Prothena Presents New Data from Robust Alzheimer's Portfolio at the Alzheimer's Association International Conference 2021

July 26, 2021

- Late-breaking PRX012 poster highlights significant *ex vivo* clearance of both pyroglutamate-modified and -unmodified Aβ plaque from AD brain at concentrations expected to be reached in CNS with subcutaneous administration
- Poster presentation demonstrates dual Aβ-tau vaccines simultaneously generate antibodies that neutralize and clear pathogenic Aβ and block pathogenic tau interaction

DUBLIN, Ireland, July 26, 2021 (GLOBE NEWSWIRE) -- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise, today announced that it presented new data at the Alzheimer's Association International Conference® 2021 (AAIC®) from two of its Alzheimer's disease (AD) programs. The presentations highlight new data for PRX012, Prothena's next-generation anti-amyloid beta (Aβ) antibody being developed for subcutaneous administration for patients with AD, as well as data on the company's dual Aβ-tau vaccine program being developed for the prevention and treatment of AD. These two programs and Prothena's anti-tau antibody partnered with Bristol Myers Squibb, PRX005, are part of Prothena's potentially best-in-class AD portfolio.

"Our presentations at AAIC reflect our commitment to leverage our protein dysregulation expertise to advance a diverse range of new medicines that are designed to offer enhanced efficacy, safety and access for patients with Alzheimer's disease worldwide," stated Hideki Garren, MD, PhD, Chief Medical Officer. "The data show that PRX012, our high-potency, next-generation anti-Aβ antibody, can clear pyroglutamate-modified and -unmodified Aβ plaque in brain tissue at concentrations that can be reached in the CNS with subcutaneous administration on a convenient treatment schedule. This has the potential to offer greater patient accessibility and compliance relative to approved therapies and treatments currently under development. We also presented preclinical data on our AD vaccine program, which simultaneously targets Aβ and tau, further reinforcing our commitment to offer multiple best-in-class therapeutic options for patients affected by and at risk of developing this devastating disease."

PRX012: Next-generation, high-potency anti-Aβ antibody for Alzheimer's disease with best-in-class potential

Preclinical PRX012 findings were featured in a late-breaking poster presentation titled: *PRX012 Induces Microglia-Mediated Clearance of Pyroglutamate-Modified and -Unmodified Aβ in Alzheimer's Disease Brain Tissue* (Poster # 57773). PRX012 is Prothena's next-generation monoclonal antibody, which binds the N-terminus of Aβ, a key component of the plaque associated with AD. Preclinical data have shown PRX012 binds to A with high affinity and avidity, consistent with the potential for more effective Aβ plaque clearance at lower concentrations than other anti-Aβ therapies. PRX012 is also designed to be administered by subcutaneous injection to provide a more convenient method and schedule of administration to facilitate patient access.

Results presented at AAIC demonstrated that PRX012 induced significant microglia-mediated clearance of both pyroglutamate-modified and -unmodified Aß plaque in brain tissue of late-stage AD patients at concentrations predicted to be clinically relevant. Both forms have been described as components of senile plaque and vascular Aβ in AD. PRX012 was observed to bind with very high affinity/avidity to full-length Aβ. PRX012 also showed higher potency and greater biologic activity than aducanumab. PRX012 Investigational New Drug Application (IND) is expected to be filed in 1Q 2022.

Dual Aβ-tau vaccine for the treatment and prevention of Alzheimer's disease

Preclinical data on Prothena's dual Aβ-tau vaccine were described in a poster presentation titled: *Development of a Dual Aβ-Tau Vaccine for the Prevention of Alzheimer's Disease* (Poster # 52980). The findings, which included results in cynomolgus monkeys and mice, support the continued development of this multi-epitope vaccine for the prevention and treatment of AD. The dual vaccine is a single agent designed to prevent the two key processes associated with AD: the formation of Aβ plaque and the development of intraneuronal tau tangles.

The poster described results from Prothena's dual Aβ-tau vaccine constructs, which generated appropriate antibody quantities with the ability to promote both phagocytosis of Aβ plaque and blockade of tau binding to a heparin-sulfate analog, which is a surrogate for neuronal uptake of tau. All three constructs generated a balanced immune response to both proteins, a common challenge with multi-epitope vaccines, and induced robust antibody titers to Aβ and tau in multiple animal experiments. The resultant titers strongly reacted with Aβ and tau pathology in human AD brain tissue. Additionally, cerebrospinal fluid (CSF) concentrations of tau and Aβ antibodies were within the expected range and similar to typical ranges achieved following administration of monoclonal antibodies (0.1-0.2% CSF/plasma).

About Alzheimer's Disease

Alzheimer's disease is the most common form of dementia causing increasingly serious symptoms, including confusion, disorientation, mood and behavioral changes, difficulty speaking, swallowing, and walking. Approximately 6.2 million Americans aged 65 and older are currently estimated to be living with Alzheimer's disease, making it 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 company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise with the potential to change the course of devastating rare peripheral amyloid and neurodegenerative diseases. Fueled by its deep scientific

expertise built over decades of research, Prothena is advancing a pipeline of therapeutic candidates for several 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 potentials, designs, and proposed mechanisms of action of PRX012, our dual Aβ-tau vaccine and PRX005; and plans for future clinical studies of PRX012. 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" section of our Quarterly Report on form 10-Q filed with the Securities and Exchange Commission (SEC) on May 11, 2021, as well as 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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Source: Prothena Corporation plc