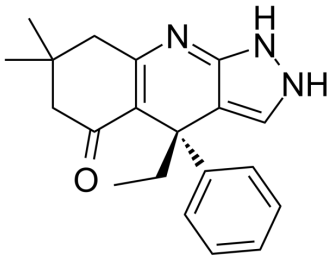
BRD0705

Cat. No.:	HY-116830
CAS No.:	2056261-41-5
Molecular Formula:	$C_{20}H_{23}N_3O$
Molecular Weight:	321.42
Target:	GSK-3
Pathway:	PI3K/Akt/mTOR; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 300 mg/mL (933.36 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1112 mL	15.5560 mL	31.1119 mL
	5 mM	0.6222 mL	3.1112 mL	6.2224 mL
	10 mM	0.3111 mL	1.5556 mL	3.1112 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 7.5 mg/mL (23.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 7.5 mg/mL (23.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BRD0705 is a potent, paralog selective and orally active GSK3α inhibitor with an IC_{50} of 66 nM and a K_d of 4.8 μM. BRD0705 displays increased selectivity for GSK3α (8-fold) versus GSK3β (IC_{50} of 515 nM). BRD0705 can be used for acute myeloid leukemia (AML) research[1].

IC_{50} & Target

GSK3α 66 nM (IC_{50})	GSK3α 4.8 μM (Kd)	GSK-3β(WT) 515 nM (IC_{50})

In Vitro

BRD0705 displays excellent selectivity in a penal of 311 kinases, the CDK family of kinases (CDK2, 3 and 5) are next most potently inhibits at values of 6.87 μM, 9.74 μM and 9.20 μM (87-fold, 123-fold and 116-fold selectivity relative to GSK3α)[1]. BRD0705 (10-40 μM; 2-24 hours; U937 cells) treatment impairs GSK3α Tyr279 phosphorylation in a time-and concentration-

dependent manner without affecting GSK3β Tyr216 phosphorylation[1].
Using a β-catenin dependent TCF/LEF luciferase reporter assay, the absence of β-catenin induced target activation after treatment with BRD0705 in AML cell lines[1].
BRD0705 impairs AML colony formation in all six tested cell lines, MOLM13, TF-1, U937, MV4-11, HL-60 and NB4, in a concentration-dependent manner, as opposed to BRD3731 which impairs colony formation in TF-1 while increasing colony forming ability in the MV4-11 cell line[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	U937 cells
Concentration:	10 μM, 20 μM and 40 μM
Incubation Time:	2 hours, 4 hours, 8 hours and 24 hours
Result:	Impaired GSK3α Tyr279 phosphorylation in a time-and concentration-dependent manner without affecting GSK3β Tyr216 phosphorylation.

In Vivo

BRD0705 (30 mg/kg; oral gavage; twice daily; NSG mice) treatment impairs leukemia initiation and prolongs survival in AML mouse models[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	8-week-old male NSG mice injected with MLL-AF9 AML cells[1]
Dosage:	30 mg/kg
Administration:	Oral gavage; twice daily
Result:	Mice survival was significantly improved.

CUSTOMER VALIDATION

- SSRN. 2023 Jun 20.

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REFERENCES

[1]. Wagner FF, et al. Exploiting an Asp-Glu "switch" in glycogen synthase kinase 3 to design paralog-selective inhibitors for use in acute myeloid leukemia. Sci Transl Med. 2018 Mar 7;10(431). pii: eaam8460.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA