ImmunityBio Announces FDA Acceptance of Biologics License Application for N-803 in BCG-Unresponsive Non-Muscle-Invasive Bladder Cancer Carcinoma In Situ

July 28, 2022

- This acceptance represents the first regulatory filing for N-803, an IL-15 superagonist, which was granted Breakthrough Therapy and Fast Track designations in combination with Bacillus Calmette-Guérin (BCG) from the U.S. Food and Drug Administration (FDA) for this indication with a target PDUFA date of May 23, 2023
- The BLA submission is based on the positive QUILT 3.032 trial results in which 71% of BCG-unresponsive NMIBC patients who had failed on previous therapies showed a complete response with a median duration of 26.6 months; cystectomy avoidance rate of 91% and 100% bladder cancer overall survival at 24 months with zero serious adverse events (SAE)

CULVER CITY, Calif.--(BUSINESS WIRE)--Jul. 28, 2022-- The FDA accepted for review a Biologics License Application (BLA) from ImmunityBio, Inc. (NASDAQ: IBRX), for its antibody cytokine fusion protein as a treatment for patients with BCG-unresponsive non-muscle-invasive bladder cancer carcinoma in situ (CIS) with or without Ta or T1 disease. ImmunityBio, a leading clinical-stage immunotherapy company, filed the BLA based on positive results from a series of studies of the investigational treatment, including the ongoing QUILT 3.032 trial. The Prescription Drug User Fee Act (PDUFA) target action date is May 23, 2023.

This combination of N-803 with BCG is ImmunityBio's first BLA to reach this stage of FDA acceptance for review. This marks an important milestone in the pursuit of ImmunityBio's vision of transforming how cancer patients are treated without high-dose chemotherapy, but instead by activating the patient's innate immune system. If approved, N-803 plus BCG would be the first immunotherapy combination for this indication in 23 years that can be delivered directly to the bladder (intravesically) to induce natural killer cells and T cells. It represents an essential step in the clinical demonstration of the Nant Cancer Vaccine hypothesis proposed by ImmunityBio's founder, Patrick Soon-Shiong, M.D. of "Quantum oncotherapeutics: a longitudinal spatiotemporal orchestration towards immunogenic cell death".

N-803 has a unique mechanism of action that leads to the proliferation of NK and T cells that are cells of the adaptive and innate immune system. Through this action, N-803 provides a secondary boost to the immunological response generated by BCG for bladder cancer, or by a checkpoint inhibitor for other indications. In the QUILT 3.032 study, 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.

"This BLA acceptance brings us a very important step closer to being able to offer this promising combination therapeutic to more people living with NMIBC and, ultimately, reduce the incidence of cystectomies," said Patrick Soon-Shiong, M.D., Executive Chairman and Global Chief Scientific and Medical Officer at ImmunityBio. "This is a compelling example of the power of inducing trained innate immune memory to potentially provide long-term, durable effects against serious, life-threatening diseases."

"We are pleased the FDA has begun its review, and ImmunityBio is prepared to move rapidly to manufacturing and marketing should the Agency approve our therapeutic for this indication," said Richard Adcock, President and CEO of ImmunityBio.

The BLA submission is supported by the results from ImmunityBio's bladder cancer trials including QUILT 3.032, an open-label, three cohort, multicenter Phase 2/3 study of intravesical BCG plus N-803 in patients with BCG-unresponsive high-grade NMIBC (NCT03022825) that was opened in 2017. The primary endpoint for Cohort A of this Phase 2/3 study is incidence of complete response (CR) of CIS at any time. Results of this trial were presented at the 2022 American Society of Clinical Oncology Annual Meeting (ASCO 2022). See link here to video presentation on *UroToday*.

ImmunityBio's IL-15 superagonist N-803

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 has been studied in more than 700 patients in multiple Phase 1 and 2 trials in both liquid and solid tumors. It is currently being studied in trials for non-muscle-invasive bladder cancer, pancreatic cancer, non-small-cell lung cancer, non-Hodgkin's lymphoma, and HIV.

N-803 has received both *Breakthrough Therapy* and *Fast Track* designations by the FDA for the treatment of BCG-unresponsive NMIBC CIS, as well as *Fast Track* designation for BCG-unresponsive NMIBC papillary and BCG-naïve NMIBC CIS. However, it is important to note such designations may not lead to a faster development process or regulatory review and may not increase the likelihood that a product candidate will receive approval. Seminal patents covering intravesical administration of BCG and N-803 were issued (US 11,173,191 B2 and US 9,925,247 B2) providing term coverage until 2035.

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). N-803 (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 data from the clinical trials for certain of ImmunityBio's product candidates, the regulatory review process and timing thereof, potential implications to be drawn from the QUILT 3.032 and other studies, whether the described mechanism of action 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 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 approve ImmunityBio's recently filed BLA and the risks and uncertainties associated with the regulatory approval process and timing thereof, (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.

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