

产品名称：**2-[[5-[3-(二甲基氨基)丙基]-2-甲基-3-吡啶基]氨基]-5,7-二氢-9-(三氟甲基)-6H-嘧啶并[5,4-D][1]苯并氮杂卓-6-硫酮**
产品别名：**MLN0905**

生物活性:				
Description	MLN0905 is a potent PLK1 inhibitor, with an IC₅₀ of 2 nM.			
IC ₅₀ & Target	PLK1			
	2 nM (IC ₅₀)			
In Vitro	MLN0905 (compound 12c) exhibits potent activities with an EC ₅₀ of 33 ± 21 nM for Cdc25C. MLN0905 shows inhibitory effects on HT29, HCT116, H460, and A375 cell lines, with LD ₅₀ s of 22, 56, 89, and 34 nM[1]. MLN0905 (125 nM) yields strong mitotic arrest and monopolar spindle formation in HT-29 cells, and these effects are associated with PLK1 inhibition. MLN0905 suppresses lymphoma cell lines with IC ₅₀ values ranging from 3 to 24 nM[2].			
In Vivo	MLN0905 (50 mg/kg, p.o.) shows a higher sustained PD response as it impressively generates a robust PD response up to 72 h in nude mice bearing HT29 xenograft tumors. MLN0905 (6.25, 12.5, 25, 50 mg/kg, p.o.) exhibits significant antitumor activities in mice bearing HT29 xenograft tumors[1]. MLN0905 has marked antitumor effects in a subcutaneous OCI LY-19-Luc lymphoma xenograft model, and the treatment are as follows: 3.12 mg/kg daily, 6.25 mg/kg daily, 10 mg/kg QD×3/wk, and 14.5 mg/kg QD×3/wk. MLN0905 (1.6, 3.12, and 6.25 mg/kg, p.o.) also induces a significant antitumor response in mice bearing disseminated (human) OCI LY-19-Luc lymphoma disease. MLN0905 (6, 8, 10, 12.5, and 14.5 mg/kg, p.o.) causes a significant antitumor response in a primary human lymphoma model (PHTX-22L). Furthermore, MLN0905 synergizes with rituximab in a disseminated OCI LY-19-Luc lymphoma model[2].			
Solvent&Solubility	In Vitro: DMSO : ≥ 30 mg/mL (61.66 mM) * "≥" means soluble, but saturation unknown.			
	<div>Preparing Stock Solutions</div>	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg
		1 mM	2.0552 mL	10.2762 mL
		5 mM	0.4110 mL	2.0552 mL
		10 mM	0.2055 mL	1.0276 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℃，6 months；-20℃，1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 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: ≥ 2.5 mg/mL (5.14 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.14 mM, 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。			

	<p>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。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.14 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.14 mM，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 生理盐水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.14 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.14 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
References	<p>[1]. Duffey MO, et al. Discovery of a potent and orally bioavailable benzolactam-derived inhibitor of Polo-like kinase 1 (MLN0905). J Med Chem. 2012 Jan 12;55(1):197-208.</p> <p>[2]. Shi JQ, et al. MLN0905, a small-molecule plk1 inhibitor, induces antitumor responses in human models of diffuse large B-cell lymphoma. Mol Cancer Ther. 2012 Sep;11(9):2045-53.</p>
实验参考：	
Cell Assay	<p>Eight μL of serially diluted test compounds are added to 75 μL of HT29 (2.66×10^4 cells/well) cells in McCoy's 5A media supplemented with 10% Fetal Calf Serum in Biocoat Poly-D lysine 384 well Black/Clear plates. Cells are incubated for 72 h at 37°C. Supernatant is aspirated from the wells, leaving 25 μL in each well. ATP-lite 1 step reagent (25 μL) is added to each well, and luminescence for each plate is read on the LeadSeeker. Percent inhibition is calculated using the values from a DMSO control set to 100%[1].</p>
Animal Administration	<p>HT29 cells are obtained from ATCC and are cultured in McCoy's 5A medium supplemented with 10% FBS. HT29 cells (2×10^6) are resuspended in Hanks buffer and injected subcutaneously into the flanks of female Nude mice. Mice (10 animals/group) are treated orally with 12c (MLN0905) for 21 days at doses based on tolerability results: QD (6.25 and 12.5 mg/kg), QD\times1/week (50 mg/kg), and QD\times3/week (25 mg/kg). Tumor growth is monitored using vernier calipers, and the mean tumor volume is calculated using the formula $V = W^2 \times L/2$. When the mean tumor volume reaches approximately 200 mm³, the animals are randomized into treatment groups (n = 10 animals/group). Tumor growth and body weights are measured twice per week[1].</p>
Kinase Assay	<p>The human PLK1 enzymatic reaction totaled 30 μL contains 50 mM Tris-HCl (pH 8.0), 10 mM MgCl₂, 0.02% BSA, 10% glycerol, 1 mM DTT, 100 mM NaCl, 3.3% DMSO, 50 μM ATP, 2 μM peptide substrate (Biotin-AHX-LDETGHLDSSGLQEVHLA-CONH₂), and 0.3 nM recombinant human PLK1[2-369]T210D. The enzymatic reaction mixture, with or without PLK inhibitors, is incubated 90 min at room temperature before termination with 50 μL of STOP buffer containing 1% BSA, 0.05% Tween 20, 100 mM EDTA. Then 50 μL of the stopped enzyme reaction mixture is transferred to a Neutravidin-coated 384-well plate and incubated at room temperature for 60 min. The wells are washed with wash buffer (25 mM Tris, 150 mM sodium chloride, and 0.1% Tween 20) and incubated for 1 h with 50 μL of antibody reaction mixture containing 1% BSA, 0.05% Tween 20, antiphospho-cdc25c rabbit monoclonal antibody (325 pM), and europium labeled antirabbit IgG (2 nM). The wells are washed, and then the bound europium is liberated using 50 μL of Enhancement</p>

	Solution. Quantification of europium is done using a Pherastar[1].
References	<p>[1]. Duffey MO, et al. Discovery of a potent and orally bioavailable benzolactam-derived inhibitor of Polo-like kinase 1 (MLN0905). J Med Chem. 2012 Jan 12;55(1):197-208.</p> <p>[2]. Shi JQ, et al. MLN0905, a small-molecule plk1 inhibitor, induces antitumor responses in human models of diffuse large B-cell lymphoma. Mol Cancer Ther. 2012 Sep;11(9):2045-53.</p>



源叶生物