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Prothena Presents Clinical Results Demonstrating Robust, Rapid Reduction in Levels of Free Serum Alpha-Synuclein of Up to 96% After Single Dose of PRX002, Novel Protein Immunotherapy for Parkinson's Disease

- **PRX002 was Safe and Well Tolerated; Phase 1 Single Ascending Dose Study Objectives Met**
- **Dose- and Time-Dependent, Statistically Significant Reduction in Free Serum Alpha-Synuclein within One Hour of PRX002 Administration**
- **Data Presented in Late Breaking Poster Session at 19th International Congress of Parkinson's Disease and Movement Disorders (Abstract #LBA19) in San Diego**
- **Investor Conference Call and Webcast Today at 5:30 p.m. EDT**

DUBLIN, Ireland, June 17, 2015 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs, today presented clinical results from a Phase 1 single ascending dose study of PRX002, a monoclonal antibody for the potential treatment of Parkinson's disease and other related synucleinopathies. PRX002 is the focus of a worldwide collaboration between Prothena and Roche.

Presented today as part of the late breaking session at the 19th International Congress of Parkinson's Disease and Movement Disorders, the data demonstrated that PRX002 was safe and well-tolerated in healthy volunteers, meeting the primary objective of the study. Further, results from this study showed that administration of PRX002 led to a mean reduction of free serum alpha-synuclein levels of up to 96%. These overall results were highly statistically significant ($p < 0.00001$). Reduction of free serum alpha-synuclein, a protein potentially involved in the onset and progression of Parkinson's disease and the target of PRX002, was shown to be robust, rapid, and dose- and time-dependent after a single dose.

"Alpha-synuclein is a protein that can be found in the blood, cerebrospinal fluid (CSF) and the brain," said Joseph Jankovic, MD, Professor of Neurology, Distinguished Chair in Movement Disorders, and Director of The Parkinson's Disease Center and Movement Disorders Clinic at the Baylor College of Medicine. "It has been shown that patients with Parkinson's disease have decreased levels of alpha-synuclein in the CSF, and this is believed to be due to an accumulation of pathogenic alpha-synuclein in the brain which plays a role in the neurodegeneration associated with the disease."

The Phase 1 double-blind, placebo-controlled, single ascending dose study enrolled 40 healthy volunteers. All volunteers enrolled were randomized 3:1 into five escalating dose cohorts (0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg or 30 mg/kg) to receive either PRX002 or placebo. No serious adverse events or hypersensitivity reactions were reported. PRX002 demonstrated favorable pharmacokinetic properties, supporting the current dosing frequency in the on-going Phase 1 multiple ascending dose study in patients with Parkinson's disease. Treatment-emergent adverse events in greater than 5% of subjects were vessel puncture site pain, headache, viral infection, nausea, neutropenia, upper respiratory infection and pruritus. All PRX002-related adverse events were mild and no dose limiting toxicities were observed. No anti-drug antibodies were detected.

"The demonstration of a positive safety profile at doses as high as 30 mg/kg and in the presence of a robust, rapid, and dose- and time-dependent mean reduction in free serum alpha-synuclein of up to 96% after a single dose of PRX002 is very encouraging," commented Gene Kinney, PhD, Chief Scientific Officer and Head of Research and Development at Prothena. "Building on these data, we are currently conducting a Phase 1 multiple ascending dose study, which will measure changes of alpha-synuclein in the periphery of patients with Parkinson's disease, and also measure levels of PRX002 in the CSF. We believe that these data will allow us to confidently proceed into advanced clinical development with doses of PRX002 selected to meaningfully reduce aggregated alpha-synuclein in the brain of patients with Parkinson's disease, with an ultimate objective of delaying or reversing disease progression."

In December 2013, Prothena and Roche entered into a worldwide collaboration to develop and commercialize antibodies that target alpha-synuclein, including PRX002. To date, Prothena has received \$45 million of the potential \$600 million in total milestones through its collaboration with Roche. Prothena has an option to co-promote PRX002 in the U.S., where the companies share all profits, as well as development and commercialization costs, on a 30/70 basis (30% Prothena and 70% Roche). Outside the U.S., Roche will have sole responsibility for developing and commercializing PRX002 and will pay Prothena up to double-digit royalties on net sales.

Conference Call and Webcast Details

Prothena management will discuss the clinical trial results from the Phase 1 single ascending dose study of PRX002 during a live audio webcast and conference call today at 5:30 p.m. EDT. The webcast and slide presentation will be made available on the company's website at www.prothena.com under the Investors tab in the Events and Presentations section. Following the live audio webcast, a replay of the webcast will be available on the Company's website for 90 days.

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 54868803. A replay of the call will be available until June 24, 2015 via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 54868803.

About Alpha-Synuclein

Alpha-synuclein is a protein found in neurons and is a major component of pathology that characterizes several neurodegenerative disorders including Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy, which collectively are termed synucleinopathies. While the normal function of synuclein is not well understood, the protein generally occurs in a soluble form. In synucleinopathies, the synuclein protein can misfold and aggregate to form soluble aggregates and insoluble fibrils that contribute to the pathology of the disease. There is also increasing evidence that this disease-causing synuclein can be propagated and transmitted from neuron to neuron, resulting in an infection-like spread of neuronal death. Recent studies in cellular and animal models suggest that the spread of synuclein-associated neurodegeneration can be disrupted by targeting aberrant forms of synuclein.

About PRX002

PRX002, a monoclonal antibody targeting alpha-synuclein, is the focus of a license agreement between Prothena and Roche. The companies are evaluating PRX002 in a multiple ascending dose study in patients with Parkinson's disease, with results expected in the first half of 2016. PRX002 is designed to slow or reduce the progressive neurodegeneration associated with synuclein misfolding and/or the cell-to-cell transmission of the pathogenic forms of synuclein in Parkinson's disease and other synucleinopathies. Prior to initiating clinical trials, Prothena demonstrated the efficacy of PRX002 in various cellular and animal models of synuclein-related disease. In transgenic mouse models of Parkinson's disease, passive immunization with 9E4, the murine version of PRX002, reduced the appearance of synuclein pathology, protected synapses and improved performance by the mice in behavioral testing. For more information on the ongoing multiple ascending dose study, please visit www.clinicaltrials.gov and search identifier NCT02157714.

About Parkinson's Disease

Parkinson's disease is a degenerative disorder of the central nervous system that affects one in 100 people over age 60, and after Alzheimer's disease is the second most common neurodegenerative disorder. There are an estimated seven to ten million patients living with Parkinson's disease worldwide. Current treatments for Parkinson's disease are only effective at managing the early motor symptoms of the disease, mainly through the use of levodopa and dopamine agonists. As the disease progresses and dopaminergic neurons continue to be lost, these drugs eventually become less effective at treating the symptoms. In contrast, PRX002 targets disease-causing alpha-synuclein, and may slow or reduce the neurodegeneration associated with aberrant forms of alpha-synuclein.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs for the potential treatment of diseases that involve amyloid or cell adhesion. The company is developing antibody-based product candidates that target a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002), and psoriasis and other inflammatory diseases (PRX003).

For more information, please visit the company's web site at www.prothena.com.

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, our ability to evaluate the effectiveness of PRX002 for the treatment of clinical synucleinopathies; our ability to advance clinical development of PRX002; whether PRX002 can reduce aggregated alpha-synuclein in the brain, delay or reverse disease progression or slow or reduce neurodegeneration; and the timing of reporting results from our Phase 1 multiple ascending dose study of PRX002. 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 March 13, 2015 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.

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