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Print Date: Aug 12th 2021

Certificate of Analysis

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Product Name: **VH 298** **Catalog No.: 6156** **Batch No.: 2**

CAS Number: 2097381-85-4

IUPAC Name: (2*S*,4*R*)-1-((*S*)-2-(1-cyanocyclopropanecarboxamido)-3,3-dimethylbutanoyl)-4-hydroxy-*N*-(4-(4-methylthiazol-5-yl) benzyl)pyrrolidine-2-carboxamide

1. PHYSICAL AND CHEMICAL PROPERTIES

Batch Molecular Formula: $C_{27}H_{33}N_5O_4S.¼H_2O$

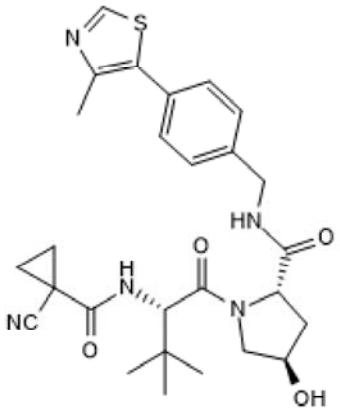
Batch Molecular Weight: 528.15

Physical Appearance: White solid

Solubility: DMSO to 100 mM
ethanol to 100 mM

Storage: Store at -20°C

Batch Molecular Structure:



2. ANALYTICAL DATA

HPLC: Shows 100.0% purity

^{1}H NMR: Consistent with structure

Mass Spectrum: Consistent with structure

Microanalysis:

	Carbon	Hydrogen	Nitrogen
Theoretical	61.4	6.39	13.26
Found	61.1	6.34	13.25

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Product Information

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Description:

VH 298 is a high-affinity inhibitor of E3 ubiquitin ligase VHL (K_d = 80-90 nM). Blocks interaction between VHL and HIF-α downstream of HIF-α hydroxylation, initiating hypoxic response. Results in time- and concentration-dependent accumulation of hydroxylated HIF-α, and upregulates mRNA and protein levels of HIF target genes, with similar transcriptional profile to hypoxia. Cell permeable. Negative control cis VH 298 also available.

Physical and Chemical Properties:

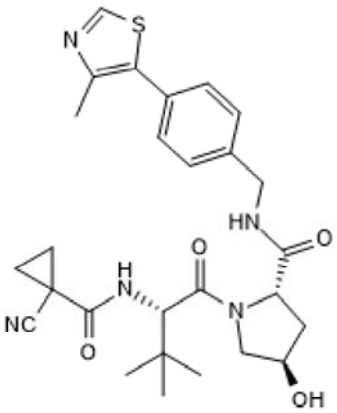
Batch Molecular Formula: $C_{27}H_{33}N_5O_4S.¼H_2O$

Batch Molecular Weight: 528.15

Physical Appearance: White solid

Minimum Purity: ≥98%

Batch Molecular Structure:



Storage: Store at -20°C

Solubility & Usage Info:

DMSO to 100 mM
ethanol to 100 mM

Stability and Solubility Advice:

Some solutions can be difficult to obtain and can be encouraged by rapid stirring, sonication or gentle warming (in a 45-60°C water bath).

Information concerning product stability, particularly in solution, has rarely been reported and in most cases we can only offer a general guide. Our standard recommendations are:

SOLIDS: Provided storage is as stated on the product label and the vial is kept tightly sealed, the product can be stored for up to 6 months from date of receipt.

SOLUTIONS: We recommend that stock solutions, once prepared, are stored aliquoted in tightly sealed vials at -20°C or below and used within 1 month. Wherever possible solutions should be made up and used on the same day.

Licensing Information:

Sold under licence from the University of Dundee

References:

Frost *et al* (2019) RNA-seq analysis of PHD and VHL inhibitors reveals differences and similarities to the hypoxia response. Wellcome Open Res. ***4*** 17. PMID: 30801039.

Soares *et al* (2018) Group-based optimization of potent and cell-active inhibitors of the von Hippel-Lindau (VHL) E3 ubiquitin ligase: structure-activity relationships leading to the chemical probe (2S,4R)-1-((S)-2-(1-Cyanocyclopropanecarboxamido)-3. J.Med.Chem. ***61*** 599. PMID: 28853884.

Frost *et al* (2015) Potent and selective chemical probe of hypoxic signalling downstream of HIF-α hydroxylation via VHL inhibition. Nat.Commun. ***7*** 13312. PMID: 27811928.