Agenus Vaccine Shows Significant Reduction in Viral Burden after HerpV Generated Immune Activation

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Phase 2 trial in patients with genital herpes shows correlation between viral load reduction and CD8 T cell activation, an important clinical surrogate

Trial shows booster shot demonstrates sustainable, long-term effect

LEXINGTON, Mass.--(BUSINESS WIRE)--Agenus Inc. (Nasdaq: AGEN), an immuno-oncology company developing a portfolio of checkpoint modulators (CPMs), heat shock protein peptide-based vaccines, and adjuvants, today announced promising Phase 2 results for HerpV, a synthetic vaccine candidate for the treatment of patients with genital Herpes Simplex Virus-2 (HSV-2). HerpV contains a defined mixture of peptides representing HSV-2 antigens plus Agenus' QS-21 Stimulon ® adjuvant.

In a randomized, Phase 2, double-blind, multi-center study, the majority of patients showed an immune response to the HSV antigens after a series of vaccinations and a booster dose at six months. More than half of those vaccinated developed a robust anti-HSV cytotoxic T-cell immune response, and in those patients there was a statistically significant 75% reduction in viral load ($P<0.001$; CI: 46.2 – 88.6%). This level of reduction in viral load has the potential to result in reduced incidence and severity of herpetic outbreaks and a reduction in viral transmission[1].

"We are pleased that the cellular immune response observed with HerpV vaccination is associated with a significant reduction in viral replication in the genital tract," said Robert Stein, MD, PhD, Chief Scientific Officer of Agenus. "The fact that our vaccine contains multiple HSV-2 antigens may contribute to its desired effects. We look forward to advancing discussions with potential partners to take this program into the next phase of clinical research."

After the booster shot, HerpV demonstrated a durable reduction in viral shedding approximating 14% (RR=0.86 and CIs: 0.58-1.26) and remains consistent with the reduction in viral shedding observed during the initial treatment period. The protocol defined secondary analyses were viral load and viral shedding after the booster shot, the primary endpoint of the study was reported in November 2013.

In this study, the booster shot was given six months after the first vaccination. Patients continue to be followed for safety and long-term immune response. HerpV reported adverse events have mostly been in line with expectations for a therapeutic vaccine and with effects commonly associated with QS-21 Stimulon® adjuvant. These adverse events are short-lived and include flu-like symptoms and injection-site reactions.

About the Phase 2 HerpV Study

In November 2013, Agenus announced the trial met its primary endpoint showing a statistically significant reduction in viral shedding. A total of 80 subjects with a history of 1-9 herpes recurrences within the prior 12 months were randomized into the trial and 70 subjects received the active treatment, HerpV and QS-21 Stimulon, and 10 subjects received placebo. Three injections of HerpV at a dose of 240 µg (includes12 µg of a mix of 32 different HSV-2 antigenic peptides) or placebo were given at two week intervals. HSV-2 activity in the genito-urinary tract was monitored by PCR for HSV-2 DNA in genital swabs for 45 days before and after the initial course of three vaccinations.

The primary analysis, which looked at viral shedding after the initial three HerpV vaccinations, demonstrated that subjects who received HerpV had a statistically significant reduction in viral shedding ($P=0.015$; RR=0.85). These results suggest a 15% reduction in viral shedding after the initial treatment period before the administration of the booster injection. The results also demonstrate a reduction in viral load of 34% ($P=0.08$). Placebo patients showed no reduction compared to baseline in either parameter. Notably, patients were not on any anti-viral treatments during their swabbing period.

About Agenus' Heat Shock Protein Platform (HSP) and Recombinant Series HerpV

HerpV is a recombinant therapeutic vaccine for genital herpes caused by the herpes simplex virus-2 (HSV-2). The vaccine is based on Agenus' HSP platform technology, and contains Agenus' proprietary QS-21 Stimulon, a plant-derived adjuvant that boosts specific immune responses. HerpV consists of recombinant human heat shock protein-70 complexed with 32 distinct 35-mer synthetic peptides from the HSV-2 proteome. This broad spectrum of herpes antigens is intended to allow for more accurate immune targeting and surveillance, reducing the likelihood of immune escape. Further, the diversity of antigens in HerpV increases the chance of providing efficacy for a wide segment of the patient population.

About HSV-2

About one in six Americans (16.2 percent) between the ages of 14 and 49 is infected with herpes simplex virus type 2 (HSV-2), according to the Centers for Disease Control and Prevention (http://www.cdc.gov/std/Herpes/STDFact-Herpes.htm). Herpes is the fastest growing STD in America, and experts predict that one in four Americans will contract an STD sometime in their life. Since two thirds of the population that gets herpes is age 25 or younger, it is a real health threat to society. HSV-2 is a lifelong and incurable infection that can cause recurrent and painful genital sores.

About Agenus

Agenus is an immuno-oncology company developing a portfolio of checkpoint modulators (CPMs), heat shock protein peptide vaccines and adjuvants. Agenus' checkpoint modulator programs target GITR, OX40, CTLA-4, LAG-3, TIM-3 and PD-1. The company's proprietary discovery engine Retrocyte Display® is used to generate fully human 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' heat shock protein vaccines for cancer and infectious disease are in Phase 2 studies. The company's QS-21 Stimulon ® adjuvant platform is extensively partnered with GlaxoSmithKline and Janssen and includes several candidates in Phase 3 trials. For more information, please visit www.agenusbio.com, or connect with the company on Facebook, LinkedIn, Twitter and Google+. For more information, please visit www.agenusbio.com.

Forward-Looking Statement

This press release contains forward-looking statements, including statements regarding clinical trial activities and results 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 March 31, 2014. 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.

[1] Schiffer JT, *et.al*. J. R. Soc. Interface 11: 2014.

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