

Product Data Sheet

Product Name: Afuresertib (hydrochloride)

Cat. No.: GC42747

Chemical Properties

Cas. No. 1047645-82-8

SMILES FC1=CC=CC(C[C@@H](CN)NC(C2=CC(C3=C(Cl)C=NN3C)=C(Cl)S2)=O)=C1.Cl

Formula $C_{18}H_{17}Cl_2FN_4OS \cdot HCl$ M.Wt 463.8

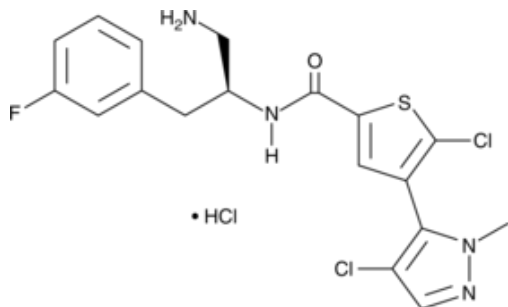
Solubility DMF: 50 mg/mL, DMSO: 100 mg/mL, Ethanol: 50 mg/mL, Ethanol: PBS (pH 7.2) (1:1): 0.5 mg/mL

Storage Store at -20°C, protect from light, stored under nitrogen

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.

Structure



Protocol

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

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Cell experiment: MPM cells are seeded in 96-well plates (cell density, 2.5×10^3 cells/well) and are incubated for 24 h at 37°C. Next, the cells are incubated in a medium containing indicated concentrations of Akt inhibitors (e.g., Afuresertib ; 50, 20, 10, 5, 2, 1, 0.5, 0.2, 0.1, and 0.01 μ M) for 72 h. Next, MTT solution is added to each well, and the cells are incubated for 4 h. Finally, the cells are incubated overnight with lysis buffer (10% SDS in 0.01 mol/L hydrogen chloride). Absorbance is measured at 550 nm using SpectraMAX M5 spectrophotometer[1].

References:

- [1]. Yamaji M, et al. Novel ATP-competitive Akt inhibitor Afuresertib suppresses the proliferation of malignant pleural mesothelioma cells. *Cancer Med.* 2017 Nov;6(11):2646-2659.
- [2]. Dumble M, et al. Discovery of novel AKT inhibitors with enhanced anti-tumor effects in combination with the MEK inhibitor. *PLoS One.* 2014 Jun 30;9(6):e100880

Background

Afuresertib hydrochloride (GSK 2110183 hydrochloride) is an orally bioavailable, selective, ATP-competitive and potent pan-Akt kinase inhibitor with K_{is} of 0.08/2/2.6 nM for Akt1/Akt2/Akt3 respectively[1][2].

Afuresertib (GSK 2110183) exhibits favorable tumor-suppressive effects on malignant pleural mesothelioma (MPM) cells. Afuresertib significantly increases caspase-3 and caspase-7 activities and apoptotic cell number among ACC-MESO-4 and MSTO-211H cells. Afuresertib strongly arrests the cell cycle in the G1 phase. Western blotting analysis shows that Afuresertib increases the expression of p21WAF1/CIP1 and decreases the phosphorylation of Akt substrates, including GSK-3 β and FOXO family proteins. Afuresertib-induced p21 expression promotes G1 phase arrest by inducing FOXO activity. Afuresertib significantly enhances cisplatin-induced cytotoxicity. Afuresertib modulates the expression E2F1 and MYC, which are associated with fibroblast core serum response[1].

Mice bearing BT474 breast tumor xenografts are dosed orally with either vehicle or GSK2110183 at 10, 30 or 100 mg/kg daily for 21 days which result in 8, 37 and 61% TGI, respectively. Mice tolerated

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GSK2110183 well, with 1-3% body weight loss reported after 5 days of dosing which recover over the course of the study. Other tumor xenograft models which possess an activation of the Akt pathway are explored to further demonstrate compound efficacy. Mice treated with GSK2110183 at 10, 30 and 100 mg/kg result in 23, 37 and 97% TGI, respectively, of SKOV3 xenografts[2].

References:

- [1]. Yamaji M, et al. Novel ATP-competitive Akt inhibitor Afuresertib suppresses the proliferation of malignant pleural mesothelioma cells. *Cancer Med.* 2017 Nov;6(11):2646-2659.
- [2]. Dumble M, et al. Discovery of novel AKT inhibitors with enhanced anti-tumor effects in combination with the MEK inhibitor. *PLoS One.* 2014 Jun 30;9(6):e100880

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