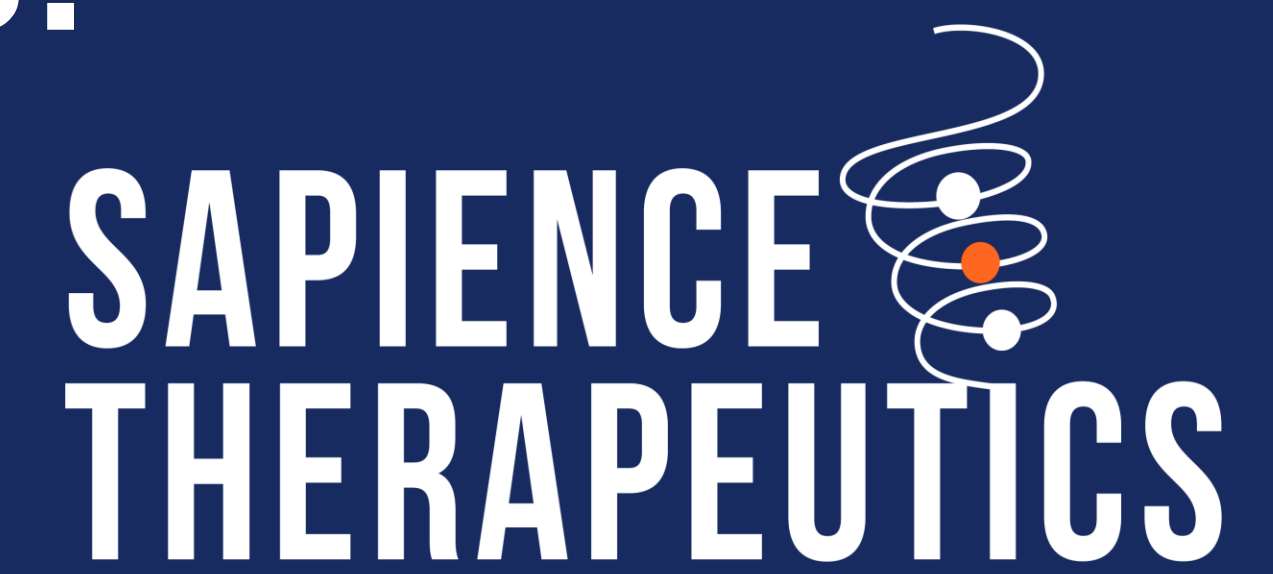




Lucicebtide (ST101) Plus Chemoradiation in Newly Diagnosed GBM Patients: Efficacy, Pharmacodynamics, and Safety in Phase 2 Window-of-Opportunity Study



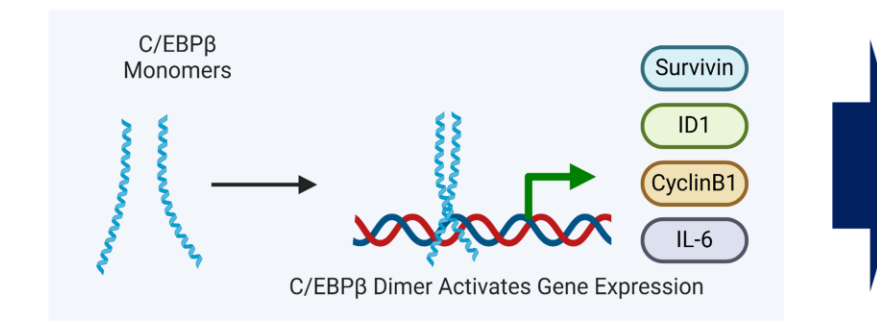
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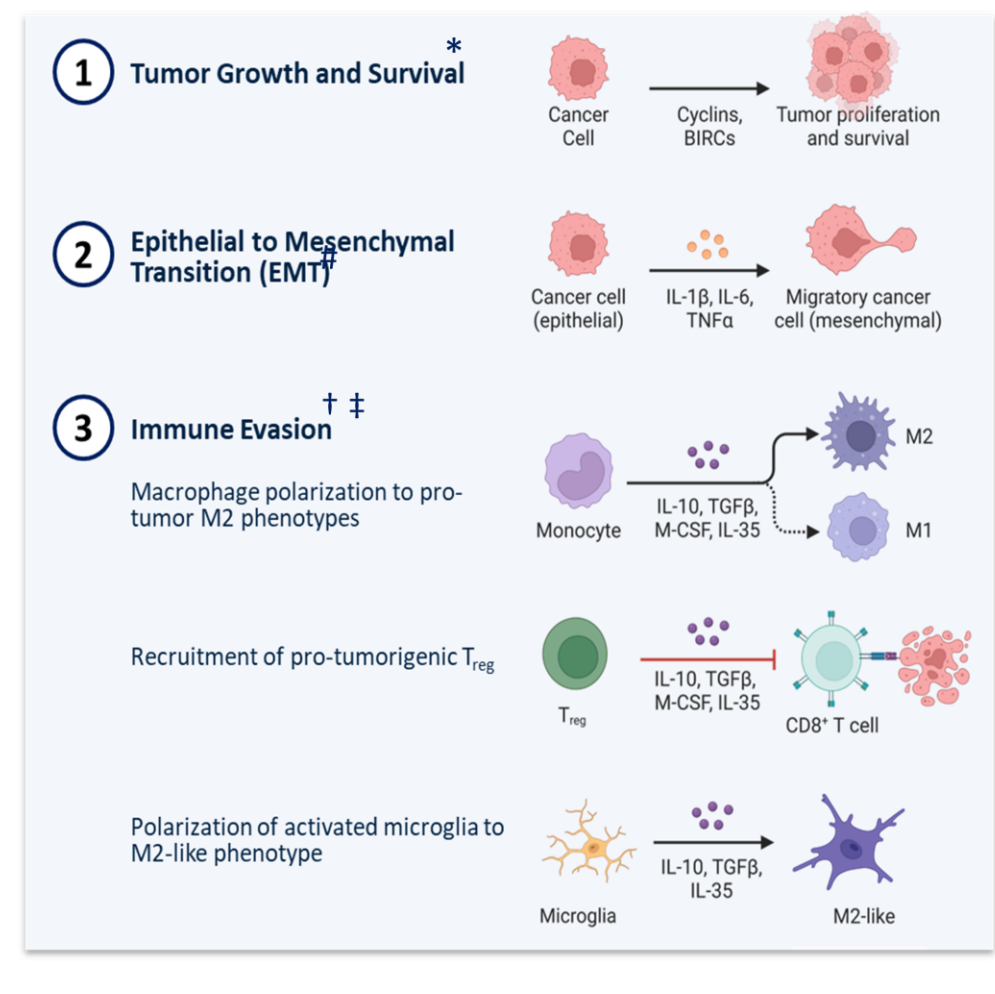
C/EBPβ Plays a Key Role in GBM

C/EBPβ is a transcription factor that supports tumor progression and an immunosuppressive TME



- Identified as a master regulator of mesenchymal transformation in GBM*
- Expression correlates with poor prognosis*
- Immunosuppressive TAMs comprise >30% of tumor and promote tumor growth and invasion**

* Homma et al., Oncol Rep 2006; # Carro et al., Nature 2010; † Yang et al., Theranostics 2024; ‡ Marigo et al., J Immunol 2010; == Sørensen et al., Neuropharmacol. Appl. Neurobiol. 2018



Lucicebtide is a C/EBPβ antagonist

- Disrupts C/EBPβ dimerization:
 - Prevents C/EBPβ-mediated transcription
 - Enhances C/EBPβ proteasomal degradation
- Decreases mesenchymal gene signature and mesenchymal transition in GBM
- Repolarizes macrophages from immune-suppressive to immune-activating

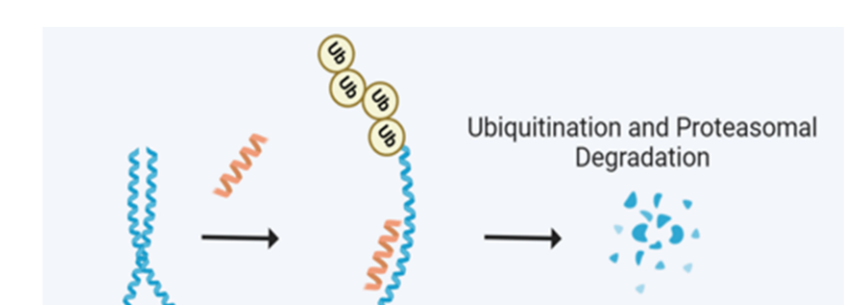
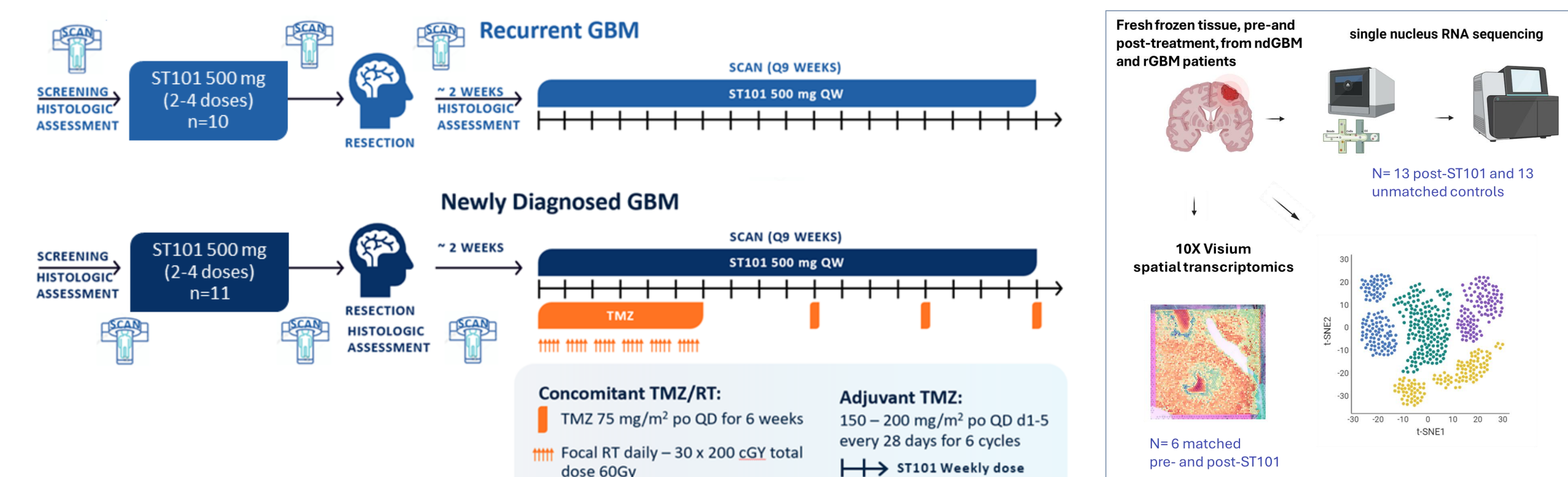


Figure 1. C/EBPβ is a Transcription Factor that Supports Tumor Progression and an Immunosuppressive Tumor Microenvironment (TME) in Glioblastoma (GBM).

Study Design

Figure 2. Study Design of a Window of Opportunity (WoO) Study to Determine the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Proof-of-Concept Efficacy of 500mg QW Lucicebtide Administered IV in Subjects with ndGBM and rGBM. Dose regimen and schedule of resections and scans indicated in left panel. Schematic for analysis of tumor sections indicated in right panel. snRNA-seq aligned using cellranger and analyzed with scanpy in Python. Pseudo-bulk differential expression was performed using pyDEseq-2 ST data was analyzed using squidpy and a custom sample-normalized spatial metaclustering algorithm.



Safety

Table 1. Most common Treatment Related Adverse Events (AEs) reported in >20% on patients.

Treatment Related AEs >20%	All AEs		Grade ≥3	
	rGBM Monotherapy (n=10)	ndGBM Luci + RT + TMZ (n=11)	rGBM Monotherapy (n=10)	ndGBM Luci + RT + TMZ (n=11)
Increased Blood Creatinine	30	72.7	-	-
Infusion Related Reaction	50	63.6	-	-
Nausea	10	36.4	-	-

- Most common AEs were:
 - IRR – resolved at the end of infusion; incidence decrease with subsequent infusions
 - Creatinine increase – decrease/stabilized with drug holidays
- No new safety concerns were raised with the combination compared to single agent

Efficacy

Figure 3. Lucicebtide Plus Chemoradiation Improves PFS and OS in ndGBM. (Top) Kaplan-Meier estimations of progression-free survival (PFS) and overall survival (OS) in newly-diagnosed GBM Cohort (n=9 evaluable). KM estimates with 95% CI (log-log transformation). Median by Brookmeyer-Crowley. Median follow-up by reverse Kaplan-Meier. Solid line: KM estimate; dashed: carried forward at last value to last censor. Bold dot last event reported. Swimmer Plot, shaded boxes represent historical benchmarks (Stupp et al., NEJM 2005; Stupp et al., JAMA 2017; Roth et al., Neuro-Onc 2024).

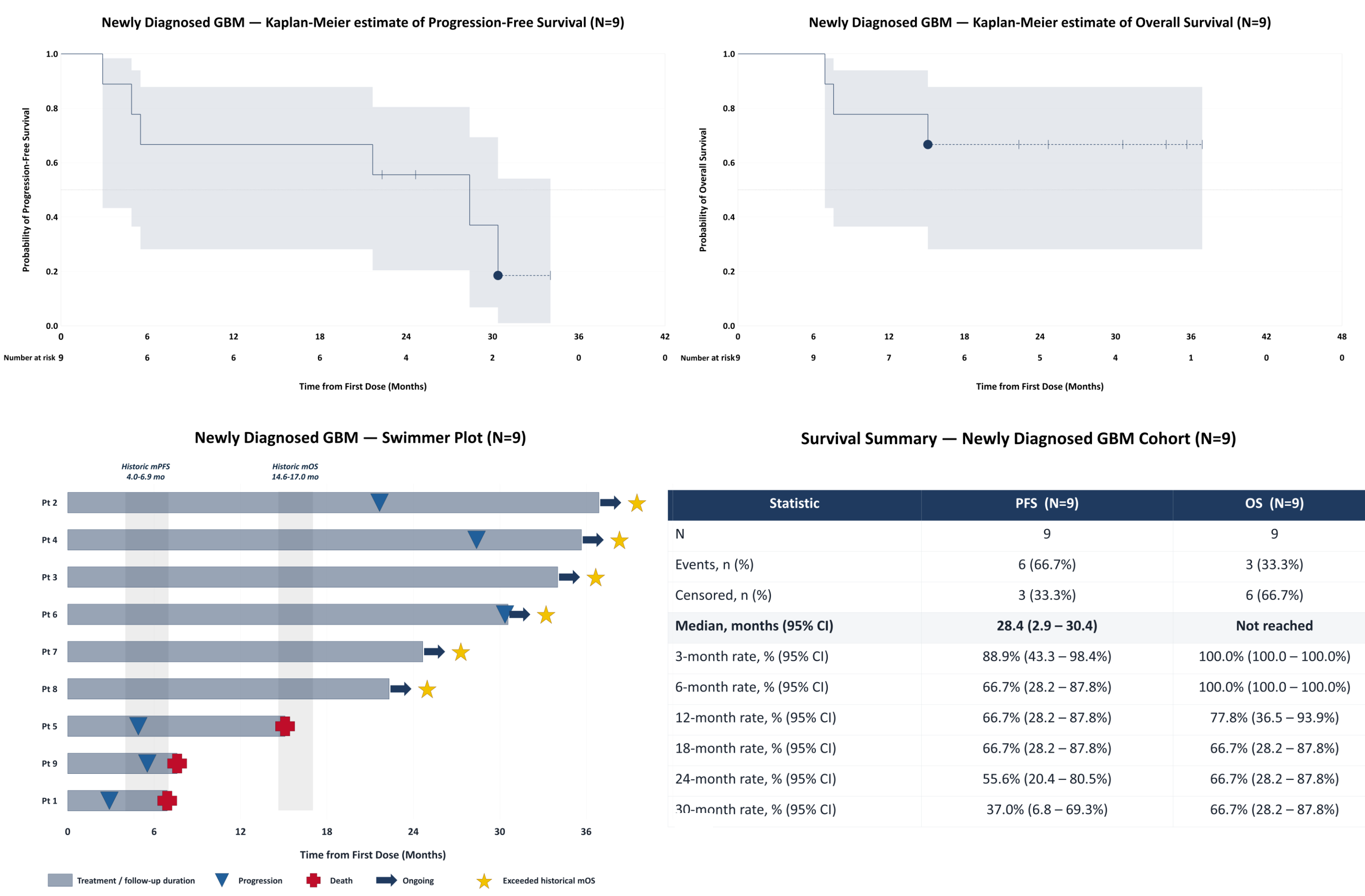


Figure 4. Lucicebtide Plus Chemoradiation Improves PFS and OS in rGBM. (Top) Kaplan-Meier estimations of PFS and OS in recurrent GBM Cohort (n=9 evaluable). KM estimates with 95% CI (log-log transformation). Median by Brookmeyer-Crowley. Median follow-up by reverse Kaplan-Meier. Solid line: KM estimate; dashed: carried forward at last value to last censor. Bold dot last event reported. Swimmer Plot, vertical dashed lines indicate historical benchmarks from Friedman et al., JCO 2009.



Transcriptomics Analyses

Figure 5. Lucicebtide Reduces C/EBPβ Regulon and Mesenchymal Signatures in Tumor and Myeloid Cells in Tumor Resections From WoO Study by snRNAseq. (A and B) UMAP of 89,000 single nuclei from control or lucicebtide-treated GBM biopsies (n=13). (C) Canonical marker gene expression by cell type. (D) Volcano plot showing up- and down-regulated genes (red and blue, respectively) following lucicebtide treatment in tumor cells. (E) Gene set enrichment analysis (GSEA) showing negative enrichment of C/EBPβ regulon and mesenchymal signatures in tumor cells. (*) denotes statistical significance (FDR-adjusted p < 0.05). (F and G) Same as (D and E) but for myeloid cells.

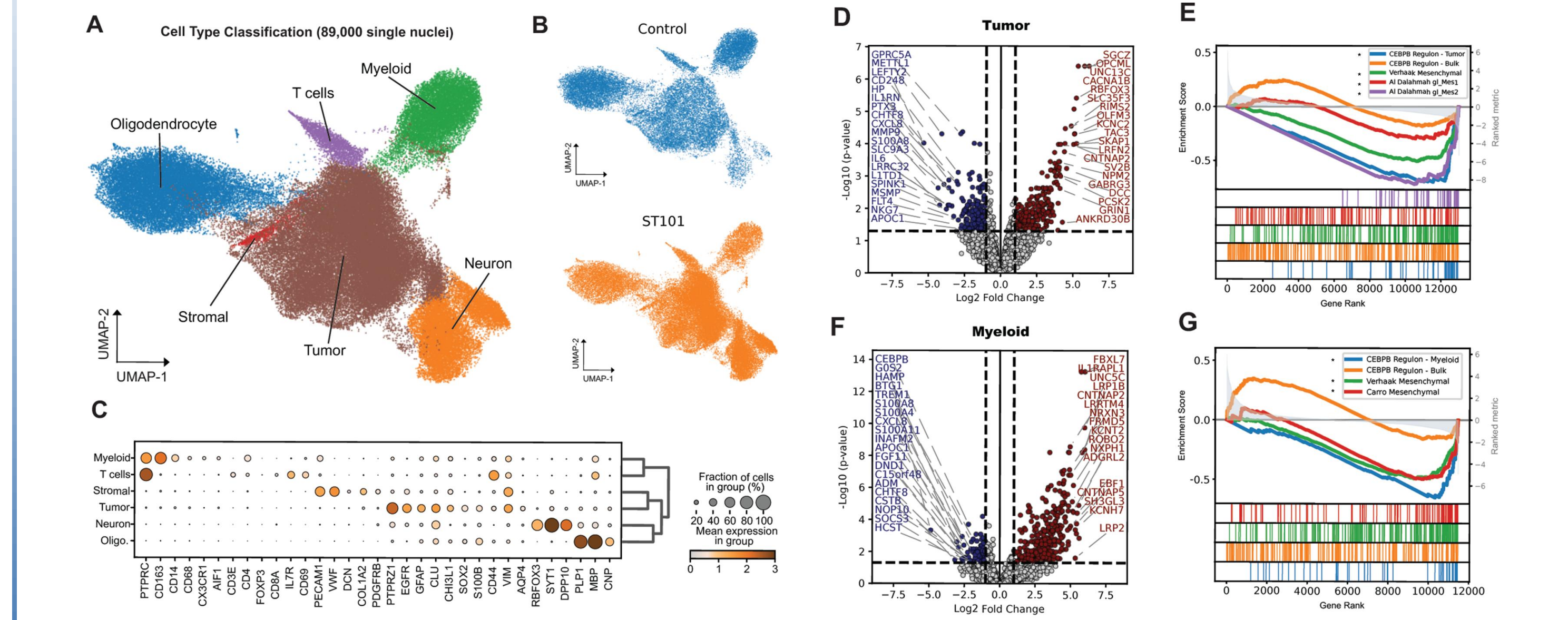
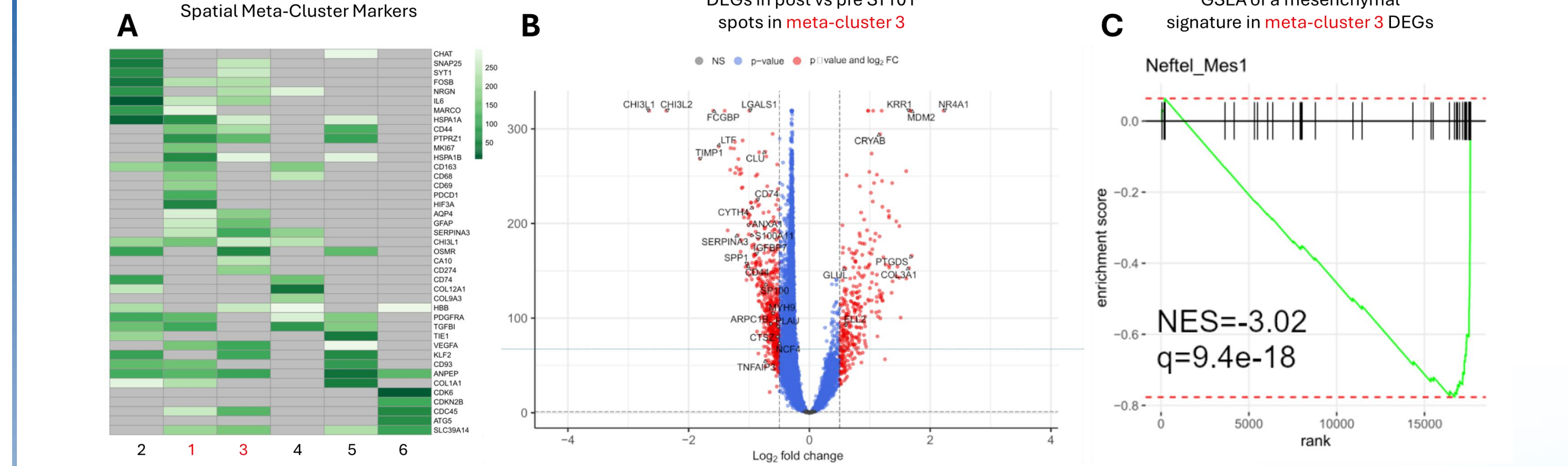


Figure 6. Spatial Transcriptomics Reveals Lucicebtide Reduces Tumor Mesenchymal Transformation in Tumor Resections in WoO Study. (A) Marker gene expression from spatially-defined clusters 1-6 identified by unsupervised clustering of tumor cell DEGs (n=6 matched tumors). The mesenchymal (Mes) niche is divided between clusters 1 and 3. B) Volcano plot showing DEGs in meta-cluster 3 comparing post- vs. pre-lucicebtide. Highlighted genes enriched in Mes signature. C) Lucicebtide significantly reduces Mes gene signature. GSEA showing negative enrichment of the Mes signature in meta-cluster 3. NES: normalized enrichment score. Adjusted q value is shown.



Conclusions

- Lucicebtide was well tolerated, with no DLTs or related SAEs observed, in a Phase 2 WoO study in patients with newly-diagnosed and recurrent GBM
- Patients with ndGBM treated with lucicebtide in combination with SOC achieved PFS and OS outcomes that exceed those reported in the published literature
 - Projected mPFS of 28.4 months, meaningfully exceeds the 4.0-6.9 month historic benchmark range
 - mOS not yet reached; 6 of 9 patients remain alive beyond 22.3 months (per April 27, 2026 cutoff date), exceeding the 14.6-17.0 month historic benchmark range
- Lucicebtide activity is supported by on-target pharmacodynamics in human GBM
 - Target engagement confirmed via negative enrichment of C/EBPβ regulon in tumor and myeloid cells
 - Suppression of the mesenchymal GBM transformation observed by spatial transcriptomics analysis
- Findings support further clinical development of lucicebtide as a novel therapeutic approach for GBM

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