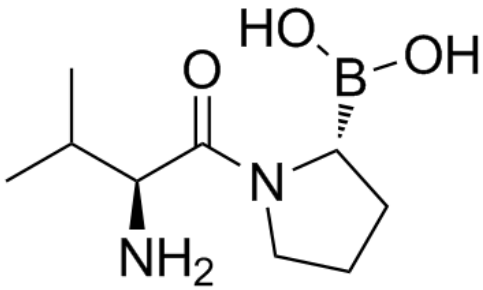
Product Data Sheet

Product Name: Talabostat (PT100)
Cat. No.: GC33853

Chemical Properties

Cas. No.	149682-77-9		
SMILES	CC(C)[C@H](N)C(N1[C@H](B(O)O)CCC1)=O		
Formula	$C_9H_{19}BN_2O_3$	M.Wt	214.07
Solubility	DMSO : ≥ 40 mg/mL (186.85 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Protocol

Cell experiment [1]:	
Cell lines	THP-1 cells, RAW 264.7 and J774 cells

Product Data Sheet

Preparation method	THP-1 cells were differentiated in 10 cm dishes in complete medium with 50 ng/mL PMA for 3 d. RAW 264.7 and J774 cells were plated at 3 × 106 cells per 10 cm plate in complete medium and incubated overnight. The cells were washed with 2 × 5 mL PBS before the addition of 10 mL of serum free media. Cells were then treated with Talabostat (PT100) (2 μM) or LPS (10 μg/mL) for 24 h.
Reaction Conditions	2 μM; 24 h
Applications	Talabostat (PT100) induces an active form of pro-caspase-1 that can sufficiently cleave a substrate (or substrates) that mediates pyroptosis, but that does not efficiently cleave IL-1β or the tetrapeptide Ac-WEHD-AFC.
Animal experiment [2]:	
Animal models	BALB/c, C56BL/6, DBA/2, and BALB/c$^{nu/nu}$ mice
Preparation method	Tumor-inoculated mice were given varying doses (5–40 μg) of Talabostat(PT100) or saline vehicle by oral gavage, twice daily at ~8h intervals. The time of tumor inoculation was defined as day 0, and PT-100 treatment was started on either day 2 or day 7 and continued daily.
Dosage form	5–40 μg twice daily at ~8h intervals；p.o.

Product Data Sheet

Applications	Treatment with Talabostat(PT100) was found to significantly inhibit the additional growth of B16-F10, WEHI 164 and EL 4 tumor cells in mice.

References:

[1] Okondo M C , Johnson D C , Sridharan R ,et al.DPP8 and DPP9 inhibition induces pro-caspase-1-dependent monocyte and macrophage pyroptosis[J].Nature Chemical Biology, 2017 Jan; 13(1): 46–53.

[2] Adams S, et al. 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.

Background

Talabostat (PT100) is an orally active and non-selective inhibitor of dipeptidyl peptidase IV (DPP-IV) (IC_{50} < 4 nM; K_i = 0.18 nM) and the first clinical inhibitor of fibroblast activation protein (FAP) (IC_{50}= 560 nM), inhibiting DPP 8/9 (IC_{50}= 4/11 nM; K_i = 1.5/0.76 nM), prolyl endopeptidase (QPP) (IC50= 310 nM), DPP2, and other DASH family enzymes[1]. Due to its inhibitory action on these proteases, the mechanism of action of Talabostat (PT100) involves the inhibition of protease activity, thereby affecting the tumor microenvironment, immune cell activity, and inflammatory responses[2]. Talabostat (PT100) is also known to stimulate hematopoiesis.

In vitro, Talabostat (PT100) at concentrations ranging from 30 pg/ml to 30 μg/ml when added to the culture medium, can induce tumor regression and rejection in WEHI 164 fibrosarcoma and EL 4 and A20/2 J lymphoma models[1]. Talabostat (PT100) (2μM, 24h) can induce the active form of caspase-1, which can efficiently cleave substrates mediating pyroptosis but not effectively cleave IL-1β or the tetrapeptide Ac-WEHD-AFC[4]. In tumors and tumor-draining lymph nodes, Talabostat (PT100) stimulates the transcriptional upregulation of various cytokines such as IL-1β, IL-6, G-CSF, and CXCL1/KC[4].

In vivo, Talabostat (PT100) significantly inhibits the extraneous growth of tumors such as B16-F10, WEHI 164, and EL 4 tumor cells in mice through delayed oral administration (5–40 μg, twice daily,

approximately 8 hours apart) [3].

References:

[1] Connolly BA, et al. Dipeptide boronic acid inhibitors of dipeptidyl peptidase IV: determinants of potencyand in vivo efficacy and safety. J Med Chem. 2008 Oct 9;51(19):6005-13.

[2] Lankas GR, et al. Dipeptidyl peptidase IV inhibition for the treatment of type 2 diabetes: potential importance of selectivity over dipeptidyl peptidases 8 and 9. Diabetes. 2005 Oct;54(10):2988-94.

[3] Adams S, et al. 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.

[4] Okondo M C , Johnson D C , Sridharan R ,et al.DPP8 and DPP9 inhibition induces pro-caspase-1-dependent monocyte and macrophage pyroptosis[J].Nature Chemical Biology, 2017 Jan; 13(1): 46–53.