Prothena Announces Presentations on Two Programs from its Alzheimer's Disease Portfolio at CTAD 2020

November 4, 2020

- **Next generation anti-Aβ antibodies being developed for subcutaneous administration to improve access for patients with Alzheimer's disease**
- **Multi-immunogen Aβ-tau vaccine being developed for the prevention and treatment of Alzheimer's disease**

DUBLIN, Ireland, Nov. 04, 2020 (GLOBE NEWSWIRE) -- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical company with expertise in protein dysregulation and a diverse pipeline of investigational therapeutics for neurodegenerative and rare peripheral amyloid diseases, today announced that it will present preclinical data from two programs in its Alzheimer's disease portfolio at the 13th Clinical Trials on Alzheimer's Disease Conference 2020 (CTAD 2020). Prothena's programs being highlighted at CTAD 2020 are next generation anti-Aβ antibodies for subcutaneous administration to improve patient access, and a multi-immunogen vaccine that targets key Aβ and tau epitopes, the two main pathological proteins involved in the cause and progression of Alzheimer's disease, for the prevention and treatment of Alzheimer's Disease. The two programs are part of Prothena's Alzheimer's disease portfolio that includes antibodies, vaccines and small molecules.

"After years of foundational research by our scientists and advances by others, we believe the field is on the precipice of being able to offer patients the first generation of drugs to slow the relentless progression of neurodegenerative diseases such as Alzheimer's," stated Wagner Zago, PhD, Chief Scientific Officer of Prothena. "Due to the high prevalence of Alzheimer's disease, these first-generation approaches will face significant challenges related to patient access due to high required dose levels, route of administration, manufacturing and distribution limitations. To address these limitations, Prothena has developed a portfolio of next generation therapies with a focus on delivering greater patient access through, for example, highly potent anti-Aβ antibodies that can be delivered through convenient subcutaneous administration. We have accomplished this by applying our knowledge around the structural binding characteristics of antibodies to design and screen novel immunotherapies with improved binding properties to key epitopes to produce the desired clinical effect."

Next generation anti-Aβ antibodies

Monoclonal antibodies targeting key epitopes within the N-terminus of Aβ have demonstrated that reducing amyloid plaque burden is associated with the slowing of clinical decline in Alzheimer's disease. To address the growing prevalence of Alzheimer's disease with a therapeutic that can be made widely accessible to patients, Prothena has developed highly potent anti-Aβ antibodies that retain or improve key attributes that are thought to underlie the observed efficacy of N-terminally directed therapeutics such as aducanumab, with the aim of offering similar or improved efficacy with convenient subcutaneous dosing regimens. Prothena antibodies demonstrated a higher binding strength to amyloid than aducanumab; specifically, antibodies with as much as an 11-fold greater affinity/avidity for fibrillar Aβ than aducanumab that also neutralized soluble, toxic (i.e., oligomeric) Aβ species. Prothena antibodies were also shown to recognize Aβ pathology to a greater extent than aducanumab, demonstrating more extensive plaque area binding at lower antibody concentrations, which are estimated to be clinically relevant exposures in the central nervous system following systemic dosing.

The poster can be found as follows:

- Title: Novel Amyloid Beta Monoclonal Antibodies with Superior Binding Properties: Potential for More Convenient Dosing and Greater Patient Access in Alzheimer's Disease
- Session: Abstract # P81, New therapies and clinical trials
- Presenter: Wagner Zago, PhD, Chief Scientific Officer

Multi-Immunogen Aβ-Tau Vaccine

Preclinical models suggest that Aβ and tau act synergistically in the development of Alzheimer's disease; however, the majority of vaccines and passive immunotherapies under development target only one of these two pathological features. Prothena is developing a multi-immunogen vaccine (MIV) that targets key epitopes wihin the Aβ and tau proteins. The MIV is a single vaccine and is being developed for the prevention and treatment of Alzheimer's disease. The Aβ-tau MIV generates polyclonal responses against key epitopes within the N-terminal of Aβ and a key region of tau to promote amyloid clearance and blockade of tau transmission. Immunohistochemistry using sera from immunized animals demonstrated an appropriate and balanced immune response with antibodies that react to both Aβ plaques and tau tangles at concentrations expected to be reached in CNS following immunization and resultant titer generation.

The poster can be found as follows:

- Title: Development of a Dual Aβ-Tau Vaccine for the Prevention and Treatment of Alzheimer's Disease
- Session: Abstract # P80, New therapies and clinical trials
- Presenter: R. Barbour, Senior Director Antibody and Assay Development

About Prothena

Prothena Corporation plc is a late-stage clinical company with expertise in protein dysregulation and a diverse pipeline of novel 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 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 (PRX005), 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 wholly-owned programs include PRX004 for the potential treatment of ATTR amyloidosis, and a portfolio of programs for the potential treatment of Alzheimer's disease including PRX012 that targets Aβ (Amyloid beta). 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 and proposed mechanisms of action of PRX005 and PRX012; and the continued advancement of our discovery and preclinical pipeline. 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 (SEC) on March 3, 2020, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings 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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