AZD5153 6-Hydroxy-2-naphthoic acid

Cat. No.: HY-100653A

CAS No.: 1869912-40-2

Molecular Formula: $C_{36}H_{41}N_7O_6$

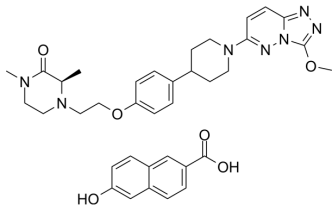
Molecular Weight: 667.75

Target: Epigenetic Reader Domain

Pathway: Epigenetics

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 1 years; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (149.76 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4976 mL	7.4878 mL	14.9757 mL
	5 mM	0.2995 mL	1.4976 mL	2.9951 mL
	10 mM	0.1498 mL	0.7488 mL	1.4976 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: ≥ 2.5 mg/mL (3.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZD5153 6-Hydroxy-2-naphthoic acid is the 6-Hydroxy-2-naphthoic acid of AZD5153. AZD5153 is a potent, selective, and orally available BET/BRD4 bromodomain inhibitor; disrupts BRD4 with an IC_{50} of 1.7 nM.

IC_{50} & Target

IC50: 1.7 nM (BRD4)[1]

In Vitro

AZD5153 demonstrates a remarkable enhancement in potency for the displacement of full-length BRD4 relative to BD1, with IC_{50} values of 5.0 nM and 1.6 μM, respectively. AZD5153 potently disrupts BRD4 foci in U2OS cells with an IC_{50} value of 1.7 nM. AZD5153 efficiently down-regulates MYC protein levels across the cell line panel irrespective of their sensitivity to AZD5153[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Administration of AZD5153 leads to tumor stasis or regression in multiple xenograft models of acute myeloid leukemia, multiple myeloma, and diffuse large B-cell lymphoma. AZD5153 treatment markedly impacts transcriptional programs of MYC, E2F, and mTOR[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: Mice are treated with either vehicle (0.5% hydroxymethylcellulose, 0.1% Tween80) or AZD5153 by oral gavage mini-pump infusion. For continuous administration of AZD5153, compound is solubilized in 20% v/v DMSO/60% v/v HP-B-CD in water, loaded into a mini pump and implanted subcutaneously in mice. Tumor fragments collected are snap frozen or fixed in 10% buffered formalin. Blood samples are collected from the same mice and stabilized in EDTA. Plasma concentrations are determined by liquid chromatography/tandem mass spectrometry method[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Rhyasen GW, et al. AZD5153: A Novel Bivalent BET Bromodomain Inhibitor Highly Active against Hematologic Malignancies. Mol Cancer Ther. 2016 Nov;15(11):2563-2574.

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