ImmunityBio Announces NIH-Led Research Affirming that PD-L1 T-haNK Therapy Overcomes T-Cell Escape in Multiple Types of Resistant Tumors

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- Checkpoint therapy alone is unlikely to lead to durable tumor control or a cure in patients with solid tumors that harbor DNA mutations that make them invisible to T cells
- This study supports ImmunityBio's hypothesis of combining NK cells with T cell activation in Phase 2/3 trials in metastatic pancreatic and lung cancers
- Preclinical study shows when tumor cells escape T cell detection or killing, tumor cell PD-L1 expression is increased thereby sensitizing these resistant cells to killing by ImmunityBio's PD-L1 t-haNK cells

CULVER CITY, Calif.--(BUSINESS WIRE)--Mar. 22, 2021-- ImmunityBio, Inc. (NASDAQ: IBRX), a clinical-stage immunotherapy company, today announced the publication of preclinical data in the Journal for ImmunoTherapy of Cancer (JITC) highlighting efficacy of ImmunityBio's PD-L1 t-haNK natural killer cell-based therapy in combination with T cell-based immunotherapy against heterogeneous tumors. ImmunityBio's novel PD-L1 t-haNKs are derived from a human, allogeneic NK cell line (NK-92) that has been engineered to express IL-2, CD16, and a chimeric antigen receptor (CAR) that recognizes PD-L1.

Human solid tumors are made of multiple clones of tumor cells, some of which harbor genomic alterations that make them invisible to T cells. These resistant clones accomplish this "cloaking ability" by preventing the presentation of the tumor antigens on MHC-I receptors, thus "hiding" from killer T cells. For these patients, maximum activation of T cells with immunotherapy is unlikely to lead to durable tumor control or a cure. However, when NK cells are activated, tumor recognition and targeting is restored. The study shows that when subpopulations of tumors cells escape T cell detection or killing, they upregulate PD-L1 in the process because of interferon in the tumor microenvironment. This increase in tumor cell PD-L1 expression sensitizes them to killing by PD-L1 t-haNKs.

"Our results suggest that sequential treatment, first with T cell immunotherapy to kill the sensitive tumor cells and upregulate PD-L1 on the remaining cells, followed by PD-L1 t-haNK treatment, may overcome the issue of tumor heterogeneity and enhance rates of durable tumor control in patients with relapsed solid cancers," said Clint T. Allen, M.D., Principal Investigator, Section on Translational Tumor Immunology in the National Institute on Deafness and Other Communication Disorders (NIH) and corresponding author of the publication.

The publication by first author Maxwell Lee et al., "Chimeric antigen receptor engineered NK cellular immunotherapy overcomes the selection of T cell escape variant cancer cells," describes the development of preclinical models with heterogenous cancers containing T cell escape variant tumor cells. T cell-based immunotherapy administered in these preclinical models resulted in IFNγ production that in turn upregulated PD-L1 expression in T cell escape variants. Subsequent administration of irradiated PD-L1 t-haNKs targeted and eliminated the tumor cell populations that had evolved to be resistant to T-cell immunotherapy alone, resulting in synergistic anti-tumor activity.

"We are excited to see this preclinical study that affirms our hypothesis of 'Quantum Oncotherapeutics,' which is currently being studied in Phase 1/2 QUILT trials across multiple tumor types. The theory we hold is that our treatment itself induces changes in the tumor immune microenvironment. By anticipating these dynamic cellular changes, we can administer and activate NK cells at the optimal time and, ultimately, outsmart the tumor. These spatial-temporal insights informing treatment have the potential to change the paradigm of cancer care with modernized immunotherapy protocols, beyond the standard-of-care therapy and beyond checkpoint therapy alone. Late-stage, randomized controlled trials in pancreatic and lung cancers that orchestrate NK cells and T cells are underway at ImmunityBio to confirm this hypothesis," said Patrick Soon-Shiong, M.D., Founder and Executive Chairman of ImmunityBio.

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 immunotherapy platform activates both the innate (natural killer cell and macrophage) and adaptive (T cell) immune systems to create long-term "immunological memory."

ImmunityBio has a comprehensive immunotherapy pipeline with more than 40 clinical trials (company sponsored or investigator initiated)—of which 25 are at Phase II and III stage of development—across 19 indications in solid and liquid cancers and infectious diseases. Currently 17 first-in human immunotherapy agents are in clinical testing and, to date, over 1,800 patients have been studied with our antibody cytokine fusion proteins, albumin chemo immunomodulators, Adeno and yeast vaccines and our off-the-shelf natural killer cell products. 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's platforms are based on the foundation of four separate modalities: Antibody cytokine fusion proteins, synthetic immunomodulators, second-generation human adenovirus (hAd5) and yeast vaccine technologies, and state-of-the-art, off-the-shelf natural killer cells, including autologous and allogenic cytokine-enhanced memory NK cells.

ImmunityBio is a leading producer of cryopreserved and clinical dose forms of off-the-shelf natural killer (NK) cell therapies. 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. 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. These 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) potential adverse effects or changes to relationships with employees, suppliers or other parties resulting from the completion of the merger, (ii) the outcome of any legal proceedings that may be instituted against the parties and others related to the merger, (iii) unexpected costs, charges or expenses resulting from the merger, (iv) uncertainty of the expected financial performance of the combined company following completion of the merger, including the possibility that the expected synergies and value creation from the merger will not be realized or will not be realized within the expected time period, (v) 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, (vi) inability to retain and hire key personnel, and (vii) the unknown future impact of the COVID-19 pandemic delay on certain clinical trial 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 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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