Principia Announces Expanded Development Program to Broaden BTK Footprint in Immune-Mediated Diseases

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Company's lead candidate PRN1008 receives generic name -- rilzabrutinib

Rilzabrutinib to enter clinical trial in IgG4-Related Disease

SOUTH SAN FRANCISCO, Calif., Jan. 07, 2020 (GLOBE NEWSWIRE) -- Principia Biopharma Inc. (Nasdaq: PRNB), a late-stage biopharmaceutical company focused on developing treatments for immune-mediated diseases, today announced an expansion in the development of rilzabrutinib (PRN1008) into IgG4-Related Disease (RD). This clinical program broadens the company's Bruton tyrosine kinase (BTK) therapeutic areas and supports the company's commitment to innovate and solve high unmet needs.

"Given BTK is critical in multiple signaling pathways across a wide range of immune-mediated diseases, we are expanding our clinical focus to advance the utility of BTK inhibition. Rilzabrutinib has now demonstrated rapid onset and proof of concept in two diverse therapeutic areas, pemphigus (dermatology) and immune thrombocytopenia (hematology) and our new clinical program in IgG4-RD (rheumatology) will allow us to further demonstrate the breadth of our lead clinical candidate," said Martin Babler, Principia's president and chief executive officer.

About IgG4 Related Diseases
IgG4-RD is an immune-mediated disease of chronic inflammation and fibrosis that, if left untreated, can lead to severe morbidity including organ dysfunction and organ failure, which can be fatal. IgG4-related disease typically manifests with multiple organ involvement including but not limited to exocrine glands, GI tract organs (liver, pancreas), and kidneys. Principia believes rilzabrutinib can potentially lead to positive outcomes in IgG4-RD by impacting many of the driving features of the disease, including inflammation, allergic components (IgE and eosinophils), monocytes, macrophages (involved in fibrosis), and B cells implicated in initiation and maintenance of disease.

"There is a tremendous need for new treatment options for patients with IgG4-RD. A clinical trial with rilzabrutinib is very exciting for the rheumatology community as it has the potential to stop the inflammation, allergic components and fibrosis without chronic steroids or immune depleting agents. Rilzabrutinib has the potential to be a single oral agent that rapidly gets to the heart of the disease," said John Stone, MD, MPH, professor of medicine in Boston and principal investigator.

Treatment is typically glucocorticoids (GCs), however, patients often relapse after GCs are tapered and thus require chronic GC dosing, which can lead to severe and debilitating side effects. Rituximab has been shown to have an effective clinical response; however, patients frequently relapse after treatment as well. Recent advances in the field have led to recognition of this disease and the many unmet needs for the patients diagnosed with it. Awareness and recognition of IgG4-RD is growing and the exact prevalence remains unknown, with estimates ranging from 40,000 to 180,000 in the United States alone. The company anticipates initiating a Phase 2 clinical trial in the first half of 2020.

Timely with the company's clinical development program, the American College of Rheumatology and European League Against Rheumatism published new IgG4-RD diagnosis and treatment guidelines in the January 2020 issue of *Arthritis and Rheumatology*. These new treatment guidelines were led by Dr. Stone who commented: "Despite the seriousness of IgG4-RD, guidelines and treatment criteria have been non-existent. Validated in 1,879 subjects, these criteria should contribute substantially to future clinical, epidemiologic, and basic investigations."

About Rilzabrutinib
Rilzabrutinib, Principia's most advanced drug candidate, is an oral, first-in-class, reversible covalent, BTK inhibitor optimized for the treatment of immune-mediated diseases. Bruton tyrosine kinase (BTK) is involved in innate and adaptive immune responses and is a critical signaling molecule in immune-mediated diseases. Rilzabrutinib data demonstrates an ability to block inflammatory immune cells, eliminate autoantibody destructive signaling, and prevent new autoantibody production without depleting B cells. Rilzabrutinib's unique attributes are based in the power of the bond from Principia's proprietary Tailored Covalency ® platform. This enabled the company to optimize rilzabrutinib's safety and efficacy profile, with prolonged and reversible action at the target site while being rapidly eliminated from the body. Principia believes this bonding and the limited systemic exposure of rilzabrutinib enables rapid clinical reversibility of effects on the immune system, and it is thus designed for safety in immune-mediated diseases.

About Principia Biopharma
Principia is a late-stage biopharmaceutical company dedicated to bringing transformative therapies to patients with significant unmet medical needs in immune-mediated diseases. Principia's proprietary Tailored Covalency ® platform differentiates the company's investigational therapies from traditional small molecules and provides the potential to deliver the potency, selectivity and safety of injectable drugs while maintaining the convenience of a pill. This highly reproducible approach enables the company to pursue multiple programs efficiently. Rilzabrutinib, a reversible covalent BTK inhibitor, is being evaluated in a Phase 3 clinical trial in patients with pemphigus -- an orphan autoimmune disease – and a Phase 2 clinical trial in patients with immune thrombocytopenia (ITP), and the company plans to initiate a Phase 2 clinical trial in patients with IgG4-related diseases. PRN2246/SAR442168, a covalent BTK inhibitor which crosses the blood-brain barrier, is being evaluated in a Phase 2 clinical trial in patients with multiple sclerosis and is partnered with Sanofi. PRN1371, a covalent inhibitor of Fibroblast Growth Factor Receptor (FGFR) is being evaluated in a Phase 1 trial in patients with bladder cancer. For more information, please visit www.principiabio.com.

Forward-Looking Statements
This press release contains forward-looking statements. These forward-looking statements reflect the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, Principia's expectations regarding the Principia pipeline of product candidates, the design of, progress of, results from, and timing of, its clinical trials and information regarding the timing, scope and success of additional clinical results. Such forward-looking statements involve known and unknown risks,

uncertainties, and other important factors that may cause Principia's actual results, performance, or achievements to be materially different from those expressed or implied by the forward-looking statements. For a description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the Principia's business in general, see the risk factors set forth in Principia's reports filed with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Principia specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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