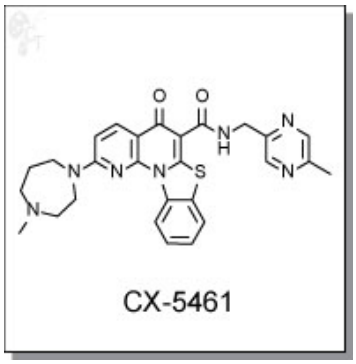
Product Specification Sheet

Product Name: CX-5461

Catalog Number: C2954



Technical information:

Chemical Formula:	$C_{24}H_{28}N_2O_3$
CAS #:	1138549-36-6
Molecular Weight:	513.61
Purity:	> 98%
Appearance:	White solid
Solubility:	Soluble in DMSO up to 1 mM
Chemical Name:	5H-Benzothiazolo[3,2-a][1,8]naphthyridine-6-carboxamide, 2-(hexahydro-4-methyl-1H-1,4-
Storage:	For longer shelf life, store solid powder or DMSO solution at -20°C desiccated.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 1 mM stock solution, add 1.947mL of DMSO for each mg of CX-5461.
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

CX-5461 is a potent, orally bioavailable small molecule inhibitor of rRNA synthesis in cancer cells. It selectively inhibits rRNA synthesis by polymerase I (Pol I) in the nucleolus, but does not inhibit mRNA synthesis by RNA Polymerase II (Pol II), DNA replication or protein synthesis. (In tested cell lines, IC50s for Pol I range from 54nmol/L to 142nmol/L, IC50s for Pol II is higher than 25umol/L.)

CX-5461 exhibits a broad range of antiproliferative activity, with wild-type (wt) p53 cells derived from hematological malignancies being the most sensitive. (p53 wt solid tumors: median IC50=164 nM; p53 wt hematologic cancers cells: median IC50=25 nM). CX-5461 selectively kills cancer cells relative to normal cells. (Median IC50 in normal cells is 5,000 nM.) CX-5461 directly targets the initiation stage of rRNA synthesis, induces both autophagy and senescene, but not apoptosis in a p53-independent process in solid tumor cell lines. In wt p53 hematologic cancer cells, however, inhibition of Pol I results in nucleolar stress and release of ribosomal proteins (RP) from the nucleolus. The RP bind to Mdm2 and release p53 to cause apoptosis in cancer cells. CX-5461 exhibits potent in vivo antitumor activity against both human solid tumor in xenograft models, and leukemia and lymphoma in animal models [1-2].

Reference:

1. Drygin D., et al. Targeting RNA polymerase I with an oral small molecule CX-5461 inhibits ribosomal RNA synthesis and solid tumor growth. Cancer Res. 2011. 71(4):1418-30. Pubmed ID: 21159662

2. Bywater MJ., et al. Inhibition of RNA polymerase I as a therapeutic strategy to promote cancer-specific activation of p53. Cancer Cell. 2012. 22(1):51-65. Pubmed ID: 22789538

To reorder: http://www.cellagentech.com/CX-5461/

For Technical Support: technical@cellagentech.com

Chemicals are sold for research use only, not for clinical or diagnostic use.