Product Data Sheet

Product Name: DT2216
Cat. No.: GC39708

Chemical Properties

Cas. No.	2365172-42-3
SMILES	CC1(C)CCC(C2=CC=C(Cl)C=C2)=C(C1)CN3CCN(C4=CC=C(C(NS(=O)(C5=CC(S(C(F)(F)F)(=O)=O)=C(N[C@@H](CSC6=CC=CC=C6)CCN7CCN(C(CCCCCC(N[C@@H](C(C)(C)C)C(N8[C@@H](C[C@@H](O)C8)C(N[C@H](C9=CC=C(C%10=C(N=CS%10)C)C=C9)C)=O)=O)=O)=O)CC7)C=C5)=O)=O)C=C4)CC3
Formula	$C_{77}H_{96}ClF_3N_{10}O_{10}S_4$
M.Wt	1542.36
Solubility	DMSO: 25 mg/mL (16.21 mM)
Storage	Store at -20°C,stored under nitrogen
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	DT2216

Protocol

Cell experiment [1]:

Cell lines	MyLa cells
Preparation Method	MyLa cells were pretreated with or without QVD for 4 h, and then treated with DT2216 for different duration.
Reaction Conditions	0, 0.01, 0.03, 0.1, 0.3μM for 16h
Applications	DT2216 dose- and time-dependently decreased the expression of Bcl-xL but had no effect on the expression of BCL2L1 (the gene that encodes Bcl-xL) mRNA in MyLa cells

Animal experiment [2]:

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal models	Pancreatic cancer PDX models were established by NSG mice
Preparation Method	Animals were treated with vehicle, gemcitabine [20 mg/kg, once a week (every 7 days), i.p.], DT2216 [15 mg/kg, every 4 days, i.p.] and a combination of gemcitabine and DT2216. DT2216 was formulated in 50% phosal 50 PG, 45% miglyol 810N and 5% polysorbate 80.
Dosage form	Intraperitoneal injection, 15 mg/kg, every 4 days
Applications	DT2216 inhibited tumor growth and increasing the survival of the tumor-bearing mice, whereas the combination treatment was more effective than either agent alone without any significant decrease in body weight.

References:

[1]: He Y, Koch R, Budamagunta V, et al. DT2216—a Bcl-xL-specific degrader is highly active against Bcl-xL-dependent T cell lymphomas[J]. Journal of hematology & oncology, 2020, 13(1): 1-13.
[2]: Thummuri D, Khan S, Underwood P W, et al. Overcoming Gemcitabine Resistance in Pancreatic Cancer Using the BCL-XL-Specific Degrader DT2216[J]. Molecular cancer therapeutics, 2022, 21(1): 184-192.

Background

DT2216 is a proteolysis targeting chimera (PROTAC), and targets Bcl-xL for degradation in T-cell lymphomas that depend on the overexpressed proteins of the Bcl-2 family, such as Bcl-2, Bcl-xL,

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

and Mcl-1[1,2].

DT2216 inhibited G-68 cells with IC50 value of 4.02 μM (72hours). Combination of 0.1μM DT2216 and 0.1μM gemcitabine treatment synergistically kills pancreatic cancer cells in vitro [3].

DT2216 showed remarkable effects in xenograft mouse model of human T-cell lymphoma (MyLa, MJ, MAC2A, and L82 cell lines) and T-cell prolymphocytic leukemia (T-PLL), with reduced platelet toxicity compared with ABT263 [1]. DT2216 effect was also present in a patient-derived xenograft tumor model of resistant T-cell ALL, when DT2216 was combined with vincristine, dexamethasone, and L-asparaginase. The median overall survival of mice reached 72 days with combination treatment versus 55 days with DT2216 monotherapy, and 47 days with chemotherapy alone [4].

References:
[1]. He Y, Koch R, Budamagunta V, et al. DT2216—a Bcl-xL-specific degrader is highly active against Bcl-xL-dependent T cell lymphomas[J]. Journal of hematology & oncology, 2020, 13(1): 1-13.
[2]. Khan, S.; Zhang, X.; Lv, D.; Zhang, Q.; He, Y.; Zhang, P.; Liu, X.; Thummuri, D.; Yuan, Y.; Wiegand, J.S.; et al. A selective BCL-XL PROTAC degrader achieves safe and potent antitumor activity. Nat Med. 2019, 25, 1938-1947.
[3]. Thummuri D, Khan S, Underwood P W, et al. Overcoming Gemcitabine Resistance in Pancreatic Cancer Using the BCL-XL-Specific Degrader DT2216[J]. Molecular cancer therapeutics, 2022, 21(1): 184-192.
[4]. Wolska-Washer A, Smolewski P. Targeting protein degradation pathways in tumors: Focusing on their role in hematological malignancies[J]. Cancers, 2022, 14(15): 3778.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA