**ALS-8176**

Cat. No.: HY-12983A  
CAS No.: 1445385-02-3  
Molecular Formula: C₁₈H₂₅ClFN₃O₆  
Molecular Weight: 433.86  
Target: RSV  
Pathway: Anti-infection  
Storage:  
- Powder: -20°C 3 years, 4°C 2 years  
- In solvent: -80°C 6 months, -20°C 1 month

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**Solvent & Solubility**

**In Vitro**

DMSO : ≥ 50 mg/mL (115.24 mM)  
* “≥” means soluble, but saturation unknown.

<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>1 mM</td>
<td></td>
<td>2.3049 mL</td>
<td>11.5245 mL</td>
<td>23.0489 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td></td>
<td>0.4610 mL</td>
<td>2.3049 mL</td>
<td>4.6098 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td></td>
<td>0.2305 mL</td>
<td>1.1524 mL</td>
<td>2.3049 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 >> 90% corn oil  
   Solubility: ≥ 2.5 mg/mL (5.76 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2.5 mg/mL (5.76 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
   Solubility: ≥ 2.5 mg/mL (5.76 mM); Clear solution

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**BIOLOGICAL ACTIVITY**

**Description**

ALS-8176 is an inhibitor of the respiratory syncytial virus (RSV) polymerase.

**In Vitro**

ALS-08176 is an orally bioavailable prodrug of the novel RSV replication inhibitor ALS-008112, a cytidine nucleoside analogue[1].
**In Vivo**

ALS-8176 demonstrates excellent anti-RSV efficacy and safety in a phase 2 clinical RSV challenge study. It exhibits good oral bioavailability and a high level of 2c-TP in vivo. ALS-8176 has excellent stability profiles in formulations (>24 h storage stability in 0.5% methylcellulose aqueous formulation at rt) and simulates gastric and intestinal fluids (half-life >2 h). Its solubility is adequate to support oral administration in solutions with relatively low percentage of organic solvent and in aqueous suspensions. High levels of NMP and NTP are obtained following oral administration of ALS-8176 to monkeys\(^2\). In an adult human challenge study, ALS-8176 has shown efficacy against RSV infection\(^1\).

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**PROTOCOL**

**Kinase Assay**\(^2\)

Cell fractionation and extraction of RSV RNP complex is performed. Nucleoside triphosphate (NTP) concentrations are: 0.1 \(\mu\)M CTP and 1 \(\mu\)M ATP, 2 \(\mu\)M UTP, and 500 \(\mu\)M GTP. The radioactive tracer is either 10 \(\mu\)Ci \([\alpha-^{33}\text{P}]r\)CTP or 15 \(\mu\)Ci MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Animal Administration**\(^2\)

Rats: ALS-8176 are formulated as solutions in PEG400-based vehicles. Pharmacokinetic studies are conducted at 5 mg/kg and for oral PK studies the prodrugs are administered at 5 mg/kg parent nucleoside equivalent doses. Blood samples are typically collected at various time points up to 24 h post dose for rats\(^2\).

Monkeys: ALS-8176 are formulated as solutions in PEG400-based vehicles. Pharmacokinetic studies are conducted at 5 mg/kg and for oral PK studies the prodrugs are administered at 5 mg/kg parent nucleoside equivalent doses. Blood samples are typically collected at various time points up to 12 h post dose for Monkeys\(^2\).

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

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**REFERENCES**
