GSK1838705A

Cat. No.: HY-13020

CAS No.: 1116235-97-2

Molecular Formula: $C_{27}H_{29}FN_8O_3$

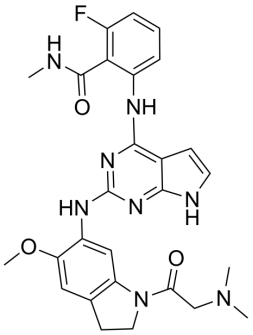
Molecular Weight: 532.57

Target: Anaplastic lymphoma kinase (ALK); IGF-1R; Insulin Receptor

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (187.77 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8777 mL	9.3884 mL	18.7769 mL
5 mM	0.3755 mL	1.8777 mL	3.7554 mL
10 mM	0.1878 mL	0.9388 mL	1.8777 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: 3 mg/mL (5.63 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GSK1838705A is a potent and reversible IGF-IR and the insulin receptor inhibitor with IC_{50}s of 2.0 and 1.6 nM, respectively. It also inhibits ALK with an IC_{50} of 0.5 nM.

IC_{50} & Target

IC50: 2.0 nM (IGF-IR), 1.6 nM (insulin receptor), 0.5 nM (ALK)[1]

In Vitro

In cellular phosphorylation assays, GSK1838705A potently inhibits IGF-IR and insulin receptor phosphorylation with IC_{50}s of 85 and 79 nM, respectively. $^{app}K_i$ values are 0.7 nM for IGF-IR and 1.1 nM for insulin receptor using the filter binding assay. GSK1838705A inhibits the proliferation in a panel of cell lines derived from solid and hematologic tumors. The EC_{50}s of GSK1838705A range from 20 nM to >8 μM, but are <1 μM in most multiple myeloma and Ewing's sarcoma cell lines[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	GSK1838705A shows robust antitumor activity in animal xenograft models. Tumor types likely to respond to GSK1838705A include multiple myeloma and Ewing's sarcoma, as well as ALK-driven tumors (e.g., ALCL, NSCLC, and neuroblastoma). A single oral dose of GSK1838705A at 0.1 and 0.3 mg/kg results in 35% and 65% inhibition of IGF-IR phosphorylation, respectively, whereas doses ≥1 mg/kg results in complete inhibition of ligand-induced IGF-IR phosphorylation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Baculovirus-expressed glutathione S-transferase–tagged proteins encoding the intracellular domain of IGF-IR (amino acids 957–1367) and IR (amino acids 979–1382) are used for determinations of IC_{50}s by a homogeneous time-resolved fluorescence assay. A filter binding assay is used for $^{app}K_i$ determinations using activated IGF-IR and IR kinases. Expanded kinase-selectivity profiling of GSK1838705A is carried out by screening the compound in the KinaseProfiler panel[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Cells are seeded in 96-well dishes, incubated overnight at 37°C, and treated with DMSO or GSK1838705A for 72 h. For the NIH-3T3/LISN proliferation assays, cells are seeded on collagen-coated 96-well tissue culture plates and allowed to adhere for 24 h. The medium is replaced with serum-free medium and the cells are treated with GSK1838705A for 2 h. Cells are incubated for 72 h after addition of IGF-I (30 ng/mL). Cell proliferation is quantified using the CellTiter-Glo Luminescent Cell Viability Assay. IC_{50}s are determined from cytotoxicity curves using a four-parameter curve fit software package[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Exponentially growing cells are implanted s.c. into the right flank of 8- to 12-wk-old female nu/nu CD-1 or SCID mice. Mice are dosed p.o. with the formulating vehicle or GSK1838705A. Mice are weighed and tumors measured by calipers twice weekly. Tumor volumes are calculated[1] MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2021 Jul 16;12(1):4360.
- ACS Chem Biol. 2017 May 19;12(5):1245-1256.
- Biochem Biophys Res Commun. 2018 Sep 3;503(1):71-78.
- Fundam Clin Pharmacol. 2020 Oct;34(5):571-580.

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REFERENCES

[1]. Sabbatini P, et al. GSK1838705A inhibits the insulin-like growth factor-1 receptor and anaplastic lymphoma kinase and shows antitumor activity in experimental models of human cancers.Mol Cancer Ther. 2009 Oct;8(10):2811-20.

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

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