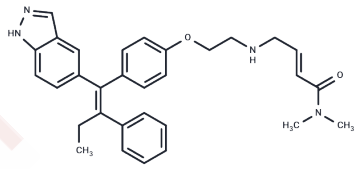
Data Sheet (Cat.No.T5633)

TargetMol

H3B-5942

Chemical Properties



CAS No. : 2052128-15-9

Formula: C31H34N4O2

Molecular Weight: 494.63

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	H3B-5942 belongs to a class of ERα antagonists referred to as selective estrogen receptor covalent antagonists (SERCA).
Targets(IC50)	Estrogen Receptor/ERR,Estrogen/progestogen Receptor
In vitro	H3B-5942 dosed once (q.d.×1) orally at 30 to 300 mg/kg showed a dose-proportional increase in plasma and tumor exposure and a concomitant dose-proportional decrease in expression of the ERα target genes PGR and NPY1R in the ERαY537S/WT ST941 tumor model.?Single or repeat dosing of H3B-5942 at 200 mg/kg suppressed a large panel of direct ERα target genes, with q.d.×1 dosing maintaining target gene suppression for up to 72 hours after dose, and q.d.×3 (3 daily doses) dosing demonstrating greatest suppression in PGR and NPY1R
In vivo	Single or repeat dosing of H3B-5942 at 200 mg/kg suppressed a large panel of direct ERα target genes, with q.d.×1 dosing maintaining target gene suppression for up to 72 hours after dose, and q.d.×3 (3 daily doses) dosing demonstrating greatest suppression in PGR and NPY1R .
Kinase Assay	ERαWT (297-554) and mutant (297-554) proteins were incubated in 50 mmol/L Tris pH 8.0, 150 mmol/L NaCl, 5% glycerol, and 1 mmol/L TCEP with a 2-fold excess of compound (2 μmol/L H3B-5942:1 μmol/L ERα protein solution) at 4°C overnight.?Mass analyses were carried out (ESI source, 4.0 kV ionization voltage, 250°C capillary temperature, 10 arb sheath gas, S-lens RF level 65) coupled with an Accela Open AS 1250.?Samples (10 μL) were desalted on a C4 column (2.1 × 150 mm, 2.6 μm) with a gradient from 5% to 95% B over 10 minutes.?Eluent A consisted of 0.1% formic acid in water, and eluent B consisted of 0.1% formic acid in acetonitrile.?The flow was set to 400 nL/minute.?All solvents were LC/MS grade .?The mass spectrometer was run in positive mode collecting full scan at R = 70,000 from m/z 500 to m/z 2,000.?Data were collected with the Xcalibur 3.1 software.
Animal Research	Animals were selected based on TV and randomized into treatment groups of 6 to 8 animals per group.?Single-agent or combination treatments were started on day 0 and continued for the duration of the study.?H3B-5942 was administered orally, tamoxifen was given Q2D, fulvestrant was given?, and palbociclib was administered orally ?Each treatment was administered based on BW (10 mL/kg).?H3B-5942 was formulated daily in 10% 2-Hydroxypropyl-β-CycloDextrin (HPβCD) in 5% dextrose, tamoxifen was

Animal Research	formulated in 95% peanut oil/5% ethanol (EtOH), clinical-grade fulvestrant was administered, and palbociclib was formulated in 25 mmol/L sodium bicarbonate, 15 mmol/L lactic acid solution with 2% Cremophor EL.?The BW measurements were performed daily, and tumor measurements were recorded twice a week.

Solubility Information

Solubility	DMSO: 50 mg/mL (101.09 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.04 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0404 mL	0.2022 mL	0.4043 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Discovery of Selective Estrogen Receptor Covalent Antagonists (SERCAs) for the treatment of ERa(WT) and ERa (MUT) breast cancer.[J]. Cancer Discovery, 2018:CD-17-1229-.