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产品名称: **XL228**
产品别名: **XL228**

生物活性:

Description	XL228 is a multi-targeted tyrosine kinase inhibitor with IC ₅₀ s of 5, 3.1, 1.6, 6.1, 2 nM for Bcr-Abl, Aurora A, IGF-1R, Src and Lyn, respectively.				
IC ₅₀ & Target	Aurora A	IGF-1R			
	3.1 nM (IC ₅₀)	1.6 nM (IC ₅₀)			
In Vitro	XL228 shows a broad pattern of protein kinase inhibition, including the tyrosine kinases IGF1R, SRC, ABL, FGFR1-3, and ALK and the serine/threonine kinases Aurora A and Aurora B. A panel of kinase inhibitors including XL228 is profiled against a series of cancer cell lines with known alterations in major signaling pathways. Approximately 30% of the lines demonstrate XL228 IC50 values of <100nM in viability assays, including many lines with characterized ALK or FGFR mutations or amplifications. XL228 eliminates the phosphorylation of Aurora A and B at concentrations above 10 nM. Short-term treatment of HeLa cells leads to disruption of mitotic spindle formation, with the majority of mitotic cells exhibiting a unipolar spindle and disorganized chromosomes[2]. It displays low nanomolar biochemical activity against wild type Abl kinase (Ki=5 nM), as well as the T315I form of Abl resistant to imatinib and dasatinib (Ki=1.4 nM). XL228 inhibits phosphorylation of BCR-ABL and its substrate STAT5 in K562 cells in vitro with IC50s of 33 and 43 nM, respectively[3].				
In Vivo	Single-dose pharmacodynamics studies demonstrate a potent effect of XL228 on BCR-ABL signaling in K562 xenograft tumors. Phosphorylation of BCR-ABL is decreased by 50% at XL228 plasma concentrations of 3.5 μM; a similar decrease in phospho-STAT5 occurred at 0.8 μM plasma concentration[3].				
Solvent&Solubility	In Vitro: DMSO : ≥ 83.33 mg/mL (190.45 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	SolventMassConcentration	1 mg	5 mg	10 mg
		1 mM	2.2855 mL	11.4275 mL	22.8551 mL
		5 mM	0.4571 mL	2.2855 mL	4.5710 mL
		10 mM	0.2286 mL	1.1428 mL	2.2855 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				



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	1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.08 mg/mL (4.75 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.75 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.75 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.75 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.75 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.75 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。
References	[1]. Cortes J, et al. Preliminary Clinical Activity in a Phase I Trial of the BCR-ABL/IGF- 1R/Aurora Kinase Inhibitor XL228 in Patients with Ph++ Leukemias with Either Failure to Multiple TKI Therapies or with T315I Mutation. Blood 2008 112:3232 [2]. Douglas O, et al. Abstract C192: Characterization of the target profile of XL228, a multi - targeted protein kinase inhibitor in phase 1 clinical development. Mol Cancer Ther 2009;8(12 Suppl):C192. [3]. Shah N, et al. Targeting Drug-Resistant CML and Ph+-ALL with the Spectrum Selective Protein Kinase Inhibitor XL228. Blood 2007 110:474;

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