Onalespib

Cat. No.: HY-14463

CAS No.: 912999-49-6

Molecular Formula: $C_{24}H_{31}N_3O_3$

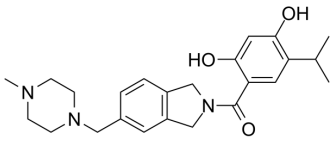
Molecular Weight: 409.52

Target: HSP

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (122.09 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4419 mL	12.2094 mL	24.4188 mL
	5 mM	0.4884 mL	2.4419 mL	4.8838 mL
	10 mM	0.2442 mL	1.2209 mL	2.4419 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 16.67 mg/mL (40.71 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Onalespib (AT13387) is a long-acting second-generation Hsp90 inhibitor with a K_d of 0.71 nM.

IC_{50} & Target

HSP90
0.71 nM (Kd)

In Vitro	Onalespib (Compound 35) is a potent inhibitor of Hsp90, with K_d of 0.71 nM. Onalespib shows potent antiproliferative activity in HCT116 cells, with an IC_{50} of 31 nM. Onalespib also strongly inhibits the proliferation of a panel of human tumor cell lines, showing IC_{50} of < 100 nM[1]. Onalespib exhibits cytotoxic activity against many of the PPTP cell lines, with median IC_{50} of 41 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Onalespib (60 mg/kg, ip 3 days on and 3 days off for four cycles) shows antitumor activity in nude BALB/c mice bearing early stage HCT116 human colon carcinoma xenografts[1]. Onalespib (40 or 60 mg/kg, i.p.) induces significant differences in EFS distribution compared to controls in 17% evaluable solid tumor xenografts, but in none of the ALL xenografts[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	In vitro testing is performed using DIMSCAN. Cells are incubated in the presence of Onalespib for 96 hours at concentrations from 1 nM to 10 μM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	HCT116 cells are injected SC into the right hind flank of male nude BALB/c mice. Tumours are apparent 7 to 10 days later. Mice are arranged into matched groups of 12 according to tumour volume giving a group mean of approximately 100 mm^3 at initiation of dosing. Tumour volumes are measured every 2 days. Statistical significance between groups is assessed using nonparametric one-way ANOVA. Mice are given the lactate salt of Onalespib using a repeated cycle of dosing of once per day for three days, no dose for three days, once per day for three days etc., for four dosing cycles at 60 mg/kg/dose (as free base equivalents) dissolved in 17.5% hydroxypropyl-β-cyclodextrin via the IP route. Control mice receive dose vehicle only via the same route. Tolerability is assessed by recording body weight, clinical observations and survival[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2019 Aug 12;9(20):5769-5783.
- Nano Res. 07 May 2022.
- Immunology. 2021 Jan;162(1):84-91.
- Sci Rep. 2017 Mar 15;7(1):201.
- J Appl Toxicol. 2017 Nov;37(11):1325-1332.

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REFERENCES

[1]. Woodhead AJ, et al. Discovery of (2,4-dihydroxy-5-isopropylphenyl)-[5-(4-methylpiperazin-1-ylmethyl)-1,3-dihydroisoindol-2-yl]methanone (AT13387), a novel inhibitor of the molecular chaperone Hsp90 by fragment based drug design. J Med Chem. 2010 Aug 26;53

[2]. Kang MH, et al. Initial testing (Stage 1) of AT13387, an HSP90 inhibitor, by the pediatric preclinical testing program. Pediatr Blood Cancer. 2012 Jul 15;59(1):185-8.

Caution: Product has not been fully validated for medical applications. For research use only.

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