ALRN-6924

Cat. No.:	HY-112283
CAS No.:	2000293-14-9
Target:	MDM-2/p53
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the COA.

BIOLOGICAL ACTIVITY

Description	ALRN-6924 is a stapled peptide that blocks interactions between **p53** and both **MDM2** and **MDMX**. ALRN-6924 induces a complete remission in angioimmunoblastic T-cell lymphoma (AITL)[1].
IC_{50} & Target	p53/MDM-2, p53/MDMX[1]

In Vitro

ALRN-6924 (0.01-10 μM; 72 hours) is potently active against all 9 TP53-wild-type cell lines (IC_{50} 100 nM-4 μM) and in MTA cells, which harbor a heterozygous S215G mutation that is believed to confer loss-of-function[1].
In TP53-wild-type lines, ALRN-6924 (1.25-10 μM; 24 hours) induces a dose-dependent increase in levels of both p53 protein and the p53-target p21, which is associated with G_0/G_1 cell cycle arrest and induction of apoptosis[1].

Cell Cytotoxicity Assay[1]

Cell Line:	MTA cells
Concentration:	0.01, 0.1, 1, and 10 μM
Incubation Time:	72 hours
Result:	Potently active in MTA cells with IC_{50} of 100 nM-4 μM.

Western Blot Analysis[1]

Cell Line:	TP53 wt (KI-JK, SUPM2, FEPD) and TP53 mutated (Karpas299) cell lines
Concentration:	1.25, 2.5, 5, and 10 μM
Incubation Time:	24 hours
Result:	Induced a dose-dependent increase in levels of both p53 protein and the p53-target p21 in TP53-wild-type lines, which was associated with G_0/G_1 cell cycle arrest and induction of apoptosis.

In Vivo

ALRN-6924 (20 mg/kg; given intravenously on days 1, 4, and 7) treatment induces p21 expression by IHC and apoptosis in treated tumors in mice. ALRN-6924 is broadly active across bone marrow, spleen and other involved compartments in all 8 models[1].

Animal Model:	Mice with patient-derived xenograft (PDX) models WCTL-91953, DFTL-28776, and WCTL-81162[1]
Dosage:	20 mg/kg
Administration:	Given intravenously on days 1, 4, and 7
Result:	Treatment induced p21 expression by IHC and apoptosis in treated tumors.

REFERENCES

[1]. Ng SY, et al. Targetable vulnerabilities in T- and NK-cell lymphomas identified through preclinical models. Nat Commun. 2018 May 22;9(1):2024.

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