ImmunityBio Announces FDA Approval of ANKTIVA®, First-in-Class IL-15 Receptor Agonist for BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

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- Designated an FDA Breakthrough Therapy, the novel immunotherapy ANKTIVA activates the body's natural killer (NK) and killer T-cell immune system to attack tumor cells
- Therapy stimulates memory T cells, leading to long duration of complete response exceeding 47 months and ongoing to date, with a median duration of response yet to be determined
- The percentage of patients with durable responses at 12 and 24 months exceeded the benchmark for magnitude of clinically meaningful results established by experts at the International Bladder Cancer Group (IBCG)
- ANKTIVA in combination with BCG is approved for maintenance therapy for up to 37 months with tolerable side effects ranging from 0% to 3% Grade 3/4 adverse events
- ANKTIVA is expected to be available in the U.S. by mid-May 2024
- Conference call and webcast are expected to be held April 26 at 11:00 am EDT

CULVER CITY, Calif.--(BUSINESS WIRE)--Apr. 22, 2024-- ImmunityBio, Inc. (NASDAQ: IBRX), an immunotherapy company, today announced that the U.S. Food and Drug Administration (FDA) has approved ANKTIVA (N-803, or nogapendekin alfa inbakicept-pmln) plus Bacillus Calmette-Guérin (BCG) for the treatment of patients with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS), with or without papillary tumors.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20240422820209/en/

ImmunityBio's ANKTIVA is approved for non-muscle invasive bladder cancer (Photo: Business Wire)

"The FDA's approval of ANKTIVA marks our launch of a next-generation immunotherapy beyond checkpoint inhibitors," said Patrick Soon-Shiong, M.D., Executive Chairman and Global Chief Scientific and Medical Officer at ImmunityBio. "ANKTIVA not only proliferates and activates the patient's own NK cells and CD8+ killer T cells, but also activates CD4+ T helper cells, thus enhancing the proliferation of memory killer T cells. This novel mechanism of action, which mimics the biology of the dendritic cell, begins the evolution of immunotherapy beyond T cells alone. The combination of the proliferation of key cancer-killing immune cells, together with the activation of T cells with memory, results in durable complete responses. The 'triangle offense' of tumor cell killing by the body's immune system with long-term memory is the foundation of our efforts to develop a therapeutic cancer vaccine across multiple tumor types, regardless of the site of origin."

ANKTIVA, a first-in-class IL-15 agonist immunotherapy for NMIBC, received Breakthrough Therapy Designation and approval from the FDA based on the safety and efficacy outcome of complete responses (CR) and duration of complete response (DOR). The 77 evaluable patients in this single-arm, multicenter trial received ANKTIVA with BCG maintenance therapy for up to 37 months. The tumor status was assessed with cystoscopy and urine cytology and will continue for up to five years after each patient began their participation in the trial.

The CR rate for the 77 evaluable patients was 62% with the upper end of the confidence interval being 73%. The duration of complete response as of the November 2023 cut-off was more than 47 months and is ongoing to date. These prolonged duration of complete response results beyond 24 months with ANKTIVA and BCG exceed the benchmark for the magnitude of meaningful clinical results suggested by a panel of experts at the IBCG.

"We are pleased that treatment with ANKTIVA now exceeds the clinically meaningful benchmarks established by the IBCG in 2016 for durable complete response," said Roger Buckley, with the IBCG. "We look forward to the global availability of ANKTIVA to potentially reduce the need for cystectomy in many patients worldwide with NMIBC."

The duration of response is ongoing, so the final median duration of response has yet to be determined. Fifty-eight percent (58%) of patients with CR had a DOR ≥ 12 months and 40% had a DOR ≥ 24 months.

"The long duration of complete response ranging over 47 months is a game changer for NMIBC patients and provides further clinical evidence of ANKTIVA's effectiveness for patients who historically have faced high rates of recurrence and significantly diminished quality of life due to radical surgeries," said Karim Chamie, M.D., Associate Professor of Urology at UCLA and principal investigator for the QUILT 3.032 study. "With this approval, ANKTIVA could represent a new standard of care for patients with NMIBC and has the potential to change the way we treat bladder cancer."

ANKTIVA is expected to be available in the U.S. by mid-May 2024.

New Hope for Patients

Bladder cancer is the 10th most commonly-diagnosed cancer globally,[1] and in the U.S., the American Cancer Society estimates there will be 83,190 new cases and 16,840 deaths from bladder cancer in 2024.[2] At the time of diagnosis, about 80% of cases are non-muscle invasive bladder cancer (NMIBC), wherein the cancer is found only on the inner layer of the bladder wall.[3] The standard therapy for NMIBC is intravesical instillation (delivery

to the bladder via a catheter) of bacillus Calmette-Guerin (BCG).[4,5] BCG is a benign bacteria that induces an immune response in the bladder in proximity to the cancer cells, leading to clearance of the cancer in many patients. In ~30-40% of patients, however, BCG will fail, and in ~50% that initially respond, cancer will recur.[6]

"A new immunotherapy that builds upon our knowledge and experience with BCG as an immune stimulant is exciting to see," said Ashish Kamat, M.D., MBBS, an Endowed Professor of Urologic Oncology and Cancer Research at University of Texas MD Anderson Cancer Center. "While patients have had limited options in the past after failure of BCG, nogapendekin alfa inbakicept-pmln, with its reported safety and efficacy, now offers them yet another choice in their quest to avoid a radical cystectomy. This is a big win for NMIBC patients everywhere."

With the approval of ANKTIVA in combination with BCG, NMIBC patients who would otherwise face highly invasive surgery with life-long consequences have an important new therapeutic option with a long-term durable complete response.

"ANKTIVA enhances natural killer cell recruitment as well as T cell stimulation. By doing this and stimulating the innate immune memory response, we get an improved ability to kill tumor cells," said Sam S. Chang, M.D., Professor of Urology and Chief Surgical Officer of the Vanderbilt Ingram Cancer Center, and a principal investigator for the QUILT 3.032 study. "It's a potent and exciting combination."

"NMIBC has a high rate of recurrence that sometimes results in major surgery to remove the bladder to prevent further disease progression," said Andrea Maddox-Smith, CEO of the Bladder Cancer Advocacy Network (BCAN). "The addition of ANKTIVA to BCG gives NMIBC patients and their physicians a much-needed, new option to effectively treat the disease and offers an important non-surgical alternative to a cystectomy."

ANKTIVA was well-tolerated with adverse events consistent with that of BCG alone. Studies of ANKTIVA in BCG-unresponsive and BCG-naive patients are ongoing. Reports of 82 subjects of high risk CIS NMIBC were reported in *NEJM Evidence* and previously presented.

The co-authors of an expert commentary on the published findings for ANKTIVA plus BCG in *European Urology* —Drs. Peter Black, Jonathan Suderman, and Marie-Pier St-Laurent—from the University of British Columbia, Vancouver, stated, "This appears to be a major advance in disease control in this patient population, especially when the low rate of serious adverse events is considered." They further stated, "One could make the argument that NAI [ANKTIVA] should now become the standard of care given its more rigorous clinical trial data."

Further updates on the ongoing analysis of QUILT-3.032 (NCT03022825) will be presented by Dr. Soon-Shiong at the upcoming American Urological Association's annual conference on May 3, 2024.

"Today's approval of ANKTIVA for patients with NMIBC marks an important milestone in our quest to develop cancer vaccines, and preventative vaccines for patients with genetic predisposition to developing cancer such as in Lynch syndrome," said Soon-Shiong. "We believe that by orchestrating the innate and adaptive immune system and driving long-term complete remission, ANKTIVA has the potential to play a key role as the immunotherapy beyond checkpoints in multiple tumor types in the years to come."

ANKTIVA has been studied in more than 700 patients in multiple Phase 1 and 2 trials in both liquid and solid tumors. In addition to trials in NMIBC, it is currently being studied in trials for non-small-cell lung cancer, colorectal cancer, non-Hodgkin's lymphoma, glioblastoma, solid tumors, and HIV. Future studies are planned for platinum-resistant ovarian cancer and acute myeloid leukemia.

How ANKTIVA (N-803) Works

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.

ANKTIVA is a novel IL-15 superagonist 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 mimics the natural biological properties of dendritic cells, and drives the generation of memory killer T cells that have specifically been trained to recognize the cancer cells, resulting in activation and proliferation of these killing cells with durable complete response. ANKTIVA has improved pharmacokinetic properties, longer persistence in lymphoid tissues, and enhanced anti-tumor activity compared to native, non-complexed IL-15 in vivo.

Selected Safety Information for ANKTIVA (N-803)

The most common (≥15%) adverse reactions, including laboratory test abnormalities, are increased creatinine, dysuria, hematuria, urinary frequency, micturition urgency, urinary tract infection, increased potassium, musculoskeletal pain, chills, and pyrexia.

Patient Assistance Program

ImmunityBio is committed to helping patients access ANKTIVA and will be offering services to overcome access barriers. ImmunityBio's Patient Assistance Program will be operational in mid May. This program is designed to help those in need, ensuring access to ImmunityBio's innovative treatment. More information for patients and healthcare professionals will be available on Anktiva.com.

Conference Call and Webcast Information

ImmunityBio management will discuss FDA approval of ANKTIVA in combination with BCG for the treatment of BCG-unresponsive NMIBC via a conference call and webcast on Fri., April 26, 2024 at 11 am EDT. The conference call registration details will be available in the IR section of the ImmunityBio website.

About ImmunityBio

ImmunityBio is a vertically-integrated 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. We are applying our science and platforms to treating cancers, including the development of potential cancer vaccines, as well as developing immunotherapies and cell therapies that we believe sharply reduce or eliminate the need for standard high-dose chemotherapy. 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.

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 and results from clinical trials and potential implications therefrom, commercialization plans and timelines, including product availability, potential regulatory pathways and approvals including outside of the United States, the regulatory review process and timing thereof, market and prevalence data, potential benefits to patients, potential treatment outcomes for patients, the described mechanism of action and results and contributions therefrom, information regarding potential benefit to patients, information regarding ongoing pre-clinical studies and clinical trials, potential future uses and applications of ANKTIVA and use in cancer vaccines, methods, conference call and webcast timing, 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," "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) the risks and uncertainties associated with commercial launch execution, success and timing, (ii) risks and uncertainties related to the regulatory submission and review process including without limitation outside of the United States, (iii) 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, (iv) ImmunityBio's ability to retain and hire key personnel, (v) ImmunityBio's ability to obtain additional financing to fund its operations and complete the development and commercialization of its various product candidates, (vi) potential product shortages or manufacturing disruptions that may impact the availability and timing of product, (vii) ImmunityBio's ability to successfully commercialize its product candidates and uncertainties around regulatory reviews and approvals, (viii) ImmunityBio's ability to scale its manufacturing and commercial supply operations for its product candidates and future approved products, and (ix) 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 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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