Product Data Sheet

Chemical Properties

**Product Name:** PTC124 (Ataluren)

**Cas No.:** 775304-57-9

**M.Wt:** 284.24

**Formula:** C15H9FN2O3

**Synonyms:** PTC 124; PTC-124

**Chemical Name:** 3-[5-(2-fluorophenyl)-1,2,4-oxadiazol-3-yl]benzoic acid

**Canonical SMILES:** C1=CC=C(C(=C1)C2=NC(=NO2)C3=CC(=CC3C(=O)O)F

**Solubility:** Soluble in DMSO > 10 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.

**Shopping Condition:** Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

**Targets:** CFTR

**Pathways:** Membrane Transporter/Ion Channel >> CFTR

**Description:**

PTC124 is a selective inhibitor of nonsense mutations with IC50 value of 0.1μM [1]. Nonsense mutation is a point mutation in a sequence of DNA which promotes premature translational termination. Different from missense mutation, nonsense mutation means a single nucleotide is changed and results in the substitution of a different amino acid. It has been reported that some genetic disorders (thalassemia, DMD, CF, Hurler syndrome) are correlated with nonsense mutation [1, 2].

PTC124 is a potent nonsense mutations inhibitor. When tested with human or mdx mice primary
muscle cells expressing dystrophin nonsense alleles, 2-8 weeks treatment of PTC124 enhanced the production of dystrophin [1]. In iPSC-derived RPE cells with nonsense mutation c.519C>T (p.R120X), PTC124 treatment restored endogenous, full-length RP2 protein with near 20% [3]. When tested with COS7 cells carrying the nonsense mutation pDsRed-EGFPmtag-Y445X, EGFP transcript level was increased after treated by PTC124 in a dose-dependent manner [2]. In mdx mice model, oral administration of PTC124 for 2-8 weeks rescued striated muscle function [1]. In a model of Cftr-/- mice expressing a human CFTR-G542X transgene, s.c. injection or oral administration of PTC124 restored a considerable amount of human (h) CFTR protein and function via suppressing G542X nonsense mutation [4].

Reference:

Protocol

Cell experiment:

Cell lines HEK293 cells

Preparation method The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions 3 μM, 16 hours

Applications Cultured HEK293 cells harbouring UAA, UAG or UGA LUC-190 nonsense alleles were treated with increasing concentrations of PTC124 for 16 h, and assayed for luciferase activity. PTC124 promoted dose-dependent readthrough of all three nonsense codons. Levels of suppression correlated inversely with established termination efficiencies, with the highest readthrough at UGA, followed by UAG and then UAA. The minimal concentration of PTC124 showing discernable readthrough was 0.01–0.1 μM, whereas the concentration promoting maximal activity was approximately 3 μM.
Animal experiment [3]:

Animal models: Cftr-/ hCFTR-G542X Mice

Dosage form: Subcutaneous injection, 60, 30, or 15 mg/kg body weight for 14–21 days

Applications: After the treatment, the mice were killed and intestinal tissues were harvested for immunofluorescence staining to determine whether hCFTR protein could be detected. No hCFTR protein was detected in intestinal tissues from untreated mice with hCFTR-specific antiserum. However, strong hCFTR staining was observed at the apical surface of epithelial cells in submucosal glands from mice treated with 60 mg/kg PTC124. Much weaker staining was detected in submucosal glands from mice treated with 30 mg/kg PTC124, whereas no signal could be detected in mice treated with 15 mg/kg PTC124. These results indicate that PTC124 can suppress the G542X mutation and partially restore hCFTR protein expression in Cftr-/ hCFTR-G542X mice.

Other notes: Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will
maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.