Avapritinib

**Cat. No.:** HY-101561  
**CAS No.:** 1703793-34-3  
**Molecular Formula:** C₂₆H₂₇FN₁₀  
**Molecular Weight:** 498.56  
**Target:** c-Kit; PDGFR  
**Pathway:** Protein Tyrosine Kinase/RTK  
**Storage:**  
<table>
<thead>
<tr>
<th>Condition</th>
<th>Temperature</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powder</td>
<td>-20°C</td>
<td>3 years</td>
</tr>
<tr>
<td></td>
<td>4°C</td>
<td>2 years</td>
</tr>
<tr>
<td>In solvent</td>
<td>-80°C</td>
<td>6 months</td>
</tr>
<tr>
<td></td>
<td>-20°C</td>
<td>1 month</td>
</tr>
</tbody>
</table>

**SOLVENT & SOLUBILITY**

**In Vitro**  
DMSO : ≥ 83.33 mg/mL (167.14 mM)  
* *≥*” means soluble, but saturation unknown.*

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent</th>
<th>Concentration</th>
<th>Mass (1 mg)</th>
<th>Mass (5 mg)</th>
<th>Mass (10 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DMSO</td>
<td>1 mM</td>
<td>2.0058 mL</td>
<td>10.0289 mL</td>
<td>20.0578 mL</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>5 mM</td>
<td>0.4012 mL</td>
<td>2.0058 mL</td>
<td>4.0116 mL</td>
</tr>
<tr>
<td></td>
<td>DMSO</td>
<td>10 mM</td>
<td>0.2006 mL</td>
<td>1.0029 mL</td>
<td>2.0058 mL</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 (5.01 mM); Clear solution

2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2.5 mg/mL (5.01 mM); Clear solution

3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 2.5 mg/mL (5.01 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**  
Avapritinib (BLU-285) is a highly potent, selective, and orally bioavailable KIT and PDGFRA activation loop mutant kinases inhibitor with IC₅₀ of 0.27 and 0.24 nM for KIT D816V and PDGFRA D842V, respectively. Avapritinib (BLU-285) binds the active conformation of the kinase and shows antitumor activity. Avapritinib (BLU-285) attenuates the transport function of both ABCB1 and ABCG2. [1][2]
<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>IC₅₀: 0.27 nM (KIT D816V), 0.24 nM (PDGFRA D842V)⁰¹</th>
</tr>
</thead>
</table>

### In Vitro
Avapritinib (BLU-285) has demonstrated biochemical in vitro activity on the KIT exon 17 mutant enzyme, KIT D816V (IC₅₀=0.27 nM). Cellular activity of Avapritinib on KIT D816 mutants is measured by autophosphorylation in the human mast cell leukemia cell line HMC1.2, and the P815 mouse mastocytoma cell line with IC₅₀=4 and 22 nM, respectively. In Kasumi-1 cells, a t(8;21)-positive AML cell line with a KIT exon 17 N822K mutation, Avapritinib potently inhibits KIT N822K mutant autophosphorylation (IC₅₀=40 nM), downstream signaling, as well as cellular proliferation (IC₅₀=75 nM)⁰³.

### In Vivo
In vivo Avapritinib (BLU-285) is well tolerated and has demonstrated dose dependent antitumor efficacy. Complete tumor growth inhibition and ≥75% KIT kinase inhibition is observed with 10 mg/kg once daily, oral dosing of Avapritinib in the aggressive KIT exon 17 mutant driven P815 mastocytoma model grown as a solid tumor allograft as well as in a disseminated model of disease. Disease burden, measured by whole body luciferase imaging (photons/second/mm²), increases 86-fold in the vehicle control animals over the 24 day dosing period with widespread disease detectable in both femurs, the pelvis and circulating in peripheral blood. Avapritinib at both doses (10 or 30 mg/kg orally, once daily) results in a marked reduction of disease burden throughout the study. Avapritinib at either 10 or 30 mg/kg results in tumor regression in all animals with disease abrogation indistinguishable from background signal measurements in several animals by the end of study. Avapritinib is also well tolerated in this in vivo model and has no adverse effects on body weight at either dose⁰³.

### PROTOCOL

**Animal Administration**⁰¹

Mice⁰¹

A Kasumi-1 luc⁺ AML NOG SCID mouse femoral injection model is used to assess the efficacy of Avapritinib (BLU-285) in KIT exon 17-mutated CBF-AML. Following a 21 day post injection latency period, mice are dosed with Avapritinib orally, once daily at 10 mg/kg or 30 mg/kg through day 45.

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

### REFERENCES

