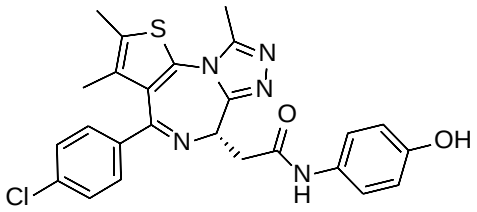
Product data sheet

MedKoo Cat#: 206116 Name: Birabresib CAS#: 202590-98-5 Chemical Formula: $C_{25}H_{22}ClN_5O_2S$ Exact Mass: 491.1183 Molecular Weight: 491.99	
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:
Birabresib, also known as OTX015 and MK-8628, a potent BET bromodomian inhibitor, which targets the BET bromodomain proteins 2, 3, and 4 (BRD2/3/4). BRDs 2, 3, and 4 are considered potential cancer targets because of their pivotal role in regulating the transcription of growth-promoting genes and cell cycle regulators. OTX015 is the first BRD2/3/4 inhibitor to enter clinical trials. OTX015 showed antiproliferative activity in a large panel of cell lines derived from mature B-cell lymphoid tumors with median IC50 of 240 nmol/L, without significant differences among the different histotypes.

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	73.50	149.39
Ethanol	98.0	199.19

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.03 mL	10.16 mL	20.33 mL
5 mM	0.41 mL	2.03 mL	4.07 mL
10 mM	0.20 mL	1.02 mL	2.03 mL
50 mM	0.04 mL	0.20 mL	0.41 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. Hu X, Schewitz-Bowers LP, Lait PJP, Copland DA, Stimpson ML, Li JJ, Liu Y, Dick AD, Lee RWJ, Wei L. The Bromodomain and Extra-Terminal Protein Inhibitor OTX015 Suppresses T Helper Cell Proliferation and Differentiation. Curr Mol Med. 2018;18(9):594-601. doi: 10.2174/1566524019666190126112238. PMID: 30683020.
2. Vázquez R, Riveiro ME, Astorgues-Xerri L, Odore E, Rezai K, Erba E, Panini N, Rinaldi A, Kwee I, Beltrame L, Bekradda M, Cvitkovic E, Bertoni F, Frapolli R, D'Incalci M. The bromodomain inhibitor OTX015 (MK-8628) exerts anti-tumor activity in triple-negative breast cancer models as single agent and in combination with everolimus. Oncotarget. 2017 Jan 31;8(5):7598-7613. doi: 10.18632/oncotarget.13814. PMID: 27935867; PMCID: PMC5352346.

In vivo study

1. Vázquez R, Licandro SA, Astorgues-Xerri L, Lettera E, Panini N, Romano M, Erba E, Ubezio P, Bello E, Libener R, Orecchia S, Grosso F, Riveiro ME, Cvitkovic E, Bekradda M, D'Incalci M, Frapolli R. Promising in vivo efficacy of the BET bromodomain inhibitor OTX015/MK-8628 in malignant pleural mesothelioma xenografts. Int J Cancer. 2017 Jan 1;140(1):197-207. doi: 10.1002/ijc.30412. Epub 2016 Sep 19. PMID: 27594045.

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2. Shi J, Song S, Han H, Xu H, Huang M, Qian C, Zhang X, Ouyang L, Hong Y, Zhuang W, Li B. Potent Activity of the Bromodomain Inhibitor OTX015 in Multiple Myeloma. Mol Pharm. 2018 Sep 4;15(9):4139-4147. doi: 10.1021/acs.molpharmaceut.8b00554. Epub 2018 Aug 9. PMID: 30048594.

7. Bioactivity

Biological target: Birabresib (OTX-015) is a bromodomain (BRD2/3/4) inhibitor with IC50s ranging from 92 to 112 nM.

In vitro activity

Naïve and memory murine and human CD4+ T cells were exposed to varying concentrations of OTX015 in vitro, and its impact on cytokine expression was quantified by flow cytometry. OTX015 suppressed both murine and human CD4+ T cell proliferation. Its impact on cytokine expression varied in murine and human naïve and memory subsets. OTX015 was similarly effective as JQ1, a previously studied BET inhibitor that was used as the control, in the suppression of cytokines and T helper cell proliferation. Higher concentrations of OTX015 also had a greater impact on the viability of murine versus human cells. IL-17 and IFN-γ expression was not altered in murine memory CD4+ T cells, whereas in human memory CD4+ T cells, OTX015 inhibited IL-17, but not IFN-γ. Across all human T cell subsets OTX015 suppressed IL-17 more effectively than IFN-γ.

Reference: Curr Mol Med. 2018;18(9):594-601. https://www.eurekaselect.com/169393/article

In vivo activity

Oral administration of the bromodomain inhibitor OTX015 displayed significant antitumor activity in a mouse model of disseminated human myeloma. OTX015 promoted osteoblast differentiation of mesenchymal stem cells (MSCs) and inhibited osteoclast formation and resorption in vivo experiments.

Reference: Mol Pharm. 2018 Sep 4;15(9):4139-4147. https://pubs.acs.org/doi/10.1021/acs.molpharmaceut.8b00554