NEWS RELEASE

Prothena Reports Third Quarter 2025 Financial Results and Business Highlights

2025-11-06

- Net cash used in operating and investing activities was $40.6 million and $140.4 million for the third quarter and first nine months of 2025, respectively; quarter-end cash and restricted cash position was $331.7 million
- Roche to initiate the Phase 3 PARAISO clinical trial evaluating prasinezumab, a potential first-in-class anti-alpha-synuclein antibody, for early-stage Parkinson's disease by end of 2025
- Novo Nordisk initiated the Phase 3 CLEOPATTRA clinical trial evaluating coramitug, a potential first-in-class amyloid depleter, for ATTR amyloidosis with cardiomyopathy
- Novo Nordisk to present Phase 2 results for coramitug during a late-breaking session at the American Heart Association Scientific Sessions on November 10, 2025
- Bristol Myers Squibb obtained Fast Track designation from the U.S. FDA for BMS-986446 (PRX005), an anti-MTBR-tau-targeting antibody, for the treatment of Alzheimer’s disease
- Prothena will convene an Extraordinary General Meeting on November 19, 2025 to obtain shareholder approval on a proposal reducing share capital to create distributable reserves to support a share redemption program to be conducted in 2026 if deemed appropriate
- Potential to earn up to $105 million in aggregate clinical milestone payments by end of 2026 related to the advancement of coramitug for ATTR amyloidosis with cardiomyopathy by Novo Nordisk and PRX019 for neurodegenerative diseases by Bristol Myers Squibb

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 reported financial results for the third quarter and first nine months of 2025 and provided business highlights.

“We are pleased with the advancement of our late-stage partnered clinical programs. Novo Nordisk recently

initiated the Phase 3 CLEOPATTRA clinical trial evaluating coramitug in ATTR-CM and Roche plans to initiate the Phase 3 PARAISO clinical trial evaluating prasinezumab in early-stage Parkinson's disease by the end of 2025. Recently, Bristol Myers Squibb obtained Fast Track designation from the U.S. FDA for BMS-986446, an anti-MTBR-tau antibody, for the treatment of Alzheimer's disease. BMS-986446 is currently in an ongoing Phase 2 trial with primary completion expected in the first half of 2027," said Gene Kinney, Ph.D., President and Chief Executive Officer, Prothena. "We look forward to Novo Nordisk presenting Phase 2 coramitug results in a late-breaking presentation at the American Heart Association Scientific Sessions 2025. In addition, our Prothena scientists will be presenting a poster on our TDP-43 CYTOPE®, a therapeutic modality enabling cytosolic delivery of macromolecules, which demonstrated a reduction in intracellular TDP-43 pathology in a preclinical ALS mouse model at Neuroscience 2025 hosted by the Society of Neuroscience. We look forward to sharing more about CYTOPE and its potential applications in the future."

Third Quarter, Recent Business Highlights and Upcoming Milestones

Updates on Active Clinical Development Portfolio

Prasinezumab, a potential first-in-class antibody for the treatment of Parkinson's disease that is designed to target a key epitope within the C-terminus of alpha-synuclein and is the focus of a worldwide collaboration with Roche.

- Partner Roche to initiate the Phase 3 PARAISO clinical trial evaluating prasinezumab for early-stage Parkinson's disease by the end of 2025 (**NCT07174310**)
- Roche has stated that prasinezumab has peak sales potential greater than $3.5 billion (unadjusted) and could be the first disease-modifying treatment for a condition that affects 10 million people worldwide

Coramitug (formerly PRX004), a potential first-in-class amyloid depleter antibody for the treatment of ATTR amyloidosis with cardiomyopathy (ATTR-CM) designed to deplete the pathogenic, non-native forms of the transthyretin (TTR) protein, is being developed by Novo Nordisk as part of its up to $1.2 billion acquisition of Prothena's ATTR amyloidosis business and pipeline.

- Novo Nordisk initiated the Phase 3 CLEOPATTRA clinical trial evaluating coramitug for ATTR-CM (**NCT07207811**)
- Novo Nordisk will present Phase 2 results during a late-breaking session at the American Heart Association Scientific Sessions on November 10, 2025
- Expect to earn a clinical milestone when prespecified enrollment criteria are met in ongoing Phase 3 clinical trial by Novo Nordisk

BMS-986446 (formerly PRX005), a potential best-in-class antibody for the treatment of Alzheimer's disease that

specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in the causal pathophysiology of Alzheimer's disease.

- Bristol Myers Squibb is conducting the Phase 2 TargetTau-1 clinical trial in approximately 310 patients with early Alzheimer's disease; primary completion expected in 1H 2027 (**NCT06268886**)
- Bristol Myers Squibb is also conducting a Phase 1 open-label single-dose clinical trial to assess a subcutaneous administration; primary completion expected in 2H 2025 (**NCT06955741**)
- BMS-986446 granted Fast Track designation by U.S. FDA as a treatment for Alzheimer's disease

PRX019, a potential treatment of neurodegenerative diseases in development in collaboration with Bristol Myers Squibb.

- Bristol Myers Squibb obtained the exclusive global license for PRX019 in 2024
- Prothena is conducting a Phase 1 first-in-human clinical trial to evaluate the safety, tolerability, immunogenicity, and pharmacokinetics of single ascending and multiple doses in healthy adults with completion expected in 2026
- Potential to earn a clinical milestone by end of 2026 should Bristol Myers Squibb decide to further develop PRX019

Upcoming Scientific and Investor Conferences

Novo Nordisk to present Phase 2 results for coramitug in a late-breaking session at the American Heart Association Scientific Sessions on November 10, 2025 in New Orleans, LA

- Title: Primary results from the phase 2 randomized, placebo controlled, blinded trial of the monoclonal antibody coramitug in transthyretin amyloid cardiomyopathy (ATTR-CM)

Prothena poster presentation on a TDP-43 CYTOPE®, a proprietary modality enabling cytosolic delivery of macromolecules for precision targeting of intracellular disease targets, in an ALS mouse model at Neuroscience 2025 annual meeting organized by Society for Neuroscience (SfN) on November 19, 2025 in San Diego, CA

- Title: Treatment with a cell-internalizing antibody targeting pTDP43 reduces intraneuronal pathology in a mouse model of ALS

Members of the senior management team will present and participate in investor meetings at the following upcoming investor conferences:

- Piper Sandler 37th Annual Healthcare Conference on Wednesday, December 3, 2025; fireside chat at 1:00 p.m. ET in New York, NY

- 8th Annual Evercore Healthcare Conference on Thursday, December 4, 2025; fireside chat at 10:50 a.m. ET in Miami, FL

Third Quarter and First Nine Months of 2025 Financial Results

For the third quarter and first nine months of 2025, Prothena reported net loss of $36.5 million and $222.5 million, respectively, as compared to a net loss of $59.0 million and $64.4 million for the third quarter and first nine months of 2024, respectively. The first nine months of 2025 includes $33.1 million of restructuring charges associated with the discontinuation of the birtamimab program and the reduction in workforce announced in June 2025, and a $43.2 million net non-cash income tax expense to book a full valuation allowance against its federal deferred tax assets. Net loss per share was $0.68 and $4.13 for the third quarter and first nine months of 2025, respectively, as compared to a net loss per share of $1.10 and $1.20 for the third quarter and first nine months of 2024, respectively.

Prothena reported total revenue of $2.4 million and $9.7 million for the third quarter and first nine months of 2025, respectively, as compared to total revenue of $1.0 million and $133.0 million for the third quarter and first nine months of 2024, respectively. Total revenue for the third quarter and first nine months of 2025 was primarily from collaboration revenue from Bristol Myers Squibb related to the partial performance of our PRX019 Phase 1 clinical trial obligation. Total revenue for the first nine months of 2024, was primarily from collaboration revenue from Bristol Myers Squibb.

Research and development (R&D) expenses totaled $28.9 million and $120.3 million for the third quarter and first nine months of 2025, respectively, as compared to $50.7 million and $172.3 million for the third quarter and first nine months of 2024, respectively. The decrease in R&D expenses for the third quarter and first nine months of 2025 compared to the same periods in the prior year was primarily due to lower clinical trial expenses, lower personnel expenses, lower manufacturing and lower consulting expenses. R&D expenses included non-cash share-based compensation expense of $2.5 million and $12.0 million for the third quarter and first nine months of 2025, respectively, as compared to $5.1 million and $16.2 million for the third quarter and first nine months of 2024, respectively.

General and administrative (G&A) expenses totaled $13.2 million and $46.7 million for the third quarter and first nine months of 2025, respectively, as compared to $16.8 million and $50.4 million for the third quarter and first nine months of 2024, respectively. The decrease in G&A expenses for the third quarter and first nine months of 2025 compared to the same periods in the prior year was primarily due to lower personnel expenses. G&A expenses included non-cash share-based compensation expense of $4.7 million and $16.5 million for the third quarter and first nine months of 2025, respectively, as compared to $5.9 million and $19.2 million for the third quarter and first nine months of 2024, respectively.

Total non-cash share-based compensation expense was $7.2 million for the third quarter of 2025 and $30.6 million for the first nine months of 2025 which included $2.1 million in non-cash share-based compensation expense related to restructuring charges, as compared to $11.0 million and $35.4 million for the third quarter and first nine months of 2024, respectively.

As of September 30, 2025, Prothena had $331.7 million in cash, cash equivalents and restricted cash, and no debt.

As of October 31, 2025, Prothena had approximately 53.8 million ordinary shares outstanding.

2025 Financial Guidance

The Company continues to expect its full year net cash used in operating and investing activities to be $170 to $178 million and to end the year with approximately $298 million (midpoint) in cash, cash equivalents, and restricted cash. The estimated full year 2025 net cash used from operating and investing activities is primarily driven by an estimated net loss of $240 to $248 million, which includes an estimated $36 million of non-cash share-based compensation expense and a $44.9 million non-cash income tax expense to book a full valuation allowance against its federal deferred tax assets.

Share Redemption Program

Prothena will convene an Extraordinary General Meeting (“EGM”) of shareholders on November 19, 2025 to vote on a proposal to approve a reduction in Prothena’s share capital to create distributable reserves, subject to confirmation by the Irish High Court, to support a potential share redemption program. The Board of Directors is seeking shareholder approval of such a proposal to create flexibility to potentially return capital to shareholders via a share redemption program through open market purchases or other permissible means in 2026. Any such program would be subject to the discretion of the Board of Directors and Prothena’s then-current financial condition.

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 ATTR amyloidosis with cardiomyopathy, 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 X (formerly Twitter) @ProthenaCorp.

Forward-Looking Statements

This press release contains forward-looking statements. These statements relate to, among other things, the sufficiency of our cash position to fund advancement of a broad pipeline and completion of our ongoing clinical trials; the continued advancement of our discovery, preclinical, and clinical pipeline, and expected milestones in 2025, 2026, 2027, and beyond; the treatment potential, designs, proposed mechanisms of action, and potential administration of prasinezumab, coramitug, BMS-986446, and PRX019; plans for ongoing and future clinical trials of prasinezumab, coramitug, BMS-986446, and PRX019; the expected timing of reporting data from pre-clinical studies and clinical trials, including data from Novo Nordisk's Phase 2 clinical trial evaluating coramitug on November 10, 2025 and our TDP-43 CYTOPE® program on November 19, 2025; projections regarding peak sales and patient population for prasinezumab; timing of and amounts we may receive under our collaborations with Novo Nordisk and Bristol Myers Squibb; our anticipated net cash burn from operating and investing activities for 2025 and expected cash balance at the end of 2025; our estimated net loss and non-cash share-based compensation expense for 2025; and the potential and ability to return capital to shareholders via a share redemption program or other permissible means if shareholders approve a reduction in share capital to create distributable reserves. 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 uncertainties related to the completion of operational and financial closing procedures, audit adjustments and other developments that may arise that would require adjustments to the preliminary financial results included in this press release, as well as those described in the "Risk Factors" sections of our Quarterly Report on Form 10-Q to be filed with the Securities and Exchange Commission (SEC) on November 6, 2025, 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.

PROTHENA CORPORATION PLC
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(unaudited - amounts in thousands except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Collaboration revenue	$ 2,415	$ 970	$ 9,613	$ 132,984
Revenue from license and intellectual property	—	—	50	50
Total revenue	2,415	970	9,663	133,034

Operating expenses:				
Research and development	28,938	50,723	120,266	172,347
General and administrative	13,238	16,760	46,746	50,351
Restructuring costs	479	—	33,088	—
Total operating expenses	42,655	67,483	200,100	222,698
Loss from operations	(40,240)	(66,513)	(190,437)	(89,664)
Other income, net	3,328	6,677	11,187	20,235
Loss before income taxes	(36,912)	(59,836)	(179,250)	(69,429)
Provision for (benefit from) income taxes	(371)	(835)	43,253	(5,075)
Net loss	$ (36,541)	$ (59,001)	$ (222,503)	$ (64,354)
Basic and diluted net loss per ordinary share	$ (0.68)	$ (1.10)	$ (4.13)	$ (1.20)
Shares used to compute basic and diluted net loss per share	53,830	53,790	53,828	53,757

PROTHENA CORPORATION PLC
CONDENSED CONSOLIDATED BALANCE SHEETS
(unaudited - amounts in thousands)

	September 30, 2025	December 31, 2024
Assets		
Cash and cash equivalents	$ 330,843	$ 471,388
Prepaid expenses and other current assets	9,131	14,024
Total current assets	339,974	485,412
Property and equipment, net	2,463	3,081
Operating lease right-of-use assets	8,849	10,708
Restricted cash, non-current	860	860
Other non-current assets	482	47,047
Total non-current assets	12,654	61,696
Total assets	$ 352,628	$ 547,108
Liabilities and Shareholders' Equity		
Accrued research and development	$ 9,544	$ 13,428
Deferred revenue, current	2,685	8,850
Restructuring liability	17,614	—
Lease liability, current	2,879	2,610
Other current liabilities	18,714	23,613
Total current liabilities	51,436	48,501
Deferred revenue, non-current	—	3,448
Lease liability, non-current	6,203	8,233
Total non-current liabilities	6,203	11,681
Total liabilities	57,639	60,182
Total shareholders' equity	294,989	486,926
Total liabilities and shareholders' equity	$ 352,628	$ 547,108

Mark Johnson, CFA, Vice President, Investor Relations

650-837-8550

IR@prothena.com

Media@prothena.com

Source: Prothena Corporation plc