上海源叶生物科技有限公司
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产品名称：dBET1
CAS 号：1799711-21-9
产品货号：S88494

生物活性：

Description	dBET1 是由 Cereblon 配体和 BRD4 配体相连的 PROTAC，其 EC50 值为 430 nM。dBET1 是一种由 BRD4 抑制剂 JQ1 与 NSC 527179 衍生物通过 linker 产生的 PROTAC，能够在低纳摩尔浓度下诱导 BRD4 降解。
IC50 & Target	BRD4 430 nM (EC_{50})　　Cereblon

Cellular Effect

Cell Line	Type	Value	Description
A549	IC_{50}	12.3 μM	Antiproliferative activity against human A549 cells assessed as cell growth inhibition measured after 4 days by CCK-8 assay
HEK293	IC_{50}	0.056 μM	Cytotoxicity against permeabilized HEK293 cells assessed as inhibition of cell viability incubated for 30 mins in presence of CRBN-tracer by nanoBRET assay
HEK293	IC_{50}	0.09 μM	Cytotoxicity against permeabilized HEK293 cells assessed as inhibition of cell viability incubated for 30 mins in presence of CRBN-tracer by nanoBRET assay
HEK293	IC_{50}	0.93 μM	Cytotoxicity against human HEK293 cells assessed as inhibition of cell viability incubated for 30 mins in presence of CRBN-tracer by nanoBRET assay
HEK293	IC_{50}	2.2 μM	Cytotoxicity against human HEK293 cells assessed as inhibition of cell viability incubated for 30 mins in presence of CRBN-tracer by nanoBRET assay
HGC-27	IC_{50}	0.88 μM	Antiproliferative activity against human HGC-27 cells assessed as cell growth inhibition measured after 4 days by CCK-8 assay
HN-6	IC_{50}	7.07 μM	Antiproliferative activity against human HN-6 cells assessed as reduction in cell viability incubated for 24 hrs by CCK-8 assay
HeLa	IC_{50}	16.06 μM	Antiproliferative activity against human HeLa cells assessed as cell growth inhibition measured after 4 days by CCK-8 assay
HepG2	IC_{50}	19.8 μM	Antiproliferative activity against human HepG2 cells assessed as cell growth inhibition measured after 4 days by CCK-8 assay
MCF7	IC_{50}	5.3 μM	Antiproliferative activity against human MCF7 cells assessed as cell growth inhibition measured after 4 days by CCK-8 assay
MM1.S	IC_{50}	0.141 μM	Antiproliferative activity against human MM1.S cells assessed as inhibition of cell growth incubated for 72 hrs MTS assay

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	MM1.S	IC_{50}	2469 nM	Antiproliferative activity against human MM1.S cells assessed as cell growth inhibition measured after 4 days by CellTitre-Glo assay
	MOLM-13	IC_{50}	140 nM	Growth inhibition of human MOLM13 cells after 96 hrs by CCK8 assay
	MOLM-13	IC_{50}	657 nM	Cytotoxicity against human MOLM13 cells assessed as cell growth inhibition after 4 days by WST-8 assay
	MV4-11	IC_{50}	0.013 μM	Antiproliferative activity against human MM4-11 cells assessed as inhibition of cell growth incubated for 72 hrs MTS assay
	MV4-11	IC_{50}	11.8 nM	Antiproliferative activity against human MV4-11 cells assessed as cell growth inhibition measured after 3 days by CellTitre-Glo assay
	MV4-11	IC_{50}	42 nM	Growth inhibition of human MV4-11 cells after 96 hrs by CCK8 assay
	MV4-11	IC_{50}	6.1 nM	Antiproliferative activity against human MV4-11 cells assessed as inhibition of cell growth incubated for 3 days by CellTiter-Glo assay
	PC-3	EC_{50}	50 nM	Cytotoxicity against human PC-3 cells assessed as reduction in cell viability measured after 5 days by Cell-Titer glo assay
	RS4-11	IC_{50}	78.8 nM	Cytotoxicity against human RS4:11 cells assessed as cell growth inhibition after 4 days by WST-8 assay
	RS4-11	IC_{50}	79 nM	Growth inhibition of human RS4:11 cells after 96 hrs by CCK8 assay

In Vitro

dBET1 处理下调 MYC 和 PIM1 的转录。dBET1 降解 BRD4，与 MV4;11 细胞系中更强的凋亡效果相关。仅 4 小时的 dBET1 处理显著增加了凋亡，并在 8 小时时增强。dBET1 还在 24 小时内对 MV4;11 细胞增殖产生显著的抑制作用 (通过 ATP 含量测量，IC50=0.14 μM，相较于 JQ1 的 IC50=1.1 μM) [1]。

In Vivo

通过连续体积测量确定，dBET1 给药可减缓肿瘤进展，并降低死后评估的肿瘤重量。在第一次或第二次每日用 dBET1(50 mg/kg IP)治疗后四小时观察到 BRD4 的急性药效学降解。与切除的肿瘤中的载体对照相比，dBET1 观察到 BRD4 的统计学显著不稳定、MYC 下调和增殖抑制。小鼠对两周的 dBET1 耐受性良好，对体重、白细胞计数、血细胞比容或血小板计数没有显著影响[1]

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 : 43.33 mg/mL (55.18 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2734 mL	6.3672 mL	12.7345 mL
	5 mM	0.2547 mL	1.2734 mL	2.5469 mL
	10 mM	0.1273 mL	0.6367 mL	1.2734 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

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	储备液的保存方式和期限：-80°C, 1 year; -20°C, 6 months。-80°C 储存时，请在 1 年内使用， -20°C 储存时，请在 6 个月内使用。 **动物实验：** 请根据您的实验动物和给药方式 选择适当的溶解方案。 以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 方案 一 请依序添加每种溶剂： 10% DMSO → 90% Corn Oil Solubility: ≥ 3 mg/mL (3.82 mM); 澄清溶液 此方案可获得 ≥ 3 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。 以 1 mL 工作液为例，取 100 μL 30.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
参考文献	[1]. Winter GE, et al. DRUG DEVELOPMENT. Phthalimide conjugation as a strategy for in vivo target protein degradation. Science. 2015 Jun 19;348(6241):1376-81.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80° C, 1 year; -20° C, 6 months。-80° C 储存时，请在 1 年内使用， -20° C 储存时，请在 6 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	1.2734 mL	6.3672 mL	12.7345 mL	31.8362 mL
	5 mM	0.2547 mL	1.2734 mL	2.5469 mL	6.3672 mL
	10 mM	0.1273 mL	0.6367 mL	1.2734 mL	3.1836 mL
	15 mM	0.0849 mL	0.4245 mL	0.8490 mL	2.1224 mL
	20 mM	0.0637 mL	0.3184 mL	0.6367 mL	1.5918 mL
	25 mM	0.0509 mL	0.2547 mL	0.5094 mL	1.2734 mL
	30 mM	0.0424 mL	0.2122 mL	0.4245 mL	1.0612 mL
	40 mM	0.0318 mL	0.1592 mL	0.3184 mL	0.7959 mL
	50 mM	0.0255 mL	0.1273 mL	0.2547 mL	0.6367 mL