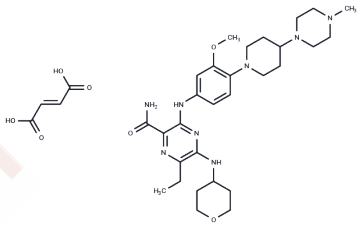
Data Sheet (Cat.No.T71973)

TargetMol

Gilteritinib hemifumarate

Chemical Properties



CAS No. : 1254053-84-3

Formula: C29H44N8O3.1/2C4H4O4

Molecular Weight: 610.75

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Gilteritinib hemifumarate (ASP2215 hemifumarate) is a potent ATP-competitive dual FLT3 (IC50: 0.29 nM) and AXL (IC50: 0.73 nM) inhibitor for the treatment of relapsed or refractory FLT3 mutant AML.
Targets(IC50)	FLT,TAM Receptor
In vitro	Gilteritinib (ASP2215) inhibits FLT3, leukocyte tyrosine kinase (LTK), anaplastic lymphoma kinase (ALK), and AXL kinases by over 50% at 1 nM, with an IC50 value of 0.29 nM for FLT3. It is approximately 800-fold more potent for FLT3 inhibition than for c-KIT [1]. In addition, Gilteritinib inhibits the activity of eight out of 78 tested kinases by over 50% at concentrations of either 1 nM (FLT3, LTK, ALK, and AXL) or 5 nM (TRKA, ROS, RET, and MER). The IC50s are 0.29 nM for FLT3 and 0.73 nM for AXL. The antiproliferative activity of Gilteritinib is evaluated against MV4-11 and MOLM-13 cells, which endogenously express FLT3-ITD. After 5 days of treatment, Gilteritinib inhibits the growth of MV4-11 and MOLM-13 cells with mean IC50s of 0.92 nM (95% CI: 0.23-3.6 nM) and 2.9 nM (95% CI: 1.4-5.8 nM), respectively. Growth suppression of MV4-11 cells is accompanied by the inhibition of FLT3 phosphorylation. Relative to vehicle control cells, phosphorylated FLT3 levels are 57%, 8%, and 1% after 2 h of treatment with 0.1 nM, 1 nM, and 10 nM Gilteritinib, respectively. Additionally, doses as low as 0.1 nM or 1 nM result in the suppression of phosphorylated ERK, STAT5, and AKT, all downstream targets of FLT3 activation. To investigate the effects of Gilteritinib on AXL inhibition, MV4-11 cells expressing exogenous AXL are treated with Gilteritinib. At concentrations of 1 nM, 10 nM, and 100 nM for 4 h, Gilteritinib treatment decreases phosphorylated AXL levels by 38%, 29%, and 22%, respectively[2].
In vivo	With oral administration of Gilteritinib (ASP2215) at 10 mg/kg for 4 days in MV4-11 xenografted mice, the concentration of Gilteritinib in tumors is more than 20-fold higher than that in plasma. Treatment with Gilteritinib for 28 days results in dose-dependent inhibition of MV4-11 tumor growth, inducing complete tumor regression at doses higher than 6 mg/kg. Additionally, Gilteritinib decreases tumor burden in the bone marrow and prolongs the survival of mice intravenously transplanted with MV4-11 cells[1].

Solubility Information

Solubility	DMSO: 3 mg/mL (4.91 mM),Sonication is recommended. H2O: 1 mg/mL (1.64 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6373 mL	8.1867 mL	16.3733 mL
5 mM	0.3275 mL	1.6373 mL	3.2747 mL
10 mM	0.1637 mL	0.8187 mL	1.6373 mL
50 mM	0.0327 mL	0.1637 mL	0.3275 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Yoko Ueno,et al. ASP2215, a novel FLT3/AXL inhibitor: Preclinical evaluation in combination with cytarabine and anthracycline in acute myeloid leukemia (AML).Journal of Clinical Oncology 2014 32:15_suppl, 7071