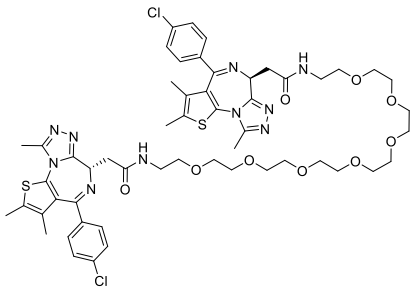
Product data sheet

MedKoo Cat#: 407972 Name: MT1 BET inhibitor CAS: 2060573-82-0 Chemical Formula: $C_{54}H_{66}Cl_2N_{10}O_9S_2$ Exact Mass: 1132.3833 Molecular Weight: 1134.203	
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:
MT1, also known as (Bis-CPI203)-PEG7, is a highly potent BET bromodomain inhibitor. MT1 is an intramolecular bivalent BRD4 binder that is more than 100-fold more potent, in cellular assays, than the corresponding monovalent antagonist, JQ1. MT1 significantly ($P < 0.05$) delayed leukemia progression in mice, as compared to JQ1.

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	150.0	132.25

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	0.88 mL	4.41 mL	8.82 mL
5 mM	0.18 mL	0.88 mL	1.76 mL
10 mM	0.09 mL	0.44 mL	0.88 mL
50 mM	0.02 mL	0.09 mL	0.18 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

Tanaka M, Roberts JM, Seo HS, Souza A, Paulk J, Scott TG, DeAngelo SL, Dhe-Paganon S, Bradner JE. Design and characterization of bivalent BET inhibitors. Nat Chem Biol. 2016 Dec;12(12):1089-1096. doi: 10.1038/nchembio.2209. Epub 2016 Oct 24. PMID: 27775715; PMCID: PMC5117811.

In vivo study

Tanaka M, Roberts JM, Seo HS, Souza A, Paulk J, Scott TG, DeAngelo SL, Dhe-Paganon S, Bradner JE. Design and characterization of bivalent BET inhibitors. Nat Chem Biol. 2016 Dec;12(12):1089-1096. doi: 10.1038/nchembio.2209. Epub 2016 Oct 24. PMID: 27775715; PMCID: PMC5117811.

7. Bioactivity
Biological target:

MT1 is a bivalent chemical probe of BET bromodomains, with an IC_{50} of 0.789 nM for BRD4(1).

In vitro activity

Significant apoptosis was observed by caspase-3 and PARP cleavage after treatment with MT1 (Fig. 5b). These cellular events followed after HEXIM1 upregulation and MYC downregulation. Early and late apoptosis were assessed with annexin-V and

propidium iodide staining to compare apoptosis induction between MT1 and JQ1 (Fig. 5c and Supplementary Fig. 12). Importantly, MT1 induced a greater degree of apoptosis at 10-fold lower concentrations than JQ1.

Reference: Nat Chem Biol. 2016 Dec;12(12):1089-1096. https://pubmed.ncbi.nlm.nih.gov/27775715/

In vivo activity

To determine whether MT1 could attenuate the growth of BRD4-dependent leukemia as a single agent *in vivo*, this study selected an aggressive disseminated leukemia model (mCherry$^+$, Luciferase$^+$, MV4;11) and treated animals with established disease using equimolar (44.2 µmol/kg) and half an equivalent (22.1 µmol/kg) of MT1 compared to JQ1 for 14 days. During the study, leukemic burden was monitored by non-invasive bioluminescence imaging. Even half an equivalent of MT1 significantly reduced leukemic burden over the course of the study compared to either vehicle or JQ1 (Fig. 6a). Post-mortem analysis of leukemic burden in bone marrow by FACS also revealed significantly decreased mCherry$^+$ disease with MT1 administration at 22.1 µg/kg (Fig. 6b).

Reference: Nat Chem Biol. 2016 Dec;12(12):1089-1096. https://pubmed.ncbi.nlm.nih.gov/27775715/