

Product Data Sheet

Product Name: BAY-299

Cat. No.: GC18508

Chemical Properties

Cas. No. 2080306-23-4

Chemical Name 2-(2,3-dihydro-1,3,6-trimethyl-2-oxo-1H-benzimidazol-5-yl)-6-(3-hydroxypropyl)-1H-benz[de]isoquinoline-1,3(2H)-dione

SMILES OCCCC1=CC=C(C(N2C3=C(C)C=C(N(C)C(N4C)=O)C4=C3)=O)C5=C1C=CC=C5C2=O

Formula $C_{25}H_{23}N_3O_4$ M.Wt 429.5

Solubility DMF: 30 mg/ml, DMSO: 20 mg/ml 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.

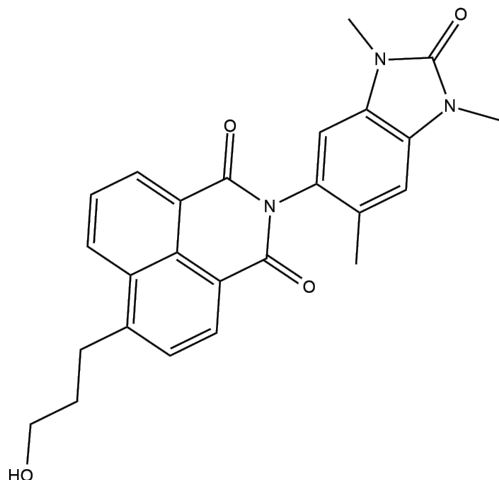
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment: MOLM-13, MV4-11, 769-P, Jurkat, NCI-H526, CHL-1, and 5637 cell lines are treated with BAY-299 while in the logarithmic growth phase, and their viability is determined by AlamarBlue staining[1].

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Animal experiment: Rats[1]BAY-299 is administered to three male Wistar rats per arm, either intravenously or intragastrally formulated as solutions. BAY-299 is given as i.v. bolus, and blood samples are taken at 2 min, 8 min, 15 min, 30 min, 45 min, 1 h, 2 h, 4 h, 6 h, 8 h, and 24 h after dosing. For pharmacokinetics after intragastral administration, BAY-299 is given intragastrally to fasted rats and blood samples are taken at 5 min, 15 min, 30 min, 45 min, 1 h, 2 h, 4 h, 6 h, 8 h, and 24 h after dosing. Blood is collected into lithium-heparin tubes and centrifuged for 15 min at 3000 rpm[1].

References:

[1]. Bouché L, et al. Benzoisoquinolinediones as Potent and Selective Inhibitors of BRPF2 and TAF1/TAF1L Bromodomains. J Med Chem. 2017 May 11;60(9):4002-4022.

Background

BAY-299 is a very potent, dual inhibitor with IC₅₀s of 67 nM for BRPF2 bromodomains (BD), 8 nM for TAF1 BD2, and 106 nM for TAF1L BD2.

BAY-299 is a dual inhibitor of the bromodomain and PHD finger (BRPF) family member BRPF2 and the TATA box binding protein-associated factors TAF1 and TAF1L. TR-FRET assays showed that BAY-299 is a potent inhibitor of BRPF2 BD with an IC₅₀ of 67 nM, and a selectivity of 47- and 83-fold over BRPF1 and BRPF3 BDs. The profile of BAY-299 is further confirmed by AlphaScreen assay, where an IC₅₀ of 97 nM and a selectivity of 23- and 25-fold over BRPF1 and BRPF3 BDs are measured. NanoBRET experiments show that the interaction of BRPF2 BD with histones H4 and H3.3 is blocked by BAY-299 with IC₅₀ values of 575 and 825 nM, respectively. For TAF1 BD2, the IC₅₀ values are 970 and 1400 nM, respectively. No inhibitory effect is observed for the interaction between BRPF1 or BRD4 and histone H4 up to 10 μM for BAY-299. BAY-299 inhibits MOLM-13, MV4-11, 769-P, Jurkat, NCI-H526, CHL-1, and 5637 cells proliferation with GI₅₀s of 1060, 2630, 3210, 3900, 6860, 7400, and 7980 nM, respectively[1].

Studies of the in vivo pharmacokinetic properties of BAY-299 in rat reveal that blood clearance is low (ca. 17% of hepatic blood flow), volume of distribution in steady-state high, terminal half-life long to very long (t_{1/2}=10 h), and bioavailability high (F=73%). In vivo blood clearance is as anticipated

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based on rat liver microsome values but lower than expected based on hepatocyte data[1].

References:

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