Inobrodib

Cat. No.: HY-111784

CAS No.: 2222941-37-7

Molecular Formula: $C_{30}H_{32}F_2N_4O_3$

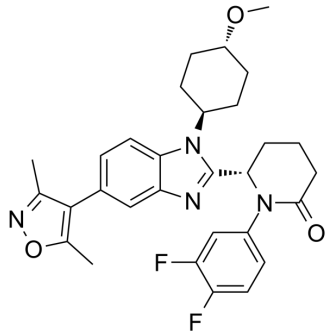
Molecular Weight: 534.6

Target: Epigenetic Reader Domain

Pathway: Epigenetics

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (187.06 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8706 mL	9.3528 mL	18.7056 mL
	5 mM	0.3741 mL	1.8706 mL	3.7411 mL
	10 mM	0.1871 mL	0.9353 mL	1.8706 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5.25 mg/mL (9.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5.25 mg/mL (9.82 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.68 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Inobrodib (CCS1477) is an orally active, potent, and selective inhibitor of the p300/CBP bromodomain. Inobrodib binds to p300 and CBP with K_d values of 1.3 and 1.7 nM, respectively, and with 170/130-fold selectivity compared with BRD4 with a K_d of 222 nM. CCS1477 inhibits cell proliferation in prostate cancer cell lines and decreases androgen receptor (AR)- and C-MYC-regulated gene expression[1].

IC_{50} & Target	p300/CBP[1]
In Vitro	Inobrodib binding to cellular histones in an in-cell BRET assay gives an IC50 of 19 nM for p300 and 1,060 nM for BRD4. Inobrodib shows potent growth-inhibitory activity in VCaP, 22Rv1, and LNCaP95 (all IC50 < 100 nM) that express both AR-FL and AR-V7[1]. Inobrodib (0-3000 nM; 48 hours) reduces expression of AR-regulated genes (KLK2, KLK3, and TMPRSS2) in both 22Rv1 and LNCaP95 cells. Inobrodib also reduces C-MYC protein expression in both 22Rv1 and LNCaP95 cells and AR-V7 protein expression in 22Rv1 cells, without clear impact on AR-FL protein expression in 22Rv1 and LNCaP95 cells. Inobrodib reduces C-MYC mRNA and downstream AR and C-MYC signaling in 22Rv1 and C4-2 cells at 16 hours. Inobrodib regulates AR signaling by affecting the recruitment of CBP, p300, and AR-FL to known AR binding sites, and has the potential to abrogate persistent AR signaling in CRPC[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Inobrodib (10-30 mg/kg; oral gavage; 10 or 20 mg/kg daily (QD) or 30 mg/kg every other day (QOD) for 28 days) suppresses growth of a 22Rv1 mouse xenograft model with associated reduction in AR signaling[1]. Inobrodib (20 mg/kg; oral gavage; daily for 8 days) decreases AR and AR-V7 signaling and inhibits growth in a patient-derived model of lethal prostate cancer (NOD/SCID gamma (NSG) male castrated mice)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Noncastrated male athymic nude mice[1]
Dosage:	10-30 mg/kg
Administration:	Oral gavage; at 10 or 20 mg/kg daily (QD) or at 30 mg/kg every other day (QOD) for 28 days
Result:	Affected tumor growth at 10 mg/kg daily, 20 mg/kg daily, and 30 mg/kg every other day.

REFERENCES

[1]. Rasool RU, et al. Toppling the HAT to Treat Lethal Prostate Cancer. Cancer Discov. 2021;11(5):1011-1013.

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