

Product Data Sheet

Product Name: GSK2798745

Cat. No.: GC39387

Chemical Properties

Cas. No. 1419609-94-1

SMILES N#CC1=CC=C2N=CN(C[C@](CCC3)(C)C[C@@]43CN(C5=NC=C(C(C)(O)C)N=C5)C(O4)=O)C2=C1

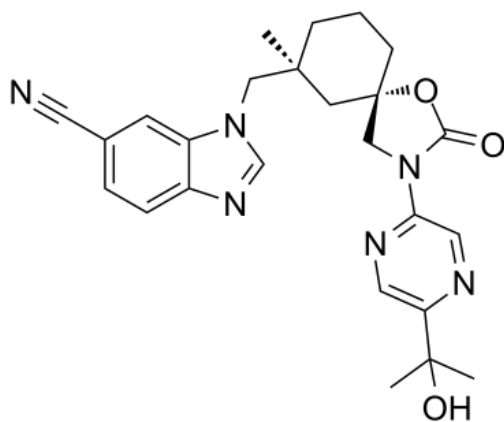
Formula $C_{25}H_{28}N_6O_3$ M.Wt 460.53

Solubility DMSO: 250 mg/mL (542.85 mM) Storage Store at -20°C, protect from light

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 293T cells transfected with wild-type or mutant TRPV4 plasmids

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

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Preparation Method	HEK293 cells were transiently transfected with human TRPV4 WT or mutation constructs and pretreated with a range of concentrations (0.3-100nM) of GSK2798745 for 1 hour. Calcium flux was measured using a FLIPR-based calcium flux assay.
Reaction Conditions	0.3-100nM; 1h
Applications	The activation activity of the mutant channels was inhibited by GSK2798745 in a dose-dependent manner. Compared with cells expressing wild-type TRPV4, all mutant channels had higher intracellular calcium levels, and these levels were inhibited by GSK2798745.

Animal experiment [1]:

Animal models	<i>Col2a1-Cre/Trpv4^{p.R594H}</i> mice
Preparation Method	Mutant mice were treated for 17 days by twice daily i.p. injections of GSK2798745. The treated mice were then subjected to radiological and morphological examinations.
Dosage form	10mg/kg; twice daily; 14-17d; i.p.
Applications	GSK2798745 inhibitor improved the qualitative appearance of the vertebral bodies and proximal tibiae. Proliferating and hypertrophic chondrocytes were morphologically normal in the treated mice and normally expressed <i>Sox9</i> and <i>Col10a1</i> , respectively.

References:

[1] Nevarez L, Ismaili TK, Zieba J, et al. Small molecule inhibition rescues the skeletal dysplasia phenotype of *Trpv4* mutant mice. *JCI Insight*. 2026;11(2):e182439.

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GSK2798745, a clinical candidate, was identified as an inhibitor of the transient receptor potential vanilloid 4 (TRPV4) ion channel with IC₅₀ of 1.8 and 1.6nM for hTRPV4 and rTRPV4, respectively [1].

In vitro, GSK2798745 (0.3-100nM) inhibited TRPV4 channel activation in a dose-dependent manner following 1h treatment in 293T cells transfected with wild-type or mutant TRPV4[2].

In vivo, Treatment with GSK2798745 at a dose of 10mg/kg by twice daily intraperitoneal injections for 17 days can treat skeletal abnormalities caused by persistent activity of the mutant channel in *Col2a1-Cre/Trpv4^{p.R594H}* mice[2].

References:

[1] Brooks CA, Barton LS, Behm DJ, et al. Discovery of GSK2798745: A Clinical Candidate for Inhibition of Transient Receptor Potential Vanilloid 4 (TRPV4). *ACS Med Chem Lett.* 2019;10(8):1228-1233.

[2] Nevarez L, Ismaili TK, Zieba J, et al. Small molecule inhibition rescues the skeletal dysplasia phenotype of *Trpv4* mutant mice. *JCI Insight.* 2026;11(2):e182439.

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