PF-3758309

Cat. No.: HY-13007
CAS No.: 898044-15-0
Molecular Formula: C_{25}H_{30}N_{8}O_{5}S
Molecular Weight: 490.62
Target: PAK; Apoptosis
Pathway: Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis
Storage: Powder
-20°C  3 years
4°C  2 years
In solvent
-80°C  6 months
-20°C  1 month

**SOLVENT & SOLUBILITY**

**In Vitro**
DMSO : ≥ 100 mg/mL (203.82 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.0382 mL</td>
<td>10.1912 mL</td>
<td>20.3824 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4076 mL</td>
<td>2.0382 mL</td>
<td>4.0765 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2038 mL</td>
<td>1.0191 mL</td>
<td>2.0382 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 (5.10 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**
PF-3758309 (PF-03758309) is a potent, orally available, and reversible ATP-competitive inhibitor of PAK4 (K_{d}= 2.7 nM; K_{i}=18.7 nM). PF-3758309 has the expected cellular functions of a PAK4 inhibitor: inhibition of anchorage-independent growth, induction of apoptosis, cytoskeletal remodeling, and inhibition of proliferation\textsuperscript{[1][2][3].}

| IC\textsubscript{50} & Target | PAK4 18.7 nM (Ki) | PAK1 13.7 nM (Ki) | PAK5 18.1 nM (Ki) | PAK6 17.1 nM (Ki) |
PAK2
190 nM (IC$_{50}$)

PAK3
99 nM (IC$_{50}$)

PAK4
2.7 nM (Kd)

**In Vitro**
PF-3758309 has similar enzymatic potency against the kinase domains of the other group B PAKs (PAK5, $K_i$=18.1 nM; PAK6, $K_i$=17.1 nM) and group A PAK1 ($K_i$=13.7 nM), but is less active against the other two group A PAKs (PAK2, IC$_{50}$=190 nM; PAK3, IC$_{50}$=99 nM)[1].

In cells, PF-3758309 inhibits phosphorylation of the PAK4 substrate GEF-H1 (IC$_{50}$=1.3 nM) and anchorage-independent growth of a panel of tumor cell lines (IC$_{50}$=4.7 nM)[1]. PF-3758309 also inhibits endogenous pGEF-H1 accumulation in HCT116 cells. PF-3758309 potently inhibits cellular proliferation (IC$_{50}$=20 nM) and anchorage-independent growth (IC$_{50}$=27 nM) of A549 cells[1].

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

**In Vivo**
PF-3758309 (7.5-30 mg/kg; p.o.; twice daily for 9-18 days) results in statistically significant tumor growth inhibition (TGI) in HCT116 and A549 models[1].

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

<table>
<thead>
<tr>
<th>Animal Model:</th>
<th>Female nu/nu, CRL breed 6–8 weeks old mice (bearing HCT116 and A549 tumors)[1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage:</td>
<td>7.5-30 mg/kg</td>
</tr>
<tr>
<td>Administration:</td>
<td>Oral administration; twice daily for 9-18 days</td>
</tr>
<tr>
<td>Result:</td>
<td>Significant tumor growth inhibition (TGI) in HCT116 and A549 models.</td>
</tr>
</tbody>
</table>

**REFERENCES**


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