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

- **All dose levels of PRX002 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**
- **Data supports advancing PRX002 into Phase 2 clinical study, planned for 2017**

DUBLIN, Ireland, Nov. 09, 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, today announced results from its Phase 1b multiple ascending dose study of PRX002, an antibody under investigation as a potentially disease-modifying treatment for Parkinson's disease. PRX002, also known as RG7935, is the focus of a worldwide collaboration between Prothena and Roche.

PRX002 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 levels in CSF, and a mean concentration of PRX002 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 confirmed after two additional monthly doses.

"These data represent the first reported assessment of an anti-alpha-synuclein antibody in patients with Parkinson's disease," stated Gene Kinney, PhD, President and Chief Executive Officer of Prothena. "In this study we observed PRX002 penetration in the CNS that exceeded our expectations based on our preclinical experience, and a highly statistically significant reduction of free serum alpha-synuclein. These Phase 1b data further support our belief that we can choose doses that target and saturate aggregated pathogenic alpha-synuclein in the brain for a Phase 2 study to further explore the potential of PRX002 as a disease-modifying treatment for Parkinson's disease. Together with Roche, we expect to initiate a Phase 2 study in 2017."

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 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 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 treated patients. No TEAEs were observed in ten percent or more of PRX002 treated patients. TEAEs greater than placebo in five percent or more of PRX002 treated patients, regardless of relationship to PRX002, 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 demonstrated acceptable pharmacokinetic properties.

"Developing new therapies for complex neurological diseases such as Parkinson's requires dedicated and disciplined science," said Todd Sherer, PhD, CEO of The Michael J. Fox Foundation for Parkinson's Research. "Targeting alpha-synuclein represents a promising path toward a potentially disease-modifying treatment for Parkinson's disease, and we are very pleased to see PRX002 advance to the next stage of development."

Prothena plans to present results from this study at an upcoming scientific conference. A Phase 2 clinical study is expected to begin in 2017.

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 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 is a monoclonal antibody under development for the potential treatment of Parkinson's disease. PRX002 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 in various cellular and animal models of alpha-synuclein-related disease. In multiple transgenic mouse models of Parkinson's disease, passive immunization with 9E4, the murine version of PRX002, 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. Prothena has an option to co-promote PRX002 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 and will pay Prothena up to double-digit royalties on net sales. A Phase 2 clinical study of PRX002 in patients with Parkinson's disease is expected to begin in 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 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, plans for and the timing of initiating a Phase 2 clinical study of PRX002; our ability to choose appropriate doses for that Phase 2 study; and the potential of PRX002 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 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.

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