



## Update on Phase 2 PASADENA Study of Prasinezumab (PRX002/RG7935) in Parkinson's Disease

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DUBLIN, Ireland, April 22, 2020 (GLOBE NEWSWIRE) -- Prothena Corporation plc (NASDAQ:PRTA), a clinical-stage neuroscience company with expertise in protein misfolding, announced that today Roche provided an update on Part 1 of the Phase 2 PASADENA study of prasinezumab in patients with early Parkinson's disease. As updated by Roche during its 1Q20 earnings [announcement](#), the study did not meet the primary objective, but showed signals of efficacy. These signals were observed on multiple prespecified secondary and exploratory clinical endpoints. Roche has begun further clinical development planning activities and is evaluating the data from Part 1 of the PASADENA study to determine next steps. Based on ongoing evaluation of the data, including potential discussions with health authorities, a further update on prasinezumab is expected later this year.

The study, which is being conducted by Roche, was designed with 80% power and a one-sided alpha of 0.10 to detect a 37.5% relative between group reduction from baseline to week 52 on the primary endpoint (i.e., the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score (parts I, II and III) vs placebo in Part 1 of the study). Part 2 of the study is ongoing. Prasinezumab was generally well tolerated with a favorable safety profile. Prasinezumab is the focus of a worldwide collaboration between Prothena and Roche.

### 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 that enrolled 316 patients to evaluate the efficacy and safety of prasinezumab in patients over 52 weeks. In Part 1, patients were randomized on a 1:1:1 basis to receive one of two active doses (1500 mg or 4500/3500 mg, depending on body weight) of prasinezumab or placebo via intravenous infusion once every 4 weeks. Eligible patients were not on dopaminergic therapy and were not expected to require dopaminergic therapy for at least 52 weeks. Part 2 of the study, which is ongoing, is a 52-week blinded extension phase in which patients from the placebo arm of the study have been re-randomized onto one of two active doses on a 1:1 basis, so that all participants are 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 are allowed to start dopaminergic therapy. Any patient who medically required initiation of dopaminergic therapy during Part 1 have had their subsequent data censored for the primary endpoint analysis.

The primary endpoint of this study is change from baseline in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score (Parts I, II and III) at the completion of Part 1 (week 52) in each treatment group vs the placebo group. The study was 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.

The 52-week blinded extension of the study (Part 2 of the Phase 2 PASADENA Study) is ongoing. Due to the COVID-19 pandemic, patients have missed assessments in Part 2 of the study. The full extent of the COVID-19 disruption to Part 2 is not yet known. 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. The understanding of the normal physiological function of alpha-synuclein is limited, but evidence indicates that soluble forms of the protein may interact with other proteins and certain intracellular membranes. In synucleinopathies, the alpha-synuclein protein appears to be abnormally aggregated intracellularly, which contributes to disease pathology. There is increasing evidence that certain aggregated forms of alpha-synuclein can be transmitted from neuron to neuron, resulting in a propagation of pathology that causes neuronal dysfunction and loss. Recent studies in cellular and animal models of synucleinopathy suggest that the spread of alpha-synuclein-associated neuronal pathology can be disrupted by targeting aberrant forms of alpha-synuclein.

### About Prasinezumab

Prasinezumab is a humanized monoclonal antibody under development for the potential treatment of Parkinson's disease. Prasinezumab targets alpha-synuclein and is designed to block the cell-to-cell transmission of the aggregated pathogenic forms of alpha-synuclein in Parkinson's disease, thereby slowing clinical decline. Prior to initiating clinical trials, the efficacy of prasinezumab was evaluated in various cellular and animal models of alpha-synuclein-related disease. In alpha-synuclein transgenic mice, the murine version of prasinezumab, reduced the appearance of alpha-synuclein pathology, protected synapses and halted the worsening of behavioral phenotypes. In December 2013, Prothena and Roche entered into a worldwide collaboration to develop and commercialize antibodies that target alpha-synuclein, including prasinezumab. Prothena has an option to co-promote prasinezumab 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 has sole responsibility for developing and commercializing prasinezumab and has agreed to pay Prothena up to double-digit royalties on net sales. To date, Prothena has earned \$75 million of a total potential \$600 million that includes clinical, regulatory and sales milestones. For more information on the Phase 2 PASADENA clinical study of prasinezumab in patients with early Parkinson's disease, visit [clinicaltrials.gov](#) and search NCT #03100149.

### About Parkinson's Disease

Parkinson's disease is a progressive degenerative disorder of the entire nervous system that affects one in 100 people over age 60. An estimated seven to 10 million people are 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. There are currently no treatments available that target the underlying cause of the disease and can slow or stop the progression.

### **Forward-Looking Statements**

*This press release contains forward-looking statements. These statements relate to, among other things, plans for the ongoing Phase 2 clinical study of prasinezumab; planning activities including potential discussions with health authorities; plans for an update on prasinezumab later this year; and the treatment potential and proposed mechanisms of action of prasinezumab. 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 effects on our business of the worldwide COVID-19 pandemic and 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 on March 3, 2020, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. 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.*

### **About Prothena**

Prothena Corporation plc is a clinical-stage neuroscience company with expertise in protein misfolding, focused on the discovery and development of novel therapies with the potential to fundamentally change the course of devastating diseases. Fueled by its deep scientific expertise built over decades of research, Prothena is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Prothena's partnered programs include prasinezumab (PRX002/RG7935), in collaboration with Roche for the potential treatment of Parkinson's disease and other related synucleinopathies, and programs that target tau, TDP-43 and an undisclosed target in collaboration with Bristol-Myers Squibb for the potential treatment of Alzheimer's disease, amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD) or other neurodegenerative diseases. Prothena's proprietary programs include PRX004 for the potential treatment of ATTR amyloidosis, and programs that target A $\beta$  (Amyloid beta) for the potential treatment of Alzheimer's disease. For more information, please visit the Company's website at [www.prothena.com](http://www.prothena.com) and follow the Company on Twitter @ProthenaCorp.

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