



Updated Phase 2 Data of Prophage In Newly Diagnosed GBM Presented at ASCO Show Improvement in Median Progression Free Survival and Overall Survival Independently of Prognostic Markers, Compared with Historical Expectations

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Most significant improvements seen in patients with less elevated PD-L1 expression in peripheral blood

Improvement in overall survival seen independent of MGMT methylation status

LEXINGTON, Mass.--([BUSINESS WIRE](#))--Agenus Inc. (NASDAQ:AGEN), an immunology company developing innovative treatments for cancers and other diseases, today announced that patients with newly diagnosed Glioblastoma Multiforme (GBM) treated with Prophage (AGEN's individualized heat shock protein (HSP)-based cancer vaccine) plus Standard of Care (SOC) show substantially longer Progression Free Survival (PFS) and median Overall Survival (mOS) compared to historical SOC data, as detailed in an oral presentation at ASCO yesterday by Orin Bloch, M.D., Khatib Professor of Neurological Surgery and Assistant Professor of Neurological Surgery and Neurology at Northwestern University Feinberg School of Medicine.

GBM patients show evidence of tumor-mediated immunosuppression prior to treatment, measurable in part by greater expression of PD-L1 (Programmed Death Receptor – Ligand 1) on monocytic white cells in their peripheral blood. These elevations of peripheral blood monocyte PD-L1 correlate with elevation of PD-L1 expressing macrophages in their brain tumors, potentially working against effective immuno-therapy. When outcomes in this study were analyzed based on the extent of monocyte PD-L1 expression, the 50% of patients with less elevated PD-L1 showed markedly better PFS and mOS than historical SOC: PFS of 27 months *versus* 5-9 months and mOS of 45 months *versus* 15-19 months. Further, more than a third of these patients remain alive for more than three years from initial treatment, and more than 80% of these have not progressed. Prophage plus SOC also gave longer PFS and mOS than historical SOC data in the 50% of patients with greater monocyte PD-L1 elevation, although the differences were less pronounced. This raises the possibility of an improved Prophage benefit by combination with Checkpoint Modulating Antibodies (CPMs) that block PD-1 or PD-L1.

Additionally, the reported data suggest that Prophage added to SOC leads to longer mPFS and mOS regardless of MGMT methylation status, a known predictor of response to SOC. When Prophage is added to SOC in MGMT methylated patients in this study, the mOS was 44.7 months, compared to ~23 months reported for comparable MGMT methylated GBM patients on SOC alone in recent controlled trials (RTOG 0825).

MGMT methylation and PD-L1 expression on monocytes appear to be independent predictive markers in these patients. Although the apparent benefit of adding Prophage to SOC was observable in all subgroups of patients compared to historical SOC outcomes, the prolongations of mPFS and mOS are especially striking in patients with high MGMT *and* less elevated circulating monocyte expression of PD-L1: in this sub-group more than half the patients live for 4 years from initial treatment.

"These data are very promising for a treatment that fits seamlessly with SOC and has very attractive tolerability and safety," commented Northwestern's Dr. Bloch, lead investigator of the study. "I am especially pleased that more than a third of patients with less elevated monocyte PD-L1 expression are alive for 3 years or more. Using PD-L1 expression on peripheral blood monocytes, we seem to identify about 50% of patients (those with lower levels of PD-L1 expression) who may derive the greatest benefit from adding Prophage to SOC. Our data also suggest that the addition of Checkpoint Modulators of PD-1 or PD-L1 to SOC plus Prophage in patients with higher monocyte PD-L1 levels may enhance the benefit of the autologous heat shock protein based vaccine regimen."

"We are very encouraged by these data that suggest that Prophage, our individualized heat shock protein based vaccine, is beneficial to patients with GBM regardless of MGMT methylation status," said Robert Stein, M.D., Ph.D., Chief Scientific Officer of Agenus. "The results in patients with lower monocyte PD-L1 expression are especially promising. We believe a well-designed, controlled Phase 3 trial of Prophage plus SOC is warranted to try to bring this potential treatment advance to patients afflicted by GBM."

Study Details

The Phase 2 single-arm trial enrolled forty-six adult patients with newly diagnosed GBM from eight centers in the U.S. Each patient received SOC (surgical resection followed by chemoradiation). Within five weeks of completing radiotherapy, patients received continuing adjuvant temozolomide as well as weekly Prophage injections for four weeks followed by monthly Prophage injections until the depletion of vaccine or tumor progression. The primary endpoints of the trial were PFS and mOS.

About Agenus

Agenus is an immunology company developing a series of Checkpoint Modulators for the treatment of patients with cancer, infectious diseases, and other immune disorders, heat shock protein (HSP)-based vaccines, and immune adjuvants. These programs are supported by three separate technology platforms. Agenus' internal and partnered checkpoint modulator programs target GITR, OX40, CTLA-4, LAG-3, TIM-3, PD-1 and other undisclosed programs. The company's proprietary discovery engine Retrocyte Display™ is used to generate fully human and humanized therapeutic antibody drug candidates. The Retrocyte Display platform uses a high-throughput approach incorporating IgG format human antibody libraries expressed in mammalian B-lineage cells. Agenus recently acquired a powerful yeast antibody display platform termed SECANT®, developed by Celexion, LLC. SECANT allows rapid generation of soluble, full-length human antibodies. SECANT and Agenus' mammalian antibody display platform have complementary strengths and further bolster Agenus' abilities to generate and optimize fully human monoclonal antibodies. Agenus' heat shock protein-based vaccines have completed Phase 2 studies in newly diagnosed glioblastoma multiforme, and in the treatment of herpes simplex viral infection; the heat shock protein-based vaccine platform can generate personalized as well as off the shelf products. The company's QS-21 Stimulon® adjuvant platform is extensively partnered with GlaxoSmithKline and with Janssen Sciences Ireland UC and includes several candidates in Phase 2 trials, as well as shingles and malaria vaccines which have successfully completed Phase 3 clinical trials.

Forward-Looking Statement

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, the potential application of the Company's product candidate in the remediation of GBM and potential future clinical trial plans. 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 most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission for the period ended March 31, 2015. 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 press release, and Agenus undertakes no obligation to update or revise the statements, other than to the extent required by law. All forward-looking statements are expressly qualified in their entirety by this cautionary statement.

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