LSZ-102

Cat. No.: HY-111486
CAS No.: 2135600-76-7
Molecular Formula: C₂₅H₁₇F₃O₄S
Molecular Weight: 470.46
Target: Estrogen Receptor/ERR
Pathway: Others
Storage: -20°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 (212.56 mM; Need ultrasonic)
H₂O: < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</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>2.1256 mL</td>
<td>10.6279 mL</td>
<td>21.2558 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4251 mL</td>
<td>2.1256 mL</td>
<td>4.2512 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2126 mL</td>
<td>1.0628 mL</td>
<td>2.1256 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: ≥ 1.67 mg/mL (3.55 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (3.55 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.55 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
LSZ-102 is a potent, orally bioavailable selective estrogen receptor degrader with an IC₅₀ of 0.2 nM.

IC₅₀ & Target
estrogen receptor[^1]

In Vitro
LSZ-102 is a potent, orally bioavailable selective estrogen receptor degrader with an IC₅₀ of 0.2 nM and currently in Phase I/Ib trials for the treatment of ERα positive breast cancer. LSZ-102 induces significant degradation of ERα after 24 h, when given as a 10 μM solution to MCF-7 cells. Robust inhibition of cell proliferation in MCF-7 cells is observed.
upon incubation with LSZ-102 with a half inhibitory concentration of 1.7 nM. Results demonstrate that LSZ-102 effectively inhibits the estrogen-induced activation of the ERE-luciferase reporter using charcoal-stripped serum treated with E2 with IC\textsubscript{50} of 0.3 nM\textsuperscript{[1]}.

### In Vivo

Treatment of the mice with LSZ-102 once daily at 20 mg/kg results in significant tumor growth inhibition as compared to the control group treated with vehicle alone, resulting in tumor stasis (mean change in tumor volume of LSZ-102 vs control=\%ΔT/ΔC of 2.4\% on day 48, p<0.05). Dosing of 3 mg/kg solution of LSZ-102 in male Sprague-Dawley rats results in 33\% bioavailability and a dose-normalized exposure of 620 nM\textbullet h\textsuperscript{[1]}.

### PROTOCOL

#### Kinase Assay \textsuperscript{[1]}

Growth factors depleted MCF-7 ERE-luc cells are used and seeded (10 000 cells/well) in 96-well plates in CSS medium. After overnight incubation, cells are treated with LSZ-102 in the presence of estradiol (0.1 nM) for 24 h. Cells are then lysed and quantified for luciferase activity using Bright-Glo assay\textsuperscript{[1]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration \textsuperscript{[1]}

Female athymic nude mice are used for tumor xenograft studies. MCF-7 cells are subcutaneously injected (200 μL/animal) in the right axillary mammary fat pad area. Tumor volume and body weights are measured twice weekly. When tumors reach an average volume of ~200 mm\textsuperscript{3}, mice are randomized into different groups. Animals are orally administered vehicle alone or 20 mg/kg LSZ-102 daily or 60 mg/kg tamoxifen 5 days per week\textsuperscript{[3]}. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### REFERENCES