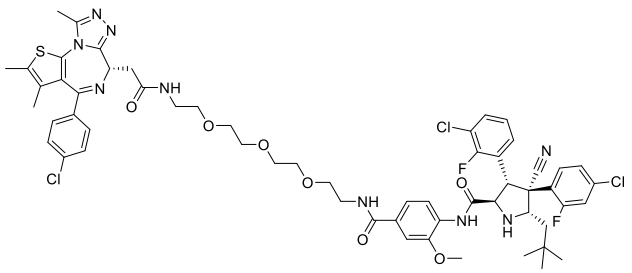
Product data sheet

MedKoo Cat#: 573175 Name: A1874 CAS#: 2064292-12-0 Chemical Formula: $C_{58}H_{62}Cl_3F_2N_9O_7S$ Exact Mass: 1171.3527 Molecular Weight: 1173.6	
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:
A1874 is a nutlin-based and BRD4-degrading PROTAC which induces BRD4 degradation in cells.

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	125.0	106.51
Ethanol	100.0	85.21

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	0.85 mL	4.26 mL	8.52 mL
5 mM	0.17 mL	0.85 mL	1.70 mL
10 mM	0.09 mL	0.43 mL	0.85 mL
50 mM	0.02 mL	0.09 mL	0.17 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. Qin AC, Jin H, Song Y, Gao Y, Chen YF, Zhou LN, Wang SS, Lu XS. The therapeutic effect of the BRD4-degrading PROTAC A1874 in human colon cancer cells. Cell Death Dis. 2020 Sep 25;11(9):805. doi: 10.1038/s41419-020-03015-6. PMID: 32978368; PMCID: PMC7519683.
2. Hines J, Lartigue S, Dong H, Qian Y, Crews CM. MDM2-Recruiting PROTAC Offers Superior, Synergistic Antiproliferative Activity via Simultaneous Degradation of BRD4 and Stabilization of p53. Cancer Res. 2019 Jan 1;79(1):251-262. doi: 10.1158/0008-5472.CAN-18-2918. Epub 2018 Nov 1. PMID: 30385614; PMCID: PMC6318015.

In vivo study

1. Qin AC, Jin H, Song Y, Gao Y, Chen YF, Zhou LN, Wang SS, Lu XS. The therapeutic effect of the BRD4-degrading PROTAC A1874 in human colon cancer cells. Cell Death Dis. 2020 Sep 25;11(9):805. doi: 10.1038/s41419-020-03015-6. PMID: 32978368; PMCID: PMC7519683.

7. Bioactivity
Biological target:
A1874 is a nutlin-based and BRD4-degrading PROTAC with a DC50 of 32 nM (induce BRD4 degradation in cells).

In vitro activity

Product data sheet

Suppression of c-Myc or induction of $p21^{CIP1/WAF1}$ -- either one alone -- will inhibit cell proliferation. HCT116 cells incubated with JQ1 or idasanutlin for 48h showed clear dose-dependent loss of viability (Figure 3A). Treatment with JQ1 resulted in 25% loss of MTS signal compared to control cells; and idasanutlin treatment caused a 62% loss. However, treatment with A1874, which combines the activities of the two inhibitors, ultimately resulted in a 97% loss in HCT116 cell viability. That the effect of A1874 was greater than either idasanutlin or JQ1 alone, and even slightly more effective than a combined treatment (Supplementary Figure S1), demonstrates that combining both activities into a single PROTAC does not result in one activity diminishing the other.

Reference: Cancer Res. 2019 Jan 1; 79(1): 251–262. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6318015/

In vivo activity

By recording tumor growth curve, this demonstrated that A1874 oral administration (20 mg/kg, daily, 21 days) potently inhibited colon cancer xenograft growth in SCID mice (Fig. 5a). Calculating the estimated daily tumor growth, using the formula: (Tumor volume at D42—Tumor volume at D0)/42 (days), this study found that colon cancer xenograft growth was largely inhibited in A1874-treated mice (Fig. 5b). Tumors from the two groups were isolated and weighted individually at experimental Day-42 (D42). Xenograft tumors with A1874 administration were significantly lighter than those of vehicle control mice (Fig. 5c). Mouse body weights were not significantly different between A1874-treated and vehicle control mice (Fig. 5d), and no noticeable toxicity was observed in the mice. These results show that oral administration of A1874 is able to inhibit colon cancer xenograft growth in SCID mice.

Reference: Cell Death Dis. 2020 Sep; 11(9): 805. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7519683/

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.