

产品名称: **PF-03814735**

产品别名: **PF-03814735**

|                           |  |   |                           |                           |                           |                            |
|---------------------------|--|---|---------------------------|---------------------------|---------------------------|----------------------------|
| 生物活性:                     |  |   |                           |                           |                           |                            |
| Description               | PF-03814735 is a potent, orally available and reversible aurora A and aurora B inhibitor with IC <sub>50</sub> s of 0.8 and 0.5 nM, respectively.  |   |                           |                           |                           |                            |
| IC <sub>50</sub> & Target | Aurora 1   | Aurora 2                                  | Flt-1                     | FAK                       | TrkA                      | Met                        |
|                           | 0.8 nM (IC <sub>50</sub> )   | 5 nM (IC <sub>50</sub> )                  | 10 nM (IC <sub>50</sub> ) | 22 nM (IC <sub>50</sub> ) | 30 nM (IC <sub>50</sub> ) | 100 nM (IC <sub>50</sub> ) |
|                           | FGFR1  |   |                           |                           |                           |                            |
|                           | 100 nM (IC <sub>50</sub> )   |   |                           |                           |                           |                            |
| In Vitro                  | In intact cells, the inhibitory activity of PF-03814735 on the Aurora1 and Aurora2 kinases reduces levels of phospho-Aurora1, phosphohistone H3, and phospho-Aurora2. PF-03814735 produces a block in cytokinesis, resulting in inhibition of cell proliferation and the formation of polyploid multinucleated cells[1]. Small cell lung cancer (SCLC) and, to a lesser extent, colon cancer lines are very sensitive to PF-03814735. The status of the Myc gene family and retinoblastoma pathway members significantly correlates with the efficacy of PF-03814735[2].   |   |                           |                           |                           |                            |
| In Vivo                   | Once-daily oral administration of PF-03814735 to mice bearing human xenograft tumors produces a reduction in phosphohistone H3 in tumors at doses that are tolerable and that result in significant inhibition of tumor growth. The combination of PF-03814735 and docetaxel in xenograft mouse tumor models shows additive tumor growth inhibition[1]. PF-03814735 is much more effective in NCI-H82 xenografts when administered on a weekly dosing schedule at 80 mg/kg compared with a daily schedule at 15 mg/kg. PF-03814735 delayed growth by 23.5 days on the weekly schedule, which corresponds to 0.9 logs of net cell kill during the course of treatment[2]. |   |                           |                           |                           |                            |
| Solvent&Solubility        | <b>In Vitro:</b><br><b>DMSO : ≥ 100 mg/mL (210.76 mM)</b><br><br>* "≥" means soluble, but saturation unknown.  |   |                           |                           |                           |                            |
|                           | <div>Preparing Stock Solutions</div>   | <div>Solvent / Mass / Concentration</div> | 1 mg                      | 5 mg                      | 10 mg                     |                            |
|                           |  | 1 mM                                      | 2.1076 mL                 | 10.5379 mL                | 21.0757 mL                |                            |
|                           |  | 5 mM                                      | 0.4215 mL                 | 2.1076 mL                 | 4.2151 mL                 |                            |
|                           |  | 10 mM                                     | 0.2108 mL                 | 1.0538 mL                 | 2.1076 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。<br>储备液的保存方式和期限: -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时, 请在 6 个月内使用, -20℃ 储存时, 请在 1 个月内使用。<br><b>In Vivo:</b><br>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 <b>In Vitro</b> 方式配制澄清的储备液, 再依次添加助溶剂:<br>——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<br><div>1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</div> <div>Solubility: ≥ 2.5 mg/mL (5.27 mM); Clear solution</div>  |   |                           |                           |                           |                            |

|                              |   |
|------------------------------|---|
|                              | <p>此方案可获得 <math>\geq 2.5</math> mg/mL (5.27 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中, 混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80, 混合均匀; 然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% (20% SBE-<math>\beta</math>-CD in saline)</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (5.27 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (5.27 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水溶液中, 混合均匀。</p> <p>3. 请依序添加每种溶剂: 10% DMSO <math>\rightarrow</math> 90% corn oil</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (5.27 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (5.27 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。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p> |
| <b>References</b>            | <p>[1]. Jani JP, et al. PF-03814735, an orally bioavailable small molecule aurora kinase inhibitor for cancer therapy. <i>Mol Cancer Ther.</i> 2010 Apr;9(4):883-94.</p> <p>[2]. Hook KE, et al. An integrated genomic approach to identify predictive biomarkers of response to the aurora kinase inhibitor PF-03814735. <i>Mol Cancer Ther.</i> 2012 Mar;11(3):710-9.</p>   |
| <b>实验参考:</b>                 |   |
| <b>Cell Assay</b>            | <p>Cell lines are grown in appropriate media and evaluated after 48 h of exposure to either PF-03814735 or vehicle. Proliferation (as measured by an increase in cell number) is expressed as a percent of untreated controls. To evaluate the PF-03814735 exposure time required for antiproliferative activity, HL-60 cell cultures are cultured in RPMI medium supplemented with 15% heat-inactivated fetal bovine serum and exposed to various PF-03814735 concentrations for 4, 8, 12, 24, and 48 h, followed by a washout step and incubation with growth media without PF-03814735 for the remainder of the 72-h assay period. Continuous exposure to PF-03814735 for 72 h is also evaluated. Cell counts are determined by a Coulter Counter[1]</p>   |
| <b>Animal Administration</b> | <p>Mice: Mice bearing s.c. HCT-116 xenograft tumors (250-400mm<sup>3</sup>) are evaluated for plasma drug concentrations and tumor levels of phosphohistone H3 Ser10. Mice are treated with a single dose of PF-03814735 or vehicle by oral gavage and are sacrificed at 0.5, 1, 2, 3, 7, 16, or 24 h postdose (3-4 mice/time point) [1]</p>  |
| <b>Kinase Assay</b>          | <p>Aurora1 and Aurora2 proteins are produced as full-length His-tag recombinant proteins expressed in insect cells. For the Aurora2 kinase assay, phosphorylation of the substrate peptide by recombinant Aurora2 protein is assessed at 3 to 300 <math>\mu</math>M ATP and various concentrations of PF-03814735 over 60 min, at a substrate peptide concentration of 2 <math>\mu</math>M. Phosphorylation is linear over this time for all conditions. For the Aurora1 kinase assay, phosphorylation of the substrate peptide by recombinant Aurora1 protein is assessed by a scintillation proximity assay in a 96-well plate format in which the incorporation of <sup>33</sup>P into the peptide substrate is measured by capturing the peptide on a streptavidin scintillation proximity assay bead[1]</p>  |
| <b>References</b>            | <p>[1]. Jani JP, et al. PF-03814735, an orally bioavailable small molecule aurora kinase inhibitor for cancer therapy. <i>Mol Cancer Ther.</i> 2010 Apr;9(4):883-94.</p> <p>[2]. Hook KE, et al. An integrated genomic approach to identify predictive biomarkers of response to</p>  |



源叶生物