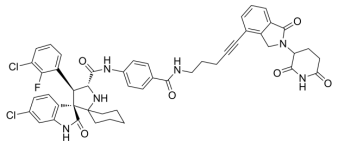
MD-224

Cat. No.:	HY-114312
CAS No.:	2136247-12-4
Molecular Formula:	$C_{48}H_{43}Cl_2FN_6O_6$
Molecular Weight:	889.8
Target:	PROTACs; MDM-2/p53; E1/E2/E3 Enzyme
Pathway:	PROTAC; Apoptosis; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (112.38 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1238 mL	5.6192 mL	11.2385 mL
	5 mM	0.2248 mL	1.1238 mL	2.2477 mL
	10 mM	0.1124 mL	0.5619 mL	1.1238 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: ≥ 7.5 mg/mL (8.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 7.5 mg/mL (8.43 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (2.81 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (2.81 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

MD-224 is a first-in-class and highly potent small-molecule human murine double minute 2 (MDM2) degrader based on the proteolysistargeting chimera (PROTAC) concept. MD-224 consists of ligands for Cereblon and MDM2. MD-224 induces rapid degradation of MDM2 at concentrations <1 nM in human leukemia cells, and achieves an IC_{50} value of 1.5 nM in inhibition of growth of RS4;11 cells. MD-224 has the potential to be a new class of anticancer agent[1]. MD-224 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules

	containing Azide groups.
IC_{50} & Target	MDM2 1 nM (IC_{50})
In Vitro	MD-224 (1-30 nM; 2 hours) effectively induces depletion of MDM2 protein and concurrently accumulation of p53 protein in a dose-dependent manner in RS4;11 cells[1]. ?MD-224 (30 nM; 6 hours) is more potent than MI-1061 in induction of transcriptional upregulation of these p53 target genes but have no effect on TP53 itself in RS4;11 cells[1]. ?MD-224 (0.001-1 μM; 24 hours) induces robust apoptosis at ≤10 nM in a dose-dependent manner upon a 24 hours treatment [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	RS4;11 cells
Concentration:	1 nM; 3 nM; 10 nM; 30 nM
Incubation Time:	2 hours
Result:	Decreased MDM2 protein and accumulated of p53 protein.

RT-PCR[1]

Cell Line:	RS4;11 cells
Concentration:	30 nM
Incubation Time:	6 hours
Result:	Upregulated p53 target gene expression.

Apoptosis Analysis[1]

Cell Line:	RS4;11 cells
Concentration:	0.001 μM, 0.003 μM, 0.01 μM, 0.03 μM, 0.1 μM, 0.3 μM, 1 μM
Incubation Time:	24 hours
Result:	Induces robust apoptosis in RS4;11 cells.

CUSTOMER VALIDATION

- Cell Rep. 2022 May 31;39(9):110879.
- bioRxiv. 2023 May 26.
- Research Square Print. November 18th, 2022
- St. Johns University. 2021 Jul.

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REFERENCES

[1]. Li Y, et al. Discovery of MD-224 as a First-in-Class, Highly Potent, and Efficacious Proteolysis TargetingChimera Murine Double Minute 2 Degrader Capable of Achieving Complete and Durable TumorRegression. J Med Chem. 2019 Jan 24;62(2):448-466

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA