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产品名称：TP-3654
产品别名：TP-3654

生物活性：

Description	TP-3654 is a second-generation Pim kinase inhibitor with K_i values of 5 and 42 nM for Pim-1 and Pim-3, respectively.
IC_{50} & Target	Ki: 5 nm(Pim-1), 239 nM (Pim-2), 42 nM (Pim-3)[1]
In Vitro	TP-3654 demonstrates potent PIM-1 specific cellular activity in the PIM-1/BAD overexpression system with an average EC_{50} of 67 nM. TP-3654 treatment reduces levels of phospho-BAD *in vitro* using the bladder cancer cell line UM-UC-3. TP-3654 reduces colony growth of T24 and UM-UC3 cells, confirming the PIM-1–dependent growth for both cell lines[1].
In Vivo	Oral dosing of 200 mg/kg TP-3654 significantly reduces both UM-UC-3 and PC-3 tumor growth measured by volume (caliper) and by final tumor weight, with no significant changes in body weight or gross adverse toxicity[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL** (**119.49 mM**; Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3897 mL	11.9486 mL	23.8971 mL
	5 mM	0.4779 mL	2.3897 mL	4.7794 mL
	10 mM	0.2390 mL	1.1949 mL	2.3897 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: ≥ 2.08 mg/mL (4.97 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.97 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 (4.97 mM); Precipitated solution; Need ultrasonic

此方案可获得 2.08 mg/mL (4.97 mM)

	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 (4.97 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.97 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]. Foulks JM, et al. A small-molecule inhibitor of PIM kinases as a potential treatment for urothelial carcinomas. Neoplasia. 2014 May;16(5):403-12.

实验参考：

Cell Assay	1 μM TP-3654 is tested against 336 kinases at a concentration of 10 μM ATP. IC_{50} determinations of phosphoinositide 3-kinase (PI3K) (α, β, δ, and γ) and all kinases inhibited by >50% from the initial screen are performed using 10-dose, three-fold serial dilutions of TP-3654 starting with 10 μM at K_m ATP concentrations for each kinase[1].
Animal Administration	When tumors of mice reaches 100 to 200 mm^3 by caliper measurement, mice are randomized, and oral dosing of TP-3654 or vehicle control began and continued every day for 5 days with 2 days off for 18 to 21 days. Tumor volumes and body weights were determined twice a week[1].
References	[1]. Foulks JM, et al. A small-molecule inhibitor of PIM kinases as a potential treatment for urothelial carcinomas. Neoplasia. 2014 May;16(5):403-12.