TGFβRI-IN-4

Cat. No.: HY-146780

CAS No.: 2421135-03-5

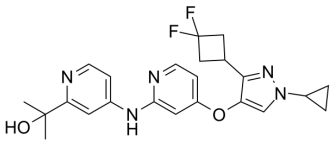
Molecular Formula: $C_{23}H_{25}F_2N_5O_2$

Molecular Weight: 441.47

Target: TGF-β Receptor

Pathway: TGF-beta/Smad

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

TGFβRI-IN-4 is a highly potent and orally active TGFβ receptor type I (TGFβRI) inhibitor, with IC_{50}s of 44 nM and 42.5 nM for ALK5 and NIH3T3. TGFβRI-IN-4 can suppress tumor growth and tumor weight in tumor xenograft model[1].

IC_{50} & Target

IC_{50}: 44 nM (ALK5), 42.5 nM (NIH3T3)[1]

In Vivo

TGFβRI-IN-4 (compound 15r) (60 mg/kg; PO; BID, for 21 days) efficiently suppresses tumor growth and tumor weight in tumor xenograft model[1].

TGFβRI-IN-4 (1 mg/kg and 10 mg/kg; IV and PO; single) exhibits good oral plasma exposure and excellent bioavailability[1].

Pharmacokinetic Parameters of TGFβRI-IN-4 in male Sprague-Dawley rats[1].

	IV (1 mg/kg)	PO (10 mg/kg)
$T_{1/2}$ (h)	0.5	1.8
CL (L/h/kg)	4.9	
C_{max} (ng/mL)		926.0
V_{SS} (L/kg)	3.0	
AUC_{0-24} (ng/mL·h)	195.2	2351.2
F (%)		120.5%

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB/C mice (5-8 weeks; injected with CT26 cells)[1]
Dosage:	60 mg/kg
Administration:	PO; BID, for 21 days

Result:	Efficiently suppressed tumor growth (tumor growth inhibition = 65.7%) and tumor weight.

Animal Model:	Male BALB/C mice[1]
Dosage:	1 mg/kg and 10 mg/kg
Administration:	IV and PO; single (Pharmacokinetic Analysis)
Result:	Exhibited good oral plasma exposure and excellent bioavailability with AUC >2000 h·ng/mL and F > 80%, respectively.

REFERENCES

[1]. Xu G, et al. Synthesis and biological evaluation of 4-(pyridin-4-oxy)-3-(3,3-difluorocyclobutyl)-pyrazole derivatives as novel potent transforming growth factor-β type 1 receptor inhibitors. Eur J Med Chem. 2020;198:112354.

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