产品名称：AGI-6780
产品别名：AGI-6780

生物活性：

Description	AGI-6780 that potently and selectively inhibits the tumor-associated mutant IDH2R140Q with IC50 of 23±1.7 nM. AGI-6780 is less potent against IDH2WT with IC50 of 190±8.1 nM.
IC_{50} & Target	IC50: 23±1.7 nM (IDH2R140Q), 190±8.1 nM (IDH2WT)[1]
In Vitro	AGI-6780 is tested in both human glioblastoma U87 and TF-1 cells expressing IDH2R140Q, as well as against IDH1R132H for 48 h incubation, with IC50 of 11±2.6 nM, 18±0.51 nM, and >1 mM, respectivly.Treatment of TF-1R140Q cells with AGI-6780, at concentrations that lower 2HG to near-normal physiologic levels, restore expression of both HBG and KLF1 genes and the color change associated with differentiation. AGI-6780 can reverse the IDH2R140Q-induced differentiation block in TF-1 cells. Pretreatment with AGI-6780 (0.2 μM and 1 μM) markedly decreased the intracellular concentration of (R)-2-hydroxyglutarate in the TF1R140Q cells and restored their ability to undergo EPO-induced differentiation[1].
Solvent&Solubility	***In Vitro:*** **DMSO : DMSO : ≥ 29 mg/mL (60.23 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0768 mL	10.3840 mL	20.7680 mL
	5 mM	0.4154 mL	2.0768 mL	4.1536 mL
	10 mM	0.2077 mL	1.0384 mL	2.0768 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.19 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 2.5 mg/mL (5.19 mM); Precipitated solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.19 mM)

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.19 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wang F, et al. Targeted inhibition of mutant IDH2 in leukemia cells induces cellular differentiation. Science. 2013 May 3;340(6132):622-6.

实验参考：

Cell Assay	Cells are sorted from fresh or frozen bone marrow aspirates and blood samples after labelling with PE-CD34, APC-CD38, PE-CD14, FITC-CD3 (clone HIT3a) and PECy7-CD19 (clone SJ25C1) antibodies using a MoFlow cell sorter. Unfractionated nucleated blood or bone marrow cells are plated in Methocult H4434 methylcellulose medium at 104 cells/dish, in duplicate dishes per condition. AGI-6780 (5 mM) is directly added to the medium. Dishes are incubated in a humidified incubator at 37°C and colonies containing at least 30 cells are counted after 13 days[1].
Kinase Assay	AGI-6780 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-ketoglutarate 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 Em590[1].
References	[1]. Wang F, et al. Targeted inhibition of mutant IDH2 in leukemia cells induces cellular differentiation. Science. 2013 May 3;340(6132):622-6.