Generex Subsidiary NuGenerex Immuno-Oncology Announces Publication of a Review Article on Cancer Vaccines Highlighting AE37 (Ii-Key-HER2) Immunotherapeutic Vaccine

Exploring Essential Issues for Improving Therapeutic Cancer Vaccine Trial Design

- Immunotherapy with cancer vaccines explained
- Review of cancer vaccine trials: design, results, opportunities
- *Cancers* **2020**, *12*(10), 2908; https://doi.org/10.3390/cancers12102908; article can be found online: (https://www.mdpi.com/2072-6694/12/10/2908)

MIRAMAR, FL, October 13, 2020 - Generex Biotechnology Corporation (www.generex.com) (OTCQB:GNBT) (http://www.otcmarkets.com/stock/GNBT/quote) is happy to announce that a review article on therapeutic cancer vaccines has been published in the peer-reviewed journal Cancers. The paper highlights the importance of proper clinical design in terms of selected groups of patients, taking into consideration (a) changes in initially established standard-of-care treatments; (b) the appropriate follow-up period necessary to achieve meaningful results; (c) statistical considerations for the delay of treatment effects (i.e., time for development of an effective immune response), thus excluding irrelevant early events; and (d) appropriate biomarkers that could guide vaccinations with clinical benefits to patients.

The authors of the paper* have extensive experience with AE37 immunotherapeutic vaccine as principal investigators in the company's breast and prostate cancer trials. The paper clearly describes why the Phase IIb clinical trial of AE37 in breast cancer demonstrated a statistically significant clinical benefit for certain subgroups of patients in the trial (advanced stage disease with low HER2 or triple negative breast cancer) while failing to meet the primary endpoint in the entire intent-to-treat (ITT) study population. The introduction of Herceptin (trastuzumab) as the standard of care during the long-term follow-up of the trial skewed the results such that the benefit of AE37 could not be detected in the statistical analysis. However, when looking at patients in subgroups that did not receive Herceptin, the positive benefits of AE37 on survival become apparent. Patient selection and protocol design that accounts for changes in standard of care are the key to future study designs.

The authors note that the survival benefit with AE37 and other cancer vaccines also require prolonged follow-up because the immune system takes time to activate against the tumor. Therefore, the survival curves only start to diverge after 12 months from treatment initiation. Future trials need to use statistical methods that account for the delayed immune response to exclude early events in order to accurately evaluate the efficacy of immunotherapeutic vaccines.

Further, responders to immunotherapy may be determined using biomarker evaluation, which for AE37 is gamma-interferon, a cytokine secreted by T-cells activated by the Ii-Key vaccine. Those patients who responded to AE37 with strong site reactions and gamma interferon induction demonstrated the most clinical benefit in survival. The use of biomarkers to evaluate

cancer vaccine efficacy can significantly improve protocol design and shorten the time from Phase II to Phase III.

“This peer-reviewed paper provides further validation of our Ii-Key immunotherapeutic cancer vaccines,” said Generex President & CEO Joe Moscato. “The recently published results of the AE37 Phase IIb breast cancer trial in over 300 women showed a statistically significant benefit to patients with advanced disease and low HER2 expression, and six of seven AE37 patients with triple negative breast cancer and advanced disease are still alive – even after 10 years. As I have said for many years, the introduction of Herceptin as standard of care during the 7-year trial masked the benefit of AE37 in this subgroup, but for those patients who are not eligible for Herceptin therapy, AE37 offers new hope.”

Mr. Moscato continued, “The paper also validates our future plans for AE37 clinical development, as we plan to initiate a trial in bladder cancer at a preeminent cancer center to evaluate the tumor microenvironment and biomarkers associated with immune system activation by Ii-Key cancer vaccines. As per the authors, and with the help of our scientific and clinical advisory board, we will conduct well-designed clinical trials to support the full potential of AE37 and our other Ii-Key vaccines for cancer and infectious diseases to activate the immune system, and to turn it effectively against a patient’s tumor.”

* The authors Drs. Constantin N. Baxevanis, Sotirios P. Fortis, Alexandros Ardavanis, and Sonia A. Perez of the St. Savas Cancer Hospital in Athens, Greece have previously been investigators for AE37 clinical trials. The company and the authors have no current affiliation.

About NuGenerex Immuno-Oncology

NuGenerex Immuno-Oncology, a public subsidiary of Generex Biotechnology, is a clinical stage oncology company developing immunotherapeutic peptide vaccines based on the CD4 T-Cell activation platform, Ii-Key. NuGenerex Immuno-Oncology (NGIO) has been spun out of Generex as a separate, independent public company to advance the platform Ii-Key technology, particularly in combination with the immune checkpoint inhibitors. 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.

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.

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