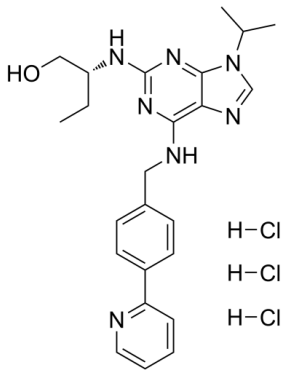
Data Sheet

Product Name:	(R)-CR8 (trihydrochloride)
Cat. No.:	CS-0107260
CAS No.:	1786438-30-9
Molecular Formula:	$C_{24}H_{32}Cl_3N_7O$
Molecular Weight:	540.92
Target:	Apoptosis; CDK; Molecular Glues
Pathway:	Apoptosis; Cell Cycle/DNA Damage; PROTAC
Solubility:	DMSO : 62.5 mg/mL (115.54 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

(R)-CR8 (CR8) trihydrochloride, a second-generation analog of Roscovitine, is a potent **CDK1/2/5/7/9** inhibitor. (R)-CR8 trihydrochloride inhibits CDK1/cyclin B (**IC_{50}**=0.09 μM), CDK2/cyclin A (0.072 μM), CDK2/cyclin E (0.041 μM), CDK5/p25 (0.11 μM), CDK7/cyclin H (1.1 μM), CDK9/cyclin T (0.18 μM) and CK1δ/ε (0.4 μM). (R)-CR8 trihydrochloride induces apoptosis and has neuroprotective effect[1][2]. (R)-CR8 trihydrochloride acts as a molecular glue degrader that depletes cyclin K[3]. ***In Vitro:*** (R)-CR8 (CR8) trihydrochloride (0.1-100 μM; 48 hours) is a potent inducer of apoptotic cell death with an IC_{50} of 0.49 μM for SH-SY5Y cell line [1].

(R)-CR8 trihydrochloride (0.25-10 μM) induces a dose-dependent induction of poly-(ADP-ribose)polymerase (PARP) cleavage[1]. The CDK-bound form of (R)-CR8 trihydrochloride has a solvent-exposed pyridyl moiety that induces the formation of a complex between CDK12-cyclin K and the CUL4 adaptor protein DDB1, bypassing the requirement for a substrate receptor and presenting cyclin K for ubiquitination and degradation ***In Vivo:*** (R)-CR8 trihydrochloride (5 mg/Kg; i.p.) results in a significant reduction in lesion size at 28 days in histological assessment[2].

References:

[1]. Bettayeb K, et al. CR8, a potent and selective, roscovitine-derived inhibitor of cyclin-dependent kinases. Oncogene. 2008 Oct 2;27(44):5797-807.

[2]. Kabadi SV, et al. CR8, a novel inhibitor of CDK, limits microglial activation, astrocytosis, neuronal loss, and neurologic dysfunction after experimental traumatic brain injury. J Cereb Blood Flow Metab. 2014 Mar;34(3):502-13.

[3]. Słabicki M, et al. The CDK inhibitor CR8 acts as a molecular glue degrader that depletes cyclin K [published online ahead of print, 2020 Jun 3]. Nature. 2020;10.1038/s41586-020-2374-x.

CAIndexNames:

1-Butanol, 2-[[9-(1-methylethyl)-6-[[[4-(2-pyridinyl)phenyl]methyl]amino]-9H-purin-2-yl]amino]-, hydrochloride (1:3), (2R)-

SMILES:

CC[C@@H](NC1=NC(NCC2=CC=C(C3=NC=CC=C3)C=C2)=C4N=CN(C(C)C)C4=N1)CO.[H]Cl.[H]Cl.[H]Cl

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

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