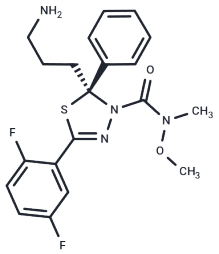
Data Sheet (Cat.No.TQ0318)

TargetMol

Filanesib

Chemical Properties



CAS No. : 885060-09-3

Formula: C20H22F2N4O2S

Molecular Weight: 420.48

Storage: Store at low temperature,Keep away from direct sunlight
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	Filanesib (ARRY 520) is a selective inhibitor of kinesin spindle protein (KSP, IC50 = 6 nM) with potent anti-proliferative activity.
Targets(IC50)	Apoptosis,Kinesin,KSP
In vitro	Filanesib shows anti-proliferative activity in multidrug-resistant cell lines including HCT-15, NCI/ADR-RES and K562/ADR with EC50 values of 3.7, 14 and 4.2 nM respectively. Filanesib (10 nM) blocks mitosis with the monopolar spindle structure typical of KSP inhibition as judged by both increased phosphorylation of histone H3 and the accumulation of cyclin B1 in four cells [2]. Filanesib (1 nM) induces a significant G2M cell cycle block in OCI-AML3 cells at 24 hours [4].
In vivo	Filanesib (10, 15, 20, 30 mg/kg, i.p.) is active in UISO-BCA-1 xenograft, and also superior to paclitaxel in mice bearing subcutaneous HT-29, HCT-116, MDA-MB-231 and A2780 xenografts. Filanesib is superior to docetaxel in the androgen receptor-negative prostate cancer xenograft model PC-3 [1]. RPMI 8226 tumor xenografts are particularly sensitive to low doses of Filanesib (12.5 mg/kg, i.p.) [2]. Filanesib significantly inhibits tumor growth in HL60 and MV4-11 xenografts of SCID mice at concentrations of 27 mg/kg and 20 mg/kg, respectively [4].
Cell Research	Exponentially growing cells (0.4×10^6/mL) are treated with ARRY-520 for up to 48 hours. For combination, HL-60 and HL-60Bcl-2 cells (0.4×10^6/mL) are incubated with ARRY-520, ABT-737, or both for up to 96 hours. DMSO is used as the control agent. Apoptosis is estimated by flow cytometry measurements of phosphatidylserine with the Annexin-V-FLUOS Staining Kit. Membrane integrity is simultaneously assessed by 7-amino-actinomycin D (7-AAD). To measure changes in the mitochondrial membrane potential (MMP), cells are loaded with CMXRos (300 nM) and MitoTracker Green (500 nM) for 1 hour at 37°C. The loss of MMP is then assessed by measuring CMXRos retention while simultaneously adjusting for mitochondrial mass [4].
Animal Research	Subcutaneous tumor xenografts are allowed to grow to a volume of 250-350 mm3. The mice are randomized into groups of 3-4 based on tumor size and are given a single dose of ARRY-520 i.p. At various time-points after administration of the drug, the mice are euthanized by CO2 inhalation and the tumors excised and placed in 10% neutral buffered formalin. The formalin-fixed tumors are processed and paraffin-embedded by

Animal Research	standard procedures. Spindle morphology is analyzed by staining tumor sections for α-tubulin, and apoptosis is analyzed by TUNEL stain. Monopolar/abnormal spindles and TUNEL positive (apoptotic) cells are counted in three ×40 fields from each sample, analyzed using algorithms developed in software [1].

Solubility Information

Solubility	DMSO: 90 mg/mL (214.04 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: 3.3 mg/mL (7.85 mM),Sonication is recommended. *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.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3782 mL	11.8912 mL	23.7823 mL
5 mM	0.4756 mL	2.3782 mL	4.7565 mL
10 mM	0.2378 mL	1.1891 mL	2.3782 mL
50 mM	0.0476 mL	0.2378 mL	0.4756 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

Woessner R, et al. ARRY-520, a novel KSP inhibitor with potent activity in hematological and taxane-resistant tumor models. Anticancer Res. 2009 Nov;29(11):4373-80.

Tunquist BJ, et al. Mcl-1 stability determines mitotic cell fate of human multiple myeloma tumor cells treated with the kinesin spindle protein inhibitor ARRY-520. Mol Cancer Ther. 2010 Jul;9(7):2046-56.

Kim KH, et al. KSP inhibitor ARRY-520 as a substitute for Paclitaxel in Type I ovarian cancer cells. J Transl Med. 2009 Jul 20;7:63.

Carter BZ, et al. Inhibition of KSP by ARRY-520 induces cell cycle block and cell death via the mitochondrial pathway in AML cells. Leukemia. 2009 Oct;23(10):1755-62.