Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

CGI-1746

Catalog No: tcsc0252

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
910232-84-7

Formula:
$C_{34}H_{37}N_5O_4$

Pathway:
Protein Tyrosine Kinase/RTK;Autophagy

Target:
Btk;Autophagy

Purity / Grade:
>98%

Solubility:
DMSO : ≥ 50 mg/mL (86.25 mM); H2O :

Observed Molecular Weight:
579.69

Product Description

CGI-1746 is a potent and highly selective inhibitor of the **Btk** with **IC_{50}** of 1.9 nM.

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IC50 & Target: IC50: 1.9 nM (Btk)

In Vitro: CGI1746 is specific for Btk, with appr 1,000-fold selectivity over Tec and Src family kinases. In an ATP-free competition binding assay, the dissociation constant for Btk is 1.5 nM. CGI1746 inhibits Btk activity in a new binding mode that stabilizes an inactive nonphosphorylated enzyme conformation. CGI1746 inhibits both auto- and transphosphorylation steps necessary for enzyme activation. CGI1746 completely inhibits anti-IgM-induced murine and human B cell proliferation, with IC_{50}s of 134 nM and 42 nM, respectively, but has no effect on anti-CD3- and anti-CD28-induced T cell proliferation. CGI1746 potently inhibits the proliferation of CD27+IgG+ B cells isolated from the tonsils of four human donors with an average IC_{50} of 112 nM. In macrophages, CGI1746 abolishes FcγRIII-induced TNFα, IL-1β and IL-6 production. CGI1746 potently inhibits TNFα, IL-1β and, to a lesser extent, IL-6 (three- to eight-fold higher IC_{50}) production in human monocytes stimulated with immobilized or soluble immune complexes[1]. CGI-1746 does not kill cells as well as the irreversible BTK inhibitors at the same drug concentration. CGI-1746 significantly reduces phosphorylation of both the BTK-A and BTK-C proteins, indicating the auto-phosphorylation of the BTK-C isoform is inhibited in a manner similar to BTK-A. CGI-1746 does not kill LNCaP or DU145 prostate cancer cells at the same concentrations as Ibrutinib or AVL-292, but it demonstrates similar inhibition of BTK phosphorylation at tyrosine 233 in the SH3 domain[2].

In Vivo: CGI1746 abrogates B cell-dependent arthritis. CGI1746 treatment (100 mg/kg, s.c, twice-daily dosing) results in significant inhibition (97%) of overall clinical arthritis scores. CGI1746 treatment substantially reduces TNFα, IL-1β and IL-6, as well as MCP1 and MIP-1α on both the mRNA and protein level in the passive anti-collagen II antibody-induced arthritis (CAIA) model. CGI1746 shows comparable efficacy to TNFα blockade and significantly reduces clinical scores, as well as joint inflammation, in mice or rats with established arthritis[1].