June 2, 2015

Prothena Presents Compelling New Data From Ongoing Phase 1/2 Study of NEOD001 in Patients With AL Amyloidosis at 2015 ASCO Annual Meeting

- **Positive NEOD001 Phase 1/2 Results Further Support the Design of The VITAL Amyloidosis Study, a Global Phase 3 Registrational Trial**
- **Increase in Best Response Rate to 60% in 15 Renal-Evaluable Patients**
- **Increase in Best Response Rate to 57% in 14 Cardiac-Evaluable Patients**
- **Results Consistent with Proposed Mechanism of Action, Indicating NEOD001 Neutralizes and Clears Amyloid to Improve Cardiac and Renal Function**
- **NEOD001 Cardiac and Renal Biomarker Responses More Than Double Published Historical Rates Reported in AL Amyloidosis Studies**
- **NEOD001 Continued to be Safe and Well-Tolerated, with No Dose Limiting Toxicities Observed**
- **Excellent Pharmacokinetic Properties and No Immunogenicity**
- **Dr. Morie A. Gertz of the Mayo Clinic to Present Data during Prothena's Investor Conference Call and Webcast Today at 3:00 p.m. EDT**

DUBLIN, Ireland, June 2, 2015 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs, today announced new clinical data from the multiple ascending dose portion of its ongoing Phase 1/2 trial of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction. With additional monthly infusions, the data continued to demonstrate an excellent safety profile as well as increased clinical biomarker activity for NEOD001, leading to best response rates of 60.0% in renal-evaluable patients and 57.1% in cardiac-evaluable patients. These data will be presented today in an oral session at the 2015 ASCO Annual Meeting by Dr. Morie A. Gertz of the Mayo Clinic at 12:45 p.m. EDT.

"These data add to, and strengthen, our previously reported results from December, further demonstrating that additional monthly infusions of NEOD001 result in increased renal and cardiac biomarker responses," said Dale Schenk, PhD, President and Chief Executive Officer of Prothena. "We believe the increase in renal responses in this data set supports NEOD001's proposed ability to clear insoluble amyloid from the glomeruli of the kidney, which leads to reduction of proteinuria. Just as decreased NT-proBNP levels correlate to increased survival, decreased proteinuria levels signal improved kidney function. These positive Phase 1/2 results allow us to continue to proceed in confidence with our global Phase 3 VITAL Amyloidosis Study."

Renal and Cardiac Biomarker Responses in NEOD001 Phase 1/2 Study

In a best response analysis, nine of 15 renal-evaluable patients (60.0%) treated with NEOD001 demonstrated a renal response, defined as a 30.0% decrease in proteinuria in the absence of estimated glomerular filtration rate (eGFR) worsening, and the remaining six patients (40.0%) achieved stable disease. The 60.0% renal best response rate is more than double the expected renal best response rate of approximately 24% 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 predict faster progression to dialysis whereas decreased levels of proteinuria and increased eGFR predict delayed time to dialysis.

In a best response analysis, eight of 14 cardiac-evaluable patients (57.1%) treated with NEOD001 demonstrated a cardiac response, defined as more than 30.0% and 300 pg/mL decrease in levels of NT-proBNP (an established cardiac biomarker that is predictive of mortality in patients with AL amyloidosis), and the remaining six patients (42.9%) achieved stable disease. Also, additional monthly infusions of NEOD001 were observed to be significantly correlated with NT-proBNP decline ($p < 0.0001$). The 57.1% cardiac best response rate is more than double the expected cardiac best response rate of 26.5% 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 predict higher mortality rates in patients with AL amyloidosis. Conversely, decreasing levels of NT-proBNP following intervention predict lower mortality rates.

"The ultimate goal of protein immunotherapy in this patient population is to reduce organ dysfunction, and the data we presented today indicates that NEOD001 induces a clinically-meaningful reduction in both renal and cardiac biomarkers," said Dr. Morie A. Gertz, Mayo Clinic. "Notably, it is unlikely that the organ response rates observed in the NEOD001 Phase 1/2 study are related to prior hematologic therapy due to the magnitude of the responses and the variable time since last plasma cell dyscrasia therapy. Organ response rates have been shown to correlate well with organ failure and mortality. These data, taken together with the excellent safety and tolerability profile, indicate that NEOD001 could transform the treatment paradigm for patients with AL amyloidosis, potentially offering the first disease-modifying therapy for this devastating disease."

Mechanism of Action

The clinical results demonstrated in this study to date expand on more than a decade of amyloid research by Prothena. The most recent results are consistent with the proposed mechanism of action demonstrating 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 continued to support that NEOD001 acts as a disease-modifying agent in AL amyloidosis, distinct from current off-label standard of care therapies that solely attempt to reduce the production of newly produced immunoglobulin light chains and often result in serious side effects, without directly clearing the residual amyloid.

Safety, Tolerability, Pharmacokinetics and Immunogenicity

Data from the Phase 1/2 study continued to demonstrate that monthly infusions (every 28 days) of NEOD001 are safe and well-tolerated in patients with AL amyloidosis and persistent organ dysfunction. An interim analysis as of February 28, 2015 showed that a total of 27 patients in seven dosing cohorts received 327 infusions, with an average treatment duration of 12 months. No hypersensitivity reactions or drug-related serious adverse events were reported and no anti-NEOD001 antibodies were detected. NEOD001 also continues to demonstrate excellent pharmacokinetic properties, supporting a dose level of 24 mg/kg on a 28 day cycle. The most frequently reported treatment-emergent adverse events (more than 10% of subjects) were fatigue, upper respiratory tract infection, cough, dyspnea, headache, anemia, increased blood creatinine, edema, diarrhea, nausea and hyponatremia. No dose limiting toxicities have been observed and no patient discontinued treatment due to drug-related adverse events. All patients remaining in the study escalated to 24 mg/kg as of December 2, 2014.

Global Clinical Development Strategy

Consistent with Prothena's commitment to provide disease-modifying therapeutic alternatives for patients suffering from AL amyloidosis, the company initiated a global, Phase 3 registrational clinical trial, The VITAL Amyloidosis Study, based on positive results from the ongoing Phase 1/2 trial. In addition, Prothena is enrolling patients with AL amyloidosis and selected persistent organ dysfunction in an open-label expansion portion of the ongoing Phase 1/2 trial.

The VITAL Amyloidosis Study - Global Phase 3 Trial

Prothena is enrolling newly-diagnosed, treatment-naïve patients in a multi-center, randomized, double-blind, placebo-controlled global Phase 3 study. 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 a 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.

A poster presentation detailing the design of The VITAL Amyloidosis Study was also presented during the 2015 ASCO Annual Meeting (Abstract #TPS8614) by Dr. Michaela Liedtke of Stanford Comprehensive Cancer Center.

Expansion Portion of Phase 1/2 Study

Due to the high level of interest from patients and physicians, we now expect to enroll up to 29 patients in the expansion portion of the Phase 1/2 study. As of May, 27, 2015, Prothena has enrolled 25 of 29 patients, including 10 of 12 patients with cardiac dysfunction, 11 of 12 patients with renal dysfunction and four of five patients with peripheral neuropathy, who are receiving, or 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 and renal biomarkers, and the modified neuropathy impairment score. The company expects to present results from the expansion portion of the NEOD001 Phase 1/2 study in the fourth quarter of 2015.

Conference Call and Webcast Details

Dr. Morie A. Gertz will join Prothena management to discuss the updated clinical data from its ongoing Phase 1/2 trial of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction during a live audio webcast and conference call today at 3:00 p.m. EDT. 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 conference 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 44777703. A replay of the call will be available until June 9, 2015 via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 44777703.

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. 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 and renal function. Separately, The VITAL Amyloidosis Study, a double-blind, placebo-controlled, global Phase 3 registrational 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. For more information on both the Phase 1/2 and VITAL Phase 3 trials, please visit www.clinicaltrials.gov, and search identifiers NCT01707264 (Phase 1/2) and NCT02312206 (VITAL Phase 3).

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 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.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapy programs 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 design and expected timing, scope, enrollment and results of our on-going Phase 1/2 and VITAL Phase 3 clinical trials of NEOD001; the potential clinical benefits of NEOD001; and the estimated timeline for reporting data from the expansion portion of the Phase 1/2 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.

CONTACT: Investors: Tran Nguyen, CFO

650-837-8535, IR@prothena.com

Media: Angela Bitting

925-202-6211, angela.bitting@prothena.com