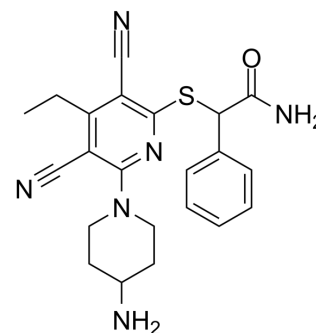


## GSK-3685032

<b>Cat. No.:</b>	HY-139664		
<b>CAS No.:</b>	2170137-61-6		
<b>Molecular Formula:</b>	C <sub>22</sub> H <sub>24</sub> N <sub>6</sub> OS		
<b>Molecular Weight:</b>	420.53		
<b>Target:</b>	DNA Methyltransferase		
<b>Pathway:</b>	Epigenetics		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 25 mg/mL (59.45 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.3780 mL	11.8898 mL	23.7795 mL
		5 mM	0.4756 mL	2.3780 mL	4.7559 mL
10 mM		0.2378 mL	1.1890 mL	2.3780 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution</li> </ol>				

### BIOLOGICAL ACTIVITY

<b>Description</b>	GSK-3685032 is a non-time-dependent, noncovalently, first-in-class reversible DNMT1-selective inhibitor, with an IC <sub>50</sub> of 0.036 μM. GSK-3685032 induces robust loss of DNA methylation, transcriptional activation, and cancer cell growth inhibition [1].
<b>IC<sub>50</sub> &amp; Target</b>	DNMT1 <sup>[1]</sup>
<b>In Vitro</b>	GSK-3685032 (6 days) has cell growth inhibition of majority cancer cell lines, with a median growth IC <sub>50</sub> value of 0.64 μM <sup>[1]</sup> .

GSK-3685032 (0.1-1000 nM, 1-6 days) exhibits growth inhibition after 3 days, with decreasing growth IC<sub>50</sub> throughout a 6 d time course<sup>[1]</sup>.

GSK3685032 (10-10000 nM, day 4) dose-dependently increases the immune-related gene transcription<sup>[1]</sup>.

GSK3685032 (3.2-10,000 nM, 2 days) inhibits DNMT1 protein expression<sup>[1]</sup>.

GSK3685032 induces DNA hypomethylation and gene activation<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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

Cell Line:	15 leukemia, 29 lymphoma and 7 multiple myeloma cell lines, e.g., EOL-1, Ki-JK, MM.1R cells.
Concentration:	0.01-100 μM
Incubation Time:	6 days
Result:	Showed cell growth inhibition of majority cancer cell lines, with a median growth IC <sub>50</sub> value of 0.64 μM.

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

Cell Line:	MV4-11 cells
Concentration:	0.1-1000 nM
Incubation Time:	1-6 days
Result:	Exhibited growth inhibition after 3 days, with decreasing growth IC <sub>50</sub> throughout a 6 d time course.

#### RT-PCR<sup>[1]</sup>

Cell Line:	MV4-11 cells
Concentration:	10-10000 nM
Incubation Time:	4 days
Result:	Dose-dependent increased of CXCL11, IFI27, HLA-DQA1 and MAGEA4 following treatment of MV4-11 cells.

#### Western Blot Analysis<sup>[1]</sup>

Cell Line:	GDM-1 cells
Concentration:	3.2-10,000 nM
Incubation Time:	2 days
Result:	Inhibited DNMT1 protein expression

#### In Vivo

GSK-3685032 (1-45 mg/kg; subcutaneous twice daily for 28 days) inhibits tumor growth in the subcutaneous MV4-11 or SKM-1 xenograft models<sup>[1]</sup>.

Summary of mouse pharmacokinetic parameters for GSK-3685032<sup>[1]</sup>

Dose,Route	C <sub>max</sub>	AUC <sub>0-8hr</sub>	DNAUC	Clearance	Volume <sub>dss</sub>	T <sub>1/2</sub>
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	(ng/mL)	(h*ng/mL)	(h*kg*ng/mL/mg)	(mL/min/kg)	(L/kg)	(h)
2 mg/kg,IV	5103	2418	1209	13	1.3	1.8
2 mg/kg,SC	252	921	461	NA	NA	2.8
2 mg/kg,SC	5473	15400	513	NA	NA	ND

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MV4-11 xenograft models (female CD1-Foxn1 mice, 12 weeks of age) or SKM-1 xenograft models (NOD. CB17-Prkdc1NCrCrI mice, 8-11 weeks of age) <sup>[1]</sup>
Dosage:	1, 5, 15, 30, 45 mg/kg (10% captisol adjusted to pH 4.5-5 with 1 M acetic acid, stored for up to 1 week at 4 °C)
Administration:	Subcutaneous injection, twice daily for 4 weeks
Result:	Revealed statistically significant dose-dependent tumor growth inhibition with clear regression at ≥30 mg/kg.

## CUSTOMER VALIDATION

- bioRxiv. 2023 May 9.

See more customer validations on [www.MedChemExpress.com](http://www.MedChemExpress.com)

## REFERENCES

[1]. Pappalardi MB, et al. Discovery of a first-in-class reversible DNMT1-selective inhibitor with improved tolerability and efficacy in acute myeloid leukemia. Nat Cancer. 2021;2(10):1002-1017.

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

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