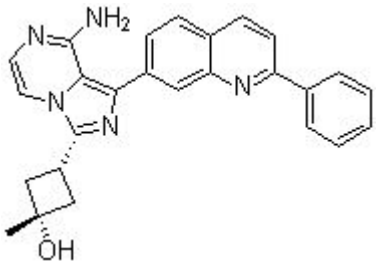
Product Introduction

OSI-906 (Linsitinib)

OSI-906 (Linsitinib) is a selective inhibitor of **IGF-1R** with **IC50** of 35 nM; modestly potent to InsR with IC50 of 75 nM, and no activity towards Abl, ALK, BTK, EGFR, FGFR1/2, PKA etc. Phase 3.

Technical Data:

Molecular Weight (MW):	421.49	
Formula:	$C_{26}H_{23}N_5O$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 84 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	867160-71-2	

Biological Activity

OSI-906 inhibits IGF-1R autophosphorylation and activation of the downstream signaling proteins Akt, ERK1/2 and S6 kinase with IC50 of 0.028 to 0.13 μM. OSI-906 enables an intermediate conformation of the target protein through interactions with the C-helix. OSI-906 displays favorable metabolic stability in liver microsomes. OSI-906 fully inhibits both IR and IGF-1R phosphorylation at a concentration of 1 μM. OSI-906 inhibits proliferation of several tumor cell lines including non-small-cell lung cancer and colorectal cancer (CRC) tumor cell line with EC50 of 0.021 to 0.810 μM. [1]

OSI-906 inhibits tumor growth in an IGF-1R-driven xenograft mouse model, with 100% TGI and 55% regression at a dose of 75 mg/kg and 60% TGI and no regression at a dose of 25 mg/kg. OSI-906 administration induces different elimination half-lives of itself in dog, rat and mice, the elimination half-lives are 1.18 hours, 2.64 hours and 2.14 hours, respectively. OSI-906 administration at different single dose once-daily in femal Sprague-Dawley rat and femal CD-1 mouse reveal that the V_{max} is not dose-proportional to OSI-906 dose. OSI-906 elevates the blood glucose levels at a dose of 25 mg/kg after 12 days administration. OSI-906 administration at a single dose of 75 mg/kg in IGF-1R-driven full-length human IGF-1R (LISN) xenograft mouse model achieve maximal inhibition of IGF-1R phosphorylation (80%) between 4 and 24 hours with plasma drug concentrations of 26.6-4.77 μM. [1] OSI-906 administered as a single dose of at 60 mg/kg in NCI-H292 xenografts mice inhibits uptake of glucose at 2, 4, and 24 hours post-treatment in vivo. OSI-906 inhibits the growth of tumors in NCI-H292 xenograft mouse model. [2]

References

[1] Mulvihill MJ, et al. Future Med Chem, 2009, 1(6), 1153-1171.

[2] McKinley ET, et al. Clin Cancer Res, 2011, 17(10), 3332-3340.

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