Memory Cytokine-Enhanced Natural Killer Cells Show Promising Results in Leukemia Patients; Data Support ImmunityBio's Scaled m-ceNK Clinical Program

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- Natural killer (NK) cells play a critical role in the innate immune system's ability to combat cancer, but the key to long-term treatment effectiveness is ensuring their persistence
- A Washington University School of Medicine study shows that increasing NK cell persistence and efficacy is possible in a study involving same-donor cytokine-stimulated NK cells as a component of hematopoietic cell transplantation (HCT) for acute myeloid leukemia
- The study demonstrated that the NK cells when stimulated with a cytokine cocktail (IL-12, IL-15 and IL-18) developed a memory-like phenotype with increased expansion and persistence *in vivo*
- The results support continued investigation of memory-like cytokine-enriched NK (m-ceNK) cells as a treatment for cancer in ImmunityBio's Phase 1 open-label trial of its m-ceNK platform combined with its IL-15 superagonist cytokine fusion protein Anktiva™
- ImmunityBio's m-ceNK platform is highly scalable, with a single extraction of white blood cells from a patient enabling multiple (10 to 20) infusions of one billion NK cells per dose

CULVER CITY, Calif.--(BUSINESS WIRE)--Mar. 2, 2022-- ImmunityBio, Inc. (NASDAQ: IBRX), a clinical-stage immunotherapy company, today announced study results that further demonstrate the potential for use of memory-like cytokine-enriched natural killer (m-ceNK) cells for the treatment of cancer. ImmunityBio has successfully scaled the process of generating over 20 billion m-ceNK cells from a single extraction of white blood cells from a donor or patient, and reports promising clinical data supporting the ongoing development of memory NK cells for the treatment of both liquid and solid tumors of all types.

In a Phase 2 study sponsored by Washington University School of Medicine (NCT02782546), white blood cells retrieved from HCT donors to treat acute myeloid leukemia (AML) patients, were stimulated with cytokines (IL-12, -15, and -18) to form memory-like NK cells, and were re-infused to the patients, who also received ImmunityBio's IL-15 superagonist Anktiva (N-803). The cytokine-stimulated NK cells safely augmented a leading treatment for AML-—HLA-haploidentical hematopoietic cell transplantation. The data showed that the cytokine-stimulated NK cells were persistent, showed increased production of interferon-gamma and functionality, and led to a complete response in 87% of patients after Day 28. The results were recently published in a peer-reviewed article ("Hematopoietic cell transplantation donor-derived memory-like NK cells functionally persist after transfer into patients with leukemia") in *Science Translational Medicine*.

NK cells are innate immune cells that are under investigation as a cell therapy for multiple types of cancer. A challenge of NK cell-based therapies, however, is ensuring that the cells persist and remain functional long-term. This study showed that memory-like NK cells derived from the same donor as the hematopoietic cell transplantation (HCT) persisted for at least two months after transplantation and were highly functional *ex vivo*. Together, these findings support the use of memory NK cells as a component of HCT for leukemia.

"This important study adds to the growing body of data that shows the cancer-fighting ability of NK cells can be enhanced by stimulating expansion *and* persistence of these cells," said Patrick Soon-Shiong, M.D., Executive Chairman and Global Chief Scientific and Medical Officer at ImmunityBio. "The study also showed that stimulated memory NK cells are effective with only a single infusion when given along with Anktiva support. To facilitate this approach, ImmunityBio has successfully scaled cytokine enrichment and expansion of m-ceNK cells, so cancer patients can receive multiple infusions of these potent and persistent m-ceNK cells generated from a single donation of white blood cells."

About Memory Cytokine-Enhanced NK Cells (m-ceNK):
ImmunityBio has successfully enriched and expanded NK cells obtained from peripheral blood of donors using a technique called apheresis to generate NK cells with a memory-like phenotype, which exhibit both high cytotoxicity and increased interferon-gamma production. These m-ceNK cells can be generated from an individual donor for autologous cell therapy, but have also been generated as an allogeneic product from cord blood. In addition to the high potential for enhanced efficacy, m-ceNK cells can be infused easily in an outpatient setting.

ImmunityBio has developed a novel method of m-ceNK cells production that yields multiple clinical-dose forms from a single apheresis (white blood cell collection) using the company's proprietary NANT 001 Bioreactor (GMP-in-a-Box), thereby alleviating pressures on supply of starting material. An optimized cryopreservation protocol for maximum shelf-life and potency upon recovery was also established, a necessity for any off-the-shelf product. ImmunityBio is leveraging their ability to generate m-ceNK cells with potent cytotoxicity, increased IFN-gamma production, proliferative capacity, activation surface markers and memory response to establish a propriety method for generation, expansion, and cryopreservation of these cells for autologous use.

The QUILT 3.076 Study of Cryopreserved M-ceNK cells
Cryopreserved m-ceNK cells in combination with Anktiva™ (N-803) will be tested in a 2-part Phase 1 study (NCT04898543) designed to evaluate safety in subjects with locally advanced or metastatic solid tumors; solid tumors comprise approximately 90% of adult cancers and 40% of all cancers in children, according to the American Cancer Society. The study will compare the quantity and characteristics of m-ceNK cells collected and cytokine-enriched from newly diagnosed patients who have not received prior treatment to m-ceNK cells generated from patients who have received at least two prior treatments for their cancer.

The study consists of two cohorts and there will be 10 participants in each cohort. Cohort 1 includes participants with newly-diagnosed, high-risk solid tumors who have not received prior treatment; and cohort 2 includes participants with relapsed/refractory (r/r) solid tumors who have progressive disease after receiving ≥ 2 prior therapies. Participants will be enrolled in the two cohorts simultaneously.

- Participants in Cohort 1 will participate in apheresis collection of lymphocytes (part A) and will not receive any investigational therapy in this study.
- Participants in Cohort 2 will undergo an apheresis collection of lymphocytes (part A) prior to receiving 4 infusions of M-ceNK on days 1, 8, 15 and 22 along with N-803 on days 1 and 15.

About ImmunityBio
ImmunityBio is a 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 26 actively recruiting clinical trials—17 of which are in Phase 2 or 3 development—across 13 indications in liquid and solid tumors (including bladder, pancreatic, and lung cancers) and infectious diseases (including SARS-CoV-2 and HIV). Anktiva™, ImmunityBio's lead cytokine fusion 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

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 scalability of ImmunityBio's m-ceNK platform, the potential use and efficacy of m-ceNK cells for the treatment of cancer, clinical trial protocol design, enrollment, and potential results, among others. 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 preclinical and 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 information may be limited or incomplete, and ImmunityBio's statements should not be read to indicate that it has conducted a thorough inquiry into, or review of, all potentially available relevant information. 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) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (iv) ImmunityBio's ability to successfully commercialize its product candidates and uncertainties around regulatory reviews and approvals, (v) ImmunityBio's ability to scale its manufacturing and commercial supply operations for its product candidates and future approved products, (vi) ImmunityBio's ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies, and (vii) the unknown future impact of the COVID-19 pandemic on certain clinical trials or their milestones and/or ImmunityBio's business 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 10-K filed with the U.S. Securities and Exchange Commission ("SEC") on March 1, 2022, 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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