ImmunityBio Receives FDA RMAT Designation for ANKTIVA® and CAR-NK for the Reversal of Lymphopenia in Patients Receiving Standard-of-Care Chemotherapy/Radiotherapy and in Treatment of Multiply Relapsed Locally Advanced or Metastatic Pancreatic Cancer

February 27, 2025

- Regenerative Medicine Advanced Therapy (RMAT) designation follows clinical data of Absolute Lymphocyte Count (ALC) and significant Overall Survival (OS) correlations in QUILT trials across multiple tumor types, including third line or greater metastatic pancreatic cancer, checkpoint relapsed NSCLC, and supportive data from healthy volunteers
- The reversal of lymphopenia by ImmunityBio's IL-15 superagonist is consistent with the mechanism of action of ANKTIVA demonstrating proliferation and activation of NK cells, CD4+ T cells, CD8+ T cells and memory T cells without upregulation of suppressive T regulatory cells and approved in the ANKTIVA label
- Company intends to submit Biologic License Application (BLA) for the indication of reversal of lymphopenia in patients receiving standard-of-care chemotherapy and/or radiation and for the treatment of locally advanced or metastatic pancreatic cancer, which includes the first-in-class CAR-NK (PD-L1 t-haNK)
- ImmunityBio to provide data from fully enrolled clinical trials in metastatic pancreatic cancer (QUILT-88) and in checkpoint relapsed NSCLC (QUILT-3.055, NSCLC Cohort) patients, as well as lymphopenia reversal across multiple tumor types (QUILT-3.055, All Cohorts), with supportive data of lymphocyte proliferation in healthy volunteers (QUILT-1.004)
- In addition, ImmunityBio intends to file an Expanded Access Policy (EAP) for ANKTIVA and PD-L1 t-haNK in combination with standard of care chemotherapy/radiotherapy within 15 days and submit the protocol to the Agency

CULVER CITY, Calif.--(BUSINESS WIRE)--Feb. 27, 2025-- ImmunityBio, Inc. (NASDAQ: IBRX), a leading immunotherapy company, today announced the U.S. Food and Drug Administration (FDA) has granted Regenerative Medicine Advanced Therapy (RMAT) designation for ANKTIVA® and CAR-NK (PD-L1 t-haNK) for the reversal of Lymphopenia in Patients Receiving Standard-of-Care Chemotherapy/Radiotherapy and in Multiply Relapsed Locally Advanced or Metastatic Pancreatic Cancer.

The complete blood count (CBC) is a standard assay widely used by oncologist to assess the status of the immune system following chemotherapy and radiation. To date, information of the cellular elements in the CBC assay provide information to the physician for the treatment of anemia, neutropenia and reduced platelet counts associated with the adverse events of chemotherapy and radiotherapy. Anemia, neutropenia and reduced platelet counts can be treated with currently approved therapies, including EPOGEN, NEUPOGEN and platelet transfusion, respectively.

However, chemotherapy and radiation has also caused a reduction in the very cells necessary to kill cancer cells. This reduction in the lymphocytes by our standard of care also inhibits the induction of T cell memory in the absence of CD4+, CD8+ T cells. A treatment for the reversal of these adverse events of lymphopenia, induced by current standard-of-care, has eluded the industry for the past 50 years. ImmunityBio and its Founder Dr. Patrick Soon-Shiong developed a vision over the past decades that activation and proliferation of these key lymphocytes was necessary if we were to win the war against cancer and indeed even prevent cancer in subjects at high-risk such as with lynch syndrome with a cancer vaccine. The founder's vision reflecting the pursuit of addressing lymphopenia over the past decades will be updated in March.

"RMAT designation for ANKTIVA combined with NK cells was applied for by the Founder in the initial 2017 IND. With the clinical results of the QUILT trials across multiple tumor types from 2017 to 2024, validating the hypothesis that high-dose chemotherapy and radiation induces lymphopenia and can be reversed by ANKTIVA together with off-the-shelf CAR-NK cells (PD-L1 t-haNK) resulting in prolongation of overall survival (OS), and enabling ImmunityBio to reapply for RMAT in 2025,"[1] said Dr. Patrick Soon-Shiong, Founder, Executive Chairman and Global Chief Scientific & Medical Officer of ImmunityBio. "I am so grateful for the FDA to have recognized the evolution of science and the need for adoption of 21 st century medicine and cell therapy, particularly the role of NK cell therapy in our war against cancer as a universal therapy in cancer, and in the potential treatment of infectious diseases such as HIV, HPV and COVID. Today's designation of ANKTIVA and the first CAR-NK (PD-L1 T-haNK), both first-in-class molecules to activate lymphocytes within the body (via subcutaneous injection of ANKTIVA) and via ex-vivo infusion of off-the-shelf PD-L1 NK cells, is an inflection point and a paradigm change of how we could treat patients with cancer and viral infections. The absolute lymphocyte count (ALC) which has been largely ignored by physicians, since no therapy existed to address lymphopenia, could now be both a prognostic biomarker but more importantly, the potential as a therapeutic biomarker."

"Multiple publications in the last five years have shown that patients with low lymphocyte counts, especially those with severe lymphopenia, have a statistically lower survival rate regardless of the tumor types.[2-5] With this RMAT designation and the attributes of a RMAT designation including all Breakthrough Therapy Designation features and statutory ways to support Accelerated Approval, we will move rapidly to file the BLA for these authorized indications provided by the RMAT designation," said Soon-Shiong. "In addition, per the requirement under section 561A(f)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), ImmunityBio will make publicly available the Expanded Access Policy of ANKTIVA and PD-L1 t-haNK in combination with standard-of-care chemotherapy/radiotherapy within 15 days."

In the authorization letter, the FDA has committed to work closely with ImmunityBio to provide guidance and advice on generating the evidence needed to "*support approval*' of the indication above " *in an efficient manner*."

About ANKTIVA®

The cytokine interleukin-15 (IL-15) plays a crucial role in the immune system by affecting the development, maintenance, and function of key immune cells—NK and CD8+ killer T cells—that are involved in killing cancer cells. By activating NK cells, ANKTIVA overcomes the tumor escape phase of clones resistant to T cells and restores memory T cell activity with resultant prolonged duration of complete response.

ANKTIVA is a first-in-class IL-15 agonist IgG1 fusion complex, consisting of an IL-15 mutant (IL-15N72D) fused with an IL-15 receptor alpha, which binds with high affinity to IL-15 receptors on NK, CD4+, and CD8+ T cells. This fusion complex of ANKTIVA mimics the natural biological properties of the membrane-bound IL-15 receptor alpha, delivering IL-15 by dendritic cells and drives the activation and proliferation of NK cells with the generation of memory killer T cells that have retained immune memory against these tumor clones. The proliferation of the trifecta of these immune killing cells and the activation of trained immune memory results in immunogenic cell death, inducing a state of equilibrium with durable complete responses. ANKTIVA has improved pharmacokinetic properties, longer persistence in lymphoid tissues, and enhanced anti-tumor activity compared to native, non-complexed IL-15 in-vivo.

ANKTIVA was approved by the FDA in 2024 for BCG-unresponsive non-muscle invasive bladder cancer CIS with or without papillary tumors. For more information, visit ImmunityBio.com (Founder's Vision) and Anktiva.com.

About CAR-NK (PD-L1 t-haNK)

PD-L1 t-haNK is a human, allogeneic, stable clonal NK cell line generated from the parental aNK cell line (NK-92), manufactured by the Sponsor under cGMP conditions.

Based on the demonstrated therapeutic efficacy of CAR targeting and on the important role of FcγR-mediated ADCC in the effectiveness of therapeutic IgG_1 monoclonal antibodies, we hypothesized that modification of the parental aNK cell line to stably express both a PD-L1–targeted CAR and the high-affinity variant of CD16 would result in potent and selective antitumor activity. Myeloid-derived suppressor cells (MDSCs) express PD-L1 in concert with MHC-I loss to induce immune escape of tumors resistant or relapsed from chemo-immunotherapy including checkpoint inhibitors. Thus, there is a rationale for the combination of Anktiva (converting a cold tumor to hot tumor and rescuing T cells by re-expressing MHC-I) and PD-L1 t-haNK to overcome the immunosuppressive effect of TGFβ secreted by MDSCs. The ability to target both the tumor and MDSCs with off-the-shelf, outpatient based safe infusion of allogeneic CAR-NKs targeting PD-L1, was the basis for the development of this CAR-NK. Preclinical studies published in the J Immunotherapy Cancer 2020 "PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations" (Fabian et al. 2020) demonstrate that PD-L1 targeting of high affinity NK cells (PD-L1 t-haNK) induced direct anti-tumor effects in TNBC tumor cell lines and target suppressive MDSCs populations.

About ImmunityBio

ImmunityBio is a leading biotechnology company addressing cancer and infectious diseases by bolstering the natural immune system. The company is developing therapeutics that coordinate innate and adaptive immune responses, stimulating robust, multifunctional immunity and sustained immune memory that results in safe, long-term protection against disease recurrence.

The company's lead asset is ANKTIVA® (nogapendekin alfa inbakicept-pmln) solution for intravesical use, approved in the U.S. by the Food and Drug Administration (FDA) indicated with Bacillus Calmette-Guérin (BCG) for the treatment of adult patients with BCG-unresponsive bladder carcinoma in situ (CIS) with or without papillary tumors.

ANKTIVA's ability to activate natural killer (NK) cells, killer T cells, and memory T cells makes it a candidate 'backbone' therapy that may enhance the effectiveness of other therapies when used in combination in various tumor types. In a Phase 2 study, combining ANKTIVA with checkpoint inhibitor (CPI) therapy has shown potential to improve overall survival of patients with advanced or metastatic non-small cell lung cancer who have become resistant to CPI treatment. Further, Phase 1 findings in healthy participants have demonstrated ANKTIVA's potential to reverse lymphopenia, a severe depletion of key immune white blood cells, that is a frequent consequence of conventional radiation or chemotherapy in cancer patients.

Based on the approved mechanism of action of proliferating and activating NK cells, CD4+, CD8+ T cells and memory T cells without proliferation of immuno-suppressive Treg cells, ANKTIVA has the potential to overcome the adverse events of chemotherapy and radiotherapy of lymphopenia. The company has received Regenerative Medicine Advanced Therapy (RMAT) designation for the development of ANKTIVA plus CAR-NK (PD-L1 t-haNK) for the reversal of lymphopenia for patients receiving standard-of-care chemotherapy/radiotherapy and in multiply relapsed locally advanced or metastatic pancreatic cancer.

ANKTIVA is just one product of ImmunityBio's vertically-integrated R&D engine comprising state-of-the-art laboratories and production facilities supporting a range of next-generation immunotherapies (Immunotherapy 2.0, beyond checkpoint inhibitors), including cell therapies, and vaccine platforms, all of which are designed to be effective, safe, easy to administer, and to reduce or eliminate the need for invasive and burdensome treatments - such as high-dose chemotherapy - that are currently standard of care.

For more information, visit ImmunityBio.com (Founder's Vision) and connect with us on X (Twitter), Facebook, LinkedIn, and Instagram.

About Regenerative Medicine Advanced Therapy (RMAT)

The RMAT designation was established under the 21st Century Cures Act to expedite the development and review of promising therapeutic candidates, including cell therapies, that are intended to treat, modify, reverse or cure a serious or life-threatening disease. RMAT designation includes benefits, such as early interactions with the FDA, including discussions on surrogate or intermediate endpoints that could potentially support accelerated approval and satisfy post-approval requirements, and potential priority review of a product's biologics license application (BLA).

References:

1. Fabian KP, Padget MR, Donahue RN, Solocinski K, Robbins Y, Allen CT, Lee JH, Rabizadeh S, Soon-Shiong P, Schlom J, Hodge JW. PD-L1 targeting high-affinity NK (t-haNK) cells induce direct antitumor effects and target suppressive MDSC populations. J Immunother Cancer. 2020 May;8(1):e000450.
2. Rubinstein MP, Williams C, Mart C, Beall J, MacPherson L, Azar J, Swiderska-Syn M, Manca P, Gibney BC, Robinson MD, Krieg C, Hill EG, Taha SA, Rock AD, Lee JH, Soon-Shiong P, Wrangle J. Phase I Trial Characterizing the Pharmacokinetic

Profile of N-803, a Chimeric IL-15 Superagonist, in Healthy Volunteers. J Immunol. 2022 Mar 15;208(6):1362-1370. doi: 10.4049/jimmunol.2100066. Epub 2022 Feb 28. PMID: 35228263.
3. Guo Z, Zhang Z, Prajapati M, Li Y. Lymphopenia Caused by Virus Infections and the Mechanisms Beyond. Viruses. 2021 Sep 20;13(9):1876.
4. Ménétrier-Caux C, Ray-Coquard I, Blay JY, Caux C. Lymphopenia in Cancer Patients and its Effects on Response to Immunotherapy: an opportunity for combination with Cytokines? J Immunother Cancer. 2019 Mar 28;7(1):85.
5. Valero C, Lee M, Hoen D, Weiss K, Kelly DW, Adusumilli PS, Paik PK, Plitas G, Ladanyi M, Postow MA, Ariyan CE, Shoushtari AN, Balachandran VP, Hakimi AA, Crago AM, Long Roche KC, Smith JJ, Ganly I, Wong RJ, Patel SG, Shah JP, Lee NY, Riaz N, Wang J, Zehir A, Berger MF, Chan TA, Seshan VE, Morris LGT. Pretreatment neutrophil-to-lymphocyte ratio and mutational burden as biomarkers of tumor response to immune checkpoint inhibitors. Nat Commun. 2021 Feb 1;12(1):729.

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 RMAT designation referenced herein and potential results therefrom, the related anticipated EAP submission and timing thereof, the related anticipated BLA submission and timing thereof, clinical trial data and potential results to be drawn therefrom, the development of therapeutics for cancer and infectious diseases, potential benefits to patients, potential treatment outcomes for patients, the described mechanism of action and results and contributions therefrom, potential future uses and applications of ANKTIVA and/or PD-L1 t-haNK and use in cancer vaccines and across multiple tumor types, and ImmunityBio's approved product and investigational agents as compared to existing treatment options, 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," "goal," "could," "estimates," "scheduled," "expects," "intends," "may," "plans," "potential," "predicts," "indicate," "projects," "is," "seeks," "should," "will," "strategy," 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) whether the RMAT designation will lead to an accelerated review or approval, of which there can be no assurance, (ii) ImmunityBio's ability to submit the regulatory submissions referenced herein on the anticipated timeline or at all, (iii) additional risks and uncertainties related to the regulatory submission, filing and review process and the timing thereof, (iv) the ability of ImmunityBio to fund its ongoing and anticipated clinical trials, (v) whether clinical trials will result in registrational pathways, (vi) whether clinical trial data will be accepted by regulatory agencies, (vii) the ability of ImmunityBio to continue its planned preclinical and clinical development of its development programs through itself and/or its investigators, and the timing and success of any such continued preclinical and clinical development, patient enrollment and planned regulatory submissions, (viii) potential delays in product availability and regulatory approvals, (ix) the risks and uncertainties associated with third party collaborations and agreements, (x) ImmunityBio's ability to retain and hire key personnel, (xi) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (xii) potential product shortages or manufacturing disruptions that may impact the availability and timing of product, (xiii) ImmunityBio's ability to successfully commercialize its approved product and product candidates, (xiv) ImmunityBio's ability to scale its manufacturing and commercial supply operations for its approved product and future approved products, and (xv) ImmunityBio's ability to obtain, maintain, protect, and enforce patent protection and other proprietary rights for its product candidates and technologies. 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 19, 2024 and the Company's Form 10-Q filed with the SEC on November 12, 2024, 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20250227880542/en/

ImmunityBio Contacts:

Investors
Hemanth Ramaprakash, PhD, MBA
ImmunityBio, Inc.
+1 858-746-9289
Hemanth.Ramaprakash@ImmunityBio.com

Media
Sarah Singleton
ImmunityBio, Inc.
+1 415-290-8045
Sarah.Singleton@ImmunityBio.com

Source: ImmunityBio, Inc.