Data Sheet (Cat.No.T88908)

JMV7048

Chemical Properties

CAS No. :

Formula:

Molecular Weight:

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	JMV7048 is an effective PROTAC degrader targeting the PXR (Pregnane X Receptor), with a DC50 of 379 nM. It induces the polyubiquitination and degradation of PXR protein by recruiting the E3 CRBN ubiquitin ligase and the 26S proteasome. This degradation of PXR significantly enhances the chemosensitivity of colorectal cancer stem cells, substantially delaying cancer recurrence in vivo. The composition of JMV7048 includes the PXR agonist JMV6944, a linker, and Thalidomide 5-fluoride.
Targets(IC50)	PROTACs
In vitro	JMV7048 (5 μM, 24 hours) inhibits the growth of cancer cells in colon cancer, liver cancer, and pancreatic cancer cell lines. When administered at the same dosage and duration, JMV7048 significantly reduces tumorigenicity in CPP1 cells xenografted into nude mice, thereby decreasing the frequency of tumor initiation in these hosts. Additionally, JMV7048 (5 μM, 48 hours) impairs the ability of CPP1, CPP14, and CPP19 cells to form spheroids under non-attached conditions, indicating its effect on the self-renewal capabilities of these cells. Moreover, treatment with JMV7048 significantly reduces the survival rate of HT29 cells following chemotherapy with drugs (5-Fluorouracil and SN38), suggesting that JMV7048 may enhance cellular sensitivity to these chemotherapeutic agents.
In vivo	JMV7048, administered intravenously at a dosage of 25 mg/kg once daily for five days per week over a period of 15 days, demonstrated good tolerability in athymic nude mice and NOD/scid mice. When tested on heterotopic xenograft models in NOD/scid mice derived from HT29 and CCP1 cells, JMV7048 (25 mg/kg, intravenously, once daily continuously for four days or for two weeks, five days per week) showed activity in degrading PXR. In combination therapy with chemotherapeutic agents (50 mg/kg 5-Fluorouracil + 25 mg/kg Irinotecan, intraperitoneal injection, twice a week for three or four weeks), JMV7048 (25 mg/kg, intravenously, once daily, five days per week for four weeks with HT29 cells; 25 mg/kg, intraperitoneal injection, twice daily, five days per week for three weeks with CCP1 cells) significantly delayed tumor recurrence in the NOD/scid mouse xenograft model with LS174T cells. Drug exposure levels in plasma were sufficiently achieved with single intraperitoneal (50 mg/kg) or intravenous (25 mg/kg) doses, while oral administration (50 mg/kg) was significantly less effective.

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