产品名称：**PHA-665752**
产品别名：**PHA-665752**

生物活性：	
Description	PHA-665752 is a selective, ATP-competitive, and active-site inhibitor of the catalytic activity of c-Met kinase (Ki=4 nM; IC50=9 nM). PHA-665752 exhibits >50-fold selectivity for c-Met compared with a panel of diverse tyrosine and serine-threonine kinases. PHA-665752 induces apoptosis and cell cycle arrest, and exhibits cytoreductive antitumor activity[1][2].
IC_{50} & Target	Ki: 4 nM[1] IC50: 9 nM (c-Met)[1]
In Vitro	PHA-665752 is a potent and ATP-competitive inhibitor of c-Met kinase activity with a Ki of 4 nM and an IC50 of 9 nM[1]. PHA-665752 exhibits >50-fold selectivity for c-Met enzyme compared with the majority of kinases evaluated[1]. PHA-665752 shows potent inhibition of c-Met RTK autophosphorylation in NIH3T3 cells engineered to express high levels of c-Met and hepatocyte growth factor (HGF)[1]. PHA-665752 inhibits HGF-stimulated or constitutive phosphorylation of mediators of downstream of c-Met such as Gab-1, ERK, Akt, STAT3, PLC-γ, and FAK in multiple tumor cell lines[1]. PHA-665752 (0-1.25 μM; 18 hours) potently inhibits HGF and c-Met-driven phenotypes such as cell growth (proliferation and survival), cell motility, invasion, and/or morphology of a variety of tumor cells[1]. PHA-665752 (0-1.25 μM; 72 hours) induces apoptosis in both the presence and absence of HGF at concentrations that inhibited tyrosine phosphorylation of c-Met in GTL-16 cells[1]. PHA-665752 (0.0125-0.2 μM; 4 hours) potent inhibits HGF-induced c-Met phosphorylation in A549 cells[1].
	Cell Proliferation Assay[1]
	Cell Line: S114 cells, GTL-16 cells, NCI-H441 cells, or BxPC-3 cells
	Concentration: 0 μM, 0.002 μM, 0.01 μM, 0.05 μM, 0.25 μM, 1.25 μM
	Incubation Time: 18 hours
	Result: Potently inhibited HGF and c-Met-driven cell growth.
	Apoptosis Analysis[1]
	Cell Line: GTL-16 cells
	Concentration: 0 μM, 0.002 μM, 0.01 μM, 0.05 μM, 0.25 μM, 1.25 μM
	Incubation Time: 72 hours
	Result: Induced apoptosis in both the presence and absence of HGF at concentrations that inhibited tyrosine phosphorylation of c-Met in GTL-16 cells. Immunoblot Analysis.
	Western Blot Analysis[1]
	Cell Line: A549 cells
	Concentration: 0.0125 μM, 0.025 μM,0.05 μM,0.1 μM,0.2 μM
	Incubation Time: 4 hours
	Result: Potent inhibited HGF-induced c-Met phosphorylation in A549 cells.
	PHA-665752 (7.5-30 mg/kg/day; i.v. ; for 9 days) exhibits statistically significant dose-dependent tumor growth inhibition of 68%, 39%, and 20% of vehicle control at the 30 mg/kg/day, 15 mg/kg/day, and 7.5 mg/kg/day doses, respectively[1]. PHA-665752 shows a potent cytoreductive activity in a gastric carcinoma xenograft model[1].

<table>
<tr><td>In Vivo</td><td>Animal Model:</td><td>Female athymic mice (nu/nu, 8–12 weeks) bearing S114 or GTL-16 tumor xenografts[1]</td></tr>
<tr><td></td><td>Dosage:</td><td>7.5 mg/kg/day, 15 mg/kg/day, 30 mg/kg/day</td></tr>
<tr><td></td><td>Administration:</td><td>Intravenous injection; for 9 days</td></tr>
<tr><td></td><td>Result:</td><td>Demonstrated statistically significant dose-dependent tumor growth inhibition.</td></tr>
<tr><td>Solvent&Solubility</td><td colspan="2">
In Vitro:
DMSO : 50 mg/mL (77.93 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)
<table>
<tr><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>1.5586 mL</td><td>7.7929 mL</td><td>15.5858 mL</td></tr>
<tr><td>5 mM</td><td>0.3117 mL</td><td>1.5586 mL</td><td>3.1172 mL</td></tr>
<tr><td>10 mM</td><td>0.1559 mL</td><td>0.7793 mL</td><td>1.5586 mL</td></tr>
</table>
*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 (3.90 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (3.90 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% corn oil
Solubility: ≥ 2.5 mg/mL (3.90 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (3.90 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。
</td></tr>
<tr><td>References</td><td colspan="2">
[1]. Christensen JG, et al. A selective small molecule inhibitor of c-Met kinase inhibits c-Met-dependent phenotypes in vitro and exhibits cytoreductive antitumor activity in vivo. Cancer Res. 2003 Nov 1;63(21):7345-55.
[2]. Ma PC. et al. A selective small molecule c-MET Inhibitor, PHA665752, cooperates with rapamycin. Clin Cancer Res. 2005 Mar 15;11(6):2312-9.
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