



GENPREX CORPORATE UPDATE

May 5, 2022

To my fellow shareholders:

Genprex has been off to a strong start for 2022. I am enthusiastic about our future as we continue to advance our leading edge gene therapy programs with the goal of extending hope and life to patients with serious disease and unmet need.

Large Markets and Unmet Need

I believe that Genprex is attracting attention for the significantly large markets and unmet need that we target. Most gene therapy companies are focused on rare diseases, characterized by serious illness but small numbers of patients. In contrast, Genprex is developing gene therapies for diseases affecting very large patient populations with correspondingly large markets. Our initial targeted diseases are lung cancer and diabetes. Lung cancer continues to be the world's leading cause of cancer death. Each year, lung cancer strikes about 236,000 people in the United States and 2 million people worldwide. The market for lung cancer therapeutics is estimated to exceed \$48 billion by 2026. Type 1 and Type 2 diabetes together affect 37 million people in the United States, or 11% of the population.

236K
LUNG CANCER CASES

There are more than 236,000 new lung cancer cases per year in the U.S.

37M
DIABETES CASES

Type 1 and Type 2 diabetes affect more than 37 million people in the U.S., or 11% of the population

We believe that the large patient populations and market sizes we are pursuing will become more widely understood and appreciated as we move forward, driving our growth and future success.

Second FDA Fast Track Designation

2022 began with the announcement of our second Food and Drug Administration (FDA) Fast Track Designation (FTD). This second FTD is for use of our most advanced drug candidate, REQORSA™ Immunogene Therapy, in combination with Merck and Co's Keytruda® (pembrolizumab) in non-small cell lung cancer (NSCLC) patients whose disease progressed on Keytruda. Merck's gross revenue from Keytruda exceeded \$17 billion in 2021. This drug combination and patient population are the subject of our Acclaim-2 clinical trial. We opened this trial for enrollment in March 2022 and treated our first patient in April 2022.

Our first FDA Fast Track Designation was received in 2020 for use of REQORSA in combination with AstraZeneca's Tagrisso® (osimertinib) in NSCLC patients whose disease progressed on Tagrisso. AstraZeneca's gross revenues from Tagrisso exceeded \$5 billion in 2021. This drug combination and patient population are the subject of our Acclaim-1 clinical trial. Patients are being enrolled and treated in the Acclaim-1 trial. Our first patient was treated in February 2022.

REQORSA consists of the TUSC2 gene inserted into a DNA plasmid and encapsulated in a nonviral delivery system made from lipid nanoparticles. REQORSA is injected intravenously where it specifically targets cancer cells. Once REQORSA is taken up into the cancer cell, the TUSC2 gene expresses the TUSC2 protein which has been shown to be capable of restoring certain functions that are often defective in the cancer cell. REQORSA has a multimodal mechanism of action whereby it:

- interrupts cell signaling pathways that cause replication and proliferation of cancer cells,
- re-establishes pathways for programmed cell death in cancer cells,
- modulates the immune response against cancer cells,
- blocks mechanisms that create drug resistance.

It should be noted that we do not seek to take market share from the companies whose drugs are combined with ours. Instead, success of REQORSA in combination with these drugs would expand the markets for these drugs. REQORSA in combination with Tagrisso or Keytruda could enable more patients to benefit from those drugs, potentially for longer periods of time, and may provide additional therapeutic benefits.

Expanding Pipeline

In early 2022, we added small cell lung cancer (SCLC) to our pipeline. SCLC represents about 13% of lung cancers. NSCLC, which is targeted in our Acclaim clinical trials, represents about 84% of lung cancers. Thus, with the addition of SCLC to our pipeline, we now target nearly 100% of the lung cancer market. We believe that this distinguishes REQORSA from almost all other lung cancer drugs in development because they only target subsets of lung cancer. By combining REQORSA with both Tagrisso and Keytruda, and including SCLC as well as NSCLC, our present program does target nearly all patients with lung cancer.

Expanding our pipeline continues to be a strategic priority. Because of this, we are continuing to sponsor research with the same major cancer research center that developed our REQORSA immunogene therapy. This includes new preclinical research exploring REQORSA's potential to treat other cancer indications, and the use of REQORSA in combination with other cancer drugs.

Strengthened Leadership



We started 2022 stronger with the addition of two seasoned, innovative drug development executives to lead our clinical and manufacturing functions. In September 2021, Mark S. Berger, M.D. joined Genprex as Chief Medical Officer, and Hemant Kumar, Ph.D., CPM, EMBA joined Genprex as Chief Manufacturing and Technology Officer.

Dr. Berger is an oncologist and senior executive with 25 years of biotech and pharmaceutical company experience in the development of oncology therapeutics. He has successfully brought two cancer drugs through the regulatory process to approval and excels in strategic development, team management and collaborative leadership.

Dr. Kumar is a recognized global expert in Chemistry, Manufacture and Controls (CMC) Technical Development and GMP manufacturing. He has more than 25 years of experience leading global CMC and regulatory approval strategy for the accelerated development of innovative vaccines, biologics, advanced cell and gene therapy drug processes and product development under current GMP and licensing processes.



These two new executives are making major contributions to the advancement of our drug candidates.

Clinical Advisory Board

In 2021, we also formed a new Clinical Advisory Board, which is comprised of world renowned medical and clinical experts, to guide our clinical development programs in cancer and diabetes. The Clinical Advisory Board's vast experience in clinical trials of cancer and diabetes therapies, combined with their expertise in consulting with small and large biotechnology companies, is invaluable as our drug candidates progress into and through the clinic.

The members of Genprex's Clinical Advisory Board include:

- Michael Morse, MD, MHS, FACP – Dr. Morse is a Professor of Medicine in the Division of Medical Oncology and Professor in the Department of Surgery at Duke University Medical Center, Durham, NC. His clinical expertise includes management of gastrointestinal malignancies including colon, hepatobiliary, gastroesophageal and pancreatic cancer. His research expertise includes the development of targeted therapies including immunotherapies for cancer.
- Col. George E. Peoples, MD, FACS – Dr. Peoples served 30 years of active duty as a surgeon and research scientist in the military. He is the Founder and Director of the Cancer Vaccine Development Program (CVDP), which has been focused on the discovery, development, and clinical testing of cancer vaccines for more than 20 years. Four of the program's cancer vaccines have been licensed for commercial development. Dr. Peoples currently serves as the CEO of Cancer Insight, LLC, CVDP's commercial counterpart, which is a boutique cancer immunotherapy Contract Research Organization conducting multiple Phase 1 and 2 clinical trials. He also serves as Professor of Surgery at the Uniformed Services University of the Health Sciences and Professor (adjunct) of Surgical Oncology at MD Anderson Cancer Center (MDACC).

- Andrew B. Becker, MD, PhD – Dr. Becker is President and Founder of Becker Pharmaceutical Consulting, a market research, competitive intelligence and strategic planning consulting firm that provides analytic and strategy services to companies ranging from small biotechnology and medical device companies up to large multinational pharmaceutical companies on a global basis. Dr. Becker received both his medical degree and PhD in Molecular Pharmacology from Stanford University where his research focused on signaling pathways for the insulin and IGF-1 receptors, deciphering the structure and function of the insulin degrading enzyme and its role in insulin processing.

REQORSA, Our Lead Gene Therapy Candidate in Oncology

Our lead therapeutic candidate is REQORSA Immunogene Therapy, which utilizes our unique, proprietary, non-viral ONCOPREX® Nanoparticle Delivery System, in combination with approved targeted therapies and immunotherapies, such as Tagrisso (osimertinib) and Keytruda (pembrolizumab) for treatment of lung cancer. We are conducting two clinical trials of REQORSA in lung cancer, which we have branded as Acclaim-1 and Acclaim-2.

Acclaim-1

In 2021, we initiated the Acclaim-1 clinical trial and in 2022 we dosed our first patient. Acclaim-1 is a Phase 1/2, open-label, dose escalation and clinical response study of the Company’s lead drug candidate, REQORSA™ Immunogene Therapy, in combination with Tagrisso in patients with advanced, EGFR-mutant metastatic NSCLC whose disease progressed after treatment with Tagrisso. As previously mentioned, in 2020, we received U.S. Food and Drug Administration (FDA) Fast Track Designation for the treatment of the Acclaim-1 patient population.



We anticipate enrolling patients at approximately 15 clinical sites. We expect the Phase 1 portion of Acclaim-1 to enroll up to 18 patients in a dose escalation study to determine the maximum tolerated dose of the combination. The Phase 2 portion of the study is expected to enroll approximately 74 patients to be randomized 1:1 to receive either REQORSA and Tagrisso combination therapy or Tagrisso monotherapy. The primary endpoint of the Phase 2 portion of the trial is progression-free survival, which is defined as time from randomization to progression or death. An interim analysis will be performed at 25 events.

We are in the process of engaging and adding premier clinical trial sites to participate in our Acclaim-1 study. We expect the Phase 1 portion of Acclaim-1 to be completed by year end 2022.

Acclaim-2

At the end of 2021, we received FDA Fast Track Designation for the treatment of the Acclaim-2 patient population. We believe this second Fast Track Designation is an important step in accelerating the clinical development of REQORSA, and it is another indication of REQORSA’s potential to treat the unmet medical need of patients with late-stage NSCLC.



In March 2022, we opened Acclaim-2 for enrollment. I am pleased to announce that we dosed our first patient in Acclaim-2 in April 2022.

Acclaim-2 is an open-label, dose escalation and clinical response study of REQORSA in combination with Keytruda in patients with advanced, metastatic NSCLC whose disease progressed after treatment with Keytruda.

We anticipate enrolling patients at approximately 15 clinical sites. We expect the Phase 1 portion of Acclaim-2 to enroll up to 30 patients to determine the maximum tolerated dose of the combination of REQORSA and Keytruda. The Phase 2 portion of the study is expected to enroll approximately 126 patients to be randomized 2:1 to receive either REQORSA and Keytruda combination therapy or docetaxel and/or ramucirumab. The primary endpoint of the Phase 2 portion of the trial is progression-free survival, which is defined as time from randomization to progression or death. An interim analysis will be performed after 50 events.

We are in the contracting process with a number of additional prestigious cancer centers across the United States to participate in the Acclaim-2 study. We expect to complete the Phase 1 portion of Acclaim-2 by the end of the first quarter of 2023.

We look forward to generating data from these two clinical trials, and we believe that positive results in either or both of them would be a major step forward for lung cancer patients and create significant value for the Company.

2021 American Association of Cancer Research (AACR) Preclinical Data

At the 2021 AACR annual meeting, our collaborators presented positive preclinical data for the combination of REQORSA in combination with chemotherapy and immunotherapies, and in combination with targeted therapies, for the treatment of NSCLC at the 2021 American Association of Cancer Research (AACR) annual meeting.

These positive data provide further support for the therapeutic potential of REQORSA in NSCLC and for the study designs of Acclaim-1 and Acclaim-2.

The first presentation at AACR, entitled “TUSC2 immunogene therapy enhances efficacy of chemo-immune combination therapy and induces robust antitumor immunity in KRAS-LKB1 mutant NSCLC in humanized mice,” showed that the combination of immunotherapy (immune checkpoint blockade) and REQORSA demonstrated strong antitumor efficacy and induced robust antitumor immunity in KRAS-LKB1 (KL)-mutant NSCLC in clinically relevant humanized mouse models. It was also reported that REQORSA and immunotherapy and chemotherapy combinations were associated with strong efficacy in xenografts in humanized mice.

This poster and its data are relevant to our Acclaim-2 clinical trial which is combining REQORSA and Keytruda, an immunotherapy in advanced NSCLC patients whose disease progressed after treatment with Keytruda. The Acclaim-2 trial is investigating whether the synergy seen with REQORSA and immunotherapy in humanized mice will translate into clinical benefits in patients.

The second poster presentation at AACR, entitled “Overcoming resistance to Osimertinib [Tagrisso] by TUSC2 gene therapy in EGFR-mutant NSCLC,” showed synergistic antitumor efficacy of REQORSA combined with Tagrisso in EGFR mutant Tagrisso resistant NSCLC tumor xenografts. The TUSC2 gene is the active ingredient in REQORSA.

The data from the second poster is particularly important as it relates to our Acclaim-1 clinical trial combining REQORSA and Tagrisso. Approximately 17% of NSCLC patients of North American and European descent and approximately 30% to 50% of NSCLC patients of Asian descent have activating EGFR mutations. Identification of these patients is clinically important, as the optimal initial therapy for them is an EGFR tyrosine kinase inhibitor (TKI), such as Tagrisso. However, among those patients who are EGFR positive and benefit from EGFR TKI therapy, nearly all eventually become resistant to and ultimately no longer respond to EGFR TKI therapy, resulting in disease progression. For example, according to the FLAURA study, sponsored by AstraZeneca, the median time to tumor progression for lung cancer patients on Tagrisso is approximately 18 months.

This AACR poster data supports the study design for the Phase 2 portion of Acclaim-1 that will enroll patients whose disease progressed on Tagrisso. Those patients may receive local therapy for progressing lesions, and will then receive either continued Tagrisso or the combination of REQORSA and Tagrisso, which we believe may extend the benefit of EGFR TKI therapy for NSCLC patients. This has the potential to change the paradigm for treatment of NSCLC patients who are no longer benefitting from Tagrisso and could provide a new treatment for NSCLC patients in desperate need of new therapies.

Key Opinion Leader Event

REQORSA’s potential in lung cancer was featured in a 2021 Key Opinion Leader event sponsored by Alliance Global Partners. The event, titled, “Advances in Gene Therapy for Oncology: New Opportunities with REQORSA™ (TUSC2),” was moderated by James Molloy, Managing Director, Equity Research at AGP and featured discussions with Andrew Becker, M.D., Ph.D. and Col. George Peoples, M.D., FACS, members of Genprex’s Clinical Advisory Board.

The presentation provided an overview of REQORSA and ONCOPREX and included discussions supporting the Company’s belief that REQORSA is the first systemic gene therapy used for cancer in human clinical trials. It also featured the large markets that REQORSA is addressing, as well as REQORSA’s potential to address a range of cancers. The discussion also reviewed highlights from Genprex’s two previous clinical trials, ONC-001, a REQORSA monotherapy clinical trial; and ONC-002, a combination of REQORSA and Roche’s Tarceva® in NSCLC. The KOLs also discussed the importance of the positive preclinical data presented at the 2021 AACR annual meeting that support the use of REQORSA in combination with immunotherapies and with targeted therapies for the treatment of NSCLC.

A replay of this discussion is available on [our website](#).

Expansion of Intellectual Property Portfolio

During 2021, we secured an amendment to the Patent and Technology License Agreement with a major cancer research center in Houston, Texas, that was originally executed in 2020. This amendment adds an additional portfolio of six patents and one patent application and related technologies to Genprex’s exclusive worldwide license. The newly

licensed intellectual property includes methods for treating NSCLC by administration of REQORSA in conjunction with EGFR inhibitors or other anti-cancer therapies, in patients who are predicted to be responsive to REQORSA therapy.

We continue to expand our intellectual property protection for our arsenal of combination therapies for REQORSA as we develop a world-class intellectual property portfolio in the gene therapy space.

Gene Therapy for Diabetes

GPX-002 is a potentially curative diabetes gene therapy that was developed by lead researcher, Dr. George Gittes, of the University of Pittsburgh. In 2021, Genprex received the inaugural “License of the Year” award from the University of Pittsburgh Innovation Institute (UPII) in recognition of the advances made with our license from University of Pittsburgh toward progressing the development of GPX-002. We are honored to receive this recognition, considering the large number of cutting-edge technologies coming out of such a distinguished university and research center.



In addition, our collaborators at the University of Pittsburgh showcased our novel, preclinical diabetes gene therapy at the 2021 American Diabetes Association Scientific Sessions. [In a video](#) produced with the University of Pittsburgh Medical Center, sponsored by Genprex, attendees were able to learn more about this gene therapy approach for the treatment of both Type 1 and Type 2 diabetes.

Meanwhile, throughout the year Dr. Gittes and his team at the Rangos Research Center at UPMC Children’s Hospital of Pittsburgh continued preclinical studies of GPX-002 in nonhuman primates as they move toward first-in-human clinical trials.

We believe this diabetes gene therapy could hold the potential to provide long-term effectiveness for this debilitating disease and become a new treatment option for the millions of diabetes patients who now must rely on insulin replacement therapy.

Corporate Highlights

Enhancing REQORSA Manufacturing

To date, we have developed a robust manufacturing process for REQORSA through years of process development activities and the manufacturing technology has been successfully transferred from an academic setting to industry contract development and manufacturing organizations (CDMOs) using current Good Manufacturing Practices (cGMP) standards.

With the addition of Dr. Kumar to Genprex’s management, we are preparing for commercial readiness of REQORSA through the development of an integrated supply chain network of vendors. Under his leadership, we also are working to identify the most advanced manufacturing technologies in our industry so that we may leverage them and continue to be on the cutting-edge of gene therapy product development and manufacturing. These efforts will enable us to continue to support our clinical programs for REQORSA at multiple cancer centers across the United States and to prepare for future commercialization.

Strengthened Balance Sheet

In 2021, we strengthened our balance sheet by raising gross proceeds of \$25 million in a registered direct offering priced at the market, with no warrants. As of December 31, 2021, we had \$38.6 million in cash and no debt, which we believe, based on certain assumptions about our expenditures, would fund our operations into 2024.

A Strong Start to 2022

We have started 2022 strong by achieving many key milestones:

- **Receipt of FDA Fast Track Designation for Acclaim-2**

This Fast Track Designation is an important achievement in our efforts to accelerate clinical development of REQORSA and another indication of the potential of REQORSA to treat the unmet medical need of patients with late-stage NSCLC.

- **Dosing the first patient in the Acclaim-1 clinical trial**

This is an exciting milestone for Genprex which we believe brings us one step closer to achieving our goal to validate the potential benefits of REQORSA in NSCLC patients who have life-limiting disease and few treatment options.

- **Opening enrollment and dosing the first patient in the Acclaim-2 clinical trial**

We recently opened enrollment and dosed the first patient in Acclaim-2, our clinical trial of REQORSA in combination with Keytruda in late-stage NSCLC patients whose disease progressed on Keytruda.

- **Expansion of our clinical development pipeline to include small cell lung cancer**

REQORSA may have the potential to treat small cell lung cancer, in addition to non-small cell lung cancer, thus making REQORSA a possible drug candidate for nearly the entire lung cancer market.

- **New preclinical data show the potential of our ONCOPREX® Nanoparticle Delivery System in treating colon cancer**

We recently announced positive preclinical data showing that the ONCOPREX Nanoparticle Delivery System may be used to deliver tumor suppressor genes other than TUSC2, which is the active ingredient in REQORSA, to address multiple types of cancer. With this compelling data, Genprex is positioned to continue expanding our oncology programs and further explore use of our delivery system for other therapeutic genes, alone or in combination with other approved cancer therapies.

As we continue to advance our clinical development strategies, I believe we are set to advance our gene therapies toward commercialization and to distinguish ourselves from other gene therapy companies. I am confident in Genprex's technologies. REQORSA, ONCOPREX and GPX-002 have the potential to provide more effective therapies for very large patient populations with cancer and diabetes who are in desperate need for new treatment options.

With numerous important milestones ahead of us, I am excited to see Genprex emerge as a leader in gene therapy. I believe in our potential to extend hope and life to patients and increase value for our shareholders.

We thank you for your continued support of our Company.

Sincerely,



Rodney Varner
Chairman, President and Chief Executive Officer, Genprex

Forward-Looking Statements:

Statements contained in this shareholder letter regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are made on the basis of the current beliefs, expectations and assumptions of management, are not guarantees of performance and are subject to significant risks and uncertainty. These forward-looking statements should, therefore, be considered in light of various important factors, including those set forth in Genprex's reports that it files from time to time with the Securities and Exchange Commission and which you should review, including those statements under "Item 1A – Risk Factors" in Genprex's Annual Report on Form 10-K for the year ended December 31, 2021.

Because forward-looking statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding: the timing and success of Genprex's clinical trials and regulatory approvals, including the extent and impact of the COVID-19 pandemic; the effect of Genprex's product candidates, alone and in combination with other therapies, on cancer and diabetes; Genprex's future growth and financial status; Genprex's commercial and strategic partnerships, including those with its third party manufacturers and their ability to successfully perform and scale up the manufacture of its product candidates; and Genprex's intellectual property and licenses.

These forward-looking statements should not be relied upon as predictions of future events and Genprex cannot assure you that the events or circumstances discussed or reflected in these statements will be achieved or will occur. If such forward-looking statements prove to be inaccurate, the inaccuracy may be material. You should not regard these statements as a representation or warranty by Genprex or any other person that Genprex will achieve its objectives and plans in any specified timeframe, or at all. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Genprex disclaims any obligation to publicly update or release any revisions to these forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this press release or to reflect the occurrence of unanticipated events, except as required by law.