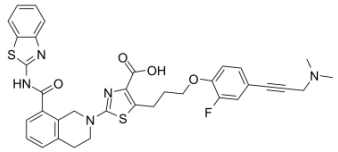
A-1155463

Cat. No.:	HY-19725
CAS No.:	1235034-55-5
Molecular Formula:	$C_{35}H_{32}FN_5O_4S_2$
Molecular Weight:	669.79
Target:	Bcl-2 Family
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (74.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4930 mL	7.4650 mL	14.9301 mL
	5 mM	0.2986 mL	1.4930 mL	2.9860 mL
	10 mM	0.1493 mL	0.7465 mL	1.4930 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 (3.73 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.73 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A-1155463 is a highly potent and selective BCL-XL inhibitor with an EC_{50} of 70 nM in Molt-4 cell.

IC_{50} & Target

Bcl-xL	Bcl-2
0.01 nM (Ki)	80 nM (Ki)

In Vitro

A-1155463 shows picomolar binding affinity to BCL-X_L (K_i≤0.01 nM), and >1000-fold weaker binding to BCL-2 (K_i= 80 nM) and related proteins BCL-W (K_i= 19 nM) and MCL-1 (K_i> 440 nM) [2]. A-1155463 demonstrates strong growth inhibition of over half

	of the colorectal cell lines as defined by EC_{50} values ≤0.5 μM in the presence of 10 % FBS[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	A-1155463 caused a mechanism-based and reversible thrombocytopenia in mice and inhibited H146 small cell lung cancer xenograft tumor growth in vivo following multiple doses[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice: Following a single 5 mg/kg IP dose of A-1155463 in nontumor bearing SCID-Beige mice, platelet counts fell dramatically as measured at 6 h postdose and then rebounded to normal levels within 72 h. A-1155463 is then administered to SCID-Beige mice that had been inoculated with BCL-XL-dependent H146 tumor cells with a daily dose at 5 mg/kg IP for 14 days[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Clin Invest. 2020 May 1;130(5):2542-2559.
- J Hematol Oncol. 2020 Jul 16;13(1):95.
- Oncogene. 2019 Jan;38(1):47-59.
- Cell Death Dis. 2019 May 21;10(6):395.
- Blood Adv. 2019 Dec 23;3(24):4202-4214.

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REFERENCES

[1]. Leverson JD, et al. Exploiting selective BCL-2 family inhibitors to dissect cell survival dependencies and define improved strategies for cancer therapy. Sci Transl Med.?2015 Mar 18;7(279):279

[2]. Tao ZF, et al. Discovery of a Potent and Selective BCL-XL Inhibitor with in Vivo Activity. ACS Med Chem Lett. 2014 Aug 26;5(10):1088-93.

[3]. Zhang H, et al. Genomic analysis and selective small molecule inhibition identifies BCL-X(L) as a critical survival factor in a subset of colorectal cancer. Mol Cancer. 2015 Jul 2;14:126.

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