Serdemetan

Cat. No.: HY-12025

CAS No.: 881202-45-5

Molecular Formula: $C_{21}H_{20}N_4$

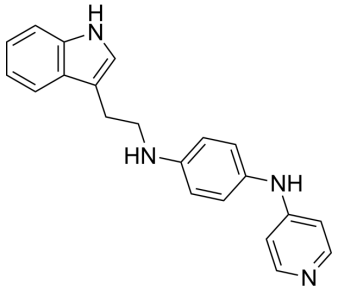
Molecular Weight: 328.41

Target: MDM-2/p53; Apoptosis; E1/E2/E3 Enzyme

Pathway: Apoptosis; 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 (152.25 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0450 mL	15.2249 mL	30.4497 mL
	5 mM	0.6090 mL	3.0450 mL	6.0899 mL
	10 mM	0.3045 mL	1.5225 mL	3.0450 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.61 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.61 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.61 mM); Suspended solution

BIOLOGICAL ACTIVITY

Description

Serdemetan(JNJ-26854165) acts as a HDM2 ubiquitin ligase antagonist and also induces early apoptosis in p53 wild-type cells, inhibits cellular proliferation followed by delayed apoptosis in the absence of functional p53.IC50 value: HDM2 ubiquitin ligaseTarget: in vitro: JNJ 26854165 is a novel tryptamine derivative which activates p53 and acts as a HDM2 ubiquitin ligase antagonist. JNJ 26854165 inhibits cell growth and induces apoptosis in leukemia cell lines with IC50 values of 0.24, 0.33, 0.32 and 0.44 μM at 72 hours for OCI-AML-3, MOLM-13, NALM-6 and REH cells, respectively. In addition, JNJ 26854165 accelerates proteasome-mediated degradation of p21 and antagonizes the transcriptional induction of p21 by p53. It also induces S-phase delay and upregulates E2F1 expression in p53 mutant cells, resulting in preferential apoptosis of

S-phase cells. JNJ 26854165 is an oral Mdm2 inhibitor which can inhibit the interaction of Mdm2-p53 complex with the proteasome and increase p53 levels by binding to RING domain of Mdm2. A recent study shows that JNJ 26854165 inhibits clonogenic survival in four human cancer cell lines: H460, A549, p53-WT-HCT116, and p53-null-HCT116.in vivo:JNJ 26854165 leads to significant differences in EFS distribution in 17 of the 36 (47%) evaluable solid tumor xenografts and in 5 of 7 (71%) of the evaluable ALL xenografts using a dose of 20 mg/kg administered via oral gavage daily for 5 days, repeated for 6 weeks.

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REFERENCES

[1]. T. Stühmer et al. A first-in-class HDM2-inhibitor (JNJ-26854165) in phase I development shows potent activity against multiple myeloma (MM) cells in vitro and ex vivo Journal of Clinical Oncology, 2008 ASCO Annual Meeting Proceedings (Post-Meeting Edition).Vol 26, No 15S (May 20 Supplement), 2008: 14694

[2]. Chargari C, Leteur C, Angevin E, Bashir T, Schoentjes B, Arts J, Janicot M, Bourhis J, Deutsch E.Preclinical assessment of JNJ-26854165 (Serdemetan), a novel tryptamine compound with radiosensitizing activity in vitro and in tumor xenografts.Cancer Lett. 2011 Dec 22;312(2):209-18.

[3]. Smith MA, Gorlick R, Kolb EA, Lock R, Carol H, Maris JM, Keir ST, Morton CL, Reynolds CP, Kang MH, Arts J, Bashir T, Janicot M, Kurmasheva RT, Houghton PJ.Initial testing of JNJ-26854165 (Serdemetan) by the pediatric preclinical testing program.Pediatr Blood Cancer. 2012 Aug;59(2):329-32.

[4]. Tabernero J, Dirix L, Sch?ffski P, Cervantes A, Lopez-Martin JA, Capdevila J, van Beijsterveldt L, Platero S, Hall B, Yuan Z, Knoblauch R, Zhuang SH.A phase I first-in-human pharmacokinetic and pharmacodynamic study of serdemetan in patients with advanced solid tumors.Clin Cancer Res. 2011 Oct 1;17(19):6313-21. Epub 2011 Aug 10.

[5]. Kojima K, Burks JK, Arts J, Andreeff M.The novel tryptamine derivative JNJ-26854165 induces wild-type p53- and E2F1-mediated apoptosis in acute myeloid and lymphoid leukemias.Mol Cancer Ther. 2010 Sep;9(9):2545-57. Epub 2010 Aug 24.

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