NEWS RELEASE

Prothena to Present New Data from Alzheimer's Disease Programs at Alzheimer's Association International Conference® 2023 (AAIC®)

7/11/2023

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 participation in the Alzheimer's Association International Conference® 2023 (AAIC®) being held July 16-20, 2023 in Amsterdam, Netherlands and virtually. Participation includes three posters highlighting the company's next generation therapies for Alzheimer's disease and a Prothena sponsored symposium.

PRX005 for the Potential Treatment of Alzheimer's Disease

Prothena will highlight results in a poster presentation from a single ascending dose (SAD) study in healthy volunteers receiving PRX005, a potentially best-in-class investigational tri-epitopic antibody for the treatment of Alzheimer's disease that specifically binds with high affinity to the R1, R2, and R3 repeats within the microtubule binding region (MTBR) of tau and targets both 3R and 4R tau isoforms.

- Poster #74181, available to view starting Sunday, July 16, 2023
- Presenting Author: Ferenc Martényi, MD, VP, Head of Neurodegeneration Clinical Development, Prothena

PRX123 Vaccine Candidate for the Potential Treatment and Prevention of Alzheimer's Disease

Prothena will present preclinical data in a late breaker poster presentation on the immunological response to the dual Aβ/Tau vaccine PRX123 surrogate and the effects on brain amyloid plaques in a rapidly depositing transgenic animal model.

- Poster #82687, available to view starting Sunday, July 16, 2023
- Presenting Author: Brian Campbell, PhD, VP, Head of Translational Medicine, Prothena

PRX012 for the Potential Treatment of Alzheimer's Disease

Prothena will present an encore poster presentation of data originally presented at the 2023 International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders (AD/PD) on preclinical data from the PRX012 program comparing a PRX012-surrogate1 (PRX012s) with lecanemab and donanemab.

- Poster #74811, available to view starting Sunday, July 16, 2023
- Presenting Author: Brian Campbell, PhD, VP, Head of Translational Medicine, Prothena

Prothena Sponsored Symposium

On Tuesday, July 18 from 5:45-7:45 PM CEST, Prothena will host an industry sponsored symposium titled "The Voice of the Patient with AD: What Progress in AD Treatment Means to People Living with the Disease".

About PRX005

PRX005 is designed to be a best-in-class anti-tau antibody that specifically binds with high affinity to the R1, R2, and R3 repeats within the MTBR of tau and targets both 3R and 4R tau isoforms. MTBR tau has been shown in preclinical studies to be involved in the pathological spread of tau. Neurofibrillary tangles composed of misfolded tau proteins, along with amyloid beta plaques, are pathological hallmarks of Alzheimer's disease. Cell-to-cell transmission of pathogenic extracellular tau and the accumulation of pathogenic tau also correlate with the progression of symptomatology and clinical decline in patients with Alzheimer's disease. Recent publications suggest that during the course of Alzheimer's disease progression, tau appears to spread throughout the brain via synaptically-connected pathways; this propagation of pathology is thought to be mediated by tau "seeds" containing the MTBR of tau. Additionally, it has been recently reported that the presence of MTBR fragments in cerebrospinal fluid correlate with dementia stages and tau tangles in Alzheimer's disease to a higher degree than fragments of other tau regions. In preclinical research, antibodies targeting this region of tau were superior in blocking tau uptake and neurotoxicity, which has been associated with efficacy in Alzheimer's disease animal models. In these preclinical models, PRX005 demonstrated significant reduction of intraneuronal tau pathology and protection against behavioral deficit in a tau transgenic mouse model and complete blockade of neuronal tau internalization in vitro.

About PRX123

PRX123, a potential first-in-class dual Aβ/tau vaccine, was designed for the treatment and prevention of Alzheimer's disease and is a dual-target vaccine targeting key epitopes within the N-terminus of Aβ and MTBR-tau to simultaneously promote amyloid clearance and blockade of pathogenic tau.

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 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, designs, proposed mechanisms of action, and potential administration of PRX005, PRX012, and PRX123. 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 4, 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.

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1 "Surrogate" is defined as an antibody with >99.5% homology, the same binding epitope and equivalent binding profile to different forms of Aβ where directly compared.

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Source: Prothena Corporation plc