Background & Historical Clinical Data

The proposed primary endpoint is overall survival (OS). The study will also confirm Progression free survival (PFS) will serve as the primary endpoint to assess VAL-083.

Results of a recent single-arm open label trial support the potential of VAL-083 to offer a clinically meaningful survival benefit in the post-bevacizumab GBM population, but must be further validated in a randomized clinical trial.

| TABLE 1: Historical data comparing randomized clinical trials of VAL-083 versus other chemotherapies used in the treatment of GBM. Reported median survival of VAL-083 in combination with radiotherapy, and the benefit versus radiotherapy alone is similar or superior to other alkylating agents. |
|-----------------|-----------------|-----------------|-----------------|
|                  | XRT + VAL-083   | TMZ             | Nitrosourea therapy |
|                  | (Egan 2017)      |                 | (Walker 2017)     |
|                  | (Stupp 2005)     |                 | (Reagan 1988)     |
| Median survival  | 16.8             | 14.6            | 12.5             |
| (months)         | 8.8              | 13.0            | 8.8              |
| Benefits vs. XRT | 8.4              | 2.5             | 2.5              |
| alone            | 1.2              | n/a             | n/a              |

DelMar Pharmaceuticals Data Demonstrates that VAL-083 Activity is Independent of MGMT-mediated Resistance

![Graph showing the effectiveness of VAL-083 in comparison to TMZ and nitrosourea therapy.](image)

Three ADDITIONAL GBM CLINICAL TRIALS ARE PLANNED:

1. A pivotal, randomized multi-center Phase 3 study measuring survival outcomes compared to a “physicians’ choice” control for the treatment of bevacizumab-failed GBM.

   **Proposed Phase 3 design**
   - Approximately 180 patients with histologically confirmed recurrent GBM who have failed both standard radiation + chemotherapy and bevacizumab will be randomized in a 2:1 fashion to receive either VAL-083 or commercially used salve chemotherapy.
   - The proposed study is projected to be enrolled at approximately 25 centers.
   - The proposed primary endpoint is overall survival (OS).
   - The proposed statistical design between the two arms of the study is 90% power, and is proposed to include an interim analysis at 50% events for futility with O’Brien-Fleming superiority boundary and non-binding, gamma(5) futility boundary.
   - The estimated length of the proposed study is less than 2 years from initiation.
   - The proposed trial design is subject to feedback from FDA and other regulatory authorities.

   **Study Design**
   - This single arm, biomarker-driven study will enroll 48 patients to determine if treatment of MGMT-unmethylated recurrent glioblastoma with VAL-083 improves overall survival (OS), compared to historical control.
   - The study is initially being enrolled at the University of Texas MD Anderson Cancer Center as a single center trial, but may be expanded to include additional centers.


   **Study Design**
   - This single-arm, biomarker-driven study will enroll 48 patients to determine if treatment of MGMT-unmethylated recurrent glioblastoma with VAL-083 improves overall survival (OS), compared to historical control.
   - The study will confirm the safety and tolerability of VAL-083 in combination with a standard of care radiation regimen.
   - The study will initially be enrolled at the Sun-Yat Sen University (Guangzhou, China) as a single center trial, but may be expanded to include additional centers.

3. An open label, single-arm, biomarker-driven, Phase 2 study of VAL-083 and radiation therapy patients with in newly diagnosed MGMT-UMGBM

   **Study Design**
   - This single-arm trial will enroll up to 30 newly diagnosed (temozolomide-naive) GBM patients to examine whether VAL-083 is active in patients with newly diagnosed GBM with unmethylated MGMT compared to historical control. This information is intended to lead to a global randomized Phase III clinical trial evaluating the efficacy of VAL-083 in newly diagnosed GBM patients with unmethylated MGMT.
   - Progression-free survival (PFS) will serve as the primary endpoint to assess VAL-083 treatment activity.
   - The study will confirm the safety and tolerability of VAL-083 in combination with a standard of care radiation regimen.
   - The study will initially be enrolled at the Sun-Yat Sen University (Guangzhou, China) as a single center trial, but may be expanded to include additional centers.

**References:**