

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 : \geq 50 mg/mL (86.25 mM); H₂O :

Observed Molecular Weight:

579.69

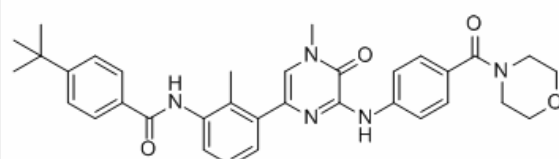
Product Description

CGI-1746 is a potent and highly selective inhibitor of the **Btk** with **IC₅₀** of 1.9 nM.

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 IC₅₀s 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 IC₅₀ 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 IC₅₀) 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].



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!