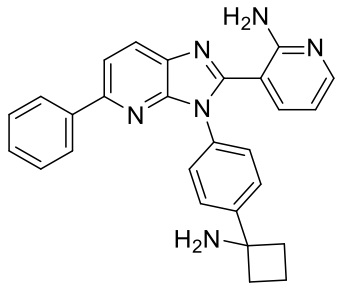
Product data sheet

MedKoo Cat#: 200281 Name: Miransertib free base CAS#: 1313881-70-7 (free base) Chemical Formula: $C_{27}H_{24}N_6$ Exact Mass: 432.2062 Molecular Weight: 432.531	
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:

Miransertib, also known as ARQ 092, is an oral activie, potent and selective AKT inhibitor with IC50 values: 5.0 nM (AKT1); 4.5 nM (AKT2); 16 nM (AKT3). ARQ 092 binds to and inhibits the activity of AKT in a non-ATP competitive manner, which may result in the inhibition of the PI3K/AKT signaling pathway. This may lead to the reduction in tumor cell proliferation and the induction of tumor cell apoptosis. ARQ-092 demonstrated high enzymatic potency against AKT1, AKT2, and AKT3, as well as potent cellular inhibition of AKT activation and the phosphorylation of the downstream target PRAS40. ARQ-092 also served as a potent inhibitor of the AKT1-E17K mutant protein and inhibited tumor growth in a human xenograft mouse model of endometrial adenocarcinoma.

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	8	18.50

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.31 mL	11.56 mL	23.12 mL
5 mM	0.46 mL	2.31 mL	4.62 mL
10 mM	0.23 mL	1.16 mL	2.31 mL
50 mM	0.05 mL	0.23 mL	0.46 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. Nandan D, Zhang N, Yu Y, Schwartz B, Chen S, Kima PE, Reiner NE. Miransertib (ARQ 092), an orally-available, selective Akt inhibitor is effective against Leishmania. PLoS One. 2018 Nov 6;13(11):e0206920. doi: 10.1371/journal.pone.0206920. PMID: 30399177; PMCID: PMC6219794.

In vivo study

1. Nandan D, Zhang N, Yu Y, Schwartz B, Chen S, Kima PE, Reiner NE. Miransertib (ARQ 092), an orally-available, selective Akt inhibitor is effective against Leishmania. PLoS One. 2018 Nov 6;13(11):e0206920. doi: 10.1371/journal.pone.0206920. PMID: 30399177; PMCID: PMC6219794.

7. Bioactivity

Biological target:

Masupirdine free base (SUVN-502 free base) is a potent, selective, orally bioavailable, and brain penetrant 5-HT6 receptor antagonist (Ki of 2.04 nM for human 5-HT6 receptor).

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In vitro activity

To determine the inhibitory effect of Miransertib on Leishmania growth, its effect on promastigotes of L. amazonensis and L. donovani was studied. First, promastigotes of L. amazonensis were treated with various concentrations of Miransertib for 24 hours. The number of viable parasites was determined by MTT assays. Fig 1 shows that increasing concentrations of Miransertib results in death of Leishmania parasites. The EC50 of Miransertib on L. amazonensis was estimated at 7.87 ± 0.93 μM (Fig 1A). For comparison, the EC50 of miltefosine on L. amazonensis was estimated at 40.83 ± 5.03 μM. The efficacy of Miransertib on L. donovani parasites was also determined to be 12.75 ± 1.14μM which was similar to the EC50 of miltefosine on L. donovani, which was 10.54 ± 3.51 μM (Fig 1B). These results show that Miransertib is as effective as miltefosine in killing L. donovani promastigotes, but it is slightly more effective on L. amazonensis promastigotes as compared to miltefosine.

Reference: PLoS One. 2018 Nov 6;13(11):e0206920. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30399177/

In vivo activity

For in vivo efficacy of Miransertib, groups of L. donovani infected BALB/c mice (seven days post infection with stationary phase promastigotes) were dosed daily, for five consecutive days per week with an oral formulation of Miransertib (50 and 75 mg/kg). On day 28 post-infection, the parasite burdens in the livers and spleens of infected mice were quantified. The only available FDA approved oral anti-leishmanial drug miltefosine (20 mg/kg, once daily, 5 days per week) was included as a positive control. Both Miransertib and miltefosine were well tolerated at both doses throughout the study, with no mice displaying any overt signs of toxicity. The results show that Miransertib effectively suppressed parasite burdens by 80–90% (Fig 3A and 3B). In fact, at 50 and 75 mg/kg, Miransertib effectively cured 50% of the study mice (2/4 mice in both treatment groups), with no detectable parasites in the livers and spleens. 50 and 75 mg/kg doses of Miransertib compared favorably with miltefosine in the spleen (Fig 3A), whereas it was more active than miltefosine in the liver (Fig 3B). These results show that Miransertib has potent anti-leishmanial activity in vivo against L. donovani.

Reference: PLoS One. 2018 Nov 6;13(11):e0206920. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30399177/