Uzansertib

Cat. No.: HY-101870

CAS No.: 1620012-39-6

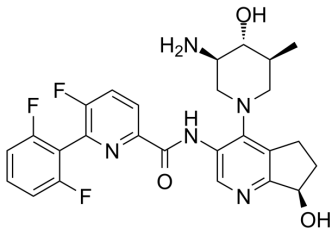
Molecular Formula: $C_{26}H_{26}F_3N_5O_3$

Molecular Weight: 513.51

Target: Pim

Pathway: JAK/STAT Signaling

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Uzansertib (INCB053914) 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 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 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 (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 (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 (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 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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