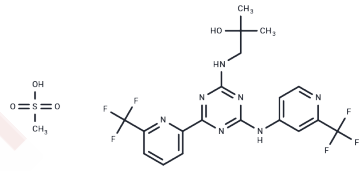
Data Sheet (Cat.No.T2346L)

TargetMol

Enasidenib mesylate

Chemical Properties



CAS No. : 1650550-25-6

Formula: C20H21F6N7O4S

Molecular Weight: 569.48

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	Enasidenib mesylate (AG-221 mesylate) is a potent and selective IDH2 mutase inhibitor that promotes differentiation of leukemia myeloid cells for the treatment of acute myeloid leukemia.
Targets(IC50)	Dehydrogenase,Isocitrate Dehydrogenase (IDH)
In vitro	Reversing the effects of mutant IDH2 on DNA methylation in mutant stem/progenitor cells, Enasidenib mesylate (AG-221) induces differentiation and impairs self-renewal of IDH2-mutant leukemia cells. Simultaneous inhibition of Flt3ITD further enhances these effects. In the context of Enasidenib mesylate (AG-221) therapy, leukemic cells undergo differentiation, resulting in an increased CD11b+ population and a decreased c-Kit+ population in the peripheral blood at 2 weeks[2].
In vivo	In an IDH2-mutant acute myeloid leukemia (AML) primary xenograft mouse model, treatment with Enasidenib mesylate (AG-221) significantly improves survival[1]. Acting as a mutant IDH2 inhibitor, enasidenib remodels the epigenetic state of IDH2-mutant cells, inducing alterations in self-renewal/differentiation in an IDH2-mutant AML model in vivo. Enasidenib mesylate treatment at doses of 10 mg/kg or 100 mg/kg bid results in a substantial reduction in 2-HG levels in vivo, reaching 96.7% below pre-treatment levels.Furthermore, Enasidenib mesylate treatment restores megakaryocyte-erythroid progenitor (MEP) differentiation, which is suppressed by mutant IDH2 expression, as indicated by a mean MEP% increase from 39% in the vehicle group to 50% in the AG-221 group. The therapy also reverses the effects of mutant IDH2 on DNA methylation, with a significant reduction observed in DNA methylation, affecting 180 genes with 20 or more hypomethylated differentially methylated cytosines (DMCs) following treatment. Enasidenib mesylate therapy, particularly at a dose of 100 mg/kg bid, applied to mice engrafted with Mx1-Cre IDH2R140QFlt3ITD AML cells, markedly reduces 2-hydroxyglutarate (2-HG) levels, consistent with on-target inhibition. Enasidenib effectively inhibits the production of 2-HG mediated by mutant IDH2[2].

Solubility Information

Solubility	DMSO: 80 mg/mL (140.48 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (5.79 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.756 mL	8.7799 mL	17.5599 mL
5 mM	0.3512 mL	1.756 mL	3.512 mL
10 mM	0.1756 mL	0.878 mL	1.756 mL
50 mM	0.0351 mL	0.1756 mL	0.3512 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

Alan H. Shih, et al. AG-221, a Small Molecule Mutant IDH2 Inhibitor, Remodels the Epigenetic State of IDH2-Mutant Cells and Induces Alterations in Self-Renewal/Differentiation in IDH2-Mutant AML Model in Vivo. Blood 2014 124: 437.

Exploring the Pathway: IDH Mutations and Metabolic Dysregulation in Cancer Cells: A Novel Therapeutic Target. MAY 29, 2015

Tong Z, Atsriku C, Yerramilli U, Wang X, Li Y, Reyes J, Fan B, Yang H, Hoffmann M, Surapaneni S. Absorption, distribution, metabolism and excretion of an isocitrate dehydrogenase-2 inhibitor enasidenib in rats and humans. Xenobiotica. 2018 Jan 22:1-11. doi: 10.1080/00498254.2018.1425511. [Epub ahead of print] PubMed PMID: 29320949.

Perl AE. The role of targeted therapy in the management of patients with AML. Blood Adv. 2017 Nov 14;1(24): 2281-2294. doi: 10.1182/bloodadvances.2017009829. eCollection 2017 Nov 14. Review. PubMed PMID: 29296877; PubMed Central PMCID: PMC5737125.