Prothena Announces FDA Clearance of IND for PRX012, a Subcutaneous Anti-Amyloid Beta Antibody Under Investigation for the Treatment of Alzheimer's Disease

- Prothena has initiated Phase 1 SAD study of PRX012, under investigation for the treatment of Alzheimer's disease

DUBLIN, Ireland, March 28, 2022 -- 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 the U.S. Food and Drug Administration (FDA) has cleared the investigational new drug (IND) application for PRX012, a potential best-in-class anti-amyloid beta (Aβ) antibody in development for the treatment of Alzheimer's disease (AD). Prothena has initiated the Phase 1 single ascending dose (SAD) study to investigate the safety, tolerability, immunogenicity and pharmacokinetics of PRX012 in both healthy volunteers and patients with AD. Prothena expects to initiate the Phase 1 multiple ascending dose study by year-end 2022.

PRX012 is a next-generation, high binding potency antibody, designed to enable subcutaneous dosing on a patient-friendly, convenient administration schedule, potentially providing greater accessibility for patients and caregivers. Preclinical data have shown that PRX012 binds to beta amyloid plaques and oligomers with high avidity, enabling effective levels of Aβ plaque occupancy at relatively lower dose ranges, which are optimal for subcutaneous delivery. Additional preclinical data 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. Compared to first generation anti-Aβ antibodies, PRX012 is expected to result in less variance of antibody concentrations in the brain.

"With Alzheimer's affecting more than 50 million people worldwide, we are committed to bringing a paradigm-shifting treatment to patients as quickly as possible. Having submitted our IND during this first quarter, we are excited to announce the initiation of this first-in-human study. PRX012's high binding potency and subcutaneous administration has the potential to serve as a foundational anti-Aβ treatment for Alzheimer's disease," said Gene Kinney, Ph. D., President and Chief Executive Officer. "We intend to leverage our multiple decades of experience and expertise in protein dysregulation together with clinical and regulatory learnings from first generation anti-Aβ therapies to maximize the probability of success for our PRX012 program to deliver a best-in-class treatment to patients with Alzheimer's and their families."

About the Phase 1 SAD Study for PRX012

The Phase 1 single ascending dose (SAD) study of PRX012 is a randomized, double-blind, placebo-controlled study to evaluate safety, tolerability, immunogenicity, and pharmacokinetics in healthy volunteers and patients with Alzheimer's disease. In this Phase 1 SAD study, healthy volunteers and patients will be randomized to receive a single subcutaneous injection of either PRX012 or placebo.

About Alzheimer's Disease

Alzheimer's disease is ultimately fatal and the most common form of dementia causing increasingly serious symptoms, including confusion, disorientation, mood and behavioral changes, difficulty speaking,

swallowing, and walking. Approximately 50 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 company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise 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, and proposed mechanism of action of PRX012; 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" sections of our Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 25, 2022, 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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