产品名称：4-[[(7R)-8-环戊基-7-乙基-5,6,7,8-四氢-5-甲基-6-氧代-2-喋啶基]氨基]-3-甲氧基-N-(1-甲基-4-哌啶基)苯甲酰胺
产品别名：BI 2536

生物活性：

Description

BI 2536 is a dual PLK1 and BRD4 inhibitor with IC50s of 0.83 and 25 nM, respectively[1]. BI-2536 suppresses IFNB (encoding IFN-β) gene transcription[4].

IC_{50} & Target

PLK1	Plk2/Snk	Plk3/Fnk	BRD4
0.83 nM (IC_{50})	3.5 nM (IC_{50})	9 nM (IC_{50})	25 nM (IC_{50})

In Vitro

Exceeding a 100-fold concentration range starting at 10 nM, BI 2536 causes HeLa cells to accumulate with a 4N DNA content, indicative of a cell-cycle block in either G2 phase or mitosis. In addition to HeLa cells, BI 2536 potently inhibits the proliferation of a panel of 32 human cancer cell lines, representing diverse organ derivations (including carcinomas of the breast, colon, lung, pancreas, and prostate, melanomas, and hematopoietic cancers) and varied patterns of tumor suppressor or oncogene mutations (including RB1, TP53, PTEN, andKRAS status). The half-maximal effective concentration (EC50) values in this cell panel ranged 2-25 nM, whereas a concentration of 100 nM of BI 2536 is typically sufficient for inducing a complete mitotic arrest. The proliferation of exponentially growing hTERT-RPE1, human umbilical vein endothelial cells (HUVECs), and normal rat kidney (NRK) cells is blocked at EC50values ranging 12-31 nM, indicating a comparable sensitivity of cycling nontransformed cells to BI 2536[3].

In Vivo

BI 2536 (40-50 mg/kg, i.v.) blocks the growth of human cancer xenografts in immunodeficient, nu/nu mice. Consecutive cycles of 40-50 mg/kg BI 2536 given i.v. once or twice per week are found to be highly efficacious in diverse xenograft models, such as the HCT 116 colon cancer with complete tumor suppression with the twice per week schedule (treated versus the control (T/C) value 0.3%) and a T/C value of 16% with once per week treatment; both schedules are well-tolerated, as judged by clinical signs and absence of major body-weight changes[3].

Solvent&Solubility

In Vitro:

DMSO： ≥ 55.5 mg/mL (106.39 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9170 mL	9.5850 mL	19.1699 mL
	5 mM	0.3834 mL	1.9170 mL	3.8340 mL
	10 mM	0.1917 mL	0.9585 mL	1.9170 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。

References

[1]. Lénárt P, et al. The Small-Molecule Inhibitor BI 2536 Reveals Novel Insights into Mitotic Roles of Polo-like Kinase 1. Curr Biol. 2007 Feb 20;17(4):304-15.

[2]. Chen L, et al. BRD4 Structure-Activity Relationships of Dual PLK1 Kinase/BRD4 Bromodomain Inhibitor BI-2536. ACS Med Chem Lett. 2015 May 18;6(7):764-9.

[3]. Steegmaier M, et al. BI 2536, a Potent and Selective Inhibitor of Polo-like Kinase 1, Inhibits Tumor

	Growth In Vivo. Current Biology (2007), 17(4), 316-322. [4]. Malik N, et al. Suppression of IFN β gene transcription by inhibitors of bromodomain and extra-terminal (BET) family members. Biochem J. 2015 Jun 15;468(3):363-72.

实验参考：

Cell Assay	Cell proliferation assays are performed by incubation in the presence of various concentrations of BI 2536 (10 nM-1 μM) for 72 hr, and cell growth is assessed by the measurement of Alamar Blue dye conversion in a fluorescence spectrophotometer. Effective concentrations at which cellular growth is inhibited by 50% (EC50) are extrapolated from the dose-response curve fit[3].
Animal Administration	Mice[3] Female BomTac:NMRI-Foxn1nu mice are grafted subcutaneously with HCT 116 colon-carcinoma, NCI-H460, or A549 lung-carcinoma cells by subcutaneous injection, respectively, of 2×10^6, 1×10^6, and 1×10^7 cells into the flank of each mouse. When tumors reached a volume of approximately 50 mm^3, animals are pair-matched into treatment and control groups of ten mice each. In regression experiments, treatment is not initiated until the mean tumor volume reached 500 mm^3. BI 2536 is injected intravenously into the tail vein at the indicated dose and schedule. The administration volume is 10 mL per kg body weight. Tumor volumes are determined three times a week with a caliper. The results are converted to tumor volume (mm^3) by the following formula: length×$width^2\times\pi/6$. The weight of the mice is determined as an indicator of tolerability on the same days. For statistical analysis, the treatment group is compared with the vehicle control group in a one-sided (decreasing) exact Wilcoxon test.
References	[1]. Lénárt P, et al. The Small-Molecule Inhibitor BI 2536 Reveals Novel Insights into Mitotic Roles of Polo-like Kinase 1. Curr Biol. 2007 Feb 20;17(4):304-15. [2]. Chen L, et al. BRD4 Structure-Activity Relationships of Dual PLK1 Kinase/BRD4 Bromodomain Inhibitor BI-2536. ACS Med Chem Lett. 2015 May 18;6(7):764-9. [3]. Steegmaier M, et al. BI 2536, a Potent and Selective Inhibitor of Polo-like Kinase 1, Inhibits Tumor Growth In Vivo. Current Biology (2007), 17(4), 316-322. [4]. Malik N, et al. Suppression of IFN β gene transcription by inhibitors of bromodomain and extra-terminal (BET) family members. Biochem J. 2015 Jun 15;468(3):363-72.