

## Product Data Sheet

Product Name: VH-298  
Cat. No.: GC19375

### Chemical Properties

Cas. No. 2097381-85-4

SMILES O=C([C@H]1N(C([C@H](C(C)(C)C)NC(C2(CC2)C#N)=O)=O)C[C@H](O)C1)NCC3=CC=C(C4=C(C)N=CS4)C=C3

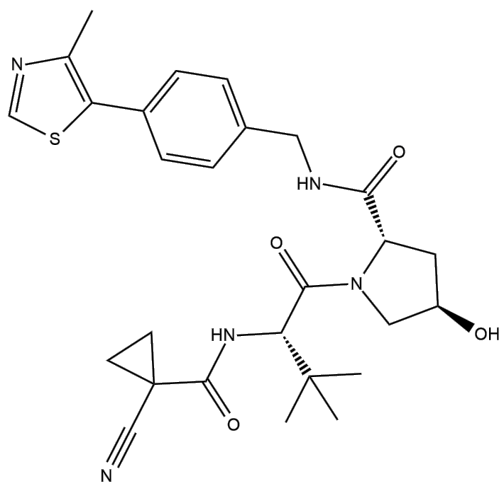
Formula  $C_{27}H_{33}N_5O_4S$  M.Wt 523.65

Solubility DMSO :  $\geq 83.3$  mg/mL (159.08 mM) 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



### Protocol

#### Cell experiment [1]:

Cell lines HeLa cells (human epithelial immortal cell line) and RPE/mRFP-EGFP-SKL cells (hTERT RPE-1 cells stably expressing monomeric red fluorescent protein-enhanced green fluorescent protein-serine-lysine-leucine)

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

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**Preparation Method** HeLa cells and RPE/mRFP-EGFP-SKL cells were maintained in Dulbecco's minimal essential medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin at 37 °C under 5% CO<sub>2</sub>. Cells were treated with VH-298 (50µM).

**Reaction Conditions** 50µM; 48h

**Applications** VH-298 promoted peroxisomal degradation (pexophagy) in an ATG5-dependent manner, increased ubiquitination of the peroxisomal membrane protein ABCD3, and required NBR1. VH-298-induced pexophagy was mediated through activation of HIF-1α transcriptional activity.

### Animal experiment [2]:

**Animal models** Sprague-Dawley rats with streptozotocin-induced hyperglycaemia

**Preparation Method** A full-thickness excisional wound (8mm) was created on the dorsal back of each rat. Rats were treated with VH-298 or PBS by local injection into the wound area every three days. Wound tissues were harvested at postoperative days 7, 14, and 21 for histological analysis.

**Dosage form** 30µM in 100µl; local injection; every three days for 21 days

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**Applications**

VH-298 treatment accelerated wound healing, improved healing pattern, increased granulation tissue area, enhanced collagen accumulation, promoted angiogenesis (more CD31-positive cell clusters), and activated the HIF-1 signalling pathway (increased HIF-1 $\alpha$ , hydroxy-HIF-1 $\alpha$ , and VEGF-A positive cells) in the wound area.

### References:

- [1] Kim YH, Park NY, Jo DS, et al. Inhibition of VHL by VH298 Accelerates Pexophagy by Activation of HIF-1 $\alpha$  in HeLa Cells. *Molecules*. 2024 Jan 18;29(2):482.
- [2] Qiu S, Jia Y, Sun Y, et al. Von Hippel-Lindau (VHL) Protein Antagonist VH298 Improves Wound Healing in Streptozotocin-Induced Hyperglycaemic Rats by Activating Hypoxia-Inducible Factor-(HIF-) 1 Signalling. *J Diabetes Res*. 2019 Feb 17;2019:1897174.

### Background

VH-298 is a selective VHL (Von Hippel-Lindau) inhibitor ( $K_d$ =80-90nM). VH-298 stabilizes HIF- $\alpha$  proteins and triggers a hypoxic response by blocking the interaction between VHL and HIF- $\alpha$  proteins. VH-298 can be used in PROTAC (Proteolysis Targeting Chimera) technology and research related to hypoxia signaling pathways<sup>[1-4]</sup>.

In vitro, VH-298 (30-100 $\mu$ M) was used to treat CD4<sup>+</sup> T cells under Th17-polarizing conditions for 72 hours. VH-298 increased HIF-1 $\alpha$  protein levels, simultaneously upregulated IL-17 and GLUT1 expression, and partially restored Th17 cell differentiation<sup>[5]</sup>. VH-298 (50 $\mu$ M) was used to treat HeLa cells and RPE/mRFP-EGFP-SKL cells for 48 hours. VH-298 significantly promoted peroxisomal degradation (pexophagy), increased ABCD3 ubiquitination, and activated HIF-1 $\alpha$ <sup>[6]</sup>.

In vivo, VH-298 (30 $\mu$ M; 100 $\mu$ l; every three days) was locally injected into the wound area of hyperglycemic rats for 21 days. VH-298 improved wound healing, activated the HIF-1 signaling pathway, and promoted vascularization in rats<sup>[7]</sup>. VH-298 (30 $\mu$ M; 100 $\mu$ l; daily) was injected into the reconstructed attachment site area of a Sprague-Dawley rat model with Achilles tendon-calcaneus rupture. VH-298 improved Achilles tendon-calcaneus healing, increased maximum load and failure energy, and activated the HIF signaling pathway in rats<sup>[8]</sup>.

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- [1] Frost J, Galdeano C, Soares P, et al. Potent and selective chemical probe of hypoxic signalling downstream of HIF- $\alpha$  hydroxylation via VHL inhibition. *Nat Commun.* 2016 Nov 4;7:13312.
- [2] Ling J, Chen H, Huang M, et al. An mRNA vaccine encoding proteasome-targeted antigen enhances CD8<sup>+</sup> T cell immunity. *J Control Release.* 2025 May 10;381:113578.
- [3] Wang Y, Cao Z, Wei Q, et al. VH298-loaded extracellular vesicles released from gelatin methacryloyl hydrogel facilitate diabetic wound healing by HIF-1 $\alpha$ -mediated enhancement of angiogenesis. *Acta Biomater.* 2022 Jul 15;147:342-355.
- [4] Qin X, Wu K, Zuo C, et al. The Expression and Role of Hypoxia-induced Factor-1 $\alpha$  in Human Tenon's Capsule Fibroblasts under Hypoxia. *Curr Eye Res.* 2021 Mar;46(3):417-425.
- [5] Zhang Q, Wang L, Jiang J, et al. Critical Role of AdipoR1 in Regulating Th17 Cell Differentiation Through Modulation of HIF-1 $\alpha$ -Dependent Glycolysis. *Front Immunol.* 2020 Aug 18;11:2040.
- [6] Kim YH, Park NY, Jo DS, et al. Inhibition of VHL by VH298 Accelerates Pexophagy by Activation of HIF-1 $\alpha$  in HeLa Cells. *Molecules.* 2024 Jan 18;29(2):482.
- [7] Qiu S, Jia Y, Sun Y, et al. Von Hippel-Lindau (VHL) Protein Antagonist VH298 Improves Wound Healing in Streptozotocin-Induced Hyperglycaemic Rats by Activating Hypoxia-Inducible Factor-(HIF-) 1 Signalling. *J Diabetes Res.* 2019 Feb 17;2019:1897174.
- [8] Qiu S, Jia Y, Tang J, et al. Von Hippel-Lindau (VHL) protein antagonist, VH298, promotes functional activities of tendon-derived stem cells and accelerates healing of entheses in rats by inhibiting ubiquitination of hydroxy-HIF-1 $\alpha$ . *Biochem Biophys Res Commun.* 2018 Nov 10;505(4):1063-1069.

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