October 15, 2015

Prothena to Initiate PRONTO, a Global Trial of NEOD001 in Patients With AL Amyloidosis With Primary Endpoint of Cardiac Response

- **Accelerates Development Timeline and Potential Path to Patients**
- **Prothena to Host Investor Conference Call and Webcast Today at 4:30 p.m. ET**

DUBLIN, Ireland, Oct. 15, 2015 (GLOBE NEWSWIRE) -- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapies, today announced it will initiate PRONTO, a global trial of NEOD001 in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction. The primary endpoint of the trial is a cardiac functional biomarker, defined by NT-proBNP best response over 12 months.

"In addition to the VITAL Amyloidosis Study, which remains on-track to provide data for full registration, the PRONTO trial enables us to explore an accelerated path forward to address the high unmet need for therapies that improve organ function in patients with AL amyloidosis," said Dale Schenk, PhD, President and Chief Executive Officer of Prothena. "NT-proBNP response is a widely validated functional biomarker that predicts survival in patients with AL amyloidosis. Demonstrating significant improvements in this key cardiac functional biomarker, along with supporting trends in key secondary endpoints, will expedite our development timeline and provide an additional opportunity to engage with European regulators on a dialogue around conditional approval for NEOD001."

The PRONTO trial was designed to align with feedback from the European Medicines Agency (EMA) related to The VITAL Amyloidosis Study, a global Phase 3 registrational trial. When combined with data from the ongoing NEOD001 Phase 1/2 trial, the PRONTO trial has the potential to expedite patient access.

In addition to the ongoing Phase 1/2 clinical trial, The VITAL Amyloidosis Study is evaluating NEOD001 in newly-diagnosed, treatment-naïve patients with AL amyloidosis with cardiac dysfunction, and will assess a composite of all-cause mortality or cardiac hospitalizations in addition to biomarker, functional and quality of life endpoints. The PRONTO trial will evaluate NEOD001 in patients with AL amyloidosis and persistent cardiac dysfunction who have been previously-treated and are not eligible for The VITAL Amyloidosis Study.

"We are encouraged with the continued consensus of leading physicians regarding NT-proBNP as a surrogate endpoint for clinical trials as exemplified by the recently announced Amyloid Research Consortium (ARC) white paper," said Gene Kinney, PhD, Chief Scientific Officer and Head of Research and Development of Prothena. "We believe an ongoing dialogue, such as the Amyloidosis Patient Forum organized by ARC on November 16 with U.S. Food and Drug Administration, may accelerate further alignment on important topics such as the use of functional biomarkers as surrogate endpoints to expedite new therapeutic options for patients."

PRONTO Registration-Directed Trial Design

The global, multi-center, randomized, double-blind, placebo-controlled Phase 2b trial further exemplifies Prothena's commitment to provide disease-modifying therapeutic alternatives for patients suffering from AL amyloidosis. The trial is designed to enroll approximately 100 patients with a primary diagnosis of AL amyloidosis and persistent cardiac dysfunction despite previous treatment with off-label, plasma cell directed therapy. Patients will be randomized on a 1:1 basis to receive 24 mg/kg of NEOD001 or placebo via infusion every 28 days.

The primary endpoint is NT-proBNP best response as measured over 12 months. Secondary endpoints include evaluations of Short-form 36 (SF-36, quality of life measure), six-minute walk test, and renal function as assessed by proteinuria. Prothena designed the study with 80% power to detect a difference of 26.5% in NT-proBNP best response rate between the treatment and placebo groups with a two-sided alpha of 0.05.

Expansion Cohort of Phase 1/2 Trial

Prothena increased enrollment to 42 patients from the originally planned 25 patients in the expansion cohort of the ongoing NEOD001 Phase 1/2 trial based on an increased level of interest from physicians and patients following data presentations at the American Society of Clinical Oncology (ASCO) and European Hematology Association (EHA) conferences in June 2015.

Enrollment is now complete and includes 15 patients with cardiac dysfunction, 16 patients with renal dysfunction and 11 patients

with peripheral neuropathy. All patients receive 24 mg/kg NEOD001 by intravenous infusion every 28 days. The expansion cohort will continue to evaluate safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 as well as the specific clinical activity against cardiac and renal functional biomarkers, and a modified neuropathy impairment score. Given the increase in enrollment, topline results for the expansion cohort of the Phase 1/2 trial are expected to be announced in the second quarter of 2016 when the trial is complete and patients have been on therapy for a minimum of 9 months. Full results are expected to be presented at a medical conference around mid-2016.

Conference Call Details

Prothena management will discuss the PRONTO trial design for NEOD001, in a live audio webcast and conference call today, Thursday, October 15 at 4:30 p.m. ET. The webcast and slide presentation will be made available on the Company's website at www.prothena.com under the Investors tab in the Events and Presentations section. Following the live audio webcast, a replay of the webcast will be available on the Company's website for at least 90 days.

To access the call via dial-in, please dial**: (877) 887-5215** (U.S. toll free) or **(315) 625-3069** (international) five minutes prior to the start time and refer to conference ID number 45152199. The webcast will be available at http://ir.prothena.com. A replay of the call will be available for at least 90 days via dial-in at **(855) 859-2056** (U.S. toll free) or **(404) 537-3406** (international), Conference ID Number **45152199**.

About NEOD001

NEOD001 is a humanized monoclonal antibody that specifically targets the circulating soluble amyloid and deposited insoluble amyloid that accumulates in both the AL and AA forms of amyloidosis. Patients with AL amyloidosis may be eligible to enroll in one of two clinical trials for NEOD001. The VITAL Amyloidosis Study, a double-blind, placebo-controlled, global Phase 3 registrational trial, is evaluating NEOD001 in newly-diagnosed, treatment-naïve patients with AL amyloidosis, and will assess a composite of all-cause mortality or cardiac hospitalizations in addition to biomarker, functional and quality of life endpoints. The PRONTO trial, a double-blind, placebo-controlled, global Phase 2b registration-directed trial, will evaluate NEOD001 in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction, and will assess NT-proBNP best response over 12 months in addition to other functional biomarker, and quality of life endpoints. More information on The VITAL Amyloidosis Study and the PRONTO trial is available or will be provided at www.clinicaltrials.gov.

About AL Amyloidosis

Systemic amyloidoses are a complex group of progressive diseases caused by tissue deposition of misfolded proteins that result in progressive organ damage. The most common type, AL amyloidosis or primary amyloidosis, involves a hematological disorder caused by plasma cells that produce misfolded immunoglobulin light chain resulting in deposits of abnormal AL protein (amyloid) in the tissues and organs of individuals with this disease. There are no approved treatments for AL amyloidosis, and none that directly target potentially toxic forms of the AL protein. AL amyloidosis is a rare disorder and it is estimated that about 30,000 to 45,000 patients in the U.S. and Europe suffer from this disease. Both the causes and origins of AL amyloidosis remain poorly understood. For more information on AL amyloidosis, please visit the websites of the Amyloidosis Support Group and the Amyloidosis Foundation. For information on the recently announced white paper and regulatory meeting please visit the website of the Amyloid Research Consortium.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapies for the potential treatment of diseases that involve amyloid or cell adhesion. The Company is developing antibody-based product candidates that target a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002), and psoriasis and other inflammatory diseases (PRX003).

For more information, please visit the Company's web site at www.prothena.com.

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the potential for the PRONTO clinical trial and use of NT-proBNP as a primary endpoint to provide a basis for conditional approval of NEOD001 and accelerate its development timeline and commercial path to patients; the PRONTO trial design; future progress on The VITAL Amyloidosis Study; the possibility that use of functional biomarkers as surrogate endpoints may accelerate; and the expected timing for announcing results from the expansion portion of the Phase 1/2 clinical trial. 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 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 13, 2015 and our subsequent Quarterly Reports on Form 10-Q filed 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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