

Product Data Sheet

Product Name: PROTAC HK2 Degrader-1

Cat. No.: GC27499

Chemical Properties

Cas. No. 3033812-84-6

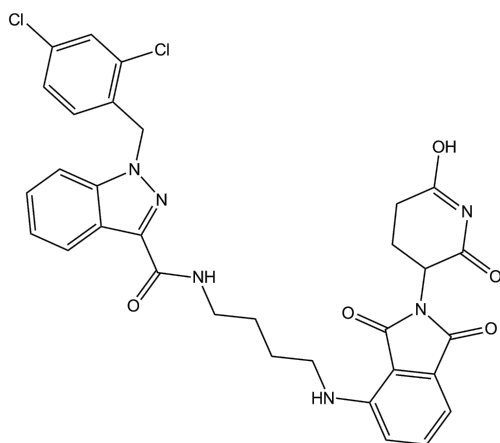
Formula $C_{32}H_{28}Cl_2N_6O_5$ M.Wt 647.51

Solubility 100 mg/mL in DMSO(154.44 mM; Storage -20°C
solubility aided by ultrasound)

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°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



Protocol

Cell experiment [1]:

Cell lines ES2 and ES2TR120 cells

ES2 and ES2TR120 cells were treated with various concentrations (0.1, 0.5, Preparation Method 1.25, 2.5, 5μM) of PROTAC HK2 Degrader-1 for 72h, then cell viability was assessed using the MTT assay.

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

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Reaction
Conditions 0.1, 0.5, 1.25, 2.5, and 5µM; 72h

Applications Treatment with PROTAC HK2 Degradator-1 dose-dependently reduced the viability of both cell types, achieving maximum inhibitory effect at a concentration of 1.25µM.

Animal experiment [2]:

Animal models High-fat-fed *Apoe*^{KO} mice

Preparation Method *Apoe*^{KO} mice fed with high-fat diet were intraperitoneally injected with PROTAC HK2 Degradator-1 (5mg/kg) every other day for 12 weeks, then the severity of atherosclerotic lesions was assessed by hematoxylin and eosin (H&E), Oil Red O, Sirius red, and Masson's trichrome staining.

Dosage form 5mg/kg; every other day; 12 weeks; i.p.

Applications Treatment with PROTAC HK2 Degradator-1 can significantly reduce the severity of atherosclerotic lesions.

References:

[1] Lin T Y, Gu S Y, Lin Y H, et al. Paclitaxel-resistance facilitates glycolytic metabolism via Hexokinase-2-regulated ABC and SLC transporter genes in ovarian clear cell carcinoma[J]. Biomedicine & Pharmacotherapy, 2024, 180: 117452.

[2] Dong M, Zhang Y, Chen M, et al. ASF1A-dependent P300-mediated histone H3 lysine 18 lactylation promotes atherosclerosis by regulating EndMT[J]. Acta Pharmaceutica Sinica B, 2024, 14(7): 3027-3048.

Background

PROTAC HK2 Degradator-1 is a proteolysis-targeting chimera (PROTAC) targeting hexokinase 2 (HK2), generated by conjugating the HK2 inhibitor Lonidamine with the CRBN E3 ubiquitin ligase

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ligand Thalidomide via a linker^[1]. PROTAC HK2 Degradator-1 selectively degrades HK2 through the ubiquitin-proteasome system^[2], leading to blocked glycolysis, mitochondrial damage, and immunogenic cell death, and is commonly used for the treatment and research of breast cancer^[3,4,5].

In vitro, treatment with PROTAC HK2 Degradator-1 (0.1, 0.5, 1.25, 2.5, 5 μ M) for 72h in ES2 and ES2TR120 cells dose-dependently reduced cell viability, achieving maximal inhibitory effect at 1.25 μ M. Treatment with PROTAC HK2 Degradator-1 (1.25 μ M) for 48h in ES2TR120 cells significantly decreased the mitochondrial oxygen consumption rate (OCR)^[6]. Treatment with PROTAC HK2 Degradator-1 (0.5 μ M) for 36h in HCAECs significantly reduced the elevation of lactate levels following stimulation with oxidized low-density lipoprotein (ox-LDL)^[7].

In vivo, PROTAC HK2 Degradator-1 (5mg/kg; every other day) was administered via intraperitoneal injection to high-fat diet-fed *Apoe*^{KO} mice for 12 weeks, significantly reducing the severity of atherosclerotic lesions^[7].

References:

- [1] Sang R, Fan R, Deng A, et al. Degradation of hexokinase 2 blocks glycolysis and induces GSDME-dependent pyroptosis to amplify immunogenic cell death for breast cancer therapy[J]. *Journal of Medicinal Chemistry*, 2023, 66(13): 8464-8483.
- [2] Huang H, Deng A, Pan F, et al. PROTAC-mediated regulation of programmed cell death: From molecular mechanisms to therapeutic breakthroughs[J]. *The Innovation*, 2026.
- [3] Chao Y L, Wang S, Luo L, et al. HIF-1 α exerts a double-edged sword regulatory role in hippocampal neuronal PANoptosis of Alzheimer's disease through HK2/VDAC1/NLRP3 axis and RIPK3 signal[J]. 2025.
- [4] Gao H, He Z, Chen J, et al. Macrocyclic Peptide-Based Dual-Sensor Platform for Linkage-Specific Visualization of Ubiquitin Chain Assembling in Live Cells[J]. *Analytical Chemistry*, 2025, 97(4): 2351-2358.
- [5] Zhang T, Zhou W, Fan T, et al. Lactic acid metabolism: gynecological cancer's Achilles' heel[J]. *Discover Oncology*, 2025, 16(1): 657.
- [6] Lin T Y, Gu S Y, Lin Y H, et al. Paclitaxel-resistance facilitates glycolytic metabolism via Hexokinase-2-regulated ABC and SLC transporter genes in ovarian clear cell carcinoma[J]. *Biomedicine & Pharmacotherapy*, 2024, 180: 117452.

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[7] Dong M, Zhang Y, Chen M, et al. ASF1A-dependent P300-mediated histone H3 lysine 18 lactylation promotes atherosclerosis by regulating EndMT[J]. Acta Pharmaceutica Sinica B, 2024, 14(7): 3027-3048.

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