

## Product Data Sheet

Product Name: TPPB ( $\alpha$ -Amyloid Precursor Protein Modulator)

Cat. No.: GC10343

### Chemical Properties

Cas. No. 497259-23-1

Chemical Name (2E,4E)-N-(5-(hydroxymethyl)-2-isopropyl-1-methyl-3-oxo-1,2,3,4,5,6-hexahydrobenzo[e][1,4]diazocin-8-yl)-5-(4-(trifluoromethyl)phenyl)penta-2,4-dienamide

SMILES CC(C1C(NC(CO)CC2=C(C=CC(NC(/C=C/C=C/C3=CC=C(C(F)(F)F)C=C3)=O)=C2)N1C)=O)C

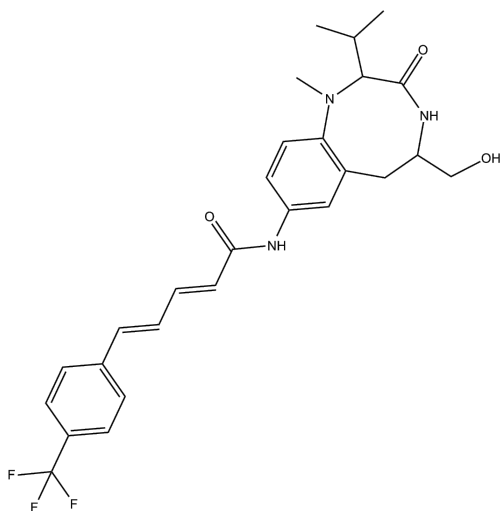
Formula  $C_{27}H_{30}F_3N_3O_3$  M.Wt 501.54

Solubility 25.08mg/mL in DMSO 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.

Structure



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

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### Protocol

#### Cell experiment [1]:

Cell lines SH-SY5Y cells

Preparation Method Cells were grown to confluency in 10 % serum-supplemented medium. Prior to experiments, culture medium was replaced with serum and protein-free (0 %) medium for 2h before drug treatments to remove APP/sAPP $\alpha$  present in FBS and to permit filter concentration of sAPP $\alpha$ . Dilutions of bryostatin-1 or TPPB were added to serum-free culture medium at various concentrations and treatments maintained for 3h, except in time course experiments where several time points up to 24h were taken. Pilot studies showed no change in SH-SY5Y appearance, attachment, or cell density for at least 24h under these conditions.

Reaction Conditions 0.1-100nM; 3h

Applications TPPB induces cell secretion of sAPP $\alpha$ .

#### Animal experiment [2]:

Animal models Experimental autoimmune encephalomyelitis (EAE) mice model

Preparation Method TPPB was dissolved in DMSO to a 1mM stock solution and then diluted to the desired concentration with sterile PBS for animal experiments. Mice were intraperitoneally injected with TPPB (50nmol/kg) or an equal volume of vehicle control three days a week. Mice were randomized and received their first treatment on the day their clinical score reached 1.0 or higher; thereafter, treatment continued three days a week.

Dosage form 50nmol/kg; ip; 21d; three days a week

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**Applications**      TPPB can alleviate the neurological deficits in EAE.

### References:

- [1]. Yi P, Schrott L, Castor T P, et al. Bryostatin-1 vs. TPPB: dose-dependent APP processing and PKC- $\alpha$ ,  $\beta$ , and  $\gamma$  isoform activation in SH-SY5Y neuronal cells[J]. Journal of Molecular Neuroscience, 2012, 48(1): 234-244.
- [2]. Shanmukha S, Godfrey W H, Gharibani P, et al. TPPB modulates PKC activity to attenuate neuroinflammation and ameliorate experimental multiple sclerosis[J]. Frontiers in Cellular Neuroscience, 2024, 18: 1373557.

### Background

TPPB ( $\alpha$ -Amyloid Precursor Protein Modulator) is a benzolactam-derived, cell-permeable protein kinase C (PKC) activator ( $K_i = 11.9\text{nM}$ ) [1]. TPPB increases  $\alpha$ -secretase activity, leading to increased secretion of sAPP $\alpha$ , while simultaneously decreasing  $\beta$ -secretase (BACE1) expression and the release of A $\beta$ 40 fragments [2-3]. TPPB is primarily used to treat Alzheimer's disease [4].

In SH-SY5Y cells, TPPB (0.1-100nM; 3h) induces cell secretion of sAPP $\alpha$  [5]. In PC12 cells, TPPB (0-10 $\mu$ M; 3h) promoted the secretion of sAPP $\alpha$  without affecting the expression of full-length APP [6].

In experimental autoimmune encephalomyelitis (EAE) mice model, TPPB (50nmol/kg; ip; 21d; three days a week) can alleviate the neurological deficits [7].

### References:

- [1]. Kozikowski A P, Nowak I, Petukhov P A, et al. New amide-bearing benzolactam-based protein kinase C modulators induce enhanced secretion of the amyloid precursor protein metabolite sAPP $\alpha$ [J]. Journal of medicinal chemistry, 2003, 46(3): 364-373.
- [2]. Yang H Q, Pan J, Ba M W, et al. New protein kinase C activator regulates amyloid precursor protein processing in vitro by increasing  $\alpha$ -secretase activity[J]. European Journal of Neuroscience, 2007, 26(2): 381-391.
- [3]. Hong-Qi Y, Zhi-Kun S, Sheng-Di C. Current advances in the treatment of Alzheimer's disease:

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- focused on considerations targeting A $\beta$  and tau[J]. Translational neurodegeneration, 2012, 1(1): 21.
- [4]. Yang H Q, Li X, Yang W M, et al. Neuroprotective Effects of New Protein Kinase C Activator TPPB Against A $\beta$ 25–35 Induced Neurotoxicity in PC12 Cells[J]. Neurochemical research, 2012, 37(10): 2213-2221.
- [5]. Yi P, Schrott L, Castor T P, et al. Bryostatin-1 vs. TPPB: dose-dependent APP processing and PKC- $\alpha$ , - $\delta$ , and - $\epsilon$  isoform activation in SH-SY5Y neuronal cells[J]. Journal of Molecular Neuroscience, 2012, 48(1): 234-244.
- [6]. Yang H Q, Pan J, Ba M W, et al. New protein kinase C activator regulates amyloid precursor protein processing in vitro by increasing  $\alpha$ -secretase activity[J]. European Journal of Neuroscience, 2007, 26(2): 381-391.
- [7]. Shanmukha S, Godfrey W H, Gharibani P, et al. TPPB modulates PKC activity to attenuate neuroinflammation and ameliorate experimental multiple sclerosis[J]. Frontiers in Cellular Neuroscience, 2024, 18: 1373557.

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