April 2, 2017

Clinical Results Presented from Prothena's Phase 1b Study of PRX002/RG7935 Demonstrating Robust Antibody CNS Penetration and Significant Reduction of Free Serum Alpha-synuclein in Patients with Parkinson's Disease

- **All dose levels of PRX002/RG7935 found to have an acceptable safety and tolerability profile, meeting the primary objective of this study**
- **Robust central nervous system (CNS) penetration demonstrated by a dose-dependent increase in PRX002 levels in cerebrospinal fluid (CSF), and mean concentration of PRX002 in CSF of 0.3 percent relative to serum across all dose levels**
- **Rapid, dose- and time-dependent mean reduction in levels of free serum alpha-synuclein of up to 97 percent**
- **Results support advancing PRX002 into Phase 2 clinical study, PASADENA, planned to begin in the second quarter of 2017**
- **Study Results Presented in Late Breaking Oral Session at 13th International Conference on Alzheimer's and Parkinson's Diseases (Symposium 58) in Vienna**
- **Joseph Jankovic, MD, Professor of Neurology, Distinguished Chair in Movement Disorders at Baylor College of Medicine to present results during Prothena's investor conference call and webcast today at 9:00 AM ET**

DUBLIN, Ireland, April 02, 2017 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapies, today presented clinical results from its Phase 1b multiple ascending dose study of PRX002/RG7935 in patients with Parkinson's disease. PRX002, also known as RG7935, is an antibody under investigation as a potentially disease-modifying treatment for Parkinson's disease and is the focus of a worldwide collaboration between Prothena and Roche.

The study results were presented as part of a late-breaking oral session at the 13th International Conference on Alzheimer's and Parkinson's Diseases (AD/PD) in Vienna, Austria today at 6:00 AM ET (12:00 PM CET), by Joseph Jankovic, MD, Professor of Neurology, Distinguished Chair in Movement Disorders at Baylor College of Medicine, Houston, Texas, and are also being discussed today in an investor webcast at 9:00 AM ET.

As highlighted in the November 2016 topline press release, PRX002/RG7935 was found to have an acceptable safety and tolerability profile in patients with Parkinson's disease, meeting the primary objective of this study. Robust CNS penetration was demonstrated by a dose-dependent increase in PRX002/RG7935 levels in CSF, and a mean concentration of PRX002/RG7935 in CSF of 0.3 percent relative to serum across all dose levels. Additional results showed a rapid, dose- and time dependent mean reduction of free serum alpha-synuclein levels of up to 97 percent after a single dose, which were statistically significant ($p<0.0001$), and maintained following two additional monthly doses.

"PRX002/RG7935 represents a promising investigational approach as a disease-modifying immunotherapy designed to target the toxic form of alpha-synuclein that accumulates in Parkinson's disease patients," stated Joseph Jankovic, MD, Professor of Neurology, Distinguished Chair in Movement Disorders, and Director of the Parkinson's Disease Center and Movement Disorders Clinic at Baylor College of Medicine. "The Parkinson's disease community is looking forward to the start of the Phase 2 clinical study that will assess how targeting alpha-synuclein may translate into a clinically meaningful delay of disease progression in patients."

"The safety, tolerability and pharmacologic properties of PRX002/RG7935 have now been demonstrated in two double-blind, placebo-controlled Phase 1 studies, which collectively enrolled 120 individuals. Based on these study results we are able to initiate a Phase 2 study with dose levels that we expect to meaningfully reduce pathogenic alpha-synuclein in the brain of patients suffering with Parkinson's disease," stated Gene Kinney, PhD, President & Chief Executive Officer of Prothena. "Together with Roche, we plan to initiate PASADENA, a global Phase 2 study in the second quarter of this year to further explore the potential of PRX002/RG7935 as a disease-modifying therapy for Parkinson's disease."

This Phase 1b double-blind, placebo-controlled multiple ascending dose study enrolled 80 patients with Parkinson's disease. Patients were randomized into six escalating dose cohorts to receive PRX002/RG7935 or placebo (2:1 randomization for 0.3, 1, 3 or 10 mg/kg, and 3:1 randomization for 30 or 60 mg/kg). In this six-month study, patients received three monthly doses (intravenous infusion once every 28 days) of PRX002/RG7935 or placebo and were followed for an observational period of three months. No serious or severe treatment emergent adverse events (TEAEs) were reported in

PRX002/RG7935 treated patients. No TEAEs were observed in ten percent or more of PRX002/RG7935 treated patients. TEAEs greater than placebo in five percent or more of PRX002/RG7935 treated patients, regardless of relationship to PRX002/RG7935, included constipation, infusion related reactions (IRRs), diarrhoea, peripheral oedema, and post lumbar puncture syndrome. Mild-to-moderate IRRs, that all resolved, were limited to the 60 mg/kg dose cohort and were observed in four of 12 treated patients. No dose-limiting toxicities were observed. PRX002/RG7935 demonstrated acceptable pharmacokinetic properties.

PASADENA, a Phase 2 study of PRX002/RG7935 of approximately 300 patients with early Parkinson's disease is expected to initiate in the second quarter of 2017.

Conference Call and Webcast Details

Dr. Joseph Jankovic of the Baylor College of Medicine will join Prothena management to discuss the clinical study results from the Phase 1b multiple ascending dose study of PRX002/RG7935 during a live audio webcast and conference call today, April 2, 2017, at 9:00 AM ET. 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 85230691. A replay of the webcast and call will be available until April 9, 2017 via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 85230691.

About Alpha-synuclein

Alpha-synuclein, a protein found in neurons and other cells, 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 alpha-synuclein is not well understood, the protein generally occurs in a soluble form. In synucleinopathies, the alpha-synuclein protein can misfold and aggregate to form soluble aggregates and insoluble fibrils that contribute to disease pathology. There is increasing evidence that this disease-causing alpha-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 alpha-synuclein-associated neurodegeneration can be disrupted by targeting aberrant forms of alpha-synuclein.

About PRX002/RG7935

PRX002**/**RG7935 is a monoclonal antibody under development for the potential treatment of Parkinson's disease. PRX002**/**RG7935 targets alpha-synuclein and is designed to slow the progressive neurodegeneration associated with alpha-synuclein misfolding and/or the cell-to-cell transmission of the aggregated pathogenic forms of alpha-synuclein found in Parkinson's disease and other synucleinopathies. Prior to initiating clinical trials, Prothena demonstrated the efficacy of PRX002**/**RG7935 in various cellular and animal models of alpha-synuclein-related disease. In multiple transgenic mouse models of Parkinson's disease, the murine version of PRX002**/**RG7935, reduced the appearance of alpha-synuclein pathology, protected synapses and improved performance in behavioral testing. In December 2013 Prothena and Roche entered into a worldwide collaboration to develop and commercialize antibodies that target alpha-synuclein, including PRX002**/**RG7935. Prothena has an option to co-promote PRX002**/**RG7935 in the U.S., where the companies share all development and commercialization costs, as well as profits, on a 30/70 basis (30 percent Prothena, 70 percent Roche). Outside the U.S., Roche will have sole responsibility for developing and commercializing PRX002**/**RG7935 and will pay Prothena up to double-digit royalties on net sales. A Phase 2 clinical study of PRX002**/**RG7935 in patients with Parkinson's disease is expected to begin in the second quarter of 2017.

About Parkinson's Disease

Parkinson's disease is a progressive degenerative disorder of the central nervous system (CNS) that affects one in 100 people over age 60. With an estimated seven to 10 million patients living with Parkinson's disease worldwide, it is the second most common neurodegenerative disorder after Alzheimer's disease. The disease is characterized by the neuronal accumulation of aggregated alpha-synuclein in the CNS and peripheral nervous system that results in a wide spectrum of worsening progressive motor and non-motor symptoms. While diagnosis relies on motor symptoms classically associated with Parkinson's disease, non-motor symptoms may present many years earlier. Current treatments for Parkinson's disease are symptomatic and only address a subset of symptoms such as motor impairment, dementia, or psychosis. Symptomatic therapies do not target the underlying cause of the disease and lose effectiveness, often leading to debilitating side effects as the disease progresses.

About Prothena

Prothena Corporation plc is a global, late-stage clinical biotechnology company establishing fully-integrated research, development and commercial capabilities. 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 seeks to fundamentally change the course of progressive diseases associated with this biology. The Company's pipeline of antibody therapeutic candidates targets a number of indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002/RG7935), inflammatory diseases, including psoriasis and psoriatic arthritis (PRX003), and ATTR amyloidosis (PRX004). The company continues discovery of additional novel therapeutic candidates where its deep scientific understanding of disease pathology can be leveraged. 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, plans for and the timing of initiating a Phase 2 clinical study of PRX002/RG7935*; whether the Phase 2 study will show meaningful reduction in pathogenic alpha-synuclein in the brain; and the design of* PRX002/RG7935 *and its potential as a disease modifying treatment for Parkinson's disease. 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 27, 2017 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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