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产品名称：CHZ868
产品别名：CHZ868

生物活性：

Description	CHZ868 is a type II JAK2 inhibitor with an IC50 of 0.17 μM in EPOR JAK2 WT Ba/F3 cell.
IC_{50} & Target	JAK2
	110 nM (IC_{50})
In Vitro	CHZ868 potently inhibits constitutive JAK2 and STAT5 phosphorylation in JAK2V617F SET2 cells. CHZ868 potently inhibits the proliferation of SET2 cells (GI_{50}=59nM), and has 6-fold less growth inhibitory activity against CMK cells (GI_{50}=378nM)[1]. At 100 nM CHZ868 has activity against 26 kinases, including JAK2 and TYK2. CHZ868 is thought to engage with the hinge region of JAK2 through two H-bonds, formed between the amino-pyridine of CHZ868 and the backbone-NH/CO of L932, while the pyridine is occupying the adenine pocket of the ATP binding site. CHZ868 potently suppresses the growth of CRLF2-rearranged human B-ALL cells, abrogates JAK2 signaling[2].
In Vivo	CHZ868 is characterized by high passive permeability, good metabolic stability, and low water solubility, as well as by moderate blood clearance and good oral bioavailability, making it suitable for in vivo use. CHZ868 improves survival in mice with human or murine B-ALL. CHZ868 and dexamethasone synergistically induces apoptosis in JAK2-dependent B-ALLs and further improves survival compared to CHZ868 alone[2].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**236.17 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3617 mL	11.8086 mL	23.6172 mL
	5 mM	0.4723 mL	2.3617 mL	4.7234 mL
	10 mM	0.2362 mL	1.1809 mL	2.3617 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: ≥ 2.5 mg/mL (5.90 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.90 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；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: ≥ 2.5 mg/mL (5.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.90 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: ≥ 2.5 mg/mL (5.90 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.90 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。
References	[1]. Meyer SC, et al. CHZ868, a Type II JAK2 Inhibitor, Reverses Type I JAK Inhibitor Persistence and Demonstrates Efficacy in Myeloproliferative Neoplasms. Cancer Cell. 2015 Jul 13;28(1):15-28. [2]. Wu SC, et al. Activity of the Type II JAK2 Inhibitor CHZ868 in B Cell Acute Lymphoblastic Leukemia. Cancer Cell. 2015 Jul 13;28(1):29-41.

实验参考：

Cell Assay	CHZ868 is dissolved in DMSO to make 10 mM stock solution and diluted in culture media. Cells are treated with CHZ868 (0, 0.05, 0.1, 0.2 μM) or vehicle (DMSO). After 48 hr (Ba/F3 cells) or 72 hr (MHH-CALL4 and PDX cells), CellTiter-Glo Luminescent Cell Viability Assay is added (10 μL undiluted or 25 μL of a 1:2 dilution in each well) and plates are read[2].
Animal Administration	Mice: CHZ868 is reconstituted in 0.5% methylcellulose / 0.5% Tween-80 and administered at doses of 10 or 30 mg/kg/day by oral gavage. Pharmacokinetic/pharmacodynamic and efficacy studies in the mouse model of rhEpo-induced polycythemia are carried out essentially as reported. Detection of STAT5 phosphorylation in spleen lysates by Meso Scale Discovery is performed[2].
References	[1]. Meyer SC, et al. CHZ868, a Type II JAK2 Inhibitor, Reverses Type I JAK Inhibitor Persistence and Demonstrates Efficacy in Myeloproliferative Neoplasms. Cancer Cell. 2015 Jul 13;28(1):15-28. [2]. Wu SC, et al. Activity of the Type II JAK2 Inhibitor CHZ868 in B Cell Acute Lymphoblastic Leukemia. Cancer Cell. 2015 Jul 13;28(1):29-41.