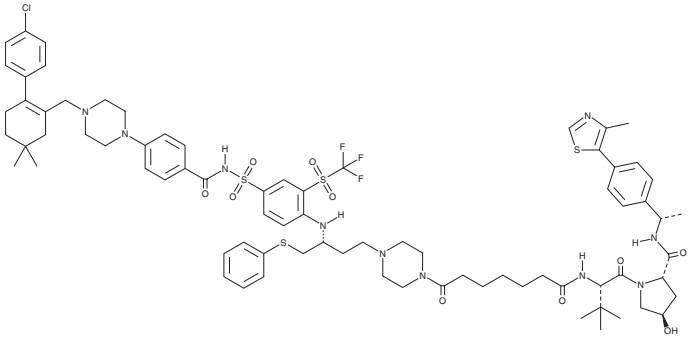
PRODUCT INFORMATION

DT2216

Item No. 37311

CAS Registry No.: 2365172-42-3
Formal Name: (2S,4R)-1-((S)-2-(7-(4-((R)-3-((4-(N-(4-(4-((4'-chloro-4,4-dimethyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methyl)piperazin-1-yl)benzoyl)sulfamoyl)-2-((trifluoromethyl)sulfonyl)phenyl)amino)-4-(phenylthio)butyl)piperazin-1-yl)-7-oxoheptanamido)-3,3-dimethylbutanoyl)-4-hydroxy-N-((S)-1-(4-(4-methylthiazol-5-yl)phenyl)ethyl)pyrrolidine-2-carboxamide
MF: $C_{77}H_{96}ClF_3N_{10}O_{10}S_4$
FW: 1,542.4
Purity: ≥98%
UV/Vis.: λ_{max}: 275, 315 nm
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

DT2216 is supplied as a solid. A stock solution may be made by dissolving the DT2216 in the solvent of choice, which should be purged with an inert gas. DT2216 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of DT2216 in ethanol and DMF is approximately 25 mg/ml and approximately 20 mg/ml in DMSO.

Description

DT2216 is a proteolysis-targeting chimera (PROTAC) composed of the Bcl-2 family inhibitor ABT-263 (Item No. 11500) conjugated to a von Hippel-Lindau (VHL) E3 ligase ligand.[1] It selectively induces degradation of Bcl-xL in MOLT-4 T cell acute lymphoblastic leukemia (T-ALL) cells with a 50% degradation concentration (DC_{50}) value of 63 nM and maximum degradation (D_{max}) of 90.8% over washed isolated human platelets with a D_{max} of 26% at 3 µM. DT2216 selectively binds to Bcl-xL and Bcl-2 over Bcl-W (K_is = 12.82, 1.82, and 300.9 nM, respectively) but does not induce degradation of Bcl-2 or Bcl-W in RS4;11 B-ALL cells at 1 µM. It is cytotoxic to MOLT-4 cells but not washed isolated human platelets (EC_{50}s = 0.052 and >3 µM, respectively) and induces cleavage of caspase-3 in MOLT-4 cells when used at concentrations of 100 and 300 nM. DT2216 (15 mg/kg) reduces tumor volume and weight in a MOLT-4 mouse xenograft model. It acts synergistically with the Bcl-2 inhibitor ABT-199 (Item No. 16233) in an NCI H146 small cell lung cancer (SCLC) mouse xenograft model and the microtubule-stabilizing anticancer agent docetaxel (Item No. 11637) in an MDA-MB-231 breast cancer mouse xenograft model.

Reference

1. Khan, S., Zhang, X., Lv, D., *et al.* A selective BCL-XL PROTAC degrader achieves safe and potent antitumor activity. *Nat. Med.* **25(12)**, 1938-1947 (2019).

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