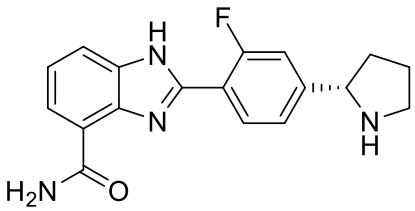
Product data sheet

MedKoo Cat#: 406362 Name: A-966492 CAS#: 934162-61-5 Chemical Formula: $C_{18}H_{17}FN_4O$ Exact Mass: 324.13864 Molecular Weight: 324.35	
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:
A-966492 is a potent PARP inhibitor, which displayed excellent potency against the PARP-1 enzyme with a K(i) of 1 nM and an EC(50) of 1 nM in a whole cell assay. In addition, A-966492 is orally bioavailable across multiple species, crosses the blood-brain barrier, and appears to distribute into tumor tissue. It also demonstrated good in vivo efficacy in a B16F10 subcutaneous murine melanoma model in combination with temozolomide and in an MX-1 breast cancer xenograft model both as a single agent and in combination with carboplatin.

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	82.0	252.81

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.08 mL	15.42 mL	30.83 mL
5 mM	0.62 mL	3.08 mL	6.17 mL
10 mM	0.31 mL	1.54 mL	3.08 mL
50 mM	0.06 mL	0.31 mL	0.62 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. Penning TD, Zhu GD, Gong J, Thomas S, Gandhi VB, Liu X, Shi Y, Klinghofer V, Johnson EF, Park CH, Fry EH, Donawho CK, Frost DJ, Buchanan FG, Bukofzer GT, Rodriguez LE, Bontcheva-Diaz V, Bouska JJ, Osterling DJ, Olson AM, Marsh KC, Luo Y, Giranda VL. Optimization of phenyl-substituted benzimidazole carboxamide poly(ADP-ribose) polymerase inhibitors: identification of (S)-2-(2-fluoro-4-(pyrrolidin-2-yl)phenyl)-1H-benzimidazole-4-carboxamide (A-966492), a highly potent and efficacious inhibitor. J Med Chem. 2010 Apr 22;53(8):3142-53. doi: 10.1021/jm901775y. PMID: 20337371.

In vivo study

1. Penning TD, Zhu GD, Gong J, Thomas S, Gandhi VB, Liu X, Shi Y, Klinghofer V, Johnson EF, Park CH, Fry EH, Donawho CK, Frost DJ, Buchanan FG, Bukofzer GT, Rodriguez LE, Bontcheva-Diaz V, Bouska JJ, Osterling DJ, Olson AM, Marsh KC, Luo Y, Giranda VL. Optimization of phenyl-substituted benzimidazole carboxamide poly(ADP-ribose) polymerase inhibitors: identification of (S)-2-(2-fluoro-4-(pyrrolidin-2-yl)phenyl)-1H-benzimidazole-4-carboxamide (A-966492), a highly potent and efficacious inhibitor. J Med Chem. 2010 Apr 22;53(8):3142-53. doi: 10.1021/jm901775y. PMID: 20337371.

7. Bioactivity

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Biological target:

A-966492 is a novel and potent inhibitor of PARP1 and PARP2 with Ki of 1 nM and 1.5 nM, respectively.

In vitro activity

While there was little difference between the two enantiomers of 25, the (S)-enantiomer of 22 (22b, A-966492) showed superior potency in both PARP enzyme and cellular assays as compared to the respective (R)-enantiomer (22a), highlighted by the 1 nM Ki and EC50 values that exhibited by 22b. This is one of the most potent PARP inhibitors identified to date.

Reference: J Med Chem. 2010 Apr 22;53(8):3142-53. https://pubmed.ncbi.nlm.nih.gov/20337371/

In vivo activity

Because of a superior profile in the B16 model, 22b (A-966492) was characterized further in vivo. Plasma and tumor levels of 22b were assessed after 5 days of oral dosing in a separate B16F10 study using a 25 mg/kg/day, bid dose of 22b in combination with TMZ (50 mg/kg/day, qd). Significant distribution of 22b to the tumor was observed 6 h after the final dose, with a concentration of 21 μg/mL in the tumor vs 0.38 μg/mL in the plasma. Similar concentrations were obtained when 22b was dosed alone (17.2 vs 0.22 μg/mL).

Reference: J Med Chem. 2010 Apr 22;53(8):3142-53. https://pubmed.ncbi.nlm.nih.gov/20337371/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.