July 5, 2016

Prothena Presents New Data from Phase 1/2 Study of NEOD001 Demonstrating Improvements in Three Organ Systems in Previously-Treated Patients with AL Amyloidosis

- **New data from Phase 1/2 dose-escalation (n=27) and expansion (n=42) study show best response rates in total cardiac- and renal- evaluable patients of 53% and 63%, respectively, that are consistent with those previously published in the Journal of Clinical Oncology**
- **Improvement of peripheral neuropathy was demonstrated by a mean 35% decrease in the Neuropathy Impairment Score-Lower Limb (NIS-LL) in peripheral neuropathy expansion cohort**
- **Continued to be safe and well tolerated**
- **Dr. Morie A. Gertz, Chair of Internal Medicine at Mayo Clinic, to present data during Prothena's investor conference call and webcast today at 10:30 AM EDT**

DUBLIN, Ireland, July 05, 2016 (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 new clinical data from the Phase 1/2 dose-escalation and expansion study of NEOD001, the company's lead program in development as a potential disease-modifying therapy for AL amyloidosis. Data from patients in the expansion cohorts (n=42), consisting of patients in three prospectively defined cohorts of cardiac (n=15), renal (n=16) and peripheral neuropathy (n=11), and from the total Phase 1/2 study population (N=69), are being presented by Morie A. Gertz MD, of Mayo Clinic in an oral session at the 15th International Symposium on Amyloidosis (ISA) in Uppsala, Sweden today at 9:15 AM ET, and also in an investor webcast at 10:30 AM EDT.

New interim data from the Phase 1/2 study as of May 9, 2016, demonstrated best response rates from total cardiac- (n=36) and renal- (n=35) evaluable patients of 53% and 63%, respectively, that are consistent with the interim analysis from the dose-escalation phase published February 2016 in the Journal of Clinical Oncology (Gertz, et al, 2016). In the first exploratory analysis of this kind, NEOD001 demonstrated improvement of peripheral neuropathy, evidenced by a mean 35% decrease in the NIS-LL in the expansion cohort (n=11), leading to an 82% response rate. Two patients in this cohort demonstrated complete resolution of their peripheral neuropathy, as measured by NIS-LL. The Phase 1/2 study (N=69) consists of previously-treated patients with AL amyloidosis and persistent organ dysfunction who received a mean of 2.5 prior lines of plasma cell directed therapy. NEOD001 continued to be safe and well tolerated, with study participants having received more than 900 monthly infusions with a mean treatment duration of 13.2 months.

"The consistent cardiac and renal response rates we see in patients in the NEOD001 Phase 1/2 study are unprecedented with current treatment options," said Morie A. Gertz, MD, of Mayo Clinic and principal investigator of the study. "The magnitude of response rates in these previously-treated patients is particularly impressive, as those of us who treat patients with AL amyloidosis would expect notably lower organ responses following prior plasma cell directed therapy. These cardiac, renal, and peripheral neuropathy data demonstrate evidence of improvement in three organ systems, providing further support for the potential for NEOD001 to transform the treatment paradigm for patients with AL amyloidosis. The improvements to three organ systems demonstrated in this Phase 1/2 study of NEOD001 provide additional evidence that targeting amyloid has the potential to improve organ function in patients with AL amyloidosis, which is the ultimate goal of treatment."

Cardiac and Renal Responses from NEOD001 Phase 1/2 Study

In a best response analysis of patients in the Phase 1/2 study who received NEOD001, 53% or 19 of 36 total cardiac-evaluable patients and 47% or seven of 15 prospectively defined cardiac expansion cohort patients, demonstrated a cardiac response, defined as more than 30% and 300 pg/mL decrease in levels of NT-proBNP. These cardiac best response rates compare favorably to cardiac response rates of 0% to 15% from available published historical data in patients previously-treated with plasma cell directed therapy (Palladini et al, Haematologica, 2013; Dispenzieri et al, Blood, 2012), and are consistent with the best response rate of 57% or 8 of 14 cardiac-evaluable patients reported in the interim analysis of the dose-escalation phase (n=27) of the NEOD001 Phase 1/2 study published in the Journal of Clinical Oncology. As consistently demonstrated in numerous peer-reviewed publications, the functional biomarker NT-proBNP predicts survival in patients with AL amyloidosis. Increasing levels of NT-proBNP predict higher mortality in patients with AL amyloidosis. Conversely, decreasing levels of NT-proBNP following intervention predict increased survival.

The 36 cardiac-evaluable patients are comprised of 14 patients from the dose-escalation phase and 22 patients from the

expansion phase, consisting of 15 from cardiac, three from renal, and four from peripheral neuropathy expansion cohorts.

In a best response analysis of patients in the Phase 1/2 study who received NEOD001, 63% or 22 of 35 total renal-evaluable patients and 63% or 10 of 16 prospectively defined renal expansion cohort patients demonstrated a renal response, defined as a 30% decrease in proteinuria in the absence of estimated glomerular filtration rate (eGFR) worsening. These renal best response rates compare favorably to renal response rates of 17% to 29% from published historical data in patients previously-treated with plasma cell directed therapy (Palladini et al, Haematologica, 2013; Dispenzieri et al, Blood, 2012; Reece et al, Blood, 2011), and are consistent with the best response rate of 60% or 9 of 15 renal-evaluable patients reported in the interim analysis of the dose-escalation phase (n=27) of the NEOD001 Phase 1/2 study published in the Journal of Clinical Oncology. 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.

The 35 renal-evaluable patients are comprised of 15 patients from the dose-escalation phase and 20 patients from the expansion phase, consisting of 16 from renal, three from cardiac, and one from peripheral neuropathy expansion cohorts.

"Best response rates of 53% and 63% demonstrated in total cardiac- and renal-evaluable patients, respectively, are consistent with those previously reported, and suggests that directly targeting amyloid has the potential to improve organ function in patients with AL amyloidosis," said Dale Schenk PhD, President and Chief Executive Officer of Prothena. "We now have a robust data set of nearly 70 patients that informs our ongoing NEOD001 clinical development program. The organ response rates from the expansion cohorts were consistent with the overall study population, and increase our confidence in the design and powering assumptions for both the PRONTO and VITAL studies. These studies remain on track and we expect the VITAL study to be fully enrolled in the second quarter of 2017 and expect topline results from the PRONTO study in late 2017 or early 2018."

Peripheral Neuropathy Expansion Cohort Data from NEOD001 Phase 1/2 Study

In addition, an improvement in peripheral neuropathy in patients in the prospectively defined peripheral neuropathy expansion cohort was demonstrated by a mean 35% (median 23%) decrease in the NIS-LL measured at month 10, indicating improvement to a third organ system in NEOD001-treated patients. Complete resolution of peripheral neuropathy, as measured by NIS-LL, was achieved in two patients in this cohort. Improvements in patient NIS-LL scores resulted in a response rate of 82% or nine of 11 patients in the peripheral neuropathy expansion cohort of the Phase 1/2 study. A response on the NIS-LL is defined as a less than 2-point increase on the 88-point scale. NIS-LL is a composite clinical scoring scale used as a clinical endpoint in peripheral neuropathy studies and measures muscle weakness, sensation and reflexes. Peripheral neuropathy is a common and progressive component of AL amyloidosis seen in 20% to 37% of patients (Bayliss M, et al, poster P784 presented at EHA 2015), which negatively affects patient quality of life and does not improve with current treatments.

"AL amyloidosis takes a toll on patients' day-to-day functioning and when multiple organs are impaired, patients' quality of life can be particularly poor," noted Isabelle Lousada, President and Chief Executive Officer of the Amyloidosis Research Consortium. "From a patient perspective, improvement in quality of life is often as important as medical improvement. I am encouraged by the new data showing NEOD001 improves multiple organ systems, and the potential that this may be shown to translate into a better quality of life."

Safety, Tolerability, and Immunogenicity from NEOD001 Phase 1/2 Study

Data from all patients (N=69) in the Phase 1/2 study continued to demonstrate that monthly infusions (every 28 days) of NEOD001 were safe and well tolerated. An interim analysis as of May 9, 2016 showed that a total of 69 patients received 913 infusions of up to 24 mg/kg, with a mean treatment duration of 13.2 months. The Phase 1/2 study (N=69) consists of previously-treated patients with AL amyloidosis and persistent organ dysfunction who received a mean of 2.5 prior lines of plasma cell directed therapy. No hypersensitivity reactions or drug-related serious adverse events were reported and no anti-NEOD001 antibodies were detected. The most commonly reported treatment-emergent adverse events, regardless of relationship to study drug were fatigue, upper respiratory tract infection, nausea, diarrhea, edema, anemia, and dizziness. No dose limiting toxicities have been observed and no patient discontinued treatment due to drug-related adverse events.

"We'd like to acknowledge and thank the patients and their caregivers, physicians and their site staff, and all involved who are helping to advance our understanding of NEOD001 as a potential treatment for AL amyloidosis," added Schenk. "In addition to the upcoming milestones in our NEOD001 program, we expect our active clinical pipeline to deliver several additional near-term R&D milestones, including topline results from the Phase 1b study of PRX002 in patients with Parkinson's disease in fourth quarter of this year, and interim data from the Phase 1b study of PRX003 in patients with psoriasis by mid-2017."

Global Clinical Development Strategy

Consistent with a commitment to develop a disease-modifying therapy for patients with AL amyloidosis, Prothena is currently enrolling two global, multi-center, randomized, double-blind, placebo-controlled clinical studies for NEOD001.

Phase 2b PRONTO Registration-Directed Study (NCT# 02632786, EudraCT# 2015-004318-14):
In October 2015, Prothena announced the PRONTO study, which is enrolling patients with AL amyloidosis and persistent cardiac dysfunction who have been previously treated with plasma cell directed therapy. PRONTO is a global, Phase 2b multi-center, randomized, double-blind, placebo-controlled, registration-directed study. The study is designed to enroll approximately 100 patients who 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 best response over 12 months of the cardiac functional biomarker NT-proBNP, defined by the consensus criteria of NT-proBNP change. Secondary endpoints include evaluations of Short-form 36 (SF-36, a quality of life measure), Six-Minute Walk Test, proteinuria (a renal functional biomarker), and NIS-LL. The study was designed with 80% power to detect an absolute difference of 26.5% in NT-proBNP best response rate between the treatment and placebo groups with a two-sided alpha of 0.05.

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

A poster presented at the 2016 ASCO Annual Meeting on the design of the PRONTO study can be found here.

Phase 3 VITAL Registrational Study (NCT# 02312206, EudraCT# 2014-003865-11):
In December 2014, Prothena announced The VITAL Amyloidosis Study, which is enrolling newly-diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction. VITAL is a global, Phase 3 multi-center, randomized, double-blind, placebo-controlled, registrational study. The study is designed to enroll approximately 230 patients who 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, proteinuria (a renal functional biomarker), SF-36, Six-minute Walk Test, and NIS-LL. The study was designed 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 VITAL Amyloidosis Study is designed to support full global registration.

A poster presented at the 2015 ASCO Annual Meeting on the design of The VITAL Amyloidosis Study can be found here.

Conference Call and Webcast Details

Dr. Morie A. Gertz of Mayo Clinic will join Prothena management to discuss the new clinical data from its Phase 1/2 study of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction during a live audio webcast and conference call on July 5, 2016 at 10:30 AM 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.

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 39206695. A replay of the webcast and call will be available until July 12, 2016 via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 39206695.

About NEOD001

NEOD001 is a 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 studies for NEOD001. The PRONTO study, a global, Phase 2b, double-blind, placebo-controlled, registration-directed study, will evaluate NEOD001 in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction, and will best response over 12 months of the cardiac functional biomarker NT-proBNP, defined by the consensus criteria of NT-proBNP change, in addition to other biomarker, quality of life and functional endpoints. The VITAL Amyloidosis Study, a global, Phase 3, double-blind, placebo-controlled, registrational study, 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, quality of life and functional endpoints. More information on the PRONTO study and The VITAL Amyloidosis Study is available at www.clinicaltrials.gov, by searching NCT #02632786 for PRONTO, and NCT #02312206 for VITAL or www.clinicaltrialsregister.eu, by searching EudraCT #2015-004318-14 for PRONTO, and EudraCT #2014-003865-

11 for VITAL.

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 global, late-stage clinical biotechnology company seeking to fundamentally change the course of progressive diseases with its clinical pipeline of novel therapeutic antibodies. Fueled by its deep scientific understanding built over decades of research in protein misfolding and cell adhesion — the root causes of many serious or currently untreatable amyloid and inflammatory diseases — Prothena has advanced several drug candidates into clinical studies while pursuing discovery of additional novel therapies. Our pipeline of antibody-based product candidates targets a number of potential indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002) and inflammatory diseases, including psoriasis (PRX003), and TTR amyloidosis (PRX004). 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 potential of NEOD001 to be a disease-modifying therapy for AL amyloidosis and transform the treatment paradigm for patients; the potential of directly targeting amyloid to improve organ function in patients with AL amyloidosis; the timing of the VITAL study being fully enrolled and announcing topline results from the PRONTO study; the potential of the PRONTO study to expedite patient access; the potential of the VITAL study design to support full global registration; the potential of our active clinical pipeline to deliver several additional near-term R&D milestones; and the timing of announcing topline results from the Phase 1b study of PRX002 in patients with Parkinson's disease and interim data from the Phase 1b study of PRX003 in patients with psoriasis. 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 February 25, 2016 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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