



Preprint Reports Curtana's CT-179 Enhances Radiotherapy in an MGMT-Unmethylated Glioblastoma Model and Extends Survival as a Single Agent

Foundational preclinical study of the first-in-class, brain-penetrant OLIG2 inhibitor supports evaluating CT-179 with standard-of-care therapy, including in MGMT-unmethylated glioblastoma, where temozolomide adds little

AUSTIN, Texas - Oct. 27, 2026 - [PRLog](#) -- Curtana Pharmaceuticals, a clinical-stage biotechnology company focused on improving outcomes for brain cancer patients, today announced that a preprint posted on bioRxiv on October 20 reports that CT-179 extended survival as a single agent in two orthotopic patient-derived models of adult glioblastoma (GBM) and enhanced radiotherapy in an orthotopic MGMT-unmethylated model. CT-179 is a first-in-class, orally bioavailable, brain-penetrant small-molecule inhibitor of the transcription factor OLIG2. The study was led by Terrance G. Johns, Ph.D., and conducted at the Hudson Institute of Medical Research and Monash University, with collaborators at QIMR Berghofer, The University of Queensland, Mayo Clinic, Huntsman Cancer Institute at the University of Utah, and UT Southwestern Medical Center. The preprint has not yet been peer reviewed.

OLIG2 is expressed throughout diffuse gliomas, sustains the stem-like tumor cells that drive recurrence, and opposes p53-mediated responses to radiation and chemotherapy. Despite its established role in GBM, it has historically been considered undruggable.

Key findings reported in the preprint:

- **Target engagement and activity across patient-derived lines.** CT-179 bound OLIG2 in patient-derived GBM cells and altered the conformation of OLIG2 on DNA. It inhibited proliferation in all 11 patient-derived GBM cell lines tested (IC₅₀ values below 360 nM), depleted the stem-like fraction, and induced apoptosis.

- **Single-agent survival benefit in orthotopic models.** Oral CT-179 crossed the blood-brain barrier and extended median survival in two independent orthotopic patient-derived xenograft models: by approximately 42% in GBM8 (P = 0.0139) and approximately 46% in MGMT-unmethylated G06 (43.0 vs. 29.5 days; P = 0.0034). Intraperitoneal dosing in GBM8 extended median survival from 46 to 70 days (P = 0.0052) and was associated with reduced intratumoral OLIG2 and Ki-67 staining.

- **Combination with chemoradiotherapy.** Added to radiotherapy and temozolomide, CT-179 eliminated all GBM8 and 7 of 8 GBM4 subcutaneous xenografts, both MGMT-methylated, with body weights comparable to controls.

- **MGMT-unmethylated intracranial disease.** In orthotopic MGMT-unmethylated GBM6 xenografts, where CT-179 alone did not significantly extend survival, adding intraperitoneal CT-179 to fractionated radiotherapy extended median survival compared with radiotherapy alone (48 vs. 38.5 days; P = 0.0248).

Cell death occurred while ERK1/2, AKT, and STAT3 survival signaling remained active, indicating that the effect is not explained by collapse of growth-factor receptor signaling. The authors also report greater-than-additive activity in vitro with Bcl-2 family inhibitors, which varied by cell line, identifying a further candidate combination strategy.

"OLIG2 has long been recognized as a central driver of glioblastoma, but it has resisted drug development,"

said Terrance G. Johns, Ph.D., corresponding author of the study. "This work shows that a small molecule can engage OLIG2 in patient-derived tumor cells, reach the brain, and add substantially to radiotherapy and temozolomide in our models."

"Seeing CT-179 deplete OLIG2-positive cells in patient-derived organoids and strengthen radiotherapy in an intracranial model gives us confidence in the translational rationale," said Bryan W. Day, Ph.D., Group Leader of the Sid Faithfull Brain Cancer Laboratory at QIMR Berghofer.

"The MGMT-unmethylated result is the most clinically relevant finding in this paper," said Gregory Stein, M.D., M.B.A., Chief Executive Officer of Curtana Pharmaceuticals. "These patients derive little benefit from temozolomide, and this data set directly informs the radiotherapy combination arm of our OPAL Phase 1 program. It adds to published reports from other laboratories of CT-179 activity in pediatric high-grade glioma and medulloblastoma, and in combination with immune checkpoint blockade."

About the Preprint

Greenall SA, Chen SC, et al. Pharmacologic inhibition of OLIG2 by CT-179 disrupts mitotic progression and enhances standard-of-care chemoradiotherapy in glioblastoma. *bioRxiv*. Posted October 20, 2026. doi: 10.64898/2026.10.14.759257. Available at <https://www.biorxiv.org/content/10.64898/2026.10.14.759257v1>. Preprints are preliminary reports that have not been peer reviewed and should not be regarded as conclusive.

About CT-179

CT-179 is a first-in-class, orally bioavailable, brain-penetrant small-molecule inhibitor of OLIG2, a master transcription factor in diffuse gliomas and OLIG2-positive medulloblastoma. CT-179 is designed to eliminate the cancer stem cells that drive recurrence, and published preclinical work shows that OLIG2 inhibition also relieves tumor-driven suppression of CXCL10 and sensitizes GBM to anti-PD-L1 therapy. The FDA has granted CT-179 Fast Track Designation, Orphan Drug Designation for gliomas, and Rare Pediatric Disease Designation for medulloblastoma and for pediatric high-grade glioma. Curtana's multi-site Phase 1 OPAL trial of CT-179 in glioblastoma will be conducted in Australia in partnership with the Cooperative Trials Group for Neuro-Oncology (COGNO).

About Curtana Pharmaceuticals

Curtana Pharmaceuticals, founded in 2013, is a privately held, clinical-stage biopharmaceutical company headquartered in Austin, Texas. Current investors include Thynk Capital, angelMD, Biosense Global, DEFTA Partners, the Musella Foundation, the Hasso Serrano Foundation, the Uncle Kory Foundation, and other anonymous investors. The company was also awarded a \$7.6 million grant from the Cancer Prevention and Research Institute of Texas (CPRIT). Curtana focuses on the development of novel, first-in-class small-molecule therapeutics targeting cancer stem cells in the central nervous system for the treatment of glioblastoma, low-grade glioma, medulloblastoma, diffuse midline glioma, and other brain cancers. For more information, visit <https://www.curtanapharma.com/>.

Forward-Looking Statements

This press release contains forward-looking statements regarding the preclinical and clinical development of CT-179, including the design and conduct of the multi-site Phase 1 OPAL study in glioblastoma and the potential of CT-179 in combination with radiotherapy and other agents. Results in preclinical models may not be predictive of results in patients. These forward-looking statements involve risks and uncertainties,

including the outcome of peer review, the complexities of clinical trial execution and patient accrual, and the need to secure additional capital to fund operations and clinical milestones. Curtana undertakes no obligation to update these statements.

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