Product Name: MLN2238
Revision Date: 6/30/2018

Product Data Sheet

Chemical Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Name</td>
<td>MLN2238</td>
</tr>
<tr>
<td>CAS No.</td>
<td>1072833-77-2</td>
</tr>
<tr>
<td>M.Wt.</td>
<td>361</td>
</tr>
<tr>
<td>Formula</td>
<td>C14H19BCl2N2O4</td>
</tr>
<tr>
<td>Chemical Name</td>
<td>[(1R)-1-[(2S,3R)-3-hydroxy-2-[(6-phenylpyridine-2-carbonyl)amino]butanoyl]amino]-3-methylbutyl]boronic acid</td>
</tr>
<tr>
<td>Canonical SMILES</td>
<td>B(C(CC(C(C)N(C(=O)CNC(=O)))C1=C(C(=C(1)Cl)Cl))Cl)(O)O</td>
</tr>
<tr>
<td>Solubility</td>
<td>$\geq 16.8$ mg/mL in DMSO</td>
</tr>
<tr>
<td>Storage</td>
<td>Store at -20° C</td>
</tr>
<tr>
<td>General tips</td>
<td>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.</td>
</tr>
<tr>
<td>Shopping Condition</td>
<td>Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request</td>
</tr>
</tbody>
</table>

Biological Activity

Targets: Ubiquitination/Proteasome
Pathways: Proteasome

Description:
MLN2238 is a potent reversible inhibitor that inhibits specific β5 site of the 20S proteasome with IC50 value of 3.4 nM and Ki value of 0.93 nM.[1] MLN2238, an N-capped dipeptidyl leucine boronic acid, preferentially bound to and inhibited the chymotrypsin-like proteolytic (β5) site of the 20S proteasome with an IC50 value of 3.4 nM (Ki value of 0.93 nM). As the concentration increased, it also inhibited the caspase-like (β1) with IC50 value of 31 nM and trypsin-like (β2) proteolytic sites with IC50 value of 3,500 nM. The clinical studies in the model of both solid-tumor and hematological xenograft have demonstrated preclinical antitumor activity. Comparing to bortezomib, MLN2238 showed the activity in
pharmacokinetics, pharmacodynamics and antitumor. It is believed that the activation of caspases, the p53 pathway, and endoplasmic reticulum stress and inhibition of NF-κB are related to MLN2238-induced MM cell death. [1,2]

MLN2238 inhibited growth and triggers apoptosis in MM cells resistant to conventional and bortezomib therapies without affecting the viability of normal cells [2]. MLN2238 has significant cytotoxic activity in RSCL and RRCL preclinical models. Although BTZ and MLN2238 have similar reversible proteasome inhibition, the proteasome dissociation half-life (t1/2) of MLN2238 was found to be approximately sixfold faster than BTZ (t1/2 of 18 vs. 110min, respectively) while has the similar LD50 values to BTZ in a variety of cultured mammalian cancer cell lines. MLN2238 is approximately two to three times more potent than BTZ in lymphoma cell models. The IC50 of MLN2238 was 2.5 nmol/l in contrast to 7.5nmol/l of BTZ in Raji parental cells. [3]

In many mouse models of hematologic malignancies, such as tumor xenograft models which derived from a human lymphoma cell line and primary human lymphoma tissue, and genetically engineered mouse models of plasma cell malignancies, the result showed the antitumor activity of MLN2238.[4]

Reference:

Protocol

Cell experiment:

Cell lines Calu-6 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 $\leq 10$ nM; 1 hr

Applications MLN2238 inhibited Calu-6 cells with an IC50 value of 9.7 nM.
Animal experiment [3]:

Animal models  DP54-Luc tumor-bearing NOD-SCID mice
Dosage form  11 mg/kg; i.v.; twice weekly for 17 consecutive days
Applications  Both Bortezomib and MLN2238 reduced tumor burden (T/C = 0.48 and 0.22, respectively).
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.

Reference:

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.