

Company Description

GeoVax Labs, Inc. (“GeoVax” or “the Company”) is a clinical-stage biotechnology company developing novel therapies and vaccines for cancers and many of the world’s most threatening infectious diseases. The Company’s lead program in oncology is a novel oncolytic solid tumor gene-directed therapy, Gedeptin®, presently in a multicenter Phase 1/2 clinical trial for advanced head and neck cancers. GeoVax’s lead infectious disease candidate is GEO-CM04S1, a next-generation COVID-19 vaccine targeting high-risk immunocompromised patient populations. GEO-CM04S1 is currently being evaluated in two Phase 2 clinical trials: (1) as a COVID-19 vaccine for immunocompromised patients; and (2) as a more robust, durable COVID-19 booster among healthy patients who previously received the mRNA vaccines. GeoVax has a leadership team who has driven significant value creation across multiple life science companies over the past several decades.

Key Points

- On March 23, 2023, GeoVax announced financial results for the year ended December 31, 2022 and provided a corporate update. The Company reported a net loss for the year ended December 31, 2022 of \$14.0 million or (\$0.83) per share versus \$18.6 million or (\$3.04) per share for the year ended December 31, 2021.
- GeoVax continues to focus on advancing its ongoing clinical programs for its Gedeptin® cancer therapy, targeting advanced head and neck cancers, as well as its SARS-CoV-2/COVID-19 vaccine. The Company recently expanded to additional clinical sites and is accelerating patient enrollment for both programs. GeoVax expects to report its progress from these trials in the coming months.
- A version of modified vaccinia Ankara (MVA) is the vaccine used and stockpiled for immunization against Monkeypox. GeoVax has acquired rights to a similar version of MVA from National Institutes of Health (NIH) to develop a Monkeypox vaccine; it is also the vaccine vector used in GeoVax’s vaccines targeting COVID-19, Hemorrhagic fever viruses, HIV, Zika, and the Company’s MVA-VLP-MUC1 cancer immunotherapy.
- In February 2023, GeoVax announced significant progress in developing a high-yield, high-capacity, continuous avian cell line system for manufacturing its MVA-based vaccines and immunotherapies. The Company expects to accelerate its efforts towards fully implementing a proprietary, continuous cell line manufacturing system that is intended to provide lower-cost, scalable versatility for broad MVA vaccine and immunotherapy applications.
- GeoVax’s intellectual property portfolio contains over 115 granted or pending patent applications across 24 patent families.
- The Company’s financing activities during 2022 have provided GeoVax with sufficient resources to advance its development programs, including producing additional drug product for use in its clinical trials. GeoVax reported cash balances of \$27.6 million at December 31, 2022 versus \$11.4 million at December 31, 2021. Contributing to the increase in cash balances were aggregate net proceeds of \$27.7 million from equity transactions during January 2022 and May 2022, and \$7.6 million from the exercise of warrants during August 2022.



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GOVX (NASDAQ) One-Year Chart



Ticker (Exchange)	GOVX (NASDAQ)
Recent Price (03/27/2023)	\$0.65
52-week Range	\$0.43 – 4.30
Shares Outstanding	26.3 million
Market Capitalization	\$18.2 million
Avg. 10-day Volume	302,500
EPS (Year ended 12/31/2022)	(\$0.83)
Employees	19

YEAR END 2022 FINANCIAL RESULTS

Net loss for the year ended December 31, 2022 was \$14.0 million or (\$0.83) per share versus \$18.6 million or (\$3.04) per share for the year ended December 31, 2021.

Research and development (R&D) expenses were \$9.1 million for 2022 versus \$15.6 million in 2021. Research and development expense for 2021 included \$12.3 million of one-time license fees and other costs related to technology licensing agreements; excluding these costs, research and development expense increased by \$5.9 million from 2021 to 2022. The increase in 2022 relates largely to higher personnel and consulting costs, costs of conducting clinical trials for GEO-CM04S1 and Gedeptin[®], costs of manufacturing materials for use in clinical trials, and a higher level of activity.

General and administrative expenses were \$5.0 million for 2022 versus \$3.6 million in 2021, with the increase primarily attributable to higher personnel and consulting costs, patent costs, investor relations costs, and travel expenses.

GeoVax reported cash balances of \$27.6 million at December 31, 2022 versus \$11.4 million at December 31, 2021. Contributing to the increase in cash balances were aggregate net proceeds of \$27.7 million from equity transactions during January 2022 and May 2022, and \$7.6 million from the exercise of warrants during August 2022.

As a result of the Company's recently completed successful financings, GeoVax is well capitalized to complete its current Phase 2 clinical programs, including expansion of the Gedeptin[®] multi-site trial as well as expansion of the GEO-CM04S1 COVID-19 vaccine trial among immunocompromised patients to additional sites. GeoVax remains focused on providing immunotherapies and vaccines that improve lives worldwide and preventing or treating some of the world's most challenging cancers and infectious diseases. The Company also recently initiated business development discussions towards partnering and collaborations to ensure worldwide access to its products.

2022 CLINICAL TRIAL PROGRESS AND OPERATIONAL DEVELOPMENTS

GeoVax is focused on advancing its ongoing clinical programs its Gedeptin[®] cancer therapy, targeting advanced head and neck cancers as well as its SARS-CoV-2/COVID-19 vaccine. The Company has expanded to additional clinical sites and is accelerating patient enrollment for both programs. For its COVID-19 vaccine program, GeoVax implemented a novel, mobile clinical research facility in Claremont, California to support its Phase 2 COVID-19 vaccine booster trial. GeoVax expects to report its milestone progress from these trials during throughout 2023.

The Company has further progressed on its MVA-VLP-MUC1 immuno-oncology candidate into IND-supportive studies, with encouraging results. GeoVax further secured rights to NIH-MVA technology for additional development and commercial use against Monkeypox (MPox) and Smallpox viruses, which is expected to provide a compelling opportunity to leverage the Company's MVA-based vaccine expertise and help expand the global public health supply options available. GeoVax believes that it could become the first U.S.-based, primary supplier of a MVA-vaccine against Mpxv and Smallpox.

The Company also recently announced important progress toward developing a high-yield, high-capacity, avian cell line system for manufacturing MVA-based vaccines. This process could prove transformational for GeoVax, biomedicine, and public health worldwide. By means of advancing the Company's MVA manufacturing to a modern, interchangeable process, GeoVax is on course to expand MVA applications from stockpile-based solutions for niche medical markets to have the capability to respond to world needs on a timely basis. This could position GeoVax to become the first U.S.-based supplier of the MVA vaccine to prevent MPox, Smallpox, and other pox-related viruses.

PHASE 2 TRIAL FOR GEDEPTIN® IN ADVANCED HEAD AND NECK CANCER

An ongoing Phase 1/2 trial is evaluating the safety and efficacy of repeat cycles of Gedeptin® therapy in patients with recurrent head and neck squamous cell carcinoma (HNSCC) with tumor(s) accessible for injection and no curable treatment options.

Gedeptin® is a novel patented product/technology to treat solid tumors through a gene therapy strategy known as Gene-Directed Enzyme Prodrug Therapy (GDEPT). In GDEPT, a vector is used to selectively transduce tumor cells with a nonhuman gene, which expresses an enzyme that can convert a nontoxic prodrug into a very toxic antitumor compound *in situ*. A Phase 1 dose-ranging study evaluating the safety of a single cycle of Gedeptin® therapy found the therapy was well-tolerated with evidence of a reduction in tumor size in patients with solid tumors.

In February 2023, GeoVax announced the expansion of the Gedeptin® Phase 1/2 trial with patients actively enrolling at National Cancer Institute (NCI) designated Cancer Centers: Stanford University Cancer Institute, Emory University Winship Cancer Institute, and the Thomas Jefferson University Sidney Kimmel Cancer Center. Funded in part by the U.S. Food & Drug Administration (FDA) under its Orphan Products Clinical Trials Grants Program, the trial will guide the design of a larger study that also may involve patients with other anatomically accessible oral and pharyngeal cancers. This may lead to labeling discussions with the FDA and initiation of further Gedeptin® investigations, including in combination with immune checkpoint inhibitors for other cancerous and non-cancerous tumor indications.

TWO PHASE 2 CLINICAL TRIALS ADVANCING IN SARS-CoV-2 VACCINES

GEO-CM04S1 is a next-generation COVID-19 vaccine that expresses spike and nucleocapsid antigens of the SARS-CoV-2 (COVID-19) virus. GEO-CM04S1 continues to advance in two Phase 2 clinical studies, one as a primary vaccine for immunocompromised cancer patients, in direct comparison to either the Pfizer or Moderna mRNA vaccine, and the second as a booster for healthy patients who have previously received either the Pfizer or Moderna vaccine as their initial inoculation.

Two 2022 peer-reviewed publications in *The Lancet Microbe* and *iScience* report data from the Phase 1 study of GEO-CM04S1 indicating robust neutralizing antibodies and T cells against SARS-CoV-2, including the Omicron and Delta variants. These data confirm the powerful dual action of the GeoVax vaccine, an important feature given the multiple mutations, leading to variants of concern and inconsistent protection from existing FDA-authorized vaccines.

These findings suggest that T cell immunity stimulated by GEO-CM04S1 may constitute a critical second line of defense to provide long-term protection against SARS-CoV-2 variants among the population in general as well as among the 15 million patients in the U.S. and over 200 million patients worldwide with compromised immune systems. A article recently published in the *New England Journal of Medicine* addressed the critical importance of addressing both antibodies and T cells in achieving protection against SARS-CoV-2.

MODIFIED VACCINIA ANKARA (MVA) FOR IMMUNIZATION AGAINST MONKEYPOX (MPOX) AND SMALLPOX

MVA is the vaccine presently used and stockpiled in the U.S. Strategic National Stockpile for immunization against the MPox and Smallpox viruses. GeoVax had previously demonstrated that an experimental HIV vaccine, using NIH-MVA as the vaccine vector, protected non-human primates challenged with a lethal dose of the MPox virus. Further, in August 2022, City of Hope, which originally developed GEO-CM04S1, published results demonstrating that both their proprietary sMVA (synthetic MVA) and GEO-CM04S1 elicited robust orthopoxvirus-specific binding and neutralizing antibody responses. The authors concluded that GEO-CM04S1 and sMVA represent unique vaccine candidates to control the unforeseen global MPox outbreak.

GeoVax secured rights from the NIH covering preclinical, clinical, and commercial uses of the NIH-MVA against MPox or Smallpox viruses. The Company is evaluating development and regulatory pathways towards expanding the public health options available to reduce and manage the risk of MPox worldwide with the intent to be the first U.S.-based supplier of a MVA-vaccine against MPox and Smallpox.

RECENT COMPANY DEVELOPMENTS

- **March 23, 2023**—GeoVax Labs, Inc. announced its financial results and key operational accomplishments for the year ended December 31, 2022 (see page 2).
- **March 15, 2023**—The Company congratulated its colleague and collaborator, Don Diamond, Ph.D. for recognition as a finalist for the Best Academic/Research Team Award, part of the Vaccine Industry Excellence (ViE) Awards which was held during the World Vaccine Congress in Washington, DC on April 3-6, 2023.
- **March 9, 2023**—Announced that it will report 2022 financial results on March 23, 2023 after the market closes.
- **February 27, 2023**—Announced the presentation of results from a clinical study of a combinational HIV therapy that included GeoVax’s HIV vaccine candidate, MVA62B. The data were presented at the Conference on Retroviruses and Opportunistic Infections (CROI) held February 19-22, 2023, in Seattle, Washington.
- **February 15, 2023**—GeoVax and EmVenio Research, a patient-focused decentralized trial global organization, announced a collaboration to deploy a mobile clinical facility in the Claremont, California area to expand GeoVax’s ongoing Phase 2 clinical trial evaluating GEO-CM04S1 as a COVID-19 booster vaccine in healthy patients.
- **February 8, 2023**—Announced significant progress in developing a high-yield, high-capacity, continuous avian cell line system for manufacturing its MVA (modified vaccinia Ankara)-based vaccines and immunotherapies.
- **February 7, 2023**—Announced its clinical trial of Gedeptin® for patients with recurrent head and neck cancers is now actively enrolling patients at three major research centers: Stanford University, Emory University, and Thomas Jefferson University.
- **January 26, 2023**—Announced that its Chairman and CEO, David Dodd, will present at the 2023 BIO CEO & Investor Conference taking place in-person in New York City at the New York Marriott Marquis and virtually on February 6-9, 2023.
- **January 25, 2023**—Announced that the U.S. Patent and Trademark Office issued a Notice of Allowance for Patent Application No. 17/000,768 titled, “Method for Generating a ZIKV Immune Response Utilizing a Recombinant Modified Vaccinia Ankara Vector Encoding the NS1 Protein.”
- **January 4, 2023**—Announced that it will present at the Biotech Showcase coinciding with the 41st Annual J.P. Morgan Healthcare Conference in San Francisco, January 9-12, 2023.
- **December 20, 2022**—Announced the appointment of Valerie Montgomery Rice, MD, FACOG, Morehouse School of Medicine President and CEO, as Special Advisor to the Chairman/CEO and Board of Directors of GeoVax.
- **December 7, 2022**—Announced that it has appointed Jayne Morgan, M.D., to its Board of Directors.
- **November 28, 2022**—Announced that Mark J. Newman, Ph.D., Chief Scientific Officer of GeoVax, will present at the World Vaccine & Immunotherapy Congress (WVIC) West Coast 2022, taking place November 28-December 1, 2022, in San Diego, California.

POTENTIAL 2023 COMPANY MILESTONES

With regard to potential 2023 milestones, GeoVax seeks to focus its efforts on accelerating support of the Gedeptin[®] and CMO4S1 Phase 2 clinical programs, moving the GeoVax MVA vaccine related to MPox and Smallpox development, and advancing its MVA manufacturing process into operational validation. During the first half, the Company anticipates reporting initial clinical results of the safety lead in for the CMO4S1 immunocompromised trial.

Presentations are scheduled for the World Vaccine Congress in early April, the Vaccine Summit 2023 in late May, as well as the ISAC Flow Cytometry (ph) International meeting in late May. In addition to the recently reported expansion of the Gedeptin[®] study, GeoVax expects to review initial data later this year.

The Company further expects to report preclinical information related to the use of the Gedeptin[®] technology in conjunction with immune checkpoint inhibitors. Additionally, GeoVax intends to provide updates relative to IND supportive studies of its advancing GeoVax MUC1 tumor associated antigen therapy. In early June, the Company is expected to participate in ASCO 2023.

Company Background

GeoVax Labs, Inc. is a clinical-stage biotechnology company focused on developing human vaccines—both preventive and therapeutic. Its technology, targeting infectious diseases and cancer, employs the Company’s proprietary GV-MVA-VLP™ vector vaccine technology platform. This GV-MVA-VLP™ vector vaccine technology utilizes a Modified Vaccinia Ankara (MVA) vector, a large virus capable of carrying several vaccine antigens. MVA is a replication-defective live vector that expresses non-infectious virus-like particles (VLPs) in the individual receiving the vaccine (*in vivo*). VLPs mimic a natural infection, stimulating both the humoral and cellular arms of the immune system to recognize, prevent, and control the target infection through durable immune responses. The Company’s development efforts are focused within the areas as summarized in Figure 1.

Figure 1
GEOVAX PIPELINE FOCUSED ON NEAR-TERM VALUE DRIVERS

	Product Candidate	Status
Coronavirus		
COVID-19 (Immunocompromised)	GEO-CM04S1	Phase 2
COVID-19 (Booster to mRNA)	GEO-CM04S1	Phase 2
Pan Coronavirus	GEO-CM02	IND-Enabling
Cancer Immunotherapy		
Solid Tumors (Advanced Head & Neck Cancer)*	Gedepin®	Phase 1/2
Solid Tumors (MUC1)	MVA-VLP-MUC1	IND-Enabling
Infectious Disease		
Ebola, Marburg, Sudan**	GEO-EM01	IND-Enabling
Zika Virus**	GEO-ZM02	IND-Enabling
Lassa Fever**	GEO-LM01	Exploratory
Malaria**	GEO-MM02	Exploratory

*: Orphan Drug status granted; **: Indication within FDA Priority Review Voucher program

Source: GeoVax Labs, Inc.

GeoVax is capitalizing on the safety and efficacy of its technology platform to address the need for a COVID-19 vaccine. Moreover, the Company is applying its MVA-VLP technology to cancer immunotherapy and plans to accelerate this program with proceeds from its recent financing. Greater details on GeoVax’s development efforts can be found in the base report (<https://bit.ly/3IjIBC0>). GeoVax’s vaccine development activities have been (and continue to be) financially supported by the U.S. Government in the form of research grants awarded directly to the Company, as well as indirect support for conducting human clinical trials.

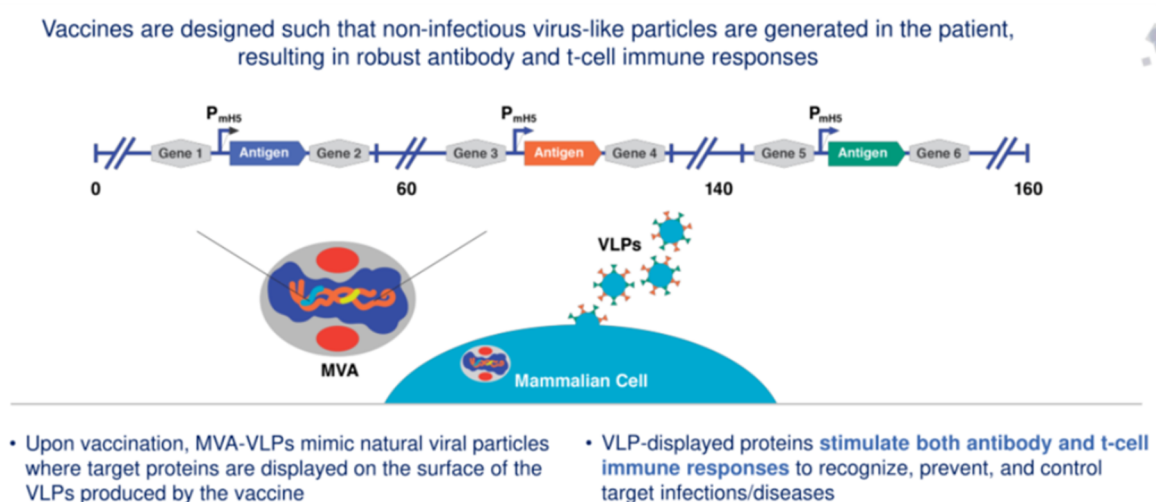
Following the Company’s recent financings, GeoVax’s cash balance now stands at approximately \$27.6 million at December 31, 2022, positioning the Company to support accelerated development of its COVID-19 vaccine development candidates, advance its cancer immunotherapy program, as well as other infectious disease vaccines.

MVA-VLP TECHNOLOGY PLATFORM

Vaccines are most often made of agents (antigens) that resemble disease-causing microorganisms and are traditionally created from weakened or killed forms of the virus. Newer vaccines largely use recombinant DNA technology to produce vaccine antigens from specific portions of the DNA sequence of the target pathogen. The most successful of these purified antigens have been non-infectious VLPs used in vaccines, such as the hepatitis B vaccines (Merck’s Recombivax® and GlaxoSmithKline’s [GSK’s] Engerix®) and human papillomavirus vaccine (GSKs Cervarix® and Merck’s Gardasil®).

GeoVax’s MVA-VLP vector vaccine technology platform combines the safety of a replication-defective live vector with the immunogenicity of VLPs and the durability of immune responses induced by vaccinia vectors. VLPs train the body’s immune system to identify and attack the authentic virus should it appear, and to recognize and kill infected cells to control infection and decrease the length and severity of disease. Among the most challenging aspects of VLP-based vaccines is to design the vaccines in such a way that the VLPs are recognized by the immune system the same way it would an authentic virus. GeoVax’s technology drives the production of VLPs in the body of the person being vaccinated (*in vivo*), thus more closely mimicking a viral infection and inducing the appropriate types of immune responses. Figure 2 provides a graphical depiction GeoVax’s GV-MVA-VLP™ vaccine technology.

Figure 2
GV-MVA-VLP™ VACCINE TECHNOLOGY



Source: GeoVax Labs, Inc.

Multiple studies have demonstrated the VLPs for enveloped viruses, such as HIV, Ebola, Sudan, Marburg, or Lassa fever, produced using the MVA-VLP platform are identical in appearance to the authentic virus because they include viral protein antigens and the viral envelope, consisting of membranes from the vaccinated individual’s cells. In contrast, VLPs produced externally have no envelope or an envelope derived from the cultured cells used to produce them. Based on its efforts to date, GeoVax believes its technology provides unique advantages by producing VLPs that more closely resemble the authentic virus, enabling the body’s immune system to recognize the authentic virus more readily. In addition, GeoVax’s MVA-VLP platform has unique advantages, summarized as follows:

- **Safety.** Clinical testing of GeoVax’s HIV vaccines have documented an optimal safety profile. This is consistent with the safety profile for MVA used as a smallpox vaccine and documented in more than 120,000 subjects throughout Europe.
- **Durability.** The Company’s vaccine technology promotes highly-durable and long-lasting immune responses.

- *Limited pre-existing immunity to vector.* Following the eradication of smallpox in 1980, smallpox vaccinations ended, which left individuals born after 1980 (except for select populations, such as vaccinated laboratory workers, first responders, etc.) unvaccinated and without pre-existing immunity.
- *No need for adjuvants.* MVA stimulates strong innate immune responses without the use of adjuvants.
- *Thermal stability.* MVA is stable in both liquid and lyophilized formats (> 6 years of storage).
- *Genetic stability and manufacturability.* MVA is genetically stable when properly engineered and can be reliably manufactured using the most modern technologies that support scalability, consistency, and efficiency.

In February 2023, GeoVax announced significant progress in developing a high-yield, high-capacity, continuous avian cell line system for manufacturing its MVA (modified vaccinia Ankara)-based vaccines and immunotherapies. Currently, MVA vaccines are manufactured in cells cultured from chicken embryonic fibroblasts (CEF), a suboptimal and time-consuming process useful primarily for niche markets and stockpile reserves. After exploring various approaches to growing MVA in continuous cell lines in bioreactors more suitable for high-yield, commercial-scale manufacturing, GeoVax intends to accelerate activities towards fully implementing a proprietary, continuous cell line manufacturing system that it expects will provide lower-cost, scalable versatility for broad MVA vaccine and immunotherapy applications.

MVA-VLP-MUC1 for Solid Tumor Cancers

The Company uses its GV-MVA-VLP vaccine platform to express abnormal, aberrantly glycosylated forms of the cell surface-associated MUC1 protein that is associated with a wide range of cancers, including breast, colon, ovarian, prostate, pancreatic, and lung with the goal of raising therapeutic anti-tumor antibodies and T cell responses in cancer patients. GeoVax's cancer immunotherapy program is based on the concept of combining a tumor-associated antigen vaccine with a potent anti-tumor agent, such as an Immune Checkpoint Inhibitor ("ICI"), with the goal of achieving regression of tumor growth and development.

The initial animal studies of the Company's MVA-VLP-MUC1 vaccine and ICI combination have been encouraging, showing that a combination of the MVA-VLP-MUC1 vaccine candidate with a MUC1 synthetic peptide was capable of breaking tolerance to human MUC1 in transgenic mice and inducing immune responses with efficacy against challenge in a lymphoma tumor model. The studies also demonstrated a significant reduction of the tumor burden in a mouse model for colorectal cancer. GeoVax plans to further these animal studies in collaboration to define the optimal course and schedule of vaccination to define a protocol that can be evaluated in a Phase 1 clinical trial.

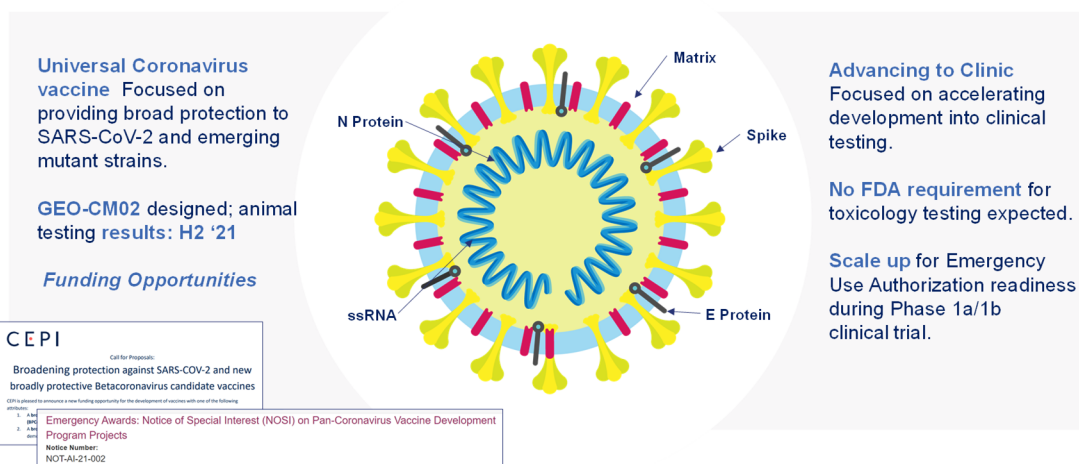
Patent update. The Company recently announced that the U.S. Patent and Trademark Office had issued a Notice of Allowance for Patent Application No. 16/068,527 entitled "Compositions and Methods for Generating an Immune Response to a Tumor Associated Antigen." In general, the claims to be granted in the patent cover GeoVax's vector platform for expressing tumor associated antigens in virus-like particles (VLPs) from a Modified Vaccinia Ankara (MVA) viral vector and encompass GeoVax's Mucin 1 (MUC1) tumor-associated antigen immunotherapy candidate.

Coronavirus (COVID-19) Vaccine Program

In January 2020, GeoVax announced initiation efforts to develop a vaccine against Coronavirus Disease 2019 (COVID-19) caused by the SARS-CoV-2 coronavirus. As of March 2023, more than 683 million cases have been reported worldwide, resulting in over 6.8 million deaths. The U.S. is still considered one of the epicenters of the disease, with roughly 106 million cases and 1.1 million deaths so far.

GeoVax has constructed novel candidate vaccines against SARS-CoV-2 based on the MVA-VLP platform. Its technology is designed to: (1) induce both neutralizing antibodies and cellular immune response; (2) induce a Th1 based cellular immune response to prevent immunopathology; (3) potentially cross-protect against other coronaviruses; and (4) induce full protection after a single dose in less than two weeks. Figure 3 (page 9) summarizes key elements of the Company's COVID-19 vaccine technology.

Figure 3
UNIVERSAL SARS-COV-X VACCINE PROGRAM



[Astuti & Ysraili, Diabetes Metab Syndr. 2020 Apr 18](#)

Source: GeoVax Labs, Inc.

The experimental COVID-19 vaccine, using the Company’s MVA-VLP technology, encodes the S protein, which is the basis for all the first-generation products in use today and the targeted neutralizing antibodies. This is used in combination with the membrane (M protein) and the envelop (E protein). The M and E proteins provide the structural components required for the VLP formation in the body. They also serve as additional targets for the cellular immune responses. This design represents a first critical step towards the COVID vaccines that could induce broad, specific immune responses that are not significantly impacted by the variants that are arising as the S protein evolves within a population. GeoVax is working with this approach to attempt to circumvent the evolution of COVID-19, rather than to chase the new variants with modifier vaccines, as is commonly done today with flu vaccines.

GeoVax is involved in animal testing with three experimental vaccines, including in transgenic mice and hamsters (and all include infectious challenged). The product design that proves to induce the most protected immune response will be the basis for the initial clinical development. Additional designs are expected to include the incorporation of other coronavirus structural proteins and non-structural proteins based on data that is being generated within a population and immune responses from the current pandemic. The goal is to expand the induction of immune responses beyond the S protein, which is the basis for GeoVax’s efforts and to develop a universal coronavirus vaccine.

The Company is in discussions with the Biomedical Advanced Research and Development Authority (BARDA) and other entities to support and accelerate its COVID-19 vaccine development efforts. While other COVID-19 vaccine candidates are in later stages of development, (with Pfizer, Moderna, and Johnson & Johnson’s COVID-19 vaccines having been approved and being distributed), the GV-MVA-VLP platform offers unique advantages, including safety and breadth of responses. This makes the Company’s platform ideal for immunization of those most vulnerable, including the immunocompromised and comorbid.

Two Phase 2 Clinical Trials Underway for SARS-CoV-2

GEO-CM04S1 for Immunocompromised Patients. GEO-CM04S1 is being studied in a first-of-its-kind Phase 2 clinical trial (NCT04977024) as a primary vaccine for immunocompromised cancer patients who have difficulty producing antibodies and largely depend on T cells to protect against the virus responsible for COVID-19. Additionally, GEO-CM04S1 is being evaluated in a Phase 2 vaccine booster trial format (NCT04639466), aimed at evaluating how GEO-CM04S1 may boost pre-existing vaccine immunity while also causing a strong immune response to nucleocapsid. GEO-CM04S1 is unique to other COVID-19 vaccines in that it targets both the spike and nucleocapsid proteins. In contrast, the current U.S. FDA-approved COVID-19 vaccines only target the spike protein.

In March 2022, data from a Phase 1 study of GEO-CM04S1 was published in the peer-reviewed journal, *The Lancet Microbe*. The publication reported data showing that GEO-CM04S1 produced robust neutralizing antibodies and T cells against SARS-CoV-2 with no significant side effects. These data confirm the strong dual action of the GeoVax vaccine, an important feature given the multiple mutations in spike, leading to variants of concern and inconsistent protection from existing FDA-approved vaccines. If a new mutation arises in the spike antigen that interferes with antibody recognition, a person vaccinated with GeoVax's vaccine may still have substantial T-Cell immunity against both the nucleocapsid and spike antigens.

In March 2022, GeoVax announced the engagement of Allucent (formerly CATO SMS) to manage GeoVax's two ongoing Phase 2 clinical trials of GEO-CM04S1 against SARS-CoV-2. Allucent is a global provider of clinical research solutions, including strategic consulting, full-service clinical trial operations, biometrics, and clinical pharmacology. With more than 30 years of experience focusing on the needs of small and emerging biopharmaceutical companies, Allucent effectively designs and executes studies (from strategy to approval) in complex indications and modalities across a variety of therapeutic areas with a proven center of excellence in oncology.

In February 2023, GeoVax Labs and EmVenio Research, a patient-focused decentralized trial global organization, announced a collaboration to deploy a mobile clinical facility in the Claremont, California area to expand GeoVax's ongoing Phase 2 clinical trial evaluating GEO-CM04S1 as a COVID-19 booster vaccine in healthy patients.

IND-Enabling Activities Progressing for Pan Coronavirus Vaccine (GEO-CM02)

Beyond to the clinical programs for GEO-CM04S1 for COVID-19, GeoVax continues to assess GEO-CM02 as a possible single-dose universal coronavirus vaccine. This program was supported by a Small Business Innovation Research (SBIR) grant from the NIH during 2021. In small animal studies, the Company measured functional immune responses after a single dose that mediated protection from infection and pathogenesis, including protection against the more virulent Beta variant. Additional studies are planned in preparation for IND filing and subsequent human clinical trials.

First-generation SARS-CoV-2 vaccines were designed to encode the spike (S) protein of the SARS-CoV-2 virus with the goal of inducing high levels of neutralizing antibodies. However, potential limitations of narrowly focusing on the spike (S) protein are becoming evident with emerging variants capable of partially escaping neutralization by vaccine induced antibodies. Consequently, the effectiveness of these vaccines against new SARS-CoV-2 variants and future coronavirus spillover events remains an enormous concern.

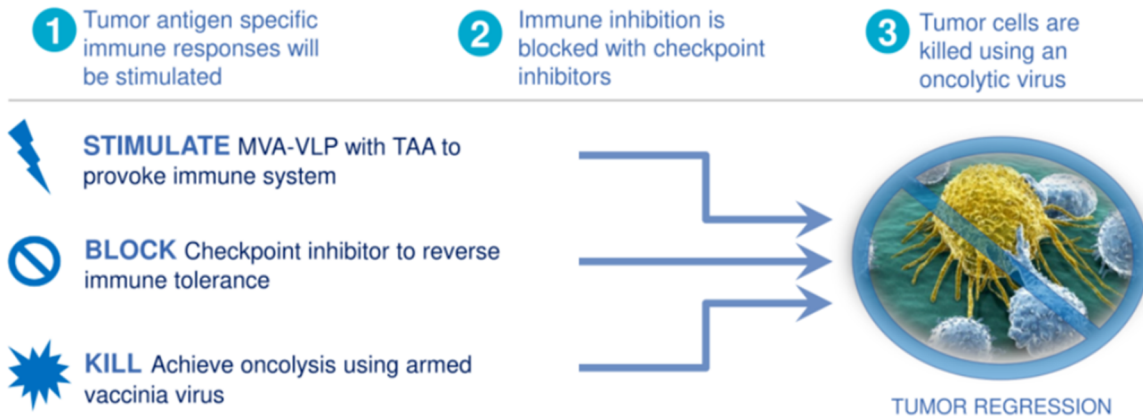
GeoVax's vaccine candidate (GEO-CM02) encodes the spike (S) protein as the neutralizing antibody target as well as the membrane (M) and envelope (E) proteins as T-cell targets and to support *in vivo* virus-like particle formation to augment potency. This strategy may provide the basis for generating a single dose universal coronavirus vaccine. Unique compared to other vaccines approved or under development, the GeoVax vaccine candidate is specifically designed to provide a broader and more durable level of protective immunity against SARS-CoV-2, which may protect against emerging variants while avoiding the potential side effects that can limit vaccine utility and acceptance.

Cancer Immunotherapy Vaccine Program

GeoVax is additionally developing the next generation of immunotherapies to address unmet medical needs in cancer (Figure 4, page 11). The Company believes that its MVA-VLP vector platform is well-suited for inducing immune responses in select tumor associated antigens (TAA). The VLPs are produced within the body of the vaccinated individual and are composed of a structural protein from a virus as well as a tumor associated antigen. These present the immune system with concentrated forms of the TAA to increase potency of the vaccine and to induce both antibody and T-cell cellular immune response. GeoVax seeks to combine a vaccine with a potential antitumor agent, such as a checkpoint inhibitors, thus resulting in immune responses that contribute to the regression of existing tumors and/or prevent the development and expansion of metastatic lesions.

Figure 4
IMMUNOTHERAPY TECHNOLOGY

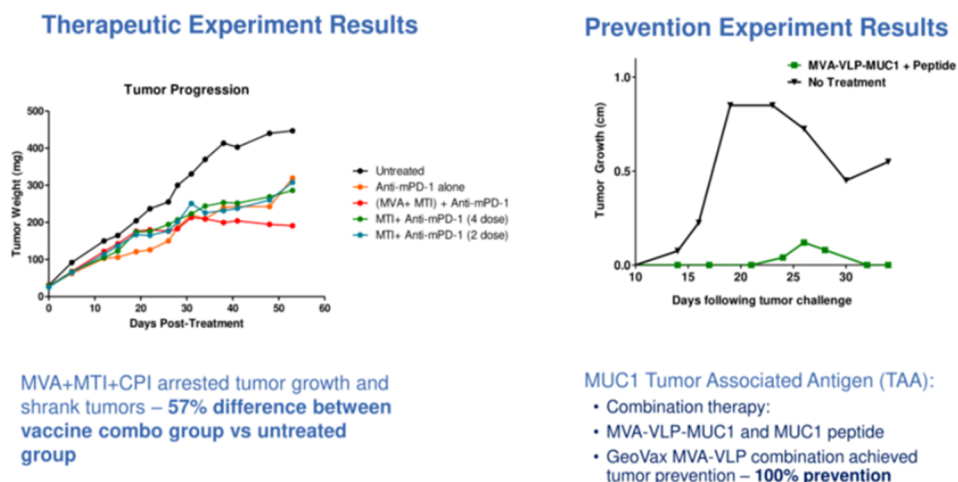
Triple-threat Approach:



Source: GeoVax Labs, Inc.

The initial focus is on the MUC1 TAA's, which is a well-studied target for both antibody and cellular immunity (noting that there are multiple associated antigens, which the Company intends to investigate with this approach). As shown in Figure 5, GeoVax has constructed a MUC1 MVA-VLP vaccine and has tested it in combination with two different experimental peptide vaccines and a checkpoint inhibitor in transgenic mouse models, which allow for the evaluation of the vaccine's effect against humanized tumors in a humanized mouse. In the treatment model, shown using the MVA-MT1 peptide, the combination induced responses that showed a 57% decrease in tumor growth when the animals were immunized with both the MVA MUC1 and the tumor associated peptide (compared to the control animal). The combination was superior to either the peptide alone or the tumor checkpoint inhibitor alone. In a prevention model, designed as a post treatment recurrence setting in cancer treatment, the GeoVax VLP MUC1 induced immune responses provided almost 100% protection against tumors reoccurring.

Figure 5
IMMUNONCOLOGY RESULTS



Source: GeoVax Labs, Inc.

Phase 1/2 Clinical Trial Underway for Advanced Head and Neck Cancer

A Phase 1/2 trial (NCT03754933) evaluating the safety and efficacy of repeat cycles of Gedeptin® therapy in patients with recurrent head and neck squamous cell carcinoma (HNSCC) that have tumor(s) accessible for injection and no curable treatment options, is ongoing at Stanford University in collaboration with Emory University. The trial design involves repeat administration using Gedeptin®, followed by systemic fludarabine, to gain additional information prior to expansion towards a larger patient trial. The initial stage of the study is being funded by the FDA under its Orphan Products Clinical Trials Grants Program. The FDA has also granted Gedeptin® Orphan Drug Status for the intra-tumoral treatment of anatomically accessible oral and pharyngeal cancers, including cancers of the lip, tongue, gum, floor of mouth, salivary gland, and other oral cavities. This trial is currently being expanded to a multi-site trial with a focus on accelerated patient enrollment. In January 2022, GeoVax engaged Allucent, a global provider of clinical research solutions, to manage the ongoing Phase 1/2 trial and to assist with the expansion of clinical sites and acceleration of patient enrollment and evaluation.

Gedeptin® is a novel, patented product/technology for the treatment of solid tumors through a gene therapy strategy, known as Gene-Directed Enzyme Prodrug Therapy (GDEPT). In September 2021, GeoVax entered into an assignment and license agreement with PNP Therapeutics, Inc. (PNP), granting GeoVax exclusive rights to develop and commercialize Gedeptin®. The Gedeptin® technology was developed with funding support from the National Cancer Institute (NCI), part of the NIH. GeoVax's license to Gedeptin® includes the rights to expand the use of Gedeptin® to all human diseases and/or conditions including, but not limited to, other cancers.

In GDEPT, a vector is used to selectively transduce tumor cells with a nonhuman gene, which expresses an enzyme that can convert a nontoxic prodrug into a very toxic antitumor compound, *in situ*. A cycle of Gedeptin® therapy consists of three intra-tumoral injections of Gedeptin® over a two-day period followed by infusion of a prodrug, fludarabine phosphate, once a day for three days. A Phase 1 dose ranging study, evaluating the safety of a single cycle of Gedeptin® therapy, found the therapy to be well tolerated, with evidence of a reduction in tumor size in patients with solid tumors.

In February 2023, GeoVax announced that its clinical trial of Gedeptin® for patients with recurrent head and neck cancers is now actively enrolling patients at three major research centers: Stanford University, Emory University, and Thomas Jefferson University. The support of the FDA and collaborations with Stanford, Emory, and Jefferson enable GeoVax to evaluate Gedeptin® rapidly in 10 patients, with the potential to subsequently expand the trial to 25 patients. A successful outcome may lead to labeling discussions with the FDA and initiation of further Gedeptin® investigations, including in combination with immune checkpoint inhibitors, for additional cancerous and non-cancerous tumor indications.

Hemorrhagic Fever (HF) Vaccine Programs (Ebola, Sudan, Marburg and Lassa)

GeoVax's initial preclinical studies in rodents and nonhuman primates for its MVA-VLP-EBOV vaccine candidate have shown 100% protection against a lethal dose of EBOV upon a single immunization. Recent studies in lethal challenge guinea pig models demonstrated that GeoVax vaccines MVA-VLP-SUDV and MVA-VLP-MARV conferred 100% protection from death. These vaccines were subsequently evaluated in a rigorous cynomolgus macaque infectious challenge model. Vaccination protected nonhuman primates from viremia, weight loss, and death following challenge with a dose of Sudan or Marburg virus that is lethal in nonvaccinated animals.

Evaluation of immune responses following vaccination demonstrated presence of both neutralizing antibodies and functional T cells, indicating a breadth of responses that combine for optimal protection. Similarly, the initial preclinical studies in rodents for GeoVax's LASV vaccine candidate have shown 100% single-dose protection against a lethal dose of LASV challenge composed of multiple strains delivered directly into the brain. The nonhuman primate studies are ongoing in collaboration with NIAID and the U.S. Army and clinical development programs will be defined based on efficacy data and global priorities as potentially dangerous outbreaks occur.

Ebola (EBOV), Sudan (SUDV), and Marburg viruses (MARV) are the most virulent species of the Filoviridae family, causing up to a 90% fatality rate in humans, and are epizootic in Central and West Africa (34 outbreaks since 1976). Lassa fever virus (LASV) also causes severe and often fatal hemorrhagic illnesses in an overlapping region to that of Ebola, but is endemic, with an annual rate of >300,000 infections and leading to 5,000-10,000 deaths.

In agreement with the WHO, GeoVax believes that an ideal vaccine against major filoviruses and LASV must provide protection with a single dose. The MVA-VLP vaccines are well suited to meet this goal because they induce both antibody and cellular immune responses, which are needed to control and clear the infections. GeoVax's preclinical studies in rodents and non-human primates have demonstrated 100% single-dose protection in lethal challenge models for its EBOV, SUDV, and LASV vaccines.

Modified Vaccinia Ankara (MVA) and Monkeypox

The vaccine used and stockpiled for immunization against Monkeypox is MVA, which is also the vaccine vector utilized in numerous GeoVax vaccines targeting COVID-19, Hemorrhagic fever viruses (e.g., Sudan ebolavirus and Zaire ebolavirus), HIV, Zika, and the GeoVax MVA-VLP-MUC1 cancer immunotherapy. Previous peer-reviewed publications examined the successful prevention of Monkeypox in non-human primate models by GeoVax MVA-based HIV vaccines:

Earl, P.L., Americo, J.L., Wyatt, L.S., Anne Eller, L., Montefiori, D.C., Byrum, R., Piatak, M., Lifson, J.D., Rao Amara, R., Robinson, H.L., Huggins, J.W., Moss, B. Recombinant modified vaccinia virus Ankara provides durable protection against disease caused by an immunodeficiency virus as well as long-term immunity to an orthopoxvirus in a non-human primate. *Virology* 15:84-97, 2007.

Nigam, P., Earl, P.L., Americo, J.L., Sharma, S., Wyatt, L.S., Edghill-Spano, Y., Chennareddi, L., Silvera, P., Moss, B., Robinson, H.L., Amara, R.R. DNA/MVA HIV-1 AIDS vaccine elicits long-lived vaccinia virus-specific immunity and confers protection against a lethal monkeypox challenge. *Virology* 366:73-83.

Evaluation is currently underway related to GEO-CM04S1 in preventing Monkeypox. It is anticipated that the results will demonstrate successful protection, validating that GEO-CM04S1 is protective against both COVID-19 and Monkeypox. GeoVax also anticipates validating its hemorrhagic fever virus vaccines as protective against Monkeypox, potentially providing unique vaccines preventing both hemorrhagic fever virus and Monkeypox virus in a single vaccine.

Malaria Vaccine Program

GeoVax has collaborated with the Burnet Institute, a leading infectious diseases research institute in Australia, for the development of a vaccine to prevent malaria infection. The project included the design, construction, and characterization of multiple malaria vaccine candidates using GeoVax's GV-MVA-VLP™ vaccine platform combined with malaria *Plasmodium falciparum* and *Plasmodium vivax* sequences identified by the Burnet Institute. The Company also collaborated separately with Leidos, Inc. with work funded by a grant to Leidos from the United States Agency for International Development (USAID) Malaria Vaccine Development Program (MVDP). This program has been inactive as GeoVax has prioritized other development programs. However, pending additional funding support via federal grants or other sources, the Company may further pursue this area.

Worldwide, as of 2020, malaria causes 241 million infections and 627,000 deaths annually (mostly in children living in sub-Saharan Africa). Despite decades of vaccine research, vaccine candidates have failed to induce substantial protection (e.g. >50%). Most of these vaccines are based on individual proteins that induce immune responses targeting only one stage of the malaria parasite's life cycle. GeoVax's MVA-VLP malaria vaccine candidates incorporate antigens derived from multiple stages of the parasite's life cycle and are designed to induce an immune response with durable functional antibodies and CD4+ and CD8+ T cell responses—all features of an ideal vaccine-induced immune response.

Patent update. On April 26, 2022, GeoVax announced that the U.S. Patent and Trademark Office has issued Patent No. 11,311,612 to GeoVax, pursuant to the Company's patent application No. 16/648,693 titled "Compositions and Methods for Generating an Immune Response to Treat or Prevent Malaria." In general, the claims granted in the patent cover GeoVax's Modified Vaccinia Ankara (MVA) vector expressing certain antigens from the malaria parasite.

ZIKA Virus (ZIKV) Vaccine Program

To address the unmet need for a vaccine against Zika virus, GeoVax is developing novel vaccine candidates constructed using its GV-MVA-VLP platform. MVA has an outstanding safety record, which is particularly important given the need to include women of child-bearing age and newborns among those being vaccinated. The Company's Zika vaccine is designed around the NS1 gene product to eliminate the risk of Antibody Dependent Enhancement (ADE), which is a serious side effect observed when a vaccinated individual does not have a fully protective immune response which causes a more virulent reaction if infected. GeoVax's initial preclinical studies in rodents using its GEO-ZM02 vaccine candidate demonstrated 100% single-dose protection against a lethal dose of ZIKV delivered directly into the brain. In rhesus macaques, vaccination with GEO-ZM02 induced immune responses that effectively controlled the virus replication despite the fact the vaccine is not designed to induce ZIKV neutralizing antibodies. Further development of the Company's Zika vaccine will be dependent upon partnering support.

Patent update. In January 2023, GeoVax announced that the U.S. Patent and Trademark Office issued a Notice of Allowance for Patent Application No. 17/000,768 titled, "Method for Generating a ZIKV Immune Response Utilizing a Recombinant Modified Vaccinia Ankara Vector Encoding the NS1 Protein."

HIV Program (being discontinued but available for out-license or partnering)

Due to the Company's corporate refocusing of development efforts in prioritizing its SARS-CoV-2 and cancer immunotherapy programs, and a lack of continuing government support for its HIV vaccine development efforts, GeoVax has recently decided to discontinue active development of these programs. The Company's technology and intellectual property will remain available for out-license or partnering but GeoVax will no longer devote any corporate resources to the programs.

Partnerships

Through its development efforts, the Company has achieved significant partnerships. Current and recent collaborators and partners include the NIAID/NIH, the HVTN, the CDC, U.S. Department of Defense (DoD), U.S. Army Research Institute of Infectious Disease (USAMRIID), U.S. Naval Research Laboratory (USNRL), Emory University, University of Pittsburgh, Georgia State University Research Foundation (GSURF), University of Texas Medical Branch (UTMB), the Institute of Human Virology (IHV) at the University of Maryland, the Scripps Research Institute (Scripps), Burnet Institute in Australia, the Geneva Foundation, ViaMune, Inc., Leidos, Inc., and UCSF, among others.

Patent Portfolio

The Company's wholly owned, co-owned, and in-licensed intellectual property portfolio now stands at over 115 granted or pending patent applications spread over 24 patent families.

Corporate Background

The Company's primary business is conducted by its wholly-owned subsidiary, GeoVax, Inc., which was incorporated under the laws of Georgia in June 2001. The predecessor to its parent company, GeoVax Labs, Inc. was originally incorporated in June 1988 under the laws of Illinois as Dauphin Technology, Inc. In September 2006, Dauphin completed a merger with GeoVax, Inc. As a result of the merger, GeoVax, Inc. became a wholly-owned subsidiary of Dauphin, and Dauphin changed its name to GeoVax Labs, Inc. In June 2008, the Company was reincorporated under the laws of Delaware.

Risks and Disclosures

This Company Update has been prepared by GeoVax Labs, Inc. (“GeoVax” or “the Company”) with the assistance of Crystal Research Associates, LLC (“CRA”) based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this Update relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in GeoVax’s statements on Forms 10-K, 10-Q, and 8-K as well as other forms filed from time to time.

The content of this report with respect to GeoVax has been compiled primarily from information available to the public released by the Company through news releases, Annual Reports, and U.S. Securities and Exchange Commission (SEC) filings. GeoVax is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by GeoVax or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, for year one of its agreement, CRA will have been compensated by the Company in cash of forty-eight thousand dollars for its services in creating the base report and for quarterly updates.

Investors should carefully consider the risks and information about GeoVax’s business. Investors should not interpret the order in which considerations are presented in its SEC filings as an indication of their relative importance. In addition, the risks and uncertainties overviewed in GeoVax’s SEC filings are not the only risks that the Company faces. Additional risks and uncertainties not presently known to GeoVax or that it currently believes to be immaterial may also adversely affect the Company’s business. If any of such risks and uncertainties develops into an actual event, GeoVax’s business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company’s shares could decline.

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