

Product Data Sheet

Product Name: AS2863619

Cat. No.: GC38736

Chemical Properties

Cas. No. 2241300-51-4

SMILES NC1=NON=C1C(N2C3=CC=C4N=C(C)NC4=C3)=NC5=C2C=CN=C5.[H]Cl.[H]Cl

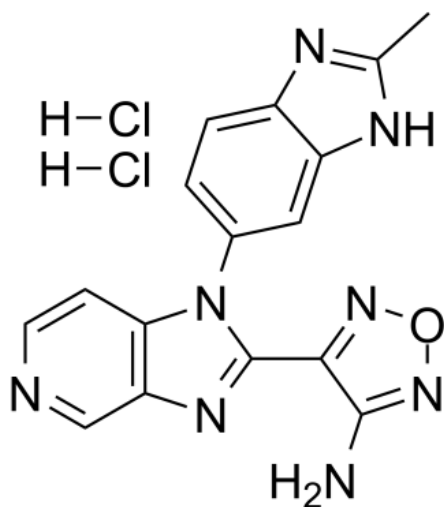
Formula $C_{16}H_{14}Cl_2N_8O$ M.Wt 405.24

Solubility DMSO: 250 mg/mL (616.92 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

Kinase experiment [1]:

AS2863619 was assessed in vitro using recombinant CDK8/cyclin C complex, Preparation Method CDK19/cyclin C complex. IC₅₀ was defined as the concentration of an inhibitor that reduced phosphorylation by half compared with the DMSO control.

Caution: Product has not been fully validated for medical applications. For research use only.

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Reaction Conditions 1.0μM

Applications AS2863619 significantly inhibits the kinase activity of CDK8 and CDK19, and its ability to induce Foxp3 expression is strongly correlated with its inhibitory potency against these kinases.

Cell experiment [2]:

Cell lines Human primary T cells

Preparation Method Human primary T cells were plated in 96-well plates with 50,000 T cells per well. Inhibitors were added 24 hours after CD3/CD28beadactivationandwererefreshlysupplemented every 48 hours. CD3/28 beads were removed on day 4 after activation.

Reaction Conditions 10^{-11} , 10^{-10} , 10^{-9} , 10^{-8} , 10^{-7} , 10^{-6} , 10^{-5} M; 15 days (per 48 hours)

Applications Cultured healthy human T cells following anti-CD3/CD28 activation with AS2863619 and observed significant increases in T cell expansion, confirming that the kinase module restrains T cell expansion.

Animal experiment [1]:

Animal models DNFB-sensitized mice

Preparation Method Mice expressing diphtheria toxin receptor under the Foxp3 promoter were sensitized epicutaneously with DNFB on the abdominal skin on days 0 and 7 and challenged on day 14 by applying DNFB on the ear, whereas some of them were orally administered with AS2863619 (30mg/kg) daily for 2 weeks.

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Dosage form 30mg/kg for two weeks; orally

Applications AS2863619 treatment dampened the degree of the secondary response, with milder infiltration of inflammatory cells into the skin and decreased ratios of interferon- γ^+ (IFN- γ^+) cells in the regional lymph nodes when compared with vehicle-treated control mice.

Reference:

- [1] Akamatsu M, Mikami N, Ohkura N, et al. Conversion of antigen-specific effector/memory T cells into Foxp3-expressing Treg cells by inhibition of CDK8/19. *Sci Immunol*. 2019;4(40):eaaw2707.
- [2] Freitas KA, Belk JA, Sotillo E, et al. Enhanced T cell effector activity by targeting the Mediator kinase module. *Science*. 2022;378(6620):eabn5647.

Background

AS2863619 is an orally administered small molecule inhibitor of cyclin-dependent kinase (CDK) 8 and 19 with IC_{50} of 0.6099nM and 4.277nM, respectively. AS2863619 inhibits serine phosphorylation in the PSP motifs of signal transducer and activator of transcription 5 (STAT5) and somehow enhances phosphorylation of tyrosine residues in the C-terminal domain, leading to enhanced activation of STAT5 and thus activation of various STAT5-binding genes, including T_{reg} signature genes such as Forkhead box p3 (Foxp3) and CD25 [1-2]. AS2863619 converts naïve and effector/memory antigen-specific CD4⁺ and CD8⁺ T cells into Foxp3⁺ Tregs in vitro through an IL-2-dependent but TGF- β -independent mechanism[3]. AS2863619 is useful in promoting the differentiation and proliferation of erythroid progenitor cells or erythroid precursor cells[4].

In vitro, healthy human T cells were cultured following anti-CD3/CD28 activation with AS2863619 and observed significant increases in T cell expansion, confirming that the kinase module restrains T cell expansion CDK19[5]. Cochlear explants from C57BL/6J were cultured for a day and treated with cisplatin for another day; over half of the OHCs were lost. In the basal region, both AS2863619 (1 μ mol/L or 5 μ mol/L) and ribociclib co-treatments effectively alleviated the cisplatin-induced damage of OHCs[6].

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In vivo, in a skin contact hypersensitivity model (sensitization with 2,4-dinitrofluorobenzene (DNFB)), mice were orally administered AS2863619 (30mg/kg) daily for 2 weeks. This treatment dampened the degree of the secondary response in a T_{reg} cell-dependent manner, with milder infiltration of inflammatory cells into the skin and decreased ratios of interferon- γ^+ (IFN- γ^+) cells in the regional lymph nodes when compared with vehicle-treated control mice^[2, 7].

References:

- [1] Wang L, Wang Y, Liu C, et al. Treg-targeted efficient-inducible platform for collagen-induced arthritis treatment. *Mater Today Bio.* 2023;19:100557.
- [2] Akamatsu M, Mikami N, Ohkura N, et al. Conversion of antigen-specific effector/memory T cells into Foxp3-expressing Treg cells by inhibition of CDK8/19. *Sci Immunol.* 2019;4(40):eaaw2707.
- [3] Bonam SR, Bayry J. For antigen-specific effector or Foxp3+ regulatory T cell fate, cyclin-dependent kinases hold the trump card. *Cell Mol Immunol.* 2020;17(4):310-312.
- [4] Gu Y, Wu L, Gao H, et al. Use of RO8191 and AS2863619 in promoting differentiation and proliferation of erythroid progenitor cells or erythroid precursor cells. *Derwent Innovations Index.* 2023;2023-913047.
- [5] Freitas KA, Belk JA, Sotillo E, et al. Enhanced T cell effector activity by targeting the Mediator kinase module. *Science.* 2022;378(6620):eabn5647.
- [6] Zheng L, Shen Q, Zhao T, et al. A Novel Functional Method of Protector Screening for Zebrafish Lateral Line Hair Cells via the Acoustic Escape Response. *Neurosci Bull.* Published online May 6, 2025.
- [7] Cully M. Treg conversion dampens autoimmunity. *Nat Rev Drug Discov.* 2019;18(12):903.

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