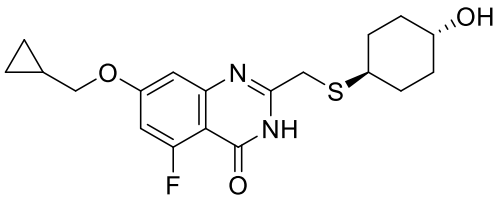
Product data sheet

MedKoo Cat#: 207164 Name: RBN012759 CAS#: 2360851-29-0 Chemical Formula: $C_{19}H_{23}FN_2O_3S$ Exact Mass: 378.1413 Molecular Weight: 378.4624	
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:
RBN012759 is a potent and selective PARP14 inhibitor which decreases protumor macrophage gene expression and elicits inflammatory responses in tumor explants. RBN012759 inhibits PARP14 with a biochemical half-maximal inhibitory concentration of 0.003 μM, exhibits >300-fold selectivity over all PARP family members, and its profile enables further study of PARP14 biology and disease association both in vitro and in vivo. Inhibition of PARP14 with RBN012759 reverses IL-4-driven protumor gene expression in macrophages and induces an inflammatory mRNA signature similar to that induced by immune checkpoint inhibitor therapy in primary human tumor explants.

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	163.0	431.06

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.64 mL	13.21 mL	26.42 mL
5 mM	0.53 mL	2.64 mL	5.28 mL
10 mM	0.26 mL	1.32 mL	2.64 mL
50 mM	0.05 mL	0.26 mL	0.53 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. Schenkel LB, Molina JR, Swinger KK, Abo R, Blackwell DJ, Lu AZ, Cheung AE, Church WD, Kunii K, Kuplast-Barr KG, Majer CR, Minissale E, Mo JR, Niepel M, Reik C, Ren Y, Vasbinder MM, Wigle TJ, Richon VM, Keilhack H, Kuntz KW. A potent and selective PARP14 inhibitor decreases protumor macrophage gene expression and elicits inflammatory responses in tumor explants. Cell Chem Biol. 2021 Aug 19;28(8):1158-1168.e13. doi: 10.1016/j.chembiol.2021.02.010. Epub 2021 Mar 10. PMID: 33705687.

In vivo study

1. Schenkel LB, Molina JR, Swinger KK, Abo R, Blackwell DJ, Lu AZ, Cheung AE, Church WD, Kunii K, Kuplast-Barr KG, Majer CR, Minissale E, Mo JR, Niepel M, Reik C, Ren Y, Vasbinder MM, Wigle TJ, Richon VM, Keilhack H, Kuntz KW. A potent and selective PARP14 inhibitor decreases protumor macrophage gene expression and elicits inflammatory responses in tumor explants. Cell Chem Biol. 2021 Aug 19;28(8):1158-1168.e13. doi: 10.1016/j.chembiol.2021.02.010. Epub 2021 Mar 10. PMID: 33705687.

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7. Bioactivity

Biological target:

RBN012759 is a selective inhibitor of PARP14, with an IC50 of <3 nM. RBN012759 displays 300-fold selectivity over the monoPARPs and 1000-fold selectivity over the polyPARPs.

In vitro activity

The ability of RBN012759 to inhibit PARP14-specific self-MARylation was evaluated. MARylation was detected by immunoblot using an antibody that binds to both MAR and PAR and a PARP14 antibody in IFN-γ-stimulated primary human macrophages. RBN012759 decreased the MAR/PAR signal corresponding to PARP14-self-MARylation in a concentration-dependent manner, further supporting its activity on endogenous PARP14. To reinforce the specificity of PARP14 autoMARylation, the CFPAC-1 cell line was used due to its high endogenous PARP14 baseline level and response to IFN-γ stimulation by increasing PARP14 and ADP-ribosylation. First, endogenous PARP14 was immunoprecipitated from IFN-γ-stimulated CFPAC-1 cells and probed for MAR/PAR. These data demonstrated that PARP14 auto-MARylation is stimulated by IFN-γ and robustly inhibited by RBN012759. In addition, CFPAC-1 cells were stimulated with IFN-γ to increase PARP14 expression and MARylation and treated with increasing concentrations of RBN012759. RBN012759 decreased the MARylation signal in a concentration-dependent manner, similar to that observed in human macrophages.

Reference: ell Chem Biol. 2021 Aug 19;28(8):1158-1168.e13. https://pubmed.ncbi.nlm.nih.gov/33705687/

In vivo activity

The ability of RBN012759 to engage PARP14 in vivo was also evaluated. C57BL/6 mice were treated with RBN012759 at 300 and 500 mg/kg BID PO for 7 days, during which it was well tolerated with no significant body weight loss observed. Treatment with RBN012759 led to an increase in PARP14 protein in vivo. The 500 mg/kg treatment group showed increased PARP14 protein, while the 300 mg/kg group did not, correlating with RBN012759 plasma exposures at the 12 h time point in which the mouse PARP14-free IC50 value was increased by 6- and <1-fold, respectively. These data support the use of RBN012759 as an in vivo chemical probe that selectively engages PARP14 in tissue.

Reference: ell Chem Biol. 2021 Aug 19;28(8):1158-1168.e13. https://pubmed.ncbi.nlm.nih.gov/33705687/

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.