Category

Best Startup

Product/Solution Name

GNOS-PV02+INO-9012 followed by intradermal electroporation. Personalized Therapeutic Cancer Vaccine

Date of Approval

N/A

Indications

Advanced hepatocellular carcinoma
Glioblastoma (GBM)

Therapeutic Categories

Advanced cancers, cancers with low tumor mutational burden

Attached Files:

- Q2 2023 Geneos Therapeutics Corporate Presentation V10.pdf

Background information and need for solution/product

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. Rather than using a one-size-fits-all approach to treatment, 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. Why not just include virtually all of a patient’s neoantigens and let nature decide which ones are relevant to unleashing the desired immune response? The fundamental importance and value of doing so is now being borne out in extensive immunological mechanism of action studies from analyses of our emerging clinical data. This could be a game-changer for cancer treatment, as it has the potential to significantly improve outcomes for patients.

Our approach has already shown promising results in early clinical studies, with improvements in overall survival rates and for some, complete eradication of their primary tumor and metastases. We are continuing to refine our approach and expand clinical studies to further validate the efficacy and safety of our treatment approach.

About Hepatocellular Carcinoma (HCC)

Advanced 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. Across these cancers, five-year survival is about 20 percent overall, but approximately 45 percent of HCC cases present as locally advanced/metastatic at the time of diagnosis.

Metastatic cases have poorer five-year overall survival (OS) rates: within this group, the five-year OS post-first line progression is approximately 3.0 percent for females and males. It is anticipated that HCC will become the third-leading cause of cancer death in the US by 2040. HCC remains a significant unmet medical need population, particularly among those with disease progression beyond first-line (1L) treatment.

HCC is distinguished by low tumor mutational burden (TMB) and immune-desert phenotype, and thus remains a challenge for immunotherapy. In patients with HCC, a median TMB of four mutations/Mb has been reported, with 95 percent of patients having a TMB of 10 mutations/Mb for classifying a tumor as high TMB. As noted above, there is low prevalence of high TMB HCCs, and in HCC, even a high TMB has not been associated with higher levels of immune infiltration. As a result, CPI therapies have provided limited benefit to HCC patients when compared to other tumors with high TMB and immune-inflamed phenotype. Objective radiological responses by anti-PD-(L)1 monotherapy (i.e., monotherapy against programmed cell death protein-1 ligand) in either 1L or second-line (2L) advanced HCC were observed in only 12-18 percent of HCC patients.

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). The anti-VEGF/CPI combination bevacizumab/atezolizumab is approved for 1L in the US, along with a second CPI combination, durvalumab and tremelimumab, which is approved for 1L therapy for adult patients with unresectable HCC.

Combining Geneos' PTCV with a CPI, whether in 1L or 2L treatment, 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. We have generated supporting data from non-clinical animal tumor model studies, as well as the ongoing GT-30 Phase 1 study of GNOS-PV02, suggesting that an immunotherapy approach including a personalized therapeutic cancer vaccine with CPI could provide clinical benefit for HCC patients.

Initial Clinical Data Reveal Four Patients Cancer-Free

The company reported data at the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting in November 2022 from the first 24 patients enrolled showing strong tumor reductions including three complete responses (complete disappearance of tumor), and four patients with a partial response.

Based on these data, we have expanded this study to include 36 patients. Geneos' GT-30 Phase 1b/2a study is designed to investigate the use of GNOS-PV02 (our personalized neoantigen-targeted immunotherapy delivered intradermally) in combination with IL-12 and pembrolizumab for the treatment of patients with second-line, advanced HCC. To date, four patients are cancer-free, whereas six additional patients had a partial response, therefore showing a 32 percent (10/31) response rate. This is unprecedented in HCC. 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 tumor-specific, neoantigen-targeted cancer vaccine 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. This industry-leading vaccine-induced CD4 and CD8 response results from the company's proprietary vaccine design and delivery methodology, optimized in extensive preclinical and clinical development. The effectiveness of Geneos' immunizations, which arises from its ability to include all targetable neoantigens as well as the use of pIL12 and EP, is resulting in meaningful tumor shrinkage and clinical benefit in the ongoing clinical trial. Equally important, to date, the treatments have been unusually well tolerated by patients. Geneos plans to report the efficacy and durability of response data from the full cohort of 36 patients in 2023. Further, planning is underway for a potentially registrational clinical trial.

"Tremendous headway has been made in the cancer immunotherapy field in recent years, but I believe that personalized approaches to treating cancer are critical given the unique nature of every patient's tumor," stated Mark Yarchoan, MD, associate professor of oncology, Johns Hopkins, and an investigator on the GT-30 study. "Geneos' approach is unique in the field of patient-specific cancer vaccines, as they have the unique ability to create a vaccine using virtually all of the patient's tumor neoantigens enabling a customized and comprehensive attack upon delivery back to the patient. I'm thrilled to be involved in Geneos' clinical program, as I believe they have the technology and the team to see this product through to commercialization for not only HCC but for many other cancers in the future as well."

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

History of the development of the solution/product

In just four 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. 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 four years after treatment and is currently pursuing a graduate degree.

"It is success stories like these that continue to motivate me and my colleagues to expedite and perfect our cancer vaccine technologies," stated founder and CEO, Niranjan Sardesai, Ph.D. "There are many more lives, and many types of cancer, that we can impact, so we are driven to effectively use our time and resources to get these important vaccines into the hands of physicians as quickly as possible."

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 has grown into a company of nine 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.

"Once manufactured, rapid delivery of our PTCVs to our patients is critical given the nature of cancer, so we have put in place key partnerships with CDMOs enabling six to eight week turnaround from biopsy to treatment of the cancer patients in our studies, in the US, Europe and other regions around the world," stated Dr. Sardesai. "This rapid turnaround is a key differentiator of our PTCVs, and we have a clear path to further reduce this time to less than three to four weeks upon commercialization, enabling accessibility of our PTCVs in most first and second line clinical settings."

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, which is providing us with many diverse opportunities to share data and network as we all work together to improve the treatment of cancer.

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- Geneos_Prix Galien_Master.mov

Why this solution/product 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 (ie Pubmed links)

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