

O-9012 followed by intradermal electroporation. Personalized Therapeutic

Category:

Best Startup

Company Name:

Geneos Therapeutics

Turnover and/or Funding:

Series B fundraising is ongoing. The Series B funding will support the Phase II Adjuvant HCC study and business operations for 3 years.

Sub-Category:

Biotechnology

Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

Geneos Therapeutics is a biotechnology company at the forefront of innovative immunotherapy solutions for personalized therapeutic cancer vaccines (PTCV). Our current focus is on advanced hepatocellular cancer (HCC), which is a particularly aggressive form of liver cancer with limited treatment options. We are developing a personalized immunotherapy approach that is tailored to the specific genetic makeup of each patient's cancer, with the goal of enhancing the patient's immune response and improving outcomes.

One of the key factors that sets us apart in the field of immunotherapy is our approach to personalized DNA-based cancer vaccines. We are focused on leveraging the individual's neoantigens to create customized, targeted therapies that are specifically designed to address the unique characteristics of his or her specific cancer. The personalized cancer vaccine approach could potentially be applied to a wide range of cancers, allowing for more effective, targeted treatment options that take into account individual variations in cancer genetics.

Hepatocellular carcinoma is a rare and aggressive cancer with poor outcomes with incidence continuing to rise in the US. NCI SEER 2022 estimates concluded that over 41,000 new cases and approximately 30,500 deaths due to liver and intrahepatic bile duct cases were reported, representing 2.2 percent of all new US cancer cases and 5

percent of all cancer deaths¹.

Patients with late-stage disease are typically treated with systemic therapies. Standard of care for treatment in both 1L and 2L advanced HCC is evolving rapidly, but all approved agents are either checkpoint inhibitors (CPI), vascular endothelial growth factor (VEGF) pathway inhibitors (anti-angiogenic monoclonal antibodies [mAbs] or tyrosine kinase inhibitors [TKIs]), or their combinations).

Combining Geneos' PTCV with a CPI is capable of inducing tumor infiltrating CD8 T cells, which can kill cancer cells and is crucial for developing effective treatments for advanced HCC patients. Targeting neoantigens has emerged as a promising approach since these antigens are patient tumor-specific and should be immunogenic since they are not subject to central tolerance.

Geneos' GT-30 Phase 1b/2a study is designed to investigate the use of GNOS-PV02 (PTCV) in combination with IL-12 and pembrolizumab for the treatment of patients with 2L, advanced HCC. Four patients are cancer-free, whereas seven additional patients had a partial response, therefore showing a 30.6 percent (11/36) response rate. Unlike other platforms, in almost every case, each patient's vaccine, designed using Geneos' proprietary GT-EPICTM platform, includes all of their tumor-specific targetable neoantigens resulting in a truly personalized vaccine. The PTCV is rapidly manufactured and administered intradermally together with plasmid-encoded IL-12 (pIL12) as an adjuvant via electroporation (EP). The use of pIL12 plus EP serve to optimize the effectiveness of peripheral vaccination and ensure an effective neoantigen-specific CD4+ and CD8+ T cell response with killing function to destroy cancer cells. Our vaccine-induced CD4 and CD8 response results from the company's proprietary vaccine design and delivery methodology. The effectiveness of Geneos' immunizations, is resulting in meaningful tumor shrinkage and clinical benefit. Treatments have been unusually well tolerated by patients. Data from this study was published in Nature Medicine, April 2024.

History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):

In just six years, Geneos has already had a significant impact on the lives of patients treated with our personalized therapeutic cancer vaccine (PTCV). Four patients to date from our Phase 1b/2a clinical trial for advanced HCC are now cancer-free following treatment with the company's PTCV and patients are continuing treatment for up to 5 years. Separately, a young lady named Julia, who was treated for anaplastic astrocytoma, a form of brain cancer, with our PTCV at the age of 21, remains cancer-free six years after treatment.

Geneos was founded in 2019 by Dr. Sardesai., who was previously head of R&D and

chief operating officer at Inovio Pharmaceuticals (Nasdaq: INO). Our proprietary plasmid delivery technology as well as our IL-12 adjuvant, originated at Inovio and was then combined with Wistar Institute's neoantigen discovery technology. These proprietary and IP protected innovations have been integrated into our GT-EPIC™ platform for the development of uniquely personalized immunotherapies for cancer. Our DNA plasmids have the ability to target one to 80+ neoantigens in the same patient-specific formulation enabling all patient-specific targetable neoantigens for virtually all patients. The addition of the second plasmid, encoding the cytokine IL-12, acts as an adjuvant locally at the injection site. Further, the administration of the PTCV at the injection site is further optimized via use of our proprietary in vivo electroporation (EP) device CELLECTRA 2000, which maximizes transfection efficiency and enhances the uptake of the DNA plasmids in all cells present at the injection site. Collectively, the optimized antigenic sequences of our PTCVs intradermal administration, pIL-12 and EP all maximize the immunogenicity of our DNA plasmids and drive induction of CD4+ and CD8+ T cells faster and in a higher percent of vaccinees than if they were not used.

Today, Geneos is a company of five employees, supported by a number of talented and experienced consultants and advisors. We also collaborate with academic institutions and other industry leaders to further enhance our research and development efforts. We have raised \$45M and have achieved significant milestones by remaining focused on what means the most, prioritizing innovation to bring life-saving therapies to patients in need.

Manufacturing of personalized therapies is fast and easy for us. Firstly, all cell and gene therapy (i.e., RNA, CAR-T, AAV) products start with the manufacturing of plasmid DNA, which for us, is the final drug product. Secondly, it is extremely important that patients receive their treatment as soon as possible. We have an experienced team of people that manage the full process from biopsy to treatment for each patient. Finally, GNOS-PV02 is very stable and doesn't require cold chain management like other personalized therapies. All three of these elements make GNOS-PV02 an optimal drug product.

We have been able to attract world class talent and have a team with a track record of success in building immunotherapy companies. Additionally, we are fortunate to be working with world renowned KOLs, thought leaders and institutions who have taken an interest in Geneos.

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:

Immunotherapies have dramatically impacted the treatment of cancer in recent years, but a significant unmet need exists for therapies that can robustly generate CD8+ T cell responses and for those which can safely be combined with checkpoint inhibitors. Checkpoint inhibitors appear only to be effective when CD8+ T cells are present in the

tumor microenvironment, and our PTCVs have been shown to reprogram the tumor microenvironment driving impactful CD8+/CD4+ T cell responses against the tumor. Further, with our industry-leading, unique ability to include virtually all of a patient's tumor neoantigens in the creation of his/her PTCV, this creates a highly targeted immune response which we are observing in extensive mechanism of action studies from ongoing analyses of our clinical data. Additionally, in the event of tumor immune escape, we can simply redesign and remanufacture an updated PTCV to resume vaccine effectiveness.

"As a physician treating cancer patients on a daily basis, the patient experience is top of mind for me. I appreciate that Geneos' protocol is both easy from the physician's perspective and non-invasive from the patient's perspective," stated Mark Yarchoan, MD at Johns Hopkins University. "Only a small tumor biopsy is needed to identify the neoantigens for the creation of the vaccine, so there is no need for apheresis or large quantities of blood or other samples. Then, once the vaccine is completed, it is administered to the patient through a simple intradermal injection."

Please provide appropriate references (PubMed, Abstract, Website):

1National Cancer Institute (NCI). Division of Cancer Control and Population Sciences (DCCPS). Surveillance Research Program (SRP). Surveillance, Epidemiology, and End Results Program. Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer. Accessed March 27, 2023.

<https://seer.cancer.gov/statfacts/html/livibd.html#:~:text=Liver%20and%20intrahepatic%20bile%20duct%20cancer%20is%20the,cancer%20deaths%20is%20highest%20among%20people%20aged%2065%E2%80%9374>

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Bhojnagarwala et al_Mol Ther_2021 A synthetic DNA vaccine targeting multiple neoantigens _ lung and ovarian tumors in mice.pdf

Duperret et al_Cancer Immunol Res_2019 A Synthetic DNA MultiNeoAg Vax Drives Predom MHC Class I CD8.pdf

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