agenusnews

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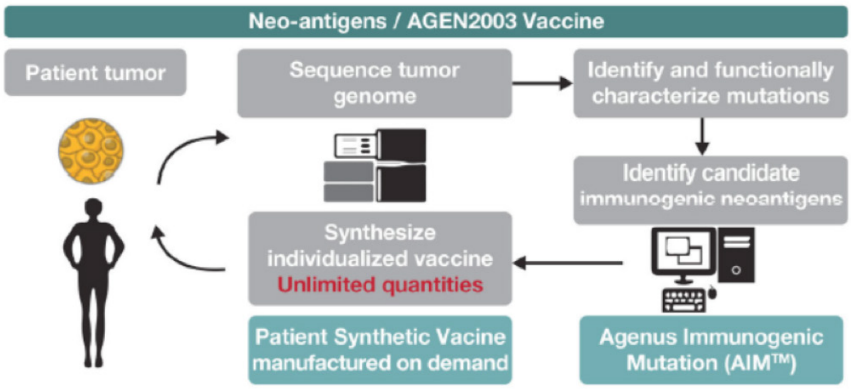
Agenus Presents at SITC 2018

The Annual Meeting of the Society for Immunotherapy of Cancer (SITC) is one of the most prominent medical conferences in immuno-oncology. SITC attendance has nearly tripled in the past four years as the field of immunotherapy continues to grow. The recently concluded SITC 2018 Conference in Washington, D.C., was estimated to have 4,000+ participants. We presented new data on our neoantigen vaccine programs and a novel anti-CD137 antibody.

Neoantigen vaccines are designed to train the immune system to recognize and attack cancers by targeting small protein fragments preferentially found in cancer tissues. Neoantigens have been extensively discussed in our previous Newsletters 2 and 9. Agenus' neoantigen vaccine platforms include: i) Individualized AutoSynVax™ (ASV™), which targets the unique antigens expressed by a patient's own tumor, and ii) Off-the-shelf (or pre-manufactured) PhosphoSynVax™ (PSV™), which targets antigens expressed across patients and tumors, thereby allowing us to treat broader categories of patients. Our vaccines are powered by our proprietary adjuvant, QS-21 Stimulon®.

Clinical Data Show Our Neoantigen Vaccine (AGEN2003) Is Safe and Stimulates Immune Responses to Individual Patient's Cancers



AGEN2003 is our first-generation neoantigen vaccine and is individually tailored to target each patient's cancer. It utilizes our proprietary data mining capabilities to identify peptides that would be expected to stimulate an immune response to a patient's cancer in an individualized vaccine. Our vaccines are formulated with our clinically validated heat shock protein (HSP) carrier molecules[1] along with our validated adjuvant, QS-21 Stimulon®. Our data mining along with our HSP and QS-21 Stimulon® are significant differentiators of our vaccine platforms as compared to other neoantigen vaccines.

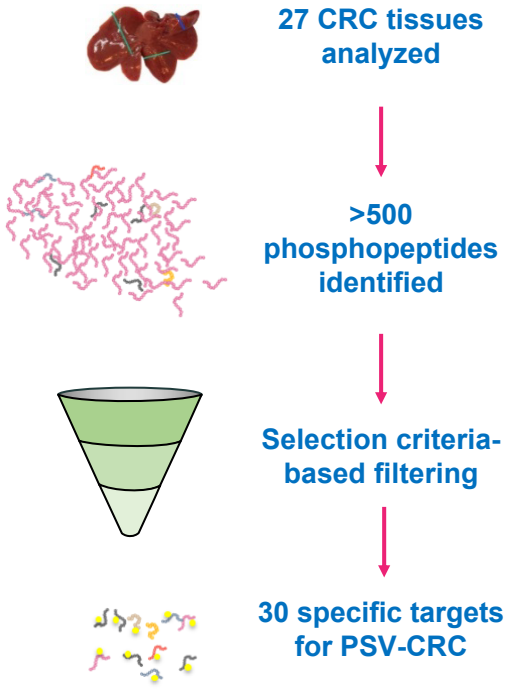
[1] Clinically validated in viral indication
[2] Agenus proprietary analysis

Forward-Looking Statements: This Agenus News Brief includes forward-looking statements, including statements regarding clinical development plans and timelines as well as expected IND filings, which are subject to risks and uncertainties. Please refer to this link for more details.

In the study which was presented at SITC, a cohort of patients with aggressive disease, who had failed multiple lines of prior therapy including PD-1 blockade, were treated with AGEN2003 in a phase 1 clinical trial (NCT02992977) or through our compassionate access program. Our results show that AGEN2003 induced tumor recognizing immune response in 3 of the 5 patients. Importantly, as of August 2018, two of these patients are alive. There were no adverse events attributed to the vaccine.

A next-generation version of this vaccine, AGEN2017, is being studied in an ongoing Phase 1a trial (NCT03673020). The next step is to combine this vaccine with immunomodulatory antibodies including Agenus' CTLA-4 antagonist (AGEN1884) and PD-1 antagonist (AGEN2034).

Agenus' Phosphopeptide Tumor Targets Represent A Breakthrough In Off-the-shelf vaccine In Colorectal Carcinoma (CRC)



Phosphopeptide Identification

As we have discussed in our most recent newsletter, our PSV™ Platform incorporates Phosphopeptide Tumor Targets (PTTs). These are neoantigens that can be used to target broader categories of patients with off-the-shelf vaccines. Hence, PSV™ has the potential to speed up patient treatment timelines and significantly reduce costs compared to individualized cancer vaccines.

Despite advancements in standard-of-care, the 5-year mortality rate for metastatic CRC patients remains close to 90%. This high mortality rate reflects limitations of current treatment modalities and provides significant opportunities for new effective treatments. We have designed a PSV-CRC vaccine aimed at benefitting a wide range of CRC patients. Our PSV-CRC vaccine utilizes a proprietary set of 30 PTTs, which are shared across CRC patients. These PTTs were identified using our proprietary algorithms to analyze a diverse set of CRC patient tissues. The samples included both primary and metastatic tumors and microsatellite unstable and stable CRC subtypes, and were taken from patients with different genetic backgrounds. By using these diverse tumor samples to identify common PTTs, we aim to increase the likelihood that our vaccine will elicit an immune response in a broad patient population, allowing use of the same vaccine in broader numbers of patients vs. the individualized vaccines. Further, this set of PTTs may be used in vaccines to treat other hematologic and solid malignancies beyond CRC.

[1] Clinically validated in viral indication
[2] Agenus proprietary analysis

The data we presented at SITC show that the majority (80%) of these 30 PTTs are presented by at least 50% of CRC patient types whose cancer tissue was evaluated. In addition, these PTTs are found in other cancer types, making them potentially useful for PSV vaccines in several other cancers. Furthermore, our analysis shows that a vaccine containing these 30 PTTs may be eligible to treat ~70% of the US/EU population[2]. This is significant, given that the lifetime risk of developing CRC is 4.5% for men and 4.2% for women.

As with our PSV-CRC vaccine, we are developing other indication-specific PSV offerings, such as in acute myeloid leukemia. By leveraging our proprietary Hsc70/QS21- based vaccine platform, which has already demonstrated clinical safety and immunogenicity[1], we plan to advance our PSV vaccine platform to the clinic in 2019.

AGEN2373: A Best-in-class Anti-CD137/4-1BB Agonist Antibody for Cancer Treatment

The primary goal of most immunotherapies is to stimulate the immune system to fight cancer. CD137/4-1BB, a co-stimulatory receptor found on immune cells, can activate multiple cancer-fighting immune responses. Our CD137/4-1BB targeting antibody represents a next generation I-O therapy based on its highly differentiated attributes versus other antibodies targeting the same receptor. The clinical development of at least one other agonist antibody that binds to the same target has been hampered by dose-limiting liver toxicity, which may be due to inflammation[a,b].

Agenus scientists are working to address these and other challenges by developing a best-in-class anti-CD137 agonist antibody, AGEN2373, with a novel mechanism of action that is expected to reduce liver toxicity. AGEN2373 is designed to stimulate CD137/4-1BB ONLY when an immune cell is undergoing activation.

We presented data at SITC showing that AGEN2373 is well-tolerated in non-human primates and may be combined with other checkpoint antibodies to enhance T cell activity. Based on these results, we plan to develop AGEN2373 as a monotherapy as well as in combination with other I-O treatments.

Having established clinical activity of our anti-PD-1 and anti-CTLA-4 programs, our scientists are sprinting to discover curative combinations. Agenus' discovery platforms have delivered 5 INDs in 2016-17 and 4 more so far this year for a total of 9 INDs. We are on track to file 2 additional INDs by year end and 2 more in 1H 2019. This would make a total of 13 INDs in ~3 years, an I-O industry record. To learn HOW, check out Issue 4. The data presented at SITC reflects on our steadfast commitment to innovation in immuno-oncology, and our strong potential to deliver transformative combinations to the clinic.

For all SITC presentations see here.

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