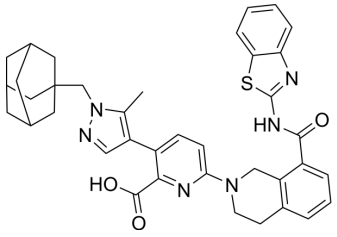
A-1331852

Cat. No.:	HY-19741
CAS No.:	1430844-80-6
Molecular Formula:	$C_{38}H_{38}N_6O_3S$
Molecular Weight:	658.81
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 (75.89 mM)
Ethanol : 4 mg/mL (6.07 mM; ultrasonic and warming and heat to 60°C)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 80°C) (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5179 mL	7.5894 mL	15.1789 mL
5 mM	0.3036 mL	1.5179 mL	3.0358 mL
10 mM	0.1518 mL	0.7589 mL	1.5179 mL

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

In Vivo

1. Add each solvent one by one: 2.5% DMSO >> 10% ethanol >> 27.5% PEG 300 >> 60% Phosal 50 PG
   Solubility: ≥ 2.5 mg/mL (3.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (3.16 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.16 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A-1331852 is an orally available BCL-XL selective inhibitor with a K_i of less than 10 pM.

IC_{50} & Target	Bcl-xL 0.01 nM (Ki)	Bcl-W 4 nM (Ki)	Bcl-2 6 nM (Ki)	Mcl-1 142 nM (Ki)

In Vitro

A-1331852 selectively disrupts BCL-XL–BIM complexes and induces the hallmarks of apoptosis in BCL-XL–dependent Molt-4 cells with IC_{50}s in the low nanomolar range but does not affect MEF cells lacking BAK or BAX. In CellTiter-Glo cell viability assay, A-1331852 inhibits NCI-H847, NCI-H1417, SET-2, HEL, OCI-M2 with EC_{50} values of 3, 7, 80, 120 and 100 nM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

A-1331852 demonstrates antitumor efficacy in the Molt-4 xenograft model, inducing tumor regressions as a single agent. Additionally, A-1331852 combines with venetoclax to recapitulate the efficacy of navitoclax in the NCI-H1963.FP5 xenograft model of SCLC. A-1331852 significantly inhibits tumor growth in seven subcutaneous xenograft models of solid tumors, including breast cancer, NSCLC, and ovarian cancer[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]

SCLC and AML cell lines are incubated with increasing concentrations of navitoclax, venetoclax, or A-1155463 for 48 hours before assessing cell viability. Cell killing EC_{50} values are calculated[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]

Mice: The growth inhibition of established tumors in SCID-bg mice is studied. A-1331852 is administered orally daily for 14 days at 25 mg/kg and RP-56976 is administered intravenously at 7.5 mg/kg. The change of tumor volume is monitored daily [1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2023 Jan;613(7942):187-194.
- Nature. 2021 Mar;591(7850):477-481.
- Cell. 2022 Apr 28;185(9):1521-1538.e18.
- Cell Res. 2023 May 11.
- Nature Cancer. 2021 Jan;2(1):34-48.

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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):279ra40.

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