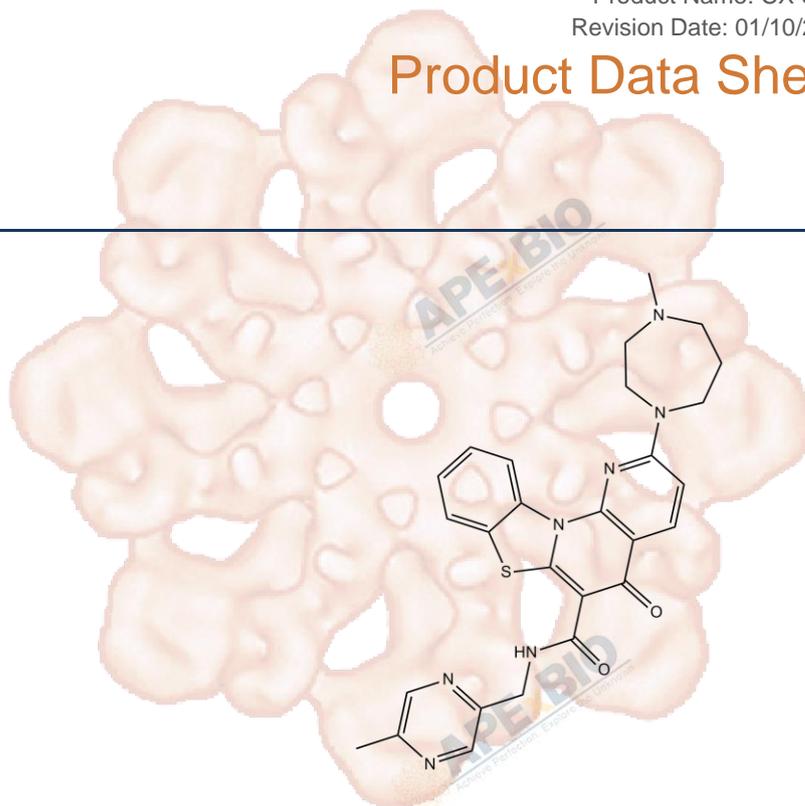


Product Data Sheet

CX-5461

Cat. No.:	A8337
CAS No.:	1138549-36-6
Formula:	C ₂₇ H ₂₇ N ₇ O ₂ S
M.Wt:	513.61
Synonyms:	CX 5461;CX5461
Target:	DNA Damage/DNA Repair
Pathway:	DNA Synthesis
Storage:	Store at -20°C



Solvent & Solubility

insoluble in H₂O; insoluble in EtOH; insoluble in DMSO

In Vitro

Preparing Stock Solutions	Solvent Concentration	Mass		
		1mg	5mg	10mg
	1 mM	1.9470 mL	9.7350 mL	19.4700 mL
	5 mM	0.3894 mL	1.9470 mL	3.8940 mL
	10 mM	0.1947 mL	0.9735 mL	1.9470 mL

Please refer to the solubility information to select the appropriate solvent.

Biological Activity

Shortsummary

Pol I-mediated rRNA synthesis inhibitor

IC₅₀ & Target

142 nM (Pol I), 167 nM (ED50) (HCT-116), 58 nM (ED50) (A375), 74 nM (ED50) (MIA PaCa-2)

In Vitro

Cell Viability Assay

Cell Line: hTERT-immortalized BJ-hTERT human fibroblasts, Human inflammatory breast cancer cell lines SUM 149PT and SUM 190PT, Human eosinophilic leukemia cell line EOL-1, human B cell precursor leukemia cell line SEM, and

	human acute monocytic leukemia cell line THP-1
Preparation method:	Stored at room temperature as 10 mmol/L stock solutions in 50 mmol/L NaH ₂ PO ₄ (pH 4.5)
Reacting conditions:	2 μmol/L, 1 hour
Applications:	Treatment of HCT-116, A375, or MIA PaCa-2 with 2 μmol/L CX-5461 resulted in 40% to 60% reduction of the Pol I enzyme association with the rDNA promoter. CX-5461 significantly depleted the binding of Pol I transcription factors (TF) to the rDNA promoter in HCT-116 cells. In dose-response studies, the IC ₅₀ for inhibition of DNA synthesis in A375 and MIA PaCa-2 cell lines ranged from 16.8 to 27.9 μmol/L. Treatment of solid tumor cell lines with CX-5461 induced cellular senescence and autophagy through selective inhibition of rRNA synthesis. CX-5461 targets the SL1 transcription factor of the Pol I complex and induces autophagy and senescence among solid tumor cell lines and selectively kills cancer cells relative to normal cells.
Animal experiment	
Animal models:	Murine xenograft models of human cancers, pancreatic carcinoma (MIA PaCa-2) and melanoma (A375)
Dosage form:	Administered orally (50 mg/kg) either once daily or every 3 day
Applications:	In murine xenograft models bearing human melanoma cancers (A375), CX-5461 demonstrated significant TGI with TGI equal to 79% on day 32. Human solid tumors grown in murine xenograft models revealed that CX-5461 can be orally administered with favorable pharmacokinetics and an antitumor efficacy. CX-5461 was well tolerated at all tested schedules as judged by the absence of significant changes in animal body weights or overt toxicity.?
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.

In Vivo

Product Citations

1. Rossetti S, Wierzbicki AJ, et al. "Undermining ribosomal RNA transcription in both the nucleolus and mitochondrion: an offbeat approach to target MYC-driven cancer." *Oncotarget*. 2017 Dec 22;9(4):5016-5031. PMID:29435159
2. Rossetti S, Wierzbicki AJ, et al. "Mammary epithelial morphogenesis and early breast cancer. Evidence of involvement of basal components of the RNA Polymerase I transcription machinery." *Cell Cycle*. 2016 Aug 2;0. PMID:27485818

See more customer validations on www.apexbt.com.

References

1. Drygin D, Lin A, Bliesath J, et al. Targeting RNA polymerase I with an oral small molecule CX-5461 inhibits ribosomal RNA

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 APEX BIO 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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