

Agenus NexGen Neoantigen Vaccines Advance in Clinical Trials to Combinations

We pioneered approaches that enable the immune system to target and destroy an individual patient's tumor. Our pipeline of clinically validated neoantigen vaccines, QS-21 Stimulon® adjuvant (driver of SHINGRIX with up to 97% efficacy), checkpoint antibodies, tumor microenvironment conditioning bispecifics, and cell therapies (see [pipeline](#)) allow us the unique ability to combine these agents for optimal efficacy. Our neoantigen vaccines include AutoSynVax™, which targets the unique antigens expressed by each patient's own tumor and PhosphoSynVax™ (PSV) which targets antigens expressed across patients and tumors which can allow us to treat categories of patients with an off the shelf vaccine. ASV will be evaluated in combination with checkpoint antibodies in 2019 and we are advancing preclinical development of PSV.

Our Neoantigen Vaccines Have Key Differentiating Features



Our neoantigen vaccines are designed with unique features, each conferring important advantages:

- 1** Proprietary methods to develop an effective and relevant “Blueprint” of immunogenic neoantigens for each patient;
- 2** Heat shock proteins (HSPs) to efficiently deliver neoantigens to the right immune cells to activate an anti-cancer immune response. Our proprietary linker technology enables efficient neoantigen loading for a robust cancer specific immune response with 10X less peptide; and
- 3** QS-21 Stimulon®, a potent immune stimulator now in GSK's approved and highly efficacious shingles vaccine, SHINGRIX® (up to 97% effective).

Case Study: Our Neoantigen Vaccine, AutoSynVax™, Triggers Immune Cell Attack on the Tumor of a Teenage Patient

An aggressive form of liver cancer in a young patient was not controlled by radiation, chemotherapy, or PD-1 antibody. We suspected the patient's tumor was hiding. We confirmed this with a quick blood test.

In order to expose the tumor to the immune system, we sequenced the tumor and applied our proprietary algorithms to identify which of the tumor's neoantigens would train the immune system to better attack the tumor, i.e., we created a vaccine "blueprint." We manufactured the vaccine and delivered it in combination with our QS-21 Stimulon® adjuvant. Agenus' ASV vaccination educated the patient's killer T cells to recognize the tumor.

The vaccine was administered alone and then in combination with a PD-1 antibody. The patient had a clinical and immunological response and has been on treatment for ~2 years.

These data support the hypothesis that effective cancer treatment requires multiple modes of attack, such as immune education (with vaccines) and immune modulation with checkpoint blockade. We will advance our ASV neoantigen vaccine in combinations with our CTLA-4 and PD-1 antibodies (AGEN1884 and AGEN2034) in 2019.



Figure 1 From blueprint to vaccine, the generation of an individualized vaccine from a patient's own tumor tissue.

Agenus Proprietary Algorithms Select Neoantigen Tumor Targets for Vaccine



Using Next Generation Sequencing (NGS) technologies, cloud computing and our cutting edge proprietary bioinformatics capabilities, we rapidly profile each patient's tumor to accurately identify the exact DNA mutations that are in the tumor cells but not in healthy cells.

Next, our proprietary Agenus Immunogenic Mutation (AIM™) algorithms sift through the terabytes of DNA data to find mutations that are present throughout the tumor and predicted to be seen by the patient's own immune system ([link to published data](#)).

QS-21 + Heat Shock Proteins (HSP)...Uniquely Powerful Platform For Peptide-based Vaccines



QS-21 is Agenus' uniquely powerful adjuvant extracted from Chilean soap bark tree

Agenus' proprietary adjuvant, QS-21 Stimulon® is a powerful adjuvant licensed to GSK and is in the highly efficacious Shingles vaccine, SHINGRIX with up to 97% efficacy. QS-21 Stimulon® with our ASV neoantigen vaccine creates a critical advantage:

- Mutation-targeting vaccines often impart CD4 "helper" T cell responses. QS-21 Stimulon® generates both CD4 helper and CD8 killer T cell responses;
- QS-21 Stimulon® activates the innate immune system which is a critical partner to the adaptive (T cell-based) immune response to cancer;
- In pre-clinical studies, the combination of HSP, peptides and QS-21 stimulates a potent memory response which is necessary for vaccine efficacy.

Agenus' heat shock protein delivery system is clinically and scientifically validated:

HSPs transport peptides in vaccines from site of injection to specialized immune cells to activate cancer fighting T cells. HSPs act as chaperones, i.e., they help peptides in vaccines efficiently reach their destination, a process which preserves peptide integrity. Therefore, Agenus' vaccines, with HSPs, require at least 10x less peptide to achieve a robust immune response. This makes our vaccines easy to manufacture and can provide efficacy and impart cost advantages.