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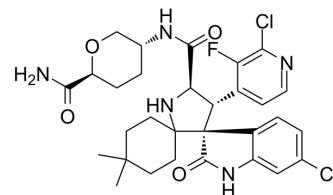
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Milademetan

Cat. No.:	HY-101266
CAS No.:	1398568-47-2
Molecular Formula:	C ₃₀ H ₃₄ Cl ₂ FN ₅ O ₄
Molecular Weight:	618.53
Target:	MDM-2/p53; E1/E2/E3 Enzyme; Apoptosis
Pathway:	Apoptosis; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 16.67 mg/mL (26.95 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	1.6167 mL	8.0837 mL	16.1674 mL
		5 mM	0.3233 mL	1.6167 mL	3.2335 mL
		10 mM	0.1617 mL	0.8084 mL	1.6167 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: ≥ 1.67 mg/mL (2.70 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 1.67 mg/mL (2.70 mM); Suspended solution; Need ultrasonic				
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 1.67 mg/mL (2.70 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	Milademetan (DS-3032) is a specific and orally active MDM2 inhibitor for the research of acute myeloid leukemia (AML) or solid tumors. Milademetan (DS-3032) induces G1 cell cycle arrest, senescence and apoptosis ^{[1][2]} .
IC ₅₀ & Target	MDM2 ^[1] .
In Vitro	Milademetan (DS-3032) can stabilize TP53 and selectively induce CDKN1A, BAX and MDM2 expression in neuroblastoma cells with wild-type TP53 ^[3] .

Milademetan (DS-3032b) treatment enhances TP53 target gene expression and induces G1 cell cycle arrest, senescence and apoptosis^[3].

Milademetan (DS-3032b, 0-2000 nM) treatment selectively inhibits viability, proliferation and migration of neuroblastoma cells with wildtype TP53 independently of MYCN status^[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay^[4]

Cell Line:	SK-N-SH, SH-SY5Y, IMR32, IMR5 and LAN5 cell lines.
Concentration:	0-2000 nM.
Incubation Time:	24-72 h.
Result:	Reduced viability in a dose- and time-dependent manner. Exhibited IC50 values of 21.9 nM, 17.7 nM, 52.63 nM, 25.7 nM and 44.1 nM in SK-N-SH, SH-SY5Y, IMR32, IMR5 and LAN5 cell lines, respectively (72 h).

In Vivo

Milademetan (DS-3032b, 50 mg/kg, oral gavage) delays tumor growth and improves survival in mice xenografted with neuroblastoma cells with functional TP53^[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SH-SY5Y xenograft tumors in nude mice ^[4] .
Dosage:	50 mg/kg.
Administration:	Oral gavage for 30 consecutive days with an alternating schedule of 4 days of daily treatment with oral gavages followed by 2 days without treatment (4+2).
Result:	Survival in the mouse cohort was significantly prolonged. Reduced neuroblastoma xenograft tumor growth by activating TP53 signaling.

CUSTOMER VALIDATION

- Biomedicines. 2022, 10(3), 638.

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REFERENCES

[1]. ARYL SULFONOHYDRAZIDES. WO 2017069289 A1.

[2]. M.M. Gounder, et al. Milademetan, an oral MDM2 inhibitor, in well-differentiated/dedifferentiated liposarcoma: results from a phase 1 study in patients with solid tumors or lymphomas. European Journal of Cancer 138S2 (2020) S1–S62.

[3]. Li, Yangbing, et al. Development of novel PROTAC Small-Molecule Degraders of MDM2 Protein and Peptidomimetic Inhibitors Targeting WDR5-MLL1 Protein-Protein Interaction.

[4]. Viktor Arnhold, et al. Reactivating TP53 signaling by the novel MDM2 inhibitor DS-3032b as a therapeutic option for high-risk neuroblastoma. ncotarget. 2018 Jan 5; 9(2): 2304–2319.

Caution: Product has not been fully validated for medical applications. For research use only.

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