

Product Data Sheet

Product Name: dBET6
Cat. No.: GC32719

Chemical Properties

Cas. No. 1950634-92-0

SMILES O=C(NCCCCCCCCNC(COC1=CC=CC(C(N2C(CC3)C(NC3=O)=O)=O)=C1C2=O)=O)C[C@H]4C5=NN=C(C)N5C6=C(C(C)=C(C)S6)C(C7=CC=C(Cl)C=C7)=N4

Formula C42H45ClN8O7S M.Wt 841.37

Solubility DMSO : ≥ 100 mg/mL (118.85 mM); Water : < 0.1 mg/mL (insoluble) 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.

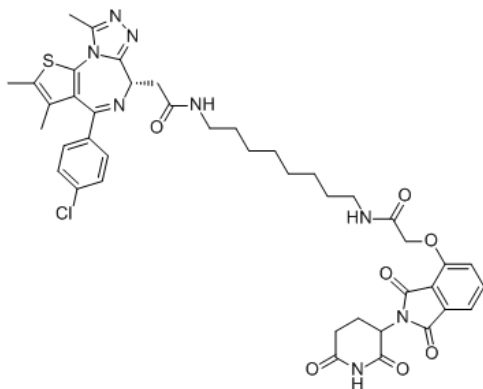
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines	Primary chronic myeloid leukemia (CML) cells, CML cell lines (KU812, K562, KCL22, KCL22T315I), and primary CML leukemic stem cells (LSC; CD34+/CD38-)
Preparation Method	Primary CML mononuclear cells (MNC) and CML cell lines were cultured in appropriate medium. Cells were treated with dBET6 (1nM-50μM) for 48 hours.
Reaction Conditions	1nM-50μM; 48 hours

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Applications dBET6 significantly inhibited proliferation and induced apoptosis in primary CML cells, including those from blast phase (BP) CML and cells harboring the BCR::ABL1 T315I mutation, overcoming resistance to the BET inhibitor JQ1.

Animal experiment [2]:

Animal models Nude mice for U87 GBM xenografts

Preparation Method dBET6 (7.5mg/kg; intraperitoneal injection; twice daily) was administered continuously for 14-18 days to mice bearing T-ALL xenograft models.

Dosage form 7.5mg/kg; intraperitoneal injection; twice daily.

Applications dBET6 significantly prolonged murine survival, reduced tumor incidence, and impaired gliomasphere-initiated tumor formation. dBET6 also downregulated BET protein levels in orthotopic GBM xenografts within 2 hours post-i.p. injection.

References:

[1] Peter B, Eisenwort G, Sadovnik I, et al. BRD4 degradation blocks expression of MYC and multiple forms of stem cell resistance in Ph⁺ chronic myeloid leukemia. Am J Hematol. 2022 Sep;97(9):1215-1225.

[2] Xu L, Chen Y, Mayakonda A, et al. Targetable BET proteins- and E2F1-dependent transcriptional program maintains the malignancy of glioblastoma. Proc Natl Acad Sci U S A. 2018 May 29;115(22):E5086-E5095.

Background

dBET6 is a novel, orally active BRD4 degrader that suppresses the transcription and expression of oncogenes such as c-Myc^[1-2]. dBET6 can be used in research related to cancers such as acute

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myeloid leukemia^[3-4].

In vitro, when chronic myeloid leukemia cells (KU812, K562, KCL22, and KCL22T315I) were treated with dBET6 (1nM–50µM) for 48 hours, dBET6 significantly inhibited cell proliferation, induced apoptosis, and blocked MYC expression. dBET6 also synergized with BCR::ABL1 tyrosine kinase inhibitors to overcome drug resistance^[5]. When various acute myeloid leukemia and acute lymphoblastic leukemia cell lines (KG1, HL60, MOLM-13, MV4-11, BV-173, NALM-1, etc.) and primary patient-derived AML and ALL cells were treated with dBET6 (0.05µM to 1µM) for 0 to 48 hours. dBET6 significantly inhibited cell growth and viability and induced apoptosis. Additionally, dBET6 overcame osteoblast-induced chemotherapy resistance and suppressed interferon-gamma and tumor necrosis factor-alpha-induced PD-L1 checkpoint antigen expression^[6].

In vivo, in a light-induced retinal degeneration model, BALB/cJ and C57BL/6J mice received intraperitoneal injections of dBET6 (10mg/kg) once one hour before light exposure and again 24 hours after exposure. dBET6 significantly improved retinal function and visual sensitivity, inhibited light damage-induced retinal thinning, photoreceptor cell death, and microglia/macrophage activation, and reduced cGAS-STING pathway activity^[7]. In a T-ALL xenograft mouse model, dBET6 (7.5mg/kg; intraperitoneal injection twice daily) was administered continuously for 14–18 days. dBET6 significantly reduced the leukemia burden and prolonged survival in the mice^[8].

References:

- [1] Winter GE, Mayer A, Buckley DL, et al. BET Bromodomain Proteins Function as Master Transcription Elongation Factors Independent of CDK9 Recruitment. *Mol Cell*. 2017 Jul 6;67(1):5-18.e19.
- [2] Bauer K, Berghoff AS, Preusser M, et al. Degradation of BRD4 - a promising treatment approach not only for hematologic but also for solid cancer. *Am J Cancer Res*. 2021 Feb 1;11(2):530-545.
- [3] Chen Z, Feng Z, Wang S, et al. Engineering Metal-Organic-Framework-Based STING Nanoagonists for PROTAC-Enhanced Cancer Chemo-Metalloimmunotherapy. *Adv Sci (Weinh)*. 2026 Jan;13(2):e15006.
- [4] Yu H, Zhao J, Wu D, et al. Exosome encapsulated albumin nanoparticles target delivery of dBET6 as a treatment for triple-negative breast cancer. *PLoS One*. 2026 Jan 12;21(1):e0335890.
- [5] Peter B, Eisenwort G, Sadovnik I, et al. BRD4 degradation blocks expression of MYC and multiple forms of stem cell resistance in Ph+ chronic myeloid leukemia. *Am J Hematol*. 2022 Sep;97(9):1215-1225.

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- [6] Bauer K, Hauswirth A, Gleixner KV, et al. BRD4 degraders may effectively counteract therapeutic resistance of leukemic stem cells in AML and ALL. Am J Hematol. 2024 Sep;99(9):1721-1731.
- [7] Zhu X, Liu W, Tang X, et al. The BET PROTAC inhibitor dBET6 protects against retinal degeneration and inhibits the cGAS-STING in response to light damage. J Neuroinflammation. 2023 May 22;20(1):119.
- [8] Xu L, Chen Y, Mayakonda A, et al. Targetable BET proteins- and E2F1-dependent transcriptional program maintains the malignancy of glioblastoma. Proc Natl Acad Sci U S A. 2018 May 29;115(22):E5086-E5095.

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