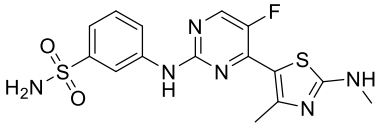
Product data sheet

MedKoo Cat#: 532808 Name: CDKI-73 CAS#: 1421693-22-2 Chemical Formula: $C_{15}H_{15}FN_6O_2S_2$ Exact Mass: 394.0682 Molecular Weight: 394.44	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
CDKI-73 is a potent CDK9 inhibitor with Ki of 4 nM. It shows selective toxicity to CLL cells(LD50=80 nM) versus normal B cell and normal CD34+ cell(LD50>20 uM). The inhibition of CDK9 induces apoptosis and potentiates the effect of cisplatin.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	52	131.83

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.54 mL	12.68 mL	25.35 mL
5 mM	0.51 mL	2.54 mL	5.07 mL
10 mM	0.25 mL	1.27 mL	2.54 mL
50 mM	0.05 mL	0.25 mL	0.51 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Lam F, Abbas AY, Shao H, Teo T, Adams J, Li P, Bradshaw TD, Fischer PM, Walsby E, Pepper C, Chen Y, Ding J, Wang S. Targeting RNA transcription and translation in ovarian cancer cells with pharmacological inhibitor CDKI-73. Oncotarget. 2014 Sep 15;5(17):7691-704. doi: 10.18632/oncotarget.2296. PMID: 25277198; PMCID: PMC4202154.

2. Sorvina A, Shandala T, Wang S, Sharkey DJ, Parkinson-Lawrence E, Selemidis S, Brooks DA. CDKI-73 is a Novel Pharmacological Inhibitor of Rab11 Cargo Delivery and Innate Immune Secretion. Cells. 2020 Feb 5;9(2):372. doi: 10.3390/cells9020372. PMID: 32033486; PMCID: PMC7072129.

In vivo study

1. Rahaman MH, Yu Y, Zhong L, Adams J, Lam F, Li P, Noll B, Milne R, Peng J, Wang S. CDKI-73: an orally bioavailable and highly efficacious CDK9 inhibitor against acute myeloid leukemia. Invest New Drugs. 2019 Aug;37(4):625-635. doi: 10.1007/s10637-018-0661-2. Epub 2018 Sep 8. PMID: 30194564.

7. Bioactivity
Biological target:

CDKI-73 (LS-007) is a potent CDK inhibitor in vitro with IC50 of 8.17 nM, 3.27 nM, 8.18 nM, and 5.78 nM for CDK1, CDK2, CDK4, and CDK9, respectively.

Product data sheet

In vitro activity

The cellular mechanism of a novel CDK9 inhibitor CDKI-73 in an ovarian cancer cell line (A2780) is herein reported. A shRNA-mediated CDK9 knockdown was used to investigate the importance of CDK9 in the maintenance of A2780 cells. This study revealed that CDKI-73 rapidly inhibited cellular CDK9 kinase activity and down-regulated the RNAPII phosphorylation. This subsequently caused a decrease in the eIF4E phosphorylation by blocking Mnk1 kinase activity. Consistently, CDK9 shRNA was also found to down-regulate the Mnk1 expression. Both CDKI-73 and CDK9 shRNA decreased anti-apoptotic proteins Mcl-1 and Bcl-2 and induced apoptosis. The study confirmed that CDK9 is required for cell survival and that ovarian cancer may be susceptible to CDK9 inhibition strategy. The data also implied a role of CDK9 in eIF4E-mediated translational control, suggesting that CDK9 may have important implication in the Mnk-eIF4E axis, the key determinants of PI3K/Akt/mTOR- and Ras/Raf/MAPK-mediated tumorigenic activity. As such, CDK9 inhibitor drug candidate CDKI-73 should have a major impact on these pathways in human cancers.

Reference: Oncotarget. 2014 Sep 15;5(17):7691-704. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/25277198/

In vivo activity

To determine the in vivo anti-leukemic efficacy of CDKI-73, two xenograft studies were performed. In the first study, two groups of MV4–11 tumor bearing mice (n = 8 per group) were administered vehicle i.e. 1% sodium carboxymethylcellulose (CMC) in water or 25 mg/kg CDKI-73 orally once every day for 33 days. Mice were observed daily during dosing and for a further 50 days afterwards. CDKI-73 caused a remarkable delay in tumor growth (Fig. 5b and c) compared to vehicle-treated mice, as reflected in a percentage for the mean tumor volume in treated to control mice (T/C, Eq. 1,Supplementary methods) of 43% at day 31 ($P < 0.00001$). There was a statistically significant reduction in tumor growth ($P < 0.05$) from day 11 onwards compared to the vehicle treated group, and tumors regressed completely in two out of eight mice. These delays in growth and regression of tumor translated to an increase in life-span (ILS) of 54.5% ($P < 0.001$) for the CDKI-73 treated animals compared to the vehicle treated group (Fig. 5d). CDKI-73 was well tolerated as evident from the absence of loss in body weight and other overt toxicities.

Reference: Invest New Drugs. 2019 Aug;37(4):625-635. https://doi.org/10.1007/s10637-018-0661-2