Generex and NuGenerex Immuno-Oncology Provide Update on Ii-Key COVID-19 Vaccine Development Program and Files Trademark Application for The Complete Vaccine™

- The trademark application can be found at USPTO.gov by searching "Complete Vaccine" in the Trademark Electronic Search System (TESS)
- Ii-Key-SARS-CoV-2 vaccine enters GMP production for clinical supply
- Ii-Key epitopes selected that elicit both CD4+ T Helper cell (Th1) and CD8+ responses that are necessary for long-term immune memory
- Ii-Key epitopes elicited no Th2 T cell responses that have been linked to antibody dependent enhancement of disease and cytokine storm
- Ii-Key epitopes have been used to purify Anti-SARS-CoV-2 antibodies from convalescent COVID-19 patient serum
- Neutralizing antibodies purified with Ii-Key epitopes have potential as a therapeutic treatment for COVID-19
- Addressing emergence of mutant coronavirus strains
- Exploring new opportunities to utilize Ii-Key-SARS-CoV-2 vaccines as a targeted universal booster designed to alleviate the immune related side effects reported with the current RNA vaccines

MIRAMAR, FL, December 31, 2020 - Generex Biotechnology Corporation (www.generex.com) (OTCQB:GNBT) (http://www.otcmarkets.com/stock/GNBT/quote) today announced that its majority owned public entity, NuGenerex Immuno-Oncology, Inc. (NGIO), has filed for and expects to receive a trademark for The Complete Vaccine™. A complete vaccine is designed to regulate the immune system to provide a targeted, neutralizing antibody response without generating off-target, non-neutralizing antibodies that can lead to antibody dependent enhancement of disease (ADE); further a complete vaccine should activate the appropriate T cell responses to yield long-term immune memory without activating detrimental Th2 responses that have been associated with immune-related complications of COVID-19 disease.

Generex also announced that significant progress has been made on the Ii-Key-SARS-CoV-2 vaccine program. The team at NGIO has completed the T Cell assays and HLA typing of blood samples from 46 convalescent COVID-19 patients and 30 healthy pre-COVID donors (from 2017 and 2018), screening the immune regulatory activity of 33 Ii-Key epitopes. The results of the T cell screen demonstrated that numerous Ii-Key epitopes activate CD4+ Th1 and CD8+ responses; none of the Ii-Key epitopes tested activated any negative Th2 responses.

Additionally, the Ii-Key epitopes have been used to bind and purify IgG antibodies from convalescent COVID-19 patient samples. These antibodies are being tested against live SARS-CoV-2 virus in a level 3 biocontainment laboratory to ensure that they neutralize the virus. Once

confirmed as neutralizing, these Ii-Key epitope binding antibodies can be purified and genetically engineered to develop antibody therapeutics against COVID-19.

Based on the results of the ex-vivo human studies, Generex has initiated GMP production of several Ii-Key-SARS-CoV-2 epitopes that will be formulated for Phase I and Phase II clinical trials; an IND is being prepared for FDA submission in early 2021. With multiple epitopes that are targeted to generate specific, neutralizing regions of the coronavirus without off-target effects, and which have demonstrated positive T cell regulation necessary for long-term immune memory, the Ii-Key COVID-19 vaccine has the potential to be a complete vaccine.

It has been widely reported that the SARS-CoV-2 virus, like all viruses, is mutating. Some of the mutational variants, with mutations that mainly occur in the virus spike protein, appear to have biological differences that may alter infectivity, transmission, and severity of infection. The Ii-Key vaccine platform is built to address issues of mutation. First, there are multiple Ii-Key-SARS-CoV-2 peptides, each containing multiple epitopes in the vaccine formulation. So even if there is one mutation, the other epitopes should provide protection. Second, if a new strain emerges, the Ii-Key platform can be rapidly deployed to make the new, mutant sequence with Ii-Key and add it to the current vaccine. This is the beauty of the Ii-Key technology. Further, the epitopes predicted by computational algorithms exclude regions of the coronavirus that are susceptible to mutation, so the Ii-Key vaccine largely eliminates mutagenic regions from the start.

With an impending IND submission for Phase I and II human clinical trials to evaluate safety and immunogenicity of the Ii-Key vaccine, NGIO is exploring additional opportunities to deploy the targeted Ii-Key COVID-19 vaccine as a universal booster for RNA, DNA, and inactivated virus vaccines that contain the entire spike protein and have the potential to elicit off-target and over-active immune responses. Recent reports of immune related side effects after booster inoculation with RNA vaccines include fever, chills, fatigue, and joint pain. These immune related side effects to the RNA vaccine mimic the immune response to coronavirus infection to provide immunity to COVID-19 as evidenced by 90+% efficacy rate. However, these strong immune responses also have the potential to lead to ADE, as has been shown in SARS-1, and questions remain as to the ability of the RNA vaccines to generate long-term immune memory. The targeted Ii-Key-SARS-CoV-2 vaccine is designed to generate long-term immune memory through specific T cell activation by the Ii-Key, and the antibody purification studies demonstrate the potential for the Ii-Key vaccine to elicit a targeted, neutralizing immune response without off-target effects. Using a targeted Ii-Key-SARS-CoV-2 vaccine as a universal booster may provide long-term immunity without causing the immune related side effects from off-target responses. Such a universal Ii-Key vaccine booster could significantly extend the currently limited supply of RNA vaccines, and with a clean side effect profile the Ii-Key booster may increase consumer acceptance.

Generex CEO, Joseph Moscato said, “Throughout this challenging year of 2020, we have overcome numerous hurdles to reach this point with our Ii-Key COVID-19 vaccine. We have filed an extensive patent application that covers our Ii-Key-SARS-CoV-2 vaccine and provides the foundation for a new patent estate for the Ii-Key platform. The results of our ex vivo human studies have been better than expected, and we have several Ii-Key epitopes that regulate the immune responses we seek in a vaccine formulation. The antibody data are especially encouraging. The results confirm that we are targeting immunologically important regions of the virus and demonstrate the ability to purify neutralizing antibodies from patient serum that can be developed as a targeted antibody therapeutic against COVID-19.

The Ii-Key vaccine is designed to be a Complete Vaccine, and we believe that our technology offers the safest and best route for the rapid development of a COVID-19 vaccine that can be safely administered to everyone, including adolescents, children and pregnant women without worry of immune related side effects. As we prepare for our first in human studies of the vaccine in healthy adults, we also plan to include underserved populations with risk factors for COVID-19, elderly subjects who are at high risk for serious complications from coronavirus infection, and working with our SAB, we are planning a focused clinical program for adolescents, children, and pregnant women.”

Mr. Moscato continued, “On the international front, we are moving forward with our partners in Malaysia and China on the development of the Ii-Key-SARS-CoV-2 vaccine. Bintai Kinden is supporting our US development efforts in exchange for exclusive distribution rights in Malaysia and Southeast Asia. We have also initiated discussions with our Chinese partners on the technology transfer, GMP production, and regulatory filings with the NMPA for the Phase I, II and III clinical programs in China. This partnership in China will also enable us to explore the potential of the Ii-Key-SARS-CoV-2 vaccine as a universal booster.”

“We look forward to an exciting 2021 as we advance the Ii-Key COVID vaccine into the clinic with the goal of gaining FDA approval for a Complete Vaccine™. On behalf of the Generex and NGIO management teams, we wish our shareholders and investors a happy, healthy, and prosperous New Year as we continue to execute our plans to build value for the future.”

About Generex Biotechnology Corp.

Generex Biotechnology is an integrated healthcare holding company with end-to-end solutions for patient centric care from rapid diagnosis through delivery of personalized therapies. Generex is building a new kind of healthcare company that extends beyond traditional models providing support to physicians in an MSO network, and ongoing relationships with patients to improve the patient experience and access to optimal care.

About NuGenerex Immuno-Oncology

NuGenerex Immuno-Oncology, a subsidiary of Generex Biotechnology, is a clinical stage oncology company developing immunotherapeutic peptide vaccines for cancer and infectious disease based on the CD4 T-Cell activation platform, Ii-Key. NuGenerex Immuno-Oncology (NGIO) has been spun out of Generex as a separate public company to advance the platform Ii-Key technology, particularly in combination with the immune checkpoint inhibitors for the treatment of cancer. NGIO is currently engaged in a Phase II clinical trial of its lead cancer immunotherapeutic vaccine AE37 in combination with pembrolizumab (Merck's Keytruda®) for the treatment of triple negative breast cancer. The company has also turned its Ii-Key technology on infectious disease, responding to the coronavirus pandemic with a SARS-CoV-2 vaccine development program.

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