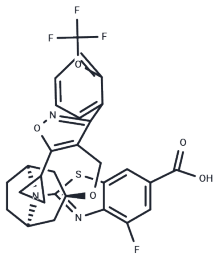
Data Sheet (Cat.No.T4379)

TargetMol

Tropifexor

Chemical Properties



CAS No. : 1383816-29-2

Formula: C29H25F4N3O5S

Molecular Weight: 603.58

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Tropifexor (LJN452) is a novel and highly potent agonist of FXR with an EC50 of 0.2 nM.
Targets(IC50)	FXR,Autophagy
In vitro	Robust induction of both BSEP and SHP genes is observed in primary cells by Tropifexor in a concentration-dependent manner. BSEP induction above vehicle (DMSO) control is observed at concentrations as low as 1 nM, while strong induction of SHP (15-fold above vehicle) is observed at 10 nM and modest induction of SHP at 1 nM (3-fold).
In vivo	Treatment of rats with Tropifexor exhibits a clear increase in plasma FGF15 protein in a dose-dependent manner, with maximal levels of FGF15 detected at 7 h postdose. Treatment with Tropifexor for 14 days results in a robust dose-dependent reduction in serum triglycerides and reaches a maximal response with a 0.3 mg/kg dose, causing a decrease of triglyceride levels to approximately 79% below the vehicle control group. Tropifexor (compound 1) demonstrates highly potent induction of SHP and FGF15 in the ileum as doses as low as 0.1 mg/kg. In the liver, robust induction of SHP is observed at 0.01 mg/kg of Tropifexor with maximal levels of gene induction achieved at 0.3 mg/kg. Expression of CYP8B1 mRNA following 14 day treatment with Tropifexor is already apparent at the lowest dose (0.003 mg/kg), and CYP8B1 gene expression is fully repressed at doses above 0.03 mg/kg.
Cell Research	Primary rat hepatocytes are plated in 24 well plates and incubated with a 5 point dose response of Tropifexor (compound 1) for 24 hours. RNA is harvested from the cells using the RNeasy 96 kit. Quantitative PCR is performed. The fold change of the transcript over no stimulation is calculated using the ΔΔCt method, with DMSO (vehicle control) being no stimulation.
Animal Research	Adult male wild-type Sprague-Dawley rats are used in this study. All animals are fasted for 3 hours before oral dosing with Tropifexor (compound 1) or with vehicle. Tropifexor is administered orally using a range of four doses (0.03, 0.1, 0.3, and 1.0 mg/kg) and compare directly to the vehicle control group (vehicle: 0.5% methylcellulose, 0.5% Tween 80, 99% water, suspension). Animals are sacrificed seven hours after dosing using CO2, liver, ileum and whole blood (in heparinized tubes) samples are collected for analysis.

Solubility Information

Solubility	DMSO: 63.75 mg/mL (105.62 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.31 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6568 mL	8.2839 mL	16.5678 mL
5 mM	0.3314 mL	1.6568 mL	3.3136 mL
10 mM	0.1657 mL	0.8284 mL	1.6568 mL
50 mM	0.0331 mL	0.1657 mL	0.3314 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Tully DC,etal.Discovery of Tropifexor (LJN452), a Highly Potent Non-bile Acid FXR Agonist for the Treatment of Cholestatic Liver Diseases and Nonalcoholic Steatohepatitis (NASH).J Med Chem. 2017 Dec 28;60(24):9960-9973.