

Product Data Sheet

Product Name: LMK 235

Cat. No.: GC13237

Chemical Properties

Cas. No. 1418033-25-6

Chemical Name N-((6-(hydroxyamino)-6-oxohexyl)oxy)-3,5-dimethylbenzamide

SMILES CC1=CC(C)=CC(C(NOCCCCC(=O)NO)=O)=C1

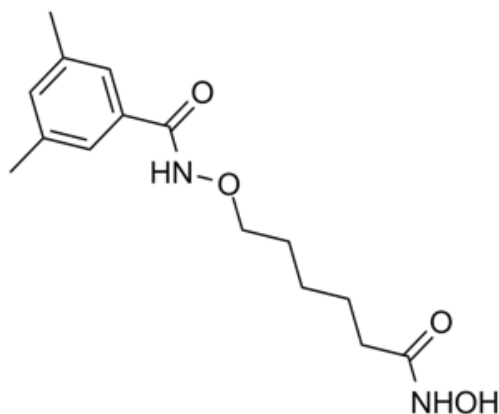
Formula $C_{15}H_{22}N_2O_4$ M.Wt 294.35

Solubility $\geq 9.95\text{mg/mL}$ in DMSO, ≥ 53.8 mg/mL in EtOH with ultrasonic 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



Protocol

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

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Cell experiment: The rate of cell survival under the action of test substances is evaluated by an improved MTT assay. The assay is based on the ability of viable cells to metabolize yellow 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) to violet formazan that can be detected spectrophotometrically. In brief, A2780, Cal27, Kyse510, and MDA-MB-231 cell lines are seeded at a density of 5000, 7000, 8000, and 10 000 cells/well in 96-well plates. After 24 h, cells are exposed to increased concentrations of the test compounds. Incubation is ended after 72 h, and cell survival is determined by addition of MTT solution (5 mg/mL in phosphate buffered saline). The formazan precipitate is dissolved in DMSO. Absorbance is measured at 544 and 690 nm in a FLUOstar microplate reader[1].

References:

- [1]. Marek L, et al. Histone deacetylase (HDAC) inhibitors with a novel connecting unit linker region reveal a selectivity profile for HDAC4 and HDAC5 with improved activity against chemoresistant cancer cells. J Med Chem. 2013 Jan 24;56(2):427-36.
- [2]. Li A, et al. HDAC5, a potential therapeutic target and prognostic biomarker, promotes proliferation, invasion and migration in human breast cancer. Oncotarget. 2016 Jun 21;7(25):37966-37978.
- [3]. Trazzi S, et al. HDAC4: a key factor underlying brain developmental alterations in CDKL5 disorder. Hum Mol Genet. 2016 Sep 15;25(18):3887-3907.

Background

Description:

IC50: cytotoxicity IC50 (490 nm for A2780; 320 nm for A2780 CisR); HDAC inhibition (650 nM for A2780; 320 nm for A2780 CisR)

Histone deacetylases (EC 3.5.1.98, HDAC) are a class of enzymes that remove acetyl groups (O=C-CH₃) from an ε-N-acetyl lysine amino acid on a histone, allowing the histones to wrap the DNA more tightly. Histone deacetylase inhibitors (HDIs) have a long history of use in psychiatry and neurology as mood stabilizers and anti-epileptics, for example, valproic acid. In more recent times, HDIs are being studied as a mitigator or treatment for neurodegenerative diseases.

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In vitro: LMK235 showed similar effects compared to vorinostat on inhibition of cellular HDACs in a pan-HDAC assay but enhanced cytotoxic effects against the human cancer cell lines A2780, Cal27, Kyse510, and MDA-MB231. LMK235 shows nanomolar inhibition of HDAC4 and HDAC5, whereas vorinostat and TSA inhibit HDAC4 and HDAC5 in the higher micromolar range. In contrast to vorinostat, LMK235 showed a novel HDAC isoform selectivity profile with preference for HDAC4 and HDAC5, which are inhibited with low nanomolar IC₅₀ values [1].

In vivo: In a mouse in-vivo study, synergistic inhibition was demonstrated for LMK235 and Cytarabine in proliferation assays and in colony formation assays. These findings demonstrate that in vivo RNAi screening for therapeutic efficacy is feasible. HDAC4 might be an important target to enhance efficacy of anti-leukemic drugs [2].

Clinical trial: LMK235 is currently in the preclinical development and no clinical trial is ongoing.

References:

[1] Marek L, Hamacher A, Hansen FK, Kuna K, Gohlke H, Kassack MU, Kurz T. Histone deacetylase (HDAC) inhibitors with a novel connecting unit linker region reveal a selectivity profile for HDAC4 and HDAC5 with improved activity against chemoresistant cancer cells. *J Med Chem.* 2013;56(2):427-36.

[2] Stephanie Lettermann, Konstantin Agelopoulos, Christian Rohde, Beate Lindtner, Linda Marek, Georg Hempel, Matthias Stelljes, Wolfgang E. Berdel, Thomas Kurz and Carsten Müller-Tidow. *In Vivo RNAi Screening Identifies HDAC4 As a Mediator Of Chemoresistance In Acute Myeloid Leukemia.* 55th ASH Annual Meeting and Exposition (2013)
(<https://ash.confex.com/ash/2013/webprogram/Paper60036.html>)

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