

# 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

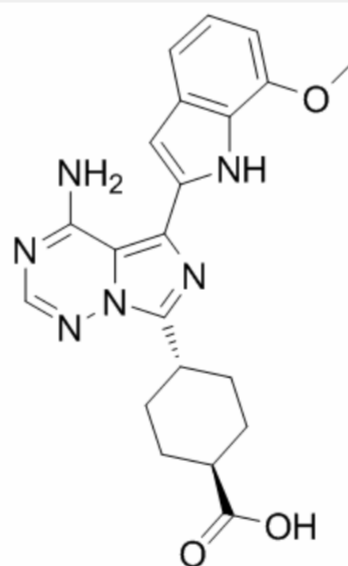
## Product Description

OSI-027 is an ATP-competitive **mTOR** kinase activity inhibitor with an **IC<sub>50</sub>** of 4 nM. OSI-027 targets both **mTORC1** and **mTORC2** with **IC<sub>50</sub>**s of 22 nM and 65 nM, respectively.

IC50 & Target: IC50: 4 nM (mTOR kinase), 22 nM (mTORC1), 65 nM (mTORC2), 0.42  $\mu$ M (PI3K- $\gamma$ ), 1.3  $\mu$ M (PI3K- $\alpha$ ), 1.0  $\mu$ M (DNA-PK)<sup>[1]</sup>

**In Vitro:** OSI-027 is an ATP-competitive inhibitor, which targets both mTORC1 and mTORC2 with IC<sub>50</sub>s of 22 nM and 65 nM. OSI-027 also inhibits PI3K- $\alpha$ , PI3K- $\gamma$  and DNA-PK with IC<sub>50</sub>s of 1.3  $\mu$ M, 0.42  $\mu$ M and 1.0  $\mu$ M. OSI-027 inhibits mTOR signaling of phospho-4E-BP1 with an IC<sub>50</sub> of 1  $\mu$ M<sup>[1]</sup>.

**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  $\mu$ M at 2 hours and 14.9  $\mu$ M at 8 hours. The in vivo efficacy of OSI-027 plus Sunitinib is tested in H292 human lung and Ovar-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. Ovar-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<sup>[1]</sup>. 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<sup>[2]</sup>.



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