ImmunityBio Submits Biologics License Application for N-803 Plus BCG for Patients with BCG-Unresponsive Non-Muscle Invasive Bladder Cancer Carcinoma in Situ

May 23, 2022

Results for this FDA-designated Breakthrough Therapy exceed historical complete response rates and duration of response of current approved therapies for this indication

CULVER CITY, Calif.--(BUSINESS WIRE)--May 23, 2022-- ImmunityBio, Inc. (NASDAQ: IBRX), a clinical-stage immunotherapy company, today announced it has submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for N-803, a first-in-class IL-15 superagonist, plus Bacillus Calmette-Guérin (BCG) for the treatment of BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) carcinoma in situ (CIS) with or without Ta or T1 disease. The BLA is supported by the results of ImmunityBio's studies in bladder cancer including the pivotal QUILT 3032 study (NCT03022825), where 71% of patients who had failed on previous therapies showed an over 50% increase in both response and median duration compared to the FDA-approved alternatives Valrubicin and Pembrolizumab, a systemic checkpoint inhibitor therapy for this indication.[1]

The FDA previously granted N-803 *Breakthrough Therapy* and *Fast Track* designations when used in combination with Bacillus Calmette-Guerin (BCG) for the treatment of BCG-unresponsive NMIBC CIS. If approved by the FDA, N-803 plus BCG would be the first new immunotherapy for this indication in 23 years that can be delivered directly to the bladder (intravesically) to induce natural killer cells and T cells, providing a new treatment option for patients with this form of bladder cancer. The results of the pivotal Phase 2/3 clinical trial demonstrated the therapeutic combination gives patients a greater chance to avoid removal of the bladder itself—a surgical procedure referred to as radical cystectomy. This surgery is one of the last remaining options for many patients that do not respond to other therapies, but is costly to the healthcare system and comes with a high risk of mortality and complications that affect patient quality of life.

"This immunotherapy represents a potential new option for bladder cancer patients who fail to respond to BCG, the current standard of care. The results of the study of N-803 plus BCG indicate that this combination provides a durable response with a reduced need for a cystectomy," said Patrick Soon-Shiong, M.D., Executive Chairman and Global Chief Scientific and Medical Officer at ImmunityBio. "We believe that the durable responses seen in this study provide further support for our hypothesis that by orchestrating natural killer cells, T cells and memory T cells, long-term durable remissions can be achieved in patients suffering from cancer. The results from the QUILT series of ongoing trials across multiple tumor types, including pancreatic, lung and other solid tumors, could lead to a paradigm shift in cancer therapy that ImmunityBio is developing. We are hopeful that this combination immunotherapy of BCG acting as a prime and N-803 as the boost to the immune system will not only provide a new path for these patients, but also help us continue to broaden our understanding of how we might apply this novel mechanism of action to other difficult-to-treat diseases."

The BLA submission for BCG-unresponsive NMIBC is based on data from 171 subjects from Phase I and 2 trials in bladder cancer and on 84 subjects treated in ImmunityBio's Pivotal Phase 2/3 QUILT 3032 study of the combination of N-803 and BCG. The combination had a well-tolerated profile and the full results of this study will be presented at an oral presentation at the 2022 American Society of Clinical Oncology (ASCO) Annual meeting to be held June 3-7 in Chicago.

ImmunityBio's IL-15 superagonist N-803 (Anktiva)

The cytokine interleukin-15 (IL-15) plays a crucial role in the immune system by affecting the development, maintenance, and function of the natural killer (NK) and T cells. N-803 is a novel IL-15 superagonist complex consisting of an IL-15 mutant (IL-15N72D) bound to an IL-15 receptor α/IgG1 Fc fusion protein. Its mechanism of action is direct specific stimulation of CD8+ T cells and NK cells through beta gamma T-cell receptor binding (not alpha) while avoiding T-reg stimulation. N-803 has improved pharmacokinetic properties, longer persistence in lymphoid tissues and enhanced anti-tumor activity compared to native, non-complexed IL-15 in vivo.

N-803 is currently being evaluated for adult patients in two clinical NMIBC trials. QUILT 2005 is investigating use of N-803 in combination with BCG for patients with BCG-naïve NMIBC; QUILT 3032 is studying N-803 in combination with BCG in patients with BCG-unresponsive NMIBC CIS and Papillary Disease.

Mechanism of Action & Contribution of N-803 and BCG for Bladder Cancer

Trained immunity is a recently discovered immune system response triggered by BCG. Natural Killer (NK) and T cells are activated by BCG resulting in bladder cancer cell death. When an appropriate secondary stimulus is administered along with BCG, that trained immune response is enhanced to induce immune *memory* resulting in a prolonged duration of immunological response. N-803, an IL-15 superagonist which proliferates NK and T cells, serves as this enhancing *secondary boost* and augments the immunological response when given in combination with BCG. ImmunityBio believes this mechanism of action of inducing *trained innate immune memory*, through the combination of N-803 and BCG, contributes to the high complete response rate and prolonged 24-month durable complete response reported in this trial.

About ImmunityBio

ImmunityBio is a clinical-stage biotechnology company developing next-generation therapies and vaccines that bolster the natural immune system to defeat cancers and infectious diseases. The company's range of immunotherapy and cell therapy platforms, alone and together, act to drive and sustain an immune response with the goal of creating durable and safe protection against disease. These platforms and their associated product candidates are designed to be more effective, accessible, and easily administered than current standards of care in oncology and infectious diseases.

ImmunityBio's clinical pipeline consists of 27 clinical trials—18 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 ImmunityBio's submission of a Biologics License Application (BLA) for N-803 plus BCG for patients with BCG-unresponsive non-muscle invasive bladder cancer carcinoma in situ with or without Ta or T1 disease, the FDA's decision regarding the filing of the BLA, regulatory review process and timing thereof, potential implications to be drawn from the QUILT 3.032 study, whether the proposed mechanism of action described herein contributes to response rate and duration, potential commercialization of ImmunityBio's product candidates, ImmunityBio's product candidates as compared to existing treatment options, and clinical trial enrollment, advancements and data, 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," "indicate," "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) whether the FDA will file and/or approve the BLA and the risks and uncertainties associated with the regulatory approval process, (ii) 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, (iii) ImmunityBio's ability to retain and hire key personnel, (iv) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (v) ImmunityBio's ability to successfully commercialize its product candidates and uncertainties around regulatory reviews and approvals, (vi) ImmunityBio's ability to scale its manufacturing and commercial supply operations for its product candidates and future approved products, (vii) ImmunityBio's ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies, and (viii) 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 the Company's Form 10-Q filed with the SEC on May 10, 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.

1. Sources: Balar, 2021; Steinberg 2000

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Investors
Sarah Singleton
ImmunityBio, Inc.
844-696-5235, Option 5
Sarah.Singleton@immunitybio.com

Media
Katie Dodge
Salutem
978-360-3151
Katie.Dodge@salutemcomms.com

Source: ImmunityBio, Inc.