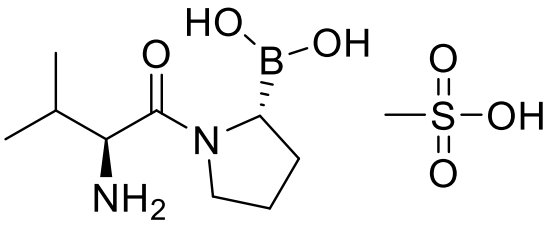
Product data sheet

MedKoo Cat#: 202730 Name: Talabostat mesylate CAS#: 150080-09-4 (mesylate) Chemical Formula: $C_{10}H_{23}BN_2O_6S$ Exact Mass: 214.15 Molecular Weight: 310.17	
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:

Talabostat, also known as PT-100 and BXCL701, is dipeptidyl peptidase inhibitor with antineoplastic and hematopoiesis- stimulating activities. By cleaving N-terminal Xaa-Pro or Xaa-Ala residues, talabostat inhibits dipeptidyl peptidases, such as fibroblast activation protein (FAP), resulting in the stimulation of cytokine and chemokine production and specific T-cell immunity and T-cell- dependent activity. This agent may also stimulate the production of colony stimulating factors, such as granulocyte colony stimulating factor (G-CSF), resulting in the stimulation of hematopoiesis. Dipeptidyl peptidases are involved in the activation of polypeptide hormones and chemokines.

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	62	199.88
Water	62	199.88
Ethanol	62	199.88

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.22 mL	16.12 mL	32.24 mL
5 mM	0.64 mL	3.22 mL	6.45 mL
10 mM	0.32 mL	1.61 mL	3.22 mL
50 mM	0.06 mL	0.32 mL	0.64 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. Okondo MC, Johnson DC, Sridharan R, Go EB, Chui AJ, Wang MS, Poplawski SE, Wu W, Liu Y, Lai JH, Sanford DG, Arciprete MO, Golub TR, Bachovchin WW, Bachovchin DA. DPP8 and DPP9 inhibition induces pro-caspase-1-dependent monocyte and macrophage pyroptosis. Nat Chem Biol. 2017 Jan;13(1):46-53. doi: 10.1038/nchembio.2229. Epub 2016 Nov 7. PMID: 27820798; PMCID: PMC5477230.

In vivo study

1. Okondo MC, Johnson DC, Sridharan R, Go EB, Chui AJ, Wang MS, Poplawski SE, Wu W, Liu Y, Lai JH, Sanford DG, Arciprete MO, Golub TR, Bachovchin WW, Bachovchin DA. DPP8 and DPP9 inhibition induces pro-caspase-1-dependent monocyte and macrophage pyroptosis. Nat Chem Biol. 2017 Jan;13(1):46-53. doi: 10.1038/nchembio.2229. Epub 2016 Nov 7. PMID: 27820798; PMCID: PMC5477230.

Product data sheet

2. Adams S, Miller GT, Jesson MI, Watanabe T, Jones B, Wallner BP. PT-100, a small molecule dipeptidyl peptidase inhibitor, has potent antitumor effects and augments antibody-mediated cytotoxicity via a novel immune mechanism. Cancer Res. 2004 Aug 1;64(15):5471-80. doi: 10.1158/0008-5472.CAN-04-0447. PMID: 15289357.

7. Bioactivity

Biological target:

Talabostat (Val-boroPro, PT-100) is a dipeptidyl peptidase inhibitor with IC50 values of <4 nM, 4 nM, 11 nM, 310 nM, 560 nM and 390 nM for DPP-IV, DPP8, DPP9, QPP, FAP and PEP respectively.

In vitro activity

The inhibition of DPP8/9 by PT-100 results in the conversion of pro-caspase-1 into an activated form of pro-caspase-1, which then induces pyroptosis in monocytes and macrophages and stimulates the immune system (Fig. 6c). The absolute dependence on caspase-1, as demonstrated by the results in caspase-1 knockout cells and mice, is in itself sufficient to establish the cytotoxic effects as pyroptosis. However, it's also shown that several other hallmarks of pyroptosis are present. These include: 1) the cleavage of GSDMD, the key effector of pyroptosis; 2) that knockout of GSDMD delays the cytotoxic response; 3) that the apoptotic caspases-3 and -7 and the apoptotic caspase substrate PARP are not cleaved; and 4) that the cell death appears lytic and not apoptotic by microscopy. Significantly, Val-boroPro's cytotoxic effects appear to be completely selective to monocytes and macrophages.

Reference: Nat Chem Biol. 2017 Jan;13(1):46-53. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5477230/

In vivo activity

Oral administration of PT-100 to mice slowed growth of syngeneic tumors derived from fibrosarcoma, lymphoma, melanoma, and mastocytoma cell lines. In WEHI 164 fibrosarcoma and EL4 and A20/2J lymphoma models, PT-100 caused regression and rejection of tumors. The antitumor effect appeared to involve tumor-specific CTL and protective immunological memory. PT-100 treatment of WEHI 164-inoculated mice increased mRNA expression of cytokines and chemokines known to promote T-cell priming and chemoattraction of T cells and innate effector cells. The role of innate activity was further implicated by observation of significant, although reduced, inhibition of WEHI 164 and A20/2J tumors in immunodeficient mice. PT-100 also demonstrated ability to augment antitumor activity of rituximab and trastuzumab in xenograft models of human CD20(+) B-cell lymphoma and HER-2(+) colon carcinoma where antibody-dependent cytotoxicity can be mediated by innate effector cells responsive to the cytokines and chemokines up-regulated by PT-100. Although CD26/DPP-IV is a potential target for PT-100 in the immune system, it appeared not to be involved because antitumor activity and stimulation of cytokine and chemokine production was undiminished in CD26(-/-) mice.

Reference: Cancer Res. 2004 Aug 1;64(15):5471-80. https://cancerres.aacrjournals.org/content/64/15/5471.long