

Product Data Sheet

Product Name: Sulanemadlin

Cat. No.: GC69968

Chemical Properties

Cas. No. 1451199-98-6

Formula $C_{95}H_{140}N_{20}O_{23}$

M.Wt 1930.25

Solubility DMSO : ≥ 100 mg/mL (51.81 mM)

Storage Store at -20°C, Sealed storage, away from moisture and light, under nitrogen

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

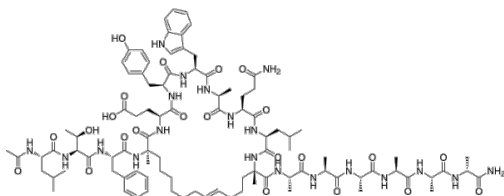
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines MCF-7、ZR-75-1 cells

Preparation Method Cells were plated and treated the following day in duplicates for 24h with either vehicle, Sulanamadlin 10μM, paclitaxel 1μM, or combination of both. Samples were collected, fixed, stained with PI, and analyzed by flow cytometry in the MDACC Flow Cytometry and Cellular Imaging Core Facility.

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Reaction
Conditions 10 μ M; 24h

Applications The cell population in S phase was decreased in both the combination and single agent Sulanemadlin treatment groups.

Animal experiment [2]:

Animal models C57/BL6 mice

Preparation Method Animals were transplanted via tail vein injections of 2.0×10^5 cells, using either MOLM13 or ML2 human AML cells and randomly assigned to experimental groups. All groups were dosed with vehicle (phosphate-buffered saline), Sulanemadlin (8mg/kg), Sulanemadlin (12mg/kg), or Sulanemadlin (20mg/kg) at a frequency of twice per week for 10 weeks or three times per week for 5 weeks. The end point of these in vivo experiments was overall survival. All animals were sacrificed upon visual signs of disease progression. Exclusion criteria included unspecified death and body weight loss of more than 20%.

Dosage form 8, 12, 20mg/kg; twice per week for 10 weeks or three times per week for 5 weeks; i.v.

Applications Sulanemadlin markedly improves survival in AML xenograft models.

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References:

- [1] Pairawan S, Zhao M, Yuca E, et al. First in class dual MDM2/MDMX inhibitor ALRN-6924 enhances antitumor efficacy of chemotherapy in TP53 wild-type hormone receptor-positive breast cancer models[J]. Breast Cancer Research, 2021, 23: 1-15.
- [2] Carvajal L A, Neriah D B, Senecal A, et al. Dual inhibition of MDMX and MDM2 as a therapeutic strategy in leukemia[J]. Science translational medicine, 2018, 10(436): eaao3003.

Background

Sulanemadlin is a membrane-permeable, potent macrocyclic peptidomimetic compound based on the p53 target, and is a stable α -helical peptide^[1]. The mechanism of action of Sulanemadlin is to selectively antagonize the protein-protein interaction between mouse double minute 4 homolog (MDMX) or mouse double minute 2 homolog (MDM2) and p53, thereby relieving the inhibitory state of p53 in tumor cells^[2]. Sulanemadlin can be used to study hematological malignancies^[3].

In vitro, Sulanemadlin (10 μ M) treatment of MCF-7 and ZR-75-1 cells for 24h increased p53 levels, reduced the S phase cell population, and induced cell apoptosis^[4].

In vivo, Sulanemadlin (8, 12, 20mg/kg) was intravenously injected into acute myeloid leukemia (AML) cell xenograft mice, significantly improving the survival rate of mice, and the animals in the treatment group appeared healthy throughout the treatment process without signs of thrombocytopenia^[5]. Sulanemadlin (2.4mg/kg) was administered intravenously to irradiated mice, inducing cell cycle arrest in the mouse bone marrow and providing significant protection against radiation-induced weight loss^[6].

References:

- [1] Guerlavais V, Sawyer T K, Carvajal L, et al. Discovery of Sulanemadlin (ALRN-6924), the first cell-permeating, stabilized α -helical peptide in clinical development[J]. Journal of Medicinal Chemistry, 2023, 66(14): 9401-9417.
- [2] Casciano F, Zauli E, Busin M, et al. State of the art of pharmacological activators of p53 in ocular malignancies[J]. Cancers, 2023, 15(14): 3593.
- [3] Carvajal L A, Ben-Neriah D, Senecal A, et al. Dual inhibition of Mdmx and Mdm2 using an α -helical P53 stapled peptide (ALRN-6924) as a novel therapeutic strategy in acute myeloid

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leukemia[J]. Blood, 2017, 130: 795.

[4] Pairawan S, Zhao M, Yuca E, et al. First in class dual MDM2/MDMX inhibitor ALRN-6924 enhances antitumor efficacy of chemotherapy in TP53 wild-type hormone receptor-positive breast cancer models[J]. Breast Cancer Research, 2021, 23: 1-15.

[5] Carvajal L A, Neriah D B, Senecal A, et al. Dual inhibition of MDMX and MDM2 as a therapeutic strategy in leukemia[J]. Science translational medicine, 2018, 10(436): eaao3003.

[6] Annis A, Sutton D, Aivado M, et al. Alrn-6924, a Dual Inhibitor of MDMX and MDM2, Transiently Induces Cell Cycle Arrest in Bone Marrow and Prevents Toxicity in Mouse Models of Acute Radiation Injury[J]. Blood, 2021, 138(Supplement 1): 2947-2947.

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