

Product Data Sheet

Product Name: VY-3-135

Cat. No.: GC64681

Chemical Properties

Cas. No. 1824637-41-3

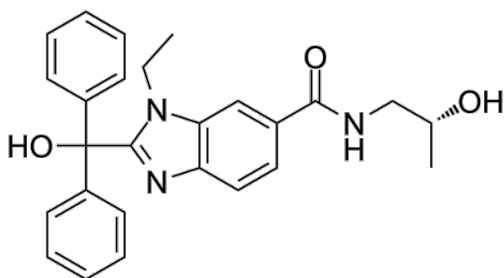
Formula C₂₆H₂₇N₃O₃ M.Wt 429.51

Solubility DMSO : 100 mg/mL (232.82 mM; Need ultrasonic) Storage 4°C, protect from light

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 [1]:

Cell lines MDA-MB-231BR cells

Preparation Method To assess colony formation survival, 1×10^5 MDA-MB-231BR cells were seeded in 6-well plates until cell confluence reached 70% to 80% and then treated with 100 μ M VY-3-135 for 24, 48, and 72h, respectively. Cells were digested with trypsin and counted with a blood cell counting plate. A total of 1×10^4 cells per treatment were seeded in 6-well plates containing fresh medium and cultured for 24h. After 24h of culture, cells were washed twice with PBS, stained with crystal violet for 30min, and washed twice more with distilled water. Colonies larger than 50 microns were counted. For crystal violet staining, 0.5% crystal violet was dissolved in a 1:1 methanol-water solution.

Reaction Conditions 100 μ M; 24, 48, 72h

Applications VY-3-135 significantly inhibited the viability of MDA-MB-231BR cells in a time-dependent manner.

Animal experiment [2]:

Animal models BALB/c mice

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Overall, 2.5×10^4 T11 cells were dissolved in 100 μ l PBS and injected into the subcutaneous hypochondrium of 12-week-old female BALB/c mice. Mice were randomized to receive vehicle (10% dimethyl sulfoxide, 20% solotol, and 70% water with 0.5% Tween-20) by intraperitoneal (ip) injection and 100mg/kg of VY-3-135 by oral gavage daily starting the day after tumor injection. The whole Preparation Method procedure lasted for 30 days. Tumors were measured with calipers three times a week, and tumor volume was calculated as the weekly mean of $(L \times W^2)/2$ (where L is the longer of the two measurements). At the end of the study, all tumors were excised, snap-frozen in liquid nitrogen and stored at -80°C for downstream analysis, or immediately stored in formalin for further analysis and processing.

Dosage form 100mg/kg/day for 30 days; p.o.

Applications VY-3-135 treatment significantly suppressed tumor growth and significantly improved the survival rate of mice.

References:

- [1] Esquea E M, Ciraku L, Young R G, et al. Selective and brain-penetrant ACSS2 inhibitors target breast cancer brain metastatic cells[J]. *Frontiers in pharmacology*, 2024, 15: 1394685.
- [2] Miller K D, O'Connor S, Pniewski K A, et al. Acetate acts as a metabolic immunomodulator by bolstering T-cell effector function and potentiating antitumor immunity in breast cancer[J]. *Nature cancer*, 2023, 4(10): 1491-1507.

Background

VY-3-135 is a potent and orally stable ACSS2 inhibitor with an IC₅₀ value of $44 \pm 3.85 \text{ nM}$ and a water solubility of $21.7 \mu\text{M}$ ^[1]. VY-3-135 is currently used in anti-breast cancer studies and derivative screening assays^[2-3].

In vitro, VY-3-135 treatment at $100 \mu\text{M}$ for 48 hours significantly inhibited the proliferation and cell survival of MDA-MB-231BR cells and 4T1 cells^[4].

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In vivo, VY-3-135 treatment (100mg/kg) through oral gavage daily for 30 days significantly inhibited tumor growth and obviously improved survival in a mouse model of breast cancer xenografts, resulting in enhanced immune cell infiltration and activation and elevated expression of interferon signaling^[5].

References:

- [1] Miller K D, Pniewski K, Perry C E, et al. Targeting ACSS2 with a transition-state mimetic inhibits triple-negative breast cancer growth[J]. Cancer research, 2021, 81(5): 1252-1264.
- [2] Miller K D, Schug Z T. Targeting acetate metabolism: Achilles' nightmare[J]. British journal of cancer, 2021, 124(12): 1900-1901.
- [3] Hlavaty S I, Salcido K N, Pniewski K A, et al. ACSS1-dependent acetate utilization rewires mitochondrial metabolism to support AML and melanoma tumor growth and metastasis[J]. Cell reports, 2024, 43(12).
- [4] Esquea E M, Ciraku L, Young R G, et al. Selective and brain-penetrant ACSS2 inhibitors target breast cancer brain metastatic cells[J]. Frontiers in pharmacology, 2024, 15: 1394685.
- [5] Miller K D, O'Connor S, Pniewski K A, et al. Acetate acts as a metabolic immunomodulator by bolstering T-cell effector function and potentiating antitumor immunity in breast cancer[J]. Nature cancer, 2023, 4(10): 1491-1507.

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