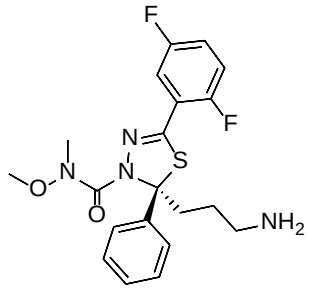
Product data sheet

MedKoo Cat#: 200292 Name: Filanesib CAS#: 885060-09-3 (free base) Chemical Formula: $C_{20}H_{22}F_2N_4O_2S$ Exact Mass: 420.1432 Molecular Weight: 420.48	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Filanesib, also known as ARRY-520, is a synthetic, small molecule targeting the kinesin spindle protein (KSP) with potential antineoplastic activity. KSP inhibitor ARRY-520 specifically inhibits KSP (kinesin-5 or Eg5), resulting in activation of the spindle assembly checkpoint, induction of cell cycle arrest during the mitotic phase, and consequently cell death in tumor cells that are actively dividing. Because KSP is not involved in postmitotic processes, such as neuronal transport, this agent does not cause the peripheral neuropathy that is often associated with tubulin-targeting agents. KSP is an ATP-dependent microtubule motor protein that is essential for the formation of bipolar spindles and the proper segregation of sister chromatids during mitosis.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	60.0	142.69
Ethanol	20.0	47.56
DMF	20.0	47.56
PBS (pH 7.2)	0.20	0.48

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.38 mL	11.89 mL	23.78 mL
5 mM	0.48 mL	2.38 mL	4.76 mL
10 mM	0.24 mL	1.19 mL	2.38 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Carter BZ, Mak DH, Woessner R, Gross S, Schober WD, Estrov Z, Kantarjian H, Andreeff M. 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. doi: 10.1038/leu.2009.101. Epub 2009 May 21. PMID: 19458629; PMCID: PMC3593228.
2. Woessner R, Tunquist B, Lemieux C, Chlipala E, Jackinsky S, Dewolf W Jr, Voegtli W, Cox A, Rana S, Lee P, Walker D. ARRY-520, a novel KSP inhibitor with potent activity in hematological and taxane-resistant tumor models. Anticancer Res. 2009 Nov;29(11):4373-80. PMID: 20032381.

In vivo study

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1. Carter BZ, Mak DH, Woessner R, Gross S, Schober WD, Estrov Z, Kantarjian H, Andreeff M. 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. doi: 10.1038/leu.2009.101. Epub 2009 May 21. PMID: 19458629; PMCID: PMC3593228.
2. Woessner R, Tunquist B, Lemieux C, Chlipala E, Jackinsky S, Dewolf W Jr, Voegtli W, Cox A, Rana S, Lee P, Walker D. ARRY-520, a novel KSP inhibitor with potent activity in hematological and taxane-resistant tumor models. Anticancer Res. 2009 Nov;29(11):4373-80. PMID: 20032381.

7. Bioactivity

Biological target: Filanesib is a kinesin spindle protein (KSP) inhibitor with an IC50 of 6 nM.

In vitro activity

Inhibition of KSP by ARRY-520 blocked cell cycle progression, leading to apoptosis in acute myeloid leukemia cell lines that express high levels of KSP. Knockdown of p53, overexpression of XIAP and mutation in caspase-8 did not significantly affect sensitivity to ARRY-520, suggesting that the response is independent of p53, XIAP and the extrinsic apoptotic pathway. Although ARRY-520 induced mitotic arrest in both HL-60 and Bcl-2-overexpressing HL-60Bcl-2 cells, cell death was blunted in HL-60Bcl-2 cells, suggesting that the apoptotic program is executed through the mitochondrial pathway. Furthermore, ARRY-520 increased Bim protein levels prior to caspase activation in HL-60 cells.

Reference: Leukemia. 2009 Oct;23(10):1755-62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3593228/

In vivo activity

SCID mice implanted with HL-60 cells were treated with ARRY-520 to evaluate its effect in vivo. As shown in Figure 8A, ARRY-520 greatly decreased tumor volumes and all 5 mice showed complete responses (CR) on day 15. Although tumor growth was significantly inhibited during ARRY-520 treatment and became undetectable shortly after the treatment, tumors eventually outgrew suggesting that prolonged/repeated treatment is required to achieve better outcome.

Reference: Leukemia. 2009 Oct;23(10):1755-62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3593228/