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产品名称：Triazolo-pyramidine derivative
产品别名：CPI-444；V81444; ciforadenant

生物活性：

Description	CPI-444 is a potent, oral and selective A2A receptor (A2AR) antagonist, which induces antitumor responses.
IC_{50} & Target	Adenosine A2A receptor[1]
In Vitro	CPI-444 is a potent, oral, selective A2AR antagonist. $CD8^+$ T cell depletion abrogates the efficacy of CPI-444 treatment as a single agent as well as in combination with anti-PD-L1, demonstrating a role for $CD8^+$ T cells in mediating primary and secondary immune responses. Anti-tumor efficacy of CPI-444±anti-PD-L1 is associated with increased CD8+ cell infiltration and activation in MC38 tumor tissues, and a corresponding rise in PD-1 expression on $CD8^+$ T cells in the spleen. Additionally, levels of immune checkpoints are modulated by treatment with CPI-444, including GITR, OX40, and LAG3 on tumor infiltrating lymphocytes and circulating T cells, suggesting a broad role for adenosine mediated immunosuppression[1].
In Vivo	Daily treatment of the syngeneic mouse model MC38 with CPI-444 (1, 10, 100 mg/kg) leads to dose-dependent inhibition of tumor growth, leading to tumor elimination in ~30% of treated mice. Combining CPI-444 (100 mg/kg, qd, 14 days) with anti-PD-L1 (200 μg, 3qw, 4 doses) treatment in MC38 models synergistically inhibits tumor growth and eliminates tumors in 90% of treated mice. When cured mice are later re-challenged with MC38 cells, tumor growth is rejected in 100% of challenged mice, indicating that CPI-444 induces systemic anti-tumor immune memory[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 67.5 mg/mL (165.67 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4544 mL	12.2720 mL	24.5441 mL
	5 mM	0.4909 mL	2.4544 mL	4.9088 mL
	10 mM	0.2454 mL	1.2272 mL	2.4544 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: ≥ 2.25 mg/mL (5.52 mM); Clear solution

此方案可获得 ≥ 2.25 mg/mL (5.52 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 22.5 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: ≥ 2.25 mg/mL (5.52 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (5.52 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 22.5 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
References	[1]. Stephen Willingham, et al. Abstract PR04: CPI-444: A potent and selective inhibitor of A2AR induces antitumor responses alone and in combination with anti-PD-L1 in preclinical and clinical studies.Cancer Immunoly Research. September 25-28, 2016.