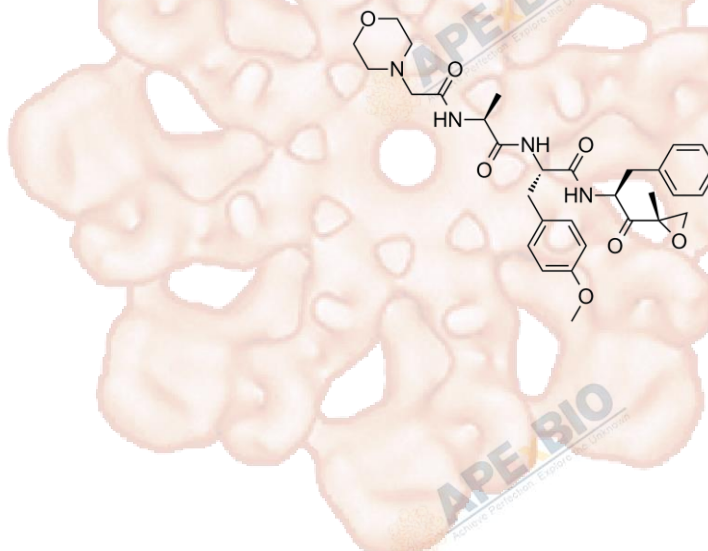


# Product Data Sheet

## ONX-0914 (PR-957)

<b>Cat. No.:</b>	A4011
<b>CAS No.:</b>	960374-59-8
<b>Formula:</b>	C31H40N4O7
<b>M.Wt:</b>	580.67
<b>Synonyms:</b>	ONX-0914, PR-957
<b>Target:</b>	Ubiquitination/ Proteasome
<b>Pathway:</b>	Proteasome
<b>Storage:</b>	Store at -20°C



### Solvent & Solubility

≥29.03 mg/mL in DMSO; insoluble in H<sub>2</sub>O; ≥69 mg/mL in EtOH

In Vitro

Preparing Stock Solutions	Solvent		Mass		
	Concentration		1mg	5mg	10mg
	1 mM		1.7221 mL	8.6107 mL	17.2215 mL
	5 mM		0.3444 mL	1.7221 mL	3.4443 mL
	10 mM		0.1722 mL	0.8611 mL	1.7221 mL

Please refer to the solubility information to select the appropriate solvent.

### Biological Activity

Shortsummary

Immunoproteasome inhibitor, potent and selective

IC<sub>50</sub> & Target

~10 nM (LMP7)

In Vitro

#### Cell Viability Assay

Cell Line:	Human peripheral blood mononuclear (PBMC) cells
Preparation method:	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting conditions:	200 nM, 1 hour

	Applications:	PBMCs were treated with 200 nM ONX-0914 for 1 hour and were exposure to 1 ng/ml LPS for 24 h. Supernatants were analyzed for expression of the inflammatory cytokines. ONX-0914 selectively inhibited LMP7 (> 80%). LMP7 inhibition blocked production of IL-23 by > 90% and of tumor necrosis factor- $\alpha$ (TNF- $\alpha$ ) and IL-6 by ~ 50%. Higher concentrations of ONX-0914, which induce inhibition of LMP2 and MECL-1, further decreased secretion of TNF- $\alpha$ and IL-6, suggesting that these subunits have a role in cytokine regulation.
In Vivo	<b>Animal experiment</b>	
	Animal models:	Collagen antibody-induced arthritis (CAIA) model in BALB/c mice Collagen-induced arthritis (CIA) model in DBA1/J mice
	Dosage form:	Intravenous injection, 2, 6 and 10 mg per kg body weight
	Applications:	ONX-0914 blocked disease progression in a dose-dependent manner and completely ameliorated visible signs of disease at the highest dose. Inhibition of LMP7 alone was sufficient to block disease progression, as evidenced by the therapeutic response to PR-957 administered at 2 mg per kg body weight. ONX-0914 treatment also induced a rapid therapeutic response in the T and B cell-dependent CIA model. Immunoproteasome inhibition was associated with a decrease in circulating levels of autoantibodies and collagen oligomeric matrix protein (COMP), a marker for cartilage breakdown.
	Other notes:	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

## Product Citations

1. Jimenez-Guardeño JM, Apolonia L, et al. "Immunoproteasome activation enables human TRIM5 $\alpha$  restriction of HIV-1." *Nat Microbiol.* 2019 Jun;4(6):933-940.PMID:30886358
2. Leslie Kirby, Jing Jin, et al. "Oligodendrocyte Precursor Cells Are Co-Opted by the Immune System to Cross-Present Antigen and Mediate Cytotoxicity." *bioRxiv.* 2018 November 4.
3. Dimasuay KG, Sanchez A, et al. "Immunoproteasomes as a novel antiviral mechanism in rhinovirus-infected airways." *Clin Sci (Lond).* 2018 Aug 16;132(15):1711-1723.PMID:29980604
4. Liu RT, Zhang P, et al. "ONX-0914, a selective inhibitor of immunoproteasome, ameliorates experimental autoimmune myasthenia gravis by modulating humoral response." *J Neuroimmunol.* 2017 Oct 15;311:71-78.PMID:28844501
5. Ortega-Atienza S, Krawiec C, et al. "20S immunoproteasomes remove formaldehyde-damaged cytoplasmic proteins suppressing caspase-independent cell death." *Sci Rep.* 2017 Apr 5;7(1):654.PMID:28381880

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## References

- [1] Muchamuel T, Basler M, Aujay M A, et al. A selective inhibitor of the immunoproteasome subunit LMP7 blocks cytokine production

## Caution

**FOR RESEARCH PURPOSES ONLY.**

**NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.**

*Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.*

**APExBIO Technology**

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