产品名称：YM155 (Sepantronium Bromide)
产品别名：YM-155

生物活性：

Description	YM-155 is a survivin inhibitor with an IC_{50} of 0.54 nM.
IC_{50} & Target	IC50: 0.54 nM (survivin)
In Vitro	YM155 (30 μM) is not sensitive to survivn gene promoter-driven luciferase reporter activity. YM155 shows significant supression on endogenous survivin expression in PC-3 and PPC-1 human HRPC cells with deficient p53 via transcriptional inhibition of the survivin gene promoter. YM155 (100 nM) does not affect protein expression of c-IAP2, XIAP, Bcl-2, Bcl-xL, Bad, α-actin, and β-tubulin. YM155 potently inhibits human cancer cell lines (mutated or truncated p53) such as PC-3, PPC-1, DU145, TSU-Pr1, 22Rv1, SK-MEL-5 and A375 with IC50s ranging from 2.3 to 11 nM, respectively[1]. YM155 resultin in an increase in sensitivity of NSCLC cells to γ-radiation. YM155 combined with γ-radiation increases both the number of apoptotic cells and the activity of caspase-3. In addition, YM155 delays the repair of radiation-induced double-strand breaks in nuclear DNA[2].
In Vivo	YM155 (3 and 10 mg/kg) inhibits the tumor growth in PC-3 xenografts, without obvious body weight loss and blood cell count decrease. YM155 is highly distributed to tumor tissue in vivo. YM155 shows 80% TGI at a dose of 5 mg/kg in PC-3 orthotopic xenografts[1]. YM155 in combination with γ-radiation shows potent antitumor activity against H460 or Calu6 xenografts in nude mice[2]. In this orthotopic renal and metastatic lung tumors models, YM155 and IL-2 additively decreases tumor weight, lung metastasis, and luciferin-stained tumor images[3].
Solvent&Solubility	***In Vitro:*** **H_2O : 100 mg/mL** (**225.59 mM;** Need ultrasonic) **DMSO : 50 mg/mL** (**112.79 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2559 mL	11.2793 mL	22.5586 mL
	5 mM	0.4512 mL	2.2559 mL	4.5117 mL
	10 mM	0.2256 mL	1.1279 mL	2.2559 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 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: ≥ 2 mg/mL (4.51 mM); Clear solution

此方案可获得 ≥ 2 mg/mL (4.51 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.0 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。
References	[1]. Nakahara T, et al. YM155, a novel small-molecule survivin suppressant, induces regression of established human hormone-refractory prostate tumor xenografts. Cancer Res. 2007 Sep 1;67(17):8014-21. [2]. Iisa T, et al. Radiosensitizing effect of YM155, a novel small-molecule survivin suppressant, in non-small cell lung cancer cell lines. Clin Cancer Res. 2008 Oct 15;14(20):6496-504. [3]. Guo K, et al. A combination of YM-155, a small molecule survivin inhibitor, and IL-2 potently suppresses renal cell carcinoma in murine model. Oncotarget. 2015 Aug 28;6(25):21137-47.

实验参考：

Cell Assay	The antiproliferative activity of YM-155 is measured. After treatment with YM-155 for 48 h, the cell count is determined by sulforhodamine B assay. The GI_{50} value is calculated by logistic analysis, which is the drug concentration resulting in a 50% reduction in the net protein increase (as measured by sulforhodamine B staining) in control cells during the drug incubation. The assay is done in triplicate, and the mean GI_{50} value is obtained from the results of four independent assays. [1]
Animal Administration	Five-week-old male nude mice (BALB/c nu/nu) are used for the assay. PC-3 cells (2×10^6-3×10^6) are injected into the flanks of the mice and allowed to reach a tumor volume of > 100 mm^3 in tumor volume (length×$width^2$×0.5). YM-155 is s.c. administered as a 3-day continuous infusion per week for 2 weeks using an implanted micro-osmotic pump or i.v. administered five times a week for 2 weeks. The percentage of tumor growth inhibition 14 days after initial YM-155 administration is calculated for each group using the following formula: MTV=100×{1-[(MTV of the treated group on day 14)-(MTV of the treated group on day 0)]/[(MTV of the control group on day 14)-(MTV of the control group on day 0)]}, where MTV is mean tumor volume. For both the frozen tumors and plasma samples, survivin expression levels are analyzed by Western blotting and YM-155 drug concentration by high-performance liquid chromatography/triple quadrupole mass spectrometry (LC/MS/MS) using validated methods. [1]
Kinase Assay	A 2,767-bp sequence of human survivin gene promoter is isolated from human genomic DNA by PCR using Pyrobest polymerase and the following primers: 5'-GCGCGCTCGAGTCTAGACATGCGGATATATTC-3' and 5'-GCGCGAA-GCTTTGGCGGTTAATGGCGCGC-3'. The resulting PCR fragment is digested with XhoI/HindIII and ligated into the XhoI/HindIII cleavage site of the pGL3-Basic vector. The resulting plasmid is named pSUR-luc. DNA sequencing is done on all amplified sequences by a DNA sequencer. The activity of pSUR-luc is confirmed by luciferase assay with transiently transfected HeLa-S3 cells. Luciferase assay is done. The pGL3 control vector, which contains the SV40 promoter and enhancer sequences, is used. HeLa cells are stably transfected with pSUR-luc and pSV2bsr by Lipofect-AMINE 2000. After blasticidin selection at 10 μg/mL, a single colony is chosen based on appropriate luciferase signals and genetic stability over time and named HeLa-SURP-luc. CHO cells are stably transfected with pGL3-control and pSV2bsr. After blasticidin selection at 10 μg/mL, a single colony is chosen based on appropriate luciferase signals and genetic stability over time and named CHO-SV40-luc. Stocked cells from the HeLa-SURP-luc and CHO-SV40-luc clones are used for chemical screening and characterization of YM155. YM155 in DMSO are added to the cells, which had been seeded the previous day on 96-well plastic plates at 5×10^3 per well. Luciferase activity is measured 24 hours later. IC_{50} is calculated by logistic analysis. [1]

References	[1]. Nakahara T, et al. YM155, a novel small-molecule survivin suppressant, induces regression of established human hormone-refractory prostate tumor xenografts. Cancer Res. 2007 Sep 1;67(17):8014-21. [2]. Iisa T, et al. Radiosensitizing effect of YM155, a novel small-molecule survivin suppressant, in non-small cell lung cancer cell lines. Clin Cancer Res. 2008 Oct 15;14(20):6496-504. [3]. Guo K, et al. A combination of YM-155, a small molecule survivin inhibitor, and IL-2 potently suppresses renal cell carcinoma in murine model. Oncotarget. 2015 Aug 28;6(25):21137-47.