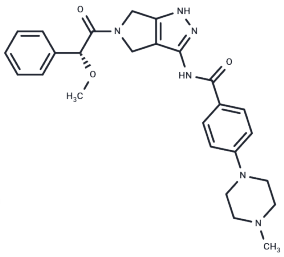
Data Sheet (Cat.No.T2094)

TargetMol

Danusertib

Chemical Properties



CAS No. : 827318-97-8

Formula: C26H30N6O3

Molecular Weight: 474.55

Storage: 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	Danusertib (PHA-739358) is a small-molecule 3-aminopyrazole derivative with potential antineoplastic activity. Danusertib binds to and inhibits the Aurora kinases, which may result in cell growth arrest and apoptosis in tumor cells in which Aurora kinases are overexpressed.
Targets(IC50)	FGFR,c-RET,Bcr-Abl,Aurora Kinase,Autophagy,Trk receptor
In vitro	Danusertib significantly inhibits the proliferation of K562 cells and suppresses tumor growth over a 10-day treatment period. Administering 25 mg/kg of Danusertib (b.d.i.v.) to HL-60 xenograft rats resulted in a 75% inhibition of tumor growth, with complete regression observed in one animal.
In vivo	In cellular assays, treatment with Danusertib in wild-type and p53-deficient mouse embryonic fibroblasts (MEFs) resulted in the arrest of wild-type cells in mitosis (4N) for up to 48 hours, whereas p53-deficient cells did not exhibit arrest at the 4N DNA stage and proceeded through mitosis, leading to DNA content >8N. Danusertib treatment was associated with increased levels of p53 protein and an upregulation of p21 protein, which is known to be transcriptionally regulated by p53. Additionally, Danusertib inhibited the activity of other kinases, such as FGFR1, Abl, Ret, and Trka, with IC50 values of 47 nM, 25 nM, 31 nM, and 31 nM, respectively.
Kinase Assay	Biochemical kinase Assays: The Km values for ATP and the specific substrate are initially determined, and each assay is then run at optimized ATP (2Km) and substrate (5Km) concentrations. This setting enabled direct comparison of IC50 values of Danusertib across the applied kinase selectivity screening panel for the evaluation of the selectivity profile.
Cell Research	For short-term expansion assays, 1 × 103 CD34+ cells are plated in triplicates in 96-well plates containing 100 µL of serum-free medium per well supplemented with human stem-cell factor (100 ng/mL), human Flt-3 Ligand (100 ng/mL), human thrombopoietin (50 ng/mL), human interleukin-3 and -6 (IL-3 and IL-6, respectively, both 20 ng/mL), and granulocyte colony-stimulating factor (20 ng/mL) along with Danusertib at the indicated concentrations. After 5 days, an additional 100 µL of cytokine and Danusertib containing medium are added. Cell numbers within each individual well are estimated on days 3, 6, and 9 or on days 3, 6, and 12 for healthy donor samples. (Only for Reference)

Solubility Information

Solubility	DMSO: 88 mg/mL (185.44 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), 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: 3.3 mg/mL (6.95 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	2.1073 mL	10.5363 mL	21.0726 mL
5 mM	0.4215 mL	2.1073 mL	4.2145 mL
10 mM	0.2107 mL	1.0536 mL	2.1073 mL
50 mM	0.0421 mL	0.2107 mL	0.4215 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

Carpinelli P, et al. Mol Cancer Ther, 2007, 12 Pt 1, 3158-3168.
Cheng S, Jin P, Li H, et al. Evaluation of CML TKI Induced Cardiovascular Toxicity and Development of Potential Rescue Strategies in a Zebrafish Model. Frontiers in Pharmacology. 2021: 2866.
Fancelli D, et al. J Med Chem, 2006, 49(24), 7247-7251.
Gontarewicz A, et al. Blood, 2008, 111(8), 4355-4364.