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Prothena Outlines Phase 2 Development Strategy for PRX003

- **Investor conference call and webcast planned today at 4:30 PM ET**

DUBLIN, Ireland, Sept. 29, 2016 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapies, will host a conference call and webcast today at 4:30 PM Eastern Time to discuss its Phase 2 clinical development strategy in psoriatic arthritis for PRX003, an antibody that targets the cellular adhesion molecule CD146, which is expressed on the surface of Th17 cells.

"We are excited to highlight development plans for PRX003, an antibody designed to block pro-inflammatory Th17 cells from infiltrating into tissue and releasing multiple cytokines that contribute to inflammatory disease pathology," stated Gene Kinney, PhD, Prothena's Chief Operating Officer. "Based on the biology of psoriatic arthritis and the novel proposed mechanism of PRX003, we believe this approach has the potential to offer an improved therapeutic option for patients suffering from this disease."

Pro-inflammatory Th17 Cells and PRX003 Potential Mechanisms of Action

Pro-inflammatory Th17 cells release multiple cytokines that contribute to inflammatory disease pathology, including IL-17, TNF-α, IL-6, IFNγ, IL-22, and CCL20 (Liuzzo, et. al., European Heart Journal, 2013; Mohan et. al., American Journal of Pathology, July 2012).

PRX003 was designed to target CD146, a cell adhesion molecule also known as melanoma cell adhesion molecule (MCAM), which is expressed on the surface of Th17 cells. CD146 facilitates Th17 cell migration from circulation into tissue, a necessary step required to initiate and/or perpetuate an inflammatory disease process. Prothena discovered that laminin α4 is the endothelial binding partner for CD146, and this binding is necessary to facilitate the migration of Th17 cells from circulation into tissue.

PRX003 is designed to occupy CD146, leading to downregulation which sequesters pro-inflammatory Th17 cells in the bloodstream, preventing their migration into tissue. PRX003 may also induce the demargination of Th17 cells that are already adherent to blood vessels or tissue.

Planned PRX003 Phase 2 Development Strategy

Prothena plans to advance a Phase 2 clinical study of PRX003 for the treatment of psoriatic arthritis, a Th17-mediated disease where multiple cytokines contribute to pathology.

Psoriatic arthritis is a potentially debilitating disease characterized by pain, stiffness and swelling in the joints and surrounding ligaments and tendons. According to the National Psoriais Foundation, as many as 45 percent of patients with psoriatic arthritis are dissatisfied with their current treatment (Armstrong AW, et. al., JAMA, 2013). There is an unmet need for more effective and tolerable therapies in this patient population.

In patients with psoriatic arthritis, there are significantly more CD146 expressing T cells at the site of inflammation than in the peripheral blood, suggesting a role for CD146 — expressed on the surface of Th17 cells — in the migration of pathogenic cells into joints (Raychaudhuri, et. al., poster presentation at 2105 ACR/ARHP Annual Meeting, abstract #982). Due to its proposed upstream mechanism of action, PRX003 is expected to block the release of multiple Th17 related cytokines that are known to contribute to psoriatic arthritis pathology including IL-17, TNF-α, IL-6, IFNγ, IL-22, and CCL20.

Prothena is conducting a Phase 1b double-blind, placebo controlled, multiple ascending dose, proof-of-biology study in approximately 56 patients with psoriasis. This study is evaluating safety, tolerability, pharmacokinetics, immunogenicity, and pharmacodynamics, and will also evaluate the Psoriasis Area and Severity Index (PASI) following treatment with PRX003 as a means to assess proof-of-biology.

Should the interim analysis of the ongoing Phase 1b multiple ascending dose proof-of-biology study in patients with psoriasis meet certain pre-specified criteria, Prothena will begin preparation for a Phase 2 study in patients with psoriatic arthritis. The interim analysis is expected by mid-2017.

Conference Call and Webcast Details

Prothena will host a webcast today at 4:30 PM Eastern Time to discuss its plans for Phase 2 development of PRX003. To access the conference call via dial-in, please dial (877) 887-5215 (U.S. toll free) or (315) 625-3069 (international) five minutes prior to the start time and refer to conference ID number 83102616. A replay of the webcast and call will be available for at least 90 days via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 83102616.

About PRX003

PRX003 is a monoclonal antibody being developed for the potential treatment of Th17-mediated inflammatory diseases where multiple cytokines contribute to pathology. PRX003 is designed to occupy and downregulate CD146, also known as melanoma cell adhesion molecule (MCAM), a cell adhesion molecule expressed on the surface of Th17 cells, sequestering cells that secrete disease-causing cytokines in the bloodstream and preventing their migration into tissues. As CD146-expressing Th17 cells appear to be disproportionately involved in propagation of inflammation, targeting the T cell, rather than any individual cytokine, may provide a highly specific way to impact multiple pathogenic processes, while leaving the vast majority of immune cells intact. In a randomized, double-blind, placebo-controlled, single ascending dose Phase 1 clinical study in healthy volunteers, PRX003 was found to be safe and well tolerated, and demonstrated greater than 95 percent neutralization of CD146 at saturating drug exposures. Prothena's plans for a Phase 2 study of PRX003 in psoriatic arthritis will be based on certain pre-specified criteria being met in an interim analysis of an ongoing Phase 1b proof-of-biology study in patients with psoriasis. For more information about Prothena's ongoing proof-of-biology Phase 1b clinical study of PRX003 in patients with psoriasis please visit www.clinicaltrials.gov and search identifier NCT02630901.

About Psoriatic Arthritis

Psoriatic arthritis is a chronic and progressive inflammatory autoimmune disease characterized by pain, stiffness and swelling in the joints and surrounding ligaments and tendons. Psoriatic arthritis impacts as many as 1 million people in the US, EU5, and Japan (Psoriatic Arthritis Disease Coverage - 2013 Datamonitor report). According to the National Psoriasis Foundation, nearly one in four people with psoriasis may have undiagnosed psoriatic arthritis. Psoriatic arthritis can be disabling and cause irreversible joint damage if left untreated.

About Prothena

Prothena Corporation plc is a global, late-stage clinical biotechnology company seeking to fundamentally change the course of progressive diseases with its clinical pipeline of novel therapeutic antibodies. Fueled by its deep scientific understanding built over decades of research in protein misfolding and cell adhesion — the root causes of many serious or currently untreatable amyloid and inflammatory diseases — Prothena is establishing a fully integrated research, development and commercial focus and has advanced several drug candidates into clinical studies while pursuing discovery of additional novel therapies. Our pipeline of antibody-based product candidates targets a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002), inflammatory diseases, including psoriasis and psoriatic arthritis (PRX003), and ATTR amyloidosis (PRX004). For more information, please visit the company's website at www.prothena.com.

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the potential of PRX003 to offer an improved therapeutic option for patients suffering from psoriatic arthritis; the design and proposed mechanisms of action of PRX003; whether PRX003 blocks infiltration of Th17 cells into tissue and sequesters them in the circulation, and induces demargination of Th17 cells; the potential for our Phase 1b study of PRX003 to provide proof-of-biology; the timing of announcing interim results of the Phase 1b study of PRX003; and our contemplated Phase 2 development strategy and clinical study of PRX003 in psoriatic arthritis. These statements are based on estimates, projections and assumptions that may prove not to be accurate, and actual results could differ materially from those anticipated due to known and unknown risks, uncertainties and other factors, including but not limited to the risks, uncertainties and other factors described in the "Risk Factors" sections of our Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 25, 2016 and our subsequent Quarterly Reports on Form 10-Q filed with the SEC. Prothena undertakes no obligation to update publicly any forward-looking statements contained in this press release as a result of new information, future events or changes in Prothena's expectations.

Contacts:

Investors: Tran Nguyen, CFO

650-837-8535, IR@prothena.com

Media: Ellen Rose, Head of Communications
650-922-2405, ellen.rose@prothena.com