Product Data Sheet

Product Name: Salirasib
Cat. No.: GC10528

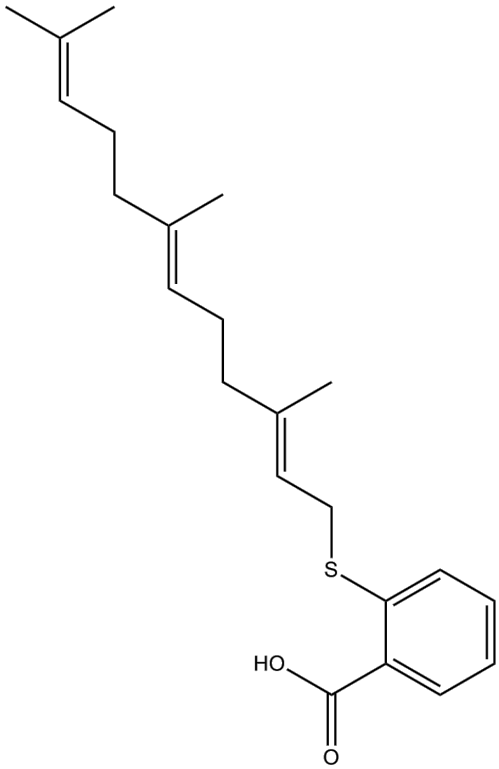
Chemical Properties

Cas. No.	162520-00-5		
Chemical Name	2-[(2E,6E)-3,7,11-trimethyldodeca-2,6,10-trienyl]sulfanylbenzoic acid		
SMILES	CC(=CCCC(=CCCC(=CCSC1=CC=CC=C1C(=O)O)C)C)C		
Formula	$C_{22}H_{30}O_2S$	M.Wt	358.54
Solubility	≥ 16.75 mg/mL in DMSO, ≥ 16.2 mg/mL in EtOH	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Structure



Protocol

Cell experiment: For time dependent response studies, cells are harvested with 0.05% Trypsin-EDTA daily for 1 to 7 days and counted under the microscope using the Trypan blue exclusion method.For dose response studies, cells are incubated in medium supplemented with salirasib or DMSO for 3 days. Cell viability is determined using a colorimetric WST-1 assay according to the manufacturer's instructions. The IC50 value, at which 50% of the cell growth is inhibited compared with DMSO control, is calculated by nonlinear regression analysis using GraphPad Prism software.

Product Data Sheet

Animal experiment: Six week old female athymic NMRI nu/nu mice are housed in filter-topped cages andreceive food and water ad libitum. Tumors are generated by subcutaneous injection into the right lower flank with 5×106 HepG2 cells suspended in 100 μL PBS in 12 mice. Two weeks after cell inoculation, when palpable tumours are established, mice are separated into salirasib-treated (n=6) and control group (n=4). Two animals do not develop tumours at that time point and had to be excluded from the study. They receive daily i.p. injections of 10 mg/kg salirasib or a similar volume of vehicle solution (PBS containing 2.5% v/v ethanol, pH 8.0) for 12 days. Tumor dimensions are recorded three times per week with a digital calliper starting with the first day of treatment. Tumor volumes are estimated as follows: V (mm3)=(length×width2)/2. Tumour weights are recorded at the time of sacrifice in order to evaluate treatment response.

References:

[1]. Makovski V, et al. Farnesylthiosalicylic acid (salirasib) inhibits Rheb in TSC2-null ELT3 cells: a potential treatment for lymphangioleiomyomatosis. Int J Cancer. 2012 Mar 15;130(6):1420-9.
[2]. Nevo Y, et al. Chapman J. The Ras antagonist, farnesylthiosalicylic acid (FTS), decreases fibrosis and improves muscle strength in dy/dy mouse model of muscular dystrophy. PLoS One. 2011 Mar 22;6(3):e18049.
[3]. Charette N, et al. Salirasib inhibits the growth of hepatocarcinoma cell lines in vitro and tumor growth in vivo through ras and mTOR inhibition. Mol Cancer. 2010 Sep 22;9:256.

Background

Salirasib (S-trans,trans-farnesylthiosalycilic acid [FTS]) is a synthetic small molecule that acts as a potent Ras inhibitor.[1]

The Ras family of small GTPases transmits extracellular signals, which are initiated by cell-surface receptors and serve to regulate various cellular processes including cell growth, differentiation, motility and cell death. Signals transmitted by activated Ras induce activation of multiple effectors. Ras signaling is activated in a large number of human cancers. Mutations of codons 12, 13 and 61 in Ras result in constitutively active Ras, and activating mutations of the three major Ras isoforms (H, K

and N) have been found in more than 33% of human cancers. [2]

Salirasib mimics the carboxy-terminal farnesylcysteine carboxymethyl ester common to all Ras proteins, which acts as part of a recognition unit for anchorage and dislodges the active Ras protein from the cell membrane. Salirasib is readily taken up by cells, and once inside the cell it specifically disrupts the association of active forms of all Ras proteins (H-ras, K-ras and N-ras) with the inner surface of the cell membrane and with other cellular membranes. [1]

The in vitro activity of salirasib has been demonstrated in pancreatic cell lines and xenograft models. In the Panc-1 cell line, salirasib decreased the amount of RAS in a dosedependent manner, with a maximum decrease in Ras of approximately 50 % seen at concentrations of 25 to 50 μM. In the mouse xenograft models, salirasib inhibites Panc-1 tumor growth and is shown to be synergistic with gemcitabine, both inhibiting tumor growth and prolonging survival. Salirasib is tested in a phase I study in patients with solid tumors twice daily for 21 days every 4 weeks. Doses are escalated from 100 to 200, 400, 600, and 800 mg. Dose-limiting toxicity is not reached, but all three patients treated with 800 mg experienced Grade 1–2 diarrhea, preventing further dose escalation. The recommended dose for phase II studies is 600 mg bid. [3]

References:
[1] Ernesto Bustinza-Linares, Razelle Kurzrock , Apostolia-Maria Tsimberidou. Salirasib in the treatment of pancreatic cance. Future Oncol. (2010) 6(6), 885–891.
[2] Sari Schokoroy, Dolly Juster, Yoel Kloog, Ronit Pinkas-Kramarski. Disrupting the Oncogenic Synergism between Nucleolin and Ras Results in Cell Growth Inhibition and Cell Death. PLOS ONESeptember 2013, Volume 8, Issue 9, e75269.
[3] Daniel Laheru , Preeti Shah, N. V. Rajeshkumar et al. Integrated preclinical and clinical development of S-trans, trans-farnesylthiosalicylic acid (FTS, Salirasib) in pancreatic cancer. Invest New Drugs (2012) 30:2391–2399.