



## **NantKwest and ImmunityBio Announce Therapeutics and Vaccines for Combatting COVID-19; Clinical Trials Anticipated to Begin This Quarter**

April 14, 2020

*Immunotherapy companies led by Dr. Patrick Soon-Shiong are developing potential coronavirus therapeutics and vaccines to address the evolving stages of disease from moderate infection to severe acute respiratory distress syndrome (SARS)*

- **Vaccine Vector to Protect Against SARS-CoV-2 Infection:**
  - ImmunityBio's Ad5: A second -generation adenovirus vaccine platform with four deletions enabling multiple homologous doses, even in patients with adenovirus immunity
- **Therapeutic Immunomodulators for Patients with Mild to Moderate COVID-19 Symptoms:**
  - NantKwest's haNK: CD-16, off-the-shelf natural killer cells to enhance antibody killing of infected cells, given alone or combined with Convalescent Plasma (CP)
  - ImmunityBio's N-803: Interleukin 15 (IL-15) 'superagonist' cytokine to stimulate natural killer cells and CD8+ T cells
- **Therapeutic for Severe and Critically Ill COVID-19 Patients on Ventilator Support:**
  - NantKwest's MSCs: Bone marrow-derived mesenchymal stem cells (MSC) to mitigate 'cytopathic storm'

EL SEGUNDO, Calif.--(BUSINESS WIRE)--Apr. 14, 2020-- NantKwest, Inc. (NASDAQ: NK) and ImmunityBio, Inc., clinical-stage immunotherapy companies within the NantWorks family of companies, today announced they are in active discussions with the U.S. Food and Drug Administration (FDA) for vaccines and therapeutics to combat COVID-19.

Leveraging ImmunityBio's expertise in vaccine development and natural killer cell activation, with a broad platform of immunomodulators currently in clinical trials for cancer and infectious diseases, and NantKwest's extensive experience in off-the-shelf, cell-based therapeutics, the companies are combining their resources to design and develop therapeutics and vaccines for COVID-19.

"We're in a race against time, but I am confident that, as a result of the incredible hard work the NantKwest, ImmunityBio, and the global scientific communities are undertaking, we will find effective therapeutics and vaccines against this coronavirus," said Patrick Soon-Shiong, M.D., Chairman & CEO of NantKwest and ImmunityBio.

### **Therapeutics:**

The biological, immunological, and physiological status of the patient's medical state should inform the treatment strategy to reverse the infectivity and tissue damage caused by this virus. ImmunityBio and NantKwest have developed immunomodulator regimens for COVID-19 based on the biological stage of the patient's infection - from the mild, moderate to the severe or critically ill state.

"In the mild-to-moderate stage of infection, we believe that the patient's infection and viral load could be mitigated with natural killer (NK) and T cell stimulation. Hence, in this early-moderate stage of the disease, we are proposing clinical trials of N-803 alone, and a second trial of haNK alone, or haNK combined with convalescent plasma," said Dr. Soon-Shiong.

Investigational New Drug (IND) applications with the FDA for these trials are pending. ImmunityBio's IL-15 'superagonist' N-803 is currently being used in clinical trials for other indications and has achieved Breakthrough Therapy Designation from the FDA<sup>[1]</sup> for the treatment of BCG-unresponsive non-muscle invasive bladder carcinoma in situ (NMIBC-CIS) patients. It has also demonstrated encouraging results in lowering the viral load in SHIV-infected monkeys<sup>[2]</sup>, as announced last month at the Annual Conference on Retroviruses and Opportunistic Infections (CROI)<sup>[3]</sup>.

"In patients requiring ventilatory support in the severe state of COVID-19 disease, we are exploring the use of bone marrow-derived allogenic mesenchymal stem cells (BM-Allo-MS) to mitigate the 'cytopathic storm,'" said Dr. Soon-Shiong.

NantKwest has proprietary isolation and expansion methods for growing MSCs and is using ImmunityBio's automated, closed system (GMP-in-a-Box) to safely and rapidly grow these stem cells from a bone marrow cell bank in approximately 7-9 days. NantKwest has filed an IND with the FDA and anticipates beginning trials in Q2 2020.

### **Vaccines: Developing a platform for both initial immunizations and subsequent booster injections**

First generation Adenovirus platforms (Ad5) currently in use are disadvantaged by inducing adenovirus neutralizing antibodies, thus limiting multiple doses and reducing the immune response to the antigen of interest. ImmunityBio has overcome this obstacle through the development of a second generation Ad5 platform. Through multiple deletions in the adenovirus genome, this next generation platform establishes a vector that is immunologically "quiet" as it relates to adenovirus protein production in the host dendritic cell and enables this same Ad5 vector to serve both as a prime and a boost treatment, even in patients with pre-existing adenovirus immunity. This second-generation Ad5 [E1-, E2b-, E3- deleted] platform has demonstrated safety in Phase I and Phase II studies in immunosuppressed cancer patients.

Furthermore ImmunityBio has extensive infectious disease experience with this second generation Ad5 platform and has published several

peer-reviewed articles on studies demonstrating humoral and cell mediated immunity in H1N1 Influenza<sup>[4]</sup>, HIV<sup>[5]</sup>, SIV<sup>[6]</sup>, Lassa Fever<sup>[7]</sup>, Chikungunya, and Zika virus infections.

"While development of therapies is urgently needed in this crisis, as urgent is the need to develop a vaccine with long-lasting cell-mediated immunity. Developing vaccines in the time of pandemics requires novel approaches and the use of modernized genomics, molecular dynamics, and vectors that are proven to induce cell-mediated immunity, with mass scale production capabilities. In 2009, with the H1N1 crisis, the scientific team developing this second generation Ad5 platform demonstrated that such a vaccine for the H1N1 pandemic could be developed in six weeks from identification of the H1N1 sequence. This experience in 2009 allows ImmunityBio to respond as rapidly as possible to the COVID-19 pandemic," continued Dr. Soon-Shiong. "I view the spike (S) protein and the nucleocapsid (N) protein as the equivalent of a neoantigen in cancer. A recent study by the National Cancer Institute (NCI) in patients with advanced cancer, published in *The Oncologist*<sup>[8]</sup> reported positive evidence that this platform could induce antigen-specific T cell immunity, even in the face of previous adenoviral immunity," said Dr. Soon-Shiong. Together with our scientific collaborators at the NCI, we have recently published evidence<sup>[9]</sup> that the Ad5 platform can successfully induce cell-mediated immunity following the administration of Ad5-Neoantigens, with total remission of the tumor in pre-clinical models. Based on these findings, we are hopeful that the Ad platform could induce a similar immune response to this novel Coronavirus antigen."

## About NantKwest

NantKwest (NASDAQ: NK) is an innovative, clinical-stage immunotherapy company focused on harnessing the power of the innate immune system to treat cancer and virally-induced infectious diseases. NantKwest is the leading producer of clinical dose forms of off-the-shelf natural killer (NK) cell therapies. The activated NK cell platform is designed to destroy cancer and virally-infected cells. The safety of these optimized, activated NK cells—as well as their activity against a broad range of cancers—has been tested in phase I clinical trials in Canada and Europe, as well as in multiple phase I and II clinical trials in the United States. By leveraging an integrated and extensive genomics and transcriptomics discovery and development engine, together with a pipeline of multiple, clinical-stage, immuno-oncology programs, NantKwest's goal is to transform medicine by delivering living drugs-in-a-bag and bringing novel NK cell-based therapies to routine clinical care. NantKwest is a member of the [NantWorks](#) ecosystem of companies. For more information, please visit [www.nantkwest.com](http://www.nantkwest.com)

haNK is a registered trademark of NantKwest, Inc.

### Forward-Looking Statements

*This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements concerning or implying that NantKwest will be successful in improving the treatment of cancer. Risks and uncertainties related to this endeavor include, but are not limited to, obtaining FDA approval of NantKwest's NK cells as well as other therapeutics as part of the NANT Cancer Vaccine platform as a cancer treatment.*

*Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements.*

*These and other risks regarding NantKwest's business are described in detail in its Securities and Exchange Commission filings, including in NantKwest's Annual Report on Form 10-K for the year ended December 31, 2019. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.*

## About ImmunityBio

ImmunityBio, Inc. is a privately-held immunotherapy company with a broad portfolio of biological molecules at clinical stages of development. The company's goals are to employ this portfolio to activate endogenous natural killer and CD8+ T cells in the fields of cancer and infectious disease. Specifically, ImmunityBio's goal is to develop a memory T-cell cancer vaccine to combat multiple tumor types—without the use of high-dose chemotherapy. Regarding infectious disease, ImmunityBio is addressing HIV, influenza, and the coronavirus.

ImmunityBio's first-in-human platform of technologies has enabled it to achieve one of the most comprehensive, late-stage clinical pipelines, activating both the innate (natural killer cell) and adaptive immune systems. The product pipeline includes an albumin-linked chemotherapeutic (Aldoxorubicin), a novel IL-15 cytokine superagonist (N-803), checkpoint inhibitors, macrophage polarizing peptides, bi-specific fusion proteins targeting TGFβ and IL-12, adenovirus, and yeast vaccine therapies targeting tumor-associated antigens and neoepitopes.

In December 2019, the U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation to N-803 for BCG-unresponsive CIS non-muscle invasive bladder cancer (NMIBC). Other indications currently at registration-stage trials include BCG-unresponsive papillary bladder cancer, first- and second-line lung cancer, and metastatic pancreatic cancer.

ImmunityBio's goal is to develop therapies, including vaccines, for the prevention and treatment of HIV, influenza, and the coronavirus SARS-CoV-2.

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*Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.*

- [1]: ImmunityBio Granted FDA Breakthrough Therapy Designation for N-803 IL-15 Superagonist in NMIBC – December 4, 2019 <https://www.businesswire.com/news/home/20191204005300/en/ImmunityBio-Granted-FDA-Breakthrough-Therapy-Designation-N-803>
- [2]: ImmunityBio Announces Durable Virus Control of SHIV Without Anti-Retroviral Therapy (ART) by Activating NK and Memory T Cells with N-803, an IL-15 Superagonist – March 10, 2020 <https://immunitybio.com/immunitybio-announces-durable-virus-control-of-shiv-without-anti-retroviral-therapy-by-activating-nk-and-memory-t-cells-with-n-803-an-il-15-superagonist/>
- [3]: Combination IL-15 Therapy in a SHIV NHP Model – Presented at Conference on Retroviruses and Opportunistic Infections (CROI) March 8-11, 2020 Boston, Massachusetts <http://www.croiconference.org/sessions/comboination-il-15-therapy-shiv-nhp-model>
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- [5]: Induction and Comparison of SIV Immunity in Ad5 Naïve and Ad5 Immune Non-Human Primates Using an Ad5 [E1-, E2b-] Based Vaccine. *Vaccine*. 2011 Oct 19; 29(45):8101-7. doi: [10.1016/j.vaccine.2011.08.038](https://doi.org/10.1016/j.vaccine.2011.08.038). Epub 2011 Aug 22.
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- [8]: A Phase I Trial Using a Multitargeted Recombinant Adenovirus 5 (CEA/MUC1/Brachyury)-Based Immunotherapy Vaccine Regimen in Patients with Advanced Cancer. *The Oncologist*. doi:[10.1634/theoncologist.2019-0608](https://doi.org/10.1634/theoncologist.2019-0608)
- [9]: Efficient Tumor Clearance and Diversified Immunity Through Neopeptide Vaccines and Combinatorial Immunotherapy. *Cancer Immunology Research* July 2019 DOI: [10.1158/2326-6066.CIR-18-0620](https://doi.org/10.1158/2326-6066.CIR-18-0620)

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