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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
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Asnuciclib

Cat. No.: HY-12445

CAS No.: 1421693-22-2

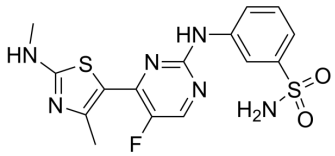
Molecular Formula: $C_{15}H_{15}FN_6O_2S_2$

Molecular Weight: 394.45

Target: CDK; Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

Storage: 4°C, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 52 mg/mL (131.83 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5352 mL	12.6759 mL	25.3518 mL
5 mM	0.5070 mL	2.5352 mL	5.0704 mL
10 mM	0.2535 mL	1.2676 mL	2.5352 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: ≥ 2.67 mg/mL (6.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Asnuciclib (CDKI-73; LS-007) is an orally active and highly efficacious CDK9 inhibitor, with K_i values of 4 nM, 4 nM and 3 nM for CDK9, CDK1 and CDK2, respectively. Asnuciclib down-regulates the RNAPII phosphorylation. Asnuciclib is also a novel pharmacological inhibitor of Rab11 cargo delivery and innate immune secretion[1][2][3][4].

IC_{50} & Target

CDK2 3.27 nM (IC_{50})	CDK9 5.78 nM (IC_{50})	CDK1 8.17 nM (IC_{50})	CDK4 8.18 nM (IC_{50})
CDK6 37.68 nM (IC_{50})	CDK7 134.26 nM (IC_{50})	CDK1 4 nM (Ki)	CDK2 3 nM (Ki)
CDK9 4 nM (Ki)	CDK7 91 nM (Ki)		

In Vitro

Asnuciclib is highly cytotoxic to primary leukemia cells derived from CLL patients (mean LD_{50} = 0.08 μM) and shows>500-fold selectivity for primary leukemia cells over normal B-lymphocytes (LD_{50}=40.5 μM)[1].
Asnuciclib (0.1 μM, 4 h) inhibits the phosphorylation of serine 2 of RNA polymerase II and MCL1 protein expression in CLL cells[1].
Asnuciclib induced caspase-dependent apoptosis that was preceded by dephosphorylation of cdk9 and serine 2 of RNA polymerase II[1].
Asnuciclib is highly effective against all cell lines tested with an IC_{50} in the range of 0.012-0.517 μM; in particular three MLL-AML cell lines, namely MOLM13, MV4-11 and THP-1, were highly sensitive to CDKI-73 with IC_{50} values <0.062 μM[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1].

Cell Line:	CLL cells.
Concentration:	0-1 μM.
Incubation Time:	48 h.
Result:	Shows preferential cytotoxicity in CLL cells.

In Vivo

Asnuciclib (25, 50, 100 mg/kg) markedly decreases tumor growth in a dose-dependent manner and results in a prolongation of animal life span (P < 0.001) without causing body weight loss and other overt toxicities.[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MV4-11 tumor bearing mice[3].
Dosage:	25 mg/kg.
Administration:	Orally once everyday for 33 days.
Result:	Caused a remarkable delay in tumor growth compared to vehicle-treated mice, as reflected in a percentage for the mean tumor volume in treated to control mice of 43% at day 31.

Animal Model:	Balb/C mice aged 6-8 weeks[3].
Dosage:	2 mg/kg (IV), 10, 20 and 40 mg/kg (PO). (Pharmacokinetic Analysis.)
Administration:	IV and PO, single dose.
Result:	The C_{max} increased from 1.29 to 3.66 μM at a mean time of 1 h and the area under the curve (AUC) of CDKI-73 increased from 3.51 to 12.8 μM.h when the oral dose was escalated from 10 to 40 mg/kg. CDKI-73 was eliminated from plasma with a mean terminal half-life (T1/2) of 2 h. Its oralbioavailability (F) ranged from 54 to 85% across the three doses.

CUSTOMER VALIDATION

- Am J Cancer Res. 2020 Apr 1;10(4):1140-1155.
- Commun Biol. 2021 Oct 29;4(1):1239.

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REFERENCES

[1]. Lam F, et al. Targeting RNA transcription and translation in ovarian cancer cells with pharmacological inhibitor CDKI-73. Oncotarget. 2014 Sep 15;5(17):7691-704.

[2]. Elisabeth Walsby, et al. A novel Cdk9 inhibitor preferentially targets tumor cells and synergizes with fludarabine. Oncotarget. 2014 Jan; 5(2): 375–385.

[3]. Muhammed H Rahaman, et al. CDKI-73: an orally bioavailable and highly efficacious CDK9 inhibitor against acute myeloid leukemia. Invest New Drugs. 2019 Aug;37(4):625-635.

[4]. Alexandra Sorvina, et al. CDKI-73 is a Novel Pharmacological Inhibitor of Rab11 Cargo Delivery and Innate Immune Secretion. Cells. 2020 Feb 5;9(2):372.

[5]. Shao Xie, et al. Antitumor action of CDK inhibitor LS-007 as a single agent and in combination with ABT-199 against human acute leukemia cells. Acta Pharmacol Sin. 2016 Nov; 37(11): 1481–1489.

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