产品名称：KW-2449
产品别名：(E)-(4-(2-(1H-indazol-3-yl)vinyl)phenyl)(piperazin-1-yl)methanone

生物活性：

Description	KW-2449 is a multi-targeted kinase inhibitor of FLT3, ABL, ABL^{T315I} and Aurora kinase with IC_{50}s of 6.6, 14, 4 and 48 nM, respectively.					
IC_{50} & Target	Abl	ABL-T315I	FGFR1	Aurora A	FLT3/D835Y	FLT3
	4nM(IC_{50})	14nM (IC_{50})	36 nM (IC_{50})	48 nM (IC_{50})	1 nM (IC_{50})	6.6nM (IC_{50})
	JAK2	SRC	PDFGRα			
	150 nM (IC_{50})	400nM(IC_{50})	1700nM(IC_{50})			
In Vitro	KW-2449 shows growth inhibitory activities against FLT3/ITD-, FLT3/D835Y-, and wt-FLT3/FL-expressing 32D cells, MOLM-13 and MV4;11 with GI50 values of 0.024, 0.046, 0.014, 0.024, and 0.011 μM, respectively. KW-2449 suppresses the phosphorylations of FLT3 (P-FLT3) and its downstream molecule phospho-STAT5 (P-STAT5) in MOLM-13 cells in a dose-dependent manner. KW-2449 increases the percentage of cells in the G1 phase of the cell cycle and reciprocally reduced the percentage of cells in the S phase, resulting in the increase of apoptotic cell population[1].					
In Vivo	Oral administration of KW-2449 shows dose-dependent and significant tumor growth inhibition in FLT3-mutated xenograft model with minimum bone marrow suppression. In FLT3 wild-type human leukemia, it induces the reduction of phosphorylated histone H3, G2/M arrest, and apoptosis. In imatinib-resistant leukemia, KW-2449 contributes to release of the resistance by the simultaneous down-regulation of BCR/ABL and Aurora kinases. Furthermore, the antiproliferative activity of KW-2449 is confirmed in primary samples from AML and imatinib-resistant patients. The inhibitory activity of KW-2449 is not affected by the presence of human plasma protein, such as α1-acid glycoprotein[1].					

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (150.42 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0084 mL	15.0421 mL	3.0084 mL
	5 mM	0.6017 mL	3.0084 mL	6.0168 mL
	10 mM	0.3008 mL	1.5042 mL	3.0084 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 (7.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.52 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 (7.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.52 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 (7.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.52 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]. Shiotsu Y, et al. KW-2449, a novel multikinase inhibitor, suppresses the growth of leukemia cells with FLT3 mutations or T315I-mutated BCR/ABL translocation. Blood. 2009 Aug 20;114(8):1607-17.

实验参考：

Cell Assay	Cell viability is determined by the sodium 3′-[1-(phenylaminocarbonyl)-3, 4-tetrazolium]-bis (4-methoxy-6-nitro) benzene sulfonic acid hydrate assay after incubation with or without KW-2449 for 72 hours at 37° C. The number of viable cells is determined using the Cell Proliferation Kit II[1].
Animal Administration	Mice: SCID mice are subcutaneously inoculated with MOLM-13 cells. Five days after inoculation, tumor volume is measured using the Antitumor test system II. The 25 mice with tumors ranging from 90 to 130 mm3 are selected and randomized using the Antitumor test system II. From the day of randomization, vehicle (0.5 wt/vol% MC400) or KW-2449 (2.5, 5.0, 10, and 20 mg/kg) is orally administered to mice twice a day for 14 days. Tumor volume is measured twice a week during the treatment[1].
References	[1]. Shiotsu Y, et al. KW-2449, a novel multikinase inhibitor, suppresses the growth of leukemia cells with FLT3 mutations or T315I-mutated BCR/ABL translocation. Blood. 2009 Aug 20;114(8):1607-17.