

Tasquinimod

Catalog No: tcsc0898



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

CAS No:

254964-60-8

Formula:

$C_{20}H_{17}F_3N_2O_4$

Pathway:

Epigenetics;Cell Cycle/DNA Damage

Target:

HDAC;HDAC

Purity / Grade:

>98%

Solubility:

DMSO : ≥ 42 mg/mL (103.36 mM)

Alternative Names:

ABR-215050

Observed Molecular Weight:

406.36

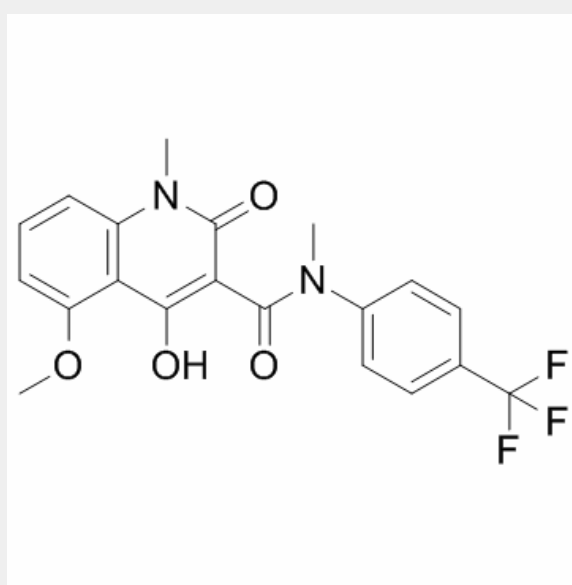
Product Description

Tasquinimod is an oral allosteric modulator of **HDAC4** with a K_d of 10–30 nM for the regulatory Zn^{2+} binding domain of HDAC4.

IC50 & Target: K_d : 10-30 nM (HDAC4)^[1]

In Vitro: Tasquinimod suppresses hypoxia induced decrease in histone acetylation without lowering HDAC expression or directly inhibiting HDAC activity. Tasquinimod binds allosterically within the regulatory Zinc domain of HDAC4 with a K_d of 10-30 nM, which results in inhibition of co-localization of N-CoR/HDAC3, thereby inhibiting deacetylation of histones and HDAC4 client transcription factors, such as HIF-1 α . TAMs secrete angiogenic factors like VEGF, FGF, TNF- α , and TGF- β when myeloid-derived suppressor cells differentiate. Tasquinimod can suppress tumor angiogenesis due to inhibition of S100A9/TLR4 dependent MDSCs tumor infiltration and/or to inhibition of HDAC4/N-CoR/HDAC3 dependent deacetylation of HIF-1 α by MDSCs suppressing their differentiation into TAMs.^[1] Tasquinimod, an orally active quinoline-3-carboxamide, binds with high affinity to HDAC4 and S100A9 in cancer and infiltrating host cells within compromised tumor microenvironment inhibiting adaptive survival pathways needed for an angiogenic response^[2]. At 10 μ M Tasquinimod, the TSP1 mRNA expression is elevated at 6 h and peaked after 72 h. Moreover, after 72 h exposure the TSP1 mRNA levels is already elevated at a dose of 1 μ M Tasquinimod, indicating that Tasquinimod-induced changes in TSP1 mRNA expression occurs in a dose range. At higher dose levels (i.e. 50-100 μ M) the mRNA levels decline at 72 h, indicating additional drug effects at these concentrations. The up-regulation of TSP1 mRNA in LNCaP cells by Tasquinimod is manifested by an increased expression of TSP1 protein, as shown by western blot analysis of cell lysates prepared from cells cultured for 24 h and 72 h. Accompanied by increased intracellular TSP1 protein levels are also a statistically significant (p[3].

In Vivo: The bioavailability and oral absorption of Tasquinimod is excellent when adult male mice (i.e., C57Bl/6J, or athymic nude mice) are given 0.1-30 mg/kg (i.e., 0.2-74 μ moles/kg) via gavage or the drinking water. The potency of Tasquinimod expressed as the daily oral dose of Tasquinimod which inhibits cancer growth by 50% ranges from 0.1-1.0 mg/kg/d (i.e., 0.24-2.40 μ moles/kg/day) against a series (n>5) of human prostate cancer xenografts in immune-deficient mice. Tasquinimod at a chronic dose of 5 mg/kg/day via the drinking water produces > 80% inhibition (p[2]. Nude mice carrying subcutaneous LNCaP tumors are treated with Tasquinimod for 3 weeks. Exposure to Tasquinimod at 1 mg/kg/day and 10 mg/kg/day started on day 7 after inoculation. There is a statistically significant dose dependent reduction in tumor weight both at 1 mg/kg/day and 10 mg/kg/day compare to the untreated control group 28 days after inoculation (p[3].



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