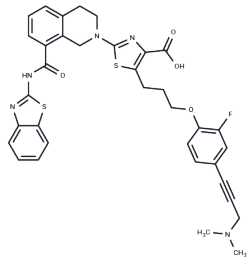
Data Sheet (Cat.No.T6748)

TargetMol

A-1155463

Chemical Properties



CAS No. : 1235034-55-5

Formula: C35H32FN5O4S2

Molecular Weight: 669.79

Appearance: no data available

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

Biological Description

Description	A-1155463, a highly potent and selective BCL-XL inhibitor, shows picomolar binding affinity to BCL-XL, and >1000-fold weaker binding to BCL-2 and related proteins BCL-W (Ki=19 nM) and MCL-1(Ki>440 nM).
Targets(IC50)	Bcl-2 Family
In vitro	A-1155463 disrupts BCL-XL-BIM but not BCL-2-BIM complexes in cells. A-1155463 kills BCL-XL-dependent Molt-4 cells (EC50=70 nM) but has no measurable cytotoxicity against BCL-2-dependent RS4;11 cells (EC50>5 mM). A-1155463 induces the hallmarks of apoptosis, as evidenced by the release of cytochrome c from mitochondria, caspase activation, and the accumulation of caspase-dependent sub-G0-G1 DNA content in BCL-XL-dependent H146 cells[2].
In vivo	Following a single 5 mg/kg IP dose of A-1155463 in nontumor bearing SCID-Beige mice, platelet counts fall dramatically as measured at 6 h postdose and then rebound to normal levels within 72 h. Daily Dosing at 5 mg/kg IP to SCID-Beige mice that had been inoculated with BCL-XL-dependent H146 tumor cells for 14 days causes a statistically significant inhibition of tumor growth (maximum tumor growth inhibition = 44%), which is alleviated upon cessation of dosing[1].
Kinase Assay	Recombinant p38 isoforms are activated by Mkk6(E) under the following conditions: p38 (100 ng/mL), Mkk6(E) (30 ng/mL), ATP (100 mM) are mixed in kinase buffer (25 mM Hepes, 25 mM b-glycerophosphate, 0.1 mM sodium orthovanadate, 25 mM MgCl2, 2.5 mM DTT, pH 7.4) and incubated for 30 min at 30°C. A typical assay reaction for Mnk1 activity contained Mnk1 (2 ng/mL), HA-eIF4E (10 ng/mL), ATP (300 mM) in kinase buffer. The reaction is started by addition of activated p38 (0.03-3 ng/mL) and stopped after 30 min at 30°C by addition of SDS loading buffer. Inhibitors of Mnk1 are identified under the same assay conditions, except that Mnk1 is pre-activated using active p38a before exposure to the substrate and inhibitors.
Cell Research	Cells are treated with increasing concentration of A-1155463. Cells are assayed for viability after 72 h using the CellTiter-Glo luminescent cell viability assay according to the manufacturer's protocol. Results are normalized to cells without treatment. EC50 is calculated using the GraphPad Prism software.(Only for Reference)
Animal Research	Animal Models: SCID-Beige MiceFormulation: 5% DMSO, 10% EtOH, 20% Cremaphor ELP, and 65% D5WDosages: 5 mg/kgAdministration: i.p.

Solubility Information

Solubility	DMSO: 100 mg/mL (149.3 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 100 mg/mL (149.3 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.493 mL	7.465 mL	14.9301 mL
5 mM	0.2986 mL	1.493 mL	2.986 mL
10 mM	0.1493 mL	0.7465 mL	1.493 mL
50 mM	0.0299 mL	0.1493 mL	0.2986 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

Tao ZF, et al. ACS Med Chem Lett. 2014, 5(10):1088-93.
Devin J, Cañeque T, Lin Y L, et al. Targeting cellular iron homeostasis with ironomycin in diffuse large B cell lymphoma. Cancer Research. 2022
Devin J, Cañeque T, Lin Y L, et al. Targeting cellular iron homeostasis with ironomycin in diffuse large B cell lymphomaTargeting cellular iron homeostasis with ironomycin in DLBCL. Cancer Research. 2022
Leverson JD, et al. Sci Transl Med. 2015, 7(279):279ra40.
Haichao Zhang, et al. Molecular Cancer. 2015, 14(1):1-9.