产品名称：**BI-847325**
产品别名：**BI-847325**

## 生物活性：

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| **Description** | BI-847325 is an ATP competitive dual inhibitor of MEK and aurora kinases (AK) with $IC_{50}$ values of 4 and 15 nM for human MEK2 and AK-C, respectively. | |
| **$IC_{50}$ & Target** | MEK2 | Aurora C |
| | 4 nM ($IC_{50}$) | 15 nM ($IC_{50}$) |
| **In Vitro** | BI 847325 inhibits the activity of X. laevis AK-B with an IC50 of 3 nM; the IC50 values for human AK-A and AK-C are 25 and 15 nM, respectively. BI 847325 also inhibits human MEK1 and MEK2 with respective IC50 values of 25 and 4 nM. BI 847325 at 1,000 nM inhibits 6 enzymes by more than 50% (LCK, MAP3K8, FGFR1, AMPK, CAMK1D and TBK1) and the IC50 values are below 100 nM only for LCK (5 nM) and MAP3K8 (93 nM). Proliferation is inhibited in A375 and Calu-6 cell lines with GI50 values of 7.5 nM and 60 nM, respectively[1]. | |
| **In Vivo** | Daily oral administration of BI 847325 at 10 mg/kg shows efficacy in both BRAF- and KRAS-mutant xenograft models. BI 847325 administered once weekly at 70 mg/kg inhibits both MEK and AK in KRAS-mutant tumors[1]. | |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO： ≥ 36 mg/mL (77.49 mM)**<br>* "≥" means soluble, but saturation unknown. | |

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| 1 mM | 2.1526 mL | 10.7629 mL | 21.5257 mL |
| 5 mM | 0.4305 mL | 2.1526 mL | 4.3051 mL |
| 10 mM | 0.2153 mL | 1.0763 mL | 2.1526 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。

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| **References** | [1]. Sini P, et al. Pharmacological Profile of BI 847325, an Orally Bioavailable, ATP-Competitive Inhibitor of MEK and Aurora Kinases. Mol Cancer Ther. 2016 Oct;15(10):2388-2398. |

## 实验参考：

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| **Cell Assay** | Cells are plated in 96-well format and BI 847325 is added 24 hours after cell seeding. At the same time, a “time zero” untreated cell plate is fixed. Compound is serially diluted and assayed over 8 concentrations in triplicates. After 72 h incubation, cells are fixed and stained with fluorescent nuclear dye. Concentration–response curves are analyzed using a four-parameter log-logistic function without upper or lower limitation. GI50 are calculated[1]. |
| **Animal Administration** | Mice: Tumor grafted female BomTac:NMRI-Foxn1$^{nu}$ mice are used in the study. BI 847325 is dissolved in 0.5% Natrosol 250 HX with 3% Tween 80 and sonicated until a homogenous suspension is obtained, then 1 M HCl is added and the suspension is vortexed and sonicated again. MEK inhibitors GSK 1120212 and AZD 6244 are suspended in 1% or 0.5% Natrosol, respectively. An administration volume of 10 mL/kg body weight is used and compounds are administered orally |

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| | with a gavage needle at the indicated dose and schedule. Tumor volumes are measured and mice are inspected daily for clinical signs and body weight is determined daily[1]. |
| **Kinase Assay** | Assays are run in the presence of 100 μM ATP using 10 μM of substrate. 30 μL PROTEIN-MIX in 25% DMSO and incubated for 15 min at room temperature. 10 μL PEPTIDE-MIX is added, the mixture is incubated for 60 min at RT and stopped by adding 180 μL 6.4% TCA (final concentration: 5%). Incorporated phosphate is measured in a scintillation counter and IC50 values are calculated using a sigmoidal curve analysis program with variable hill slope[1]. |
| **References** | [1]. Sini P, et al. Pharmacological Profile of BI 847325, an Orally Bioavailable, ATP-Competitive Inhibitor of MEK and Aurora Kinases. Mol Cancer Ther. 2016 Oct;15(10):2388-2398. |