# Product Data Sheet

Product Name: GSK2850163 hydrochloride
Cat. No.: GC34205

## Chemical Properties

| | | | |
|---|---|---|---|
| Cas. No. | 2319838-09-8 | | |
| SMILES | O=C(N(CCC1)C[C@]21CCN(CC3=CC=C(Cl)C(Cl)=C3)C2)NCC4=CC=C(C)C=C4.Cl | | |
| Formula | $C_{24}H_{30}Cl_3N_3O$ | M.Wt | 482.87 |
| Solubility | Soluble in DMSO | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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 | GSK2850163 hydrochloride | | |

## Protocol

**Kinase experiment:**

In the ADP-Glo assay, GSK2850163 hydrochloride’s potency toward pIRE1α kinase activity is measured as its inhibition of an intrinsic, slowing ATP hydrolysis activity. One hundred nanoliters of dimethylsulfoxide solution of GSK2850163 hydrochloride at various concentrations is added into a 384-well plate. The reaction is carried out with 5 nM pIRE1α and 60 mM ATP in 10 mL of 50 mM Hepes buffer, pH 7.5, containing 30 mM NaCl, 10 mM MgCl2, 1 mM DTT, 0.02% Chaps, and 0.01 mg/mL bovine serum albumin. The reaction is stopped after 2 hours by adding 5 mL of ADP-Glo reagent I, which also depletes the remaining ATP. Following 1-hour incubation, 5 mL of ADP-Glo reagent II is added into the reaction, which converts the ADP product into ATP to serve as the substrate for the coupled luciferin/luciferase reaction. After 30 minutes, the plate is read on a microplate imager[1].


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**Cell experiment:**

PANC-1 cells are seeded into six-well plates at a density of 5.0×103 cells/well in RPMI 1640 media containing 10% FBS. Cells are cotransfected with a pGL3-5x unfolded protein response element (UPRE)-luciferase reporter containing five repetitions of the XBP-1 DNA binding site and pRL-SV40 using the FuGENE6 transfection reagent. Forty-eight hours later, cells are treated with 2.5 mg/mL tunicamycin for 1 hour, followed by GSK2850163 hydrochloride treatment for 16 hours. Luciferase expression is measured using Dual-Glo Luciferase Assay kit and normalized to Renilla expression levels[1].

References:

[1]. Nestor O. Concha, et al. Long-Range Inhibitor-Induced Conformational Regulation of Human IRE1α Endoribonuclease Activity. Molecular Pharmacology December 2015, 88 (6) 1011-1023.

### Background

GSK2850163 hydrochloride is a novel inhibitor of inositol-requiring enzyme-1 alpha (IRE1α) which can inhibit IRE1α kinase activity and RNase activity with IC50s of 20 and 200 nM, respectively.

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respectively. The increased autophosphorylation of IRE1α can be reduced in a dose-dependent manner by GSK2850163 hydrochloride. Increasing concentrations of GSK2850163 hydrochloride are capable of reducing the increased XBP 1 transcriptional activity. Two additional kinases are weakly inhibited by GSK2850163 hydrochloride: Ron (IC50=4.4 μM) and FGFR1 V561M (IC50=17 μM)[1].

[1]. Nestor O. Concha, et al. Long-Range Inhibitor-Induced Conformational Regulation of Human IRE1α Endoribonuclease Activity. Molecular Pharmacology December 2015, 88 (6) 1011-1023.