



Prothena Q4/YE Financial Results

February 11, 2021

Agenda and Speakers

- **Prothena Highlights and Path for Sustainable Growth**

- Gene Kinney, PhD, President & Chief Executive Officer

- **2020 Financial Results and 2021 Guidance**

- Tran Nguyen, Chief Operating Officer & Chief Financial Officer

- **Concluding Remarks and Upcoming R&D Milestones**

- Gene Kinney, PhD, President & Chief Executive Officer

- **Q&A**

- Radhika Tripuraneni, MD, MPH, Chief Development Officer & ATTR Program Head
- Wagner Zago, PhD, Chief Scientific Officer

Forward Looking Statements

This overview 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 2021 and beyond; our goal of building a protein dysregulation platform; the treatment potential, designs, and proposed mechanisms of action of birtamimab, prasinezumab, PRX004, PRX005, PRX012 and multi-immunogen A β -tau vaccine; plans for future clinical studies of birtamimab, prasinezumab, PRX004, PRX005, and PRX012; amounts we might receive under our collaborations with Roche and Bristol-Myers Squibb; the expected timing of reporting data from prior clinical studies of birtamimab, the Phase 2 clinical study of prasinezumab, and preclinical studies of PRX005; potential indications and the potential superior attributes and efficacy of novel epitopes and antibodies we have identified in our programs, including our TDP-43 and undisclosed programs; our potential to advance, initiate and complete IND enabling studies for our discovery and preclinical programs; our anticipated net cash burn from operating and investing activities for 2021 and expected cash balance at the end of 2021; and our estimated net loss and non-cash share-based compensation expense for 2021. These forward-looking 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 effects on our business of the worldwide COVID-19 pandemic and 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 March 3, 2020, 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 2020. We undertake no obligation to update publicly any forward-looking statements contained in this presentation as a result of new information, future events, or changes in our expectations.



Prothena Highlights and Path for Sustainable Growth

Gene Kinney, PhD

President & Chief Executive Officer

Highlights for Today

- **2020 financial guidance met**

- 2021 financial guidance

- **Rare peripheral amyloid portfolio**

- Birtamimab – Phase 3 AFFIRM-AL under SPA at unprecedented $p \leq 0.10$ for AL amyloidosis
- PRX004 – improvements in neuropathy and cardiac function in ATTR amyloidosis

- **Neurodegenerative portfolio**

- Prasinezumab (α -synuclein) advancing in Phase 2b study in early Parkinson's disease
- Alzheimer's disease portfolio advancing with PRX005 (tau) and PRX012 ($A\beta$)

Our Proven Scientific Platform for Delivering Transformational Therapeutics

**Proven protein
dysregulation platform
specifically targeting
pathogenic forms that
cause disease**

**Scientific platform
consistently translating
into clinical
proof-of-concept**

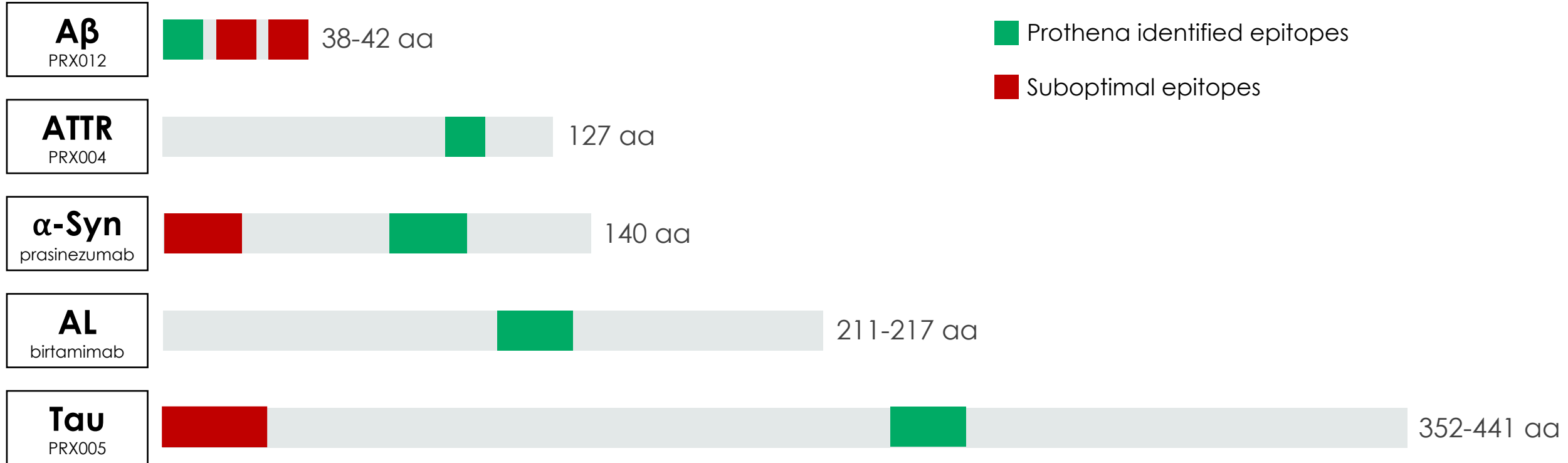
**Blockbuster indications
with high unmet need**

STRONG CORPORATE FOUNDATION

Epitope Matters

Identifying Novel Epitopes and Antibodies with Superior Attributes

Target: listed in order of protein length



Zago et al., 2012, *Journal of Neuroscience*; Higaki et al. 2016, *Amyloid*; Games et al., 2014, *Journal of Neuroscience*; Renz et al, 2016, *Amyloid*; Wall et al, 2011, *Frontiers in Immunology*; Data on file, to be presented at ADPD 2021

Growing Clinical Evidence Supporting Our Platform

Rare Peripheral Amyloid Disease

- **Birtamimab** – Significant survival benefit observed with 59% relative risk reduction on all-cause mortality in Mayo Stage IV patients with AL amyloidosis over 9 months¹
- **PRX004** – First depleter MOA in ATTR amyloidosis with observed improvement in neuropathy and cardiac systolic function²

Neurodegenerative Disease

- **Prasinezumab** – First potentially disease modifying anti- α -synuclein antibody to significantly slow progression of Parkinson's disease³
- **Alzheimer's portfolio**, including:
 - **PRX005**, anti-tau antibody targeting novel epitope
 - **PRX012**, anti-A β antibody with superior binding properties and subcutaneous delivery⁴

¹ Phase 3 VITAL study post hoc analysis presented Feb. 1, 2021

² Phase 1 study results presented Dec. 9, 2020

³ Phase 2 PASADENA study results presented Sept. 11, 2020

⁴ CTAD 2020 abstract presented Nov. 2020

Blockbuster Indications with High Unmet Need

Rare Peripheral Amyloid Diseases

Orphan market opportunities

60k to 120k¹

**ADVANCED
AL AMYLOIDOSIS**
(Mayo Stage IV)

BIRTAMIMAB

130k to 490k²

**MODERATE-TO-
ADVANCED ATTR-CM**
(NYHA Class III and IV)

PRX004

Neurodegenerative Diseases

2.6 Million³

EARLY PD
(Hoehn & Yahr 1-3)

PRASINEZUMAB

37 Million⁴

PRODROMAL-MILD AD
(MMSE 24-30)

PRX005, PRX012

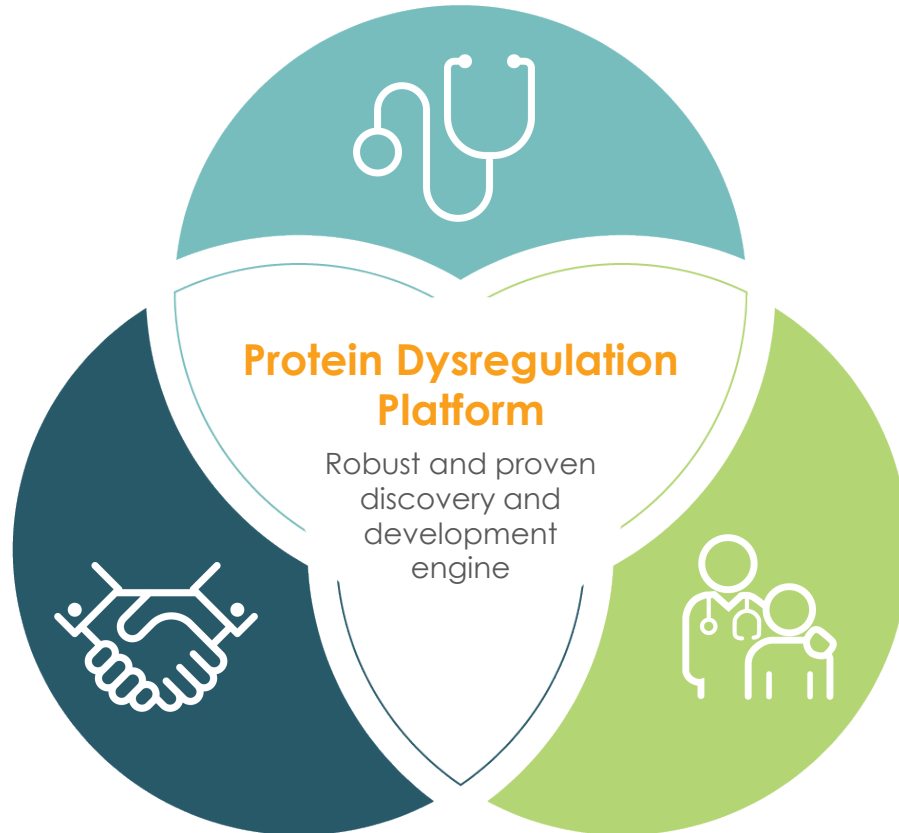
¹ Zhang et al, 2019; Kumar et al 2012; VITAL study; Clearview Analysis

² GlobalData epidemiology for major markets (US, EU5, Japan, China); Gonzalez-Lopez et al, 2015; Gonzalez-Lopez et al, 2017; Maurer et al, 2016; Gagliardi et al, 2018

³ Internal estimates

⁴ Decision Resources Group epidemiology

Path for Sustainable Growth



Clinical

3 Late-stage programs

6 Potential INDs from internal discovery engine

Collaboration

Strong collaborations with Roche and Bristol-Myers Squibb

Significant potential partner payments add to current cash of \$298 million¹

Commercial

Transition to fully-integrated commercial biotech

¹ Includes cash, cash equivalents and restricted cash at end of 4Q20



2020 Financial Results and 2021 Guidance

Tran Nguyen

Chief Operating Officer & Chief Financial Officer

2020 Actuals vs. Guidance

	2020 Actuals	2020 Guidance	Description
Net Cash Used in Operating and Investing Activities	\$81M	\$75 – 85M	Met
Net Loss	\$111M ¹	\$101 – 118M	Met
YE Cash Balance ²	\$298M	\$294 – 304M	Met

¹ Includes non-cash share-based compensation expense of \$22 million

² Includes cash, cash equivalents, and restricted cash

2021 Financial Guidance

	2021 Financial Guidance ¹
Net Cash Used in Operating and Investing Activities	\$51 – 74M
Net Loss	\$79 – 111M ²
YE Cash Balance ³ (midpoint)	\$235M

¹ Includes \$60M payment from Roche upon first patient dosed in Phase 2b study of prasinezumab

² Includes an estimated \$20M of non-cash share-based compensation expense

³ Includes cash, cash equivalents, and restricted cash



Concluding Remarks and Upcoming R&D Milestones

Gene Kinney, PhD

President & Chief Executive Officer

Robust R&D Pipeline

Focused on Rare Peripheral Amyloid and Neurodegenerative Diseases

Program/Target	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights	Next Milestone
Birtamimab / AL <i>AL Amyloidosis</i>	AFFIRM-AL (Phase 3, under SPA ¹ agreement with FDA)					 prothena	• P3 initiation mid-2021
Prasinezumab / α-Syn <i>Parkinson's Disease</i>	PASADENA (Phase 2)					 prothena 	• AD/PD oral presentation March • P2b initiation 2Q21; \$60M at FPI ²
PRX004 / ATTR <i>ATTR Amyloidosis</i>	Phase 1 Complete					 prothena	• P2/3 initiation 4Q21
PRX005 / Tau <i>Alzheimer's Disease</i>	Preclinical					 Bristol Myers Squibb™	• AD/PD oral presentation in March • IND 3Q21; \$80M U.S. opt-in ³
PRX012 / Aβ <i>Alzheimer's Disease</i>	Preclinical					 prothena	• IND 1Q22
Undisclosed <i>AD in Down Syndrome</i>	Discovery					 prothena	• IND 2022
Undisclosed <i>Neurodegeneration</i>	Discovery					 Bristol Myers Squibb™	• IND
Vaccine / Aβ + Tau <i>Alzheimer's Disease</i>	Discovery					 prothena	• IND
TDP-43 <i>ALS</i>	Discovery					 Bristol Myers Squibb™	• IND

mAb

Small
Molecule

Vaccine

Undisclosed

¹ Primary endpoint of all-cause mortality at p≤0.10 under the Special Protocol Assessment (SPA) agreement with FDA; ² \$60 million milestone payment at Phase 2b first patient dosed; ³ \$80 million potential option payment for US rights
Aβ, Abeta; AD, Alzheimer's disease; ALS, amyotrophic lateral sclerosis; mAb, monoclonal antibody



Q&A

Upcoming R&D Milestones

Birtamimab for potential treatment of AL amyloidosis

- ☐ Phase 3 AFFIRM-AL Study initiation expected mid-2021
- ☐ VITAL study 9-month results expected to be presented at medical conference in 2021

Prasinezumab for potential treatment of Parkinson's disease (collaboration with Roche)

- ☐ New pre-specified exploratory subgroup analyses as well as previously presented results from Part 1 of the Phase 2 PASADENA study to be presented at ADPD 2021
- ☐ \$60 million clinical milestone payment upon first patient dosed in Phase 2b; further details expected 2Q21
- ☐ Results from Part 2 of the Phase 2 PASADENA study expected to be presented at a medical conference

PRX004 for potential treatment of ATTR-cardiomyopathy

- ☐ Initiation of Phase 2/3 study expected 4Q21
- ☐ Phase 1 study results expected to be presented at medical conference in 2021

PRX005 for potential treatment of Alzheimer's disease (collaboration with BMS)

- ☐ Preclinical data to be presented at ADPD 2021
- ☐ IND filing expected 3Q21, with potential \$80 million US option payment

PRX012 for potential treatment of Alzheimer's disease

- ☐ IND filing expected 1Q22