



## Positive Phase 2 Results from Agenus' Brain Cancer Vaccine Published in Neuro-Oncology

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Agenus Inc. (Nasdaq: AGEN), a biotechnology company developing novel immune system activating treatments for cancers and infectious diseases, today announced results published from a Phase 2 study demonstrated that more than 90% of the patients treated with Prophage Series G-200 were alive at six months after surgery and 30% were alive at twelve months. Additionally, the median overall survival was approximately eleven months. This compares favorably to the expected median survival for recurrent Glioblastoma multiforme (GBM) patients of three to nine months<sup>1-7</sup>. The primary objective of this multi-center, single arm Phase 2 trial was to assess the survival rate at six months.

The data was published in a manuscript in Neuro-Oncology, the official journal of the Society of Neuro-Oncology. GBM is the most common and most aggressive form of primary brain cancer. Despite approved therapy patients with GBM face a poor prognosis. Prophage Series vaccines are currently being studied in both newly diagnosed and recurrent GBM.

"Glioblastoma tumors are often resistant to standard therapies and the extended survival observed in patients treated with Prophage Series vaccine is very promising," said Andrew Parsa, MD, PhD, corresponding author of the study and chair of neurological surgery at Northwestern Memorial Hospital and the Michael J. Marchese Professor and chair of the department of neurological surgery at the Feinberg School of Medicine at Northwestern University. "The next phase of development is underway with an NCI funded, large-scale, randomized trial investigating Prophage Series G-200 in combination with Avastin (bevacizumab). Avastin is approved for the treatment of recurrent GBM and we believe there is the potential for a synergistic effect of a targeted anti-tumor immunotherapy and anti-angiogenic agent that could benefit patients."

Prophage Series vaccines are individualized cancer vaccines. Each Prophage Series vaccine is manufactured using a patient's own tumor after surgical removal. Each vaccine contains the 'antigenic fingerprint' of the patient's particular cancer and is designed to activate the patient's immune system to specifically target and destroy cancer cells bearing this fingerprint.

### Prophage Series G-200 Study Design

The Phase 2 trial enrolled 41 patients with a mean age of 55 years with surgically resectable recurrent high-grade GBM, the deadliest form of brain cancer. Patients underwent surgery to remove  $\geq 90\%$  of their tumors (also referred to as gross total resection), which were then used to manufacture Prophage Series G-200, a patient-specific heat shock protein based therapeutic vaccine. Eligible patients were treated after surgery with Prophage Series G-200 once weekly for four weeks, followed by biweekly injections until vaccine depletion. There were no serious adverse events associated with vaccine administration. For further information about this manuscript, please visit <http://neuro-oncology.oxfordjournals.org>.

The trial was supported through funding from the American Brain Tumor Association, Accelerated Brain Cancer Cure, National Brain Tumor Society, and National Cancer Institute Special Programs of Research Excellence. Dr. Parsa has not received any financial support or travel expense reimbursement for this work or for consulting activities on behalf of Agenus. Dr. Parsa does not have an equity interest in Agenus or a financial relationship with the company.

### About the Randomized Prophage Series G-200 ALLIANCE Trial with Avastin in Recurrent GBM

The National Cancer Institute (NCI) is supporting a study of the Prophage Series G-200 vaccine in a large-scale, multi-center, randomized Phase 2 trial in combination with bevacizumab (Avastin®) in patients with surgically resectable recurrent GBM. The study is being sponsored by the Alliance for Clinical Trials in Oncology (ALLIANCE), a cooperative group of the NCI.

This trial is the largest brain tumor trial ever funded by the NCI and the largest vaccine study ever conducted with Avastin. The study aims to advance the treatment of GBM, the most common and malignant form of brain cancer.

The ALLIANCE trial is investigating the potential benefits of treatment with a combination of Prophage Series G-200 and bevacizumab in a three-arm study of approximately 222 patients with surgically resectable recurrent GBM using a primary endpoint of overall survival. The study will compare efficacy of the Prophage Series G-200 vaccine administered with bevacizumab either concomitantly or at progression, versus treatment with bevacizumab alone. This study design is supported in part by previous research indicating a potential synergistic effect between the mechanisms of action of Prophage Series G-200 and bevacizumab. For additional information about the ALLIANCE trial visit ClinicalTrials.gov using Identifier NCT01814813.

### About Glioblastoma Multiforme (GBM)

The incidence rates of primary malignant brain and central nervous system cancers have increased over the last three decades.<sup>8</sup> The American Cancer Society estimates that more than 23,000 malignant tumors of the brain or spinal cord will be diagnosed during 2013 in the US, and that more than 14,000 people will die from these tumors.<sup>9</sup> GBM is the most common primary malignant brain tumor and accounts for the majority of diagnoses. It has been associated with a particularly poor prognosis, with survival rates at one and five years equaling 33.7% and 4.5%, respectively.<sup>10</sup> The current standard of care for patients with newly diagnosed GBM is surgical resection followed by fractionated external beam radiotherapy and systemic temozolomide<sup>11</sup> resulting in a median OS of 14.6 months<sup>12</sup> based on data from a randomized Phase 3 trial. Although this treatment can prolong survival, it is not curative and the vast majority of patients with GBM experience recurrent disease, with a median time to recurrence of seven months.<sup>13</sup> From the time of recurrence, the median survival is three to nine months.<sup>1-7</sup> Currently there is no standard treatment for patients with recurrent GBM, although additional surgery, chemotherapy (i.e., CCNU, temozolomide), bevacizumab, and radiotherapy are used.

### About Prophage Series Vaccines

Prophage Series vaccines are individualized cancer vaccines derived from each patient's own tumor. As a result of its individualized nature, each

Prophage Series vaccine contains the precise signals (antigenic fingerprint) of the patient's particular cancer and allows the body's immune system to target only cells bearing this specific fingerprint. Such high precision in immunological targeting represents a distinctly different method for treating cancer compared to conventional anti-cancer treatments such as chemotherapy or radiation therapy. These therapies cause side effects which are sometimes debilitating.

Prophage Series vaccines are based on Agenus' heat shock protein platform technology. For more information about Prophage Series vaccines and Agenus' heat shock protein platform, please visit <http://agenusbio.com/science/prophage.php>.

### **About Agenus**

Agenus Inc. is a biotechnology company developing treatments for cancers and infectious diseases. The company has multiple immunotherapeutic products based on strong technology platforms that are advancing through the clinic. Agenus' technology is further validated through partnerships with major pharmaceutical companies, with several product candidates in late-stage clinical trials with corporate partners. Between Agenus and its partners, 23 programs are in clinical development. For more information, please visit [www.agenusbio.com](http://www.agenusbio.com), or connect with the company on Facebook, LinkedIn, Twitter and Google+. For more information, please visit [www.agenusbio.com](http://www.agenusbio.com).

### **References**

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- <sup>10</sup> Central Brain Tumor Registry of the United States (CBTRUS) 2010 CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2004-2006. <http://www.cbtrus.org/reports/reports.html>
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Avastin is a registered trademark of Genentech.

### **Forward-Looking Statement**

*This press release contains forward-looking statements, including statements regarding clinical trial activities, the publication of data, and the potential application of the Company's technologies and product candidates in the prevention and treatment of diseases. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially. These risks and uncertainties include, among others, the factors described under the Risk Factors section of our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission for the period ended September 30, 2013. Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this release. These statements speak only as of the date of this document, and Agenus undertakes no obligation to update or revise the statements. All forward-looking statements are expressly qualified in their entirety by this cautionary statement. Agenus' business is subject to substantial risks and uncertainties, including those identified above. When evaluating Agenus' business and securities, investors should give careful consideration to these risks and uncertainties.*