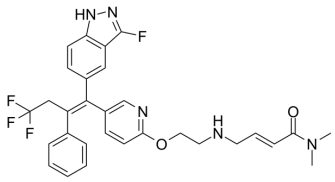
H3B-6545

Cat. No.:	HY-112596
CAS No.:	2052130-80-8
Molecular Formula:	$C_{30}H_{29}F_4N_5O_2$
Molecular Weight:	567.58
Target:	Estrogen Receptor/ERR
Pathway:	Vitamin D Related/Nuclear Receptor
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 (176.19 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7619 mL	8.8093 mL	17.6187 mL
5 mM	0.3524 mL	1.7619 mL	3.5237 mL
10 mM	0.1762 mL	0.8809 mL	1.7619 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 (3.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

H3B-6545 is an oral, selective estrogen receptor covalent antagonist (SERCA) for the research of metastatic ER-positive, HER2-negative breast cancer[1][2].

IC_{50} & Target

Estrogen receptor[1]

In Vitro

H3B-6545 is a highly selective small molecule that potently antagonizes wild-type and mutant ERα in biochemical and cell based assays. In vitro comparisons with standard of care and other experimental agents confirm increased cell potency of H3B-6545 under continuous as well as washout treatment conditions[1]. H3B-6545, a member of a novel class of ERα antagonists refer to as selective ER covalent antagonist (SERCA), which inactivates both wild-type and mutant ERα by targeting C530 and enforcing a unique antagonist conformation. H3B-6545 is a first-in-class selective ER covalent antagonist

	(SERCA). H3B-6545 inhibits ERα^{WT} activity and growth of ERα^{WT} -positive breast cancer lines. H3B-6545 potently inhibits ERα^{WT} activity and suppresses proliferation of ERα^{WT} -positive breast cancer lines. With GI_{50}s of 0.3-0.4, 1.0, 0.5, 5.2, and 0.2 nM for MCF7, HCC1428, BT483, T47D and CAMA-1 cell lines[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In vivo, once daily oral dosing of H3B-6545 shows potent activity and superior efficacy to fulvestrant in the MCF-7 xenograft model with maximal antitumor activity at doses >10x below the maximum tolerated dose in mice. In addition, H3B-6545 shows superior antitumor activity to Tamoxifen and Fulvestrant in patient derived xenograft models of estrogen receptor positive breast cancer including models carrying ERα mutations in rat and monkeys, H3B-6545 is well tolerated across a broad dose range and at exposures that significantly exceed those required for efficacy in mouse xenograft models[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Pharm Biomed Anal. 2019 Aug 5;172:189-199.
- Biol Trace Elem Res. 2020 Feb;34(2):e4746.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Peter G. Smith, et al. Abstract DDT01-04: Discovery and development of H3B-6545: A novel, oral, selective estrogen receptor covalent antagonist (SERCA) for the treatment of breast cancer.AACR Annual Meeting 2017; April 1-5.

[2]. Amy H Kim, et al. H3B-6545, a selective estrogen receptor covalent antagonist, prevents bone loss in ovariectomized Sprague-Dawley rats. J Pharmacol Toxicol Methods. Sep-Oct 2019;99:106595.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA