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Prothena Announces Initiation of Phase 2 PASADENA Study of PRX002/RG7935 in Patients with Early Parkinson's Disease

- **First potentially disease-modifying anti-alpha-synuclein antibody to be evaluated for efficacy in patients with Parkinson's disease**
- **Prothena to receive $30 million milestone payment under collaboration agreement with Roche**

DUBLIN, Ireland, July 05, 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 announced that the first patient has been enrolled in PASADENA, a global Phase 2 study of PRX002/RG7935 in patients with early Parkinson's disease. PRX002/RG7935 is an anti-alpha-synuclein antibody under investigation as a disease-modifying treatment for Parkinson's disease and is the focus of a worldwide collaboration between Prothena and Roche. The start of the study triggered a $30 million milestone from Roche to Prothena, which was earned in the second quarter of 2017. Prothena had previously received $45 million in upfront and development milestone payments.

"Building upon the data from two completed Phase 1 studies of PRX002/RG7935, which demonstrated favorable safety, tolerability and pharmacologic properties, the Phase 2 study will evaluate the impact of targeting alpha-synuclein on the slowing of progression of Parkinson's disease in patients," stated Gene Kinney, PhD, President & Chief Executive Officer of Prothena. "Two dose levels have been selected for the Phase 2 study of PRX002/RG7935 that, based on our preclinical and clinical data, we expect to meaningfully reduce pathogenic alpha-synuclein in the brains of patients with Parkinson's disease."

Phase 2 PASADENA Study Design

PASADENA is a two-part Phase 2 clinical study in early Parkinson's disease patients that is being conducted by Roche. Part 1 is a randomized, double-blind, placebo-controlled, three-arm study designed to enroll approximately 300 patients to evaluate the efficacy and safety of PRX002/RG7935 in patients over 52 weeks. In part 1, patients will be randomized on a 1:1:1 basis to receive one of two active doses (1500 mg or 4500 mg) of PRX002/RG7935 or placebo via intravenous infusion once every 4 weeks. Eligible patients must not be on dopaminergic therapy and must not be expected to require dopaminergic therapy for at least 52 weeks. Part 2 of the study is a 52-week blinded extension phase in which patients from the placebo arm of the study will be re-randomized onto one of two active doses on a 1:1 basis, so that all participants will be on active treatment. Patients who were originally randomized to an active dose will continue at that dose level for the additional 52 weeks. In part 2, patients will be allowed to use concomitant dopaminergic therapy. Any patient who medically requires initiation of dopaminergic therapy during part 1 will have their subsequent data censored for the primary endpoint analysis.

The primary endpoint of this study is the comparison of change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score (sections 1, 2 and 3) at the completion of part 1 (week 52) in each treatment group vs. the placebo group. The study is designed with 80 percent power and a one-sided alpha of 0.10 to detect a 37.5 percent relative between group reduction from baseline to week 52. A prespecified exploratory analysis will compare the results of the two pooled treatment arms vs. placebo. Key secondary endpoints include safety, tolerability and DaT-SPECT imaging.

For more information on the Phase 2 PASADENA study, please visit clinicaltrials.gov and search NCT #03100149.

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. To date, Prothena has earned $75 million of a potential $600 million in clinical, regulatory and sales milestones. For more information on the Phase 2 clinical study of PRX002/RG7935 in patients with Parkinson's disease, visit clinicaltrials.gov and search NCT #03100149.

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, whether the PRX002/RG7935 dose levels in the Phase 2 study will meaningfully reduce pathogenic alpha-synuclein in the brain of patients with Parkinson's disease; the design of PRX002/RG7935 and its potential as a disease-modifying antibody for patients with 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 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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