A Phase 1 Ascending Dose Trial of the Safety and Tolerability of Toca 511, a Retroviral Replicating Vector, Administered to Subjects at the Time of Resection for Recurrent High Grade Glioma and Followed by Treatment with Toca FC, Extended-Release 5-FC

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Primary Objective

1. To identify the highest, safe and well tolerated dose of Toca 511 administered to the resection cavity of subjects with rHGG undergoing planned resection ≥ 80%

Secondary Objectives

1. To evaluate the safety and tolerability of treatment with 5-fluorocytosine (5-FC) at approximately 130 mg/kg/day for 8 days beginning approximately 7 weeks after administration of Toca 511 and repeated approximately every 8 weeks

2. To assess the percentage of subjects who have not progressed or died at 6 months (PFS-6)

All of the following questions must be answered “Yes” in order for the subject to participate in the study.

1. Has the subject given written informed consent?

2. Is the subject between 18 years old and 80 years old inclusive?

3. Has the subject undergone at least one prior surgical gross-total or subtotal tumor resection and a course of postoperative radiation therapy with concurrent temozolomide?

4. Does the subject have a single tumor recurrence/progression that is
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<td>1. Has the subject received cytotoxic chemotherapy within the past 3 weeks (6 weeks for nitrosoureas) of the planned surgery date?</td>
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<td>2. Does the subject have, or has the subject had, within the past 4 weeks any infection requiring antibiotic, antifungal or antiviral therapy?</td>
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<td>3. Does the subject have any bleeding diathesis, or must the subject take any anticoagulants, or antiplatelet agents, including NSAIDs that</td>
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### Exclusions

1. Can surgery be completed without delay?

2. Does the subject have a history of allergy or intolerance to flucytosine?

3. Is the subject HIV positive?

4. Does the subject have any gastrointestinal disease that would prevent him or her from being able to ingest or absorb flucytosine?

5. Has the subject received any investigational treatment within the past 30 days?

6. Has the subject received Avastin® (bevacizumab) for this recurrence/progression, or within the past 5 weeks?