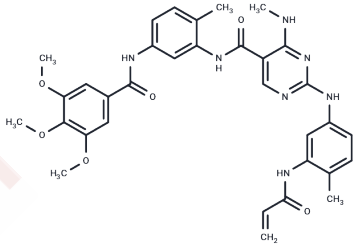
Data Sheet (Cat.No.T4268)

TargetMol

CHMFL-BMX-078

Chemical Properties



CAS No. : 1808288-51-8

Formula: C33H35N7O6

Molecular Weight: 625.67

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	CHMFL-BMX-078 is a highly potent and selective type II irreversible inhibitor of BMX kinase, with an IC50 of 11 nM.
Targets(IC50)	BTK
In vitro	CHMFL-BMX-078 displays a high selectivity profile against the 468 kinases/mutants in the KINOMEscan evaluation and achieves at least 40-fold selectivity over BTK kinase (IC50=437 nM). For inactive state of BMX kinase, CHMFL-BMX-078 displays a binding Kd of 81 nM, while for the active state of BMX kinase, it exhibits a binding Kd of 10200 nM. CHMFL-BMX-078 exhibits antiproliferative effects against BaF3-TEL-BMX cells (GI50=0.016 μM) and selectivity over parental BaF3 cells. CHMFL-BMX-078 is about 80-fold more potent against BMX wt (EC50=5.8 nM) than C496S mutant (EC50=459 nM) for the inhibition of BMX total tyrosine phosphorylation.
In vivo	CHMFL-BMX-078 also displays an acceptable Cmax (13565.23 ng/mL) and AUC0-t (1386.41 ng/mL h) in iv injection. However, it is not absorbed by oral administration, indicating that this compound could be administrated through i.v. or i.p. injection when used as a research tool.
Kinase Assay	The kinase reaction system contains BMX or BTK, 1 μL of serially diluted CHMFL-BMX-078, and substrate Poly peptidewith 100 μM ATP. The reaction in each tube is started immediately by adding ATP and kept going for an hour under 37 °C. After the tube cooled for 5 min at room temperature, 5 μL solvent reactions are carried out in a 384-well plate. Then 5 μL of ADP-Glo reagent is added into each well to stop the reaction and consume the remaining ATP within 40 min. At the end, 10 μL of kinase detection reagent is added into the well and incubated for 30 min to produce a luminescence signal. Luminescence signal is measured with an automated plate reader.
Animal Research	CHMFL-BMX-078 is dissolved in 55% saline containing 5% DMSO and 40% PEG400 by vortex. The final concentration of the stock solution is 1 mg/mL for administration.Rat: Six 8-week-old male Sprague?Dawley rats are fasted overnight before starting drug treatment via intravenous and oral administration. Animal blood collection time points are as follows. For groups 1, 3, and 5 (intravenous): 1 min, 5 min, 15 min, 30 min, 1 h, 2 h, 4 h, 6 h, and 8 h before and after administration is selected. For group 2, 4, and 6 (oral): 5 min, 15 min, 30 min, 1 h, 2 h, 4 h, 6 h, 8 h, and 24 h before and after dosing. The plasma is collected for analysis.

Solubility Information

Solubility	DMSO: 30 mg/mL (47.95 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.5983 mL	7.9914 mL	15.9829 mL
5 mM	0.3197 mL	1.5983 mL	3.1966 mL
10 mM	0.1598 mL	0.7991 mL	1.5983 mL
50 mM	0.032 mL	0.1598 mL	0.3197 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.

Reference

Liang X, et al. Discovery of 2-((3-Acrylamido-4-methylphenyl)amino)-N-(2-methyl-5-(3,4,5-trimethoxybenzamido) phenyl)-4-(methylamino)pyrimidine-5-carboxamide (CHMFL-BMX-078) as a Highly Potent and Selective Type II Irreversible Bone Marrow Kinase in the X Chromosome (BMX) Kinase Inhibitor. J Med Chem. 2017 Mar 9;60(5):1793-1816.