

Product Data Sheet

Product Name: GSK2982772

Cat. No.: GC19182

Chemical Properties

Cas. No. 1622848-92-3

SMILES O=C(C1=NC(CC2=CC=CC=C2)=NN1)N[C@H]3COC4=CC=CC=C4N(C)C3=O

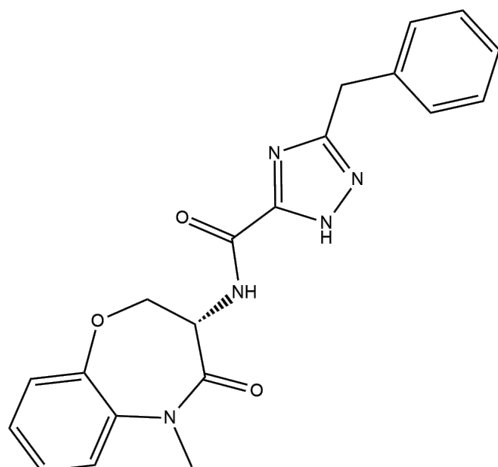
Formula C20H19N5O3 M.Wt 377.4

Solubility DMSO : ≥ 100 mg/mL (264.97 mM) 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

Animal experiment:

Mice: A total of 7 mice per dose group are orally predosed with saline or GSK2982772 at doses of 3, 10, and 50 mg/kg 15 min before i.v. administration of mouse TNF (30 µg/ mouse). Temperature loss in the mice is measured by a rectal probe. The study is terminated after 6 h when the control group lost 7 °C[1].

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:

[1]. Harris PA, et al. Discovery of a First-in-Class Receptor Interacting Protein 1 (RIP1) Kinase Specific Clinical Candidate (GSK2982772) for the Treatment of Inflammatory Diseases. J Med Chem. 2017 Feb 23;60(4):1247-1261.

Background

GSK2982772 is a potent and ATP competitive RIP1 inhibitor with an IC₅₀ of 16 nM.

GSK2982772 shows more than 1,000-fold selectivity for ERK5 over a panel of over 339 kinases at 10 uM. In stimulated cellular systems, GSK2982772 is also able to reduce spontaneous production of cytokines (IL-1 β and IL-6) in a concentration-dependent fashion from ulcerative colitis explant tissue in overnight incubations. GSK2982772 produces a weak concentration dependent inhibition of hERG in human embryonic kidney (HEK-293) cells, with an estimated IC₅₀ of 195 uM, and also shows a weak activation of the human Pregnane X receptor (hPXR) with an EC₅₀ of 13 uM[1].

GSK2982772 is dosed orally 15 min prior to TNF and shows 68, 80, and 87% protection from temperature loss over 6 h, at doses of 3, 10, and 50 mg/kg, respectively. In the corresponding TNF/zVAD model, GSK2982772 shows 13, 63, and 93% protection from temperature loss over 3 h. GSK2982772 displays a good free fraction in blood in rats (4.2%), dogs (11%), cynomolgus monkeys (11%), and humans (7.4%). The inhibitor has a good pharmacokinetic profile across both rats and monkeys. GSK2982772 distributes into a range of tissues including the colon, liver, kidney, and heart at concentrations comparable to those of blood. However, GSK2982772 has low brain penetration in rat (4%) despite possessing good cell permeability (21×10^{-6} cm/s)[1].

References:

[1]. Harris PA, et al. Discovery of a First-in-Class Receptor Interacting Protein 1 (RIP1) Kinase Specific Clinical Candidate (GSK2982772) for the Treatment of Inflammatory Diseases. J Med Chem. 2017 Feb 23;60(4):1247-1261.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA