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PROTHENA CORP PLC

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(Current report filing)

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the

Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 28, 2017

PROTHENA CORPORATION PUBLIC LIMITED COMPANY

(Exact Name of Registrant as Specified in its Charter)

Ireland	001-35676	98-1111119
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

Adelphi Plaza
Upper George's Street
Dún Laoghaire
Co. Dublin, A96 T927, Ireland

(Address of principal executive offices including Zip Code)

Registrant's telephone number, including area code: 011-353-1-236-2500

(Former Name or Former Address, if Changed Since Last Report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events

On September 28, 2017, Prothena Corporation plc issued a press release announcing results from a Phase 1b multiple ascending dose study of PRX003, an investigational monoclonal antibody for the potential treatment of inflammatory diseases. That press release is attached as Exhibit 99.1 to this Current Report on Form 8-K.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits .

Exhibit No.	**Description**
99.1	Press Release dated September 28, 2017.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 28, 2017

PROTHENA CORPORATION PLC

By: /s/ Tran B. Nguyen
Name: Tran B. Nguyen
Title: Chief Financial Officer

Exhibit 99.1

Prothena Reports Results from Phase 1b Multiple Ascending Dose Study of PRX003 in Patients with Psoriasis

- **Data demonstrated consistent safety, tolerability and pharmacodynamic effects as previously reported from Phase 1a single ascending dose (SAD) study**
- **Observed clinical efficacy and reductions in markers of inflammation were insufficient to advance PRX003 into mid-stage clinical development**

DUBLIN, Ireland, September 28, 2017- Prothena Corporation plc (Nasdaq:PRTA), a late-stage clinical biotechnology company focused on the discovery, development and commercialization of novel protein immunotherapies, today announced clinical results of a Phase 1b multiple ascending dose (MAD) study of PRX003 in patients with psoriasis. PRX003 is a monoclonal antibody targeting CD146, also known as melanoma cell adhesion molecule (MCAM), a cell adhesion molecule located on the surface of T helper 17 cells (Th17). While the primary objectives of the study were achieved, advancing PRX003 into mid-stage clinical development required a well-defined relationship between biological activity and meaningful clinical effects, and these prerequisites were not met. In this study, PRX003 administration resulted in dose- and time-dependent occupancy and downregulation of CD146 on Th17 cells, consistent with prior Phase 1a SAD study results. However, the pharmacodynamic effects did not translate into meaningful clinical benefit in patients with psoriasis treated with PRX003, as measured by responses in the Psoriasis Area and Severity Index 75 (PASI 75), a clinical assessment used to evaluate psoriasis severity in patients. Additionally, skin biopsy data demonstrated insufficient reduction in measurements of Th17 cell infiltration and other inflammatory markers required to advance PRX003 into mid-stage clinical development for psoriasis or psoriatic arthritis as previously planned.

“While we observed occupancy and downregulation of CD146 following administration of PRX003 consistent with our previous Phase 1a SAD study, the clinical results in this study did not meet our pre-specified criteria for evidence of a well-defined relationship between biological activity and meaningful clinical effects required to advance PRX003 into mid-stage clinical development for psoriasis or psoriatic arthritis as previously planned,” said Sarah Noonberg, MD, PhD, Chief Medical Officer of Prothena. “Moreover, these results indicate the need for a deeper understanding of CD146 modulation in the treatment of complex disease states. We want to thank the patients, clinicians and site coordinators who have helped us execute this thorough study.”

The Phase 1b double-blind, placebo-controlled, MAD study enrolled 33 patients with psoriasis and was designed to assess the safety, tolerability, and pharmacokinetics of PRX003. Further effects of PRX003 were evaluated through multiple exploratory endpoints of pharmacodynamic activity, including measures of CD146 occupancy and downregulation, efficacy evaluations of psoriasis severity as measured by PASI 75 response rates, and histopathologic and RNA transcript assessment of skin biopsies to measure changes in cytokines that are known markers of inflammation. All patients enrolled were randomized 3:1 to receive PRX003 at 1 mg/kg (n=7), 3 mg/kg (n=6), 10 mg/kg (n=6), or 30 mg/kg (n=6) or placebo (n=8) every 28 days for three months and were then observed for an additional three months. The study results demonstrated,

in PRX003 treated-patients, near-complete (>99 percent) occupancy of CD146 with a dose- and time-dependent effect. Occupancy led to a statistically significant ($p<0.0001$) dose- and time-dependent downregulation of CD146 on Th17 cells at saturating drug exposures. These results were consistent with pharmacodynamic effects observed in the previous Phase 1a SAD study in healthy volunteers. Across all PRX003 dose levels in the Phase 1b MAD study, no clinically relevant or statistically significant benefit on PASI 75 response was observed. At week 12, 29 percent of PRX003-treated patients (2 out of 7) in the 1 mg/kg dose cohort achieved a PASI 75 response ($p=0.2$ relative to placebo), and no patients in the 3 mg/kg, 10 mg/kg or 30 mg/kg dose cohorts achieved a PASI 75 response. Evaluation of Th17 cell migration revealed insufficient decreases in Th17 cell infiltration into tissue. Additionally, as measured from skin biopsies there were no clinically meaningful or dose-dependent changes in RNA transcript levels of genes associated with Th17-mediated inflammation, including IL-17A, IL-17F, IL-6, TNFα, and IFNγ. Despite modest evidence of a clinical effect on PASI 75 response at the lowest dose level, there was no relationship between dose levels, RNA transcript levels or other markers of inflammatory activity that provided evidence of a meaningful therapeutic effect. Collectively, these data demonstrated that near-complete downregulation of CD146 is insufficient to inhibit Th17 cell infiltration and associated inflammation to the degree necessary to achieve meaningful clinical benefit in patients with psoriasis.

PRX003 was shown to be generally safe and well tolerated up to and including the highest dose level tested at 30 mg/kg. There were no serious adverse events in PRX003-treated patients and two patients discontinued study drug due to adverse events. Treatment-emergent adverse events reported in ≥2 PRX003-treated patients, regardless of relationship to study drug, were arthralgia, fatigue, gamma-glutamyl transferase increases, presyncope, and upper respiratory tract infection.

“As an organization guided by science and data-driven decision-making, we will only advance programs into mid- or late-stage clinical development that have the potential to offer clear and differentiated clinical benefits to patients,” stated Gene Kinney, PhD, President and Chief Executive Officer of Prothena. “While we are disappointed that these data do not support moving PRX003 into mid-stage development at this time, we continue to focus on advancing NEOD001 (Phase 2b and Phase 3), PRX002 (Phase 2) and PRX004 (expected to enter Phase 1 by mid-2018), as well as our active discovery programs for new clinical candidates.”

About PRX003

PRX003 is a monoclonal antibody that targets CD146, also known as MCAM, a cell adhesion molecule expressed on the surface of Th17 cells. Within the immune system, a small population of approximately three to six percent of T cells known as Th17 cells, are known to be a key participant in both normal inflammatory reactions as well as pathogenic autoimmune diseases. CD146, also known as MCAM, is a cell adhesion molecule expressed on the surface of Th17 cells, and facilitates their interaction with vasculature.

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), 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 timing of advancing PRX004 into a Phase 1 clinical study. 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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