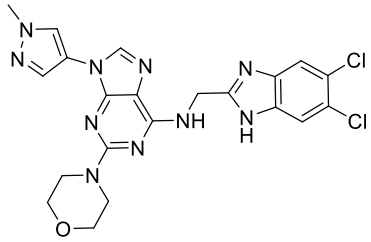
Product data sheet

MedKoo Cat#: 593163 Name: SR-4835 CAS#: 2387704-62-1 Chemical Formula: $C_{21}H_{20}Cl_2N_{10}O$ Exact Mass: 498.1199 Molecular Weight: 499.36	
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:
SR-4835 is a highly selective dual inhibitor of CDK12 and CDK13, which disables triple-negative breast cancer (TNBC) cells. Mechanistically, inhibition or loss of CDK12/CDK13 triggers intronic polyadenylation site cleavage that suppresses the expression of core DNA damage response proteins. This provokes a "BRCAness" phenotype that results in deficiencies in DNA damage repair, promoting synergy with DNA-damaging chemotherapy and PARP inhibitors.

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	5.0	10.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.00 mL	10.01 mL	20.03 mL
5 mM	0.40 mL	2.00 mL	4.01 mL
10 mM	0.20 mL	1.00 mL	2.00 mL
50 mM	0.04 mL	0.20 mL	0.40 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. Houles T, Boucher J, Lavoie G, MacLeod G, Lin S, Angers S, Roux PP. The CDK12 inhibitor SR-4835 functions as a molecular glue that promotes cyclin K degradation in melanoma. Cell Death Discov. 2023 Dec 16;9(1):459. doi: 10.1038/s41420-023-01754-x. PMID: 38104154; PMCID: PMC10725499.
2. Hopkins JL, Zou L. Induction of BRCAness in Triple-Negative Breast Cancer by a CDK12/13 Inhibitor Improves Chemotherapy. Cancer Cell. 2019 Nov 11;36(5):461-463. doi: 10.1016/j.ccell.2019.10.012. PMID: 31715127.

In vivo study

1. Li Y, Zhang H, Li Q, Zou P, Huang X, Wu C, Tan L. CDK12/13 inhibition induces immunogenic cell death and enhances anti-PD-1 anticancer activity in breast cancer. Cancer Lett. 2020 Dec 28;495:12-21. doi: 10.1016/j.canlet.2020.09.011. Epub 2020 Sep 15. PMID: 32941949.
2. Quereda V, Bayle S, Vena F, Frydman SM, Monastyrskyi A, Roush WR, Duckett DR. Therapeutic Targeting of CDK12/CDK13 in Triple-Negative Breast Cancer. Cancer Cell. 2019 Nov 11;36(5):545-558.e7. doi: 10.1016/j.ccell.2019.09.004. Epub 2019 Oct 24. PMID: 31668947.

Product data sheet

7. Bioactivity

Biological target:

SR-4835 is a highly selective dual inhibitor of CDK12 and CDK13 with IC50 of 99 nM and Kd of 98 nM for CDK12 and IC50 of 4.9 nM for CDK13. SR-4835 disables triple-negative breast cancer (TNBC) cells.

In vitro activity

SR-4835 acts as a molecular glue that recruits the CDK12-cyclin K complex to the CUL4-RBX1-DDB1 ubiquitin ligase complex to target cyclin K for degradation. SR-4835 uniquely promotes cyclin K degradation via the proteasome. SR-4835 promotes DDB1 interaction with the CDK12-cyclin K complex. Docking studies and structure-activity relationship analyses of SR-4835 revealed the importance of the benzimidazole side-chain in molecular glue activity.

Reference: Cell Death Discov. 2023 Dec 16;9(1):459. https://pubmed.ncbi.nlm.nih.gov/38104154/

In vivo activity

SR-4835's anti-tumor activity was assessed in a PDX model (PDX4013) derived from a triple-negative breast cancer (TNBC) patient with limited response to dasatinib and docetaxel treatment. Tumor growth markedly decreased in SR-4835-treated mice compared to controls. Endpoint studies revealed reduced expression of DDR genes and elevated levels of γ-H2AX protein. SR-4835 treatment did not induce weight loss. Additionally, SR-4835 significantly impaired tumor growth.

Reference: Cancer Cell. 2019 Nov 11;36(5):545-558.e7. https://pubmed.ncbi.nlm.nih.gov/31668947/

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.