

Product Data Sheet

Product Name: RG2833
Cat. No.: GC10423

Chemical Properties

Cas. No. 1215493-56-3

Chemical Name N-[6-(2-aminoanilino)-6-oxohexyl]-4-methylbenzamide

SMILES CC1=CC=C(C=C1)C(=O)NCCCCC(=O)NC2=CC=CC=C2N

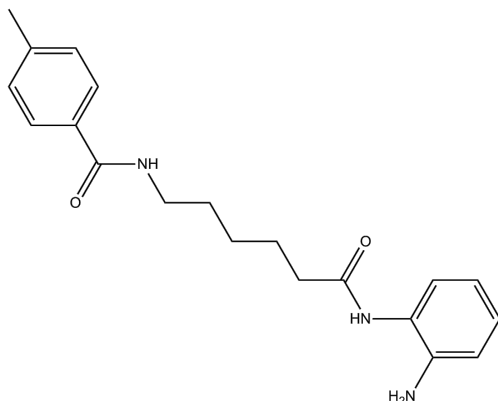
Formula $C_{20}H_{25}N_3O_2$ M.Wt 339.43

Solubility ≥ 16.95 mg/mL in DMSO, ≥ 8.05 mg/mL in EtOH with ultrasonic and warming
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 Unstimulated peripheral blood mononuclear cells (PBMC) from FRDA Patients.

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

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Preparation method The solubility of this compound in DMSO is >17mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 1, 2.5, 5 or 10 µM for 48 hours

Applications RG2833 dose-dependently upregulates frataxin mRNA and protein levels in cultures of unstimulated peripheral blood mononuclear cells (PBMC) from FRDA patients.

Animal experiment [2]:

Animal models GAA knock-in mice

Dosage form 150 mg/kg, subcutaneous injection

Application RG2833 corrected frataxin deficiency and increases histone acetylation in the brain and heart of KIKI mice (a GAA repeat based FRDA mouse model) without acute toxicity signs.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Rai M, et al. Two new pimelic diphenylamide HDAC inhibitors induce sustained frataxin upregulation in cells from Friedreich's ataxia patients and in a mouse model. PLoS One. 2010, 5(1), e8825.

Background

RG2833 is a brain-penetrant HDAC inhibitor with IC₅₀ of 60 nM and 50 nM for HDAC1 and HDAC3, respectively.

The Ki values of RG2833 for HDAC1 and HDAC3 are 32 nM and 5 nM, respectively. RG2833 is highly active in the whole tested concentration range from 1 to 10 µM. Continuous incubation with RG2833 slows the increase in frataxin protein, and when the compound is removed, frataxin protein levels rapidly increased in the cells from patient P13^[1]. RG2833 produces significant increases in brain aconitase enzyme activity, together with reduction of neuronal pathology of the dorsal root ganglia (DRG)^[2].

RG2833 (150 mg/kg) is able to correct frataxin deficiency in the brain and heart of KIKI mice 24 hours after a single injection, but not when lower doses are used. When followed in time, the frataxin mRNA increase induced by RG2833 in the KIKI mouse can be first detected at 12 hours and reach a maximum at 24 hours in both brain and heart^[1]. RG2833 (100 mg/kg, s.c.) is well tolerated in chronic dosing of mice without toxicity. RG2833 improves motor coordination of YG8R FRDA mice. RG2833 increases frataxin protein expression in the brain of YG8R FRDA mice^[2]. RGFP109 (30 mg/kg, p.o. once daily for 6 days) has no acute effects on dyskinesia after single or 6 days once-daily treatment. One week following cessation of RGFP109, dyskinesia and duration of ON-time with disabling dyskinesia are reduced by 37% and 50%, respectively^[3].

References:

[1]. Rai M, et al. Two new pimelic diphenylamide HDAC inhibitors induce sustained frataxin upregulation in cells from Friedreich's ataxia patients and in a mouse model. PLoS One. 2010, 5(1), e8825.

[2]. Sandi C, et al. Prolonged treatment with pimelic o-aminobenzamide HDAC inhibitors ameliorates the disease phenotype of a Friedreich ataxia mouse model. Neurobiol Dis. 2011, 42(3), 496-505.

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[3]. Johnston TH, et al. RGFP109, a histone deacetylase inhibitor attenuates L-DOPA-induced dyskinesia in the MPTP-lesioned marmoset: a proof-of-concept study. *Parkinsonism Relat Disord.* 2013, 19(2), 260-264.

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