**Background and Rationale**

- GLIOblastoma (GBM) Background
  - GBM is the most common primary malignant central nervous system tumor in adults.
  - Approximately 12,000 individuals in the US.
  - Aggressive, difficult to treat, poor prognosis. Median overall survival (OS) is 13-15 months for newly diagnosed patients despite aggressive multi-modality therapy including surgical resection, RT, and TMZ chemotherapy.
  - Recurrence in GBM essentially all patients, salvage therapies have limited efficacy.
  - Prognosis at recurrence: Median OS ~ 6 months; PFS 4-5 months; median survival from diagnosis ~ 1 year.
  - Median RT: 4 months
  - Radiographic response rate: 5-10%
  - Clear need for effective therapies.

- **Glioblastoma (GBM)emons.**

- **Stage 1**
  - Median age: 62 years
  - Male: 64%
  - IDH1 mutated: 66%
  - IDH2 mutated: 3%
  - TUG 368
  - Partial or Complete response: 46/46 (100%)
  - Duration of disease control: months

- **Stage 2**
  - Median age: 56 years
  - Male: 66%
  - IDH1 mutated: 70%
  - IDH2 mutated: 6%
  - TUG 368
  - Partial or Complete response: 46/46 (100%)
  - Duration of disease control: months

**Phase 2 Trial Design (S7901-0114)**

- **Stage 1 Eligibility: Second-line GBM**
  - ECOG PS ≤ 1
  - No prior standard of care immunotherapy
  - No prior RT to target glioma
  - No serious active infection
  - No serious uncontrolled medical condition
  - No prior neuroendocrine tumor
  - No prior cranial radiation therapy
  - No prior bevacizumab
  - No prior temozolomide
  - No prior lenvatinib
  - No prior durvalumab
  - No prior pembrolizumab
  - No active or recent malignancy

- **Stage 2 Eligibility: Second-line GBM**
  - ECOG PS ≤ 1
  - No prior standard of care immunotherapy
  - No prior RT to target glioma
  - No serious active infection
  - No serious uncontrolled medical condition
  - No prior neuroendocrine tumor
  - No prior cranial radiation therapy
  - No prior bevacizumab
  - No prior temozolomide
  - No prior lenvatinib
  - No prior durvalumab
  - No prior pembrolizumab
  - No active or recent malignancy

**Glioblastoma (GBM) Prospects**

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**Mechanism of Action**

- **Glioblastoma targets**
  - IDH1/IDH2, H3K27M, MGMT
  - Specific CD8+ T cell responses

**Safety and Tolerability**

- **Treatment-related adverse events (TRAEs, 2.5%) (n=74)**

**Disease Control, Including Major Responses**

- **Modified RANO Criteria (IT)**
  - Stage 1: 44/46 (95.6%)
  - Stage 2: 23/28 (82.1%)

**Overall Survival (OS)**

- **OS-12 + 44% (65.4, 69.6)**
  - Median OS: 11 months (65.4, 69.6)
  - Modified OS: 11.7 months (65.4, 69.6)

**Conclusions and Next Steps**

- **Long-term survivors: 80% 12-month OS with SL-701 + bevacizumab**
  - OS - 50% at 2 and 4 years
  - Median OS - 11 months (65.4, 69.6)
  - Modified OS - 11.7 months (65.4, 69.6)

- **Potential immune-related biomarker**
  - NCT02527737
  - NCT02966015
  - NCT02966016

**Duration of Disease Control**

- **Stage 1 (n=46)**
  - Time (months)
  - Partial Response (PR), n (rate)
  - Stable Disease (SD), n (rate)

- **Stage 2 (n=28)**
  - Time (months)
  - Partial Response (PR), n (rate)
  - Stable Disease (SD), n (rate)

**Disease Control Rate (DCR)**

- **Stage 1**
  - CR, n (rate)
  - PR, n (rate)
  - SD, n (rate)

- **Stage 2**
  - CR, n (rate)
  - PR, n (rate)
  - SD, n (rate)

**Potential immune-related biomarker**

- T cell responses
  - Targeted expression
  - CR after 4 months
  - DCR - 44% (95% CI: 28.9, 58.9)
  - p = 0.001

**Conclusion**

- Identifies potential correlation of immune-related biomarker with clinical outcome
  - Long-term survivors, including OS, and prior state in glioblastoma
  - Worldwide, very manageable side effect profile
  - Given the major unmet medical need in GBM and promising safety and efficacy data generated to date with SL-701, Stemline is considering next steps, including leveraging potential immune-related biomarker in future clinical trials.