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

CH5132799

Catalog No: tcsc0981

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
1007207-67-1

Formula:
$C_{15}H_{19}N_7O_3S$

Pathway:
PI3K/Akt/mTOR

Target:
PI3K

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Observed Molecular Weight:
377.42

Product Description

CH5132799 is a selective class I **PI3K** inhibitor. CH5132799 inhibits class I PI3Ks, particularly PI3Kα, with an $\mathbf{IC_{50}}$ of 14 nM.

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IC50 & Target: IC50: 14 nM (PI3Kα), 36 nM (PI3Kγ), 120 nM (PI3Kβ), 500 nM (PI3Kδ)[1]

In Vitro: CH5132799 is a selective class I PI3K inhibitor with potent antitumor activity against tumors harboring the PIK3CA mutations. CH5132799 selectively inhibits class I PI3Ks and PI3Kα mutants in in vitro kinase assays. CH5132799 inhibits class I PI3Ks, particularly PI3Kα, with an IC_{50} of 14 nM. IC_{50} values against class II PI3Ks (C2α and C2β), a class III PI3K (Vps34), and a class IV PI3K (mTOR) are more than 100-fold higher than that against PI3Kα. Interestingly, slightly lower IC_{50} values are observed against PI3Kα with oncogenic mutations E542K, E545K, and H1047R than against wild-type (WT) PI3Kα. In an analysis of cocrystal structure with PI3Kγ (PBD ID: 3APC), CH5132799 is shown to interact with ATP-binding sites of the enzyme, suggesting an ATP competitive mode of inhibition. No significant inhibitory activities of CH5132799 are observed against a representative panel of 26 protein kinases, including RTKs, nonreceptor tyrosine kinases, and serine/threonine kinases. These data indicate that CH5132799 is a selective class I PI3K inhibitor, especially against PI3Kα and its mutants. CH5132799 shows superior antiproliferative activity across the 4 tumor types, with 75% (45/60) of lines having an IC_{50} below 1 μM and 38% (23/60) of lines having an IC_{50} below 0.3 μM[1].

In Vivo: Mice bearing BT-474 tumors (n=14) are orally administered 50 mg/kg of Everolimus on a daily basis for 31 days and then randomized. After randomization, the mice are orally administered 50 mg/kg of Everolimus (n=4) and 12.5 mg/kg (n=5), and 25 mg/kg (n=5) of CH5132799 on a daily basis for 7 days. C, the vehicle-, Everolimus, and CH5132799-treated (25 mg/kg) tumors are resected at 4 hours after terminal administration in B, lysed, and analyzed by Western blotting. CH5132799 administration leads to a remarkable regression in a dose-dependent manner of the tumors regrown after the long-term Everolimus treatment. The tumors are resected at the end of treatment and analyzed by Western blotting with respect to PI3K pathway inhibition. CH5132799 suppresses various effectors in the PI3K pathway, including Akt, FoxO1, S6K, S6, and 4E-BP1, whereas Everolimus inhibits only phosphorylation of S6K and S6, both downstream effectors of mTORC1[1].