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Inhibitors, Screening Libraries, Proteins

# p97

VCP; Cdc48

p97 (also referred to as VCP) is a highly conserved and abundant AAA+ (ATPases associated with diverse cellular activities) ATPase that plays an essential role in cellular proteostasis. p97 participates in a large number of important cellular activities, including (i) proteasomal degradation, through its roles in extracting proteins from membranes or molecular complexes; (ii) lysosomal degradation via autophagy and endolysosomal sorting; (iii) membrane fusion; and (iv) regulation of intracellular signaling, cell proliferation, and survival. These diverse cellular functions are powered by the chemical energy from ATP hydrolysis and coordinated through the interaction of p97 with as many as 40 cofactors that recruit it to specific subcellular locations and to designated substrates for their remodeling and processing.

Mutations in p97 have been linked to a number of neurodegenerative diseases, and overexpression of wild type p97 is observed in numerous cancers. Furthermore, p97 activity has been shown to be essential for the replication of certain viruses, including poliovirus, herpes simplex virus (HSV), cytomegalovirus (CMV), and influenza. These observations highlight the potential for targeting p97 as a therapeutic approach in neurodegeneration, cancer, and certain infectious diseases.

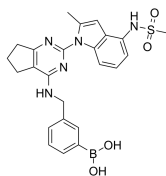
## p97 Inhibitors

<p><b>CB-5083</b></p> <p>Cat. No.: HY-12861</p>	<p><b>DBeQ</b> (JRF 12)</p> <p>Cat. No.: HY-15945</p>
<p>CB-5083 is a first-in-class, potent, selective, and orally bioavailable inhibitor of the p97 AAA ATPase/VCP. CB-5083 selectively inhibits p97 through its D2 site with the <math>IC_{50}</math> of 11 nM.</p> <p><b>Purity:</b> 99.90%</p> <p><b>Clinical Data:</b> Phase 1</p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg</p>	<p>DBeQ is a selective, potent, reversible, and ATP-competitive p97 inhibitor, with an <math>IC_{50}</math> value of 1.5 <math>\mu</math>M and 1.6 <math>\mu</math>M for p97(wt) and p97(C522A), respectively; DBeQ also inhibits Vps4 with an <math>IC_{50}</math> of 11.5 <math>\mu</math>M.</p> <p><b>Purity:</b> 99.68%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 50 mg</p>
<p><b>Eyarestatin I</b></p> <p>Cat. No.: HY-110078</p>	<p><b>ML240</b></p> <p>Cat. No.: HY-19795</p>
<p>Eyarestatin I, a potent endoplasmic reticulum-associated protein degradation (ERAD) inhibitor, is a potent protein translocation inhibitor.</p> <p><b>Purity:</b> 98.14%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 5 mg, 10 mg</p>	<p>ML240 is a potent p97 inhibitor, inhibiting p97 ATPase with <math>IC_{50}</math> value of 100 nM.</p> <p><b>Purity:</b> 99.85%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg</p>
<p><b>ML241 hydrochloride</b></p> <p>Cat. No.: HY-19797A</p>	<p><b>MSC1094308</b></p> <p>Cat. No.: HY-123872</p>
<p>ML241 hydrochloride is a potent p97 inhibitor, inhibiting p97 ATPase with <math>IC_{50}</math> value of 100 nM.</p> <p><b>Purity:</b> 99.78%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg</p>	<p>MSC1094308 is a reversible and allosteric inhibitor of the type II AAA ATPase human ubiquitin-directed unfoldase (VCP)/p97 and the type I AAA ATPase VPS4B, with <math>IC_{50}</math> values of 0.71 <math>\mu</math>M and 7.2 <math>\mu</math>M for VPS4B and p97, respectively.</p> <p><b>Purity:</b> 99.75%</p> <p><b>Clinical Data:</b></p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg</p>
<p><b>NMS-859</b></p> <p>Cat. No.: HY-15714</p>	<p><b>NMS-873</b></p> <p>Cat. No.: HY-15713</p>
<p>NMS-859 is a potent, covalent VCP (p97) inhibitor, with <math>IC_{50}</math>s of 0.37 and 0.36 <math>\mu</math>M for wild-type VCP in the presence of 60 <math>\mu</math>M and 1 mM ATP in cells, respectively.</p> <p><b>Purity:</b> 98.01%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg</p>	<p>NMS-873 is a potent, selective allosteric VCP/p97 inhibitor with an <math>IC_{50}</math> value of 30 nM.</p> <p><b>Purity:</b> 99.86%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 10 mM × 1 mL, 5 mg, 10 mg, 50 mg, 100 mg</p>
<p><b>p97-IN-1</b></p> <p>Cat. No.: HY-128724</p>	<p><b>UPCDC-30245</b></p> <p>Cat. No.: HY-123636</p>
<p>p97-IN-1 is a potent p97 inhibitor with an <math>IC_{50}</math> &lt;30 nM (WO2015109285A1, compound FF07).</p> <p><b>Purity:</b> &gt;98%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 1 mg, 5 mg</p>	<p>UPCDC-30245 is an allosteric p97 inhibitor with an <math>IC_{50}</math> of approximately 27 nM. UPCDC-30245 inhibits the p97 mutant N660K similar to wild type (WT; <math>IC_{50}</math>=300 nM) and shows 3-fold resistance for p97 mutant T688A. UPCDC-30245 can be used in the research of cancer.</p> <p><b>Purity:</b> &gt;98%</p> <p><b>Clinical Data:</b> No Development Reported</p> <p><b>Size:</b> 1 mg, 5 mg</p>

## VCP/p97 inhibitor-1

Cat. No.: HY-139606

VCP/p97 inhibitor-1 is a potent inhibitor of VCP/p97 (also called Cdc48, CDC-. 48, or Ter94) with an  $IC_{50}$  of 54.7 nM.



**Purity:** >98%

**Clinical Data:** No Development Reported

**Size:** 1 mg, 5 mg