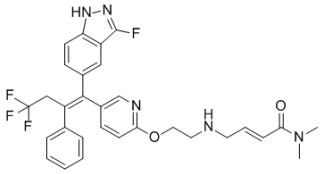
H3B-6545

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:	Others
Storage:	Please store the product under the recommended conditions in the COA.



BIOLOGICAL ACTIVITY

Description	H3B-6545 is an oral, selective **estrogen receptor** covalent antagonist (**SERCA**).
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].
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].

CUSTOMER VALIDATION

- **J Pharmaceut Biomed**. 2019 Apr.

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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]. Manav Korpal, et al. Development of a First-in-Class Oral Selective ER Covalent Antagonist (SERCA) for the Treatment of ERα^{WT} and ERα^{MUT} Breast Cancer.

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