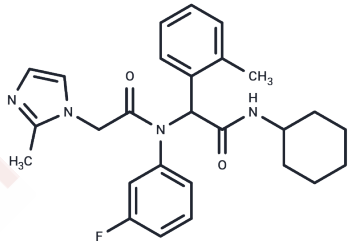
Data Sheet (Cat.No.T2104)

TargetMol

AGI-5198

Chemical Properties



CAS No. : 1355326-35-0

Formula: C27H31FN4O2

Molecular Weight: 462.56

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	AGI-5198 (IDH-C35) is a potent and selective inhibitor of IDH1 R132H and R132C mutants, with IC50 values of 0.07 μM and 0.16 μM, respectively.
Targets(IC50)	Dehydrogenase,Isocitrate Dehydrogenase (IDH)
In vitro	AGI-5198 showed some anti-tumor efficacy against TS603 glioma cell line and dose-dependently inhibited R-2HG production. Under the condition of almost complete inhibition of R-2HG, AGI-5198 induced demethylation of histone H3K9me3, and induced the expression of genes related to glial gene differentiation. In genome-wide DNA methylation, AGI-5198 inhibited the growth of mIDH1-impaired IDH1 mutant, but wild-type growth was hardly affected.AGI-5198 significantly inhibited mutant IDH1 (R132H-IDH1 and R132C-IDH1), but did not inhibit the growth of wild-type IDH1 (IC50>100 μM) or IDH1 (IC50>100 μM) or wild-type IDH1 (IC50>100 μM), but very weakly inhibited any of the IDH2 isoforms (R140Q, R172K, wild-type) (IC50>100 μM).
In vivo	AGI-5198 showed some anti-tumor efficacy against TS603 glioma cell line and dose-dependently inhibited R-2HG production. Under the condition of almost complete inhibition of R-2HG, AGI-5198 induced demethylation of histone H3K9me3, and induced the expression of genes related to glial gene differentiation. In genome-wide DNA methylation, AGI-5198 inhibited the growth of mIDH1-impaired IDH1 mutant, but wild-type growth was hardly affected.AGI-5198 significantly inhibited mutant IDH1 (R132H-IDH1 and R132C-IDH1), but did not inhibit the growth of wild-type IDH1 (IC50>100 μM) or IDH1 (IC50>100 μM) or wild-type IDH1 (IC50>100 μM), but very weakly inhibited any of the IDH2 isoforms (R140Q, R172K, wild-type) (IC50>100 μM).
Kinase Assay	IDH enzyme activity: Compound is prepared as 10 mM stock in DMSO and diluted to 50X final concentration in DMSO, for a 50 μL reaction mixture. IDH enzyme activity converting alpha-ketogluta rate to 2-hydroxyglutarate is measured using a NADPH depletion assay. In the assay the remaining cofactor is measured at the end of the reaction with the addition of a catalytic excess of diaphorase and resazurin, to generate a fluorescent signal in proportion to the amount of NADPH remaining. IDH enzyme activity in the direction of isocitrate to alpha-ketoglutarate conversion is measured by direct coupling of the NADPH production to conversion of resazurin to resorufin by diaphorase. In both cases, resorufin is measured fluorometrically at Ex544 Em 590.
Cell Research	AGI-5198 is dissolved in DMSO.TS603 cells are grown in medium containing either AGI-5198 (1.5 μM) or DMSO vehicle control.One week prior to harvest cells are ransferred to

differentiation medium (DMEM F12; 15 mM HEPES; 0.06% glucose; B27 without vitamin A; N2; Insulin/transferrin; 1% FBS) containing freshly added retinoic acid (1 μM).ChIP of non-crosslinked cells is then carried out using established ChIP methods.350 μg of lysate is immunoprecipitated-using anti-H3K9Me3,H3K27me3 or Rabbit Control IgG.After washing,ChIP DNA is eluted from protein G beads and analyzed by RT-PCR using SYBR green.Relative occupancy is calculated using the standard curve method and fold enrichment versus IgG.Enrichment in AGI- 5198-treated cells is normalized to vehicle control.Means and standard deviation are calculated from 4 technical replicates.

Solubility Information

Solubility	DMSO: 23 mg/mL (49.72 mM),Sonication is recommended. Ethanol: 12 mg/mL (25.94 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1619 mL	10.8094 mL	21.6188 mL
5 mM	0.4324 mL	2.1619 mL	4.3238 mL
10 mM	0.2162 mL	1.0809 mL	2.1619 mL
50 mM	0.0432 mL	0.2162 mL	0.4324 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.

Reference

Rohle D, et al. Science, 2013, 340(6132), 626-630.