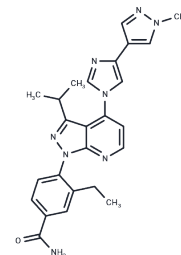


Pimitespib

Chemical Properties

CAS No. :	1260533-36-5
Formula:	C ₂₅ H ₂₆ N ₈ O
Molecular Weight:	454.53
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



Biological Description

Description	Pimitespib (TAS-116) is an ATP-competitive and highly specific HSP90 α /HSP90 β inhibitor with inhibition constants (K _i) of 34.7 nM and 21.3 nM, respectively.
Targets(IC50)	HSP
In vitro	Pimitespib binds not only to the conventional-binding pockets as existing Hsp-90 inhibitors but also to a novel-binding pocket. Such a unique binding mode makes Pimitespib highly specific for Hsp-90 α / β . Pimitespib (0-5 μ M, 48 hours) inhibits human retinal pigment epithelial ARPE-19 cell lines and NCI-H929 MM cell growth. Compared 17-AAG in INA6 and NCI-H929 MM cells, more significant degradation of p-C-Raf and p-MEK1/2, HSP90 client proteins, and key RAS/RAF/MEK pathway regulators, is triggered by Pimitespib (0.125-1 μ M, 24 hours) [2][3].
In vivo	TAS-116 is orally absorbed and has a bioavailability of almost 100% in mice, and 69.0% in rats. TAS-116 has moderate terminal elimination half-life (t _{1/2} =8.2 h, 2.5 h, 4.4 h and 2.2 h for mouse (3.6 mg/kg, p.o.), mouse (7.1 mg/kg, p.o.), mouse (14.0 mg/kg, p.o.), rat (4 mg/kg, p.o.)). TAS-116 is more rapidly eliminated from retina (t _{1/2} =3.4 hours) than the other HSP90 inhibitors (t _{1/2} =7.1-19.1 hours). TAS-116 is distributed less in retina than in plasma in rats; consequently, TAS-116 does not produce any detectable photoreceptor injury. TAS-116 triggers enhanced in vivo anti-MM activities, both alone and in combination with Bortezomib (BTZ), with a favorable safety profile. TAS-116 (12.0 mg/kg, p.o., 14 days) displays antitumor activity without inducing eye injury in rats. Mice treated with TAS-116 (10 mg/kg and 15 mg/kg, orally, 38 days), BTZ, or TAS-116 plus BTZ show significantly enhance growth inhibition versus the vehicle control group. Median overall survival of treated animals (TAS-116, orally, 10 mg/kg=33 days, 15 mg/kg=37 days, BTZ=36 days, and the combination=56.5 days) is significantly longer than vehicle control. The favorable pharmacokinetic profile of TAS-116 is reflected in its dose-dependent antitumor activity; the T/C (tumor volume of TAS-116-treated mice vs. vehicle-treated mice) is 47%, 21%, and 9% for doses of 3.6 mg/kg, 7.1 mg/kg, and 14.0 mg/kg, respectively [1][2].

Solubility Information

A DRUG SCREENING EXPERT

Solubility	DMSO: 50 mg/mL (110 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (8.8 mM), Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2001 mL	11.0004 mL	22.0007 mL
5 mM	0.440 mL	2.2001 mL	4.4001 mL
10 mM	0.220 mL	1.100 mL	2.2001 mL
50 mM	0.044 mL	0.220 mL	0.440 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

- Ohkubo S, et al. TAS-116, a highly selective inhibitor of heat shock protein 90 α and β , demonstrates potent antitumor activity and minimal ocular toxicity in preclinical models. *Mol Cancer Ther.* 2015 Jan;14(1):14-22.
- Suzuki R, et al. Anti-tumor activities of selective HSP90 α / β inhibitor, TAS-116, in combination with bortezomib in multiple myeloma. *Leukemia.* 2015 Feb;29(2):510-4.
- Utsugi T. New challenges and inspired answers for anticancer drug discovery and development. *Jpn J Clin Oncol.* 2013 Oct;43(10):945-53.

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Tel: 781-999-4286 E_mail: info@targetmol.com Address: 34 Washington Street, Wellesley Hills, MA 02481