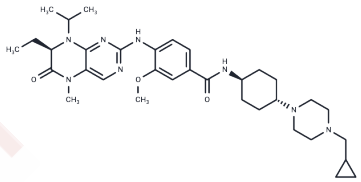
Data Sheet (Cat.No.T6019)

TargetMol

Volasertib

Chemical Properties



CAS No. : 755038-65-4

Formula: C34H50N8O3

Molecular Weight: 618.81

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Volasertib (BI 6727) (BI-6727) is a potent inhibitor of PLK1 (IC50: 0.87 nM), inducing mitotic arrest and apoptosis. It also inhibits PLK2/PLK3 (IC50s: 5/56 nM).
Targets(IC50)	Apoptosis,PLK
In vitro	Volasertib (BI 6727) potently inhibited Plk1 as well as the two closely related kinases Plk2 and Plk3 (IC50 values 0.87, 5, and 56 nmol/L, respectively). BI 6727 inhibited proliferation of multiple cell lines derived from various cancer tissues, including carcinomas of the colon (HCT 116, EC50 = 23 nmol/L) and lung (NCI-H460, EC50 = 21 nmol/L), melanoma (BRO, EC50 = 11 nmol/L), and hematopoietic cancers (GRANTA-519, EC50 = 15 nmol/L; HL-60, EC50 = 32 nmol/L) with EC50 values of 11 to 37 nmol/L [1]. BI 6727 showed nanomolar activity on NB TICs, with an EC50 of 21 nmol/L, and an excellent selectivity profile, with an EC50 of 2.8 μmol/L on SKPs [2]. Volasertib inhibited proliferation in all 40 cell lines tested, with a mean half-maximal growth inhibitory concentration of 313 nmol/l (range: 4-5000 nmol/l) [3].
In vivo	BI 6727 has physicochemical and pharmacokinetic properties that allow in vivo testing of i.v. as well as oral formulations, adding flexibility to dosing schedules. Finally, BI 6727 shows marked antitumor activity in multiple cancer models, including a model of taxane-resistant colorectal cancer [1]. Volasertib was highly active against RMS-1 alveolar rhabdomyosarcoma xenografts, resulting in 100% tumor regression. Activity was associated with complete and prolonged G2/M arrest and subsequent apoptotic cell death. Volasertib showed synergistic activity with vincristine but antagonistic effects with etoposide [3].
Kinase Assay	Recombinant human Plk1 (residues 1-603) was expressed as NH2-terminal, GST-tagged fusion protein using a baculoviral expression system and purified by affinity chromatography using glutathione-agarose. Enzyme activity assays for Plk1, Plk2, and Plk3 were done in the presence of serially diluted inhibitor using 20 ng of recombinant kinase and 10 μg casein from bovine milk as substrate. Kinase reactions were done in a final volume of 60 μL for 45 min at 30°C [15 mmol/L MgCl2, 25 mmol/L MOPS (pH 7.0), 1 mmol/L DTT, 1% DMSO, 7.5 μmol/L ATP, 0.3 μCi γ-32P-ATP]. Reactions were terminated by the addition of 125 μL of ice-cold 5% TCA. After transferring the precipitates to MultiScreen mixed ester cellulose filter plates, plates were washed with 1% TCA and quantified radiometrically. Dose-response curves were used for calculating IC50 values.

Kinase Assay	To establish a kinase selectivity profile, additional kinase assays were done by contract research organizations or reagents were purchased from commercial sources and assays were done according to the supplier's instructions. Appropriate positive and negative controls were included in the assay design [1].
Cell Research	Cell proliferation assays were done by incubating cells in the presence of various concentrations of BI 6727 for 72 h and cell growth was assessed by measuring Alamar blue dye conversion in a fluorescence spectrophotometer. Effective concentrations at which cellular growth was inhibited by 50% (EC50) were extrapolated from the dose-response curve fit [1].
Animal Research	Female BomTac:NMRI-Foxn1nu mice were grafted s.c. with 2 × 10^6 HCT 116 human colon carcinoma cells (ATCC CCL-247), 1 × 10^6 NCI-H460 non-small cell lung cancer cells (ATCC HTB-177), or CXB1 human colon carcinoma tumor pieces derived from patient material by serial transplantation in nude mice. When tumors had reached a volume of ~50 to 100 mm^3, animals were randomized into treatment and control groups of 10 mice each. BI 6727 was formulated in hydrochloric acid (0.1 N), diluted with 0.9% NaCl, and injected i.v. into the tail vein at the indicated dose and schedule. For oral treatment, BI 6727 was resuspended in 0.5% Natrosol 250 hydroxyethyl-cellulose and given intragastrally via gavage needle. An administration volume of 10 mL per kilogram of body weight was used for both administration routes. Tumor volumes were determined thrice a week using a caliper. The results were converted to tumor volume (mm^3) by the formula length × width2 × π/6. The weight of the mice was determined as an indicator of tolerability on the same days. Median tumor volumes on the last day of the experiment were used to calculate treated versus control values (= tumor volume treated mice × 100/tumor volume control mice) [1].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 25.38 mg/mL (41.01 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.23 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.616 mL	8.080 mL	16.160 mL
5 mM	0.3232 mL	1.616 mL	3.232 mL
10 mM	0.1616 mL	0.808 mL	1.616 mL
50 mM	0.0323 mL	0.1616 mL	0.3232 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Rudolph D, et al. BI 6727, a Polo-like kinase inhibitor with improved pharmacokinetic profile and broad antitumor activity. Clin Cancer Res. 2009 May 1;15(9):3094-102.
Yu Z, Deng P, Chen Y, et al. Inhibition of the PLK1-Coupled Cell Cycle Machinery Overcomes Resistance to Oxaliplatin in Colorectal Cancer. Advanced Science. 2021: 2100759.
Cheng M, Yang Q, Liu Y, et al. SETD3 Methyltransferase Regulates PLK1 Expression to Promote In Situ Hepatic Carcinogenesis. Frontiers in oncology. 2022, 12: 882202.
Grinshtein N, et al. Small molecule kinase inhibitor screen identifies polo-like kinase 1 as a target for neuroblastoma tumor-initiating cells. Cancer Res. 2011 Feb 15;71(4):1385-95.
Qu Y, Gong X, Zhao Z, et al.Establishment and Validation of Novel Prognostic Subtypes in Hepatocellular Carcinoma Based on Bile Acid Metabolism Gene Signatures Using Bulk and Single-Cell RNA-Seq Data.International Journal of Molecular Sciences.2024, 25(2): 919.
Abbou S, et al. Polo-like Kinase Inhibitor Volasertib Exhibits Antitumor Activity in Pediatric Malignancies. Anticancer Res. 2016 Feb;36(2):599-609.