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# Prothena Presents New Research Supporting Clinical Relevance of Cardiac Biomarker NT-proBNP in AL Amyloidosis

- **Preclinical Research Demonstrating a Direct Relationship Between Misfolded Light Chain Toxicity and NT-proBNP Production**
- **Clinical Outcomes Research Showing a Correlation between NT-proBNP Response and Health-related Quality of Life**
- **Data Presented at Heart Failure Society of America Annual Meeting**

DUBLIN, Ireland, Sept. 18, 2017 (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 highlighted research from two new studies being presented at the Heart Failure Society of America (HFSA) Annual Scientific Meeting in Dallas, Texas that further supports the important role of the cardiac biomarker NT-proBNP in both the biology and clinical aspects of AL amyloidosis. Preclinical data presented in a moderated poster talk and poster session at the conference demonstrated the relationship between misfolded light chain toxicity to heart cells and production of NT-proBNP. In addition, a clinical outcomes study also presented by Prothena showed a correlation between NT-proBNP response and quality of life measures in patients who have AL amyloidosis with cardiac involvement. NT-proBNP is a cardiac biomarker that has been shown in multiple independent studies to predict survival in patients with AL amyloidosis (Merlini, et. al, *Leukemia,* 2016).

"These results provide new insights into the important role of NT-proBNP in AL amyloidosis, unique from other forms of heart failure, and offer further support for the clinical utility of NT-proBNP as a surrogate biomarker in AL amyloidosis studies," said Sarah Noonberg, MD, Ph.D., Chief Medical Officer of Prothena. "Furthermore, data from our clinical outcomes research demonstrate a clinically meaningful relationship between NT-proBNP response and quality of life improvements that are highly relevant to patients, and will be further evaluated in our two late-stage studies of NEOD001."

**New preclinical research supports relationship between lowering of NT-proBNP and improved survival in patients with AL amyloidosis**

New preclinical research presented at HFSA provides mechanistic insight into how misfolded light chains induce cardiotoxicity and increase NT-proBNP production. Prothena's research demonstrated that aggregated light chain induces oxidative stress and leads to an increase in expression of the oxidative response marker heme oxygenase-1 (Hmox-1) in cardiomyocytes. The research further showed that NT-proBNP secretion is increased by aggregated light chain, via a mechanism dependent on Hmox-1 catalytic activity. Aggregated light chain exhibited dose-dependent binding to cardiomyocytes, suggesting that the observed effect is driven by the direct interaction between aggregated light chains and cardiomyocytes.

Taken together, these results support the finding that aggregated light chain induces cardiomyocyte toxicity and provides a direct link between the misfolded protein and NT-proBNP elevation in AL amyloidosis.

Furthermore, these data indicate that the role of NT-proBNP in AL amyloidosis is differentiated from other forms of heart failure, and support the relationship that has been reported between lowering of NT-proBNP and improved cardiac function and survival in patients with AL amyloidosis.

**Clinical outcomes research demonstrates NT-proBNP response is associated with clinically meaningful improvements in health-related quality of life in patients with AL amyloidosis**

New clinical outcomes research also presented by Prothena at HFSA establishes for the first time a correlation between NT-proBNP response and health-related quality of life measures. In this study, data were extracted from a community-based sample of 108 patients with AL amyloidosis and validated against patient health records from an AL amyloidosis Center of Excellence (COE) sample of 95 patients. All patients in both samples had AL amyloidosis with cardiac involvement. Patients' health-related quality of life was evaluated using the SF-36® Health Survey for eight domains of functional health and well-being that provided two summary scores, one physical and one mental. Patients in the community-based sample were also evaluated by the Kansas City Cardiomyopathy Questionnaire — Short Form (KCCQ-12), a validated health-related quality of life measure that is specific to heart failure.

In the community-based sample (n=108), cardiac response was defined as a 30 percent or greater decrease in NT-proBNP. Differences in SF-36 scores for patients with and without a previous response in NT-proBNP were statistically significant ($p<0.05$ for all domains and both summary scores) and clinically meaningful. In addition, patients with a history of cardiac response reported SF-36 scores that were significantly better than existing congestive heart failure (CHF) benchmarks across all SF-36 domains and both summary components.

Differences in burden of disease as measured by KCCQ-12 scores for patients with and without previous NT-pro-BNP response were also statistically significant ($p < 0.05$ for all subscales). The average total KCCQ-12 score for patients with a history of NT-proBNP response (n=75) was 66, which corresponds to scores previously observed in patients with New York Heart Association (NYHA) functional class II symptoms, indicating slight limitation in physical activity. The average score for patients with no history of NT-proBNP response (n=33) was 42, which corresponds to scores previously observed in patients with NYHA functional class III symptoms, indicating a marked limitation in physical activity.

Results from the AL amyloidosis Center of Excellence validation patient cohort (n=95) showed comparable findings.

This study demonstrates the relationship between the cardiac biomarker NT-proBNP with health-related quality of life using multiple data sources and different analytic approaches. The data further support that NT-proBNP may be a useful surrogate measure for health-related quality of life and burden of disease classification of patients.

**About NEOD001**

NEOD001 is an investigational first-in-class antibody that specifically targets disease-causing misfolded light chain aggregates in AL amyloidosis. There are two ongoing global clinical studies for NEOD001. The PRONTO study, a global, Phase 2b, double-blind, placebo-controlled, registration-directed study, will evaluate NEOD001 vs. placebo in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction, and will assess best response over 12 months of the cardiac 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 vs. placebo in newly-diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction, with both arms of the study receiving standard of care. The VITAL study will assess a composite endpoint 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 diseases caused by tissue deposition of misfolded proteins that result in progressive organ damage. AL amyloidosis, the most common type, is a rare, progressive, and typically fatal disease caused by extracellular deposition of misfolded immunoglobulin light chains. An excess of light chains prone to misfolding are produced by clonal plasma cells. Soluble toxic aggregates and deposited fibrils (amyloid) lead to progressive failure of vital organs including the heart, kidneys and nervous system, causing significant morbidity and mortality. It is estimated that approximately 30,000 — 45,000 patients in the U.S. and Europe suffer from this disease. There are no approved treatments for AL amyloidosis, although patients may be treated with off-label therapies directed at the plasma cell dyscrasia. There is a large unmet need for therapies that specifically target soluble toxic aggregates and deposited fibrils, thereby improving vital organ function. For more information on AL amyloidosis, please visit the websites of the Amyloidosis Support Groups, The Amyloidosis Research Consortium, and the Amyloidosis Foundation.

**About Prothena**

Prothena Corporation plc is a global, late-stage clinical biotechnology company establishing fully-integrated research, development and commercial capabilities. 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 seeks to fundamentally change the course of progressive diseases associated with this biology. The Company's pipeline of antibody therapeutic candidates targets a number of indications including AL amyloidosis (NEOD001), Parkinson's disease and other related synucleinopathies (PRX002/RG7935), inflammatory diseases, including psoriasis and psoriatic arthritis (PRX003), and ATTR amyloidosis (PRX004). The Company continues discovery of additional novel therapeutic candidates where its deep scientific understanding of disease pathology can be leveraged. 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 relationship between misfolded light chain toxicity and NT-proBNP production; the correlation between NT-proBNP response and health-*

*related quality of life; whether aggregated light chain induces cardiomyocyte toxicity; the clinical utility of NT-proBNP as a surrogate biomarker in AL amyloidosis; and the correlation between lowering of NT-proBNP and improved cardiac function and survival in patients with AL amyloidosis. 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 27, 2017 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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