March 19, 2015

Prothena Reports Robust Reduction of Free Serum Alpha-Synuclein of up to 96% After Single Dose of PRX002, a Novel Protein Immunotherapy for Parkinson's Disease

- **All Doses of PRX002 Found to be Safe and Well Tolerated, Meeting Primary Objective of Phase 1 Single Ascending Dose Study**
- **Results of Study Demonstrate Rapid and Dose-Dependent Reduction of Free Serum Alpha-Synuclein, Potential Disease-Causing Protein in Parkinson's Disease**

DUBLIN, Ireland, March 19, 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 announced positive 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.

PRX002 was safe and well-tolerated, meeting the primary objective of the study. Further, results from this study showed that administration of PRX002 leads to 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-dependent after just a single dose.

"There is genetic and pathological evidence that supports a causal role of alpha-synuclein in Parkinson's disease," said Todd Sherer, PhD, CEO of the Michael J. Fox Foundation for Parkinson's Research. "We applaud Prothena and Roche for their pioneering work in developing a potentially disease-modifying therapy for this progressive neurodegenerative disease that affects millions worldwide."

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 hypersensitivity reactions or drug-related serious adverse events 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. There were no treatment emergent adverse events (TEAEs) in greater than 10% of subjects. The only TEAEs in greater than 5% of subjects were vessel puncture site pain, headache and viral infection. All PRX002-related adverse events were mild and no dose limiting toxicities were observed.

"We are extremely pleased with the results of the Phase 1 single ascending dose study as the mean reduction of free serum alpha-synuclein of up to 96% demonstrates the pharmacodynamic effects of PRX002," commented Gene Kinney, PhD, Chief Scientific Officer and Head of Research and Development at Prothena. "Importantly and for the first time in humans, we demonstrated that this robust, rapid and dose-dependent reduction of free serum alpha-synuclein was safe and well-tolerated. Thus, this approach may translate into a clinically meaningful delay or reversal of disease progression in patients with Parkinson's disease. We look forward to building upon these data with results from the on-going, multiple ascending dose study in patients with Parkinson's disease expected in the first half of 2016, where we will also be measuring levels of PRX002 in the cerebrospinal fluid and assessing additional biochemical, imaging and clinical biomarker endpoints. Separately, we are excited to co-host a symposium with Roche on March 21 at the 12th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD™ 2015) to continue to raise awareness of the role of alpha-synuclein as a target for Parkinson's disease."

"The results of the PRX002 study exemplify Prothena's deep domain expertise to develop novel disease-modifying protein immunotherapies with unique specificities to their targets," stated Dale Schenk, PhD, President and Chief Executive Officer of Prothena. "Prothena's consistent ability to develop targeted potential therapeutics has resulted in a strong and promising pipeline to transform patient's lives, with NEOD001 in Phase 3 clinical studies for the treatment of AL amyloidosis, PRX002 continuing in a Phase 1 multiple ascending dose study in patients with Parkinson's disease and PRX003 ready to begin clinical studies for the treatment of psoriasis and potentially other inflammatory diseases."

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.

Roche and Prothena to Co-Host Symposium During AD/PD™ 2015

Leading researchers in the field of Parkinson's disease will present during a Roche and Prothena co-hosted symposium entitled 'Alpha-Synuclein as a Target in Parkinson's Disease,' during the 12th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD™ 2015) in Nice, France. The symposium will be held on March 21, 2015 at 9:15 a.m. local time, and will feature leading experts from Europe and the United States including Wilma van de Berg, PhD, of the VU University Medical Center in the Netherlands; Patrik Brundin, MD, PhD, of the Van Andel Research Institute in Michigan; Eliezer Masliah, MD, of the University of California, San Diego; Mark Frasier, PhD, of the Michael J. Fox Foundation in New York; and, Wagner Zago, PhD, of Prothena Biosciences Inc in South San Francisco.

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, the timing of reporting data from our Phase 1 multiple ascending dose study for PRX002; the possible clinical benefit of PRX002 in patients with Parkinson's disease; the potential of Prothena's development pipeline; and the timing of initiating clinical trials for PRX003. 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 12, 2015. 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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