Product Datasheet

Siremadlin

Catalog No. **BP-02135** · CAS **1448867-41-1** · Form **free base** · Physical state **other** · Color **White to off-white** · Version **1.0** · Revision **2026-09-03**

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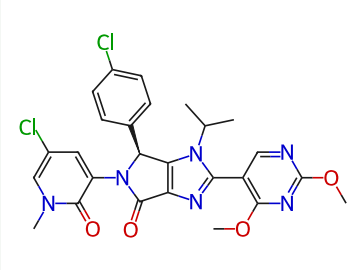
Target	Research area
MDM-2/p53; E1/E2/E3 Enzyme	**Cancer**

Molecular formula	$C_{26}H_{24}Cl_2N_6O_4$
Molecular weight	**555.4130**

STRUCTURE



DESCRIPTION

Siremadlin (NVP-HDM201) is a potent and highly specific MDM-2/p53 inhibitor.

BIOLOGICAL ACTIVITY

In Vitro

Siremadlin (NVP-HDM201) disrupts both human and murine TP53- MDM2 interactions, with nanomolar cellular IC50 values, blocking TP53 degradation.

In Vivo

Siremadlin (NVP-HDM201) is an imidazolopyrrolidinone analogue, showing a very advantageous in vivo profile. NVP-HDM201 has recently entered Phase 1 clinical trials in cancer patients[2]. Constitutive PB mutagenesis in Arf / mice provides a collection of spontaneous tumors with characterized insertional genetic landscapes. Tumors are allografted in large cohorts of mice to assess the pharmacologic effects of Siremadlin (NVP-HDM201). Sixteen out of 21 allograft models are sensitive to Siremadlin (NVP-HDM201) but ultimately relapse under treatment. A comparison of tumors with acquired resistance to Siremadlin (NVP-HDM201) and untreated tumors identified 87 genes that are differentially and significantly targeted by the PB transposon[1]. Siremadlin (NVP-HDM201) administered either daily at a low dose or once at a high dose revealed a differentiated engagement of the p53 molecular response. In contrast to the daily low dose treatment regimen, the single high dose Siremadlin (NVP-HDM201) regimen results in a rapid and dramatic induction of p53-dependent PUMA expression and apoptosis. This is consistent with the finding that a single high dose Siremadlin (NVP-HDM201) treatment, administered orally or intravenously, results in a robust and sustained tumor regression. Overall, both daily and once every 3 weeks dosing regimen shows comparable long term efficacy in preclinical studies. The ongoing clinical trial is currently designed to compare both dosing regimens with regard to efficacy and tolerability.

SOLUBILITY

Soluble in DMSO > 50mg/mL

REFERENCES

[1]. Chapeau EA, et al. Resistance mechanisms to TP53-MDM2 inhibition identified by in vivo piggyBac transposon mutagenesis screen in an Arf-/- mouse model. Proc Natl Acad Sci U S A. 2017 Mar 21;114(12):3151-3156.

[2]. Furet P, et al. Discovery of a novel class of highly potent inhibitors of the p53-MDM2 interaction by structure-based design starting from a conformational argument. Bioorg Med Chem Lett. 2016 Oct 1;26(19):4837-41.

[3]. Holzer, Philipp. “Discovery of Potent and Selective p53-MDM2 Protein-Protein Interaction Inhibitors as Anticancer Drugs.” Chimia vol. 71,10 (2017): 716-721.