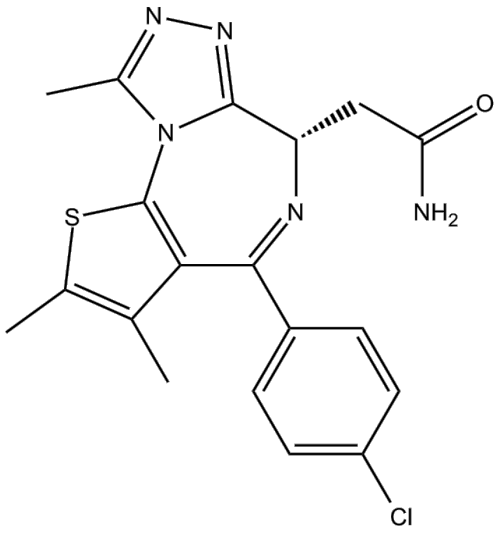
Product Data Sheet

Product Name: CPI-203
Cat. No.: GC14699

Chemical Properties

Cas. No.	1446144-04-2		
Chemical Name	(S)-2-(4-(4-chlorophenyl)-2,3,9-trimethyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-6-yl)acetamide		
SMILES	CC1=C(C)C(C(C2=CC=C(Cl)C=C2)=N[C@@H](CC(N)=O)C3=NN=C(C)N43)=C4S1		
Formula	$C_{19}H_{18}ClN_5OS$	M.Wt	399.9
Solubility	≥ 40mg/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.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	9 MCL cell lines and 2 PBMCs
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 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.
Reacting condition	72 hrs
Applications	In 9 MCL cell lines, CPI-203 exerted a cytostatic effect, with a mean GI50 value of 0.23 μM. At this concentration, the cytotoxicity of CPI-203 to PBMCs was below 25%, which demonstrated its selectivity. In 2 Bortezomib-resistant MCL cell lines with high MYC expression (REC-1 and JBR) and 2 Bortezomib-sensitive MCL cell lines with lower MYC expression (GRANTA-519 and JVM-2), CPI-203 at the dose of 5 μM effectively reduced MYC expression, without causing apoptosis.

Animal experiment [1]:

Animal models	REC-1 tumor-bearing mice
Dosage form	2.5 mg/kg; i.p.; b.i.d.

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Applications	In REC-1 tumor-bearing mice, CPI-203 alone or in combination with Lenalidomide reduced tumor volume by 44% and 62%, respectively. Moreover, tumor glucose uptake was reduced by 86% in the CPI-203 + Lenalidomide group. Immunohistochemical analysis of tumors collected from the CPI-203 + Lenalidomide group showed a decrease in the mitotic index, almost complete disappearance of MYC- and IRF4-positive cells, as well accumulation of cleaved caspase-3-positive cells.
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.

References:

[1]. Moros A, Rodríguez V, Saborit-Villarroya I, Montraveta A, Balsas P, Sandy P, Martínez A, Wiestner A, Normant E, Campo E, Pérez-Galán P, Colomer D, Roué G. Synergistic antitumor activity of lenalidomide with the BET bromodomain inhibitor CPI203 in bortezomib-resistant mantle cell lymphoma. Leukemia. 2014 Mar 18.

Background

CPI-203 is a potent, selectivie and competitive small molecule inhibitor of BET bromodomain with a mean GI50 value of 0.23μM in MCL cell lines [1].

As an inhibitor of BET proteins, CPI-203 inhibits BRD4 in vitro and in cells. It inhibits the specific Ser2 phosphorylation of both endogenous BRD4 and exogenous mutant BRD4 (BRD4 FEE-AAA) in vivo, thus blocking the recruitment of BRD4 to chromatin. CPI-203 is shown to suppress cell growth of 9 MCL cell lines. And in REC-1 cells, treatment of CPI-203 causes the effects of IRF4 expression. CPI-203 marginally activates the apoptotic program in these cells. The CPI-203-lenalidomide combination is reported to be a promising strategy in MCL cases refractory to proteasome inhibition [1, 2].

References:

[1] Moros A, Rodríguez V, Saborit-Villarroya I, Montraveta A, Balsas P, Sandy P, Martínez A,

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Wiestner A, Normant E, Campo E, Pérez-Galán P, Colomer D, Roué G. Synergistic antitumor activity of lenalidomide with the BET bromodomain inhibitor CPI203 in bortezomib-resistant mantle cell lymphoma. Leukemia. 2014 Mar 18.
[2] Devaiah BN, Lewis BA, Cherman N, Hewitt MC, Albrecht BK, Robey PG, Ozato K, Sims RJ 3rd, Singer DS. BRD4 is an atypical kinase that phosphorylates serine2 of the RNA polymerase II carboxy-terminal domain. Proc Natl Acad Sci U S A. 2012 May 1;109(18):6927-32.

Caution: Product has not been fully validated for medical applications. For research use only.
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