NEWS RELEASE

Prothena to Present Data on Survival Benefit Observed in Completed Phase 3 Study of Drug Candidate Birtamimab in Patients with Mayo Stage IV AL Amyloidosis at the ASH 2022 Meeting

11/3/2022

DUBLIN--(BUSINESS WIRE)-- Prothena Corporation plc (NASDAQ:PRTA), a late-stage clinical biotechnology company with a robust pipeline of investigational therapeutics built on protein dysregulation expertise, today announced that it will present survival data from the phase 3 VITAL study at an oral presentation at the American Society of Hematology Conference 2022 (ASH). The meeting will be held December 10-13, 2022 in New Orleans, LA.

Phase 3 VITAL study data on observed survival benefit in Mayo Stage IV AL amyloidosis patients treated with birtamimab was consistent after adjusting for baseline variables. The observed survival benefit adds to the totality of existing data supporting birtamimab in this patient population. Prothena has advanced birtamimab into the confirmatory Phase 3 AFFIRM-AL study in patients with Mayo Stage IV AL amyloidosis under a Special Protocol Assessment (SPA) with the FDA with a primary endpoint of all-cause mortality at $p \leq 0.10$.

Following are details of the VITAL oral presentation at ASH:

- Oral Presentation #760: Survival Benefit of Birtamimab in Mayo Stage IV AL Amyloidosis in the Phase 3 VITAL Study Consistent after Adjustment for Key Baseline Variables
- Presenting Author: Morie Gertz, MD
- Session Date: December 12, 2022
- Presentation Time: 11:15 AM ET

About Birtamimab

Birtamimab is an investigational monoclonal antibody designed to specifically and selectively target and clear the amyloid that accumulates and causes organ dysfunction and failure in patients with AL amyloidosis. Birtamimab is the only investigational therapeutic that has shown a significant survival benefit in patients with Mayo Stage IV AL amyloidosis in a placebo-controlled study. Birtamimab has been granted orphan drug designation for AL Amyloidosis by both the U.S. FDA and the European Medicines Agency and has been granted Fast Track designation by the FDA. A SPA was agreed to between Prothena and the FDA for the AFFIRM-AL trial which represents FDA's agreement that the design and planned analysis for the primary endpoint of time to all-cause mortality adequately address the objectives necessary to support a regulatory submission. Results from the AFFIRM-AL trial are anticipated in 2024. Final marketing approval is predicated upon FDA's complete review of the entire application.

About Confirmatory Phase 3 AFFIRM-AL Trial

The AFFIRM-AL study is a global, multi-center, double-blind, placebo-controlled, 2:1 randomized, time-to-event trial expected to enroll approximately 150 newly diagnosed, treatment naïve patients with AL amyloidosis categorized as Mayo Stage IV. The trial is being conducted under a SPA agreement with FDA and supported by the significant survival benefit observed in the previous analysis of birtamimab-treated patients categorized as Mayo Stage IV at baseline in the VITAL study. For more information on the clinical trial please visit **https://affirm-al.com/**.

About AL Amyloidosis

AL amyloidosis is a rare, progressive and fatal disease where clonal plasma cells overproduce light chain proteins that misfold, aggregate and deposit as amyloid in vital organs such as the heart. It is estimated that there are 60,000 – 120,000 patients worldwide living with Mayo Stage IV AL amyloidosis. Patients with AL amyloidosis can present with a wide range of general symptoms that are common to other conditions such as fatigue, shortness of breath or edema. Current treatment strategies target plasma cells to reduce production of new amyloid, but do not address the amyloid already deposited in organs. Mortality is driven primarily by cardiac failure. There is an urgent unmet medical need for therapies that improve survival in patients at risk for early mortality due to amyloid deposition.

About Prothena

Prothena Corporation plc is a late-stage clinical biotechnology company with expertise in protein dysregulation and a pipeline of investigational therapeutics with the potential to change the course of devastating neurodegenerative and rare peripheral amyloid diseases. Fueled by its deep scientific expertise built over decades of research, Prothena is advancing a pipeline of therapeutic candidates for a number of indications and novel targets for which

its ability to integrate scientific insights around neurological dysfunction and the biology of misfolded proteins can be leveraged. Prothena's pipeline includes both wholly-owned and partnered programs being developed for the potential treatment of diseases including AL amyloidosis, ATTR amyloidosis, Alzheimer's disease, Parkinson's disease and a number of other neurodegenerative diseases. For more information, please visit the Company's website at **www.prothena.com** and follow the Company on Twitter @ProthenaCorp.

Forward-looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the treatment potential, design, proposed mechanism of action, and potential administration of birtamimab; and the expected timing of reporting data from clinical studies of birtamimab. 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 those described in the "Risk Factors" sections of our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 8, 2022, and discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. We undertake 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 our expectations.

View source version on **businesswire.com**: **https://www.businesswire.com/news/home/20221103005351/en/**

Media and Investor Contact:

Media
Michael Bachner, Senior Director, Corporate Communications
609-664-7308, **michael.bachner@prothena.com**

Investors
Jennifer Zibuda, Director, Investor Relations & Communications
650-837-8535, **jennifer.zibuda@prothena.com**

Source: Prothena Corporation plc