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# 产品名称：NVS-PAK1-1
# 产品别名：NVS-PAK1-1

## 生物活性：

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| **Description** | NVS-PAK1-1 is a potent and selective allosteric PAK1 inhibitor with an IC50 of 5 nM. |
| **$IC_{50}$ & Target** | IC50: 5 nM (PAK1)[1] |
| **In Vitro** | NVS-PAK1-1 demonstrates high selectivity for inhibition of PAK1 over other PAK isoforms and the kinome in general. NVS-PAK1-1 has a biochemical PAK1 $K_d$ of 7 nM and a PAK2 $K_d$ of 400 nM. NVS-PAK1-1 shows excellent activity in biochemical assays and an exceptional selectivity profile against other known kinases. NVS-PAK1-1 at 6-20 μM inhibits the phosphorylation of the downstream substrate MEK1 Ser289. Consistent with the observation, NVS-PAK1-1 inhibits proliferation of Su86.86 cell line only above a concentration of 2 μM. In contrast, by applying a mixture of NVS-PAK1-1 and PAK2 shRNA, inhibition of downstream signaling and cell proliferation at a significantly lower 0.21 μM concentration are achieved[1]. |
| **In Vivo** | NVS-PAK1-1 shows a relatively poor stability in rat liver microsomes (RLM) and this would limit its application for in vivo studies ($t_{1/2}$ in RLM 3.5 min)[1]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO： ≥ 125 mg/mL (260.45 mM)**<br>* "≥" means soluble, but saturation unknown. |

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.0836 mL | 10.4182 mL | 20.8364 mL |
| | 5 mM | 0.4167 mL | 2.0836 mL | 4.1673 mL |
| | 10 mM | 0.2084 mL | 1.0418 mL | 2.0836 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 (5.21 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.21 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 (5.21 mM); Clear solution

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| | 此方案可获得 ≥ 2.5 mg/mL (5.21 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。<br>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]. Karpov AS, et al. Optimization of a Dibenzodiazepine Hit to a Potent and Selective Allosteric PAK1 Inhibitor. ACS Med Chem Lett. 2015 May 22;6(7):776-81. |
| **实验参考：** | |
| **Kinase Assay** | Inhibition of PAK1 kinase activity is measured using the Caliper assay. The assay is performed using 384-well microtiter plates. Compounds (NVS-PAK1-1) are tested as 8-point dose responses. The assays are prepared by addition of 50 nL of compound solution in 90% DMSO directly into the empty plate. Subsequently, 4.5 μL of the enzyme solution is added to each well and the resulting solution is pre-incubated at 30°C for 60 min, followed by addition of 4.5 μL of the peptide/ATP-solution. After 60 min incubation at 30°C, reactions are terminated by addition of 16 μL per well of the stop solution. Plates with terminated kinase reactions are transferred to the Caliper LC3000 workstations for reading. Product formation is measured in a microfluidic mobility shift assay. $IC_{50}$ values are derived from percent inhibition values at different compound concentrations by non-linear regression analysis[1]. |
| **References** | [1]. Karpov AS, et al. Optimization of a Dibenzodiazepine Hit to a Potent and Selective Allosteric PAK1 Inhibitor. ACS Med Chem Lett. 2015 May 22;6(7):776-81. |