

Product Data Sheet

Product Name: TG101209

Cat. No.: GC10035

Chemical Properties

Cas. No. 936091-14-4

Chemical Name N-tert-butyl-3-[[5-methyl-2-[4-(4-methylpiperazin-1-yl)anilino]pyrimidin-4-yl]amino]benzenesulfonamide

SMILES CC1=CN=C(N=C1NC2=CC(=CC=C2)S(=O)(=O)NC(C)(C)C)NC3=CC=C(C=C3)N4CCN(CC4)C

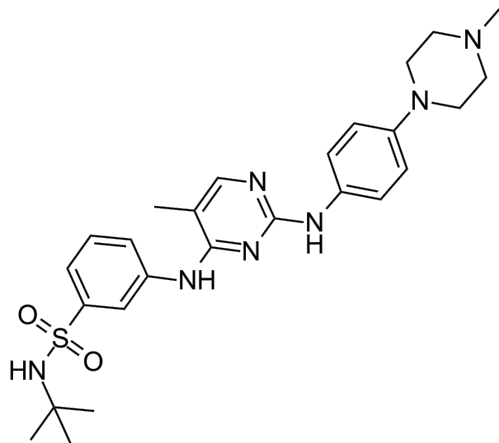
Formula $C_{26}H_{35}N_7O_2S$ M.Wt 509.67

Solubility ≥ 25.5 mg/mL in DMSO Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ 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.

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Cell experiment: In brief, approximately 2×10^3 cells are plated into microtiterplate wells in 100 mL RPMI-1640 growth media with indicated concentrations of TG101209. The relative growth of cells is quantified at 24-hour intervals using Cell Proliferation Kit II (XTT) as per manufacturer's guidelines. After incubation, 20 mL of XTT is added to the wells and allowed to incubate for 4-6 hours. The colored formazan product is measured spectrophotometrically at 450 nm with correction at 650 nm, and IC₅₀ values are determined using the GraphPad Prism 4.0 software. Data are subjected to a non-linear regression-fit analysis and IC₅₀ values are determined as the concentration that inhibits proliferation by 50%. All experiments are done in triplicate and the results normalized to growth of untreated cells.

Animal experiment: Severe combined immunodeficiency (SCID) mice are intravenously injected with 10 times 10⁶ sorted GFP-positive BaF/3 cells expressing JAK2V617F (Ba/F3-V617F-GFP). TG101209 is administered by oral gavage at the indicated doses beginning day +3 after tumor cell infusion and ending on day +20. On day +11 following tumor cell injection, 1 mL blood is collected by terminal cardiac bleeding from the mouse that receives vehicle, and 0.1 mL of blood is collected by non-lethal retro-orbital collection from each of the three six-mouse groups dosed with 10, 30 or 100 mg/kg b.i.d. (twice daily) of TG101209, and samples pooled within the dose groups. Blood mononuclear cells are isolated by a Ficoll cushion centrifugation method (600 RCF and 30 min). The isolated cells are subjected to FACS analysis to determine the percentage of GFP-positive tumor cells (that is, Ba/F3-V617F-GFP cells).

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References:

- [1]. Pardanani A, et al. TG101209, a small molecule JAK2-selective kinase inhibitor potently inhibits myeloproliferative disorder-associated JAK2V617F and MPLW515L/K mutations. *Leukemia*. 2007 Aug;21(8):1658-68.
- [2]. Ma AC, et al. A novel zebrafish jak2a(V581F) model shared features of human JAK2(V617F) polycythemia vera. *Exp Hematol*. 2009 Dec;37(12):1379-1386.e4.
- [3]. Sun Y, et al. Inhibition of JAK2 signaling by TG101209 enhances radiotherapy in lung cancer models. *J Thorac Oncol*. 2011 Apr;6(4):699-706
- [4]. Cuesta-Dominguez A, et al. Transforming and tumorigenic activity of JAK2 by fusion to BCR: molecular mechanisms of action of a novel BCR-JAK2 tyrosine-kinase. *PLoS One*. 2012;7(2):e3245

Background

TG101209, a small-molecule identified by structure based design, is a selective inhibitor of janus kinase 2 (Jak2) that potently inhibits Jak/Stat pathway in multiple myeloma (MM) cell lines, such as cell harboring JAK2V617F or MPLW515L/K mutations which are commonly associated with polycythemia vera (PV) and primary myelofibrosis (PMF) respectively. According to results of multiple studies, it has revealed that TG101209 exhibits a dose and time dependent cytotoxicity, which is associated with inhibited cell cycle progression and induced apoptosis, in a wide range of MM cell lines through suppressing the expression of pJak2, pStat3 and Bcl-xl and inducing the overexpression of pErk and pAkt.

Reference

[1]. Ramakrishnan V, Kimlinger T, Haug J, Timm M, Wellik L, Halling T, Pardanani A, Tefferi A, Rajkumar SV, Kumar S. TG101209, a novel JAK2 inhibitor, has significant in vitro activity in multiple myeloma and displays preferential cytotoxicity for CD45+ myeloma cells. *Am J Hematol*. 2010;85(9):675-686.

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