Print Date: Dec 15th 2022

Certificate of Analysis

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Product Name: **SIM1** **Catalog No.: 7432** **Batch No.: 1**

CAS Number: 2719051-84-8

IUPAC Name: *N*,*N*'-(11-((2-(((*S*)-1-((2*S*,4*R*)-4-Hydroxy-2-((4-(4-methylthiazol-5-yl)benzyl)carbamoyl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxoethoxy)methyl)-11-methyl-3,6,9,13,16,19-hexaoxahenicosane-1,21-diyl)bis(2-((*S*)-4-(4-chlorophenyl)-2,3,9-trimethyl-6*H*-thieno[3,2-*f*][1,2,4]triazolo[4,3-*a*][1,4]diazepin-6-yl)acetamide)

1. PHYSICAL AND CHEMICAL PROPERTIES

Batch Molecular Formula: $C_{79}H_{98}Cl_2N_{14}O_{13}S_3.¾H_2O$

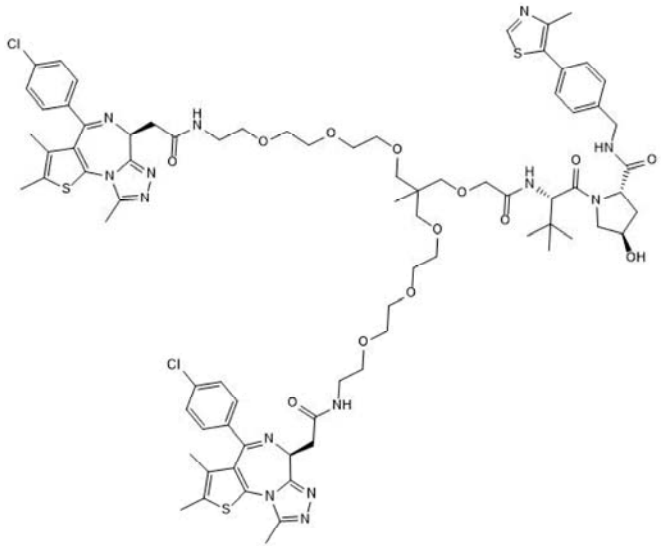
Batch Molecular Weight: 1632.33

Physical Appearance: White solid

Solubility: DMSO to 50 mM

Storage: Store at -20°C

Batch Molecular Structure:



2. ANALYTICAL DATA

HPLC: Shows 99.6% purity

^{1}H NMR: Consistent with structure

Mass Spectrum: Consistent with structure

Microanalysis:

	Carbon	Hydrogen	Nitrogen
Theoretical	58.13	6.14	12.01
Found	57.76	6.1	11.91

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Product Information

Product Name: **SIM1** **Catalog No.: 7432** **1**

CAS Number: 2719051-84-8

IUPAC Name: *N*,*N*'-(11-((2-(((*S*)-1-((2*S*,4*R*)-4-Hydroxy-2-((4-(4-methylthiazol-5-yl)benzyl)carbamoyl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)amino)-2-oxoethoxy)methyl)-11-methyl-3,6,9,13,16,19-hexaoxahenicosane-1,21-diyl)bis(2-((*S*)-4-(4-chlorophenyl)-2,3,9-trimethyl-6*H*-thieno[3,2-*f*][1,2,4]triazolo[4,3-*a*][1,4]diazepin-6-yl)acetamide)

Description:

SIM1 is a potent and selective trivalent PROTAC® Degrader based on BET bromodomain inhibitors linked to a Von Hippel Lindau (VHL) ligand via branched linkers. SIM1 degrades all BET family proteins with a preference for BRD2 (DC_{50} values = 0.7 nM, 1.1 nM and 3.3 nM for BRD4, BRD2 and BRD3, respectively). SIM1 degrades BRD2 more significantly and rapidly than BRD3 and BRD4, and degrades BET proteins with a higher potency than a bivalent degrader. SIM1 also decreases protein levels for Myc and HMOX1 and induces apoptosis in prostate cancer cells.

Physical and Chemical Properties:

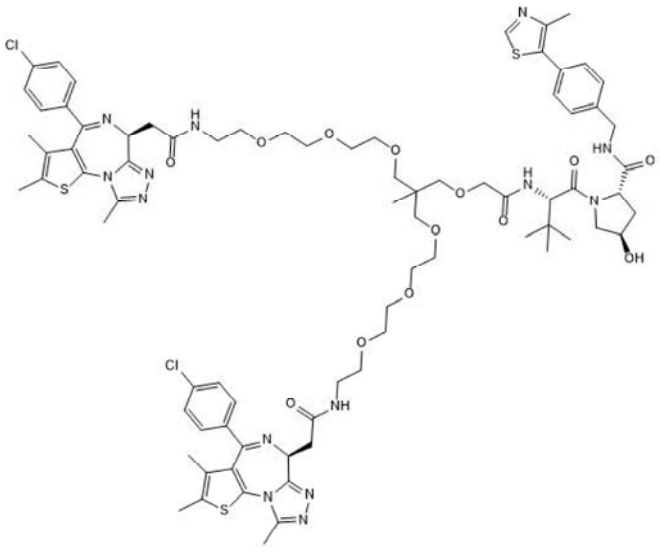
Batch Molecular Formula: $C_{79}H_{98}Cl_2N_{14}O_{13}S_3.¾H_2O$

Batch Molecular Weight: 1632.33

Physical Appearance: White solid

Minimum Purity: ≥98%

Batch Molecular Structure:



Storage: Store at -20°C

Solubility & Usage Info:

DMSO to 50 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:

Imaide *et al* (2021) Trivalent PROTACs enhance protein degradation via combined avidity and cooperativity Nat.Chem.Biol. ***17*** 1157. PMID: 34675414.