

Product Data Sheet

Product Name: AI-10-49
Cat. No.: GC11189

Chemical Properties

Cas. No. 1256094-72-0

Chemical Name 2,2'-(5,5'-((oxybis(ethane-2,1-diyl))bis(oxy))bis(pyridine-5,2-diyl))bis(5-(trifluoromethoxy)-1H-benzo[d]imidazole)

SMILES FC(F)(F)OC1=CC2=C(C=C1)NC(C(C=C3)=NC=C3OCCOCCOC(C=C4)=CN=C4C5=NC6=CC(OC(F)(F)F)=CC=C6N5)=N2

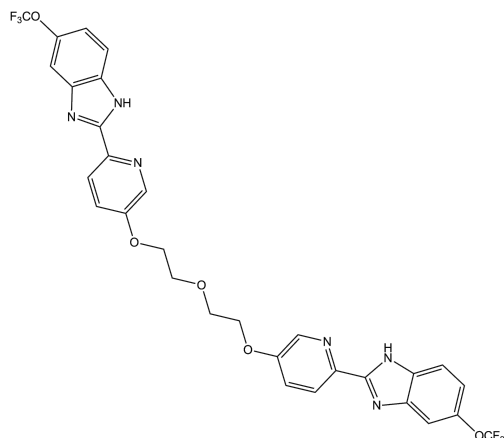
Formula $C_{30}H_{22}F_6N_6O_5$ M.Wt 660.52

Solubility $\geq 16.53\text{mg/mL}$ 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]:

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

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Cell lines ME-1 (human leukemia cell lines)

Limited solubility. General tips for obtaining a higher concentration: Please warm Preparation method 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.

Reaction Conditions 6 h

Applications After 6 hours of treatment, AI-10-49 effectively dissociates RUNX1 from CBFb-SMMHC with 90% dissociation, by contrast, it has a mild effect on CBFb-RUNX1 association. The ChIP assays indicates that AI-10-49 treatment on ME-1 cells for 6 hours increases RUNX1 occupancy 8-, 2.2-, and 8-fold at the RUNX3, CSF1R, and CEBPA promoters.

Animal experiment [1]:

Animal models Transplanted mice with Cbfb+/MYH11:Ras+/G12D leukemic cells

Dosage form 200 mg/kg; 10 days

Applications Mice treated with AI-10-49 survives markedly longer (median latency = 61 days) and transient AI-10-49 treatment also reduces leukemia spreading in vivo.

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. Illendula A, Pulikkan JA, Zong H et.al A small-molecule inhibitor of the aberrant transcription factor CBF β -SMMHC delays leukemia in mice. *Science*. 2015 Feb 13;347(6223):779-84.

Background

AI-10-49 is a selective inhibitor of CBF β –SMMHC and RUNX1 interaction with a FRET IC₅₀ value of 260nM.

AI-10-49 restores RUNX1 transcriptional activity, displays favorable pharmacokinetics, and delays leukemia progression in mice. Treatment of primary inv(16) AML patient with AI-10-49 triggers selective cell death. Direct inhibition of the oncogenic CBF β -SMMHC fusion protein may be an effective therapeutic approach for inv(16) AML, and they provide support for transcription factor targeted therapy in other cancers. The stability of RUNX1, CBF β , and CBF β -SMMHC was not affected by AI-10-49 [1].

In 11 human leukemia cell lines, ME-1 cells were the only cell line highly sensitive to AI-10-49. In ME-1 cell, AI-10-49 has enhanced inhibitory activity on growth (IC₅₀ = 0.6 mM) compared with the parent protonated bivalent compound AI-4-83 (IC₅₀ of ~3 mM). In normal human bone marrow cells, AI-10-49 showed negligible activity (IC₅₀ > 25 mM), which indicated a robust potential therapeutic window. In chromatin-immunoprecipitation (ChIP) assays, treatment of ME-1 cells for 6 hours with AI-10-49 increased RUNX1 occupancy 8-, 2.2-, and 8-fold at the RUNX3, CSF1R, and CEBPA promoters, respectively.

After treatment with AI-10-49 to leukemia mice significantly prolonged their lives, and after 7 days of administration of AI-10-49, we observe no evidence of toxicity [1].

Reference:

1. Illendula A, Pulikkan JA, Zong H et al. A small-molecule inhibitor of the aberrant transcription factor CBF β -SMMHC delays leukemia in mice. *Science*. 2015 Feb 13;347(6223):779-784.

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