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产品名称: **Debio 0932**
产品别名: **CUDC-305**

生物活性:					
Description		Debio 0932 is an orally active HSP90 inhibitor, with IC50s of 100 and 103 nM for HSP90α and HSP90β, respectively.			
IC ₅₀ & Target	HSP90α	HSP90β			
	100 nM (IC ₅₀)	103 nM (IC ₅₀)			
In Vitro		Debio 0932 is an orally active HSP90 inhibitor, with IC50s of 100 and 103 nM for HSP90α and HSP90β, respectively. Debio 0932 (CUDC-305) binds to the tumor HSP90 complex with a mean IC50 of 48.8 nM. Debio 0932 (1 μM) promotes degradation of multiple HSP90 client proteins in cancer cell lines. Debio 0932 also shows inhibitory activities against the proliferation of 40 cancer cell lines (containing 34 solid and 6 hematologic tumor-derived lines) with an IC50 ranging from 40 to 900 nM (mean IC50, 220 nM)[1]. Debio 0932 strongly binds to cancer-derived HSP90 complex with an IC50 of 61.2 nM in H1975 cells and 74.2 nM in H1993 cells, respectively. Debio 0932 (CUDC-305, 1 μM) durably induces oncoprotein degradation in NSCLC cell lines with mutations that can confer resistance to erlotinib[3].			
In Vivo		Debio 0932 (CUDC-305, 30 mg/kg, p.o.) exhibits favorable pharmacokinetic profiles in tumor-bearing nude mice. Debio 0932 (160 mg/kg, p.o.) causes degradation of HSP90 client proteins, suppresses tumor growth, and also prolongs survival in various animal models of U87MG glioblastoma. Debio 0932 (40, 80, or 160 mg/kg, p.o.) also dose-dependently inhibits tumor growth in the U87MG s.c. tumor model by every-other-day (q2d) dosing[1]. Debio 0932 (80 mg/kg, p.o.) significantly alleviates psoriasis by day 11 and decreases epidermal thickness in psoriasis xenograft transplantation model[2]. Debio 0932 (CUDC-305) is able to cross the blood-brain barrier. Debio 0932 (80, 120, and 160 mg/kg, p.o.) shows dose-dependent inhibition of tumor growth in the H1975 subcutaneous tumor model. Debio 0932 (160 mg/kg, p.o.) also promotes antitumor activity in the erlotinib-resistant H1975 subcutaneous tumor model[3].			
In Vitro: DMSO : ≥ 33 mg/mL (74.56 mM) * "≥" means soluble, but saturation unknown.					
Preparing Stock Solutions		<div>Solvent Mass Concentration</div>	1 mg	5 mg	10 mg
		1 mM	2.2595 mL	11.2974 mL	22.5948 mL
		5 mM	0.4519 mL	2.2595 mL	4.5190 mL
		10 mM	0.2259 mL	1.1297 mL	2.2595 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					
Solvent&Solubility					



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	<p>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</p> <p>1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (5.65 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.65 mM, 饱和度未知) 的澄清溶液。</p> <p>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)</p> <p>Solubility: ≥ 2.5 mg/mL (5.65 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.65 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>3.请依序添加每种溶剂: 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (5.65 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.65 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。</p> <p>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]. Bao R, et al. CUDC-305, a novel synthetic HSP90 inhibitor with unique pharmacologic properties for cancer therapy. Clin Cancer Res. 2009 Jun 15;15(12):4046-57.</p> <p>[2]. Stenderup K, et al. Debio 0932, a new oral Hsp90 inhibitor, alleviates psoriasis in a xenograft transplantation model. Acta Derm Venereol. 2014 Nov;94(6):672-6.</p> <p>[3]. Bao R, et al. Targeting heat shock protein 90 with CUDC-305 overcomes erlotinib resistance in non-small cell lung cancer. Mol Cancer Ther. 2009 Dec;8(12):3296-306.</p>
实验参考:	
Cell Assay	<p>Human cancer cell lines are plated at 5,000 to 10,000 per well in 96-well plates with culture medium. The cells are then incubated with compounds (Debio 0932) at various concentrations for 120 h. Growth inhibition is assessed by ATP content assay using the ATPlite kit. Briefly, a 25-μL cell lysis solution is added to the 50-μL phenol red-free culture medium per well to lyse cells and stabilize ATP. Then 25-μL substrate solutions are added to the wells, and subsequently, luminescence is measured with a TopCount liquid scintillation analyzer. Values are expressed as a percentage relative to those obtained in untreated controls. IC₅₀ values are calculated using PRISM software with sigmoidal dose-response curve fitting[1].</p>
Animal Administration	<p>When tumors are established after implantation, animals with proper tumor size are randomly assigned into different groups. Debio 0932 is formulated in 30% Captisol and delivered by oral gavage based on the body weight of each individual animal. The control group is treated with vehicle (30% Captisol) using the same dosing paradigm. In combination studies, paclitaxel or camptothecin-11 is diluted in 0.9% normal saline and injected i.p. twice weekly[1].</p>
	<p>COOH terminal His-tagged human HSP90α and HSP90β proteins are expressed in Escherichia coli.</p>



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Kinase Assay	Fluorescence polarization competition binding assays are done with purified HSP90 α or HSP90 β and FITC-labeled geldanamycin in the presence of different concentrations of test articles (Debio 0932). The final reaction contains 10 and 50 nM of labeled geldanamycin and purified HSP90 protein, respectively. The assay buffer contains 20 mM HEPES (pH 7.3), 50 mM KCl, 1 mM DTT, 50 mM MgCl ₂ , 20 mM Na ₂ MoO ₄ , and 0.01% NP40 with 0.1 mg/mL bovine γ -globulin. Polarization degree (mP) values are determined using a Synergy II plate reader with background subtraction after 24 h of incubation at 4°C[1].
References	<p>[1]. Bao R, et al. CUDC-305, a novel synthetic HSP90 inhibitor with unique pharmacologic properties for cancer therapy. Clin Cancer Res. 2009 Jun 15;15(12):4046-57.</p> <p>[2]. Stenderup K, et al. Debio 0932, a new oral Hsp90 inhibitor, alleviates psoriasis in a xenograft transplantation model. Acta Derm Venereol. 2014 Nov;94(6):672-6.</p> <p>[3]. Bao R, et al. Targeting heat shock protein 90 with CUDC-305 overcomes erlotinib resistance in non-small cell lung cancer. Mol Cancer Ther. 2009 Dec;8(12):3296-306.</p>

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