ImmunityBio Announces Promising Clinical Study Results for ‘Kick and Kill’ HIV Cure Strategy to Reduce HIV Viral Load with Anktiva (N-803) Therapy

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- Data from the Phase 1 “HIV Cure” Study as published in *Nature Medicine* showed that Anktiva (N-803) stimulates latent HIV replication in CD4+ cells (the kick) and increases immune cell activation (the kill)
- Activated CD4, CD8, and NK immune cells are necessary for finding and killing HIV-infected cells
- No treatment-related serious adverse events were reported
- Multiple Phase 1 and 2 trials with Anktiva in patients with HIV are ongoing
- The need for this therapeutic approach is significant: Globally there are an estimated 38 million people living with HIV; in the US, with 1.2 million people living with HIV, the average annual cost of antiretrovirals is $36,000, while nearly $2 billion is spent on those therapies in developing countries[1 & 2]

CULVER CITY, Calif.--(BUSINESS WIRE)--Jan. 31, 2022-- ImmunityBio, Inc. (NASDAQ: IBRX), a clinical-stage immunotherapy company, today announced promising study results that demonstrate the activation of CD4+ and CD8+ T cells and natural killer (NK) cells in people living with HIV by ImmunityBio’s IL-15 superagonist Anktiva (N-803). Anktiva stimulates latent HIV replication (the “kick”) in CD4 memory cells allowing the previously hidden infected cells to be revealed and eliminated (the “kill”) by CD8 and NK cells. This mechanism is key for killing cells that harbor latent virus, thereby reducing viral reservoirs in antiretroviral (ART)-suppressed HIV patients and ultimately ridding the body of the virus and the threat of re-activation. These positive clinical findings support ImmunityBio’s “Kick-and-Kill” strategy to cure HIV.

The study was conducted by Timothy W. Schacker, M.D., a leading HIV researcher and Vice Dean for research at the University of Minnesota Medical School, and the results were published today in *Nature Medicine*. The goal of the Phase 1 study was to assess the effects of Anktiva on these viral reservoirs, along with safety and tolerability, as a precursor to larger human studies.

“Today there are 38 million people living with HIV in every corner of the world, and most of them depend on a daily cocktail of antiretroviral drugs to keep the virus at bay. These can cost thousands of dollars a month, a huge cost in wealthy countries and unaffordable for people in poorer nations,” said Patrick Soon-Shiong, M.D., Executive Chairman and Global Chief Scientific and Medical Officer at ImmunityBio. “This study is one of several ImmunityBio is undertaking to validate the potential role of Anktiva in activating the innate (NK) and adaptive (T cell) immune system to attack and kill cancerous or virus-infected cells. In this case, the target is HIV, and our ultimate goal is to develop our immunotherapy platforms of IL-15 fusion proteins combined with NK cell therapy as a therapeutic approach to rid the body of the virus for good and eliminate the need for antiretroviral therapy. The company is pursuing multiple studies in patients with HIV in hopes of meeting this goal of curing the disease.”

Study Adds to Existing Results

In both pre-clinical and clinical research, ImmunityBio’s IL-15 superagonist Anktiva has exhibited three activities that could potentially help the immune system eliminate HIV reservoirs and control virus rebound. First, Anktiva has been shown to reverse HIV latency—whereby genetic code for the virus persists, but virus is not made, allowing the infected cells to evade detection and elimination by the immune system—by stimulating HIV replication within long-lived immune cells such as memory CD4 cells, allowing the infected cells to be recognized and cleared. Second, it activates NK cells and CD8+ T cells, two elements of the immune system that specialize in killing virus-infected cells. Third, it enables NK cells and CD8+ T cells to move to lymphoid tissues where they will encounter and have an increased likelihood of eliminating HIV-infected cells.

Study Details (NCT02191098)

ART-suppressed individuals were enrolled into a dose-escalation study of N-803 in four different cohorts (0.3, 1.0, 3.0, and 6.0 mcg/kg). Each cohort received three doses total, separated by at least one week. The study enrolled 16 individuals, of which 11 completed all three doses. The maximum tolerated dose was 6.0 mcg/kg. The primary clinical adverse events (AEs) reported were an injection site rash and adenopathy and four participants experienced a grade 1 or 2 QTc prolongation, which was deemed unrelated to the N-803 administration. There were no significant laboratory AEs attributable to N-803. In exploratory analyses, N-803 was associated with proliferation and/or activation of CD4+ and CD8+ T cells, and NK cells, that peaked at four days post dosing. IFN, IP10, MCP-1, and IL-15 increased during treatment. HIV transcription in memory CD4 T cells and intact proviral DNA initially increased after N-803 treatment and there was a small but significant decrease in the frequency of PBMCs with an inducible HIV provirus that persisted for up to six months post therapy.

Additional HIV-related studies involving N-803

The ACTG **A5386** trial is studying whether Anktiva can control HIV alone or together with combination broadly neutralizing antibodies (bNABs) after participants stop their antiretroviral therapy (ART) and they are carefully monitored. The “HIV Cure” study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) and conducted by the AIDS Clinical Trials Group (ACTG), the largest global HIV research network.

A second study, which is in Phase 2, will evaluate Anktiva in combination with antiretroviral therapy during acute HIV infection. This study is being conducted by the Walter Reed Army Institute of Research’s U.S. Military HIV Research Program (MHRP) at the Thai Red Cross AIDS Research Centre in Bangkok. Both studies were announced in 2021.

About ImmunityBio

ImmunityBio is a leading late-clinical-stage immunotherapy company developing next-generation therapies that drive immunogenic mechanisms for defeating cancers and infectious diseases. The company's broad immunotherapy and cell therapy platforms—including Antibody cytokine fusion proteins, synthetic immunomodulators, vaccine technologies (hAd5 viral vector, mRNA, recombinant protein, and adjuvant), and genetically-modified, off-the-shelf natural killer cells (autologous and allogenic cytokine-enhanced memory NK cells)—activate both the innate (natural killer cell and macrophage) and adaptive (T cell) immune systems to create long-term "immunological memory."

ImmunityBio's clinical pipeline consists of 21 clinical trials—13 of which are in Phase II or III development—across 12 indications in solid and liquid cancers (including bladder, pancreatic, and lung cancers) and infectious diseases (including SARS-CoV-2 and HIV). Anktiva™, ImmunityBio's lead cytokine infusion protein, is a novel interleukin-15 (IL-15) superagonist complex and has received Breakthrough Therapy and Fast Track Designations from the U.S. Food and Drug Administration (FDA) for BCG-unresponsive CIS non-muscle invasive bladder cancer (NMIBC).

The company has established GMP manufacturing capacity at scale with cutting-edge cell manufacturing expertise and ready-to-scale facilities, as well as extensive and seasoned R&D, clinical trial, and regulatory operations, and development teams. For more information, please visit: www.immunitybio.com.

1. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2759735
2. Clinton Health Access Initiative, 2021 HIV Market Report

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, such as statements regarding the development of therapeutics for HIV, cancer and infectious diseases, clinical trial results, the efficacy of ImmunityBio's product candidates as compared to existing treatment options, and regulatory approval, commercialization and commercial success of ImmunityBio's product candidates and related matters. Statements in this press release that are not statements of historical fact are considered forward-looking statements, which are usually identified by the use of words such as "anticipates," "believes," "continues," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "seeks," "should," "will," and variations of such words or similar expressions. Statements of past performance, efforts, or results of our clinical trials, about which inferences or assumptions may be made, can also be forward-looking statements and are not indicative of future performance or results. Forward-looking statements are neither forecasts, promises nor guarantees, and are based on the current beliefs of ImmunityBio's management as well as assumptions made by and information currently available to ImmunityBio. Such statements reflect the current views of ImmunityBio with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about ImmunityBio, including, without limitation, (i) the ability of ImmunityBio to continue its planned preclinical and clinical development of its development programs, and the timing and success of any such continued preclinical and clinical development and planned regulatory submissions, (ii) ImmunityBio's ability to retain and hire key personnel, (iii) whether interim, initial, "top-line" and preliminary data from ImmunityBio's clinical trials that it announces or publishes from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data, (iv) the ability of clinical trial sites to initiate and complete ImmunityBio's clinical trials on time, or at all, and the cost associated with such clinical trials, (v) risks and uncertainties regarding the regulatory review and approval process, (vi) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (vii) ImmunityBio's ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies, (viii) ImmunityBio's ability to successfully commercialize its product candidates and (ix) the unknown future impact of the COVID-19 pandemic delay on certain clinical trials or their milestones and/or ImmunityBio's operations or operating expenses. More details about these and other risks that may impact ImmunityBio's business are described under the heading "Risk Factors" in the Company's Form 8-K filed with the U.S. Securities and Exchange Commission ("SEC") on March 10, 2021, Form 10-Q filed with the SEC on November 12, 2021 and in subsequent filings made by ImmunityBio with the SEC, which are available on the SEC's website at www.sec.gov. ImmunityBio cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. ImmunityBio does not undertake any duty to update any forward-looking statement or other information in this press release, except to the extent required by law.

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