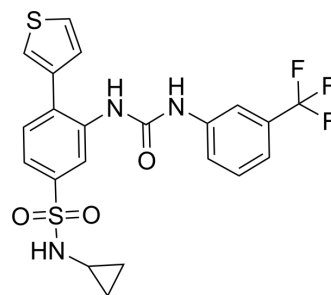


## AGI-6780

<b>Cat. No.:</b>	HY-15734		
<b>CAS No.:</b>	1432660-47-3		
<b>Molecular Formula:</b>	C <sub>21</sub> H <sub>18</sub> F <sub>3</sub> N <sub>3</sub> O <sub>3</sub> S <sub>2</sub>		
<b>Molecular Weight:</b>	481.51		
<b>Target:</b>	Isocitrate Dehydrogenase (IDH)		
<b>Pathway:</b>	Metabolic Enzyme/Protease		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 29 mg/mL (60.23 mM)  
 \* "≥" means soluble, but saturation unknown.

Concentration	Mass		
	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

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 2.5 mg/mL (5.19 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

AGI-6780 that potently and selectively inhibits the tumor-associated mutant IDH2<sup>R140Q</sup> with IC<sub>50</sub> of 23±1.7 nM. AGI-6780 is less potent against IDH2<sup>WT</sup> with IC<sub>50</sub> of 190±8.1 nM.

#### IC<sub>50</sub> & Target

IDH2

#### In Vitro

AGI-6780 is tested in both human glioblastoma U87 and TF-1 cells expressing IDH2<sup>R140Q</sup>, as well as against IDH1<sup>R132H</sup> for 48 h incubation, with IC<sub>50</sub> of 11±2.6 nM, 18±0.51 nM, and >1 mM, respectively. Treatment of TF-1<sup>R140Q</sup> 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 IDH2<sup>R140Q</sup>-induced differentiation block in TF-1 cells.

Pretreatment with AGI-6780 (0.2  $\mu$ M and 1  $\mu$ M) markedly decreased the intracellular concentration of (R)-2-hydroxyglutarate in the TF1<sup>R140Q</sup> cells and restored their ability to undergo EPO-induced differentiation<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Kinase Assay <sup>[1]</sup>

AGI-6780 is prepared as 10 mM stock in DMSO and diluted to 50X final concentration in DMSO, for a 50  $\mu$ L 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<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### Cell Assay <sup>[1]</sup>

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 10<sup>4</sup> 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<sup>[1]</sup>.  
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cell Metab. 2020 Dec 8;S1550-4131(20)30655-0.
- Clin Cancer Res. 2018 Apr 1;24(7):1705-1715.
- Cell Commun Signal. 2020 Apr 3;18(1):55.
- Br J Pharmacol. 2024 Jul 27.
- J Med Chem. 2023 Mar 23.

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## 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.

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

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