Prothena Reports Fourth Quarter and Full Year 2021 Financial Results, and Provides Financial Guidance and Business Highlights

- **Net cash used in operating and investing activities was $22.8 million in the fourth quarter and net cash provided by operating and investing activities was $92.0 million for the full year 2021; quarter-end cash and restricted cash position was $580.4 million**
- **Reached SPA agreement with FDA at p≤0.10 for confirmatory Phase 3 study of birtamimab and initiated the study in Mayo Stage IV patients with AL amyloidosis**
- **Received $80 million option payment from Bristol Myers Squibb for U.S. license to PRX005 for the treatment of Alzheimer's disease; initiated Phase 1 study**
- **Novo Nordisk acquired ATTR amyloidosis business for up to $1.23 billion; includes $60 million upfront payment received**
- **Received $60 million milestone from Roche for first patient dosed in Phase 2b study of prasinezumab in patients with early Parkinson's disease**
- **Presented preclinical data at AAIC 2021 from two Alzheimer's disease programs: PRX012, a next-generation anti-Aβ antibody, and the dual Aβ/tau vaccine**

DUBLIN, Ireland, February 17, 2022 -- 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 fourth quarter and full year 2021. In addition, the Company provided 2022 financial guidance and an update on business highlights.

"Prothena made meaningful progress in multiple therapeutic indications across our portfolio in 2021 with the advancement of three clinical stage programs. We announced the initiation of the confirmatory Phase 3 AFFIRM-AL study of birtamimab, Phase 2b PADOVA study of prasinezumab, and Phase 1 study of PRX005. Additionally, we presented positive preclinical findings for our anti-Aβ PRX012 and our dual Aβ/tau vaccine at AAIC in June last year," said Gene Kinney, Ph.D., President and Chief Executive Officer of Prothena. "In 2021, we also received $200 million from strategic partnerships with leading pharmaceutical companies and bolstered our cash position with $175 million raised through equity offerings. In 2022, we look forward to multiple scientific congresses starting with the presentation of additional preclinical data at AD/PD in March. Our strong capital position funds Prothena through multiple value-creating milestones as we transition into a fully integrated commercial company."

2021 Business Highlights and Upcoming Milestones

Neurodegenerative Diseases Portfolio

Alzheimer's Disease (AD)

PRX012, a potential best-in-class treatment for AD, is an investigational monoclonal antibody targeting a key epitope at the N-terminus of amyloid beta (Aβ) with high binding potency

- Presented preclinical results at the Alzheimer's Association International Conference® in 2021 (AAIC®) demonstrating that PRX012 significantly cleared both pyroglutamate-modified and -unmodified Aβ plaque in post-mortem brain tissue of late-stage AD patients
- Investigational New Drug (IND) application filing expected 1Q 2022

PRX005, a potential best-in-class treatment for AD, is an investigational antibody that specifically targets a key epitope within the microtubule binding region (MTBR) of tau, a protein implicated in diseases including AD, frontotemporal dementia (FTD), progressive supranuclear palsy (PSP), chronic traumatic encephalopathy (CTE), and other tauopathies. PRX005 is part of the global neuroscience research and development collaboration with Bristol Myers Squibb

- Received $80 million option payment from Bristol Myers Squibb for execution of U.S. license agreement in 2021
- Phase 1 study initiated in 2021
- Topline Phase 1 data expected in 2022

Dual Aβ/tau vaccine, a potential first-in-class treatment and prevention for AD, is a dual-target vaccine targeting key epitopes within the Aβ and tau proteins to promote amyloid clearance and blockade of pathogenic tau

- AAIC® presentation in 2021 showcased preclinical data demonstrating that Prothena's dual Aβ/tau vaccine generated appropriate and balanced antibody titers promoting both phagocytosis of Aβ plaque and blockade of tau transmission in vitro
- Presentation of preclinical data at the International Conference on Alzheimer's and Parkinson's Diseases (AD/PD) expected in March 2022
- IND filing expected in 2023

Parkinson's Disease (PD)

Prasinezumab, a potential first-in-class treatment for PD, is a humanized monoclonal antibody designed to target key epitopes within the C-terminus of alpha-synuclein and is the focus of the worldwide collaboration with Roche

- Earned $60 million clinical milestone payment in 2021 upon dosing of the first patient in the global Phase 2b PADOVA study for prasinezumab (NCT#04777331)
- Presentation of additional data by Roche at AD/PD expected in March 2022
- Phase 2b PADOVA study results expected in 2024

Rare Peripheral Amyloid Diseases Portfolio

AL Amyloidosis (AL)

Birtamimab, a potential best-in-class amyloid depleter treatment for AL, is an investigational humanized monoclonal antibody designed to directly neutralize soluble toxic aggregates and promote clearance of amyloid that causes organ dysfunction and failure

- Reached Special Protocol Assessment (SPA) agreement with FDA at $p \leq 0.10$ and initiated confirmatory Phase 3 AFFIRM-AL study of birtamimab in Mayo Stage IV patients with AL amyloidosis in 2021 (NCT#04973137)

- Confirmatory Phase 3 AFFIRM-AL study results expected in 2024

ATTR Amyloidosis (ATTR)

PRX004, a potential first-in-class treatment for ATTR, is a humanized monoclonal antibody designed to deplete the pathogenic, non-native forms of the TTR protein, and is being developed by Novo Nordisk for the treatment of ATTR cardiomyopathy

- Announced Novo Nordisk acquisition of ATTR business for a total aggregate of up to $1.23 billion and Prothena received $60 million up front payment in 2021
- Novo Nordisk expected to initiate a Phase 2 trial in 1H 2022 with PRX004 for the treatment of ATTR cardiomyopathy

2021 Organizational Highlights

- Sanjiv Patel, MBBS, MA, MBA, appointed to the Board of Directors
- Hideki Garren, M.D., Ph.D., appointed to Chief Medical Officer
- Tran Nguyen, Chief Financial Officer, appointed to the additional, newly created role of Chief Strategy Officer
- Brandon Smith promoted from Chief Business Officer to Chief Operating Officer

Upcoming Investor Conference

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

- Oppenheimer 32nd Annual Healthcare Conference, March 15, 2022, at 1:20 PM ET

Fourth Quarter and Full Year of 2021 Financial Results

For the fourth quarter and full year of 2021, Prothena reported a net loss of $33.2 million and net income of $67.0 million, respectively, as compared to a net loss of $30.7 million and $111.1 million for the fourth quarter and full year of 2020, respectively. Net loss per share for the fourth quarter of 2021 was $0.71 and net income per share on a diluted basis for the full year of 2021 was $1.38, as compared to net loss per share of $0.77 and $2.78 for the fourth quarter and full year of 2020, respectively.

Prothena reported total revenue of $1.2 million and $200.6 million for the fourth quarter and full year of 2021, respectively. Revenue for the fourth quarter of 2021 related to $1.2 million from Bristol Myers Squibb. Revenue for the full year of 2021, included $79.7 million from Bristol Myers Squibb for PRX005 U.S. License and U.S. Development Services and $60.7 million from the sale of the intellectual property and related rights to the Company's ATTR amyloidosis business and pipeline to Novo Nordisk. In addition, the full year revenue included $60.0 million in clinical milestone payment from Roche related to the global Phase 2b PADOVA study for prasinezumab and a nominal amount of license revenue from Roche. This compares to total revenue of $0.4 million and $0.9 million for the fourth quarter and full year of 2020, primarily from collaboration revenue from Roche.

Research and development (R&D) expenses totaled $22.1 million and $82.3 million for the fourth quarter and full year of 2021, respectively, as compared to $20.8 million and $74.9 million for the fourth quarter and full year of 2020, respectively. The increase in R&D expense for the fourth quarter and full year of 2021 compared to the same periods in the prior year was primarily due to higher personnel expenses, higher clinical trial expenses primarily related to the birtamimab and PRX005 programs (offset in part by lower PRX004 clinical trial expense); offset in part by lower collaboration expenses related to the

prasinezumab program with Roche as a result of the cost share opt-out exercised in May 2021 and lower manufacturing costs primarily related to PRX005 and birtamimab programs (offset in part by higher PRX012 preclinical expense). R&D expenses included non-cash share-based compensation expense of $2.9 million and $9.5 million for the fourth quarter and full year of 2021, respectively, as compared to $2.1 million and $8.2 million for the fourth quarter and full year of 2020, respectively.

General and administrative (G&A) expenses totaled $12.2 million and $46.3 million for the fourth quarter and full year of 2021, respectively, as compared to $9.9 million and $38.7 million for the fourth quarter and full year of 2020, respectively. The increase in G&A expenses for the fourth quarter and full year of 2021 compared to the same periods in the prior year was primarily related to higher personnel expenses, legal expenses, consulting and expense for our director and officer insurance premium. G&A expenses included non-cash share-based compensation expense of $4.0 million and $15.1 million for the fourth quarter and full year of 2021, respectively, as compared to $3.2 million and $13.8 million for the fourth quarter and full year of 2020, respectively.

Total non-cash share-based compensation expense was $6.9 million and $24.7 million for the fourth quarter and full year of 2021, respectively, as compared to $5.2 million and $22.0 million for the fourth quarter and full year of 2020.

As of December 31, 2021, Prothena had $580.4 million in cash, cash equivalents and restricted cash, and no debt. This includes net proceeds raised of $175 million raised through equity offerings and a total of $200 million in payments from partners Bristol Myers Squibb, Novo Nordisk and Roche.
As of February 11, 2022, Prothena had approximately 46.7 million ordinary shares outstanding.

2022 Financial Guidance

The Company expects the full year 2022 net cash used in operating and investing activities to be $120 to $132 million, which includes an expected $40 million clinical milestone payment from Novo Nordisk, and expects to end the year with approximately $454 million in cash, cash equivalents and restricted cash (midpoint). The estimated full year 2022 net cash used in operating and investing activities is primarily driven by an estimated net loss of $154 to $170 million, which includes an estimated $32 million of non-cash share-based compensation expense.

Conference Call Details

Prothena management will discuss these results and its 2022 financial guidance during a live audio conference call today, Thursday, February 17, 2022, at 4:30 PM ET. The conference call 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 live audio webcast, a replay will be available on the Company's website for at least 90 days.

To access the call via dial-in, please dial (888) 440-6385 (U.S. and Canada toll free) or +00 1 646 960-0180 (international) five minutes prior to the start time and refer to conference ID number 92750. A replay of the call will be available until March 3, 2022, via dial-in at (800) 770-2030 (U.S. toll free) or +00 1 647 362-9199 (international), Conference ID Number 92750.

About Prothena

Prothena Corporation plc is a late-stage clinical company with a robust pipeline of novel investigational therapeutics built on protein dysregulation expertise 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 sufficiency of our cash position to fund advancement of a broad pipeline; the continued advancement of our discovery, preclinical, and clinical pipeline, and expected milestones in 2022 and beyond; our goal to continue building a biology-directed discovery engine targeting protein dysregulation and to change the Alzheimer's disease treatment paradigm; the treatment potential, designs, proposed mechanisms of action, and potential administration of birtamimab, prasinezumab, PRX004, PRX005, PRX012, and our dual Aβ/tau vaccine; plans for future clinical studies of birtamimab, prasinezumab, PRX004, PRX005, PRX012, and our dual Aβ/tau vaccine; the expected timing of reporting data from clinical studies of birtamimab, prasinezumab, and PRX005, and preclinical studies of PRX012 and our dual Aβ/tau vaccine; our anticipated net cash burn from operating and investing activities for 2022 and expected cash balance at the end of 2022; and our estimated net loss and non-cash share-based compensation expense for 2022. 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 November 4, 2021, discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC, and our Annual Report on Form 10-K to be filed with the SEC for our fiscal year 2021. 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
CONSOLIDATED STATEMENTS OF OPERATIONS
(unaudited - amounts in thousands except per share data)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Collaboration revenue	$ 1,172	$ 121	$ 139,833	$ 564
Revenue from license and intellectual property	—	239	60,744	289
Total revenue	1,172	360	200,577	853
Operating expenses:				
Research and development	22,058	20,760	82,284	74,884
General and administrative	12,206	9,908	46,318	38,703
Total operating expenses	34,264	30,668	128,602	113,587
Income (loss) from operations	(33,092)	(30,308)	71,975	(112,734)
Other income (expense), net	(4)	(55)	(54)	1,307
Income (loss) before income taxes	(33,096)	(30,363)	71,921	(111,427)
Provision for (benefit from) income taxes	83	353	4,946	(283)
Net income (loss)	$ (33,179)	$ (30,716)	$ 66,975	$ (111,144)
Basic net income (loss) per ordinary share	$ (0.71)	$ (0.77)	$ 1.51	$ (2.78)
Diluted net income (loss) per ordinary share	$ (0.71)	$ (0.77)	$ 1.38	$ (2.78)
Shares used to compute basic net income (loss) per share	46,618	39,921	44,228	39,915
Shares used to compute diluted net income (loss) per share	46,618	39,921	48,464	39,915

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

	December 31, 2021	December 31, 2020
Assets		
Cash and cash equivalents	$ 579,094	$ 295,380
Accounts receivable	—	15
Prepaid expenses and other current assets	5,715	2,537
Restricted cash, current	—	1,352
Total current assets	584,809	299,284
Property and equipment, net	2,012	2,551
Operating lease right-of-use assets	12,123	17,811
Restricted cash, non-current	1,352	1,352
Other non-current assets	9,070	11,977
Total non-current assets	24,557	33,691
Total assets	$ 609,366	$ 332,975
Liabilities and Shareholders' Equity		
Accrued research and development	6,351	9,044
Deferred revenue, current	7,657	—
Lease liability, current	5,940	5,512
Other current liabilities	13,504	11,292
Total current liabilities	33,452	25,848
Deferred revenue, non current	102,933	110,242
Lease liability, non-current	6,386	12,326
Other non-current liabilities	553	553
Total non-current liabilities	109,872	123,121
Total liabilities	143,324	148,969
Total shareholders' equity	466,042	184,006
Total liabilities and shareholders' equity	$ 609,366	$ 332,975

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