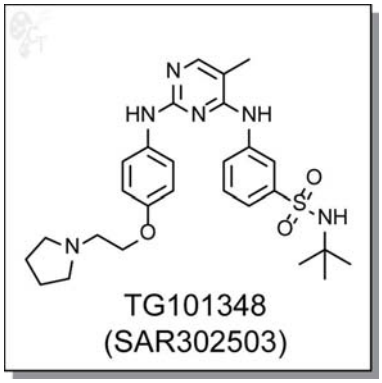
Cellagen Technology

Product Specification Sheet

Product Name: TG101348 (SAR302503)

Catalog Number: C8134



Technical information:

Chemical Formula:	$C_{27}H_{36}N_6O_3S$
CAS #:	936091-26-8
Molecular Weight:	524.68
Purity:	> 98%
Appearance:	Pale Yellow solid
Solubility:	Soluble in DMSO up to 100mM
Chemical Name:	N-tert-butyl-3-(5-methyl-2-(4-(2-(pyrrolidin-1-yl)ethoxy)phenylamino)pyrimidin-4-ylamino)benzenesulfonamide
Storage:	Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 10 mM stock solution, add 0.191mL of DMSO for each mg of TG101348 (SAR302503).
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

TG101348 is an orally-available, aminopyrimidine-based inhibitor of JAK2 and JAK2V617F at an IC50 of 3 nM, with marked selectivity over JAK3 (IC50 >1 uM). [1, 2] TG101348 inhibits proliferation of HMC-1.1 and HMC-1.2 cells at IC50s of 740 and 407 nM, respectively. [1]

In a UT7/EPO cell line, TG101348 inhibited STAT5 phosphorylation much more potently at lower concentrations than known JAK2/3 inhibitor AG490 (600 nM vs 100 uM). In the same study, TG101348 inhibited AKT phosphorylation while reducing GATA-1 S310 phosphorylation. [2]

In human erythroleukemia and Ba/F3-JAK2V617F cells, TG101348 inhibited the cytokine-independent growth at IC50s of 300 and 580 nM, respectively. [3]

TG101348 induces apoptosis in both HEL and Ba/F3 JAK2V617F cells, but not in normal human dermal fibroblasts at concentrations up to 10 uM; antiproliferative IC50 against fibroblasts is > 5 uM.

Reference:

1. Lasho et al., Inhibition of JAK-STAT signaling by TG101348: a novel mechanism for inhibition of KITD816V-dependent growth in mast cell leukemia cells. Leukemia, 2010, 24, 1378-1380. Pubmed ID: 20485374
2. Geron et al., Selective inhibition of JAK2-driven erythroid differentiation of polycythemia vera progenitors. Cancer Cell, 2008, 13(4), 321-330. Pubmed ID: 18394555
3. Lasho et al., TG101348, a JAK2-selective antagonist, inhibits primary hematopoietic cells derived from myeloproliferative disorder patients with JAK2V617F, MPLW515K or JAK2 exon 12 mutations as well as mutation negative patients. Leukemia, 2008, 22, 1790-1792. Pubmed ID: 18354492
4. Wernig et al., Efficacy of TG101348, a selective JAK2 inhibitor, in treatment of a murine model of JAK2V617F-induced polycythemia vera. Cancer Cell 2008, 13(4), 311-320. Pubmed ID: 18394554

To reorder: http://www.cellagentech.com/TG101348-SAR302503/

For Technical Support: technical@cellagentech.com

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