Product Name: A-1210477

Revision Date: 6/30/2016

Product Data Sheet

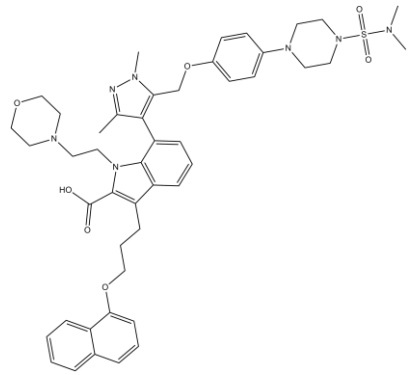
Chemical Properties

Product Name: A-1210477

Cas No.: 1668553-26-1

M.Wt: 850.04

Formula: C46H55N7O7S



Chemical Name: 7-(5-((4-(4-(N,N-dimethylsulfamoyl)piperazin-1-yl)phenoxy)methyl)-1,3-dimethyl-1H-pyrazol-4-yl)-1-(2-morpholinoethyl)-3-(3-(naphthalen-1-yloxy)propyl)-1H-indole-2-carboxylic acid

Canonical SMILES: CC1=NN(C(COC2=CC=C(N3CCN(S(N(C)C)(=O)=O)CC3)C=C2)=C1C4=CC=CC(C(CCCOC5=CC=CC6=CC=CC=C65)=C7C(O)=O)=C4N7CCN8CCOCC8)C

Solubility: Soluble 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 : Bcl-2 Family

Pathways: Apoptosis >> Bcl-2 Family

Description:

A-1210477 is an effective and specific MCL-1 inhibitor with an EC50 value below 5 μmol/L [1]. Selectively, it binds to MCL-1 with an affinity of 0.45 nM [2].

MCL-1, an anti-apoptotic Bcl-2 family member, is an anti-apoptotic protein. It is a key regulator of cancer cell survival [3, 4].

In MCL-1-dependent SVEC cells, treatment with A-1210477 at varying doses, induced cell death in a dose-dependent manner. SYTOX Green exclusion and live-cell imaging were used to determine cell viability. In line with increased potency, cell death was more rapidly induced by A-1210477. To examine the selectivity of A-1210477 for targeting Bcl-2 family members, BcL-xL-, BcL-2-, and MCL-1-dependent SVEC cells were treated with A-1210477. A-1210477 only killed MCL-1-dependent cells. Compared with UMI-77, A-1210477 showed greater potency and specificity as an MCL-1 inhibitor, the EC50 value of UMI-77 is 10 μmol/L [1]. In living cells, A-1210477 disrupted BIM/MCL-1 complexes. In MCL-1-dependent cancer cells, A-1210477 induced the hallmarks of mitochondrial apoptosis. In various malignant cell lines, A-1210477 induced apoptosis, synergizing with navitoclax. Data also demonstrate that A-1210477 acted through an on-target mechanism. It appeared as the first BH3 mimetic targeting MCL-1 [2].

The pharmacokinetics of A-1210477 are not favorable for in vivo use [5].

***Reference**:*

[1]. Lopez J, Bessou M, Riley JS, et al. Mito-priming as a method to engineer Bcl-2 addiction. Nature communications, 2016, 7:10538.
[2]. Besbes S, Mirshahi M, Pocard M, et al. New dimension in therapeutic targeting of BCL-2 family proteins. Oncotarget, 2015, 6(15): 12862.
[3]. Leverson JD, Zhang H, Chen J, et al. Potent and selective small-molecule MCL-1 inhibitors demonstrate on-target cancer cell killing activity as single agents and in combination with ABT-263 (navitoclax). Cell death & disease, 2015, 6(1): e1590.
[4]. Mott JL, Kobayashi S, Bronk SF, et al. mir-29 regulates Mcl-1 protein expression and apoptosis. Oncogene, 2007, 26(42): 6133-6140.
[5]. Opferman JT. Attacking cancer's Achilles heel: antagonism of anti-apoptotic BCL-2 family members. FEBS Journal, 2015.

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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