Web: www.taiclone.com
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OSI-027

Catalog No: tcsc0257

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Specifications

CAS No:
936890-98-1

Formula:
$C_{21}H_{22}N_6O_3$

Pathway:
PI3K/Akt/mTOR;Autophagy

Target:
mTOR;Autophagy

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Observed Molecular Weight:
406.44

Product Description

OSI-027 is an ATP-competitive **mTOR** kinase activity inhibitor with an **IC_{50}** of 4 nM. OSI-027 targets both **mTORC1** and **mTORC2** with **IC_{50}**s of 22 nM and 65 nM, respectively.

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IC50 & Target: IC50: 4 nM (mTOR kinase), 22 nM (mTORC1), 65 nM (mTORC2), 0.42 μM (PI3K-γ), 1.3 μM (PI3K-α), 1.0 μM (DNA-PK)[1]

In Vitro: OSI-027 is an ATP-competitive inhibitor, which targets both mTORC1 and mTORC2 with IC_{50}s of 22 nM and 65 nM. OSI-027 also inhibits PI3K-α, PI3K-γ and DNA-PK with IC_{50}s of 1.3 μM, 0.42 μM and 1.0 μM. OSI-027 inhibits mTOR signaling of phospho-4E-BP1 with an IC_{50} of 1 μM[1].

In Vivo: Effects on GEO colorectal xenograft growth treated with Rapamycin or OSI-027 for 12 days are consistent with our in vitro experiments. Treatment with Rapamycin (20 mg/kg) inhibits phospho-S6 and phospho-4E-BP1, while Akt phosphorylation is increased by 29%. In contrast, OSI-027 (65 mg/kg) inhibits both mTORC1 and mTORC2 effectors. After 2 hours, decreased 4E-BP1, Akt, and S6 phosphorylation is observed and inhibition of S6 and Akt is sustained for 24 hours. The plasma drug concentration of OSI-027 inversely correlated with these effects on mTORC1 and mTORC2 signaling. The median plasma drug concentration with OSI-027 is 21.3 μM at 2 hours and 14.9 μM at 8 hours. The in vivo efficacy of OSI-027 plus Sunitinib is tested in H292 human lung and Ovcar-5 human ovarian xenograft tumors. H292 tumors, treated with OSI-027 (50 mg/kg) for 21 days have 61% median tumor growth inhibition for the duration of treatment (TGI). Sunitinib (40 mg/kg) for 21 days had 47% median TGI. Combining OSI-027 with Sunitinib, however, has a median TGI of 100% with 59% maximal tumor regression, a statistically significant improvement over either agent alone. Ovcar-5 xenograft tumors treated with OSI-027 or Sunitinib have a 55% and 68% median TGI, respectively. OSI-027 administered with Sunitinib has a significantly better median TGI of 100% with 38% maximal tumor regression[1].In the Rapamycin (RAPA) group, three rats exhibit symptoms typical of LTx-aGVHD and die 27 to 35 days after liver transplantation (LT); the remaining five rats do not develop LTx-aGVHD symptoms and survive for more than 100 days. In contrast, seven rats in the OSI-027 group survive for more than 100 days without symptoms of LTx-aGVHD, and only one rat exhibits LTx-aGVHD symptoms and dies on day 33 after LT[2].