Principia Biopharma Presents Phase 1 Clinical Data from CNS Penetrating BTK Inhibitor Candidate PRN2246/SAR442168 at ACTRIMS 2019

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-- Orally administered PRN2246 achieved full BTK occupancy in peripheral blood --
-- PRN2246 exhibited blood-brain barrier permeability and CNS exposure --
-- Sanofi to lead Phase 2 development for people with Multiple Sclerosis --

SOUTH SAN FRANCISCO, Calif., March 01, 2019 (GLOBE NEWSWIRE) -- Principia Biopharma Inc. (Nasdaq: PRNB), a late-stage biopharmaceutical company dedicated to bringing transformative oral therapies to patients with significant unmet medical needs in immunology and oncology, announced the presentation of Phase 1 clinical data for PRN2246, now known as SAR442168, at the American Consortium for Therapy and Research in Multiple Sclerosis (ACTRIMS) annual meeting in Dallas, Texas. PRN2246/SAR442168 is a Bruton's tyrosine kinase (BTK) inhibitor that crosses the blood-brain barrier and modulates immune cell function in both the periphery and in the brain. PRN2246/SAR442168 is being developed for the treatment of multiple sclerosis (MS) and potentially other central nervous system (CNS) diseases under a license agreement with Sanofi, a company committed to discovering and developing new treatment options for people living with MS. In this Phase 1 study, PRN2246/SAR442168 was found to be well tolerated at all dose levels studied and all related treatment-emergent adverse events were mild in nature.

"We are pleased with the tolerability profile of PRN2246/ SAR442168 to date, the exposure of the compound in the CNS, and therapeutic levels of BTK occupancy in peripheral blood in this first-in-human study," said Martin Babler, Chief Executive Officer of Principia. "We are looking forward to our partner, Sanofi, advancing PRN2246/SAR442168 into Phase 2 development for people living with MS."

The Phase 1 Trial: Phase 1 Clinical Trial of PRN2246 (SAR441268), a Covalent BTK Inhibitor Demonstrates Safety, CNS Exposure and Therapeutic Levels of BTK Occupancy (Abstract #3790, poster presentation)

The Phase 1 trial was a first-in-human randomized, double-blind, placebo-controlled study that included five single ascending dose (SAD) cohorts (5 to 120 mg), and five multiple ascending dose (MAD) cohorts (7.5 to 90 mg once daily). The MAD cohorts consisted of ten days of treatment. In an additional cohort, cerebral spinal fluid (CSF) exposure was measured through lumbar puncture after a single 120 mg dose. The primary objective of the study was to evaluate the safety and tolerability of single ascending doses and multiple ascending doses of PRN2246/SAR442168 in healthy subjects. Secondary objectives included assessment of pharmacokinetics (PK) and a pharmacodynamic (PD) assessment of peripheral BTK occupancy. The study enrolled 94 subjects, 74 of whom received study drug while the remaining 20 subjects received placebo. Key findings, which were presented by Tim Owens, Ph.D, Principia's PRN2246/ SAR442168 Team Lead, include:

- PRN2246/SAR442168 was well tolerated in the study, with all treatment related events being mild in nature (Grade 1);
- PRN2246/SAR442168 exposure increased with dose and with the expected rapid absorption and clearance profile;
- BTK occupancy increased in a dose dependent manner—high levels of peripheral BTK occupancy were achieved after single doses of 30 mg and higher. In the MAD portion of the study, after 10 days, BTK occupancy approached maximal levels in the lowest dose group (7.5 mg) studied; and
- CSF exposure was achieved in all subjects who underwent lumbar puncture, confirming blood-brain barrier permeability. The potential to impact B cell driven inflammation in the CNS will be evaluated in the next phase of development.

The poster may be found on the ACTRIMS website or the Principia website.

About PRN2246/SAR442168
PRN2246/SAR442168 is being developed to potentially treat MS and other CNS diseases, in part by penetrating the blood-brain barrier and modulating B cells and other immune cells in the CNS. During neuro-inflammation, the number of B cells in the brain increases, which is thought to play a central role in the pathology of MS and other CNS diseases. This provides the potential of targeting the adaptive and innate immunity in both the periphery and also within the CNS. In late 2017, Principia formed a collaboration with Sanofi under which Principia granted Sanofi an exclusive, worldwide license to develop and commercialize PRN2246/SAR442168. Principia is responsible for completion of Phase 1 activities. Phase 2 and any further development will be conducted by Sanofi.

About Principia Biopharma
Principia is a late-stage biopharmaceutical company dedicated to bringing transformative oral therapies to patients with significant unmet medical needs in immunology and oncology. Principia's proprietary Tailored Covalency ® platform enables Principia to design and develop reversible and irreversible covalent, small molecule inhibitors with potencies and selectivities that have the potential to rival those of injectable biologics yet maintain the convenience of a pill. PRN1008, a reversible covalent BTK inhibitor, is being evaluated in a Phase 3 clinical trial in patients with pemphigus, an orphan autoimmune disease, and in a Phase 2 clinical trial in patients with immune thrombocytopenic purpura, a rare hematological disease. PRN2246/SAR442168, a covalent BTK inhibitor which crosses the blood-brain barrier, has completed a Phase 1 clinical trial in healthy volunteers, and has been partnered with Sanofi for development in multiple sclerosis and, potentially, for other diseases of the CNS. 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. All statements other than statements of historical fact contained herein are forward-looking statements reflecting 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, Sanofi's advancement of PRN2246/SAR442168 into Phase 2 development for people living with MS; the potential for PRN2246/SAR442168 to treat CNS

diseases, including MS; the potential for PRN2246/SAR442168 to impact B cell driven inflammation in both the periphery and the CNS; the peripheral BTK occupancy of PRN2246/SAR442168; and the safety and tolerability of PRN2246/SAR442168. 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 any future results, performance, or achievements expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the risks and uncertainties of the clinical development process and of clinical trial recruitment; risks and uncertainties about the efficacy, safety and tolerability of our product candidates; risks that early research or clinical results may be materially different from future clinical results; risks and uncertainties regarding Principia's reliance on third-party organizations, such as contract research organizations, contract manufacturing organizations, and partners such as Sanofi; risks of third party claims alleging infringement of patents and proprietary rights or seeking to invalidate Principia's patents or proprietary rights; and the risk that Principia's proprietary rights may be insufficient to protect its technologies and product candidates. For a further 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, including its Quarterly report on form 10-Q for the period ending September 30, 2018. 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.

Investor Contact
Christopher Chai, CFO
ir@principiabio.com
Media Contact
Denise Powell
denise@redhousecomms.com

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