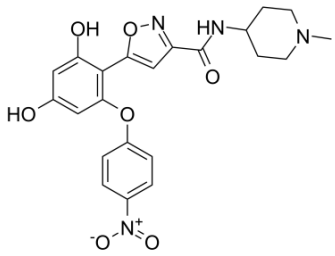
NMS-E973

Cat. No.:	HY-17547
CAS No.:	1253584-84-7
Molecular Formula:	$C_{22}H_{22}N_4O_7$
Molecular Weight:	454.43
Target:	HSP
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the COA.



BIOLOGICAL ACTIVITY

Description	NMS-E973 is a potent and selective inhibitor of **HSP90**. NMS-E973 binds to the ATP binding site of **Hsp90α** with a **DC 50** of <10 nM. NMS-E973 is able to cross the blood-brain barrier (BBB). Antitumor efficacy[1].
IC_{50} & Target	HSP90α 10 nM (DC50)
In Vitro	NMS-E973 inhibits cancer cell proliferation. NMS-E973 shows a widespread antiproliferative activity, with an average IC_{50} of 1.6 μM and 15 cell lines with an IC_{50} <100 nM[1].

Cell Proliferation Assay[1]

Cell Line:	Carcinoma breast DU-4475, EVSA-T, CAL-51, HCC1954, BT-474, HCC1419, HDQ-P1 cells; Leukemia MV-4-11 and MOLM-13 cells; Melanoma A-375 cells
Concentration:	
Incubation Time:	24, 48, 72 hours
Result:	IC_{50}s of 13, 16, 56, 61, 73, 76, and 89 nM for DU-4475, EVSA-T, CAL-51, HCC1954, BT-474, HCC1419, HDQ-P1 cells, respectively. IC_{50}s of 29 and 35 nM for MV-4-11, MOLM-13 cells, respectively. The IC_{50} of 133 nM for A-375 cell.

In Vivo

NMS-E973 (60 mg/kg; i.v.) inhibits the growth of A375 tumors subcutaneously or intracranially implanted in mice[1]. NMS-E973 exhibits moderate elimination half-lives (5.55±1.07 h) due to high plasma clearance (39.9±1.70 mL/min/kg) combined with large volumes of distribution (5.83±3.18 L/kg) following intravenous administration (10 mg/kg) in mice[1].

Animal Model:	Balb/c male nude mice (aged 6 to 8 weeks) xenografted with the A375 tumors[1]
Dosage:	60 mg/kg
Administration:	Administered twice daily i.v. according to 2 schedules: (i) every other day for 12 days

	and (ii) 3 days on/1 day off/3 days on (3-1-3, one cycle).
Result:	Both schedules resulted in tumor shrinkage and TGI of 74% and 89%, respectively.

REFERENCES

[1]. Gianpaolo Fogliatto, et al. NMS-E973, a novel synthetic inhibitor of Hsp90 with activity against multiple models of drug resistance to targeted agents, including intracranial metastases. Clin Cancer Res. 2013 Jul 1;19(13):3520-32.

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