上海源叶生物科技有限公司
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产品名称：NVP-AUY922 Synonyms:Luminespib ；VER-52296

CAS 号：747412-49-3

产品货号：S86397

生物活性：

Description	Luminespib (VER-52296) 是有效的 HSP90 抑制剂，抑制 HSP90α 和 HSP90β 的 IC50 分别为 7.8 和 21 nM。

IC50 & Target[1]	HSP90α	HSP90β	GRP94	TRAP-1
	7.8 nM (IC_{50})	21 nM (IC_{50})	535 nM (IC_{50})	85 nM (IC_{50})

Cellular Effect

Cell Line	Type	Value	Description
A2780	IC_{50}	0.001 μM	Antiproliferative activity against human A2780 cells after 72 hrs
A549	GI_{50}	0.01 μM	Antiproliferative activity against human A549 cells measured after 48 hrs by SRB assay
A549	GI_{50}	0.026 μM	Growth inhibition of human A549 cells after 72 hrs by SRB assay
A549	IC_{50}	39 nM	Antiproliferative activity against human A549 cells assessed as reduction in cell viability after 72 hrs by SRB assay
A549	IC_{50}	60 nM	Antiproliferative activity against human A549 cells after 72 hrs by SRB assay
BT-474	IC_{50}	0.01 μM	Induction of Her2 degradation in human BT474 cells assessed as inhibition of signal by immunocytochemistry
BT-474	IC_{50}	14 nM	Antiproliferative activity against human BT474 cells after 72 hrs by SRB assay
CAPAN-1	IC_{50}	657 nM	Antiproliferative activity against human Capan1 cells assessed as reduction in cell viability after 72 hrs by SRB assay
DU-145	GI_{50}	0.005 μM	Growth inhibition of human DU145 cells by SRB assay
DU-145	IC_{50}	21 nM	Antiproliferative activity against human DU145 cells after 72 hrs by SRB assay
EBC-1	IC_{50}	13 nM	Antiproliferative activity against human EBC1 cells after 72 hrs by SRB assay
Fibroblast	CC_{50}	0.008 μM	Cytotoxicity against Huntington's disease patient derived fibroblasts after 48 hrs by CellTiter Glo assay
HCC827	IC_{50}	7 nM	Cytotoxicity against gefitinib-resistant human HCC827 cells assessed as inhibition of cell proliferation by MTS assay
HCT-116	GI_{50}	0.016 μM	Growth inhibition of human HCT116 cells after 24 hrs by SRB assay
HCT-116	IC_{50}	121 nM	Antiproliferative activity against human HCT116 cells assessed as reduction in cell viability after 72 hrs by SRB assay
HCT-116	IC_{50}	16 nM	Antiproliferative activity against human HCT116 cells after 72 hrs by SRB assay
L02	IC_{50}	1364 nM	Cytotoxicity agains human HL7702 cells assessed as reduction in cell viability after 72 hrs by SRB assay
MDA-M	IC_{50}	21 nM	Antiproliferative activity against human MDA-MB-231 cells

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	B-231			after 72 hrs by SRB assay
	MIA PaCa-2	IC_{50}	38 nM	Antiproliferative activity against human MIAPaCa2 cells assessed as reduction in cell viability after 72 hrs by SRB assay
	NCI-H1975	GI_{50}	0.02 μM	Antiproliferative activity against human NCI-H1975 cells measured after 48 hrs by SRB assay
	NCI-H3122	IC_{50}	0.014 μM	Antiproliferative activity against human NCI-H3122 cells after 72 hrs by SRB assay
	NCI-H3122	IC_{50}	12.4 nM	Antiproliferative activity against human NCI-H3122 cells after 72 hrs by SRB assay
	NCI-H460	IC_{50}	0.0024 μM	Cytotoxicity against human NCI-H460 cells assessed as growth inhibition after 72 hrs by sulforhodamine B assay
	NCI-H460	IC_{50}	0.0024 μM	Cytotoxicity against human NCI-H460 after 72 hrs by sulforhodamine B assay
	NCI-H460	GI_{50}	0.03 μM	Antiproliferative activity against human NCI-H460 cells measured after 48 hrs by SRB assay
	NCI-H460	IC_{50}	2.4 nM	Cytotoxicity against human NCI-H460 cells assessed as growth inhibition after 72 hrs by SRB assay
	NCI-H460	IC_{50}	23 nM	Antiproliferative activity against human NCI-H460 cells after 72 hrs by SRB assay
	NCI-N87	IC_{50}	83 nM	Antiproliferative activity against human NCI-N87 cells after 72 hrs by SRB assay
	PC-3M	GI_{50}	0.006 μM	Growth inhibition of human PC3M cells by SRB assay
	SF-268	GI_{50}	0.006 μM	Growth inhibition of human SF268 cells by SRB assay
	Sf9	IC_{50}	8 nM	Displacement of GM-BODIPY from human full length HSP90 alpha expressed in baculovirus-infected Sf9 cells after 16 hrs by fluorescence polarization assay
	SK-MEL-28	GI_{50}	0.005 μM	Growth inhibition of human SKMel28 cells by SRB assay
	U-87MG ATCC	GI_{50}	0.008 μM	Growth inhibition of human U87MG cells by SRB assay
	U-87MG ATCC	IC_{50}	31 nM	Antiproliferative activity against human U87MG cells after 72 hrs by SRB assay

In Vitro

Luminespib 是一种强效且选择性的 HSP90 抑制剂，对 HSP90β 的 IC50s 值和 Kis 值分别为 21 ± 16、8.2 ± 0.7 nM，对 HSP90α 的 IC50s 值和 Kis 值分别为 7.8 ± 1.8、9.0 ± 5.0 nM。Luminespib 对 GRP94 和 TRAP-1 表现出较弱的活性，IC50s 值分别为 535 ± 51 nM（Ki，108 nM）和 85 ± 8 nM（Ki，53 nM）。Luminespib 对各种人类肿瘤细胞系的增殖有抑制作用 (2.3-49.6 nM)，诱导细胞周期停滞和凋亡，并消耗人类癌细胞中的客户蛋白 (80 nM)[1]。Luminespib (100 nM) 显著降低 CD40L 成纤维细胞诱导的免疫表型和 STAT3 信号传导变化，但对慢性淋巴细胞白血病 (CLL) 细胞的活力没有影响。Luminespib (500 nM) 与 NSC 118218 联合使用比单独使用任何一种药物更有效地诱导共培养细胞凋亡，并克服成纤维细胞对 Hsp90 抑制剂的耐药性[2]。Luminespib 对胰腺癌细胞表现出很强的抑制作用，IC50 值为 10 nM。Luminespib (10 nM) 可降低 EGFR 的表达和表皮生长因子 (EGF) 介导的激活，并通过降低 ERKThr202/Tyr204 的下游磷酸化来显著破坏 EGF 信号传导。Luminespib (10 nM) 可在没有和存在 EGF 的情况下显著阻止胰腺癌细胞的迁移和侵袭[3]。

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In Vivo

Luminespib（50、75 mg/kg，腹腔注射）显著抑制肿瘤生长速度，降低人类肿瘤异种移植模型中第 11 天肿瘤的平均重量[2]。

Luminespib（50 mg/kg/周，3×25 mg/kg/周）显著降低 L3.6pl 胰腺癌细胞小鼠模型中的肿瘤生长速度并降低肿瘤重量[3]。

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 :≥ 62 mg/mL (133.18 mM; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

* "≥" means soluble, but saturation unknown

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1480 mL	10.7402 mL	21.4804 mL
	5 mM	0.4296 mL	2.1480 mL	4.2961 mL
	10 mM	0.2148 mL	1.0740 mL	2.1480 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：

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 (5.37 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% (20% SBE-β-CD in Saline)

Solubility: ≥ 2.5 mg/mL (5.37 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。

2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。

方案 三

请依序添加每种溶剂： 10% DMSO → 90% Corn Oil

Solubility: ≥ 2.5 mg/mL (5.37 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。

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	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。 方案 四 请依序添加每种溶剂： 5% DMSO → 40% PEG300 → 5% Tween-80 → 50% Saline Solubility: ≥ 2.5 mg/mL (5.37 mM); 澄清溶液 方案 五 请依序添加每种溶剂： 5% DMSO → 95% (20% SBE-β-CD in Saline) Solubility: ≥ 2.5 mg/mL (5.37 mM); 澄清溶液。
参考文献	[1]. Eccles, Suzanne A., et al. NVP-AUY922: A Novel Heat Shock Protein 90 Inhibitor Active against Xenograft Tumor Growth, Angiogenesis, and Metastasis. Cancer Research (2008), 68(8), 2850-2860. [2]. Best OG, et al. Heat shock protein-90 inhibitor, NVP-AUY922, is effective in combination with NSC 118218 against chronic lymphocytic leukemia cells cultured on CD40L-stromal layer and inhibits their activated/proliferative phenotype. Leuk Lymphoma. 2012 Jul 9. [3]. Moser C, et al. Stoeltzing O.Targeting HSP90 by the novel inhibitor NVP-AUY922 reduces growth and angiogenesis of pancreatic cancer. Anticancer Res. 2012 Jul;32(7):2551-61.

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**	2.1480 mL	10.7402 mL	21.4804 mL	53.7011 mL
	5 mM	0.4296 mL	2.1480 mL	4.2961 mL	10.7402 mL
	10 mM	0.2148 mL	1.0740 mL	2.1480 mL	5.3701 mL
	15 mM	0.1432 mL	0.7160 mL	1.4320 mL	3.5801 mL
	20 mM	0.1074 mL	0.5370 mL	1.0740 mL	2.6851 mL
	25 mM	0.0859 mL	0.4296 mL	0.8592 mL	2.1480 mL
	30 mM	0.0716 mL	0.3580 mL	0.7160 mL	1.7900 mL
	40 mM	0.0537 mL	0.2685 mL	0.5370 mL	1.3425 mL
	50 mM	0.0430 mL	0.2148 mL	0.4296 mL	1.0740 mL
	60 mM	0.0358 mL	0.1790 mL	0.3580 mL	0.8950 mL
	80 mM	0.0269 mL	0.1343 mL	0.2685 mL	0.6713 mL
	100 mM	0.0215 mL	0.1074 mL	0.2148 mL	0.5370 mL