

Product Data Sheet

Product Name: AS-99
Cat. No.: GC62615

Chemical Properties

Cas. No. 2323623-93-2

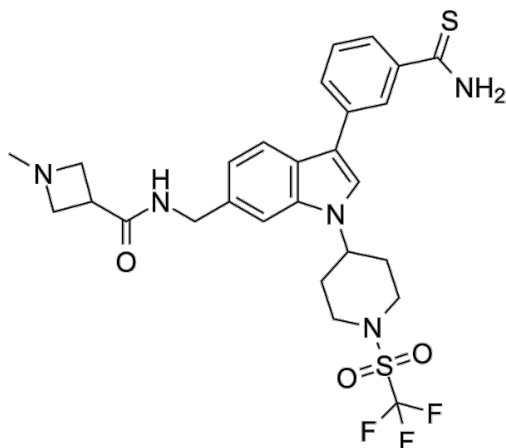
Formula $C_{27}H_{30}F_3N_5O_3S_2$ M.Wt 593.68

Solubility Storage Store at -20°C

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.

Structure



Background

AS-99 is a first-in-class, potent and selective ASH1L histone methyltransferase inhibitor (IC_{50} = 0.79 μ M, K_d = 0.89 μ M) with anti-leukemic activity. AS-99 blocks cell proliferation, induces apoptosis and differentiation, downregulates MLL fusion target genes, and reduces the leukemia burden in vivo[1].

AS-99 is tested against a panel of 20 histone methyltransferases, including NSD1, NSD2, NSD3, and SETD2. NO significant inhibition is observed at 50 μ M of AS-99 on any of the tested histone methyltransferases, indicating over 100-fold selectivity towards ASH1L[1]. AS-99 shows effect on the growth of the MLL leukemia cells (MV4;11, MOLM13, KOPN8, RS4;11) with the GI50 values ranging

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

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from 1.8 μ M to 3.6 μ M[1]. AS-99 (1-8 μ M; 7 days) also induces apoptosis in the MLL leukemia cells, but not in the K562 cells, as assessed by the quantification of the Annexin V positive cells[1]. AS-99 suppresses MLL fusion driven transcriptional programs[1].

AS-99 (30 mg/kg; i.p.; q.d., treated for 14 consecutive days) reduces leukemia burden in mice[1]. AS-99 is used for in vivo studies in mice, which reveals favorable exposure in plasma upon i.v. and i.p. administration (AUC = 9701 hr* ng/mL and 10,699 hr* ng/mL, respectively), suitable half-life (~5-6 h) and C_{max} >10 μ M[1].

[1]. David S. Rogawski, Jing Deng, Hao Li, Tomasz Cierpicki, Jolanta Grembecka, et al. Discovery of first-in-class inhibitors of ASH1L histone methyltransferase with anti-leukemic activity. Nat Commun. 2021 May 14;12(1):2792.

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