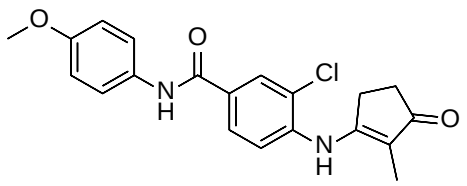
Product data sheet

MedKoo Cat#: 525592 Name: MS402 CAS#: 1672684-68-2 Chemical Formula: $C_{20}H_{19}ClN_2O_3$ Exact Mass: 370.1084 Molecular Weight: 370.83	
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:
MS402 is a novel BD1-selective BET BrD inhibitor, inhibiting primarily Th17 cell differentiation with a little or almost no effect on Th1 or Th2 and Treg cells. MS402 preferentially renders Brd4 binding to Th17 signature gene loci over those of housekeeping genes and reduces Brd4 recruitment of p-TEFb to phosphorylate and activate RNA polymerase II for transcription elongation. MS402 prevents and ameliorates T-cell transfer-induced colitis in mice by blocking Th17 cell overdevelopment.

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

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.70 mL	13.48 mL	26.97 mL
5 mM	0.54 mL	2.70 mL	5.39 mL
10 mM	0.27 mL	1.35 mL	2.70 mL
50 mM	0.05 mL	0.27 mL	0.54 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. Cheung K, Lu G, Sharma R, Vincek A, Zhang R, Plotnikov AN, Zhang F, Zhang Q, Ju Y, Hu Y, Zhao L, Han X, Meslamani J, Xu F, Jaganathan A, Shen T, Zhu H, Rusinova E, Zeng L, Zhou J, Yang J, Peng L, Ohlmeyer M, Walsh MJ, Zhang DY, Xiong H, Zhou MM. BET N-terminal bromodomain inhibition selectively blocks Th17 cell differentiation and ameliorates colitis in mice. Proc Natl Acad Sci U S A. 2017 Mar 14;114(11):2952-2957. doi: 10.1073/pnas.1615601114. Epub 2017 Mar 6. PMID: 28265070; PMCID: PMC5358349.

In vivo study

1. Cheung K, Lu G, Sharma R, Vincek A, Zhang R, Plotnikov AN, Zhang F, Zhang Q, Ju Y, Hu Y, Zhao L, Han X, Meslamani J, Xu F, Jaganathan A, Shen T, Zhu H, Rusinova E, Zeng L, Zhou J, Yang J, Peng L, Ohlmeyer M, Walsh MJ, Zhang DY, Xiong H, Zhou MM. BET N-terminal bromodomain inhibition selectively blocks Th17 cell differentiation and ameliorates colitis in mice. Proc Natl Acad Sci U S A. 2017 Mar 14;114(11):2952-2957. doi: 10.1073/pnas.1615601114. Epub 2017 Mar 6. PMID: 28265070; PMCID: PMC5358349.

7. Bioactivity

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Biological target: MS402 is a BD1-selective BET BrD inhibitor with Kis of 77 nM, 718 nM, 110 nM, 200 nM, 83 nM, and 240 nM for BRD4(BD1), BRD4(BD2), BRD3(BD1), BRD3(BD2), BRD2(BD1) and BRD2(BD2), respectively.

In vitro activity

To study the role of BET proteins in Th cell differentiation, murine primary naïve CD4+ T cells were isolated from mouse spleen and lymph nodes and treated with IL-12, IL-4 plus α-IL-12, TGF-β plus IL-6, or TGF-β plus IL-2, respectively, to promote Th1, Th2, Th17, or Treg linage-specific differentiation over 3.5 d with or without MS402 added daily to cell culture (Fig. 2A). Strikingly, as shown by flow cytometry analysis, MS402, in a dose-dependent manner, inhibited IL-17 release from 18.6 to 8.0% in the Th17 polarizing condition and to a lesser extent IFN-γ production from 49.7 to 38.6% in the Th1 condition; it had little, if any, effect on IL-4 and Foxp3 expression during Th2 and Treg cell differentiation, respectively (Fig. 2B).

Reference: Proc Natl Acad Sci U S A. 2017 Mar 14;114(11):2952-2957. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5358349/

In vivo activity

An in vivo experimental colitis study to explore therapeutic potential of MS402 was conducted. Mice treated with MS402 exhibited a reversal of weight loss after 1 wk (Fig. 4G). Consistently, the MS402-treated mice showed an almost minimal degree of inflammation in the colon, as demonstrated by much improved colon length and appearance (Fig. S4A), a lower disease score of 0–1 (Fig. S4B), and markedly reduced inflammatory cell infiltrates in colon sections as compared with those of the disease-group mice (Fig. 4H). Further, the MS402-treated mice also had a lower population of IFN-γ–producing CD4+ T cells and exhibited a much more dramatic reduction of IL-17–producing CD4+ T cells in colon than the group of T-cell-transfer disease mice (Fig. 4I). Finally, the MS402-treated mice had much lower mRNA expression levels of key cytokines and Th17- and Th1-specific transcription factors including il17, il21, il22, il6, rorc, Tbet, and ifng compared with the disease-group mice (Fig. 4J). Collectively, these results show that MS402 is an effective inhibitor of Th17 cell development and ameliorates adaptive T-cell transfer-induced colitis in mice.

Reference: Proc Natl Acad Sci U S A. 2017 Mar 14;114(11):2952-2957. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5358349/