ImmunityBio Announces Positive Durable Responses in BCG Unresponsive Bladder Cancer Patients with a Complete Response Rate of 72%, Median Duration of Complete Response of 19.9 Months, and 85% Remaining Cystectomy-free in Phase 2/3 Trial

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- 58 out of 81 (72%) patients achieved a complete response at any time (three or six months), which compares favorably to historical complete response rates of 41% and 18% for FDA-approved therapies pembrolizumab and valrubicin, respectively
- Median duration of complete response in all responders is 19.9 months and 85% of patients enrolled in the study have avoided a cystectomy as of May 2021
- 61% probability of initial responders (complete response at three months) remaining disease free at 18 months
- 0% treatment- or immune-related adverse events (AEs) or serious adverse events (SAEs) reported

CULVER CITY, Calif.--(BUSINESS WIRE)--Sep. 13, 2021-- ImmunityBio, Inc. (NASDAQ: IBRX), a clinical-stage immunotherapy company, today announced updated data from an ongoing bladder cancer trial showing sustained complete response rates in patients with BCG-unresponsive non-muscle invasive carcinoma in situ (CIS) bladder cancer (Cohort A). Of the 81 patients in the QUILT 3.032 study, 58 patients (72%) had a complete response (CR) at any time (three or six months) to intravesical BCG plus N-803 (Anktiva) with median duration of CR of 19.9 months.

The data also showed a 59% probability (95% confidence interval; 43.1%, 71.2%) that responding patients would maintain a complete response for more than 12 months, based on Kaplan-Meier analysis. For the patients who had a CR within the first three months, the CR rate was 77%, with a 61% probability of remaining disease free at 18 months with the median duration of complete response having not yet been reached in that group. 85% of patients in the cohort avoided a cystectomy with a median duration of follow-up of 20.4 months.

Of note, the therapy was extremely well tolerated with 0% treatment-related SAEs, 0% immune-related AEs and 0% grade 4 or 5 treatment-related AEs. In contrast, the currently approved checkpoint therapy for this indication is associated with an incidence of 21% immune-related adverse events.

“The data suggest that a high percentage of patients who respond within the first three months to treatment will maintain that complete response for 18 months and possibly beyond. But most importantly, 85% of the patients in the cohort avoided a cystectomy,” said Principal Investigator Karim Chamie, M.D., Associate Professor of Urology at UCLA. “The AUA-FDA workshop set a lofty, clinically meaningful benchmark: 30% of patients receiving treatment for their BCG-unresponsive bladder cancer remaining disease-free 18–24 months. Unfortunately, none of the FDA-approved (or under FDA evaluation) agents have come close to the goal; by 12 months, only 20% of patients are disease-free. But for the first time, we now have a product with N-803 + BCG that has hit the AUA-FDA 30% 18-month milestone. With its well-tolerated safety profile, I am confident that N-803 + BCG will make a meaningful impact on the lives of patients with BCG-unresponsive bladder cancer.”

The data was announced on Friday, Sept. 10 during an oral presentation at the American Urological Association’s Annual Meeting titled “PD09-05: Phase 2/3 clinical results of IL-15aFc superagonist N-803 with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) carcinoma in-situ (CIS).”

Bladder cancer has a high incidence worldwide; in 2020, an estimated 573,278 new cases were diagnosed and it was the cause of 212,536 deaths[1]. In the United States, bladder cancer is the fourth most commonly diagnosed solid malignancy in men and the twelfth for women. In the US, the American Cancer Society estimated 81,400 new cases and 17,980 deaths[2]. Approximately 75-85% of all newly diagnosed cases of bladder cancer are non-muscle invasive bladder cancer (NMIBC)[3].

“We are pleased with the sustained durable response and the significant avoidance of cystectomy in this patient population. In those patients who responded by three months after the initial treatment, it is encouraging to see that the median duration of that response, even after 18 months, has not yet been reached,” said Patrick Soon-Shiong, M.D., Founder and Executive Chairman and Global Chief Scientific and Medical Officer of ImmunityBio. “In the resistant patients who were re-induced after failing to respond to N-803 and BCG in the first three months, but who responded following a “rescue reinduction” at six months, the median duration of response was shorter, but nonetheless, this immunotherapy candidate delayed cystectomy.”

Soon-Shiong continued, “We are encouraged by these results showing the potential for a higher and longer-lasting rate of complete response than with the current standards of care in patients facing removal of the bladder as an alternative. This study provides insights into the power of harnessing the immune system, including NK cells and T cells, which are activated by N-803. What is more, the novel IL15 fusion protein N-803 being studied was designed to be administered safely in the urologist’s office, potentially enabling ease of administration and increasing access for patients.”

The Urgent, Unmet Need to Treat NMIBC and Avoid Cystectomy

For the last 30 years, BCG immunotherapy has been the standard for treating NMIBC. However, disease recurrence and progression rates remain unacceptably high. Standard-of-care recommendations for these patients include lifetime invasive surveillance and rapid treatment of recurrences, creating a substantial financial burden and drastic impact on quality of life. Of those patients who experience recurrence, approximately 30% will progress and succumb to their disease over a 15-year period, and another 50% will undergo radical cystectomy of the bladder— a surgery to remove the entire bladder that may require removal of other surrounding organs—in an attempt to control their disease[4].

Despite the advent of minimally invasive procedures and robotic techniques, the 90-day mortality and morbidity rates in patients who undergo cystectomy remain unacceptably high at 3-6% and 28-64%, respectively[5 & 6]. Based on this urgent need, FDA published guidance in February 2018 to address BCG unresponsive non-muscle invasive bladder cancer (NMIBC), stating that the goal of therapy in patients with BCG-unresponsive NMIBC is to avoid cystectomy.

About the Study and Breakthrough Designation

QUILT 3.032 is an open-label, three cohort, multicenter Phase 2/3 study of intravesical BCG plus Anktiva (N-803) in patients with BCG-unresponsive high-grade NMIBC (NCT03022825) and 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. The FDA had granted Fast Track Designation to the pivotal trial based on Phase I data. In December 2019, the FDA granted ImmunityBio Breakthrough Therapy Designation based on interim Phase 2 data indicating the primary endpoint of the trial was already met.

ImmunityBio's IL-15 superagonist Anktiva (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 is currently being evaluated for adult patients in two clinical NMIBC trials. QUILT 2.005 is investigating use of N-803 in combination with BCG for patients with BCG-naïve NMIBC; QUILT 3.032 is studying N-803 in combination with BCG in patients with BCG-unresponsive NMIBC.

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 stages 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 currently developing a dual construct COVID-19 vaccine candidate using its hAd5 platform.

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, such as statements regarding the development of therapeutics for cancer and infectious diseases, the advancement of our Phase II and III trials, and regulatory approval, commercialization and commercial success of ImmunityBio's product candidates and related matters. 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 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 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) inability to retain and hire key personnel, (iii) uncertainty of the expected financial performance and successful integration of the combined company following completion of the recent merger of ImmunityBio with NantCell (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, (iv) whether interim, initial, "top-line" and preliminary data from ImmunityBio's clinical trials that it announces or publishes from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data, (v) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (vi) ImmunityBio's ability to obtain, maintain, protect and enforce patent protection and other proprietary rights for its product candidates and technologies, (vii) ImmunityBio's ability to successfully commercialize its product candidates and (viii) the unknown future impact of the COVID-19 pandemic delay on certain clinical trials or their 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, Form 10-Q filed with the SEC on August 12, 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.

Contacts

1. Global cancer statistics: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries: https://gco.iarc.fr/
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3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3263923/
4. https://doi.org/10.1016/j.eururo.2018.09.028
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1945091/
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