TIP-08

Open-Label, Single-Arm, Exploratory Cohort Evaluating Safusidenib in Chemotherapy- and Radiotherapy-Naïve Patients With Grade 3 Isocitrate Dehydrogenase 1 (*IDH1*)-Mutant Oligodendroglioma

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Background

- *IDH*-mutant oligodendrogliomas are a distinct category of adult-type diffuse glioma per WHO CNS 2021 criteria[1]
- IDH inhibitors represent a paradigm shift in neuro-oncology, giving select patients with Grade 2 *IDH*-mutant glioma their first targeted treatment option[2]
- However, standard-of-care treatment for Grade 3 *IDH1*-mutant oligodendrogliomas remains maximal safe resection followed by RT and CT[2,3]
  - Although RT and CT prolongs PFS and OS, it can be associated with substantial detrimental short- and long-term impacts for patients[2,4–6]
  - There is, therefore, an unmet need for effective targeted treatments for Grade 3 *IDH1*-mutant oligodendroglioma that can delay use of RT/CT after surgery, be better tolerated, and preserve HRQoL for patients

Rationale

- Safusidenib is an investigational mutant-IDH1 inhibitor with high potency, selectivity, and blood-brain barrier permeability,[7] that has recently been granted fast track designation by the US FDA for treatment of *IDH1*-mutant glioma[8]
  - Safusidenib demonstrated encouraging clinical activity and a favorable risk-benefit profile in patients with *IDH1*-mutant glioma in Phase 1 (NCT03030066) and Phase 2 (NCT04458272) studies, including responses across histological grades and risk groups[9,10]
  - Safusidenib has also demonstrated encouraging clinical activity in patients with RT/CT-naïve *IDH1*-mutant glioma in the Phase 2 study[10]
  - These findings support further evaluation of safusidenib in patients with Grade 3 *IDH1*-mutant oligodendroglioma

See poster CTNI-11 at this meeting for updated data from this Phase 2 study

Study Aim

- This ongoing, open-label, single-arm exploratory cohort of the SIGMA study (NCT05303519) is evaluating the efficacy and safety of **safusidenib** in **RT/CT-naïve patients** with **Grade 3 *IDH1*-mutant oligodendroglioma**[11]
- A preceding dose-finding part of this study confirmed the RP2D of safusidenib as 250 mg BID
- This cohort study is being conducted in parallel with the ongoing Phase 3, randomized, double-blind SIGMA study (NCT05303519) evaluating maintenance safusidenib vs placebo following RT/CRT and adjuvant TMZ in patients with *IDH1*-mutant astrocytoma with high grade or high-risk features[11]

See poster TIP-06 at this meeting for more information on the Phase 3 SIGMA study

Study Design: Exploratory Cohort (NCT05303519)

Key Eligibility Criteria

Inclusion Criteria

- Histologically confirmed Grade 3 *IDH1*-mutant, 1p/19q-codeleted oligodendroglioma, per INV assessment according to WHO CNS 2021 criteria[1]
- Age ≥18 years
- KPS ≥60
- Measurable residual or recurrent disease per RANO 2.0 by BICR
- ≥1 prior surgery for glioma with most recent surgery ≥90 days and ≤5 years before enrollment
- RT/CT-naïve and not in need of immediate RT/CT

Exclusion Criteria

- Prior anticancer therapy other than surgery for glioma
- Prior treatment with anti-angiogenic agents, agents known to target IDH1 or IDH2, or other investigational agents for glioma

Treatment

Patients with **Grade 3 *IDH1*-mutant oligodendroglioma** with measurable residual or recurrent disease who are RT/CT-naïve
(N≈40)

Open Label

Safusidenib
250 mg PO BID

28-day continuous cycles until PD or discontinuation

Study Endpoints

Primary Endpoint

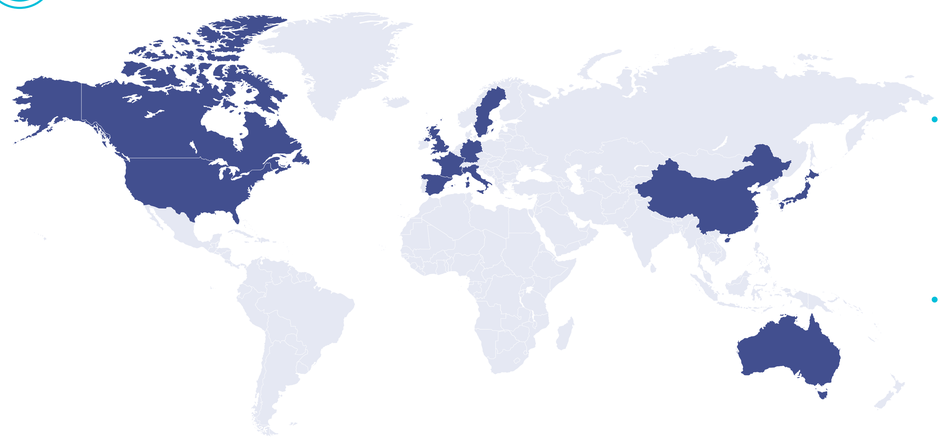
- ORR (CR, PR, MR) per RANO 2.0 by BICR

Secondary Endpoints

- ORR (CR, PR, MR) per RANO 2.0 by INV
- Duration of response[a]
- PFS[a]
- Time to next intervention
- Disease control rate[a]
- Time to response[a]
- Overall survival
- Safety
- Seizure activity
- HRQoL by FACT-Br and QOLIE-10-P scores
- Pharmacokinetics

[a]BICR and INV assessed, per RANO 2.0.

Trial Progress



- The international Phase 3 SIGMA study (NCT05303519) is ongoing, with approximately 80 sites across Australia, Canada, China, France, Germany, Italy, Japan, Spain, Sweden, UK, and USA selected as of October 2026
- The first patient in the exploratory cohort was enrolled in July 2026

Summary

- For patients with Grade 3 *IDH1*-mutant oligodendroglioma, there is an unmet need for effective targeted treatments that can delay use of RT/CT after surgery
- Safusidenib is an investigational mutant-IDH1 inhibitor with high potency, selectivity, and blood-brain barrier permeability that has shown encouraging efficacy in patients with *IDH1*-mutant glioma[7,9,10]
- This ongoing, open-label, single-arm, exploratory cohort study will evaluate the efficacy and safety of safusidenib in RT/CT-naïve patients with Grade 3 *IDH1*-mutant oligodendroglioma

Abbreviations

BICR, blinded independent central review; BID, twice daily; CNS, central nervous system; CR, complete response; CRT, chemoradiotherapy; CT, chemotherapy; FACT-Br, Functional Assessment of Cancer Therapy-Brain; FDA, Food and Drug Administration; HRQoL, health-related quality of life; IDH1/2, isocitrate dehydrogenase 1/2; INV, investigator; KPS, Karnofsky Performance Status; MR, minor response; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, orally; PR, partial response; QOLIE-10-P, Patient Weighted Quality of Life in Epilepsy Questionnaire; RANO, Response Assessment in Neuro-Oncology; RP2D, recommended Phase 2 dose; RT, radiation therapy; TMZ, temozolomide; UK, United Kingdom; USA, United States of America; WHO, World Health Organization.

References

1. Louis DN, et al. *Neuro Oncol* 2021;23:1231–1251
2. Lin MD, et al. *NPJ Precis Oncol* 2024;8:149
3. Mohile NA, et al. *J Clin Oncol* 2022;40:403–426
4. Blonski M, et al. *Front Oncol* 2022;12:827897
5. Cayuela N, et al. *Neuro Oncol* 2019;21:1470–1479
6. Cairncross G, et al. *J Clin Oncol* 2013;31:337–343
7. Machida Y, et al. *Mol Cancer Ther* 2020;19:375–383
8. Nuvation Bio Press Release. Accessed October 1, 2026; https://investors.nuvationbio.com/news/news-details/2026/Nuvation-Bio-Granted-FDA-Fast-Track-Designation-for-Safusidenib-for-Treatment-of-IDH1-Mutant-Glioma/default.aspx
9. Natsume A, et al. *Neuro Oncol* 2023;25:326–336
10. Arakawa Y, et al. *Neuro Oncol* 2026;28:717–727
11. ClinicalTrials.gov. NCT05303519. Accessed October 1, 2026; https://clinicaltrials.gov/study/NCT05303519

Acknowledgments

We would like to thank all patients who are participating in this ongoing study, the study investigators, and their staff. This study is sponsored by Nuvation Bio Inc. Medical writing support was provided by Jane Blackburn, PhD, of Ashfield MedComms, an Inizio company, and was funded by Nuvation Bio Inc.

Presented at the Society for Neuro-Oncology Annual Meeting | November 12–15, 2026 | Philadelphia, PA, USA

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