PNU-159682

Cat. No.: HY-16700
CAS No.: 202350-68-3
Molecular Formula: $C_{32}H_{35}NO_{13}$
Molecular Weight: 641.62
Target: ADC Cytotoxin; Topoisomerase
Pathway: Antibody-drug Conjugate/ADC Related; Cell Cycle/DNA Damage
Storage: 4°C, stored under nitrogen
* In solvent: -80°C, 6 months; -20°C, 1 month (stored under nitrogen)

SOLVENT & SOLUBILITY

**In Vitro**

DMSO: 100 mg/mL (155.86 mM; ultrasonic and warming and heat to 60°C)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Concentration</td>
<td>1 mM</td>
<td>5 mM</td>
<td>10 mM</td>
</tr>
<tr>
<td>1 mM</td>
<td></td>
<td>1.5586 mL</td>
<td>7.7928 mL</td>
<td>15.5855 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.3117 mL</td>
<td>1.5586 mL</td>
<td>3.1171 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.1559 mL</td>
<td>0.7793 mL</td>
<td>1.5586 mL</td>
<td></td>
</tr>
</tbody>
</table>

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

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.90 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.90 mM); Suspended solution; Need ultrasonic

3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PNU-159682, a metabolite of the anthracycline Nemorubicin, is a highly potent DNA topoisomerase II inhibitor with excellent cytotoxicity. PNU-159682 acts as a more potent and tolerated ADC cytotoxin than Doxorubicin for ADC synthesis. PNU-159682 can be used in EDV-nanocell technology to overcome agent resistance.

**IC₅₀ & Target**

Daunorubicins/Doxorubicins | Topoisomerase I

**In Vitro**

PNU-159682 (0-500 nM; exposed to the compounds for 1 hour and then cultured in compound-free medium for 72 hours) has cytotoxic effects on human tumor cell lines in a sulforhodamine B assay. The IC₅₀ values are 0.577 nM, 0.39 nM, 0.128 nM, and 0.081 nM, 0.086 nM and 0.075 nM for HT-29, A2780, DU145, EM-2, Jurkat and CEM cells, respectively[1]. It against human
tumor cell lines with IC$_{50}$ in the ranging 68 nM-578 nM and 181 nM-1717 nM towards MMDX and doxorubicin, respectively$^{[1]}$. PNU-159682 is more potent than MMAE on NHL cell lines. In a cell viability assay, PNU-159682 is against BJAB.Luc, Granta-519, SuDHL4.Luc, and WSU-DLCL2 with IC$_{50}$ values of 0.10 nM, 0.020 nM, 0.055 nM, and 0.1 nM, respectively. While MMAE is against BJAB.Luc, Granta-519, SuDHL4.Luc, and WSU-DLCL2 with IC$_{50}$ values of 0.54 nM, 0.25 nM, 1.19 nM and 0.25 nM, respectively$^{[2]}$. PNU-159682 is thousands of times more cytotoxic than doxorubicin and can be used to develop a new class of ADCs. PNU159682?to?anti-CD22?antibody (anti-CD22-NMS249) exhibits strong anti-tumor effects in vitro. Anti-CD22-NMS249 (PNU159682?to?anti-CD22?antibody) is active in in vitro viability assays of NHL cell lines and is 2 to 20 fold more potent than pinatuzumab vedotin, the ADC anti-CD22-NMS249 is against BJAB.Luc, Granta-519, SuDHL4.Luc, and WSU-DLCL2 with IC$_{50}$ values of 0.058 nM, 0.030 nM, 0.0221 nM, and 0.01 nM, respectively$^{[3]}$. PNU-159682 (100 μM) weakly inhibits topoisomerase II unknotting activity. PNU-159682 shows cytotoxic effect on CAIX-expressing SKRC-52 cells with IC$_{50}$ of 25 nM$^{[4]}$.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### Cell Viability Assay$^{[2]}$

<table>
<thead>
<tr>
<th>Cell Line:</th>
<th>HT-29, A2780, DU145, EM-2, Jurkat and CEM cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration:</td>
<td>0-500 nM</td>
</tr>
<tr>
<td>Incubation Time:</td>
<td>Exposed to the PNU-159682 for 1 hour and then cultured in compound-free medium for 72 hours</td>
</tr>
<tr>
<td>Result:</td>
<td>Was 2,360- to 790-fold and 6,420- to 2,100-fold more potent than MMDX and doxorubicin, respectively. Exhibited IC$_{70}$ values of PNU-159682 are in the subnanomolar range (0.07-0.58 nM) and noticeably lower than that recorded for both MMDX and doxorubicin.</td>
</tr>
</tbody>
</table>

### In Vivo

PNU-159682 (single-dose; i.v.15 μg/kg) is a maximum tolerated dose in murine L1210 leukemia model. PNU-159682 shows an improved antitumor activity in vivo. The antitumor effect of PNU-159682 (increase in life span=29%) is comparable to that afforded by 90 μg/kg MMDX (increase in life=36%)$^{[1]}$. PNU-159682 (i.v. 4 μg/kg; q7dx3; 40 days) has a therapeutic response in MX-1 human mammary carcinoma mice. What’s more, from day 39, four out of seven mice receiving PNU-159682 exhibits complete tumor regression$^{[1]}$. PNU-159682 is more cytotoxic than doxorubicin and can be used to develop a new class of ADCs. PNU159682?to?anti-CD22?antibody (anti-CD22-NMS249) exhibits strong anti-tumor effects in vivo. ADC dose (anti-CD22-NMS249; 50 μg/m2 conjugated PNU-159682) is well tolerated in mice and results in less than 10% weight loss$^{[2]}$. In the BJAB.Luc model the efficacy of antiCD22-NMS249 (single dose; 2 mg/kg) is similar to anti-CD22-vc-MMAE. At 2 mg/kg dosage, antiCD22-NMS249 gives complete remission of the tumors (NMS249: 110-134%TGI vs. vc-MMAE: 114-143%TGI). Additionally, a single dose of antiCD22-NMS249 at 2 mg/kg results in tumor stasis for three weeks$^{[1]}$.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>Four- to six-week-old female CD-1 athymic nude mice with MX-1 tumor fragments$^{[1]}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>4 μg/kg</td>
</tr>
<tr>
<td>Administration:</td>
<td>Intravenous injection; q7dx3; 40 days</td>
</tr>
<tr>
<td>Result:</td>
<td>Exhibited anti-cancer effects in MX-1 human mammary carcinoma xenografts to PNU-159682.</td>
</tr>
</tbody>
</table>

### REFERENCES


www.MedChemExpress.com


[4]. Joanne Lundy, Interim data: Phase I/IIa study of EGFR-targeted EDV nanocells carrying cytotoxic drug PNU-159682 (E-EDV-D682) with immunomodulatory adjuvant EDVs carrying α-galactosyl ceramide (EDV-GC) in patients with recurrent, metastatic pancreatic cancer. GASTROINTESTINAL CANCER—GASTROESOPHAGEAL, PANCREATIC, AND HEPATOBLIARY

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: 609-228-6898           Fax: 609-228-5909           E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA