

## Product Data Sheet

Product Name: Evacetrapib (LY2484595)

Cat. No.: GC14061

### Chemical Properties

Cas. No. 1186486-62-3

Chemical Name 4-[[[(5S)-5-[[3,5-bis(trifluoromethyl)phenyl]methyl-(2-methyltetrazol-5-yl)amino]-7,9-dimethyl-2,3,4,5-tetrahydro-1-benzazepin-1-yl]methyl]cyclohexane-1-carboxylic acid

SMILES CC1=CC(=C2C(=C1)C(CCCN2CC3CCC(CC3)C(=O)O)N(CC4=CC(=CC(=C4)C(F)(F)F)C(F)(F)F)C5=NN(N=N5)C)C

Formula  $C_{31}H_{36}F_6N_6O_2$  M.Wt 638.65

Solubility  $\geq 32.1$  mg/mL in DMSO,  $\geq 50.4$  mg/mL in EtOH with ultrasonic Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility, please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while. Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

**Caution: Product has not been fully validated for medical applications. For research use only.**

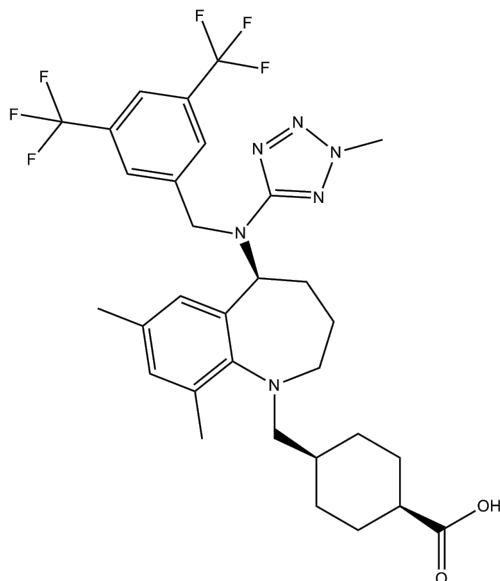
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

## Product Data Sheet

---

### Structure



### Protocol

**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: [tech@glpbio.com](mailto:tech@glpbio.com)

Address: 10292 Central Ave. #205, Montclair, CA, USA

## Product Data Sheet

---

**Kinase  
experiment:**

Human CETP cDNA is amplified from a human liver cDNA library and the sequence is confirmed to be identical to the published sequence. The cDNA is subcloned into a pcDNA3.1 vector, under the control of CMV promoter. A stable line is established in CV1 cells in which the above-mentioned construct is used to express the recombinant human CETP. The medium contained the secreted recombinant CETP protein and the amount (19 ng/ $\mu$ L) is quantified by an ELISA kit. The medium is then aliquoted in 0.2% BSA and stored at -80°C. The stock CETP protein is diluted 150-fold in CETP buffer (10 mM Tris, 150 mM NaCl, and 2 mM EDTA) before use. The assay is set up in a 96-well plate. Each well received 97.5  $\mu$ L diluted CETP protein (final concentration 7 nM) and 2.5  $\mu$ L of compound stock. After a 30 min incubation at 37°C, 5  $\mu$ L of substrate stock (the same stock used in the human plasma CETP assay), 0.16  $\mu$ L of VLDL stock (2.5 mg/mL, Intracel) and 145  $\mu$ L of CETP buffer are added, and the incubation is continued for another 4 h. Signal is read for the human plasma CETP assay[1].

**Animal  
experiment:**

Rats[1] The blood pressure study is carried out using telemetered, male, obese Zucker Diabetic rats (ZDF fa/fa rats, 8 weeks of age on arrival; n=4). All rats underwent surgical implantation of a telemetry transmitter for continuous monitoring of hemodynamic parameters throughout the study. The rats are acclimated on Purina 5008 chow and house water ad libitum until 11 weeks of age. Mean daily blood pressure for the 24-h period immediately prior to administration of compound is taken as the baseline blood pressure. On the day of an experiment, a single 160 mg/kg dose (in 10% acacia) of Evacetrapib as the lysine salt is administered by oral gavage, and the drug effect is taken as the average daily mean arterial pressure (MAP) during the 24 h period following the dose. Data are expressed as the change in MAP from baseline. Following the last day of blood pressure monitoring, samples are collected from the orbital sinus at 1, 2, 4, 8, and 24 h post dose into tubes containing EDTA and processed into plasma. Plasma concentrations of Evacetrapib are measured using liquid chromatography tandem mass spectrometry.

**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: [tech@glpbio.com](mailto:tech@glpbio.com)

Address: 10292 Central Ave. #205, Montclair, CA, USA

## Product Data Sheet

---

### References:

[1]. Cao G, et al. Evacetrapib is a novel, potent, and selective inhibitor of cholesteryl ester transfer protein that elevates HDL cholesterol without inducing aldosterone or increasing blood pressure. J Lipid Res. 2011 Dec;52(12):2169-76.

### Background

Evacetrapib is a potent and selective inhibitor of cholesteryl ester transfer protein (CETP) with IC<sub>50</sub> value of 5.5nM [1].

As a benzazepine-based inhibitor of CETP, evacetrapib is developed to increase HDL cholesterol for the treatment of coronary artery disease. Evacetrapib is efficacious both in vitro and in vivo. The IC<sub>50</sub> values of evacetrapib against CETP are 5.5nM and 26nM, respectively in the buffer assay using human recombinant CETP and in the plasma assay using human plasma CETP. In the animal model of human CETP/ApoA1 double transgenic mouse line, oral administration of evacetrapib at 30mg/kg significantly inhibits the CETP activity as well as increases the level of HDL. Besides that, the ED<sub>50</sub> value of evacetrapib is less than 5mg/kg. Compared to the previous inhibitors of CETP, evacetrapib has less side effects. It is found no to increase blood pressure Zucker diabetic fatty rats and not to induce aldosterone or cortisol synthesis in H295R cells [1].

### References:

[1] Cao G, Beyer TP, Zhang Y, Schmidt RJ, Chen YQ, Cockerham SL, Zimmerman KM, Karathanasis SK, Cannady EA, Fields T, Mantlo NB. Evacetrapib is a novel, potent, and selective inhibitor of cholesteryl ester transfer protein that elevates HDL cholesterol without inducing aldosterone or increasing blood pressure. J Lipid Res. 2011 Dec;52(12):2169-76.

**Caution: Product has not been fully validated for medical applications. For research use only.**

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA