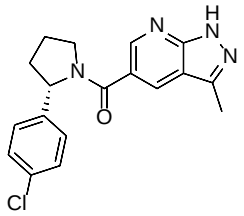
Product data sheet

MedKoo Cat#: 406828 Name: MSC2530818 CAS: 1883423-59-3 Chemical Formula: $C_{18}H_{17}ClN_4O$ Exact Mass: 340.1091 Molecular Weight: 340.811	
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:
MSC2530818 is a Potent, Selective, and Orally Bioavailable CDK8 Inhibitor with CDK8 IC50 = 2.6 nM; Human PK prediction: Cl ~ 0.14 L/H/Kg; t1/2 ~ 2.4h; F > 75%. MSC2530818 displays excellent kinase selectivity, biochemical and cellular potency, microsomal stability, and is orally bioavailable. MSC2530818 demonstrates suitable potency and selectivity to progress into preclinical in vivo efficacy and safety studies.

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
DMF	30.0	88.03
DMF:PBS (pH 7.2) (1:1)	0.50	1.47
DMSO	64.33	188.77
Ethanol	39.0	114.43

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.93 mL	14.67 mL	29.34 mL
5 mM	0.59 mL	2.93 mL	5.87 mL
10 mM	0.29 mL	1.47 mL	2.93 mL
50 mM	0.06 mL	0.29 mL	0.59 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

Czodrowski P, Mallinger A, Wienke D, Esdar C, Pöschke O, Busch M, Rohdich F, Eccles SA, Ortiz-Ruiz MJ, Schneider R, Raynaud FI, Clarke PA, Musil D, Schwarz D, Dale T, Urbahns K, Blagg J, Schiemann K. Structure-Based Optimization of Potent, Selective, and Orally Bioavailable CDK8 Inhibitors Discovered by High-Throughput Screening. J Med Chem. 2016 Oct 27;59(20):9337-9349. doi: 10.1021/acs.jmedchem.6b00597. Epub 2016 Oct 7. PMID: 27490956.

In vivo study

Czodrowski P, Mallinger A, Wienke D, Esdar C, Pöschke O, Busch M, Rohdich F, Eccles SA, Ortiz-Ruiz MJ, Schneider R, Raynaud FI, Clarke PA, Musil D, Schwarz D, Dale T, Urbahns K, Blagg J, Schiemann K. Structure-Based Optimization of Potent, Selective, and Orally Bioavailable CDK8 Inhibitors Discovered by High-Throughput Screening. J Med Chem. 2016 Oct 27;59(20):9337-9349. doi: 10.1021/acs.jmedchem.6b00597. Epub 2016 Oct 7. PMID: 27490956.

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7. Bioactivity

Biological target:

MSC2530818 is a potent, selective and orally available CDK8 inhibitor with an IC_{50} of 2.6 nM for CDK8.

In vitro activity

In a commercially available reporter displacement assay, compound 25 (MSC2530818) binds to CDK8 and CDK19 with similar affinity (4 nM), as this study has previously observed across multiple chemotypes. Furthermore, compound 25 demonstrated potent inhibition of WNT-dependent transcription in human cancer cell lines that have constitutively activated WNT signaling. For example, 25 inhibited the reporter-based luciferase readout in several cell lines bearing activating WNT-pathway mutations; LS174T (β-catenin mutant, IC50 = 32 ± 7 nM), COLO205 (APC mutant, IC_{50} = 9 ± 1 nM) and demonstrated inhibition of WNT3a ligand-dependent reporter readout in PA-1 cells (IC_{50} = 52 ± 30 nM).

Reference: J Med Chem. 2016 Oct 27;59(20):9337-9349. https://pubmed.ncbi.nlm.nih.gov/27490956/

In vivo activity

Compound 25 (MSC2530818) was then assessed in vivo in an established SW620 human colorectal cancer xenograft model in female NCr athymic mice. Tumor-bearing mice were treated orally with compound 25 (50 mg/kg bid or 100 mg/kg qd) for 16 days. Both schedules gave a similar reduction in tumor growth (Figure 6A) with T/C ratios (based on final tumor weights) of 49% and 57%, respectively.

Reference: J Med Chem. 2016 Oct 27;59(20):9337-9349. https://pubmed.ncbi.nlm.nih.gov/27490956/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.