CHMFL-BMX-078

Cat. No.: HY-101267

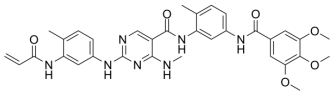
CAS No.: 1808288-51-8

Molecular Formula: $C_{33}H_{35}N_7O_6$

Molecular Weight: 625.67

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 30 mg/mL (47.95 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CHMFL-BMX-078 is a highly potent and selective type II irreversible BMX kinase inhibitor with an IC_{50} of 11 nM.

IC_{50} & Target

IC50: 11 nM (BMX)[1]

In Vitro

Bone marrow kinase in the X chromosome (BMX, also called ETK) is a nonreceptor tyrosine kinase involved in tumorigenicity, cell motility, adhesion, angiogenesis, proliferation, and differentiation. CHMFL-BMX-078 exhibits an IC_{50} of 11 nM by formation of a covalent bond with cysteine 496 residue in the DFG-out inactive conformation of BMX. It displays a high selectivity profile against the 468 kinases/mutants in the KINOMEscan evaluation and achieves at least 40-fold selectivity over BTK kinase (IC_{50}=437 nM). For inactive state of BMX kinase, CHMFL-BMX-078 displays a binding K_d of 81 nM, while for the active state of BMX kinase, it exhibits a binding K_d of 10200 nM. CHMFL-BMX-078 exhibits antiproliferative

	effects against BaF3-TEL-BMX cells (GI_{50}=0.016 μM) and selectivity over parental BaF3 cells. CHMFL-BMX-078 is about 80-fold more potent against BMX wt (EC_{50}=5.8 nM) than C496S mutant (EC_{50}=459 nM) for the inhibition of BMX total tyrosine phosphorylation. CHMFL-BMX-078 would serve as a useful pharmacological tool to elucidate the detailed mechanism of BMX mediated signaling pathways[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CHMFL-BMX-078 exhibits a short half-life ($T_{1/2}$=0.80 h) in iv injection. CHMFL-BMX-078 also displays an acceptable C_{max} (13565.23 ng/mL) and AUC_{0-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 iv or ip injection when used as a research tool[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: 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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Blood Adv. 2022 Jul 7;bloodadvances.2022007952.

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