April 23, 2014

Prothena's NEOD001 Demonstrates Encouraging Cardiac Biomarker Responses in Ongoing Phase 1 Study in Patients With Immunoglobulin Light Chain (AL) Amyloidosis

- **NEOD001 appears generally safe, well-tolerated, has acceptable pharmacokinetic properties and no immunogenicity at studied dose levels**
- **No dose limiting toxicities have been observed**
- **Eight of nine evaluable patients with AL amyloidosis with cardiac involvement either achieved responses (N=5) or were considered stable (N=3)**
- **Additional Phase 1 data updates of NEOD001 expected at medical conferences later this year**
- **Expect to initiate Phase 2/3 clinical trial of NEOD001 in the fourth quarter of 2014**

DUBLIN, Ireland, April 23, 2014 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a clinical stage biotechnology company focused on the discovery, development and commercialization of novel antibodies for the potential treatment of diseases that involve protein misfolding or cell adhesion, announced today that an abstract was published by the XIV International Symposium on Amyloidosis (ISA) and described interim data from an ongoing Phase 1 study of NEOD001, a monoclonal antibody in clinical development for the treatment of patients with AL amyloidosis and persistent organ dysfunction, as of the abstract submission date. Updated data will be presented for the first time at ISA in Indianapolis, Indiana.

"AL amyloidosis is a hematological disorder caused by plasma cells that produce misfolded AL protein. The abnormal AL protein forms deposits, known as amyloid, in the tissues and organs of individuals suffering from this disease," said Michaela Liedtke, MD, Assistant Professor of Medicine at Stanford University. "Autologous stem cell therapy and off-label use of chemotherapy is often used in an effort to reduce or eliminate the plasma cells producing the misfolded protein, but even after treatment, residual organ dysfunction remains the primary cause of morbidity and mortality for patients suffering from AL. It is exciting to observe that some patients are potentially responding to NEOD001 as we look to confirm these interim results in a larger Phase 2/3, controlled clinical trial. A therapy that works effectively for AL would be welcomed by the amyloidosis community."

"NEOD001 is the first potential treatment that directly targets the toxic forms of the AL protein and offers hope for this unmet medical need," said Dale Schenk, PhD, President and Chief Executive Officer of Prothena. "The encouraging signals observed in this ongoing Phase 1 study, both in safety and tolerability and in the cardiac biomarker responses, suggest that a Phase 2/3 study is warranted to further evaluate the safety and efficacy of NEOD001."

The Phase 1 study is evaluating the safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction. It is also designed to define a maximally tolerated dose and/or recommended dose(s) for a Phase 2/3 study and to evaluate exploratory biomarkers of cardiac, renal and hepatic function.

At the date of the abstract submission, 15 patients, with a median age of 60 years and a median of two organs involved, had been treated with NEOD001, administered intravenously once per month at five dose levels ranging from 0.5 to 8.0 mg/kg for a period of one to nine months. At the time of enrollment into the study, all patients completed one or more prior anti-plasma cell therapies, did not require additional chemotherapy, and had persistent organ dysfunction.

Key data from the published abstract include:

Safety and Tolerability

The interim data demonstrate that NEOD001 was generally safe and well-tolerated at the doses studied. In addition, NEOD001 demonstrated acceptable pharmacokinetic properties and immunogenicity was not observed in any patient. The most frequently reported adverse events were musculoskeletal (N=4), infection (N=4), and fatigue (N=3). All adverse events were mild to moderate and no dose limiting toxicities have been observed. A total of three patients had discontinued the trial at the time of abstract submission: one due to hematological progression, one due to organ progression and one due to withdrawal of consent.

Evidence of Cardiac Biomarker Activity

Of the 15 patients enrolled in the study at the time of abstract submission, 9 patients (56%) had pre-specified baseline levels of the N-terminal prohormone of brain natriuretic peptide (NT-proBNP) that were ≥ 650 pg/mL (required baseline level for

evaluation) and at least one post-baseline NT-proBNP determination. Of those 9 patients, one patient met the progression criteria based on an increase of NT-proBNP, and the remaining 8 patients either met the response criteria based on a decrease in NT-proBNP or were considered stable. Specifically, 5 of 9 (56%) patients had NT-proBNP levels that decreased to a level that met pre-defined response criteria, 3 of 9 (33%) patients had stable NT-proBNP levels, and 1 of 9 (11%) patients showed an increase in NT-proBNP levels in a manner that met pre-defined progression criteria.

Presentation of NEOD001 Poster at ISA

Presentation of the NEOD001 poster at ISA will include updated safety, tolerability, pharmacokinetic and NT-proBNP data from the ongoing Phase 1 study as of March 11. The full poster will be made available at www.prothena.com on April 29 at 8:00 a.m. EDT (concurrent with when it will be made available for viewing at ISA).

(Abstract #PB-48) Preliminary cardiac biomarker responses demonstrated in an ongoing phase 1 study of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction

- Presenter: Dr. Michaela Liedtke, Stanford Cancer Institute, Stanford, California
- Presentation Date and Time: Tuesday, April 29, 4:30-6:00 p.m. EDT

About NEOD001

NEOD001 is a humanized monoclonal antibody that specifically targets the amyloid that accumulates in both 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 clinical trial is evaluating the safety, tolerability, pharmacokinetics and immunogenicity of NEOD001 in patients with AL amyloidosis and persistent organ dysfunction. The study is designed to define a maximally tolerated dose and/or recommended dose(s) for Phase 2/3. The study is also evaluating exploratory biomarkers for cardiac, renal and hepatic function. For more information, please visit www.clinicaltrials.gov and search identifier NCT01707264.

About AL Amyloidosis

Systemic amyloidoses are a complex group of 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 currently 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. 1,200 to 3,200 new cases of AL amyloidosis are reported each year in the United States. Both the causes and origins of AL amyloidosis remain poorly understood.

About Prothena

Prothena Corporation plc. is a clinical stage biotechnology company focused on the discovery, development and commercialization of novel antibodies for the potential treatment of diseases that involve protein misfolding or cell adhesion. We focus on therapeutic monoclonal antibodies directed specifically to disease-causing proteins. Our antibody-based product candidates target a number of potential indications including AL and AA forms of amyloidosis (NEOD001), Parkinson's disease and related synucleinopathies (PRX002) and novel cell adhesion targets involved in inflammatory diseases and cancers (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 within the meaning of the Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These statements relate to, among other things, the potential safety, efficacy, benefits and acceptance of our product candidates, including NEOD001; the nature and timing of our development programs, including the design of our Phase 1 study of NEOD001 and need for additional studies of NEOD001; evidence of cardiac biomarker activity in NEOD001; and the poster presentation of our abstract at the ISA. These forward-looking statements are identified by their use of terms and phrases such as "anticipate," "believe," "could," "should," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "target," "will" and similar terms and phrases, including references to assumptions. These statements are based on assumptions that may not prove accurate. 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 and uncertainties described in Prothena's SEC filings, including the "Risk Factors" section of Prothena's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. 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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