Uzansertib phosphate

Cat. No.: HY-101870B

CAS No.: 2088852-47-3

Molecular Formula: $C_{26}H_{29}F_3N_5O_7P$

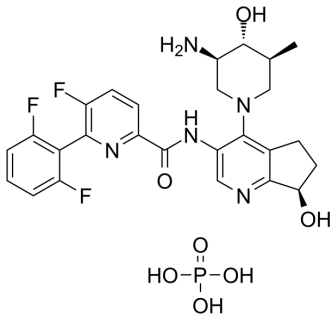
Molecular Weight: 611.51

Target: Pim

Pathway: JAK/STAT Signaling

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 18 mg/mL (29.44 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.6353 mL	8.1765 mL	16.3530 mL
	5 mM	0.3271 mL	1.6353 mL	3.2706 mL
	10 mM	0.1635 mL	0.8176 mL	1.6353 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.8 mg/mL (2.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.8 mg/mL (2.94 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.8 mg/mL (2.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Uzansertib (INCB053914) phosphate is an orally active, ATP-competitive pan-PIM kinase inhibitor with IC_{50}s of 0.24 nM, 30 nM, 0.12 nM for PIM1, PIM2, PIM3, respectively. Uzansertib phosphate has broad anti-proliferative activity against a variety of hematologic tumor cell lines[1].

IC_{50} & Target

PIM1	PIM2	PIM3
0.24 nM (IC_{50})	30 nM (IC_{50})	0.12 nM (IC_{50})

In Vitro

Uzansertib phosphate inhibits proliferation in all multiple myeloma (MM) cell lines tested, with mean GI_{50} values ranging from 13.2 nM to 230.0 nM in AML, MM, DLBCL, MCL, and T-ALL cell lines[1].

	Uzansertib phosphate (0.1, 0.3, 1, 3, 10, 30, 100, 300, 1000 nM) inhibits the phosphorylation of downstream PIM kinase substrates (p70S6K/S6 and 4E-BP1) in a dose-dependent manner in MOLM-16 (AML), Pfeiffer (DLBCL), and KMS-12-PE/BM (MM) cell lines[1]. PIM kinase-mediated phosphorylation of BAD in MOLM-16 and KMS-12-BM cells is particularly sensitive to inhibition by Uzansertib phosphate (mean IC_{50}, 4 nM and 27 nM, respectively)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Uzansertib phosphate (25-100 mg/kg; PO; twice a day; for 15 days) inhibits tumor growth in a dose-dependent manner in mice bearing MOLM-16 (AML) or KMS-12-BM (MM) [1]. Uzansertib phosphate demonstrates a dose-dependent inhibition of BAD phosphorylation relative to vehicle at 4 hours post dose (MOLM-16 tumors, IC_{50}=70 nM; KMS-12-BM tumors, IC_{50}=145 nM) [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female immune compromised (severe combined immunodeficiency [SCID]) mice (5-9 weeks of age) bearing MOLM-16 (AML) or KMS-12-BM (MM)[1]
Dosage:	25, 50, 75, 100 mg/kg
Administration:	PO; twice a day; for 15 days
Result:	Inhibited tumor growth in a dose-dependent manner in mice.

REFERENCES

[1]. Koblish H, et al. Preclinical characterization of INCB053914, a novel pan-PIM kinase inhibitor, alone and in combination with anticancer agents, in models of hematologic malignancies. PLoS One. 2018 Jun 21;13(6):e0199108.

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