NEWS RELEASE

Prothena Announces Phase 3 VITAL Clinical Trial Results Published in Blood Showing Survival Benefit in Patients with Mayo Stage IV AL Amyloidosis Treated with Birtamimab

6/27/2023

• First time published in a peer-reviewed journal: birtamimab is the only investigational drug that has shown a significant survival benefit in patients with Mayo Stage IV AL amyloidosis in a double-blind placebo-controlled clinical trial
• A significant improvement in time to all-cause mortality at month 9 was observed with birtamimab versus placebo and remained consistent across all key baseline variables in a post hoc analysis of patients with Mayo Stage IV AL amyloidosis
• Birtamimab is currently being studied in the confirmatory Phase 3 clinical trial, AFFIRM-AL, in patients with Mayo Stage IV AL amyloidosis; topline data is expected in 2024

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 the publication of the Phase 3 VITAL clinical trial in Blood, a journal of the American Society of Hematology (ASH). The published data demonstrate that in a post hoc analysis of patients with Mayo Stage IV AL amyloidosis, a statistically significant survival benefit of 74 percent was observed for those treated with birtamimab plus standard of care (SOC) versus 49 percent in patients on placebo plus SOC at 9 months (HR 0.413, p=0.021). All participants in the clinical trial received concomitant bortezomib-containing chemotherapy regimens as part of SOC.

“For the first time, we have these important data published in a prestigious, peer-reviewed journal which show that treatment with birtamimab led to a survival benefit in patients with Mayo Stage IV AL amyloidosis and affirms its
potential as a safe, well-tolerated and effective therapy,” said Morie Gertz, MD, Hematologist, Chair emeritus Internal Medicine, Mayo Clinic. “AL amyloidosis is a rare and life-threatening disease in which patients have no treatment options despite the high fatality rate. We look forward to learning more about the survival benefit of birtamimab in patients with Mayo Stage IV AL amyloidosis from the confirmatory Phase 3 AFFIRM-AL clinical trial.”

The article, entitled “Birtamimab plus standard of care in light chain amyloidosis: the phase 3 randomized placebo-controlled VITAL clinical trial”, also includes new data showing that there was no observed difference in hematologic response rates between the control arm and the treatment arms which suggests the survival benefit of birtamimab was not due to improved hematologic response, which is consistent with birtamimab’s depleter mechanism of action.

For two secondary endpoints, birtamimab demonstrated statistically significant improvements over placebo in a post hoc assessment of patients with Mayo Stage IV AL amyloidosis. The secondary endpoints were quality of life (assessed with the Short Form-36 version 2 physical component score, SF-36v2 PCS) and cardiac function (assessed with the 6-minute walk test). Patients treated with birtamimab showed a slower decline in quality of life with a mean decrease of 0.75 in the SF-36v2 PCS at 9 months compared to a mean decrease of 5.40 in the SF-36v2 PCS for patients on placebo at 9 months (a mean difference of 4.65 favoring birtamimab; p=0.046). Patients treated with birtamimab after 9 months demonstrated an increase in mean distance of 15.22 meters in the 6-minute walk test, compared to a decrease in mean distance of 21.15 meters for patients on placebo (a mean difference of 36.37 meters favoring birtamimab; p=0.022).

In safety evaluations, the rates of treatment emergent adverse events (TEAEs) were balanced between treatment arms among patients with Mayo Stage IV AL amyloidosis (38 TEAEs in patients treated with birtamimab compared to 39 TEAEs in patients receiving placebo). The rates of treatment-related TEAEs were similar or lower with birtamimab than in the placebo arms. Cardiac disorder was the most common class of fatal TEAEs, which is consistent with patients who have AL amyloidosis. There were no fatal TEAEs that were considered treatment related.

Birtamimab is a potential best-in-class amyloid depleter treatment for AL amyloidosis. Birtamimab specifically binds to a defined epitope on kappa and lambda AL protein involved in the disease process. Based on the totality of data generated to date, including results from the VITAL clinical trial, Prothena has advanced birtamimab into the confirmatory Phase 3 AFFIRM-AL clinical trial in patients with Mayo Stage IV AL amyloidosis under a Special Protocol Assessment (SPA) agreement with the U.S. Food and Drug Administration (FDA) with a primary endpoint of all-cause mortality at a significance level of 0.10. Phase 3 AFFIRM-AL topline data is expected in 2024. Birtamimab has also been granted orphan drug designation for AL amyloidosis by both the FDA and the European Medicines Agency and has been granted Fast Track designation by the FDA.
Blood is the weekly, peer-reviewed journal published by The American Society of Hematology (ASH). A copy of the Phase 3 VITAL publication can be found here:

https://doi.org/10.1182/blood.2022019406

Prothena previously presented data on the Phase 3 VITAL clinical trial in an oral presentation at the 64th ASH Annual Meeting and Exposition.

About VITAL Phase 3 Clinical Trial

VITAL was a phase 3 multicenter, randomized, double-blind, placebo-controlled clinical trial that evaluated the efficacy and safety of birtamimab plus standard of care versus placebo plus standard of care in newly diagnosed, treatment-naïve patients with AL amyloidosis. The clinical trial was terminated early based on a futility analysis. The primary endpoint in the full clinical trial population was the composite of time to all-cause mortality and cardiac hospitalization in patients with AL amyloidosis. The primary endpoint in the overall clinical trial population favored birtamimab over placebo, but the difference was not statistically significant at the time of early clinical trial termination. The primary clinical trial population included 260 patients with AL amyloidosis, of which patients who received birtamimab and placebo were evenly split. Approximately one-third of patients in the clinical trial had Mayo Stage IV AL amyloidosis (n=77). Patient demographics were generally balanced between the birtamimab and placebo groups in the clinical trial population and the Mayo Stage IV sub population.

About Phase 3 AFFIRM-AL Clinical Trial

The AFFIRM-AL clinical trial is a global, multi-center, double-blind, placebo-controlled, 2:1 randomized, time-to-event clinical trial expected to enroll approximately 150 newly diagnosed, treatment naïve patients with AL amyloidosis categorized as Mayo Stage IV. The clinical 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 clinical trial. For more information on the clinical trial please visit https://affirm-al.com/.

About Birtamimab

Birtamimab is an investigational, humanized 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 specifically binds to a defined epitope on kappa and lambda AL protein involved in the disease process. Birtamimab is the only investigational drug that has shown a significant survival benefit in patients with Mayo Stage IV AL amyloidosis post-hoc in a placebo-controlled clinical trial. 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 clinical 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 clinical trial are anticipated in 2024. Final marketing approval is predicated upon FDA’s complete review of the entire application.

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 a clinical trial 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 May 4, 2023, 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.

Media and Investor Contact:

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

Investors: IR@prothena.com

Source: Prothena Corporation plc