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产品名称：Rigosertib (sodium)
产品别名：瑞格色替钠；ON-01910 sodium

生物活性：

Description	Rigosertib sodium (ON-01910 sodium) is a multi-kinase inhibitor and a selective anti-cancer agent, which induces apoptosis by inhibition the PI3K/Akt pathway, promotes the phosphorylation of histone H2AX and induces G2/M arrest in cell cycle[1][2]. Rigosertib sodium is a selective and non-ATP-competitive inhibitor of PLK1 with an IC50 of 9 nM[3].

IC_{50} & Target					
PLK1	PLK2	PDGFR	Src	BCR-ABL	Cdk1
9 nM (IC_{50})	260 nM (IC_{50})	18 nM (IC_{50})	155 nM (IC_{50})	32 nM (IC_{50})	260 nM (IC_{50})
Flt1	Fyn				
42 nM (IC_{50})	182 nM (IC_{50})				

In Vitro	Rigosertib is non-ATP-competitive inhibitor of PLK1 with IC50 of 9 nM. Rigosertib also exhibits inhibition of PLK2, PDGFR, Flt1, BCR-ABL, Fyn, Src, and CDK1, with IC50 of 18-260 nM. Rigosertib shows cell killing activity against 94 different tumor cell lines with IC50 of 50-250 nM, including BT27, MCF-7, DU145, PC3, U87, A549, H187, RF1, HCT15, SW480, and KB cells. While in normal cells, such as HFL, PrEC, HMEC, and HUVEC, Rigosertib has little or no effect unless its concentration is greater than 5-10 μM. In HeLa cells, Rigosertib (100-250 nM) induces spindle abnormalities and apoptosis[3]. Rigosertib also inhibits several multidrug resistant tumor cell lines, including MES-SA, MES-SA/DX5a, CEM, and CEM/C2a, with IC50 of 50-100 nM. In DU145 cells, Rigosertib (0.25-5 μM) blocks cell cycle progression in G2/M phase, results in an accumulation of cells containing subG1 content of DNA, and activates apoptotic pathways. In A549 cells, Rigosertib (50 nM-0.5 μM) induces loss of viability and caspase 3/7 activation[4]. Rigosertib sodium (2 μM) induces apoptosis in chronic lymphocytic leukemia (CLL) cells without toxicity against T-cells or normal B-cells. Rigosertib sodium (2 μM) also abrogates the pro-survival effect of follicular dendritic cells on CLL cells and reduces SDF-1-induced migration of leukemic cells[5].
In Vivo	Rigosertib (250 mg/kg, i.p.) markedly inhibits tumor growth in mouse xenograft models of Bel-7402, MCF-7, and MIA-PaCa cells[3]. Rigosertib (200 mg/kg, i.p.) shows inhibition on tumor growth in a mouse xengraft model of BT20 cells[4].

In Vitro:

DMSO : 150 mg/mL (**316.81 mM;** Need ultrasonic)

H_2O : ≥ 52 mg/mL (**109.83 mM**)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1121 mL	10.5603 mL	21.1207 mL
5 mM	0.4224 mL	2.1121 mL	4.2241 mL
10 mM	0.2112 mL	1.0560 mL	2.1121 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, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C

Solvent&Solubility	储存时，请在 1 个月内使用。 ***In Vivo:*** 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 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 5.25 mg/mL (11.09 mM); Clear solution 此方案可获得 ≥ 5.25 mg/mL (11.09 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 52.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 5.25 mg/mL (11.09 mM); Clear solution 此方案可获得 ≥ 5.25 mg/mL (11.09 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 52.5 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 5.25 mg/mL (11.09 mM); Clear solution 此方案可获得 ≥ 5.25 mg/mL (11.09 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 52.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Xu F, et al. Rigosertib as a selective anti-tumor agent can ameliorate multiple dysregulated signalingtransduction pathways in high-grade myelodysplastic syndrome. Sci Rep. 2014 Dec 4;4:7310. [2]. Hyoda T, et al. Rigosertib induces cell death of a myelodysplastic syndrome-derived cell line by DNA damage-induced G2/M arrest. Cancer Sci. 2015 Mar;106(3):287-93. [3]. Gumireddy K, et al. ON01910, a non-ATP-competitive small molecule inhibitor of Plk1, is a potent anticancer agent. Cancer Cell. 2005 Mar;7(3):275-86. [4]. Reddy MV, et al. Discovery of a clinical stage multi-kinase inhibitor sodium (E)-2-{2-methoxy-5-[(2',4',6'-trimethoxystyrylsulfonyl)methyl]phenylamino}acetate (ON 01910.Na): synthesis, structure-activity relationship, and biological activity. J Med Chem. [5]. Chapman CM, et al. ON 01910.Na is selectively cytotoxic for chronic lymphocytic leukemia cells through a dual mechanism of action involving PI3K/AKT inhibition and induction of oxidative stress. Clin Cancer Res. 2012 Apr 1;18(7):1979-91

实验参考：

Cell Assay	Tumor cells are plated into six-well dishes at a density of 1×10^5 cells/mL/well, and Rigosertib is added 24 hours later at various concentrations. Cell counts are determined from duplicate wells after 96-hour of treatment. The total number of viable cells is determined by trypan blue exclusion.

	[2]
Animal Administration	Bel-7402 tumor models: twenty female athymic (NCR-nu/nu) nude mice are injected with 1 × 10^7 Bel-7402 tumor cells subcutaneously, and 10-14 days later, when the tumor volumes reach 200-250 mm, the mice are divided into four groups such that each group harbors tumors of the same volume. Rigosertib (ON01910, 250 mg/kg) dissolved in PBS is administered alone or in combination with NSC 266046 (100 mg/kg) intraperitonially on alternate days. Tumor measurements are done two times/week using traceable digital vernier calipers. Body weight is determined during each measurement. The animals are observed for signs of toxicity[1].
References	[1]. Xu F, et al. Rigosertib as a selective anti-tumor agent can ameliorate multiple dysregulated signalingtransduction pathways in high-grade myelodysplastic syndrome. Sci Rep. 2014 Dec 4;4:7310. [2]. Hyoda T, et al. Rigosertib induces cell death of a myelodysplastic syndrome-derived cell line by DNA damage-induced G2/M arrest. Cancer Sci. 2015 Mar;106(3):287-93. [3]. Gumireddy K, et al. ON01910, a non-ATP-competitive small molecule inhibitor of Plk1, is a potent anticancer agent. Cancer Cell. 2005 Mar;7(3):275-86. [4]. Reddy MV, et al. Discovery of a clinical stage multi-kinase inhibitor sodium (E)-2-{2-methoxy-5-[(2',4',6'-trimethoxystyrylsulfonyl)methyl]phenylamino}acetate (ON 01910.Na): synthesis, structure-activity relationship, and biological activity. J Med Chem. [5]. Chapman CM, et al. ON 01910.Na is selectively cytotoxic for chronic lymphocytic leukemia cells through a dual mechanism of action involving PI3K/AKT inhibition and induction of oxidative stress. Clin Cancer Res. 2012 Apr 1;18(7):1979-91