上海源叶生物科技有限公司
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产品名称：Pomalidomide
CAS 号： 19171-19-8
产品货号：S89235

生物活性：

Description	Pomalidomide 是第三代免疫调节剂，以分子胶的方式作用。Pomalidomide 与 E3 连接酶 cereblon 相互作用，诱导必需的 Ikaros 转录因子的降解。
IC50 & Target[5]	Cereblon

Cellular Effect

Cell Line	Type	Value	Description
A-375	IC_{50}	> 10 μM	Cytotoxicity against human A375 cells assessed as reduction in cell viability after 72 hrs by MTT assay
A549	IC_{50}	> 33.3 μM	Antiproliferative activity against human A549 cells assessed as inhibition of cell growth measured after 72 hrs by MTS assay
B16-F10	IC_{50}	> 10 μM	Cytotoxicity against mouse B16F10 cells assessed as reduction in cell viability after 72 hrs by MTT assay
BXPC-3	IC_{50}	<= 30 μM	Antiproliferative activity against human BxPC-3 cells assessed as reduction in cell viability incubated for 3 days by MTT assay
HCT-116	IC_{50}	> 33.3 μM	Antiproliferative activity against human HCT-116 cells assessed as inhibition of cell growth measured after 72 hrs by MTS assay
HCT-116	IC_{50}	> 50 μM	Antiproliferative activity against human HCT-116 cells expressing wildtype ATM incubated for 72 hrs by CCK8 assay
HeLa	IC_{50}	1.27 μM	Inhibition of IL-1-alpha-induced NF-kappaB activation in HeLa cells assessed as blocking of p50/p65 nuclear translocation
JeKo-1	IC_{50}	2617.33 nM	Antiproliferative activity against human Jeko-1 cells assessed as cell viability measured after 7 days by CCK-8 assay
JeKo-1	IC_{50}	> 20000 nM	Antiproliferative activity against human Jeko-1 cells expressing CRBN-knockout assessed as cell viability measured after 7 days by CCK-8 assay
Jurkat	IC_{50}	> 33.3 μM	Antiproliferative activity against human Jurkat cells assessed as inhibition of cell growth measured after 72 hrs by MTS assay
K562	IC_{50}	> 10 μM	Antiproliferative activity against human K562 cells assessed as cell growth inhibition measured after 48 hrs by CCK8 assay
K562	IC_{50}	> 10 μM	Antiproliferative activity against human K562 cells assessed as inhibition of cell growth incubated for 2 days by CCK8 assay
KARPAS-2	IC_{50}	> 10 μM	Antiproliferative activity against human KARPAS-299

	99			cells assessed as inhibition of cell growth measured after 72 hrs by MTT assay
	LP-1	GI_{50}	> 10 μM	Antiproliferative activity against human LP-1 cells assessed as growth inhibition incubated for 3 days by fluorescence based assay
	LoVo	IC_{50}	> 50 μM	Antiproliferative activity against ATM deficient human LoVo cells incubated for 72 hrs by CCK8 assay
	MCF7	IC_{50}	17 μM	Cytotoxicity against human MCF7 cells assessed as inhibition of cell proliferation measured after 72 hrs by MTT assay
	MCF7	IC_{50}	> 100 μM	Antiproliferative activity against human MCF7 cells assessed as inhibition of cell proliferation incubated for 72 hrs by MTT assay
	MCF7	IC_{50}	> 100 μM	Antiproliferative activity against human MCF-7 cells assessed as inhibition of cell proliferation incubated for 72 hrs by MTT assay
	MDA-MB-231	IC_{50}	> 100 μM	Antiproliferative activity against human MDA-MB-231 cells assessed as inhibition of cell proliferation incubated for 72 hrs by MTT assay
	MDA-MB-231	IC_{50}	> 100 μM	Antiproliferative activity against human MDA-MB-231 cells assessed as inhibition of cell proliferation incubated for 72 hrs by MTT assay
	MDA-MB-468	IC_{50}	> 100 μM	Antiproliferative activity against human MDA-MB-468 cells assessed as inhibition of cell proliferation incubated for 72 hrs by MTT assay
	MIA PaCa-2	IC_{50}	<= 30 μM	Antiproliferative activity against human MIA PaCa-2 cells assessed as reduction in cell viability incubated for 3 days by MTT assay
	MM1.S	IC_{50}	21.93 nM	Antiproliferative activity against human MM1.S cells assessed as cell viability measured after 7 days by CCK-8 assay
	MM1.S	IC_{50}	837.8 nM	Antiproliferative activity against human MM1.S cells assessed as cell viability measured after 3 days by CCK-8 assay
	MX1	IC_{50}	> 100 μM	Antiproliferative activity against human MX1 cells assessed as inhibition of cell proliferation incubated for 72 hrs by MTT assay
	NAMALVA	IC_{50}	0.03 μM	Antiproliferative activity against human NAMALWA cells assessed as inhibition of [3H]thymidine incorporation after 72 hrs by scintillation counting
	NCI-H929	CC_{50}	0.035 μM	Antiproliferative activity against human NCI-H929 cells after 72 hrs by WST-1 assay
	OCI-Ly10	IC_{50}	1.4 μM	Antiproliferative activity against human OCI-Ly10 cells

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				measured after 4 days by CellTiter-Glo Luminescent Cell Viability Assay
	PBMC	IC_{50}	0.013 μM	Inhibition of TNF-alpha production in LPS-stimulated human PBMC preincubated for 1 hr before LPS challenge measured after 28 to 20 hrs by ELISA
	PBMC	IC_{50}	13 nM	Inhibition of lipopolysaccharide stimulated TNF-alpha release in human PBMC
	T-cell	EC_{50}	0.008 μM	Inhibition of IL-2 production in human T cells measured after 2 to 3 days by ELISA
	THP-1	IC_{50}	> 33.3 μM	Antiproliferative activity against human THP-1 cells assessed as inhibition of cell growth measured after 72 hrs by MTS assay
	TMD8	IC_{50}	187 nM	Cytotoxicity against human TMD8 cells incubated for 48 hrs by celltitre glo 2.0 assay

In Vitro

Pomalidomide 还抑制全血 TNF-α，IC50 为 25 nM[1]。与载体处理的对照相比，将淋巴瘤细胞暴露于 Pomalidomide (CC-4047) 会导致细胞增殖减少 40%。Pomalidomide 抑制 Raji 细胞 40% 的 DNA 合成 (P=0.036)[2]。在 CD4+ 和 CD8+ 细胞中，Pomalidomide (CC-4047) 是最有效的 IL-2 升高剂，其次是 CC-6032 和 CC-5013。Pomalidomide 在升高 IL-2、IL-5 和 IL-10 方面明显强于 CC-5013，在升高 IFN-γ 方面略强于 CC-5013[3]。

In Vivo

在 mAb 处理前连续两天给予 Pomalidomide (CC-4047) 可增强利妥昔单抗的抗肿瘤活性，并使荷淋巴瘤小鼠的中位生存期增加一倍。在统计学上，观察到用 Rituximab 处理的动物与 Pomalidomide + Rituximab 处理的动物之间存在显著差异。接受 Pomalidomide 和利妥昔单抗处理的动物的中位生存时间 (中位生存期，74 天；95% CI，70-78) 长于接受利妥昔单抗单一疗法处理的动物 (中位生存期，38 天；95% CI，26-50；log-秩检验，P=0.002)。如流式细胞术分析所示，在荷淋巴瘤 SCID 小鼠中，连续两天施用 CC-5013 或 Pomalidomide 会导致循环 NK 细胞数量显著增加[2]。对大鼠口服 Pomalidomide (POM) 50 mg/kg 后，血液中未结合的浓度在 4.6±2.4 小时时达到 1100±82 ng/mL 的 Cmax 值，同时 AUC(0-10) 值为 6800 ng hr/mL。然而，大脑中未结合的 POM 在 4.1h 时的 Cmax 值为 430 ng/mL，AUC(0-10) 值为 2700 ng hr/mL，未结合的 AUCbrain 与 AUCblood 的比率为 0.39。这些值与出色的血脑屏障穿透力一致。本研究中获得的结果与同时进行的研究中观察到的结果一致，该研究观察了小鼠口服 POM 后的全脑内容[4]。

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：50 mg/mL (182.99 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	3.6598 mL	18.2989 mL	36.5979 mL
5 mM	0.7320 mL	3.6598 mL	7.3196 mL
10 mM	0.3660 mL	1.8299 mL	3.6598 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。

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：

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	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 → 40% PEG300 → 5% Tween-80 → 45% Saline Solubility: ≥ 2.5 mg/mL (9.15 mM); 澄清溶液 此方案可获得 ≥ 2.5 mg/mL（饱和度未知）的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。 生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。 方案 二 请依序添加每种溶剂： 10% DMSO → 90% Corn Oil Solubility: ≥ 2.5 mg/mL (9.15 mM); 澄清溶液 此方案可获得 ≥ 2.5 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 以下溶解方案，请直接配制工作液。建议现用现配，在短期内尽快用完。 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： 0.5% CMC-Na/0.5% Tween-80 in Saline water Solubility: 10 mg/mL (36.60 mM); 悬浊液; 超声助溶。
参考文献	[1]. Zhu YX, et al. Molecular mechanism of action of the immune-modulatory drugs, thalidomide, lenalidomide and pomalidomide in multiple myeloma. Leuk Lymphoma. 2013 Apr;54(4):683-7. [2]. Hernandez-Ilizaliturri FJ1, et al. Immunomodulatory drug CC-5013 or CC-4047 and rituximab enhance antitumor activity in a severe combined immunodeficient mouse lymphoma model. Clin Cancer Res. 2005 Aug 15;11(16):5984-92. [3]. Schafer PH, et al. Enhancement of cytokine production and AP-1 transcriptional activity in T cells by thalidomide-related immunomodulatory drugs. J Pharmacol Exp Ther. 2003 Jun;305(3):1222-32. [4]. Li Z, et al. Pomalidomide shows significant therapeutic activity against CNS lymphoma with a major impact on the tumor microenvironment in murine models. PLoS One. 2013 Aug 5;8(8):e71754. [5]. Lu J, et al. Hijacking the E3 Ubiquitin Ligase Cereblon to Efficiently Target BRD4. Chem Biol. 2015 Jun 18;22(6):755-63. [6]. Liu D, et al. Tumour necrosis factor-α inhibits hepatic lipid deposition through GSK-3β/β-catenin signaling in juvenile turbot (Scophthalmus maximus L.). Gen Comp Endocrinol. 2016 Mar 1;228:1-8.

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。

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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。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	3.6598 mL	18.2989 mL	36.5979 mL	91.4947 mL
	5 mM	0.7320 mL	3.6598 mL	7.3196 mL	18.2989 mL
	10 mM	0.3660 mL	1.8299 mL	3.6598 mL	9.1495 mL
	15 mM	0.2440 mL	1.2199 mL	2.4399 mL	6.0996 mL
	20 mM	0.1830 mL	0.9149 mL	1.8299 mL	4.5747 mL
	25 mM	0.1464 mL	0.7320 mL	1.4639 mL	3.6598 mL
	30 mM	0.1220 mL	0.6100 mL	1.2199 mL	3.0498 mL
	40 mM	0.0915 mL	0.4575 mL	0.9149 mL	2.2874 mL
	50 mM	0.0732 mL	0.3660 mL	0.7320 mL	1.8299 mL
	60 mM	0.0610 mL	0.3050 mL	0.6100 mL	1.5249 mL
	80 mM	0.0457 mL	0.2287 mL	0.4575 mL	1.1437 mL
	100 mM	0.0366 mL	0.1830 mL	0.3660 mL	0.9149 mL