NEWS RELEASE

Prothena to Highlight Next Generation Treatments for Alzheimer’s and Parkinson’s Disease at the AD/PD 2023 Meeting

3/14/2023

- Broad participation at this year's congress highlights Prothena's leadership in advancing next generation treatments for Alzheimer’s and Parkinson’s disease
- Oral presentation on PRX012, Prothena’s next generation anti-amyloid beta antibody for Alzheimer’s disease, demonstrates higher affinity binding to amyloid beta protofibrils and greater clearance of pyroglutamate-amyloid beta plaques compared to other approved and investigational molecules
- Prothena participating in AD/PD Alzheimer’s Forum Discussions and hosting an industry-sponsored Symposium
- Poster and Symposium presentations by partner Roche on Phase 2 PASADENA study of prasinezumab for Parkinson’s disease

DUBLIN--(BUSINESS WIRE)-- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical biotechnology company with a robust pipeline of investigational therapeutics built on protein dysregulation expertise, today announced broad participation at the 2023 International Conference on Alzheimer’s and Parkinson’s Diseases and related neurological disorders (AD/PD) being held March 28 – April 1, 2023 in Gothenburg, Sweden, highlighting Prothena's leadership in advancing next generation treatments for Alzheimer’s and Parkinson’s disease.

PRX012 for the Treatment of Alzheimer’s Disease

In an oral presentation, Prothena will highlight new preclinical data from its PRX012 program, a potential best-in-class anti-amyloid beta (Aβ) product candidate in development for the treatment of Alzheimer’s disease. To build a more in-depth understanding of PRX012’s binding profile to Aβ protofibrils and its ability to clear pyroglutamate-Aβ

from Alzheimer's disease brain tissue, nonclinical studies compared a PRX012-surrogate* (PRX012s) to approved and investigational molecules. Findings demonstrated that PRX012s had superior binding of 20-fold higher affinity to Aβ protofibrils as compared to lecanemab+ and mediated more robust phagocytic clearance of pyroglutamate-modified Aβ when compared to donanemab+.

These findings further support the ongoing clinical development of PRX012 as a potential best-in-class treatment for Alzheimer's disease that could enable greater accessibility and more convenient administration for patients and caregivers.

Following are details of the PRX012 oral presentation at AD/PD 2023:

- Session Type: Symposium
- Title: Abeta targeting therapies in AD 02
- Oral Presentation: Binding Characteristics of Surrogate PRX012 Demonstrate Potent Engagement of Toxic Abeta Protofibrils and Robust Clearance of Pyroglutamate-Modified Abeta
- Presenting Author: Brian Campbell
- Abstract number: 2480
- Date: Friday, March 31, 2023
- Time: 14:20 CET (9:20 AM EDT)
- Location: Hall C at the Swedish Exhibition Center Gothenburg
- Abstract: **https://cslide.ctimeetingtech.com/adpd23/attendee/confcal/show/session/92**

Additional Prothena Sponsored Activities at AD/PD 2023

Prothena will host leaders in Alzheimer's disease research to define the next generation of care for patients in a company-sponsored Symposium:

- Title: Entering the Era of Disease-Modifying Treatments for AD: Taking Stock of Today and Looking to Tomorrow
- Symposium Chair: Dr. Dennis Selkoe, Co-director, Ann Romney Center for Neurologic Diseases, Department of Neurology, Brigham and Women's Hospital, Harvard Medical School
- Speakers: Dr. Jeffrey Cummings, Joy Chambers-Grundy Professor of Brain Science and Director, Chambers-Grundy Center for Transformative Neuroscience, University of Nevada Las Vegas (UNLV); and Dr. Alireza Atri, Director, Banner Sun Health Research Institute, Banner Health, Sun City, Arizona
- Date: Thursday, March 30, 2023
- Time: 08:40-10:40 CET (3:40-5:40 AM EDT)

- Location: Hall C at the Swedish Exhibition Center Gothenburg

Prothena will also participate in two AD/PD 2023 Forum Discussions:

- Title: Immunotherapies in AD: From Basics to Approval
- Panelist: Wagner Zago, Chief Scientific Officer, Prothena
- Date: Wednesday, March 29, 2023
- Time: 15:55-16:55 CET (11:55 AM-12:55 PM EDT)
- Location: Hall C at the Swedish Exhibition Center Gothenburg

- Title: Anti-Tau Therapies in Clinical Trials
- Panelist: Phillip Dolan, Sr. Director, Head of Exploratory Research, Prothena
- Date: Friday, March 31, 2023
- Time: 17:20-18:20 CET (12:20-1:20 PM EDT)
- Location: Hall C at the Swedish Exhibition Center Gothenburg

Roche (partner) Presentations on Prasinezumab for the Treatment of Parkinson's Disease

- Poster: Exploratory delayed-start analysis of PASADENA Part 3 52-week OLE evaluating prasinezumab efficacy on motor progression and complications in early-stage PD (Poster 338 / #2095)

- On-Demand Symposium: Digital health technologies can reduce sample size and enable shorter proof of concept clinical trial in Parkinson's disease (OD059 / #1444)
- Date: Wednesday, March 29, 2023
- Time: 07:00-08:30 CET (2:00-3:30 AM EDT)

- On-Demand Symposium: Reliability and validity of digital speech features as biomarkers of dysarthria severity and progression in individuals with early Parkinson's disease (OD058 / #1082)
- Date: Wednesday, March 29, 2023
- Time: 07:00-08:30 CET (2:00-3:30 AM EDT)

About PRX012

PRX012, an investigational next-generation anti-Aβ antibody, was designed as a subcutaneous IgG1 mAb to target aggregated forms of Aβ, including protofibrils and plaques, with high binding affinity. PRX012 is currently being investigated in a Phase 1 clinical study for the treatment of Alzheimer's disease. Preclinical data have demonstrated binding of PRX012 to beta amyloid plaques and oligomers with high affinity, allowing effective Aβ plaque occupancy and removal at relatively lower dose ranges, optimal for subcutaneous delivery. Preclinical data have also demonstrated clearance of both pyroglutamate modified and unmodified Aβ plaque in brain tissue at concentrations of PRX012 estimated to be clinically achievable in the central nervous system with subcutaneous delivery.

About Alzheimer’s Disease

Alzheimer’s disease is a fatal disease and the most common form of dementia causing increasingly serious symptoms, including confusion, disorientation, mood and behavioral changes, and difficulty speaking, swallowing, and walking. Approximately 55 million people worldwide are estimated to be living with Alzheimer’s disease or other dementias. Alzheimer’s disease is the most common neurodegenerative disorder. There is an urgent need for therapies that slow the progression and ultimately prevent Alzheimer’s disease to address this global healthcare crisis. Prothena’s Alzheimer’s disease portfolio spans next generation antibody immunotherapy, small molecule, and vaccine approaches, geared toward building upon first generation treatments to advance the treatment paradigm.

About Prasinezumab

Prasinezumab is a humanized monoclonal antibody that targets a carboxyl terminal epitope of alpha-synuclein, a protein found in neurons that can aggregate and spread from cell to cell, resulting in the neuronal dysfunction and loss that causes Parkinson’s disease. Prasinezumab 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. In December 2013, Prothena and Roche entered into a worldwide collaboration to develop and commercialize antibodies that target alpha-synuclein, including prasinezumab. For more information on the Phase 2b PADOVA clinical study of prasinezumab in patients with early Parkinson's disease, visit **clinicaltrials.gov** (NCT#04777331).

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 central nervous system 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 its progression.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid 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 pipeline includes both wholly-owned and partnered programs being developed for the potential treatment of diseases including AL amyloidosis, ATTR amyloidosis, Alzheimer's disease, Parkinson's disease and a number of other neurodegenerative diseases. For more information, please visit the Company's website at **www.prothena.com** and follow the Company on Twitter @ProthenaCorp.

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the treatment potential, design, proposed mechanism of action, and potential administration of PRX012 and 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 those described in the "Risk Factors" sections of our Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 28, 2023, and discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. We undertake 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 our expectations.

* surrogate is defined as an antibody recognizing the same epitope as PRX012 and with the same Aβ binding properties

+ lecanemab and donanemab used in these studies were generated by Prothena from publicly available sequences

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