

Product Data Sheet

Product Name: ML 348
Cat. No.: GC18039

Chemical Properties

Cas. No. 899713-86-1

Chemical Name N-(2-chloro-5-(trifluoromethyl)phenyl)-2-(4-(furan-2-carbonyl)piperazin-1-yl)acetamide

SMILES C1C=C(NC(CN2CCN(C(C3=CC=CO3)=O)CC2)=O)C=C(C(F)(F)F)C=C1

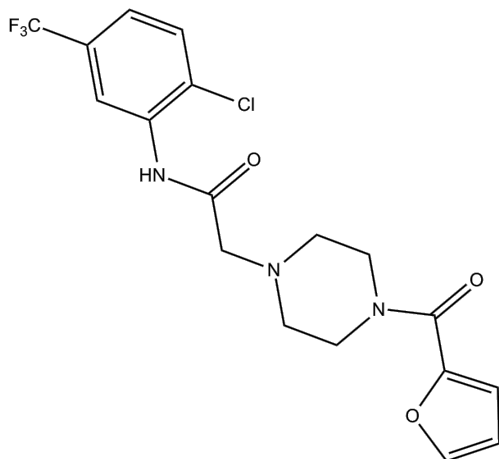
Formula $C_{18}H_{17}ClF_3N_3O_3$ M.Wt 415.79

Solubility $\geq 19.1\text{mg/mL}$ in DMSO 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

Cell experiment [1]:

Cell lines NRAS mutant melanoma cells

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

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Preparation Method Cells were treated with ML 348 ($\leq 12.5\mu\text{M}$) for 6 hours to assess acute signaling changes.

Reaction Conditions $\leq 12.5\mu\text{M}$; 6h

Applications ML 348 caused minor increases in AKT phosphorylation but did not alter ERK or S6 phosphorylation, indicating no biologically significant impact on NRAS downstream signaling pathways.

Animal experiment [2]:

Animal models CAG140 knock-in HD mice (Huntington disease model)

Preparation Method Mice were subcutaneously infused with ML 348 (0.3mg/kg/day) via Alzet osmotic pumps for 28 days. Behavioral tests and tissue analyses were conducted during and after treatment.

Dosage form 0.3mg/kg; subcutaneous infusion; Chronic administration; Daily for 28 days.

Applications ML 348 treatment restored motor coordination in the horizontal ladder test (reduced error rate and crossing time), improved balance in rotarod tests, and alleviated anxio-depressive behaviors in novelty-suppressed feeding tests. ML 348 increased brain palmitoylation levels, reduced mutant huntingtin (mHTT) nuclear accumulation, and restored corticostriatal synapse density.

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References:

- [1] Vujic I, Sanlorenzo M, Esteve-Puig R, et al. Acyl protein thioesterase 1 and 2 (APT-1, APT-2) inhibitors palmostatin B, ML348 and ML349 have different effects on NRAS mutant melanoma cells. *Oncotarget*. 2016 Feb 9;7(6):7297-306.
- [2] Virlogeux A, Scaramuzzino C, Lenoir S, et al. Increasing brain palmitoylation rescues behavior and neuropathology in Huntington disease mice. *Sci Adv*. 2021 Mar 31;7(14):eabb0799.

Background

ML 348 is a selective and reversible lysophospholipase 1 (LYPLA1) inhibitor with an IC₅₀ of approximately 210nM, exhibiting 14-fold selectivity for LYPLA1 over LYPLA2^[1-2]. ML 348 can be used to study protein palmitoylation and the biological functions of LYPLA1, and it significantly inhibits enzymatic activity in heart, lung, and kidney tissues^[3-4].

In vitro, pretreatment of porcine alveolar macrophages (PAMs) with ML 348 (1μM) for 24–36 hours, followed by infection with porcine reproductive and respiratory syndrome virus (PRRSV-2; MOI=0.1), significantly suppressed viral ORF7 mRNA transcription and nucleocapsid protein (N protein) expression, while reducing viral titers^[5]. Pretreatment of NRAS-mutant melanoma cells with ML 348 (≤12.5μM) for 6 hours did not significantly affect cell viability and did not markedly inhibit phosphorylation of the NRAS downstream signaling pathways ERK and AKT^[6].

In vivo, chronic subcutaneous infusion of ML 348 (0.3mg/kg) for 28 days in 7-month-old symptomatic CAG140 Huntington's disease knock-in mice effectively crossed the blood-brain barrier, significantly improved motor coordination and alleviated anxiety-depressive-like behaviors, and reversed neuropathological changes^[7]. Oral administration of ML 348 (70mg/kg) for 90 days in 12-month-old symptomatic 3KL α-synucleinopathy model mice significantly enhanced motor coordination, spatial memory, and long-term memory, and restored hippocampal synaptic plasticity^[8].

References:

- [1] Adibekian A, Martin BR, Chang JW, et al. Characterization of a Selective, Reversible Inhibitor of Lysophospholipase 1 (LYPLA1). National Center for Biotechnology Information (US); 2010- 2013 Apr 08.
- [2] Hulce JJ, Joslyn C, Speers AE, et al. An in Vivo Active Carbamate-based Dual Inhibitor of

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Lysophospholipase 1 (LYPLA1) and Lysophospholipase 2 (LYPLA2). National Center for Biotechnology Information (US); 2013 Dec 9.

[3] Won SJ, Davda D, Labby KJ, et al. Molecular Mechanism for Isoform-Selective Inhibition of Acyl Protein Thioesterases 1 and 2 (APT1 and APT2). ACS Chem Biol. 2016 Dec 16;11(12):3374-3382.

[4] Gu M, Jiang H, Tan M, et al. Palmitoyltransferase DHHC9 and acyl protein thioesterase APT1 modulate renal fibrosis through regulating β -catenin palmitoylation. Nat Commun. 2023 Oct 21;14(1):6682.

[5] Jing H, Liu Y, Song Y, et al. ZDHHC3-LYPLA1 regulates PRRSV-2 replication through reversible palmitoylation. Vet Microbiol. 2025 Feb;301:110368.

[6] Vujic I, Sanlorenzo M, Esteve-Puig R, et al. Acyl protein thioesterase 1 and 2 (APT-1, APT-2) inhibitors palmostatin B, ML348 and ML349 have different effects on NRAS mutant melanoma cells. Oncotarget. 2016 Feb 9;7(6):7297-306.

[7] Virlogeux A, Scaramuzzino C, Lenoir S, et al. Increasing brain palmitoylation rescues behavior and neuropathology in Huntington disease mice. Sci Adv. 2021 Mar 31;7(14):eabb0799.

[8] Moors TE, Li S, McCaffery TD, et al. Increased palmitoylation improves estrogen receptor alpha-dependent hippocampal synaptic deficits in a mouse model of synucleinopathy. Sci Adv. 2023 Nov 15;9(46):eadj1454.

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