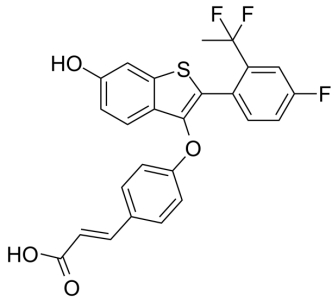
LSZ-102

Cat. No.:	HY-111486
CAS No.:	2135600-76-7
Molecular Formula:	$C_{25}H_{17}F_3O_4S$
Molecular Weight:	470
Target:	Estrogen Receptor/ERR
Pathway:	Vitamin D Related/Nuclear Receptor
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 (212.77 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.1277 mL	10.6383 mL	21.2766 mL
5 mM	0.4255 mL	2.1277 mL	4.2553 mL
10 mM	0.2128 mL	1.0638 mL	2.1277 mL

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 IC_{50} of 0.2 nM.

IC_{50} & Target

estrogen receptor[1]

In Vitro

LSZ-102 is a potent, orally bioavailable selective estrogen receptor degrader with an IC_{50} 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_{50} of 0.3 nM [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment of the mice with LSZ-102 once daily at 20 mg/kg results in significant tumor growth inhibition as compare to the control group treated with vehicle alone, resulting in tumor stasis (mean change in tumor volume of LSZ-102 vs control=%Δ T/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•h[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [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^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[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Tria GS, et al. Discovery of LSZ102, a Potent, Orally Bioavailable Selective Estrogen Receptor Degrader (SERD) for the Treatment of Estrogen Receptor Positive Breast Cancer. J Med Chem. 2018 Apr 12;61(7):2837-2864.

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