AT-02. INTRATUMORAL DELIVERY OF THE RETROVIRAL REPLICATING VECTOR (RRV) TOCA 511 IN SUBJECTS WITH RECURRENT HIGH GRADE GLIOMA: INTERIM REPORT OF PHASE 1 STUDY (NCT 01156584)

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INTRODUCTION: High grade glioma (HGG) remains resistant to standard therapies. Newer approaches, such as immunotherapy, hold great promise. Viral infection and killing of tumor cells can stimulate antitumor immune responses. A Phase 1 clinical study using an investigational retroviral replicating vector, Toca 511, injected intratumorally, in combination with investigational oral Toca FC (extended-release 5-FC) is being conducted.

METHODS: The primary purpose of this study is to identify the highest safe and well tolerated dose of Toca 511 administered transcranially into recurrent HGG tumors. The starting dose was $3.9 \times 10^6$ Transducing Units (TU). Using a standard 3 + 3 design, doses have been escalated at half log intervals to $1.5 \times 10^9$ TU. 24 subjects were injected using a brain biopsy needle. Addition of gadolinium to the vector with post-operative iMRI suggested variable delivery of vector to the tumor. Subsequently 12 subjects have been treated using CED under real-time MRI-guidance. Monthly cycles of oral 5-FC are started 4 weeks after injection of the vector.

RESULTS: 36 subjects across 5 vector dosing cohorts have been studied. Real-time MRI-guidance demonstrated vector delivery with confirmation of vector RNA and CD protein in tumor samples. The injection procedures and vector and 5-FC dosing have been safe and well tolerated to date. No DLTs have been observed. Tumors have been observed to regress in the area around vector infusion and some subjects have experienced improvement in clinical symptoms. A number of subjects have experienced prolonged survival with 8 of the first 17 subjects with Grade 4 tumors surviving more than 1 year.

CONCLUSION: This study confirms the feasibility and safety of transcranial, intratumoral delivery of an RRV. Continued dose escalation is planned and may yield further gains in efficacy.