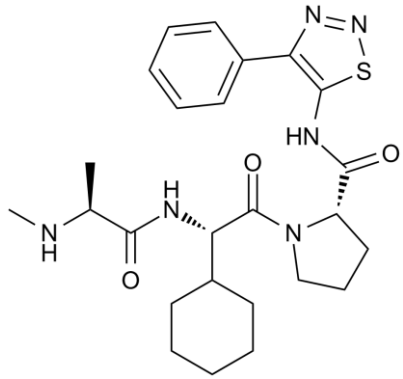
Product Name: GDC-0152

Revision Date: 6/30/2016

Product Data Sheet

Chemical Properties



Product Name:	GDC-0152
Cas No.:	873652-48-3
M.Wt:	498.64
Formula:	C25H34N6O3S
Synonyms:	GDC0152, GDC 0152
Chemical Name:	(2S)-1-[(2S)-2-cyclohexyl-2-[[(2S)-2-(methylamino)propanoyl]amino] acetyl]-N-(4-phenylthiadiazol-5-yl)pyrrolidine-2-carboxamide
Canonical SMILES:	CC(C(=O)NC(C1CCCCC1)C(=O)N2CCCC2C(=O)NC3=C(N=NS3)C4=CC=CC=C4)NC
Solubility:	>25mg/mL in DMSO
Storage:	Store at -20°C
General tips:	For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.
Shopping Condition:	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets :	IAP
Pathways:	Apoptosis >> IAP

Description:

GDC-0152 is a potent small-molecule antagonist of inhibitor of apoptosis (IAP) proteins, including ML-IAP, XIAP, cIAP1 and cIAP2, that binds to the BIR domain of ML-IAP and the BIR3 domains of XIAP, cIAP1 and cIAP2 with values of inhibition constant Ki of 14 nM, 28 nM, 17 nM and 43 nM respectively. GDC-0152 potentially inhibits tumor growth of breast cancer by promoting cIAP1

degradation and inducing caspase-3/7 activation which result in the decreasing of cell viability of breast cancer cells with normal epithelial cells unaffected. In recent studies, GDC-0152 shows its ability to disrupt the binding of XIAP to caspase-9 and the association of ML-IAP, cIAP1 and cIAP2 with Smac in HEK293T cells.

***Reference**:*
Flygare JA, Beresini M, Budha N, Chan H, Chan IT, Cheeti S, Cohen F, Deshayes K, Doerner K, Eckhardt SG, Elliott LO, Feng B, Franklin MC, Reisner SF, Gazzard L, Halladay J, Hymowitz SG, La H, LoRusso P, Maurer B, Murray L, Plise E, Quan C, Stephan JP, Young SG, Tom J, Tsui V, Um J, Varfolomeev E, Vucic D, Wagner AJ, Wallweber HJ, Wang L, Ware J, Wen Z, Wong H, Wong JM, Wong M, Wong S, Yu R, Zobel K, Fairbrother WJ. Discovery of a potent small-molecule antagonist of inhibitor of apoptosis (IAP) proteins and clinical candidate for the treatment of cancer (GDC-0152). J Med Chem. 2012;55(9):4101-4113

Protocol

Cell experiment:

Cell lines	U87MG, GL261, GBM6, GBM9 cell lines, and MDA-MB-231 breast carcinoma cells
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	
Applications	GDC-0152 treatment triggered apoptosis and decreased IAP protein expression in glioblastoma cell lines. Moreover, GDC-0152 (10 nM-10μM) dose-dependently promoted degradation of cIAP1, induced caspase-3/7 activation, and lead to decreased viability of breast cancer cells.

Animal experiment [3]:

Animal models	100 000 U87MG-iRFP cells were injected into the corpus callosum of athymic nude mice; MDA-MB-231 breast cancer xenograft model;
Dosage form	10, 20, 50, and 100 mg/kg; intravenous injection or oral gavage; weekly for 2 months
Applications	GDC-0152 (10 mg/kg or 20 mg/kg) dose-dependently increased survival and slowed down tumor growth of mice bearing intracranial tumors. Moreover, GDC-0152 (10, 50, and 100 mg/kg) suppressed

	tumor growth in dose-dependent manner in the MDA-MB-231 breast cancer xenograft model.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

***Reference**:*

1Flygare, J. A., Beresini, M., Budha, N., Chan, H., Chan, I. T., Cheeti, S., Cohen, F., Deshayes, K., Doerner, K., Eckhardt, S. G., Elliott, L. O., Feng, B., Franklin, M. C., Reisner, S. F., Gazzard, L., Halladay, J., Hymowitz, S. G., La, H., LoRusso, P., Maurer, B., Murray, L., Plise, E., Quan, C., Stephan, J. P., Young, S. G., Tom, J., Tsui, V., Um, J., Varfolomeev, E., Vucic, D., Wagner, A. J., Wallweber, H. J., Wang, L., Ware, J., Wen, Z., Wong, H., Wong, J. M., Wong, M., Wong, S., Yu, R., Zobel, K. and Fairbrother, W. J. (2012) Discovery of a potent small-molecule antagonist of inhibitor of apoptosis (IAP) proteins and clinical candidate for the treatment of cancer (GDC-0152). J Med Chem. 55, 4101-41132Tchoghandjian, A., Souberan, A., Tabouret, E., Colin, C., Denicolai, E., Jiguet-Jiglaire, C., El-Battari, A., Villard, C., Baeza-Kallee, N. and Figarella-Branger, D. (2016) Inhibitor of apoptosis protein expression in glioblastomas and their in vitro and in vivo targeting by SMAC mimetic GDC-0152. Cell Death Dis. 7, e2325

2Tchoghandjian, A., Souberan, A., Tabouret, E., Colin, C., Denicolai, E., Jiguet-Jiglaire, C., El-Battari, A., Villard, C., Baeza-Kallee, N. and Figarella-Branger, D. (2016) Inhibitor of apoptosis protein expression in glioblastomas and their in vitro and in vivo targeting by SMAC mimetic GDC-0152. Cell Death Dis. 7, e2325

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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