

Product Data Sheet

Product Name: LYN-1604 hydrochloride

Cat. No.: GC36517

Chemical Properties

Cas. No. 2216753-86-3

SMILES ClC1=CC=C(C(CN2CCN(C(CN(CC(C)C)CC(C)C)=O)CC2)OCC3=CC=C(C=CC=C4)C4=C3)C(Cl)=C1.[H]Cl

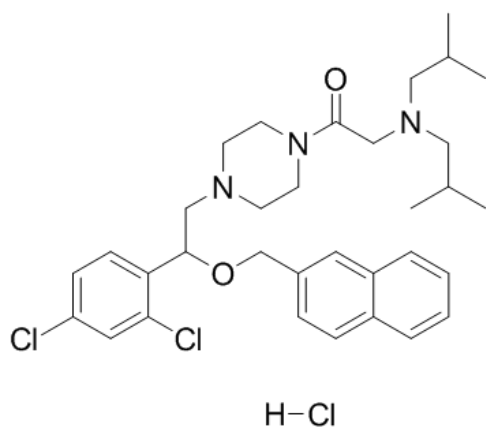
Formula $C_{33}H_{44}Cl_3N_3O_2$ M.Wt 621.08

Solubility DMSO: 100 mg/mL (161.01 mM) 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.

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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- Kinase experiment:** The ULK1 kinase enzyme, substrate, ATP and compound (include LYN-1604) are diluted in kinase buffer. Then, 1 μ L of compound or (5% DMSO), 2 μ L of ULK1 kinase enzyme or purified wild-type and mutant ULK1 (K50A, L53A, Y89A) (10 ng), or 2 μ L of MBP (0.1 μ g/ μ L)/ATP (10 μ M) mix are added to the wells of a 384 well low volume plate. After incubation at room temperature for 60 minutes, 5 μ L of kinase assay reagent is added per well. The plates are incubated at room temperature for 40 minutes and then 10 μ L of kinase detection reagent is added. After incubation at room temperature for 30 minutes, the luminescence is recorded. The EC50 values are calculated using nonlinear regression with normalized dose response fitting[1].
- Cell experiment:** MCE-7, MDA-MB-231 and MDA-MB-468 cells are treated with LYN-1604, cell viability is measured by the MTT assay[1].
- Animal experiment:** Mice: Mice are injected subcutaneously with MDA-MB-231 cells. When the tumors reach 100 mm³ in volume, the mice are divided into four groups. Three groups are treated with different doses of LYN-1604 once a day by intragastric administration for 14 days (low dose, 25 mg/kg; median dose, 50 mg/kg; high dose, 100 mg/kg), whereas the control group is treated with vehicle control. During the treatment, the tumor volumes and body weight are measured every day until the end of the study. At the end of treatment, all mice are sacrificed. The spleen, liver, kidney and tumor tissue are harvested, weighed, and photographed, then immediately frozen in liquid nitrogen or fixed in formalin[1].

References:

[1]. Zhang L, et al. Discovery of a small molecule targeting ULK1-modulated cell death of triple negative breast cancer in vitro and in vivo. Chem Sci. 2017 Apr 1;8(4):2687-2701.

Background

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LYN-1604 hydrochloride is a potent ULK1 activator with an EC₅₀ of 18.94 nM. EC₅₀: 18.94 nM (ULK1)[1]

LYN-1604 is found as a potential ULK1 activator with enzymatic activity of 195.7% at 100 nM and IC₅₀ of 1.66 μM against MDA-MB-231 cells. LYN-1604 displays a good effect on ULK1 activation with an EC₅₀ of 18.94 nM. LYS50, LEU53, and TYR89 are key to the activation site of LYN-1604. LYN-1604 induces cell death in MDA-MB-231 cells. LYN-1604 could modulate ATF3 and RAD21 through ULK1 in MDA-MB-231 cells. LYN-1604 can also increase cleavage of caspase3 and induce apoptosis. LYN-1604 induces cell death involved in ATF3, RAD21, and caspase3, accompanied by autophagy and apoptosis[1].

LYN-1604 could significantly inhibit the growth of xenograft MDA-MB-231 cells. The body weights of mice are stable. LYN-1604 induces remarkable autophagy in vivo. LYN-1604 has good therapeutic potential by targeting ULK1-modulated cell death of TNBC, thus making a ULK1 agonist that can be utilized as a new drug for triple negative breast cancer therapy[1].

[1]. Zhang L, et al. Discovery of a small molecule targeting ULK1-modulated cell death of triple negative breast cancer in vitro and in vivo. Chem Sci. 2017 Apr 1;8(4):2687-2701.

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