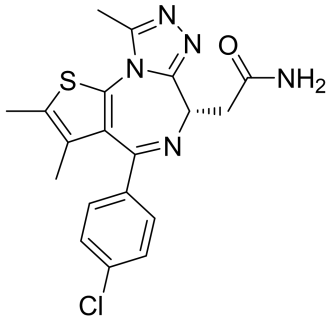
Xcess Biosciences Inc.
7144 N Harlem Ave #169
Chicago, IL 60631 USA

http://www.xcessbio.com
Toll free: 1-866-706-2330
Fax: 1-619- 810-0718
Email: info@xcessbio.com

BET Inhibitor CPI203

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



Molecular Weight:	399.90
Formula:	$C_{19}H_{18}ClN_5OS$
Purity:	≥98%
CAS#:	1446144-04-2
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

CPI203 is a novel potent, selective and cell permeable inhibitor of the bromodomain and extra terminal (BET) family protein BRD4 with an IC_{50} of ~37 nM (BRD4 α-screen assay). It has an IC_{50} of ~99 nM in inhibiting Myc expression in MV4-11 cells and an IC_{50} of ~30 nM in inhibiting IL-6 production in THP-1 cells stimulated with LPS, decreases specific Ser2 phosphorylation of the carboxyl-terminal domain (CTD) of the RNA polymerase II (Pol II) by either endogenous BRD4 or a BRD4 mutant, BRD4 FEE-AAA, that is incapable of binding PTEFb. CPI203 is an analog of JQ-1 but has shown superior bioavailability with oral or intraperitoneal (IP) administration. When mice that were transplanted with primary mouse T-ALL cells, either Fbxw7+/+ or Fbxw7mut/+, were treated with CPI203 at 5 mg/Kg orally twice per day, a significant and rapid reduction in leukemia burden was observed. CPI203 is a useful chemical probe to study the suppression of Myc-dependent cancer development.

How to Use:

In vitro: CPI203 was used at 0.5-1 μM final concentration in various in vitro assays.

In vivo: CPI203 could be dosed to the mice by oral administration at 5 mg/kg twice per day for 7 days.

Reference:

1. Devaiah BN, et al. BRD4 is an atypical kinase that phosphorylates serine2 of the RNA polymerase II carboxy-terminal domain. (2012) Proc Natl Acad Sci U S A. 109(18):6927-32.
2. Bryan King, et al. The Ubiquitin Ligase Fbxw7 Modulates Leukemia-Initiating Cell Activity by Regulating Myc Stability. (2013) Cell 153(7):1552-66.
3. Moros A, et al. Synergistic antitumor activity of lenalidomide with the BET bromodomain inhibitor CPI203 in bortezomib-resistant mantle cell lymphoma. (2014) Leukemia. In press.