H3B-5942

Cat. No.: HY-112611

CAS No.: 2052128-15-9

Molecular Formula: $C_{31}H_{34}N_4O_2$

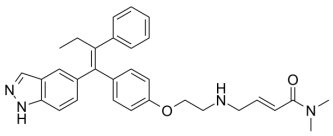
Molecular Weight: 494.63

Target: Estrogen Receptor/ERR

Pathway: Vitamin D Related/Nuclear Receptor

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (168.47 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0217 mL	10.1086 mL	20.2171 mL
	5 mM	0.4043 mL	2.0217 mL	4.0434 mL
	10 mM	0.2022 mL	1.0109 mL	2.0217 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: ≥ 2.08 mg/mL (4.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

H3B-5942 is a selective, irreversible and orally active estrogen receptor covalent antagonist, inactivates both wild-type and mutant ERα by targeting Cys530, with K_is of 1 nM and 0.41 nM, respectively. H3B-5942 reduces ERα target gene GREB1, shows potent antitumor activity both in multiple cell lines or animals bearing $ERα^{WT}$ or ERα mutations[1].

IC_{50} & Target

$ERα^{Y537S}$	$ERα^{WT}$
0.41 nM (Ki)	1 nM (Ki)

In Vitro

H3B-5942 is a selective and irreversible estrogen receptor covalent antagonist, inactivates both wild-type and mutant ERα by targeting Cys530, with K_is of 1 nM and 0.41 nM, respectively[1].
H3B-5942 elevates ERα protein level distinct from SERMs/SERD, blocks ERα-dependent transcription in breast cancer cells.

H3B-5942 (0.01-10 μM) reduces ERα target gene GREB1 in MCF7-ERα^{WT}, various MCF7-ERαMUT lines, and the PDX-ERα^{Y537S} /WT line[1].
H3B-5942 also decreases proliferation of MCF7-Parental, MCF7-LTED-ERα^{WT}, and MCF7-LTED-ERα^{Y537C} lines with GI_{50}s of 0.5, 2, and 30 nM, respectively. H3B-5942 (10-25 nM) in combination with CDK4/6 inhibitors (≥25 pM) has synergic inhibitory effect on multiple cell lines bearing ERα^{WT} or clinically frequent ERα mutations[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

H3B-5942 (1, 3, 10, or 30 mg/kg, p.o, q.d. for 17 days) dose-dependently inhibits tumor growth in MCF7 xenograft model in athymic female nude mice[1].
H3B-5942 (3, 10, 30, 100, and 200 mg/kg, p.o, q.d.) exhibits similar anti-tumor activity in the ERα$^{Y537S/WT}$ ST941 model in athymic female nude mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MCF7 xenograft model in athymic female nude mice[1]
Dosage:	1, 3, 10, or 30 mg/kg
Administration:	P.O. once a day (q.d.×1) for 17 days
Result:	Exhibited tumor growth inhibition (TGI) on day 17 of 19%, 41%, 68%, and 83%, respectively.

REFERENCES

[1]. Puyang X, et al. Discovery of Selective Estrogen Receptor Covalent Antagonists for the Treatment of ERαWT and ERαMUT Breast Cancer. Cancer Discov. 2018 Sep;8(9):1176-1193.

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