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Confirmatory Phase 3 *AFFIRM-AL* Study of Birtamimab in Mayo Stage IV Patients with AL Amyloidosis

February 2, 2021

Agenda and Speakers

- **Introduction and Background**
  - Gene Kinney, PhD, President & Chief Executive Officer
- **Birtamimab Overview**
  - Wagner Zago, PhD, Chief Scientific Officer
- **AL Amyloidosis Patient Journey, VITAL Study Results and AFFIRM-AL Study**
  - Morie Gertz, MD, MACP, Division of Hematology, Mayo Distinguished Clinician, Mayo Clinic
- **AL Amyloidosis Market Opportunity**
  - Tran Nguyen, Chief Operating Officer & Chief Financial Officer
- **Concluding Remarks**
  - Gene Kinney, PhD, President & Chief Executive Officer
- **Q&A**

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 and preclinical pipeline and the expected milestones in 2021 and beyond; our goal of building a neurotherapeutics engine; the design, proposed mechanism of action and possible clinical benefits of birtamimab, and its potential as a treatment for Mayo Stage IV patients with AL amyloidosis; the design, expected enrollment and expected timing of the Phase 3 AFFIRM-AL study of birtamimab; the results from post hoc analyses that reveal a potential survival benefit of birtamimab in Mayo Stage IV patients; the design, proposed mechanism of action and possible clinical benefits of prasinezumab (PRX002/RG7935), and its potential as a treatment for Parkinson's disease; the design of the Phase 2 PASADENA study of prasinezumab; the expected timing of announcing additional data from the Phase 2 study of prasinezumab; the design and timing of future clinical studies of prasinezumab; amounts we might receive under our collaboration with Roche; the design, proposed mechanism of action and possible clinical benefits of PRX004, and its potential as a treatment for ATTR amyloidosis; the potential of PRX004 to complement proven therapies and offer superior efficacy; the design and capabilities of our misTTR assay for hereditary ATTR; the design of the Phase 1 study of PRX004; the design and timing of future clinical studies of PRX004; amounts we might receive under our collaboration with Bristol-Myers Squibb; potential Tau and abeta indications; the potential superior attributes and efficacy of novel epitopes and antibodies we have identified in our Tau, abeta and TDP-43 programs, including PRX005 and PRX012; our potential to advance, initiate and complete IND enabling studies for our tau and abeta programs; and our ability to progress our vaccine and small molecule programs. 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, as well as 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 presentation as a result of new information, future events or changes in our expectations.

Introduction and Background

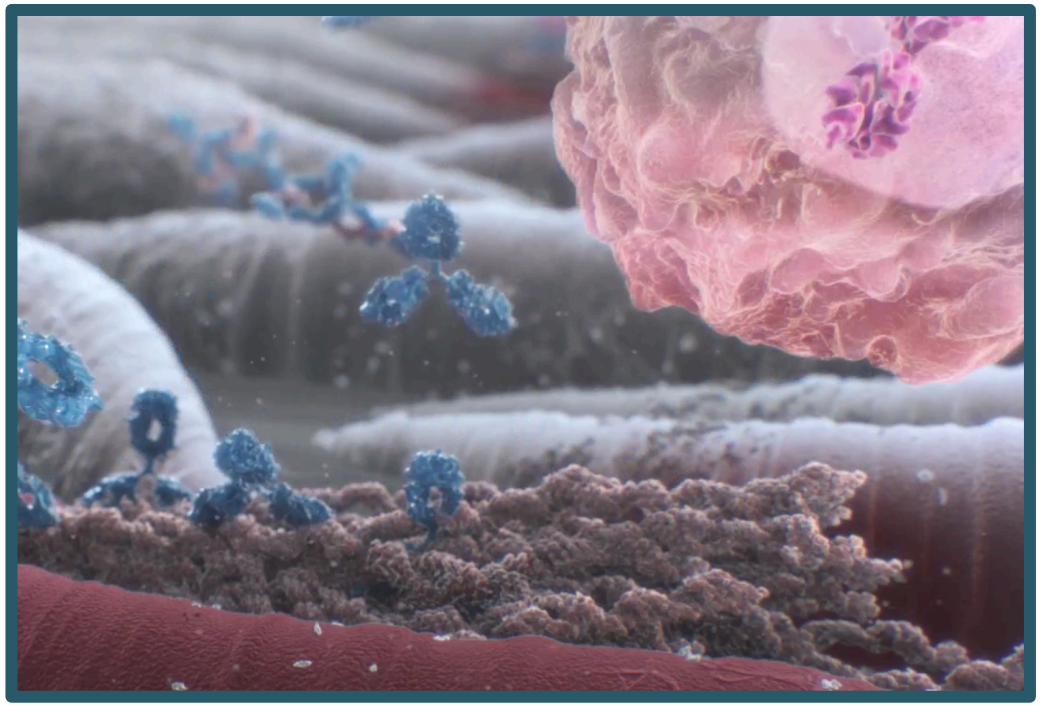
Gene Kinney, PhD

President & CEO

Protein Dysregulation and Amyloid Causes Multiple Fatal Diseases

Expertise in **protein dysregulation** applied to **rare peripheral amyloid disease** and **neurodegeneration**

- ✓ Understanding protein dysregulation in the context of disease
- ✓ Expertise in targeting toxic proteins to alleviate detrimental effects
- ✓ Translating science into clinical benefit across multiple programs



The Path Leading to Today's News

VITAL results analyzed

- Results **analyzed** with **input from external advisors** and **KOLs**
- **Greater than 50% relative risk reduction on all-cause mortality** in Mayo Stage IV patients at high risk for early mortality

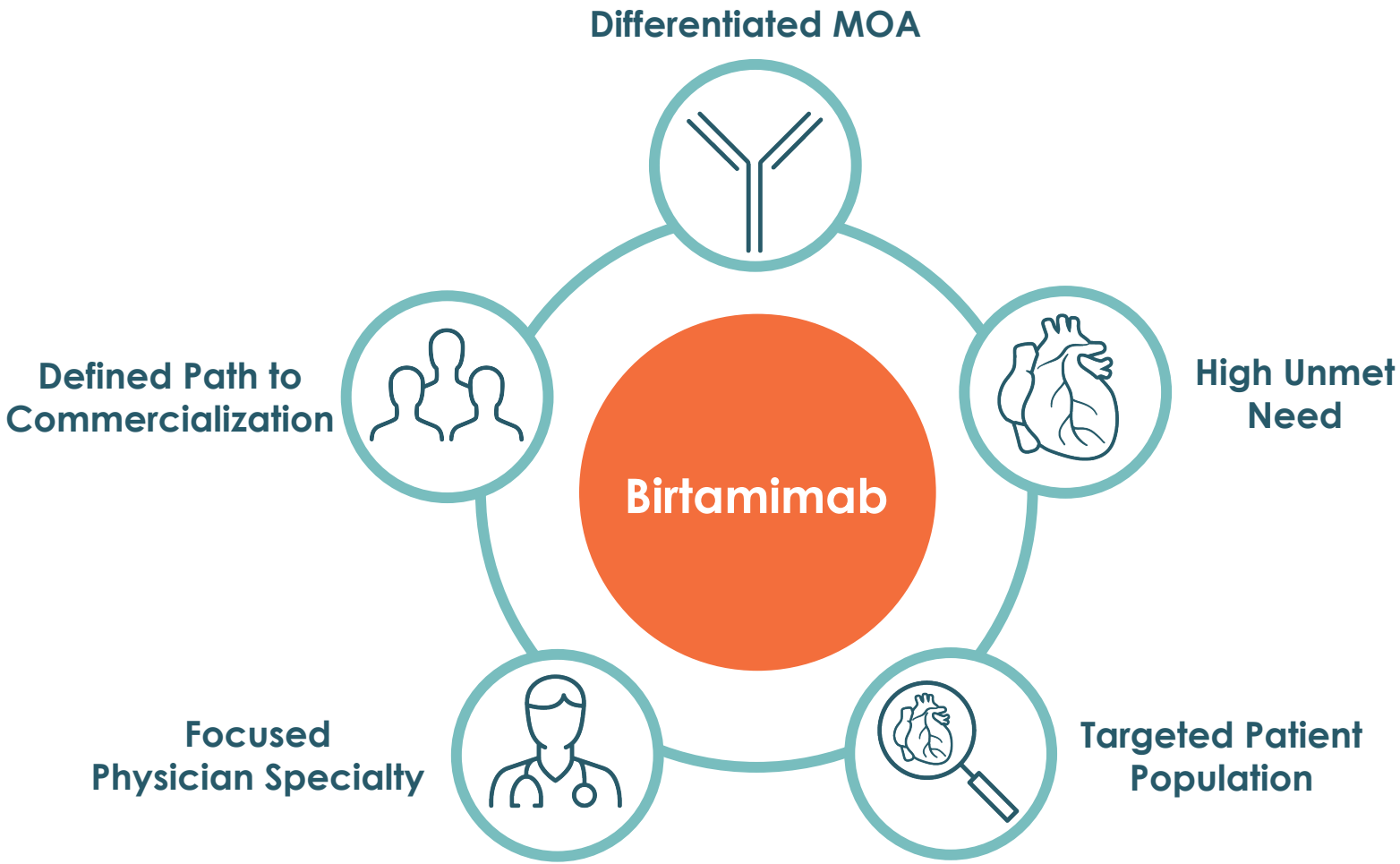
Collaboration and alignment with FDA

- Multiple **in-depth discussions** with FDA
- **VITAL enables path forward under SPA**

AFFIRM-AL

- **Confirmatory Phase 3 global study of birtamimab in Mayo Stage IV patients** with AL amyloidosis
- **Primary endpoint all-cause mortality**
- **SPA** agreement with significance level of **$p \leq 0.10$**
- Expected to **initiate mid-2021**

Birtamimab: Anti-Amyloid Immunotherapy for AL Amyloidosis



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Birtamimab Overview

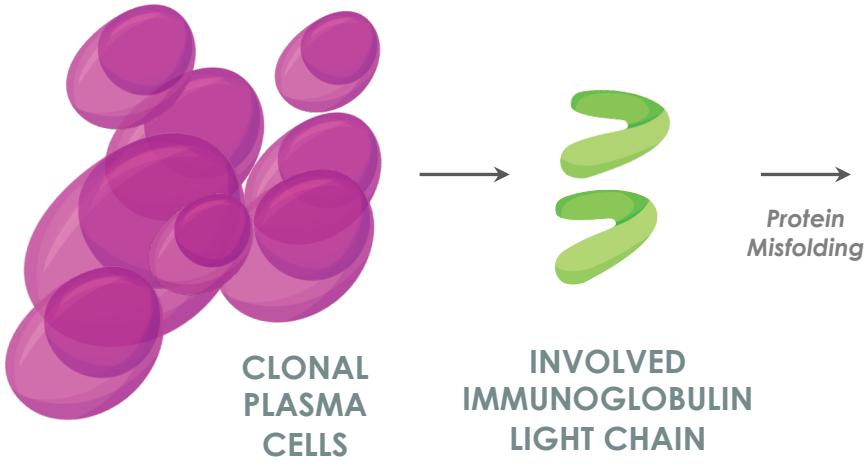
Wagner Zago, PhD

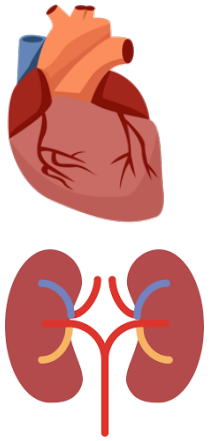
Chief Scientific Officer

Amyloid Causes Organ Dysfunction and Failure in AL Amyloidosis

Amyloid accumulates over time and is present in organs at diagnosis

PATHOGENIC PATHWAY





HEART
Restrictive cardiomyopathy
Heart failure

KIDNEY
Proteinuria
Kidney failure

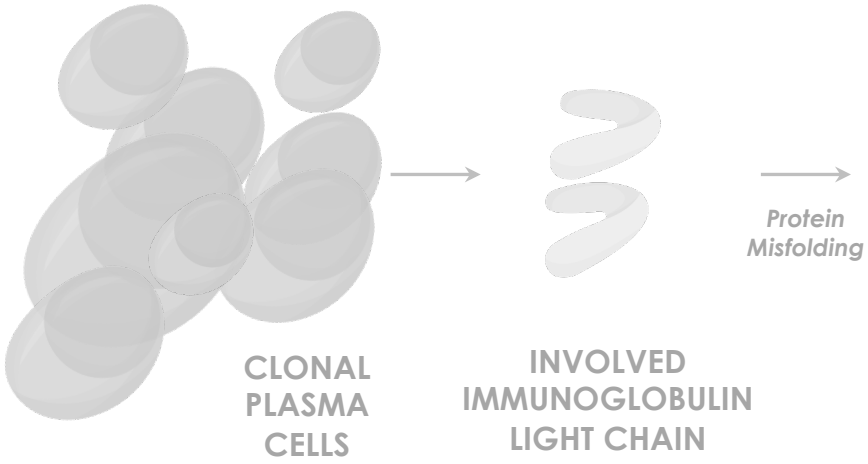
Current treatment approach:
Reduce new protein production

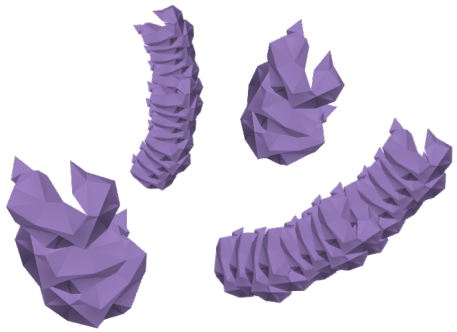
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Birtamimab: Anti-Amyloid Immunotherapy

Depleter mechanism designed to clear pathogenic light chain amyloid

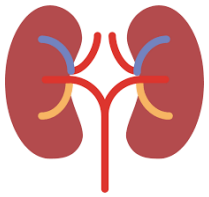
PATHOGENIC PATHWAY







HEART
Restrictive cardiomyopathy
Heart failure



KIDNEY
Proteinuria
Kidney failure

Current treatment approach:
Reduce new protein production

Birtamimab:
Uniquely suited for patients at high risk for early mortality
Survival benefit observed in placebo-controlled study

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Birtamimab Key Characteristics and Preclinical Findings

Molecule

- ✓ Fully humanized IgG1 antibody
- ✓ No immunogenicity detected to date
- ✓ Half-life supports monthly IV infusions

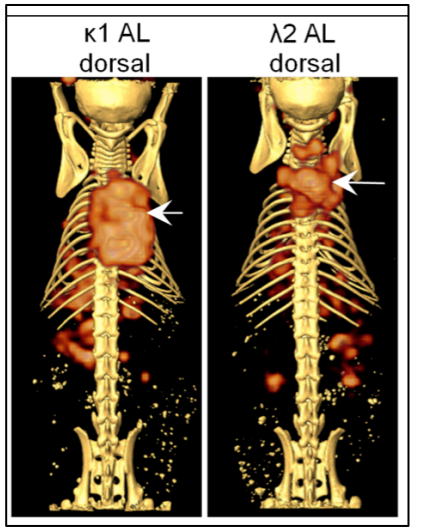
Binding characteristics

- ✓ Broadly binds to both kappa and lambda aggregated light chain (LC)
- ✓ Epitope well defined, highly conserved, and specific to misfolded form of LCs exposed through all stages of aggregation including soluble aggregates and deposited amyloid
- ✓ Binds to aggregates in multiple organs

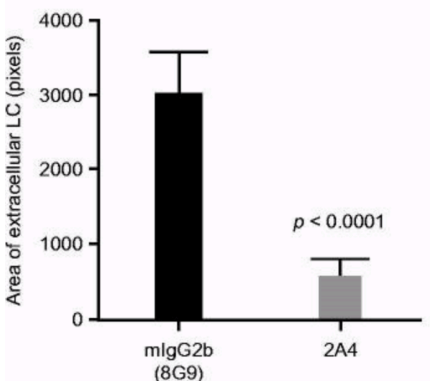
Mechanism

- ✓ Broad perfusion from vasculature to bind kappa and lambda LC amyloid in vivo
- ✓ Promotes clearance of amyloid deposits via phagocytosis

Birtamimab* binds LC amyloid fibrils in vivo



Birtamimab* induces LC amyloid clearance by phagocytosis

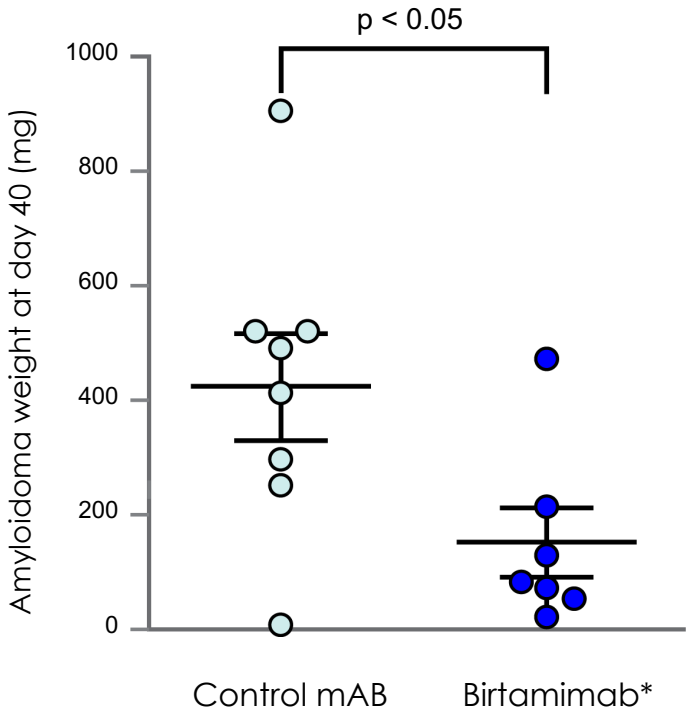


*murine version of birtamimab, 2A4
Wall et al., PLOS ONE, 2012, Renz et al., Amyloid, 2016

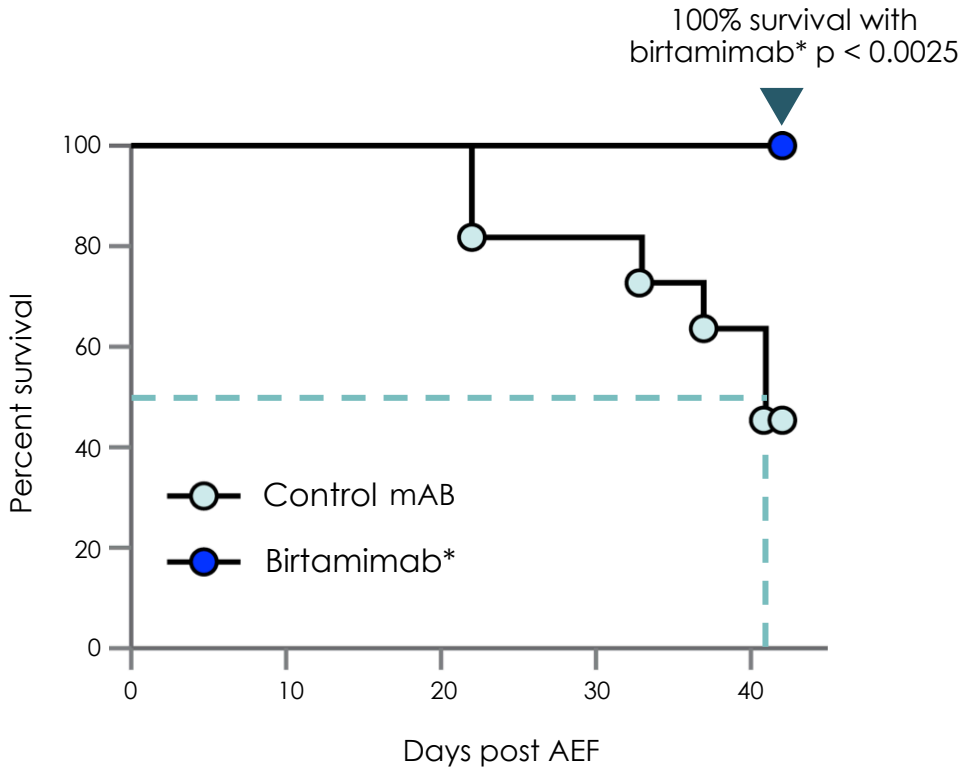
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Birtamimab* Demonstrates Significant Amyloid Clearance and Prolonged Survival in Preclinical Model

Birtamimab* Removes Amyloid In Vivo



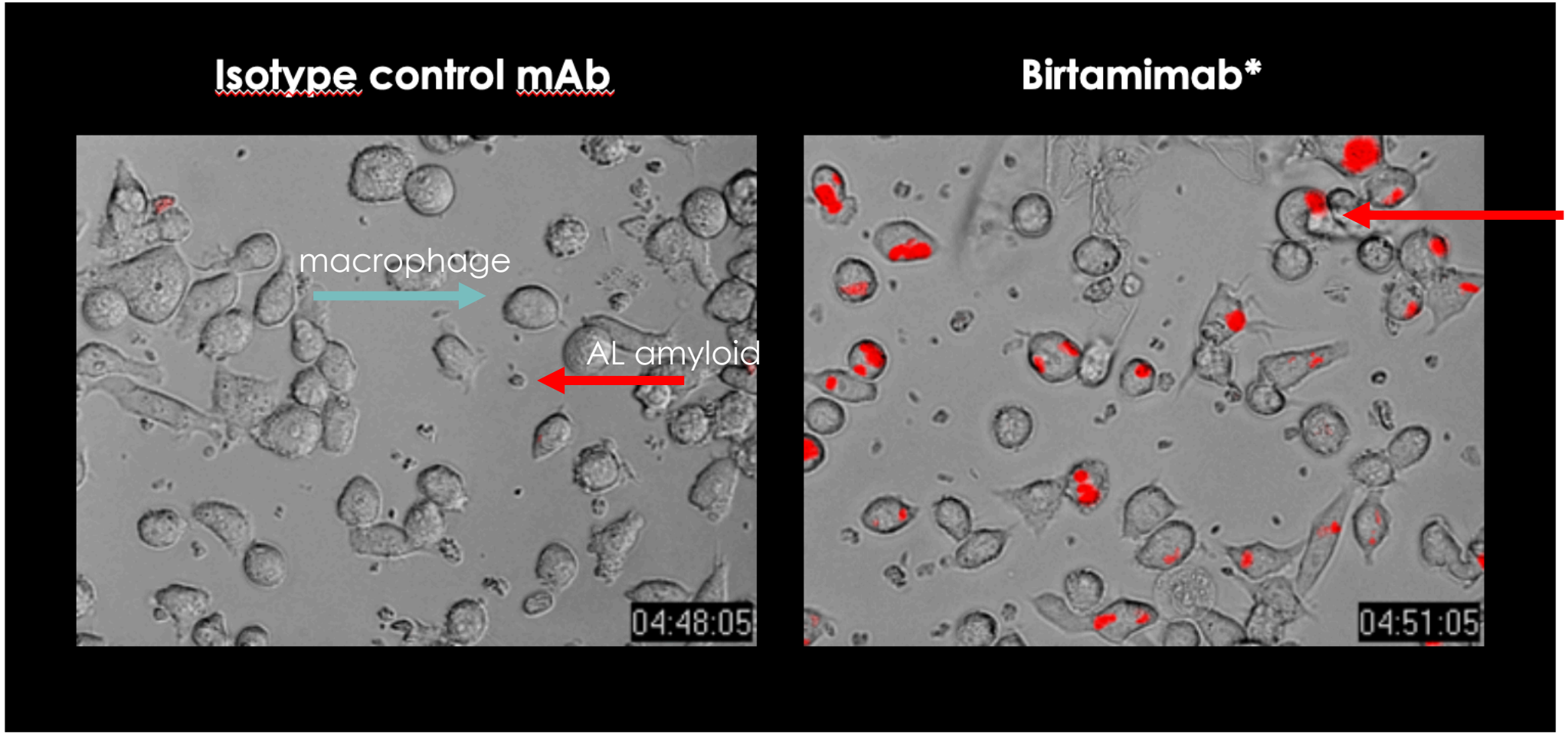
Birtamimab* Prolongs Survival in Transgenic Mouse Model



*murine version of birtamimab, 2A4
Wall et al., PLOS ONE, 2012, data on file

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Birtamimab* Induces Phagocytosis of Light Chain Amyloid (AL)



In the presence of birtamimab, phagocytes engulf amyloid, indicated by red fluorescence

*murine form of birtamimab, 2A4
Renz et al., Amyloid, 2016

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AL Amyloidosis Patient Journey

VITAL and *AFFIRM-AL* Studies

Morie Gertz, MD, MACP

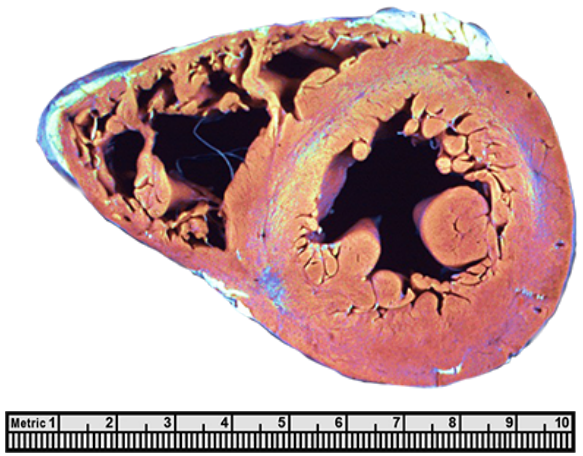
Division of Hematology

Mayo Distinguished Clinician, Mayo Clinic

AL Amyloidosis is Caused by Amyloid Deposition

- AL amyloidosis is a rare, progressive, and fatal disease caused by amyloid deposition leading to organ dysfunction and failure
- In AL amyloidosis, immunoglobulin light-chain misfolds, forms toxic aggregates and deposits as amyloid in vital organs, most commonly the heart
- Clinical manifestations of the disease depend on impacted organs and the degree of deposition
- Morbidity and mortality are driven by progressive restrictive cardiomyopathy and heart failure

Normal Heart[1]



Amyloidosis[2]

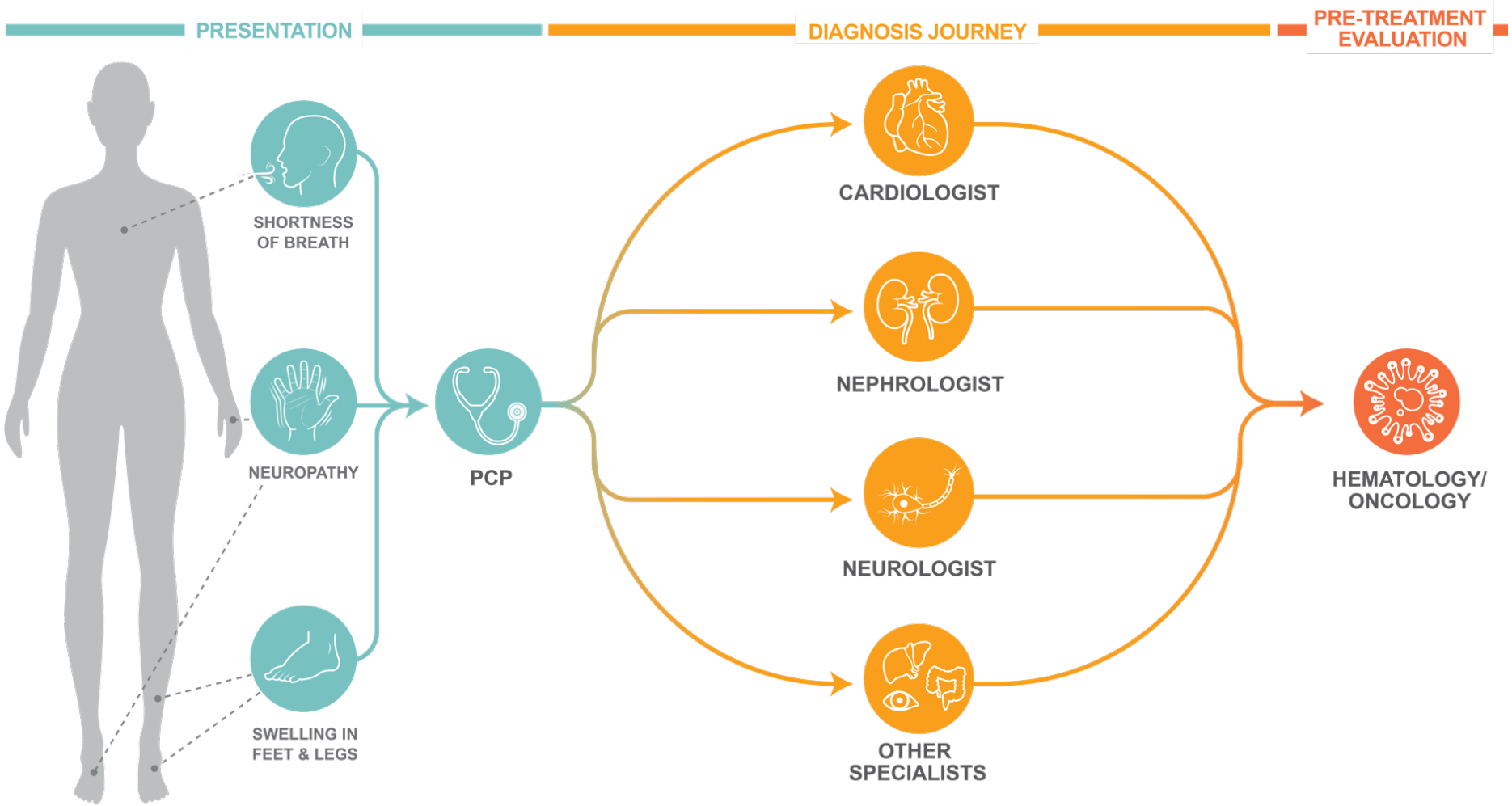


By the time they are diagnosed, patients have accumulated significant cardiac amyloid deposition

[1]Modified from http://www.med.uottawa.ca/patho/eng/Public/cardio/lab2.html
[2]Seward et al., 2010

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AL Amyloidosis Patients Face a Long Journey Before Diagnosis



- 37% of patients are diagnosed >12 months after initial symptoms
- 32% of patients are seen by ≥ 5 doctors before diagnosis
- Only 8% of patients see 1 doctor before diagnosis

Lousada et al, ARC Online Survey, 2015

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Confirming AL Amyloidosis Diagnosis Requires a Patchwork of Clinical Assessments



AL Amyloidosis Diagnostic Tests

- ☐ Blood test
- ☐ Urinalysis
- ☐ Bone marrow biopsy
- ☐ Fat pad aspirate biopsy
- ☐ Echocardiogram, MRI, or nuclear imaging
- ☐ Biopsy of other affected organs

AL Amyloidosis Diagnostic Dynamics

- Bone marrow biopsies, blood tests, and urinalyses confirm AL amyloidosis diagnoses
  - Blood and urine tests show the presence of elevated monoclonal light chain levels
  - Bone marrow biopsies demonstrate abnormally high plasma cell levels
- Abdominal fat pad aspirate biopsies followed by histological tests confirm amyloid involvement
- Imaging tests and biopsies of affected organs (e.g., heart, kidneys) highlight the extent of disease progression
- Mayo Staging used as prognostic risk classification system that informs potential treatment options

Sanchorawala. CJASN. 2006; Mayo Clinic; ClearView Analysis

Mayo Staging Criteria (Kumar et al., 2012)

A prognostic risk classification system

Stratification for Mayo Staging Criteria		
Test	**Value**	**Score**
NT-proBNP	<1800 pg/mL	0
	≥ 1800 pg/mL	1
Troponin-T	≤ 0.03 ng/mL[1]	0
	> 0.03 ng/mL[1]	1
dFLC	< 18 mg/dL	0
	≥ 18 mg/dL	1

Total Score:

0 = Mayo Stage I

1 = Mayo Stage II

2 = Mayo Stage III

3 = Mayo Stage IV

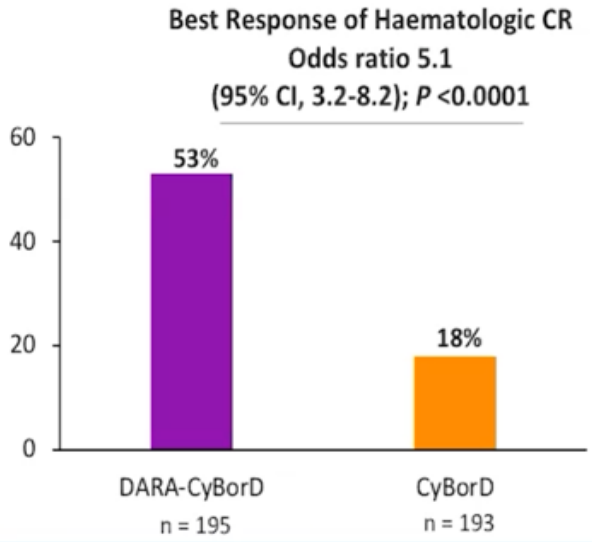
[1] Modified from the value of 0.025 ng/mL cited in Kumar et al., to 0.03 ng/mL, which is the lowest validated determination for this commercially available test.
NT-proBNP, N-terminal pro hormone B-type natriuretic peptide; dFLC = differential free light chain

Advances in Plasma-Cell Directed Approaches Have Resulted in Significantly Higher Hematologic Complete Response Rates

EHA EUROPEAN HEMATOLOGY ASSOCIATION

EHA25 VIRTUAL

Haematologic CR: Primary Endpoint



- Assessed by blinded Independent Review Committee
- CR per Comenzo criteria[1] with clarifications:
  - Abnormal FLC ratio does not preclude CR[2]
  - CR requires confirmation
- The CR rate at 6 months was consistent with overall CR rate
  - 50% DARA-CyBorD vs 14% CyBorD (odds ratio 6.1; *P* <0.0001)
- Median time to CR[a]:
  - DARA-CyBorD: 60 days
  - CyBorD: 85 days

Responses with DARA-CyBorD were deeper and achieved more rapidly

CI, confidence interval; FLC, free light chain.
[a]Among CR responders (DARA-CyBorD, n = 104; CyBorD, n = 35).
1. Comenzo RL, et al. *Leukemia*. 2012;26(11):2317-2325. 2. Sidana S, et al. *Leukemia*. 2019;34(5):1472-1475.

Primary Results from the Daratumumab Phase 3 ANDROMEDA Study, Presented at EHA June 2020

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However, Plasma-Cell Directed Approaches Have Not Improved Survival in Studies Conducted to Date

EHA EUROPEAN HEMATOLOGY ASSOCIATION

EHA25 VIRTUAL

Safety: Most Common Any Grade (≥25%) and Grade 3 or 4 (>5%) TEAEs

Median duration of treatment was 9.6 months for DARA-CyBorD and 5.3 months CyBorD

	DARA-CyBorD (n = 193)		CyBorD (n = 188)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Patients experiencing a TEAE, %	98	59	98	57
Diarrhoea	36	6	30	4
Peripheral oedema	36	3	36	6
Constipation	34	2	29	0
Peripheral sensory neuropathy	31	3	20	2
Fatigue	27	4	28	3
Nausea	27	2	28	0
Upper respiratory tract infection	26	<1	11	<1
Anaemia	24	4	23	5
Insomnia	24	0	25	1
Lymphopaenia	19	13	15	10
Neutropaenia	11	5	6	3
Pneumonia	11	8	6	4
Syncope	7	5	6	6
Cardiac failure[a]	9	6	7	5

- Infections: 12% DARA-CyBorD vs 9% CyBorD
- Serious TEAEs: 43% DARA-CyBorD vs 36% CyBorD
  - Most common was pneumonia
- Rate of discontinuation due to TEAEs (overall): 4% both arms
- In the first 6 months, 25 deaths with DARA-CyBorD vs 20 with CyBorD were observed
  - >90% were related to underlying AL amyloidosis (both arms)

The safety profile of DARA-CyBorD was consistent with the known profiles of DARA SC and CyBorD

AE, treatment-emergent adverse event.
cludes overall and congestive cardiac failure.

Primary Results from the Daratumumab Phase 3 ANDROMEDA Study, Presented at EHA June 2020

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VITAL Study Results

Phase 3 VITAL Study Overview

- **Global, randomized, double-blinded, placebo-controlled study**
  - Sample size and randomization
    - N=260
    - 1:1
  - Key eligibility criteria
    - Confirmed diagnosis of AL amyloidosis
    - Newly diagnosed and treatment naïve
    - Cardiac involvement
  - Treatment regimen
    - Birtamimab 24 mg/kg vs. placebo, with concurrent standard of care (SoC) in both arms
- **Primary endpoint**
  - Composite endpoint of time to all-cause mortality or time to cardiac hospitalizations (≥90 days) as adjudicated by the Clinical Events Committee
- **Secondary endpoints**
  - SF-36v2 PCS, 6MWT
- **Randomization stratification**
  - Mayo Stage I-II vs III-IV, renal stage I vs II-III and 6MWT distance < 300 m vs ≥ 300m

- **30% of patients enrolled in VITAL (N=77) were characterized as Mayo Stage IV at baseline**
  - 38 in birtamimab + SoC arm
  - 39 in placebo + SoC arm

SF-36v2 PCS = Short Form-36 Physical Component Score; 6MWT = 6-Minute Walk Test

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VITAL Study Demographics and Key Baseline Characteristics: Mayo Stage IV Subjects

	Birtamimab + SOC (n=38)	Placebo + SOC (n=39)	Total (N=77)
Age Median (Q1, Q3)	63.56 (55.71, 69.78)	63.74 (56.97, 68.40)	63.74 (56.89, 68.59)
Gender N (%)			
Male	25 (65.8)	28 (71.8)	53 (68.8)
Female	13 (34.2)	11 (28.2)	24 (31.2)
Race N (%)			
Black or African American	2 (5.3)	2 (5.1)	4 (5.2)
White	36 (94.7)	36 (92.3)	72 (93.5)
Other	0	1 (2.6)	1 (1.3)
Ethnicity N (%)			
Not Hispanic or Latino	34 (89.5)	36 (92.3)	70 (90.9)
Not Provided or Unknown	4 (10.5)	3 (7.7)	7 (9.1)
Screening NT-proBNP N (%)			
≥ 1800 pg/mL	38 (100)	39 (100)	77 (100)
NT-proBNP (pg/mL) Median (Q1, Q3)	5142 (3228, 5939)	5415 (4054, 8073)	5254 (3724, 7048)
dFLC* (mg/dL) Median (Q1, Q3)	44.44 (25.13, 56.17)	57.42 (35.52, 106.28)	49.56 (29.49, 72.05)
FLC ratio Median (Q1, Q3)	0.05 (0.02, 0.08)	0.05 (0.03, 11.14)	0.05 (0.03, 0.10)
Troponin-T (ng/mL) Median (Q1, Q3)	0.05 (0.04, 0.09)	0.09 (0.06, 0.13)	0.06 (0.05, 0.11)
6MWD (meters), Median (Q1, Q3)	343.4 (290.2, 422.0)	332.0 (248.4, 410.9)	342.6 (271.6, 410.9)

*Baseline dFLC is only calculated for subjects with an abnormal baseline FLC ratio (Kappa/Lambda <0.26 or >1.65) and is defined as the difference between involved and uninvolved free light chains.
NT-proBNP, N-terminal proB natriuretic peptide; 6MWD = 6-Minute Walk Distance

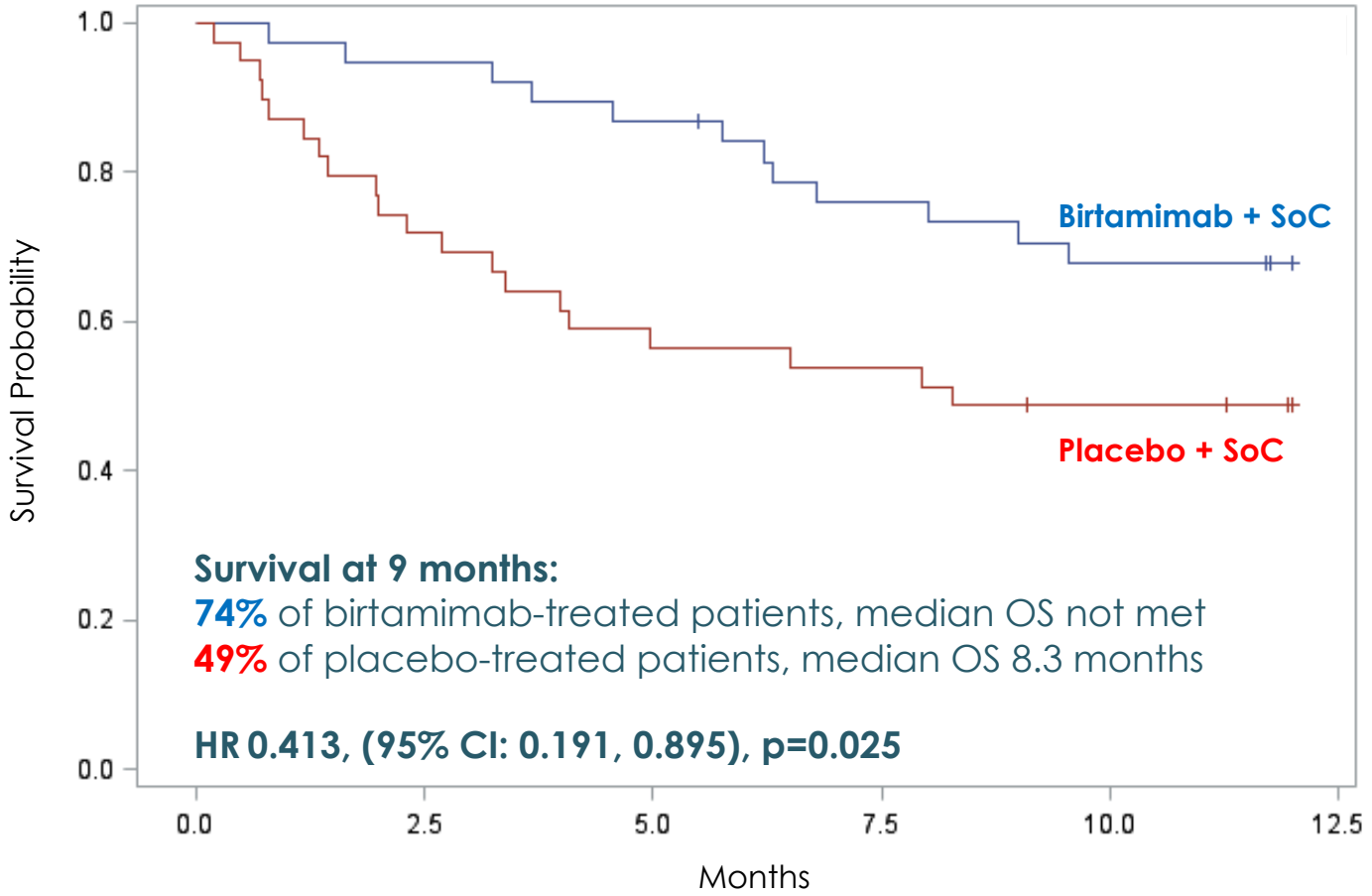
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Phase 3 VITAL Study Safety Summary for Mayo Stage IV Subjects:
Treatment-Emergent Adverse Events (TEAEs)

- **Multiple infusions of 24 mg/kg were safe and well-tolerated in the VITAL Study:**
  - The most commonly reported TEAEs (fatigue, nausea, peripheral edema, constipation and diarrhea) were similar in both groups
  - None of the subjects developed anti-birtamimab antibodies

Number (%) of subjects reporting at least 1 of the following:	Birtamimab + SoC (n=38) n (%)	Placebo + SoC (n=39) n (%)
TEAE	38 (100)	39 (100)
TEAE considered related to study drug	12 (31.6)	9 (23.1)
TEAE Grade ≥3	30 (78.9)	35 (89.7)
TEAE Grade ≥3 considered related to study drug	1 (2.6)	3 (7.7)
Related TEAE leading to death	0	0

VITAL Study of Birtamimab in AL Amyloidosis: All-Cause Mortality, Mayo Stage IV (N=77), 9 Months

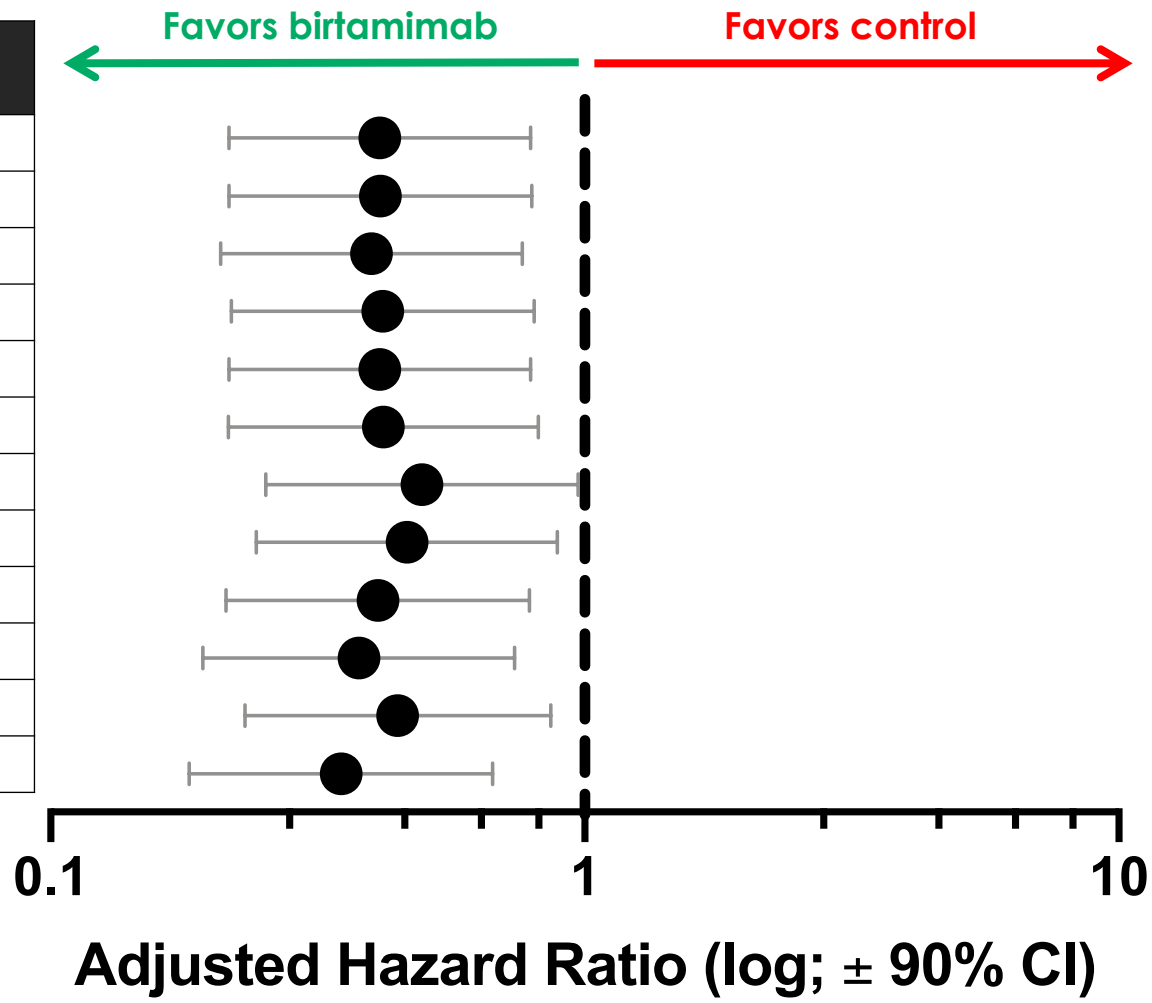


Birtamimab (NEOD001) Phase 3 VITAL study was discontinued for futility; results including Mayo Stage IV mITT analysis announced April 18, 2019, www.prothena.com
All-cause mortality regardless of prior cardiac hospitalization
SOC = Standard of Care (hematologic directed chemotherapy); OS = Overall Survival

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Birtamimab Survival Benefit Adjusted for Key Baseline Variables

Baseline Variable	Adjusted HR
Age	0.414
Sex	0.415
Race	0.399
Ethnicity	0.419
Age at diagnosis	0.414
Duration since diagnosis	0.420
NT-proBNP	0.496
dFLC	0.465
FLC	0.410
NYHA class	0.378
Troponin-T	0.447
6MWT distance	0.350



Cox Proportional Hazards Model for all-cause mortality through the first 9 months of treatment, adjusted for randomization stratification factors (Renal Stage and 6MWT distance category)

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Secondary Endpoints: Mayo Stage IV Patients (N=77)

SF-36v2 PCS Quality of Life	Placebo + SoC (n=39)	Birtamimab + SoC (n=38)	
Baseline score	31.2	31.1	**+5 points favoring birtamimab (p=0.026)**
Mean change from baseline at 9 months	**–6 points**	**–1 point**	

6MWT Functional Capacity	Placebo + SoC (n=39)	Birtamimab + SoC (n=38)	
Baseline distance (meters)	327.6	339.1	**+27 meters favoring birtamimab (p=0.046)**
Mean change from baseline at 9 months	**–22 meters**	**+5 meters**	

Mean baseline PCS and 6MWT distance by treatment group. Mean paired change from baseline to month 9 summarized by treatment group.
Missing values due to death imputed as zero, other missing values imputed as minimum of previous values.
SF-36v2 PCS, Short-Form 36 Version 2 Physical Component Score, 6MWT, 6-Minute Walk Test

Summary of Phase 3 VITAL Study Results Mayo Stage IV

- **First and only observed survival benefit in Mayo Stage IV patients**
  - 74% of birtamimab-treated patients alive at 9 months versus 49% of patients in the control group at 9 months
  - Hazard ratio = 0.413, over 9 months (p = 0.025)
- **Clinical benefit on secondary endpoints, with significant mean changes from baseline observed at 9 months on:**
  - Quality of Life: SF-36v2 PCS, +5 points favoring birtamimab (p=0.026)
  - Functional Capacity: 6MWT distance, +27 meters favoring birtamimab (p=0.046)
- **Safe and well-tolerated, Mayo Stage IV consistent with overall study**
  - Birtamimab 24 mg/kg has been safe and well tolerated in the 294 patients treated across all studies to date, with mean of 14.7 infusions over ~15 months



AFFIRM-AL STUDY

AFFIRM-AL Global Study Design

Key Eligibility Criteria

- Newly diagnosed and treatment naïve
- Confirmed diagnosis of AL amyloidosis with cardiac involvement
- Mayo Stage IV

Key Exclusion Criteria

- NT-proBNP >8500 pg/mL
- Autologous stem cell transplant

Randomize 2:1
N = 150

Birtamimab (IV q28d)
+ SoC
n = 100

Placebo (IV q28d)
+ SoC
n = 50

Primary endpoint

- All-Cause Mortality

Secondary endpoints

- SF-36v2 PCS
- 6MWT

- Designed under SPA agreement with significance level of $p \leq 0.10$
- Interim analysis when ~50% events have occurred
- Expected to initiate mid-2021

Primary endpoint of all-cause mortality at p<0.10 under the SPA agreement with FDA
NT-proBNP, N-terminal pro hormone B-type natriuretic peptide; SOC, Standard of Care; IV, intravenous; q28d, infusion once every 28 days; SF-36v2 PCS, Short-Form 36 Version 2 Physical Component Score; 6MWT, 6-Minute Walk Test

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AL Amyloidosis Market Opportunity

Tran Nguyen
Chief Operating Officer &
Chief Financial Officer

Mayo Stage IV Patients Lack Effective Treatment Options

Represent 60k-120k Patients Globally

Global Population



32-71[1] **Patients Per Million**

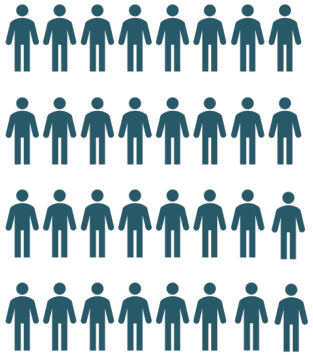
AL Amyloidosis Dx Prevalence



200k-400k patients

30%[2,3,4]

Mayo Stage IV



60k-120k patients

[1]Zhang et al, 2019; [2]Kumar et al 2012; [3]VITAL study; [4]Clearview Analysis

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Mayo Stage IV Patients in Major Markets

Targeted Opportunity in Orphan Population

					
AL Amyloidosis Dx Prevalence	~13,000	~17,500	~4,500	~30,500 Urban Only	~6,800
Mayo Stage IV Dx Prevalence	~3,900	~5,200	~1,300	~9,100	~2,000

Kyle Mayo Clin Proc. 2019; Kyle Blood 1992; Quock Blood Adv. 2018; Shimazaki The Japanese Journal of Clinical Hematology. 2018; Duhamel Blood 2017; Hemminki BMC Public Health 2012; Pinney BJ Haem 2013; Merlini Nature 2018; Desport Orphanet J Rare Diseases 2012; Schulman Eur J Haematol 2020; Zhang J CLML 2019; VITAL study; World Bank Databank; ClearView Analysis

Mayo Stage IV Patients are Primarily Treated in Amyloidosis Centers

Treatment Setting	Mayo Stage IV Patients
Amyloidosis Centers of Excellence (COEs)	17-24%
Amyloidosis Specialty Centers	43-51%
Community Centers / Private Practice	25-40%

~75% of patients primarily treated in ~500 Amyloidosis COE and specialty centers

Estimates based on US/EU/UK Market Research, LEK Analysis

Concluding Remarks

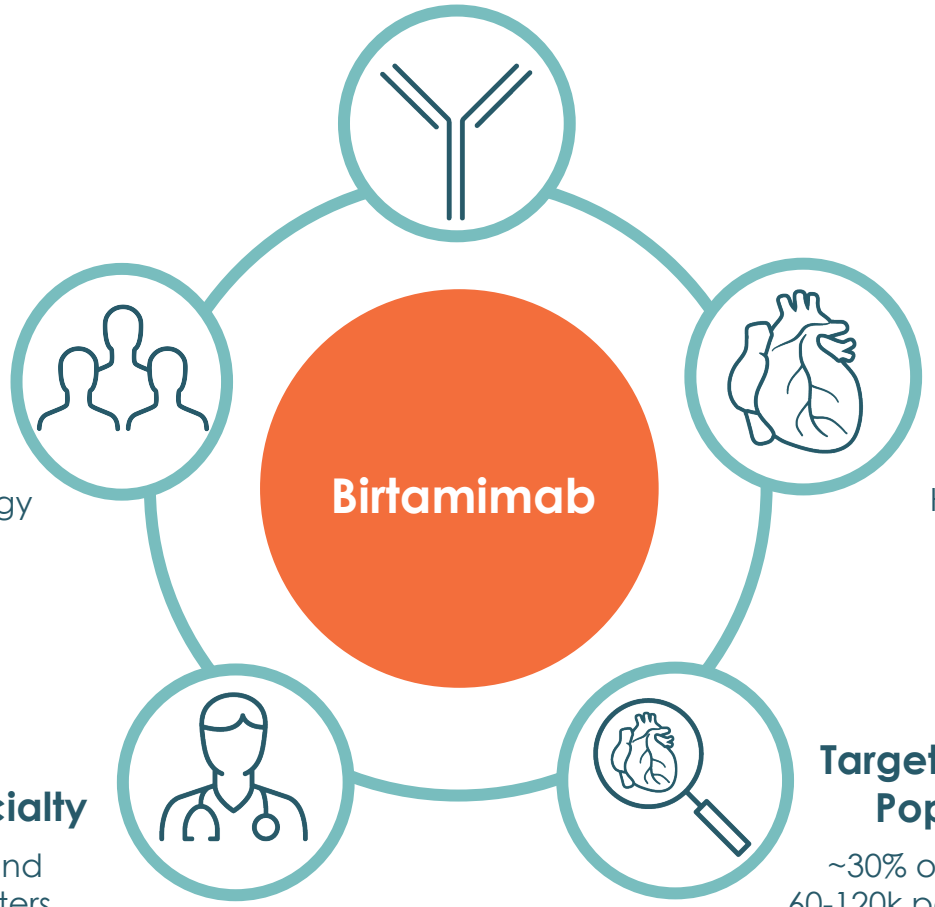
Gene Kinney, PhD

President & CEO

Birtamimab:
Opportunity to Address Urgent Unmet Need in Orphan Disease

Differentiated MOA

First-in-class anti-amyloid immunotherapy



Defined Path to Commercialization

AFFIRM-AL under SPA
Clear go-to-market strategy

High Unmet Need

Mayo Stage IV
High mortality risk

Focused Physician Specialty

AL academic and amyloidosis centers

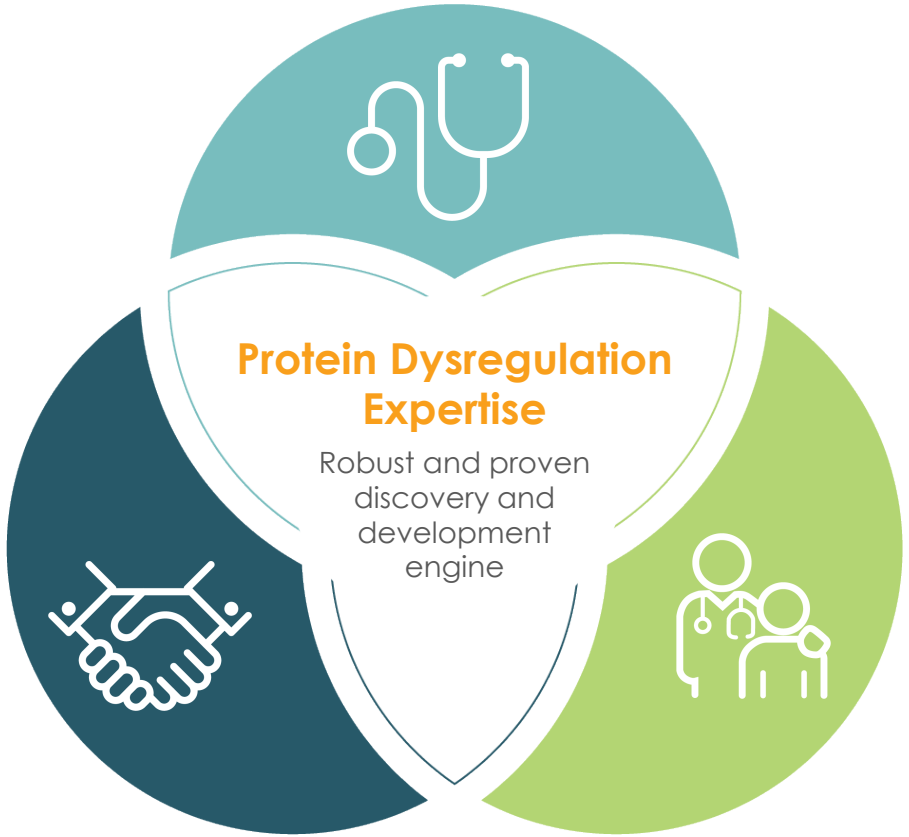
Targeted Patient Population

~30% of AL patients
60-120k patients globally

- **Depleter mechanism that clears amyloid**
- **VITAL Study**
  - First and only observed survival benefit in Mayo Stage IV patients
  - Rapid response with early survival benefit
  - Favorable safety and tolerability
- **AFFIRM-AL confirmatory, registration-enabling Phase 3 study under SPA**
- **Opportunity to establish premium product with blockbuster potential**

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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 $317 million[1]

Commercial

Transition to fully-integrated commercial biotech

[1]Includes cash, cash equivalents and restricted cash at end of 3Q20

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Q&A

Robust R&D Pipeline

Focused on neurodegenerative and rare peripheral amyloid diseases

Program/Target	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Commercial Rights	Next Milestone
Birtamimab / AL *AL Amyloidosis*				AFFIRM-AL (Phase 3, under SPA[1] agreement with FDA)		prothena	• P3 initiation mid-2021
Prasinezumab / αSyn *Parkinson's Disease*				PASADENA (Phase 2)		prothena Roche	• P2b initiation 2Q21 • $60M at FPI in P2b[2]
PRX004 / ATTR *ATTR Amyloidosis*			Phase 1 Complete			prothena	• P2/3 initiation 4Q21
PRX005 / Tau *Alzheimer's Disease*		Preclinical				Bristol Myers Squibb	• IND mid-2021 • $80M U.S. opt-in[3]
PRX012 / Aβ *Alzheimer's Disease*		Preclinical				prothena	• IND 1Q22
Undisclosed *AD in Down Syndrome*	Discovery					prothena	• IND 2022
Undisclosed *Neurodegeneration*	Discovery					Bristol Myers Squibb	• IND
Vaccine / Aβ + Tau *Alzheimer's Disease*	Discovery					prothena	• IND
TDP-43 *ALS*	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 opt in payment for US rights
Aβ, Abeta; AD, Alzheimer's disease; ALS, amyotrophic lateral sclerosis; mAb, monoclonal antibody

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Recently Achieved R&D Milestones

Birtamimab for potential treatment of AL amyloidosis

- ✓ Confirmatory AFFIRM-AL study in Mayo Stage IV patients with AL amyloidosis, under SPA with FDA

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

- ✓ Part 1 of Phase 2 PASADENA study in patients with early PD presented at MDS Congress 2020
- ✓ Announced plans to advance into a Phase 2b study in patients with early Parkinson's disease

PRX004 for potential treatment of ATTR amyloidosis

- ✓ Phase 1 study results reported 4Q 2020

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

- ✓ Advanced IND-enabling activities for the internally discovered tau antibody

PRX012 for potential treatment of Alzheimer's disease

- ✓ Initiated cell line development of a lead candidate
- ✓ Presented preclinical data at CTAD 2020
- ✓ Initiated IND-enabling studies for the internally discovered Aβ antibody

Upcoming R&D Milestones

Birtamimab for potential treatment of AL amyloidosis

- Phase 3 AFFIRM-AL Study initiation expected mid-2021

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

- $60 million clinical milestone payment upon first patient dosed in Phase 2b; further details expected 2Q21

PRX004 for potential treatment of ATTR-cardiomyopathy

- Initiation of Phase 2/3 study expected 4Q21

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

- IND filing expected mid-2021, with potential $80 million US option payment

PRX012 for potential treatment of Alzheimer's disease

- IND filing expected 1Q22