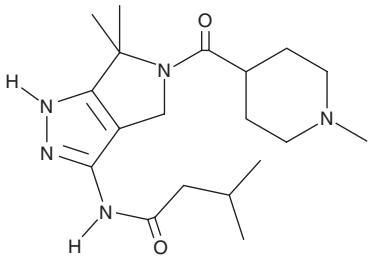
PRODUCT INFORMATION

PHA-793887

Item No. 18388

CAS Registry No.:	718630-59-2
Formal Name:	3-methyl-N-[1,4,5,6-tetrahydro-6,6-dimethyl-5-[(1-methyl-4-piperidinyl)carbonyl]pyrrolo[3,4-c]pyrazol-3-yl]-butanamide
MF:	$C_{19}H_{31}N_5O_2$
FW:	361.5
Purity:	≥95%
UV/Vis.:	λ_{max}: 235 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

PHA-793887 is supplied as a crystalline solid. A stock solution may be made by dissolving the PHA-793887 in the solvent of choice, which should be purged with an inert gas. PHA-793887 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of PHA-793887 in these solvents is approximately 30 mg/ml.

PHA-793887 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, PHA-793887 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. PHA-793887 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

PHA-793887 is an inhibitor of cyclin-dependent kinases (CDKs; IC_{50}s = 8, 8, 5, and 10 nM for Cdk2/cyclin A, Cdk2/cyclin E, Cdk5/p25, and Cdk7/cyclin H, respectively).[1] It is selective for these CDKs over Cdk1/cyclin B, Cdk4/cyclin D1, Cdk9/cyclin T1, and glycogen synthase kinase 3β (GSK3β; IC_{50}s = 60, 62, 138, and 79 nM, respectively), as well as a panel of 36 other kinases at 10 µM. PHA-793887 inhibits the proliferation of A2780 ovarian, HCT116 colon, and BxPC-3 pancreatic cancer cells (IC_{50}s = 88, 163, and 3,444 nM, respectively). It inhibits reactivation of latent HIV-1 induced by prostratin (Item No. 10272), panobinostat (Item No. 13280), or JQ-1 in 24ST1NLESG cells (IC_{50}s = 0.004, 0.0082, and 0.016 µM, respectively).[2] PHA-793887 (20 mg/kg) reduces tumor growth and increases survival in HL-60 and K562 leukemia mouse xenograft models.[3]

References

1. Brasca, M.G., Albanese, C., Alzani, R., *et al.* Optimization of 6,6-dimethyl pyrrolo[3,4-c]pyrazoles: Identification of PHA-793887, a potent CDK inhibitor suitable for intravenous dosing. *Bioor. Med. Chem.* **18(5)**, 1844-1853 (2010).
2. Vargas, B., Giacobbi, N.S., Sanyal, A., *et al.* Inhibitors of signaling pathways that block reversal of HIV-1 latency. *Antimicrob. Agents Chemother.* **63(2)**, e01744-18 (2019).
2. Alzani, R., Pedrini, O., Albanese, C., *et al.* Therapeutic efficacy of the pan-cdk inhibitor PHA-793887 *in vitro* and *in vivo* in engraftment and high-burden leukemia models. *Exp. Hematol.* **38**, 259-269 (2010).

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