM) |



## BIOLOGICAL ACTIVITY:

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. IC50 & 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].

## PROTOCOL (Extracted from published papers and Only for reference)

**Animal Administration:** GW788388 is formulated in 1% carboxymethyl cellulose solution.[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.

## 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

## CAIndexNames:

Benzamide, 4-[4-[3-(2-pyridinyl)-1H-pyrazol-4-yl]-2-pyridinyl]-N-(tetrahydro-2H-pyran-4-yl)-

## SMILES:

O=C(C1=CC=C(C=C1)C2=NC=CC(C3=CNN=C3C4=NC=CC=C4)=C2)NC5CCOCC5

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

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