TAS6417

Cat. No.: HY-112299
CAS No.: 1661854-97-2
Molecular Formula: C₂₃H₂₀N₆O
Molecular Weight: 396.44
Target: EGFR
Pathway: JAK/STAT Signaling; Protein Tyrosine Kinase/RTK
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 : ≥ 125 mg/mL (315.31 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 mM</td>
<td>2.5224 mL</td>
<td>12.6122 mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 mM</td>
<td>0.5045 mL</td>
<td>2.5224 mL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 mM</td>
<td>0.2522 mL</td>
<td>1.2612 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: ≥ 2.25 mg/mL (5.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.25 mg/mL (5.68 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.25 mg/mL (5.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
TAS6417 is an EGFR inhibitor and an efficacious drug candidate for patients with NSCLC, with IC₅₀ values ranging from 1.1-8.0 nM.

IC₅₀ & Target
EGFR
1.1-8.0 nM (IC₅₀)
In Vitro

TAS6417 inhibits the in vitro phosphorylation activity of EGFR and its mutants including an exon 20 insertion mutation, with IC\textsubscript{50} values ranging from 1.1±0.1 to 8.0±1.1 nM. TAS6417 suppresses the growth of cells expressing exon 20 insertion mutations of the EGFR gene, with a GI\textsubscript{50} value of 86.5±28.5 nM for LXF 2478L cells and 45.4±2.6 nM for NCI-H1975 EGFR D770_N771insSVD cells. TAS6417 also potently inhibits proliferation in other cell lines harboring activating mutations or acquired resistance mutations, with mean GI\textsubscript{50} values of 1.92±0.21 nM to 7.12±0.60 nM. In contrast, the effect of TAS6417 on cell proliferation in normal human epidermal keratinocytes (NHEK-Neo), of which WT EGFR is implicates in the growth and survival, is moderate\cite{1}.

In Vivo

TAS6417 causes persistent tumor regression in vivo in EGFR exon 20 insertion-driven tumor models. TAS6417 inhibits mutant EGFR in tumors but not WT EGFR in skin tissues. TAS6417 prolongs survival of animals bearing lung cancer\cite{1}.

**PROTOCOL**

**Animal Administration** \cite{1}

Mice bearing NCI-H1975 EGFR D770_N771insSVD xenografts are orally administered TAS6417 (50, 100, 200 mg/kg). One and 2 hours after administration of TAS6417, xenograft tumors and skin tissues are collected\cite{1}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**