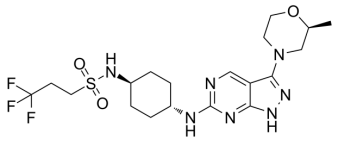
GSK3186899

Cat. No.:	HY-112622
CAS No.:	1972617-87-0
Molecular Formula:	$C_{19}H_{28}F_3N_7O_3S$
Molecular Weight:	491.53
Target:	Parasite
Pathway:	Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (508.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0345 mL	10.1723 mL	20.3446 mL
	5 mM	0.4069 mL	2.0345 mL	4.0689 mL
	10 mM	0.2034 mL	1.0172 mL	2.0345 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: ≥ 2.08 mg/mL (4.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.23 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK3186899 (DDD-853651) is an inhibitor of cdc-2-related kinase 12 (CRK12), with an EC_{50} of 1.4 μM for L. donovani in an intra-macrophage assay.

IC_{50} & Target

CRK12[1].

In Vitro

GSK3186899 (Compound 7) is active against L. donovani in an intra-macrophage assay with an EC_{50} value of 1.4 μM, and shows good selectivity against mammalian THP-1 host cells (EC_{50} value>50 μM). This is not as potent as reported data for

	amphotericin B (EC_{50} value of 0.07 μM in the intra-macrophage assay), but is comparable to the clinically used drugs miltefosine and paromomycin (EC_{50} values of 0.9 μM and 6.6 μM, respectively). GSK3186899 is also active in cidal axenic amastigote assay (EC_{50} value of 0.1 μM). At a concentration of 0.2 μM, GSK3186899 is cytocidal at 96 h; increasing the concentration to 1.8 μM reduced this time to 48 h. GSK3186899 demonstrates a less than 10-fold variation in potency against a panel of Leishmania-derived lines. GSK3186899 is also more active in a panel of Leishmania lines using human peripheral blood mononuclear cells as the host cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In the mouse model of infection, GSK3186899 demonstrates comparable activity to the front-line drug miltefosine, reducing parasite levels by 99% when dosed orally twice a day for 10 days at 25 mg/kg. The efficacy of treatment is dependent on dose, frequency, and duration (10 days better than 5). The non-clinical safety data for GSK3186899 suggests a suitable therapeutic window for progression into regulatory preclinical studies. Non-GLP preclinical assessment of cardiovascular effects and genotoxicity does not reveal any issues that would prevent further development. In addition, there are no notable adverse effects in a rat seven-day repeat-dose oral toxicity study with respect to clinical chemistry and histopathology at all doses tested. Both the in vivo efficacy and safety profile of GSK3186899 support progression to definitive safety studies[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wyllie S, et al. Cyclin-dependent kinase 12 is a drug target for visceral leishmaniasis. Nature. 2018 Aug;560(7717):192-197.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA