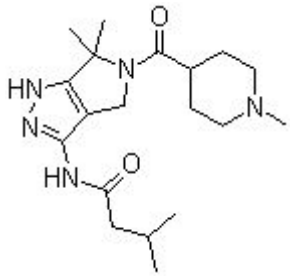
Product Introduction

PHA-793887

PHA-793887 is a novel and potent inhibitor of CDK2, CDK5 and CDK7 with IC50 of 8 nM, 5 nM and 10 nM. It is greater than 6-fold more selective for CDK2, 5, and 7 than CDK1, 4, and 9. Phase 1.

Technical Data:

Molecular Weight (MW):	361.48	
Formula:	$C_{19}H_{31}N_5O_2$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 72 mg/mL	
	Water <1 mg/mL	
	Ethanol 72 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	718630-59-2	

Biological Activity

PHA-793887 has low activity against CDK1, CDK4, CDK9 and GSK3β with IC50 of 60 nM, 62 nM, 138 nM and 79 nM, respectively. PHA-793887 inhibits cell proliferation of many tumor cell lines, including A2780, HCT-116, COLO-205, C-433, DU-145, A375, PC3, MCF-7, and BX-PC3, with IC50 of 88 nM–3.4 μM. PHA-793887 (1 μM) shows a decrease in the S phase, a subsequent increase of the G1 phase and a slight accumulation of G2/M phase in A2780 cells. PHA-793887 (3 μM) significantly increases G2/M phase and reduces DNA synthsis. [1]PHA-793887 is cytotoxic for leukemic cell lines, including K562, KU812, KCL22, and TOM1, with IC50 of 0.3–7 μM, but it is not cytotoxic for normal unstimulated peripheral blood

mononuclear cells or CD34+ hematopoietic stem cells. In colony assays, PHA-793887 shows very high activity against leukemia cell lines with IC50 less than 0.1 μM. PHA-793887 induces cell-cycle arrest, inhibits Rb and nucleophosmin phosphorylation, and modulates cyclin E and cdc6 expression at 0.2–1 μM and induces apoptosis at 5 μM. [2]

PHA-793887 (10–30 mg/kg) shows good efficacy in the human ovarian A2780, colon HCT-116, and pancreatic BX-PC3 carcinoma xenograft models. [1] PHA-793887 (20 mg/kg) is effective in xenograft models of K562 and HL60 cells, primary leukemic disseminated model, and a high-burden disseminated ALL-2 model derived from a relapsed Philadelphia-positive acute lymphoid leukemia patient. [2]

Multi-CDK inhibitor.

References

[1] Brasca MG, et al. Bioorg Med Chem, 2010, 18(5), 1844-1853.

[2] Alzani R, et al. Exp Hematol, 2010, 38(4), 259-269.

[3] Pevarello P, et al. J Med Chem, 2004, 47(13), 3367-3380.

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