



April 23, 2018

Prothena Discontinues Development of NEOD001 for AL Amyloidosis

- | **Phase 2b PRONTO study did not meet its primary or secondary endpoints**
- | **Phase 3 VITAL Amyloidosis Study being discontinued based on futility analysis**
- | **Investor conference call and webcast today at 8:30 AM ET**

DUBLIN, Ireland, April 23, 2018 (GLOBE NEWSWIRE) -- Prothena Corporation plc (Nasdaq:PRTA), a clinical stage biotechnology company focused on the discovery and development of novel therapies in the neuroscience and orphan categories, today announced that the Company is discontinuing development of NEOD001, an investigational antibody that was being evaluated for the treatment of AL amyloidosis. The decision was based on results from the Phase 2b PRONTO study and a futility analysis of the Phase 3 VITAL study.

Based on the results from the Phase 2b PRONTO study, which did not meet its primary or secondary endpoints, the Company asked the independent data monitoring committee (DMC) of the Phase 3 VITAL study to review a futility analysis of the ongoing VITAL study. The DMC recommended discontinuation of the VITAL study for futility. The Company therefore decided to discontinue all development of NEOD001, including the VITAL study as well as the open label extension studies.

"We are deeply disappointed by this outcome, particularly for patients suffering from this devastating disease," said Gene Kinney, PhD, President and Chief Executive Officer of Prothena. "We are surprised by the results from these two placebo-controlled studies and will continue to analyze the resulting data to share insights with our collaborators in the scientific, medical and advocacy communities. We thank all of the patients, their families, caregivers, investigators, study staff and our employees. Their participation in and commitment to these studies are indispensable to advancing our shared goal of improving the lives of patients with amyloidosis."

The Phase 3 VITAL Study

The VITAL Amyloidosis Study was a Phase 3 global, multi-center, randomized, double-blind, placebo-controlled clinical study of NEOD001 vs. placebo in treatment-naïve patients with AL amyloidosis and cardiac dysfunction, with both arms of the study receiving standard of care. The composite primary endpoint was event-based, with all-cause mortality or cardiac hospitalizations as events.

- | The futility analysis, based on 103 adjudicated events of the 156 events specified to complete the study, was not statistically significant.
- | The hazard ratio was 0.84 favoring NEOD001 vs. control arm.

The Phase 2b PRONTO Study

The PRONTO study was a Phase 2b global, multi-center, randomized, double-blind, placebo-controlled clinical study of NEOD001 vs. placebo in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction.

No statistically significant differences were observed between treatment groups as summarized in the table below.		
	NEOD001	Placebo
Primary Endpoint		
Cardiac best response (NT-proBNP, modified consensus criteria) through 12 months of treatment	39.4%	47.6%
Key Secondary Endpoints		
Change in Short-form 36 (SF-36v2) Physical Component Summary Score (PCS) after 12 months of treatment (mean)	0.19	0.97
Change in 6-Minute Walk Test distance (meters) after 12 months of treatment (median)	19.25	8.00
NT-proBNP rate of change (slope) through 12 months of treatment	9.80	81.42
Additional Secondary Endpoints		
Renal best response (proteinuria and eGFR consensus criteria) through 12 months of treatment	53.8%	33.3%
Change in NIS-LL (total score) after 12 months of treatment (mean)	- 1.20	- 0.60
Exploratory Endpoint		
	4.5%	9.5%

In the PRONTO study, NEOD001 was generally safe and well tolerated.

"Prothena has a deep pipeline of novel therapeutics in clinical and preclinical development, including several partnered with leading strategic collaborators," stated Lars Ekman, MD, PhD, Chairman of Prothena's Board of Directors. "We have the resources and scientific expertise to continue to advance our pipeline through meaningful development milestones towards our goal of transforming patients' lives."

Investor Conference Call and Webcast Details

Prothena management will host a conference call and webcast to discuss the PRONTO study results today, April 23, 2018, at 8:30 AM 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 conference call and webcast, a replay will be available on the Company's website for at least 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 6976689. A replay of the webcast and call will be available until April 30, 2018 via dial-in at (855) 859-2056 (U.S. toll free) or (404) 537-3406 (international), Conference ID Number 6976689.

About the Phase 3 VITAL Study

The VITAL Amyloidosis Study was a Phase 3 global, multi-center, randomized, double-blind, placebo-controlled clinical study for NEOD001 in patients with AL amyloidosis. The study enrolled 260 newly diagnosed, treatment-naïve patients with AL amyloidosis and cardiac dysfunction. Patients were randomized on a 1:1 basis to receive 24 mg/kg of NEOD001 or placebo via intravenous infusion every 28 days, with both groups receiving concurrent standard of care therapy. The composite primary endpoint was event-based with all-cause mortality or cardiac hospitalizations counted as events. Secondary endpoints of the study included Short Form-36v2 Physical Component Summary Score, 6-Minute Walk Test distance and NT-proBNP best response.

About the Phase 2b PRONTO Study

The PRONTO study was a Phase 2b global, multi-center, randomized, double-blind, placebo-controlled clinical trial for NEOD001 in previously-treated patients with AL amyloidosis and persistent cardiac dysfunction. The study enrolled 129 previously-treated patients with AL amyloidosis with persistent cardiac dysfunction. Patients were randomized on a 1:1 basis to receive 24 mg/kg of NEOD001 (n=66) or placebo (n=63) via intravenous infusion every 28 days. The primary endpoint was cardiac best response as assessed by NT-proBNP through 12 months of treatment. Key secondary endpoints included Short Form-36v2 Physical Component Summary Score, 6-Minute Walk Test distance and NT-proBNP rate of change (slope). Additional secondary endpoints included the renal best response as assessed by proteinuria and estimated glomerular filtration rate, and Neuropathy Impairment Score-Lower Limb.

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 improve organ function and quality of life. 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, clinical biotechnology company focused on the discovery and development of novel therapies in the neuroscience and orphan categories. Fueled by its deep scientific understanding built over decades of research in protein misfolding, Prothena seeks to fundamentally change the course of progressive, life-threatening diseases associated with this biology. Prothena's pipeline of antibody therapeutic candidates targets a number of indications including Parkinson's disease and other related synucleinopathies (PRX002/RG7935) and ATTR amyloidosis (PRX004). The Company continues to advance additional discovery programs against targets including tau, A β (Amyloid beta) and

ALECT2 where its deep scientific understanding of disease pathology can be leveraged. For more information, please visit the Company's website at www.prothena.com and follow us @ProthenaCorp.

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the depth of our pipeline of novel therapeutics; whether we have the resources and scientific expertise to continue to advance our pipeline through meaningful development milestones; and our ability to transform patients' lives. 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 26, 2018 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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