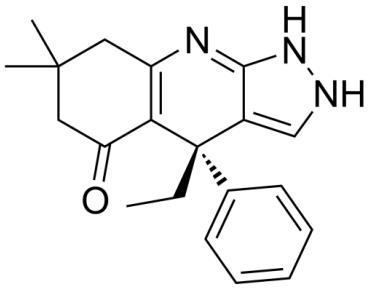
Data Sheet

Product Name:	BRD0705
Cat. No.:	CS-0066622
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
Solubility:	DMSO : 300 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

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]. ***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]. ***In Vivo:*** BRD0705 (30 mg/kg; oral gavage; twice daily; NSG mice) treatment impairs leukemia initiation and prolongs survival in AML mouse models[1].

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.

CAIndexNames:

5H-Pyrazolo[3,4-b]quinolin-5-one, 4-ethyl-1,2,4,6,7,8-hexahydro-7,7-dimethyl-4-phenyl-, (4S)-

SMILES:

O=C1C2=C(N=C3C([C@]2(CC)C4=CC=CC=C4)=CNN3)CC(C)(C)C1

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

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