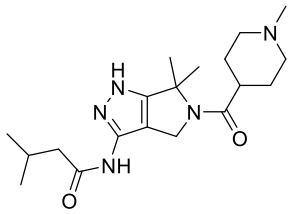
Product data sheet

MedKoo Cat#: 206024 Name: PHA-793887 CAS#: 718630-59-2 (free base) Chemical Formula: $C_{19}H_{31}N_5O_2$ Exact Mass: 361.24778 Molecular Weight: 361.48	
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:

PHA-793887 is an inhibitor of multiple cyclin dependent kinases (CDK) with activity against CDK2, CDK1 and CDK4. PHA-793887 was cytotoxic for leukemic cell lines in vitro, with IC(50) ranging from 0.3 to 7 microM. In colony assays PHA-793887 showed very high activity against leukemia cell lines, with an IC(50) <0.1 microM indicating that it has efficient and prolonged antiproliferative activity. PHA-793887 induced cell-cycle arrest, inhibited Rb and nucleophosmin phosphorylation. PHA-793887 has promising therapeutic activity against acute leukemias in vitro and in vivo.

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	30.0	83.0
Ethanol	30.0	83.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.77 mL	13.83 mL	27.66 mL
5 mM	0.55 mL	2.77 mL	5.53 mL
10 mM	0.28 mL	1.38 mL	2.77 mL
50 mM	0.06 mL	0.28 mL	0.55 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. Wu B, Yang W, Fu Z, Xie H, Guo Z, Liu D, Ge J, Zhong S, Liu L, Liu J, Zhu D. Selected using bioinformatics and molecular docking analyses, PHA-793887 is effective against osteosarcoma. Aging (Albany NY). 2021 Jun 21;13. doi: 10.18632/aging.203165. Epub ahead of print. PMID: 34156352.
2. Alzani R, Pedrini O, Albanese C, Ceruti R, Casolaro A, Patton V, Colotta F, Rambaldi A, Introna M, Pesenti E, Ciomei M, Golay J. Therapeutic efficacy of the pan-cdk inhibitor PHA-793887 in vitro and in vivo in engraftment and high-burden leukemia models. Exp Hematol. 2010 Apr;38(4):259-269.e2. doi: 10.1016/j.exphem.2010.02.004. Epub 2010 Feb 16. PMID: 20167248.

In vivo study

1. Alzani R, Pedrini O, Albanese C, Ceruti R, Casolaro A, Patton V, Colotta F, Rambaldi A, Introna M, Pesenti E, Ciomei M, Golay J. Therapeutic efficacy of the pan-cdk inhibitor PHA-793887 in vitro and in vivo in engraftment and high-burden leukemia models. Exp Hematol. 2010 Apr;38(4):259-269.e2. doi: 10.1016/j.exphem.2010.02.004. Epub 2010 Feb 16. PMID: 20167248.
2. Brasca MG, Albanese C, Alzani R, Amici R, Avanzi N, Ballinari D, Bischoff J, Borghi D, Casale E, Croci V, Fiorentini F, Isacchi A, Mercurio C, Nesi M, Orsini P, Pastori W, Pesenti E, Pevarello P, Roussel P, Varasi M, Volpi D, Vulpetti A, Ciomei M.

Product data sheet

Optimization of 6,6-dimethyl pyrrolo[3,4-c]pyrazoles: Identification of PHA-793887, a potent CDK inhibitor suitable for intravenous dosing. Bioorg Med Chem. 2010 Mar 1;18(5):1844-53. doi: 10.1016/j.bmc.2010.01.042. Epub 2010 Jan 25. PMID: 20153204.

7. Bioactivity

Biological target:

PHA-793887 is an ATP-competitive CDK inhibitor, can inhibit Cdk2, Cdk1, Cdk4, and Cdk9 with IC50s of 8 nM, 60 nM, 62 nM and 138 nM, respectively, and also inhibits glycogen synthase kinase 3β with an IC50 of 79 nM.

In vitro activity

Subsequently, this study examined the effects of PHA-793887 on osteosarcoma cells in vitro. A 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay indicated that the viability of MG63, U20S and 143B cells decreased with increasing drug concentrations ($P < 0.05$; Figure 5A). Moreover, in a colony formation assay, the PHA-793887-treated cells exhibited lower clonogenicity than the control cells in both number and size (Figure 5B, 5D).

Reference: Aging (Albany NY). 2021 Jun 21;13. https://www.aging-us.com/article/203165/text

In vivo activity

On the basis of these data compound 31 (PHA-793887) was evaluated for its in vivo antitumor activity in the human ovarian A2780 xenograft mouse model. The doses of 10, 20 and 30 mg/kg were selected and administered by iv route, once a day, for 10 consecutive days, on the basis of the plasma levels reached in the preliminary in vivo PK study. Compound 31 was dissolved in 5% dextrose solution and caused a dose-dependent inhibition of the A2780 tumor growth up to 76% at the dose of 30 mg/kg at the end of treatment (Fig. 4a). With the same schedule, compound 31 was tested at the doses of 10 and 20 mg/kg also on a model of human colon carcinoma (HCT-116) causing a dose-dependent inhibition of the tumor growth up to 81% at the dose of 20 mg/kg at the end of treatment (Fig. 4b) and on a model of human pancreatic carcinoma (BX-PC3) with a 84% of tumor growth inhibition at the end of treatment with 20 mg/kg (Fig. 4c). Compound 31 was well tolerated upon daily treatments by iv administration. In fact, in all experiments, body weight reduction was always marginal (<10% vs control mice) and no toxic effects were reported after gross autopsy.

Reference: Bioorg Med Chem. 2010 Mar 1;18(5):1844-53. https://pubmed.ncbi.nlm.nih.gov/20153204/