December 2, 2014

Prothena Initiates NEOD001 Global Phase 3 Registrational Trial Based on Positive Results in Ongoing Phase 1/2 Study of NEOD001 in Patients With AL Amyloidosis

- **New and Updated Results Show 50% Response Rate in 14 Cardiac-Evaluable Patients**
- **New Data Show 43% Best Response Rate in 14 Renal-Evaluable Patients**
- **Cardiac and Renal Biomarker Responses of Single-Agent NEOD001-Treated Patients Compare Favorably with Historical Data in Patients with AL Amyloidosis**
- **NEOD001 Continues to be Safe and Well-Tolerated, with No Dose Limiting Toxicities Observed**
- **Excellent Pharmacokinetic Properties and No Immunogenicity**
- **Currently Enrolling Expansion Portion of Phase 1/2 Trial with New Data Expected to be Presented Annually at Appropriate Medical Conferences, Beginning in 2015**
- **Prothena to Host Investor Conference Call and Webcast Today at 4:30 p.m. ET**

DUBLIN, Ireland, Dec. 2, 2014 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel antibodies for the potential treatment of diseases that involve amyloid or cell adhesion, today announced the initiation of the VITAL Amyloidosis Study, an international, multi-center, registrational Phase 3 clinical trial, based on positive results from an ongoing Phase 1/2 clinical study of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction.

"The results of our ongoing Phase 1/2 clinical study confirm and strengthen data presented in April 2014 at the XIV International Symposium on Amyloidosis and I'm pleased to report that as of September 30, 2014, we believe that the primary and secondary endpoints of the trial have been met. Importantly, we believe the robust 50.0% cardiac and 42.9% renal best response rates in patients treated with NEOD001 compare favorably with historical data that would have predicted 26.5% cardiac and approximately 24% renal response rates in patients treated solely with off-label standard of care," said Gene Kinney, PhD, Chief Scientific Officer and Head of Research and Development at Prothena. "We look forward to further evaluation of NEOD001 in the expansion portion of our Phase 1/2 study that is currently enrolling additional patients with AL amyloidosis and selected persistent organ dysfunction for which we expect to present initial results in 2015, and annually thereafter. Today, following favorable conversations with the US and EU regulatory bodies, we are excited to announce initiation of the VITAL study, our registrational Phase 3 trial in newly-diagnosed, treatment-naïve patients with AL amyloidosis."

Cardiac and Renal Biomarker Responses in Phase 1/2 Study

Seven of 14 cardiac-evaluable patients (50.0%) treated with NEOD001 demonstrated a cardiac response, defined as more than 30.0% and 300 pg/mL decrease in levels of NT-proBNP (a validated cardiac biomarker associated with mortality). Cardiac responders, on average, showed more NT-proBNP decline with added monthly NEOD001 infusions. The 50.0% cardiac response rate compares favorably with the expected results of a 26.5% cardiac response rate from historical data in patients treated solely with off-label standard of care (Comenzo, et al., Leukemia. 2012;26:2317-2325). As noted in numerous peer-reviewed publications, increasing levels of NT-proBNP predicts higher mortality rates in patients with AL amyloidosis. Conversely, decreasing levels of NT-proBNP predicts lower mortality rates.

In a best response analysis of renal-evaluable patients treated with NEOD001, six of 14 renal-evaluable patients (42.9%) demonstrated a response, defined as a 30.0% decrease in proteinuria in the absence of estimated glomerular filtration rate (eGFR) worsening. The 42.9% renal response rate compares favorably with the expected results of an approximately 24% renal response rate from historical data in patients treated solely with off-label standard of care (Palladini, et al., Blood. 2014 124: 2325-2332). Increased levels of proteinuria and decreased eGFR predicts faster progression to dialysis where decreased levels of proteinuria and increased eGFR predicts delayed time to dialysis.

"NEOD001 potentially holds significant promise for patients with AL amyloidosis as we now see clinically meaningful decreases in both cardiac and renal biomarkers with monthly NEOD001 infusions," said Raymond L. Comenzo, MD, Professor of Medicine and Pathology at Tufts University School of Medicine. "NEOD001 appears to be the first agent that works directly to address the buildup of light-chain (AL) amyloid in organs. The results presented today strongly support moving into a Phase 3 trial, which I believe is designed to test whether or not NEOD001 provides meaningful clinical benefit for patients with AL amyloidosis."

Mechanism of Action

The clinical results demonstrated to date expand on more than a decade of amyloid research. NEOD001 elicits a rapid response initially, and a deepening response with additional monthly infusions. The results are consistent with the mechanism of

action showing that NEOD001 functions in two ways: neutralization of circulating soluble amyloid and clearance of deposited insoluble amyloid within affected organs. The Phase 1/2 data supports that NEOD001 acts as a disease-modifying agent in AL amyloidosis which is distinct from current off-label standard of care therapies that attempt to solely reduce production of immunoglobulin light chain and are associated with adverse events.

Safety, Tolerability, Pharmacokinetics and Immunogenicity

Data from the Phase 1/2 study continued to demonstrate that chronic monthly infusions of NEOD001 are safe and well-tolerated in patients with AL amyloidosis and persistent organ dysfunction. A database analysis as of September 30, 2014 showed a total of 27 patients in seven dosing cohorts received 209 infusions, with each patient treated on average for approximately eight months. No hypersensitivity reactions or drug-related serious adverse events were reported and no anti-NEOD001 antibodies were detected. NEOD001 demonstrated excellent pharmacokinetic properties, supporting a dose level of 24 mg/kg on a 28 day cycle. The most frequently reported adverse events (more than 10% of subjects) were fatigue, cough, dyspnea, diarrhea, upper respiratory infection, anemia, headache, hyponatremia, nausea and edema. All adverse events were mild to moderate and no dose limiting toxicities have been observed. As of September 30, 2014, 19 patients continue on therapy (eight patients discontinued). No patient discontinued due to drug-related adverse events. Following selection of 24 mg/kg as the Phase 3 recommended dose, in consultation with their treating physician, 13 out of 14 eligible patients continuing in the dose escalation portion of the Phase 1/2 study have chosen to escalate to 24 mg/kg.

Expansion Portion of Phase 1/2 Study

Prothena is now enrolling up to an additional 25 patients, with AL amyloidosis and selected persistent organ dysfunction, in an open-label expansion portion of the Phase 1/2 study. The company plans to enroll 10 patients with cardiac dysfunction, 10 patients with renal dysfunction and five patients with peripheral neuropathy, all of whom will receive 24 mg/kg intravenously every 28 days. The expansion phase will continue to evaluate safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 as well as the specific clinical activity against cardiac, renal and neuropathy biomarkers. The company expects to present results from the NEOD001 expansion portion of the Phase 1/2 study at least once annually at appropriate medical conferences, beginning in 2015.

VITAL Phase 3 Registrational Trial Design

The multi-center, randomized, double-blind, placebo-controlled Phase 3 study continues Prothena's commitment to provide disease-modifying therapeutic alternatives for patients suffering from AL amyloidosis. The trial is designed to support global regulatory approvals and to enroll approximately 230 newly-diagnosed, treatment-naïve patients with cardiac dysfunction. Patients will be randomized on a 1:1 basis to receive 24 mg/kg of NEOD001 or placebo via infusion every 28 days, with both arms receiving concurrent standard of care therapy.

The composite primary endpoint is event-based, with all-cause mortality or cardiac hospitalizations as qualifying events. Secondary endpoints of the study include evaluation of the cardiac biomarker NT-proBNP, renal biomarker proteinuria, six-minute walk test, and multiple quality of life evaluations including SF-36 and the Kansas City Cardiomyopathy Questionnaire. Prothena designed the study with 90% power to detect as little as 30% change in the event rate between the treatment and placebo groups with a two-sided alpha of 0.05. The trial allows for an interim analysis to assess the primary endpoint for efficacy and futility.

"Based on the encouraging results from our ongoing NEOD001 Phase 1/2 clinical study, which confirms safety, tolerability and pharmacokinetic properties, and noteworthy responses in patients with organ dysfunction, we are pleased to initiate the VITAL study, our global Phase 3 trial for newly-diagnosed, treatment-naïve patients with AL amyloidosis," said Dale Schenk, PhD, President and Chief Executive Officer of Prothena. "We believe the responses in multiple organs of NEOD001-treated patients compare favorably to historic data in AL amyloidosis, and support and inform the initiation of the VITAL study, our global Phase 3 registrational trial."

"This is an important event for the AL amyloidosis community, who is in desperate need of new safe and well tolerated therapeutic alternatives for this deadly, progressive disease. It is also a significant corporate milestone for Prothena, as it marks the first Phase 3 program to evaluate a disease-modifying agent targeting toxic amyloid in AL amyloidosis," continued Dr. Schenk.

Conference Call Details

Prothena management will discuss these new Phase 1/2 study results with NEOD001 for the treatment of AL amyloidosis in addition to the Phase 3 study design for NEOD001, in a live audio webcast and conference call today, Tuesday, December 2, 2014 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 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 42271521. The webcast will be available at http://ir.prothena.com. A replay of the call will be available until December 9, 2014 via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 42271521.

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. NEOD001 was granted orphan drug designation for the treatment of AL and AA amyloidosis by the U.S. Food and Drug Administration in 2012 and for the treatment of AL amyloidosis by the European Medicines Agency in 2013. The ongoing multi-center Phase 1/2 clinical trial is evaluating the safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction. The study is also evaluating exploratory biomarkers for cardiac, renal and hepatic function. The VITAL study, a double-blind, placebo-controlled Phase 3 trial, will evaluate NEOD001 in newly-diagnosed, treatment-naïve patients with AL amyloidosis, and will assess all-cause mortality and cardiac hospitalizations in addition to biomarker, functional and quality of life endpoints. More information on both the Phase 1/2 and VITAL Phase 3 trials 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 AL protein 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 that directly target potentially toxic forms of the AL protein. AL amyloidosis is a rare disorder and it is estimated that about 15,000 patients in the U.S. and Europe suffer from AL amyloidosis. Both the causes and origins of AL amyloidosis remain poorly understood.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel antibodies for the potential treatment of diseases that involve amyloid or cell adhesion. The Company focuses on therapeutic monoclonal antibodies directed specifically to disease-causing proteins and its antibody-based product candidates target a number of potential indications including AL and AA forms of amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002) and novel cell adhesion targets involved in psoriasis and other inflammatory diseases (PRX003).

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

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the design and expected timing, scope and enrollment of the expansion portion of our Phase 1/2 study and the VITAL study, our Phase 3 trial for NEOD001; the potential clinical benefit of NEOD001; and the timing of reporting additional data from the ongoing Phase 1/2 clinical trial of NEOD001. 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 7, 2014, 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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