The study population includes subjects with Grade IV Malignant Glioma (including glioblastoma and gliosarcoma) who are in first or second relapse and who have not previously received any bevacizumab (BEV) or other anti-angiogenic agents, including sorafenib, sunitinib, axitinib, pazopanib, everolimus, or cilengitide, or marizomib (MRZ) or any other proteasome inhibitor, including bortezomib (BTZ), carfilzomib (CFZ), or ixazomib (IXZ).

The objective of this trial is to assess the activity of a once weekly dose for 3 weeks of a 28-day cycle of MRZ in subjects with progressive or recurrent Grade IV Malignant Glioma, who have not previously been treated with either an anti-angiogenic agent or a proteasome inhibitor.

Marizomib (MRZ) is a novel, second generation proteasome inhibitor that prevents the breakdown of proteins involved in signal transduction which blocks growth and survival of cancer cells.

Inclusion Criteria:
- Written informed consent; age ≥18 years
- Histologic evidence of Grade IV Malignant Glioma (including glioblastoma and gliosarcoma) and radiographic evidence of recurrence or disease progression
- Previously completed standard radiation therapy and been exposed to temozolomide. Patients must be in first or second relapse
- Subjects with archival tumor tissue suitable for proteasome activity and genetic testing must give permission to access and test the tissue; subjects without archival tumor tissue are eligible.
- No prior treatment with MRZ or any other proteasome inhibitors, including BTZ, CFZ, or IXZ or BEV or any other anti-angiogenic agents, including sorafenib, sunitinib, axitinib, pazopanib, everolimus, or cilengitide.
- No investigational agent within 4 weeks prior to first dose of study drug.
- At least 4 weeks from surgical resection and 12 weeks from end of radiotherapy prior to enrollment in this study.
- Subjects with a history of seizures must be on a stable dose of anti-epileptic drugs (AEDs) for 7 days prior to enrollment.
- All AEs resulting from prior chemotherapy, surgery, or radiotherapy, must have resolved to NCI-CTCAE (v. 4.03) Grade ≤1
- Karnofsky Performance Status (KPS) score ≥ 70%.
- For women of child-bearing potential and for men with partners of childbearing potential, subject must agree to take contraceptive measures for duration of treatments and 6 months after the last dose.