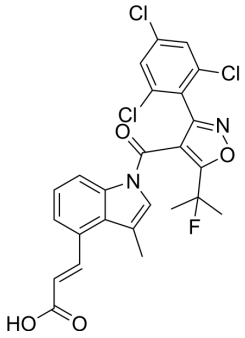
Safusidenib

Cat. No.:	HY-145594
CAS No.:	1898206-17-1
Molecular Formula:	$C_{25}H_{18}Cl_3FN_2O_4$
Molecular Weight:	535.78
Target:	Isocitrate Dehydrogenase (IDH)
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Safusidenib (AB-291; DS-1001) is an orally bioavailable, selective mutant IDH1 inhibitor. Safusidenib strongly inhibits mutant IDH1 but not wild-type IDH1. Safusidenib impairs tumor activity in chondrosarcoma[1]. Safusidenib exhibits activity against IDH1R132H, and IDH1R132C with IC_{50}s of 15, and 130 nM in assays without any preincubation, respectively[2].
IC_{50} & Target	IDH1

In Vitro

Safusidenib (DS-1001b) impairs the proliferation of IDH1-mutated chondrosarcoma cell lines and decreases 2-HG levels[1].
Safusidenib impairs the proliferation of IDH1 mutant chondrosarcoma cell lines in a dose-dependent manner, whereas Safusidenib has little effect on the proliferation of the IDH wild-type cell lines OUMS27 and NDCS-1; GI_{50} values for JJ012, L835, OUMS27, and NDCS-1 cells are 81?nM (day 14), 77?nM (6 weeks), >10?μM (day 10), and >10?μM (day 10), respectively[1].
Safusidenib (1, and 10?μM; for 6 weeks) markedly upregulates SOX9, a key regulator of chondrocyte differentiation, at the protein level[1].
Safusidenib (1 μM) significantly upregulates CDKN1C at the protein level[1].
Safusidenib (DS-1001b) exhibits activity against IDH1 or IDH2 enzymes with IC_{50}s of 8.4, 11, and 180 nM for IDH1R132H, IDH1R132C, and IDH1WT in assays conducted with a 2-hour preincubation step[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	The IDH1 mutant cell lines JJ012 and L835 cells
Concentration:	0.1, 1, and 10 μM
Incubation Time:	0, 3, 6, 9, 12, and 15 days
Result:	Impaired proliferation in both cell lines in a dose-dependent manner.

Western Blot Analysis[1]

Cell Line:	L835 cells
Concentration:	0, 1, and 10 μM
Incubation Time:	6 weeks
Result:	Markedly upregulated SOX9 at the protein level.

In Vivo	Safusidenib (DS-1001b) has antineoplastic activity in JJ012 xenografts. Continuous administration of Safusidenib (mixed with sterilized pellet food and fed continuously for 6 weeks) impairs tumor growth in xenograft mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NOD-SCID bearing JJ012 xenograft[3]
Dosage:	Mixed with sterilized pellet food (CRF-1; Oriental Yeast) and fed ad libitum for 6 weeks.Mixed with sterilized pellet food (CRF-1; Oriental Yeast) and fed ad libitum for 6 weeks.
Administration:	Fed continuously starting at 3 weeks
Result:	Continuous administration significantly impaired tumor growth in JJ012 xenograft mice.

CUSTOMER VALIDATION

- Nat Commun. 2022 Aug 15;13(1):4785.

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REFERENCES

[1]. Makoto Nakagawa, et al. Selective inhibition of mutant IDH1 by DS-1001b ameliorates aberrant histone modifications and impairs tumor activity in chondrosarcoma. Oncogene. 2019 Oct;38(42):6835-6849.

[2]. Yukino Machida, et al. A Potent Blood-Brain Barrier-Permeable Mutant IDH1 Inhibitor Suppresses the Growth of Glioblastoma with IDH1 Mutation in a Patient-Derived Orthotopic Xenograft Model. Mol Cancer Ther. 2020 Feb;19(2):375-383.

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