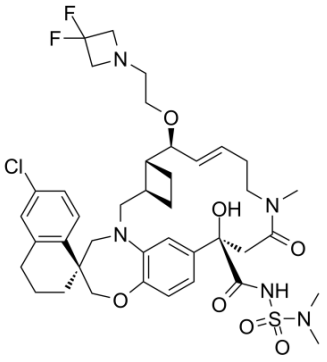
Mcl-1 inhibitor 3

Cat. No.:	HY-133015
CAS No.:	2376774-73-9
Molecular Formula:	$C_{40}H_{52}ClF_2N_5O_7S$
Molecular Weight:	820.38
Target:	Bcl-2 Family
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Mcl-1 inhibitor 3 (compound 1) is a highly potent and orally activate macrocyclic Mcl-1 inhibitor (K_i= 0.061 nM; IC_{50}=19 nM in an OPM-2 cell viability assay). Mcl-1 inhibitor 3 shows good pharmacokinetic properties and excellent in vivo efficacy without toxicity[1]. .

IC_{50} & Target	Mcl-1 19 nM (IC_{50})	Mcl-1 0.061 nM (Ki)

In Vitro

Mcl-1 inhibitor 3 shows an IC_{50} value of 19 nM in an OPM-2 cell viability assay, and a K_i value of 0.061 nM in Mcl-1 HTRF/TR-FRET assay[1].

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

In Vivo

Mcl-1 inhibitor 3 (oral administration; 3, 10, or 30 mg/kg; 6 hours) causes a significant loss of luminescence (-40%) over vehicle at 30 mg/kg,This effect was observed with unbound drug levels in plasma, the $[plasma]_u$/OPM-2 IC_{50} values are 0.24, 0.93 and 3.65 μM in 3, 10, 30 mg/kg doses,respectively[1].

Mcl-1 inhibitor 3 (oral administration; 10, 30, or 60 mg/kg; 6 hours) activates Bak by 8-fold at 30 mg/kg and by 14-fold at 60 mg/kg in this OPM-2 Luc assay,this test is based on the detection of activated Bak in nude mice subcutaneously injected with via electrochemiluminescence.[1].

Mcl-1 inhibitor 3 (oral administration; 10, 30, or 60 mg/kg; 30 days) led to a robust dose-dependent tumor growth inhibition at 30 mg/kg (44% TGI) and 34% tumor regression when the animals were dosed at 60 mg/kg.Lastly, no body weight loss is observed in any of the mice in this study efficacy models[1].

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

Animal Model:	Nude miceinjected with HEK293 cells[1]
Dosage:	3, 10, or 30 mg/kg
Administration:	Oral administration
Result:	Showed a disruption of the Mcl-1/Bak interaction in this in vivo model.

Animal Model:	Nude mice injected with human OPM-2 multiple myeloma tumor cells[1]

Dosage:	10, 30, or 60 mg/kg
Administration:	Oral administration
Result:	Exhibited a inhibition of tumor growth without any toxicity.

REFERENCES

[1]. Rescourio G, Discovery and in Vivo Evaluation of Macrocyclic Mcl-1 Inhibitors Featuring an α-Hydroxy Phenylacetic Acid Pharmacophore or Bioisostere.J Med Chem. 2019 Nov 27;62(22):10258-10271.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA