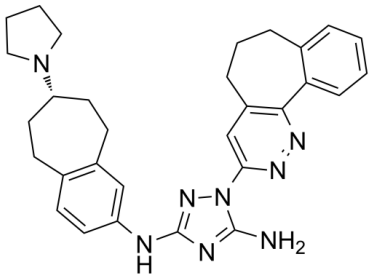
Data Sheet

Product Name:	Bemcentinib
Cat. No.:	CS-1046
CAS No.:	1037624-75-1
Molecular Formula:	C30H34N8
Molecular Weight:	506.64
Target:	TAM Receptor
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : 10.25 mg/mL (20.23 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

Bemcentinib (R428) is a potent and selective inhibitor of **Axl** with an **IC_{50}** of 14 nM. IC50 & Target: IC50: 14 nM (Axl kinase) **In Vitro:** Bemcentinib (R428) (2μM) significantly interferes with mechanisms of migration and invasion of Axlpos melanoma cells at levels comparable to Axl knockdown[1]. Bemcentinib (R428) synergizes with CDDP to enhance suppression of liver micrometastasis[2]. Bemcentinib (R428) (50 nM-1μM) causes a concentration-dependent inhibition of preadipocyte differentiation into mature adipocytes, as evidenced by reduced lipid uptake[3]. **In Vivo:** Bemcentinib (R428) (125 mg/kg, p.o.) significantly blocks MDA-MB-231-luc-D3H2LN metastases development in two independent mouse models of breast cancer dissemination, suppresses both tumor angiogenesis and vascular endothelial growth factor (VEGF)-induced corneal neovascularization in vivo[2]. Bemcentinib (R428) (75 mg/kg/day, 25 mg/kg twice daily, p.o.) makes mice keep on a high-fat diet resulted in significantly reduced weight gain and subcutaneous and gonadal fat mass[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Bemcentinib (R428) is dissolved in 0.25% DMSO at a concentration of 2 μM.[1]Cells maintained for 24 hours in serum-free medium are harvested and transferred to the upper chamber (1.5×10^5 cells per well) of uncoated (migration) or matrigel-coated (invasion) 24-well chambers. RPMI medium containing 10% fetal bovine serum is added to the lower chamber. Bemcentinib (R428) (2 μM) or vehicle (DMSO, 0.25%) is added for 2 hours to cells before loading them in the upper chambers. Both the upper and lower chambers contain the drug or vehicle. Quantification of migrating/invading cells is obtained by measuring their fluorescent signals with a 480/520 nm filter set on an Infinite M1000 microplate reader 20 or 42 hours later, respectively. **Animal Administration:** Bemcentinib (R428) R428 is formulated in 0.5% hydroxypropylmethylcellulose + 0.1% Tween 80 at a concentration of 125 mg/kg.[2] Seven- to 8-wk-old female NCr nu/nu mice are injected intracardially with bioluminescent MDA-MB-231-luc-D3H2LN cell suspension. Oral dosing with Bemcentinib (R428) (125 mg/kg, p.o.) or vehicle twice daily begins 2 h before cell implantation and continue to day 21 (n=20). Metastatic burden is quantified by in vivo bioluminescence imaging on day 22 and analyzed using the Wilcoxon rank sum test.

References:

[1]. Sensi M, et al. Human cutaneous melanomas lacking MITF and melanocyte differentiation antigens express a functional Axl receptor kinase. J Invest Dermatol. 2011 Dec;131(12):2448-57.

[2]. Holland SJ, et al. R428, a selective small molecule inhibitor of Axl kinase, blocks tumor spread and prolongs survival in models of metastatic breast cancer. Cancer Res. 2010 Feb 15;70(4):1544-54.

[3]. Lijnen HR, et al. Growth arrest-specific protein 6 receptor antagonism impairs adipocyte differentiation and adipose tissue development in mice. J Pharmacol Exp Ther. 2011 May;337(2):457-64.

CAIndexNames:

1H-1,2,4-Triazole-3,5-diamine, 1-(6,7-dihydro-5H-benzo[6,7]cyclohepta[1,2-c]pyridazin-3-yl)-N3-[(7S)-6,7,8,9-tetrahydro-7-(1-pyrrolidinyl)-5H-benzocyclohepten-2-yl]-

SMILES:

NC1=NC(NC2=CC(CC[C@@H](N3CCCC3)CC4)=C4C=C2)=NN1C(N=N5)=CC6=C5C7=CC=CC=C7CCC6

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