CORPORATE PRESENTATION

September 2021

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1. Pharnext

Snapshot

Management Team with Proven Track Record

Dr. David Horn Solomon
Chief Executive Officer

COLUMBIA UNIVERSITY

ZEAL&
ZEALAND PHARMA

SILENCE
THERAPEUTICS

Dr. Adrian Hepner
Chief Medical Officer

AVANIR
pharmaceuticals

ucb

EAGLE
PHARMACEUTICALS

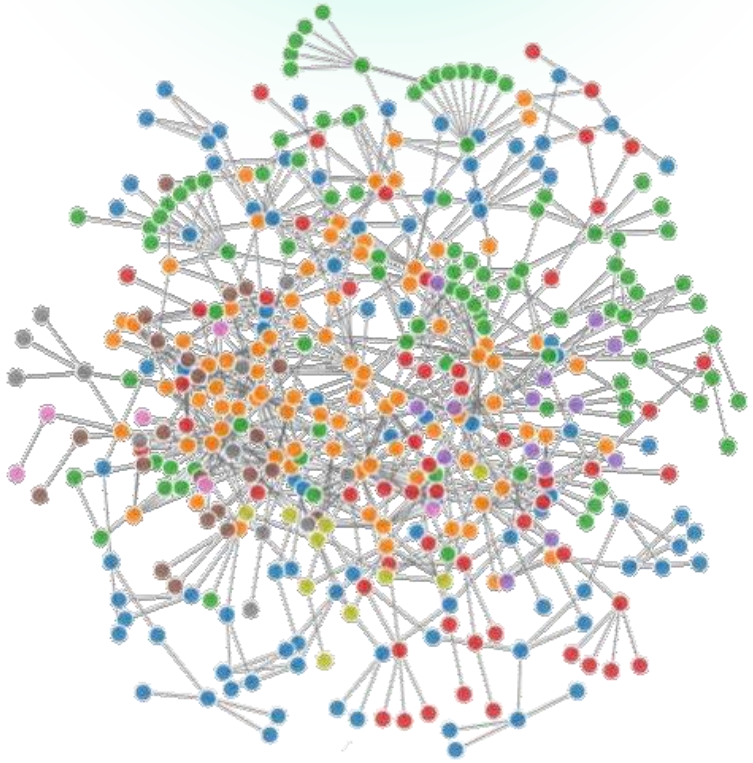
Xavier Paoli, MSc
Chief Commercial Officer

ALEXION

ucb

gsk

PHARNEXT



Pharnext is a

late clinical stage

biopharmaceutical company focused on advancing **innovative Pleotherapy™** drug candidates in diseases with **high unmet need,** including PXT3003 in Phase 3 for Charcot-Marie-Tooth Disease Type 1A

Pharnext Highlights

PIPELINE

PXT3003: Pivotal Stage Program for CMT1A

- PXT3003 in Phase III for Charcot-Marie-Tooth disease type 1A (CMT1A)
- ~$1Bn WW sales potential
- Promising results from first Phase III and extension studies
- Clear FDA guidance on upcoming pivotal studies and path to NDA Submission
- Further potential upside in other demyelinating neuropathies

PXT864: Ph IIb ready program for AD

- Encouraging Phase IIa data in Alzheimer's Disease
- Opportunity to explore additional combinations with NCEs
- Further potential upside in other CNS diseases including Amyotrophic Lateral Sclerosis (ALS)

PLEOTHERAPY PLATFORM

Large Opportunity Set

- Scalable platform across multiple Tx areas
- Combinations using both NCEs and approved medicines

Enhanced Probability of Clinical Success

- Superior targeting within disease molecular network

Capital Efficiency / Speed to Approval

- Discovery and development to pre-Phase II POC can be done in ~ 2.5 years

External Validation from Collaborations

Galápagos TASLY

Pharnext Transformation Establishes a New Foundation for Value Creation

New Senior Management Team

Strong Industry and Financial Expertise

Board Transformation

Six new members
Deep expertise in clinical development, neuroscience and strategy

Clear FDA Guidance on Regulatory Pathway to Approval for PXT3003

Shareholders approved a share capital increase delegation to the Board of Directors

(Annual General Meeting of July 17, 2020)

Six New Board Members Providing Deep Expertise in Clinical Development, Neuroscience and Strategy

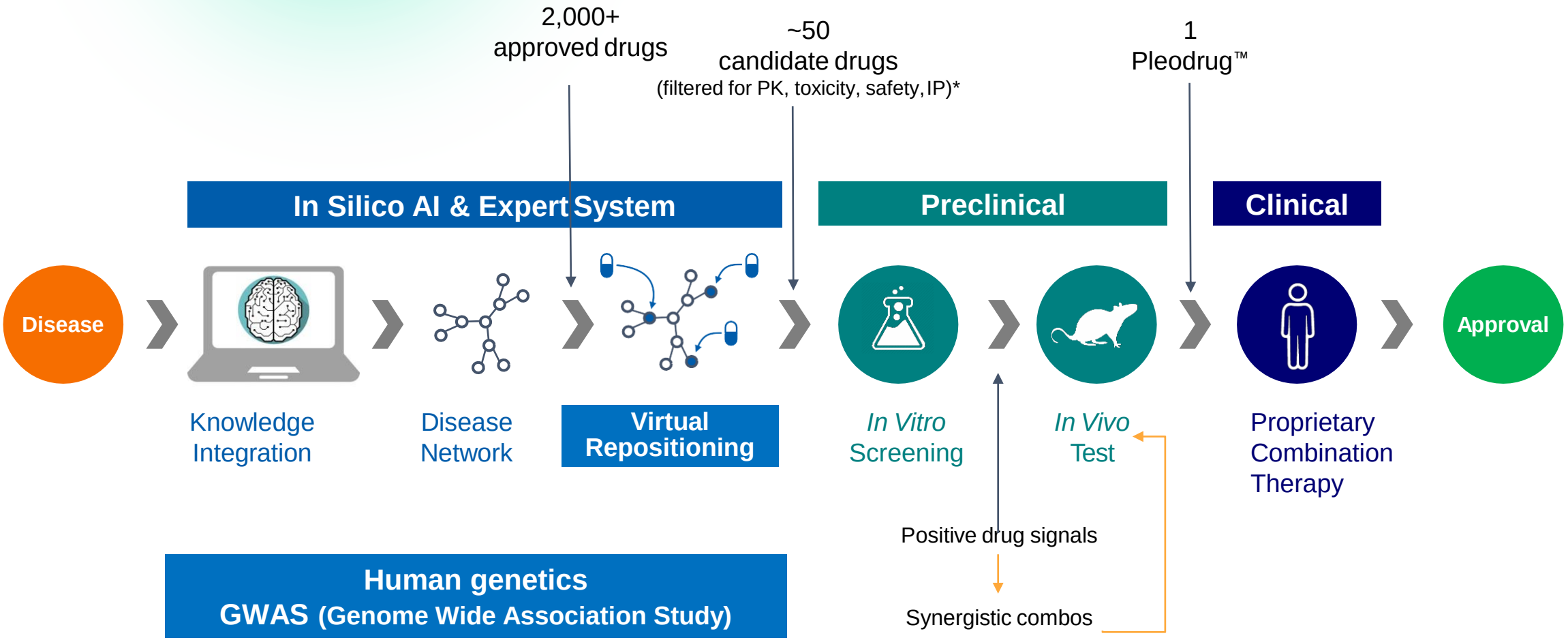
Pharnext Board of Directors

- **Michel de Rosen (Chairman)**
  Former CEO ***Rhône Poulenc Rorer, Viropharma***
  Chairman of ***DBV Technologies*** and Board member of ***Idorsia***
  Chairman of ***Faurecia***
- **Pierre Bastid**
  Former President and CEO of ***Converteam Group***, acquired by ***General Electric***
  Board member of ***Cellectis, Carmat***
- **Alexandre Berda**
  Managing Director of CB Lux, Pharnext's largest shareholder
- **Piers Morgan**
  20 years of senior biotech roles, principally as CFO
  Led the Nasdaq IPOs of ***COMPASS Pathways***, ***uniQure*** and ***Verona Pharma***
  Board member of ***Ikarovec Ltd***, and previously at ***Quethera***
- **Kenneth Lee**
  Represents ***Tasly (Hong-Kong) Pharmaceuticals Ltd***
- **Philippe Pouletty, MD**
  Co-founder and CEO of Truffle Capital
- **Joshua Schafer**
  Chief Strategy and BD Officer of ***Mallinckrodt Pharmaceuticals***
  Board member of ***Shuttle Pharmaceuticals***
  Former Head of oncology at ***Astellas*** and senior roles at ***Takeda***
- **David H. Solomon**
  CEO of ***Pharnext SA***
  Former CEO of ***Zealand, Bionor, Akari, Silence Therapeutics***
  Chairman of ***Advicenne*** and ***Rexgenero***
- **Prof. Lawrence Steinman, MD**
  Professor of Neurology and Neurological Sciences, Pediatrics and Genetics at ***Stanford University***
- **Elisabeth Svanberg, MD, PhD**
  Chief Development Officer at ***Ixaltis SA***
  Board member of ***Galapagos NV*** and ***SOBI***
  Former senior development roles at ***BMS, J&J*** and ***Serono***

Shading denotes new Board members

PLEOTHERAPY™ R&D Platform

Starting with Big Data

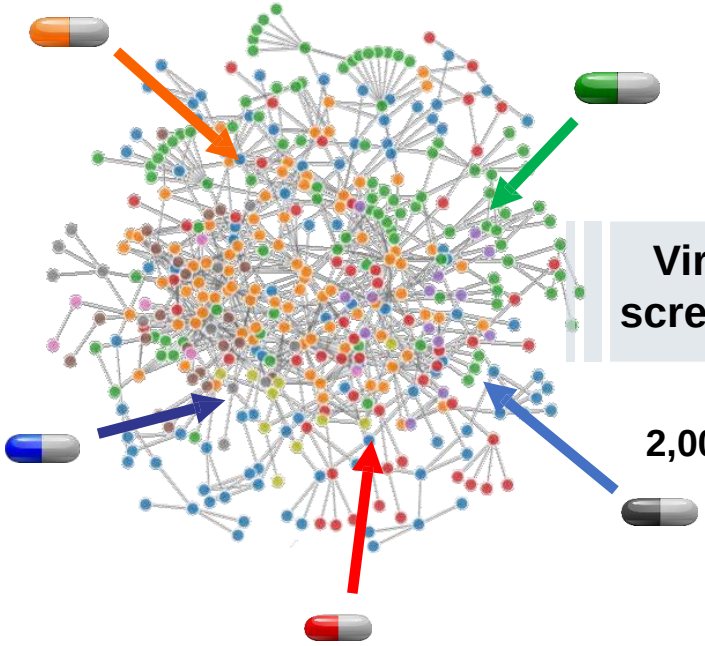


* Based on currently available external data.

Discovery of PXT3003 for CMT1A

Led to Positive Phase II and Promising Phase III Data

CMT1A disease molecular network

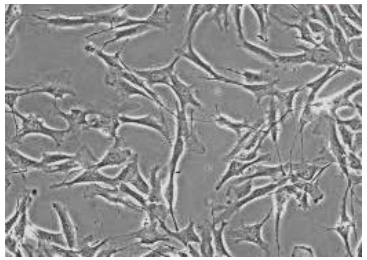


Virtual screening

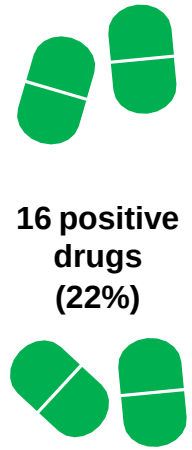
2,000+ drugs*

72 Drugs selected to screen

Down-regulation of *PMP22* in Schwann cells



In CMT1A, excess PMP22 protein is produced, leading to demyelination and progressive disease



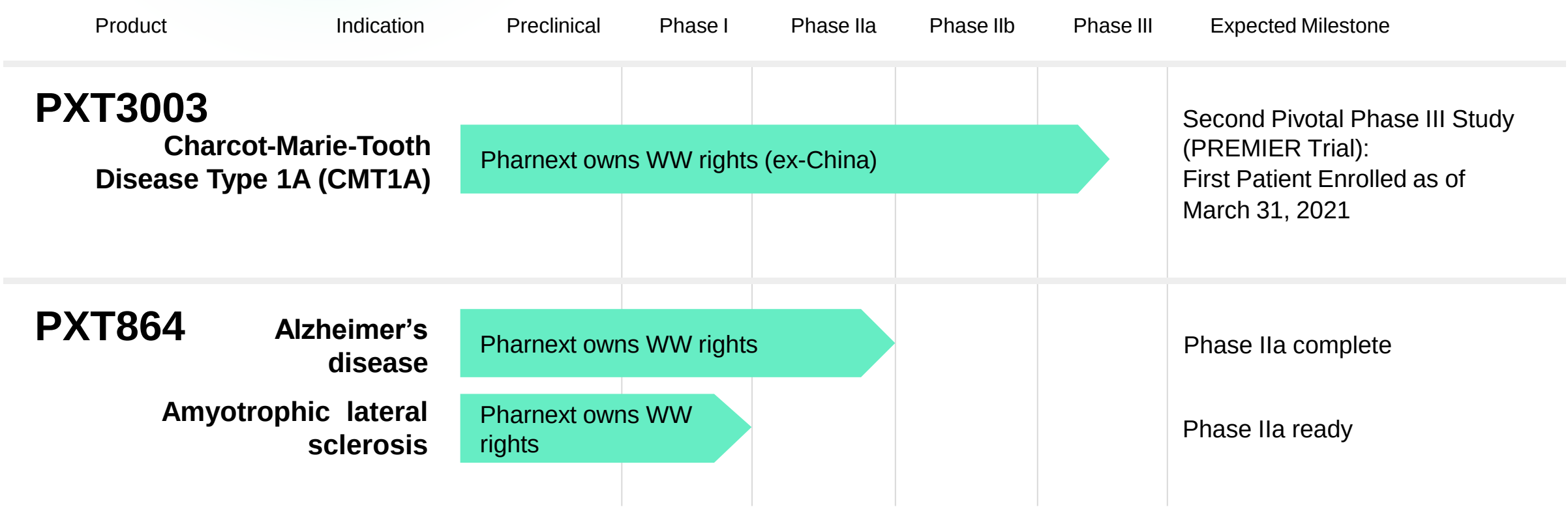
16 positive drugs (22%)

3 combinations prioritized

1 combination selected

* All currently approved for marketing by FDA.

Pipeline and Expected Milestones



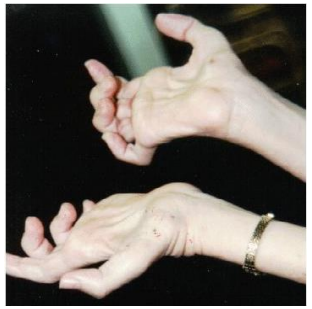
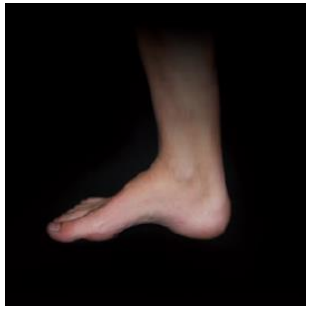
2. PXT3003

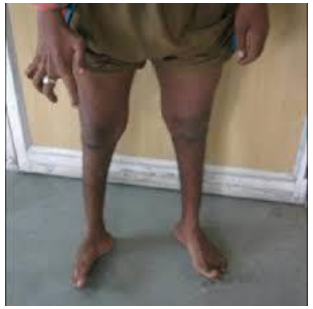
Overview

Charcot-Marie-Tooth Disease Type 1A

Chronic, Severe, Debilitating Inherited Neuropathy

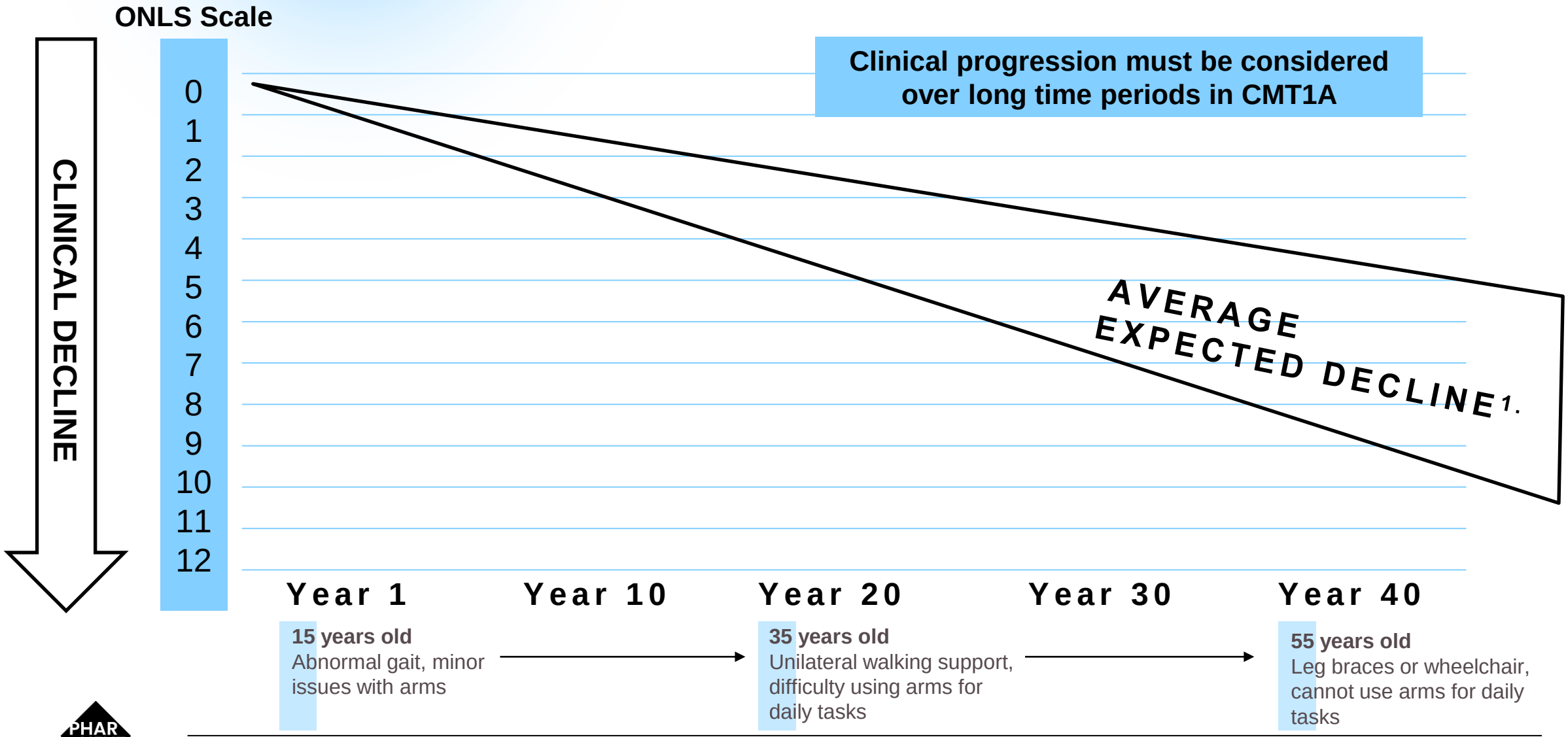
CMT1A	Most common form of CMT (~50%) Chronic, severe, progressively debilitating, inherited neuropathy resulting from a duplication of the PMP22 gene, causing demyelination of peripheral nerves
SYMPTOMS	Muscle atrophy in extremities causing severe leg and arm disabilities, pain, cramps and fatigue
DIAGNOSIS	~50% of patients have symptoms before the age of 20, confirmed by genetic testing
NATURAL HISTORY	Genetic disease; symptoms starting in teenage years, progressively declining through life, often requiring braces, surgery and wheelchair
POPULATION	More than 100,000 people affected with mild to moderate CMT1A in US and EU5 (core market)
TREATMENT OPTIONS	No approved drugs; only limited supportive care available No other candidates in late stage clinical development



Charcot-Marie-Tooth Disease Type 1A

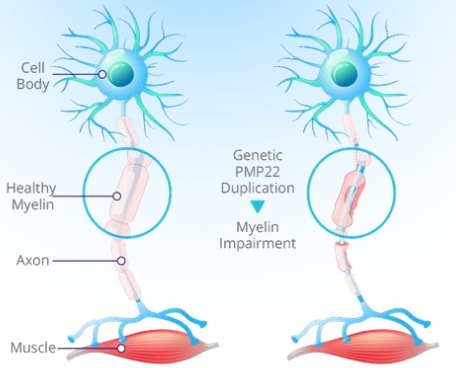
Natural Long-Term Progression of Disease on ONLS Scale



1. Natural progression estimate based on Shy, et al (2008) and placebo group decline in Pharnext Phase II and III studies.

PXT3003 Novel Targeted Design and Mechanism of Action

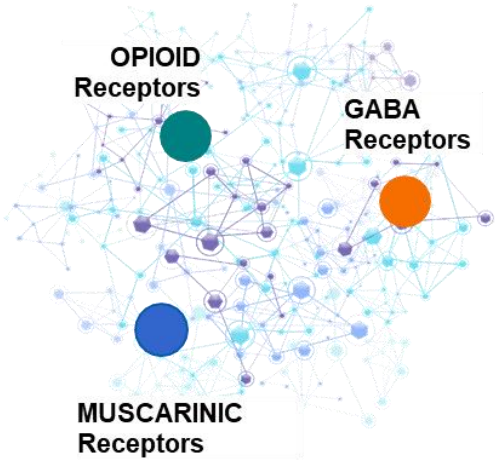
CMT1A



Normal

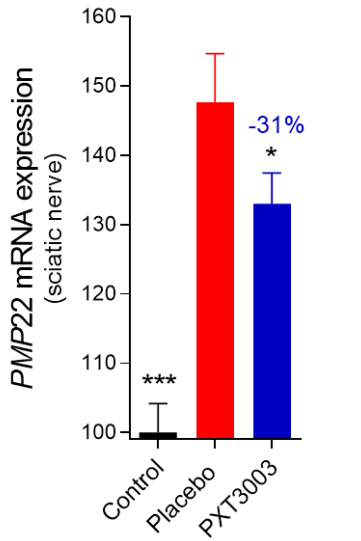
CMT1A - Axonal dysfunction and muscle loss

	Current Approved Dose*	Pharnext Dose
NAL	50 mg	1.4 mg
BAC	120 mg	12 mg
SOR	15,000 mg	420 mg

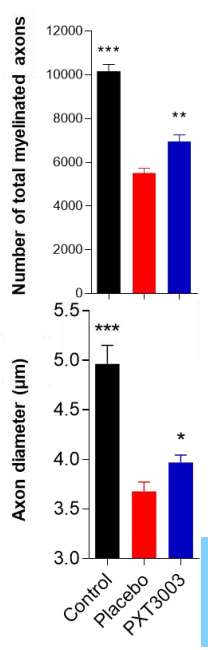


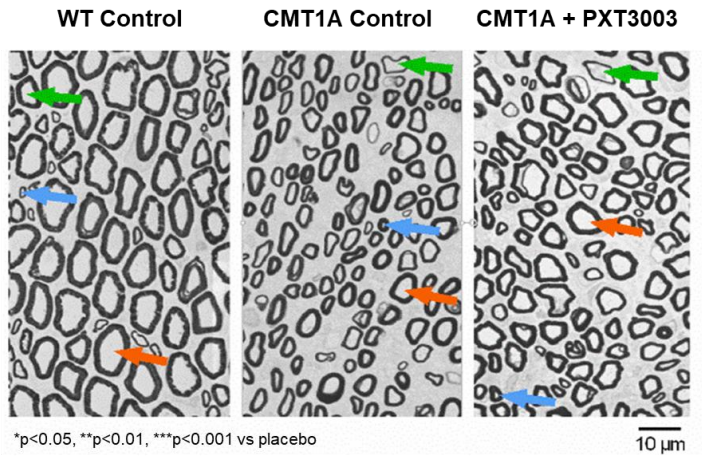
Targeted Disease Network

Downregulation of PMP22 in CMT1A rats



*p<0.05, **p<0.01, ***p<0.001 vs placebo





Increased number of myelinated axons and their diameter in CMT1A rats

NAL = Naltrexone; BAC = Baclofen; SOR = Sorbitol
*Approved dose in original indications
Source: Prukop, et al (2019)

Mechanism of Action of PXT3003 in CMT1A

PXT3003 Targets are Ubiquitous Along the Peripheral Nerve

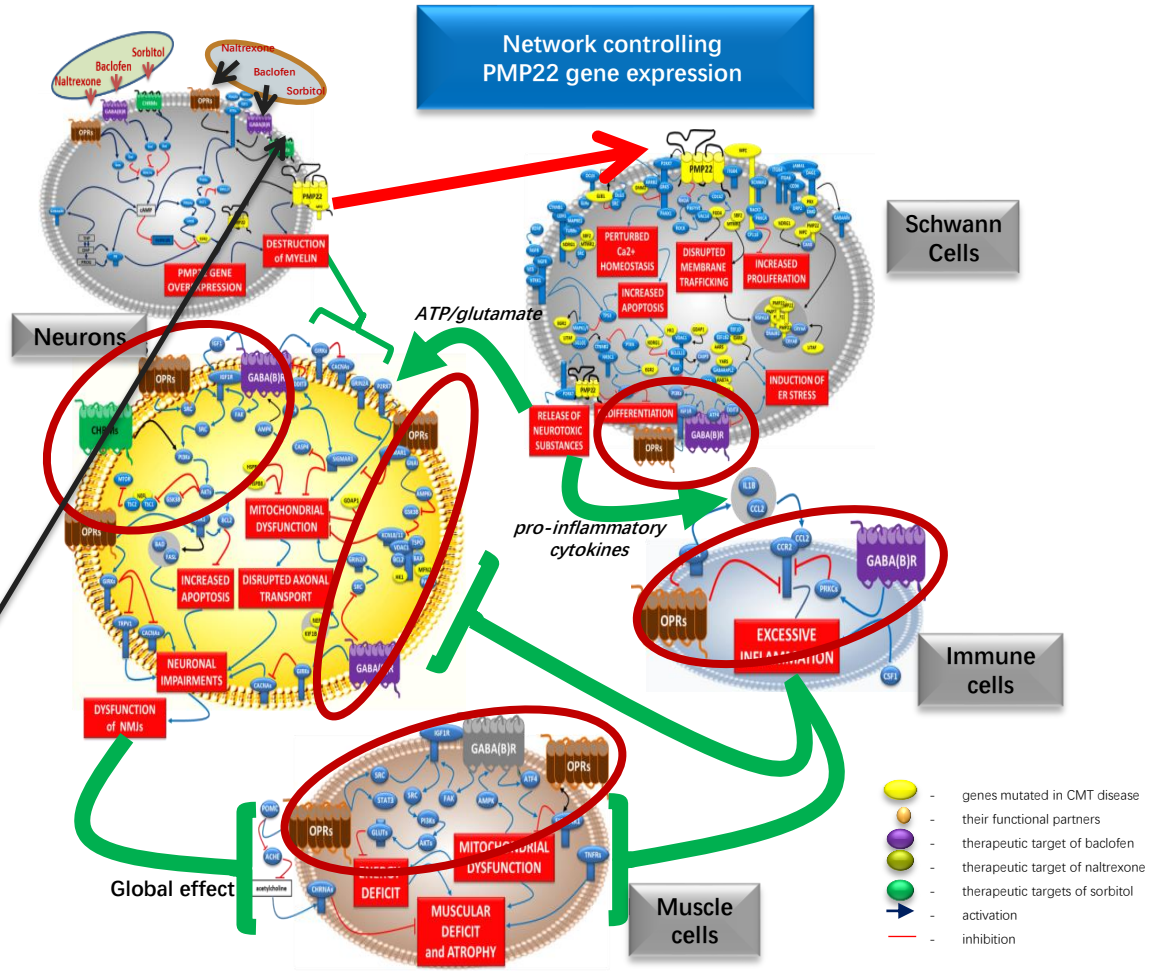
PXT3003 modulation of opioid, GABA and muscarinic receptors lowers PMP22 overexpression

Improved Myelination

Axon Preservation

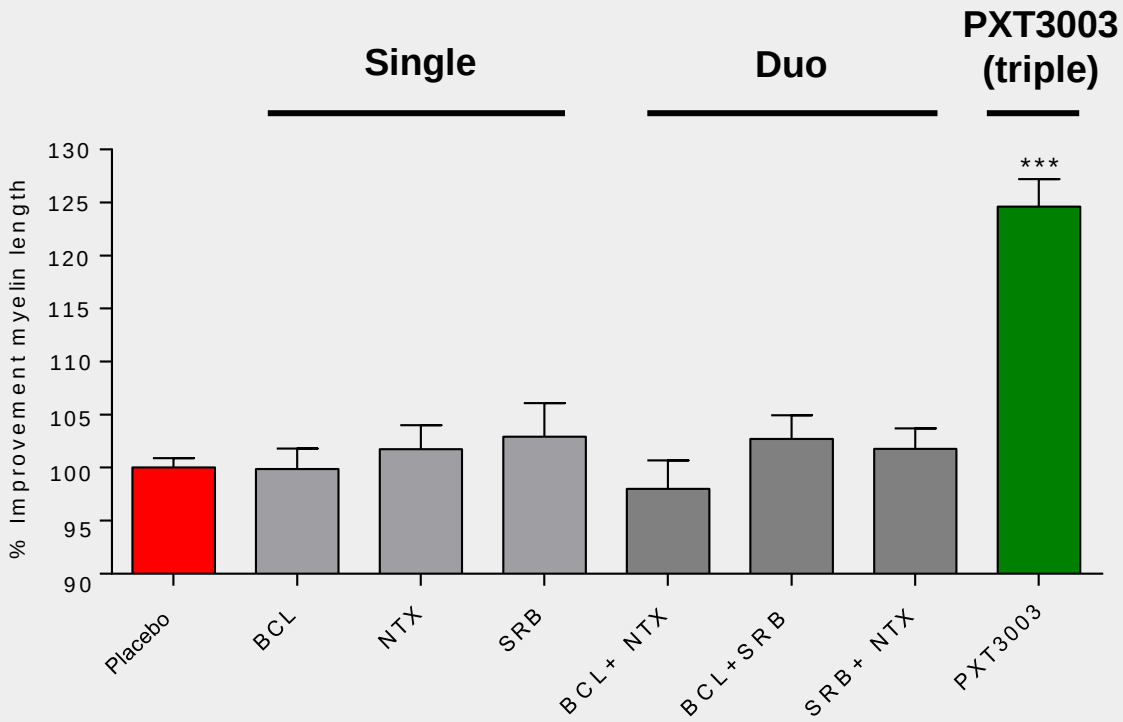
Improvement of Motor Function

CMT1A Disease Modification



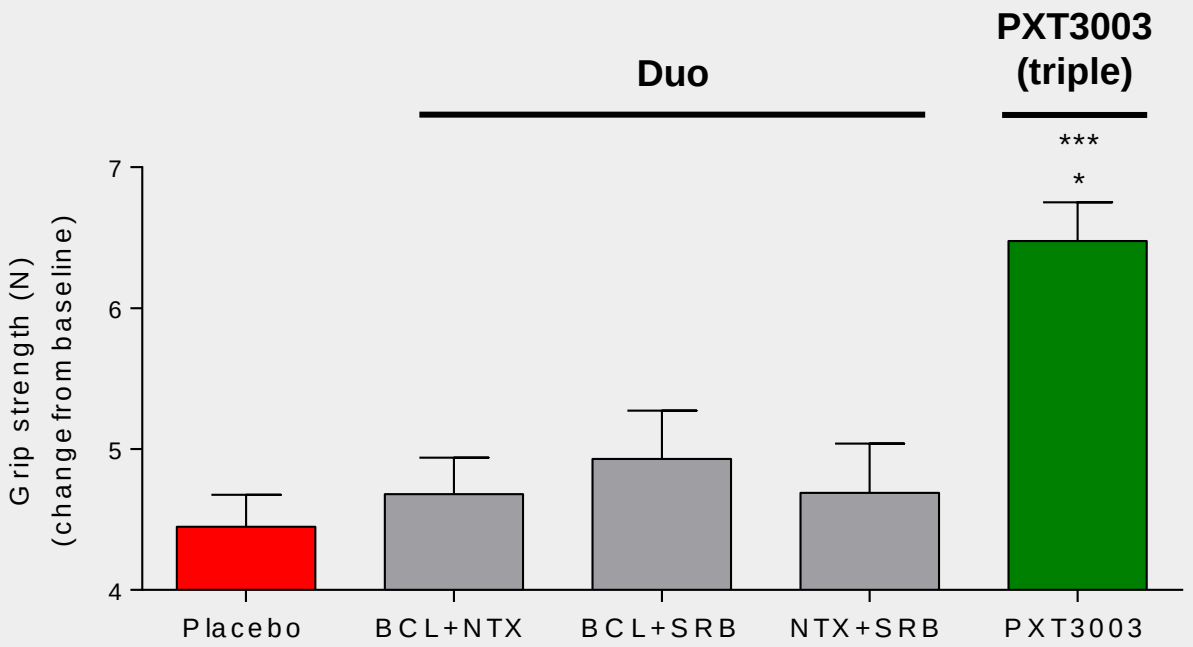
PXT3003 Has Demonstrated Superiority to the Single or Dual Component Medicines

CMT1A neurons *in vitro* (myelination)



*** p<0.001 vs placebo, all singles and all duals, ANOVA + Dunnett test

CMT1A animals in vivo (grip strength at end of trial)



*** p<0.001 vs placebo, all singles, BCL+NTX and NTX+SRB, ANOVA + Dunnett test

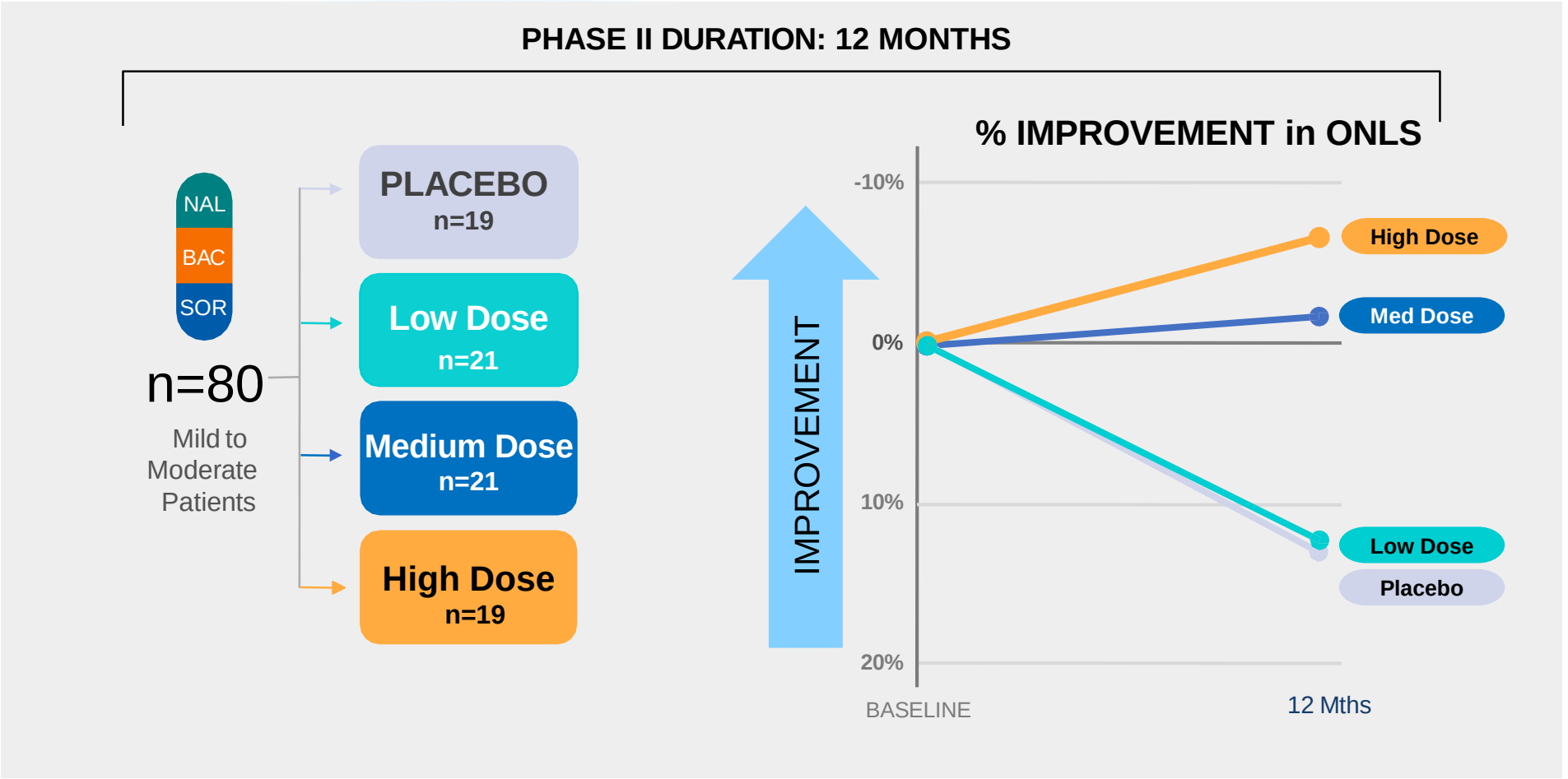
* p<0.05 vs BCL+SRB, ANOVA + Dunnett test

BCL = Baclofen (GABA receptor), NTX = Naltrexone (opioid receptor), SRB = Sorbitol (muscarinic receptor)

Phase II Results for PXT3003 in CMT1A

Exploratory multi-center, randomized, double-blind, placebo-controlled Phase II study

Efficacy and dose-effect demonstrated with Overall Neuropathy Limitation Scale (ONLS)



- All doses safe and well tolerated
- Effect achieved at 12 months with High Dose, which was used to design the first Ph III study

Source: Attarian et al, Orphanet Journal of Rare Diseases (2014),9:199

ONLS Grading Scale

Arms Scale			
Does the patient have any symptoms in their hands or arms, e.g. tingling, numbness or weakness? (if no, go to legs section)	Yes		No
Is the patient affected in their ability to:	**Not affected**	**Affected but not prevented**	**Prevented**
Wash and brush their hair			
Turn a key in a lock			
Use a knife and fork together (or spoon, if knife and fork not used)			
Do or undo buttons or zips			
Dress the upper part of their body excluding buttons or zips			
If all these functions are prevented can the patient make purposeful movements with their hands or arms?	Yes	No	Not applicable

Arms grade score

- 0 = Normal
- 1 = Minor symptoms in one or both arms but not affecting any of the functions listed
- 2 = Disability in one or both arms affecting but not preventing any of the functions listed
- 3 = Disability in one or both arms preventing at least one but not all functions listed
- 4 = Disability in both arms preventing all functions listed but purposeful movement still possible
- 5 = Disability in both arms preventing all purposeful movements

Legs Scale	Yes	No	Not applicable
Does the patient have difficulty running or climbing stairs?			
Does the patient have difficulty with walking?			
Does their gait look abnormal?			
How do they mobilise for about 10 metres (i.e. 33 feet)?			
Without aid			
With one stick or crutch or holding to someone's arm			
With two sticks or crutches or one stick or crutch holding onto someone's arm or frame			
With a wheelchair			
If they use a wheelchair, can they stand and walk 1 metre with the help of one person?			
If they cannot walk as above are they able to make some purposeful movements of their legs, e.g. reposition legs in bed?			
Does the patient use ankle foot orthoses/braces? (If yes, please indicate, Right or Left)			

Legs grade score

- 0 = Walking/climbing stairs/running not affected
- 1 = Walking/climbing stairs/running is affected, but gait does not look abnormal
- 2 = Walks independently but gait looks abnormal
- 3 = Requires unilateral support to walk 10 metres (stick, single crutch, one arm)
- 4 = Requires bilateral support to walk 10 metres (sticks, crutches, crutch and arm, frame)
- 5 = Requires wheelchair to travel 10 metres but able to stand and walk 1 metre with the help of one person
- 6 = Restricted to wheelchair, unable to stand and walk 1 metre with the help of one person, but able to make some purposeful leg movements
- 7 = Restricted to wheelchair or bed most of the day, unable to make any purposeful movements of the legs

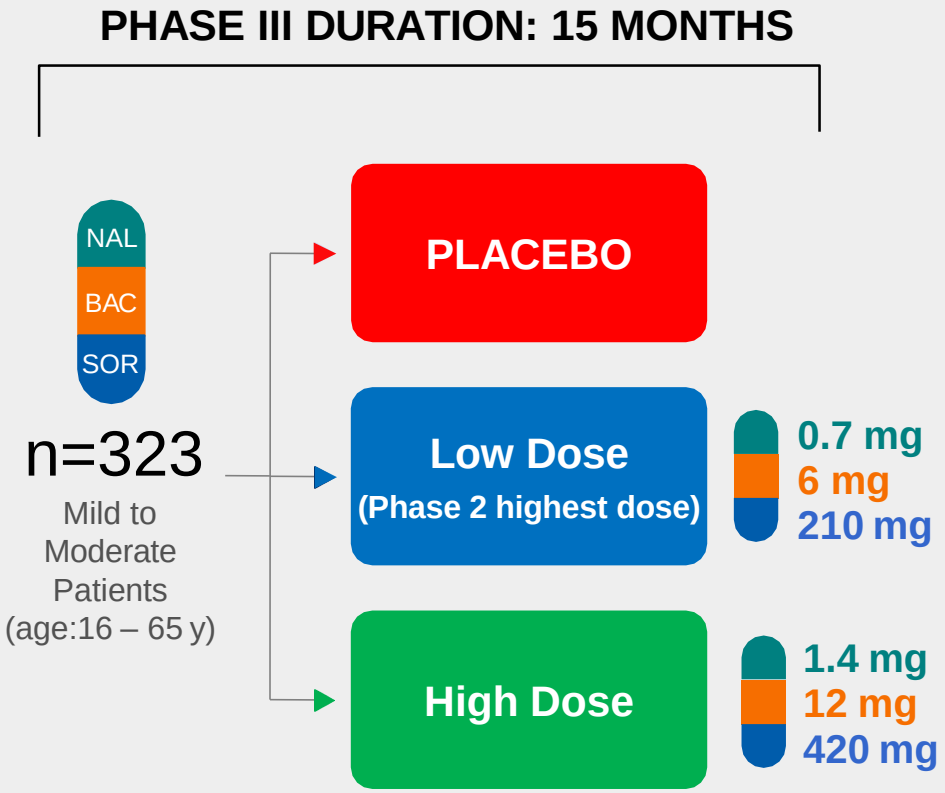
Overall Neuropathy Limitation Scale Score				
Arm scale score (0 to 5)	5	+	**Leg scale score (0 to 7)**	7

Range: 0 (no disability) to 12 (maximum disability).

Total ONLS score (please enter into BloodSTAR): 12

First Phase III Study Design and Endpoints (PLEO-CMT Trial)

International, randomized, double-blind, placebo-controlled



Primary endpoint: ONLS after 12-15 months (avg)

- ONLS: a 12-point scale evaluating disability
- 90% of the patients scored 2-4 (mild-to-moderate)
- **A 0.3-point ONLS improvement vs. placebo was determined to be clinically meaningful**
  - **Stabilizing or even improving disease *versus* placebo or natural yearly evolution estimated at 0.1 to 0.2-point decline**
- FDA and EMA agreed on using ONLS as the primary endpoint for this study.

Secondary endpoints:

- 10-meter walk test (10-MWT)
- Nine-hole peg test (9-HPT)
- 2 subsets of CMTNSv2 (CMT Impairment Score)
  (Clinical + Electrophysiological items = CMTNSv2)
  - Sensory subset*
  - Clinical subset = purely clinical items (CMTES)**

ONLS = Overall Neuropathy Limitation Scale
* Sensory subset of CMTNSv2: items 1,4 and 5
** CMTES is derived from CMTNSv2, items 1 to 7 excluding nerve conductions

Clinical Effect Size – What is Meaningful in CMT1A?

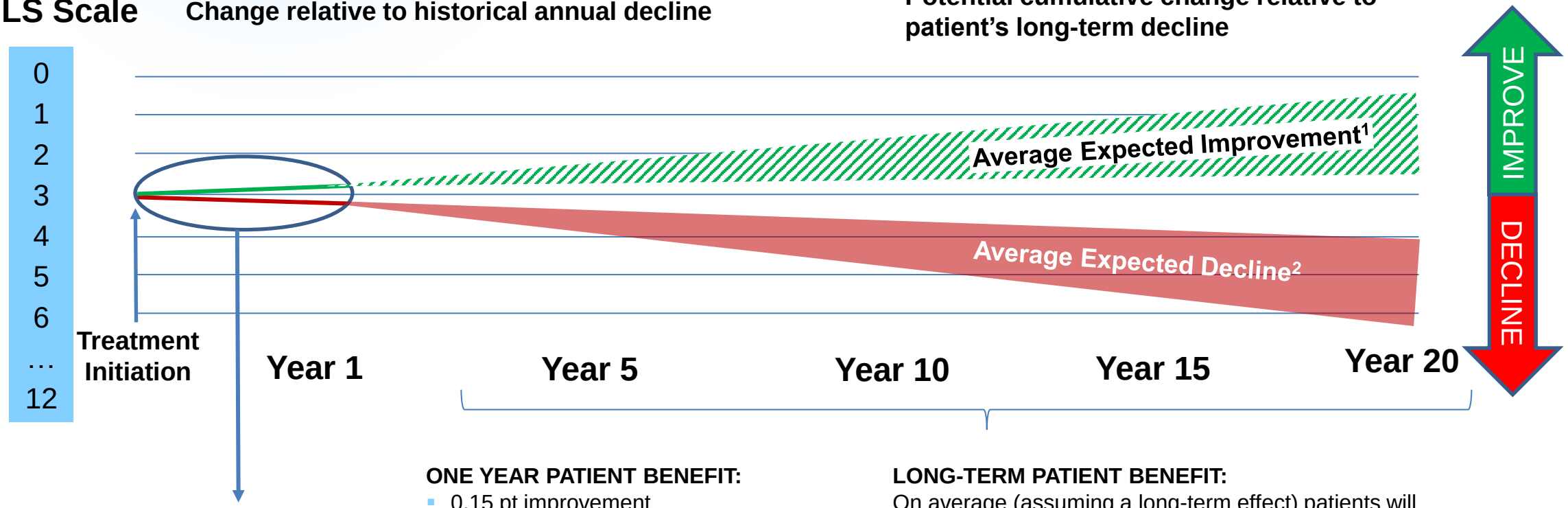
1

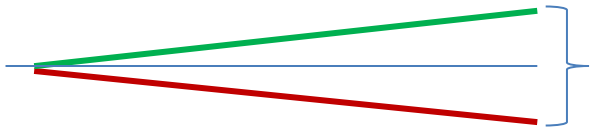
ONLS Scale

Change relative to historical annual decline

2

Potential cumulative change relative to patient's long-term decline





ONE YEAR PATIENT BENEFIT:

- 0.15 pt improvement
  vs
- 0.15 pt decline

A 0.3 pt difference in ONLS represents **2x change vs level of decline**

LONG-TERM PATIENT BENEFIT:

On average (assuming a long-term effect) patients will likely achieve disease stabilization and avoid declining by several points to a severely disabled state

1. Pharnext estimated by extrapolating treatment effect in our first Phase III study.
2. Natural progression estimate based on Shy, et al (2008) and placebo group decline in Pharnext Phase II and III studies.

The Importance of Ameliorating Decline in Chronic Progressive Disorders

Chronic neurological, neuromuscular and neurodegenerative disorders are often characterized by relentless progression, leading to growing disability and decline in activities of daily living and quality of life.

The ultimate treatment objective is stopping or ameliorating the declining natural progression of the disease.

Generalized Myasthenia Gravis (gMG)

FDA Approval of Soliris (eculizumab) was based on a limited change over 26 weeks

-1.9 points difference vs placebo in MG-ADL (0-24).

-3.0 points difference vs placebo in QMG (0-39).

Source: Soliris US Prescribing Information (11/2020)

Primary Progressive Multiple Sclerosis (PPMS)

FDA Approval of Ocrevus (ocrelizumab) was supported by a milder decline vs placebo over 120 weeks

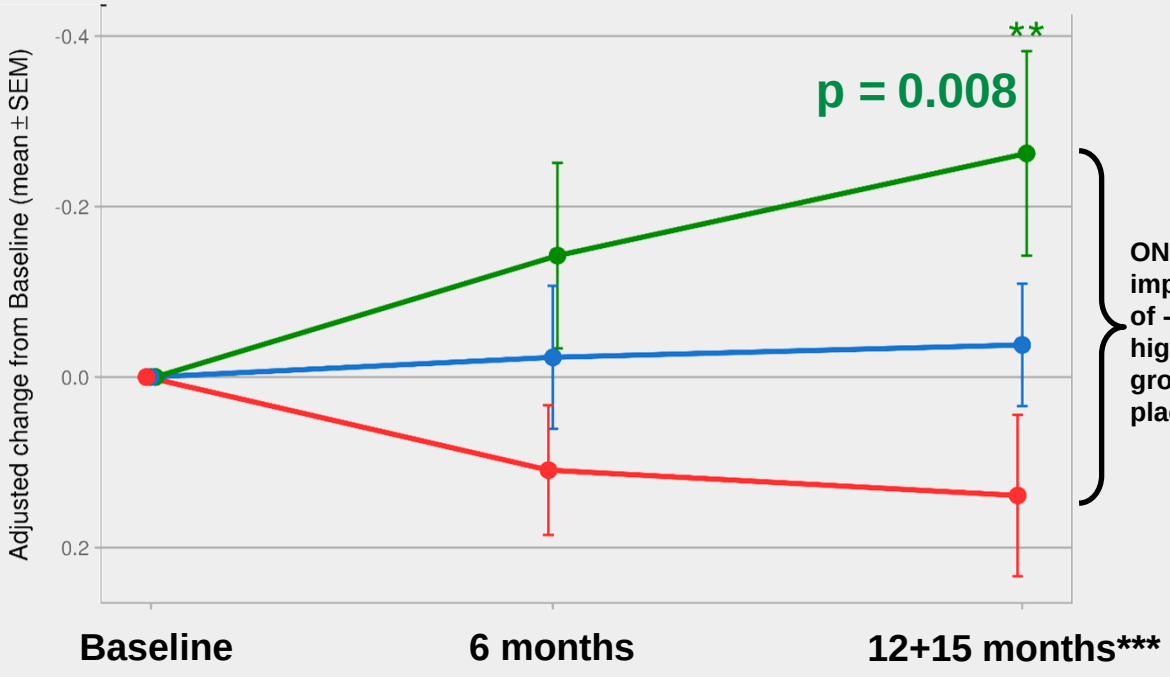
32.9% of patients receiving Ocrevus had confirmed disability progression compared to 39.3% on placebo, representing a 25% reduction in the risk of decline in favor of Ocrevus.

Source: Ocrevus US Prescribing Information (03/2021)

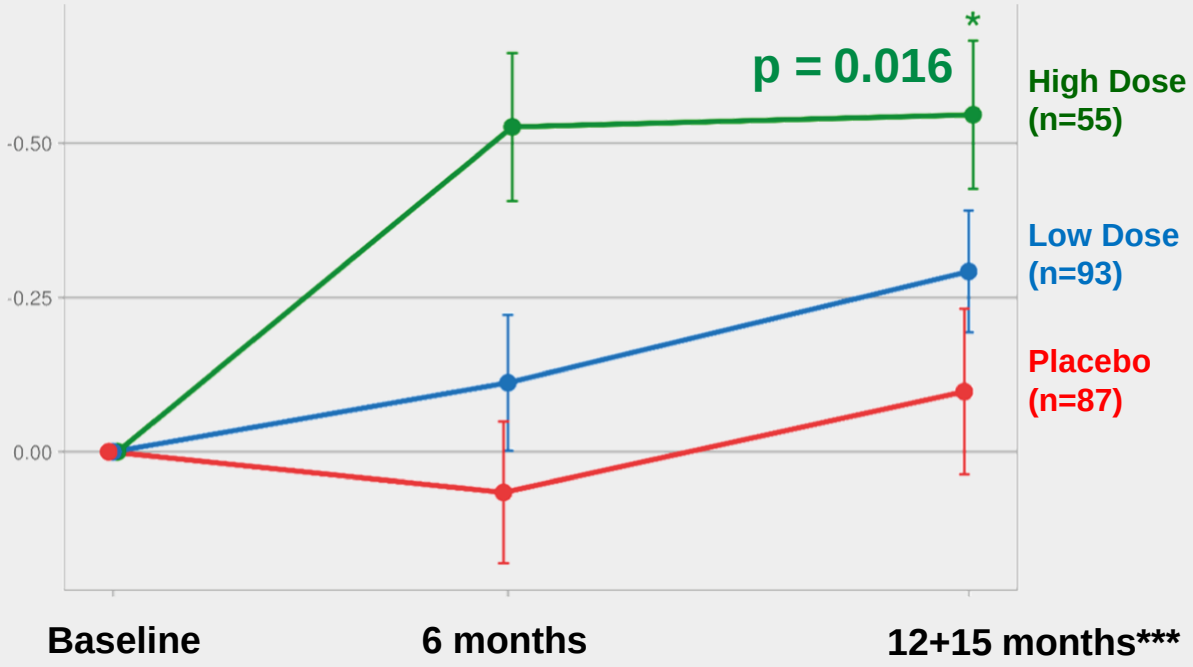
MG-ADL: Myasthenia Gravis-Specific Activities of Daily Living scale
QMG: Quantitative Myasthenia Gravis total score

First Phase III Study (PLEO-CMT Trial) Results: ONLS and 10 Meter Walk Test in SAP Primary Population

ONLS



10mWT



*, ** Dose 4 vs Placebo, ANCOVA with multiple imputation (Missing data implemented by multiple imputations following the placebo trend)

*** Average of 12 and 15 Month, or 12 Month if 15 Month is missing

First Phase III Study (PLEO-CMT Trial) - Analysis of Completers

Start Dec 2015 — Apr 2017 — **Completion** Mar 2018

	Completers*	Total discontinued before 12-months		P-Value (ONLS)	
		CMC-related	All Other**	Orig protocol	SAP
PLACEBO n=101	80	21 (21%)	12 (12%) / 9 (9%)	N/A	N/A
LOW DOSE n=109	85	24 (22%)	13 (12%) / 11 (10%)	p = 0.287	p = 0.143
HIGH DOSE n=113	49	64 (57%)	53 (47%) / 11 (10%)	p = 0.04	p = 0.008

Early discontinuation due to CMC event

Crystal formation (~2% by volume consisting of baclofen and an excipient, paraben) was observed in some high dose bottles, ultimately leading to the stoppage of the high dose arm approximately halfway through the trial resulting in 53 patients of "missing data"

Due to the unanticipated CMC event, original protocol was adapted to account for atypical amount of "missing data" due to patients' discontinuation

- Original protocol → primary population (n=323), all dropouts imputed like placebo for all study arms.
- Statistical Analysis Protocol (SAP) → primary population (n=235) including completers + dropouts related to treatment-related AEs,
- Dropouts related to treatment-related AEs imputed like Placebo for all study arms, dropouts unrelated to treatment-related AEs excluded from analysis.

* Completers = patients with at least 12 months of treatment
**Other reasons include: lost to follow-up, protocol violation, withdrawal by patient and AEs

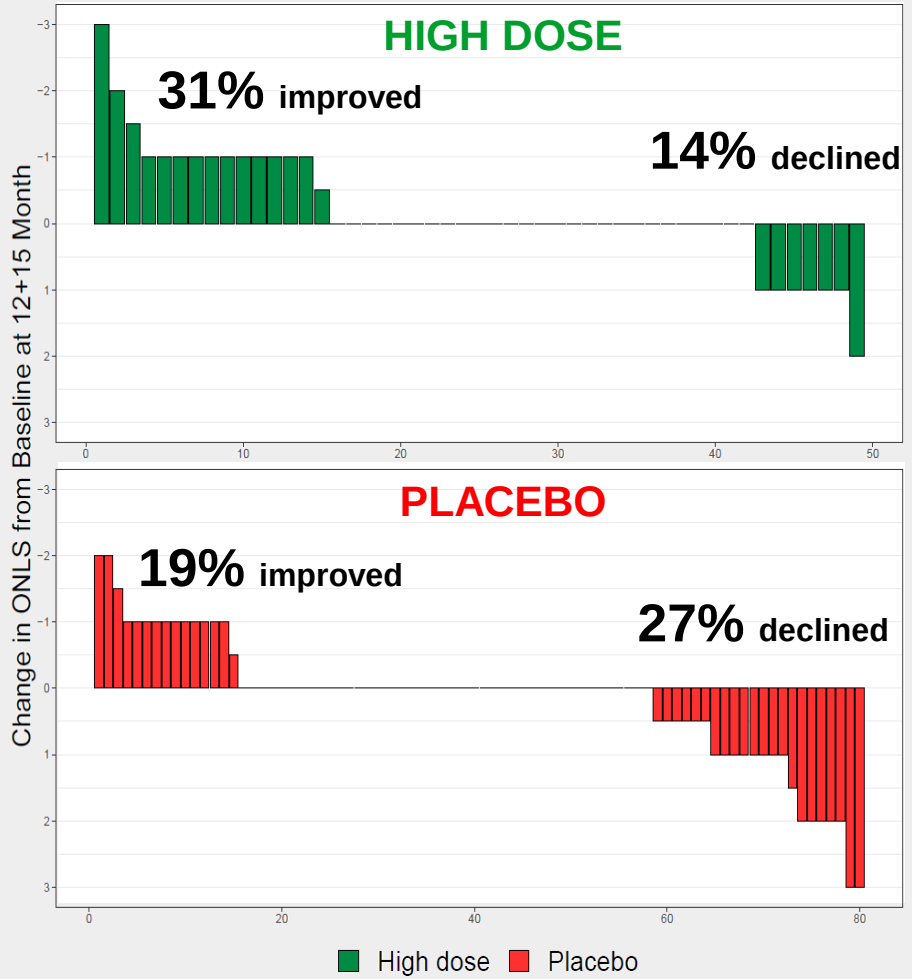
First Phase III Study (PLEO-CMT Trial): ONLS Responder Analysis

Natural progression of CMT1A results in continuous deterioration of motor and sensory function in lower and upper limbs

Treatment with PXT3003 demonstrated greater improvement compared to placebo (31% vs. 19%)

Additional efficacy analysis demonstrated that untreated patients experienced double incidence of disease progression compared to PXT3003-treated patients (27% vs. 14%)

For patients receiving high-dose, the **odds ratio (OR)*** of being a non-decliner (responder) was **3.39 (p=0.026)**, compared to patients receiving placebo



*OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure

CMC Overview

De-risking our Dose Format for Second Phase III Study

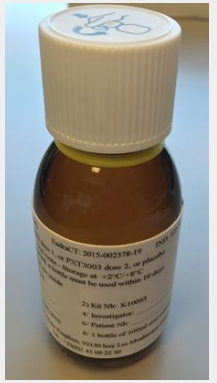
- 10mL of low dose = 5mL of high dose
- For the second Phase III study, we are delivering the high dose by dosing patients with 10mL of the low dose concentration, since the low dose concentration does not have the issue with crystals
- This same approach was used for the prior Phase III extension study with the approval of regulatory agencies
- We are also planning to use unit dose “stick packs” for better convenience and compliance

Why?

- High dose solution in 100mL bottles exhibited a small amount of crystal precipitate (~ 2% by volume) in some batches due to a reaction between baclofen and paraben

Future

- In parallel, we are developing both a room temperature oral solution as well as a solid oral dosage form which will better serve patients on a commercial basis

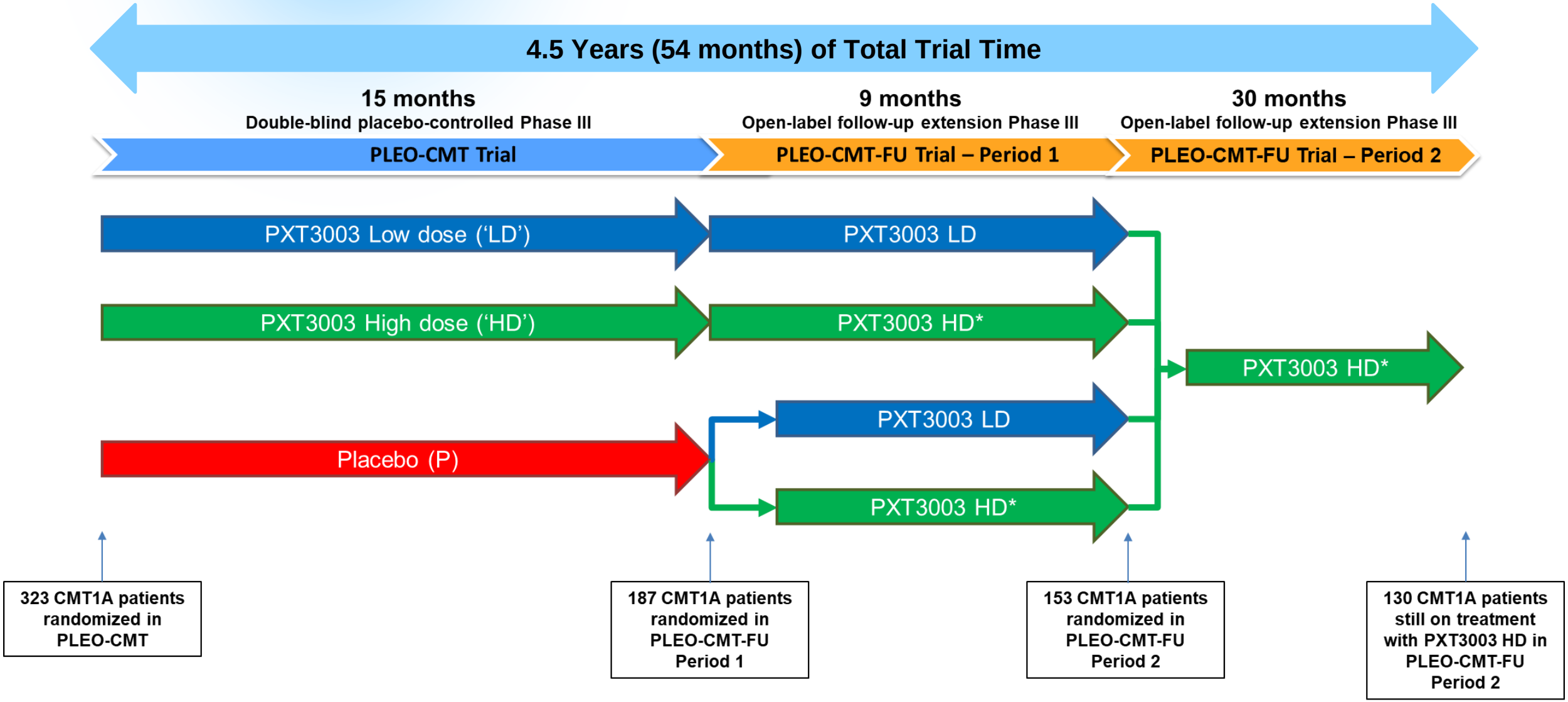


First Phase III

Second Phase III

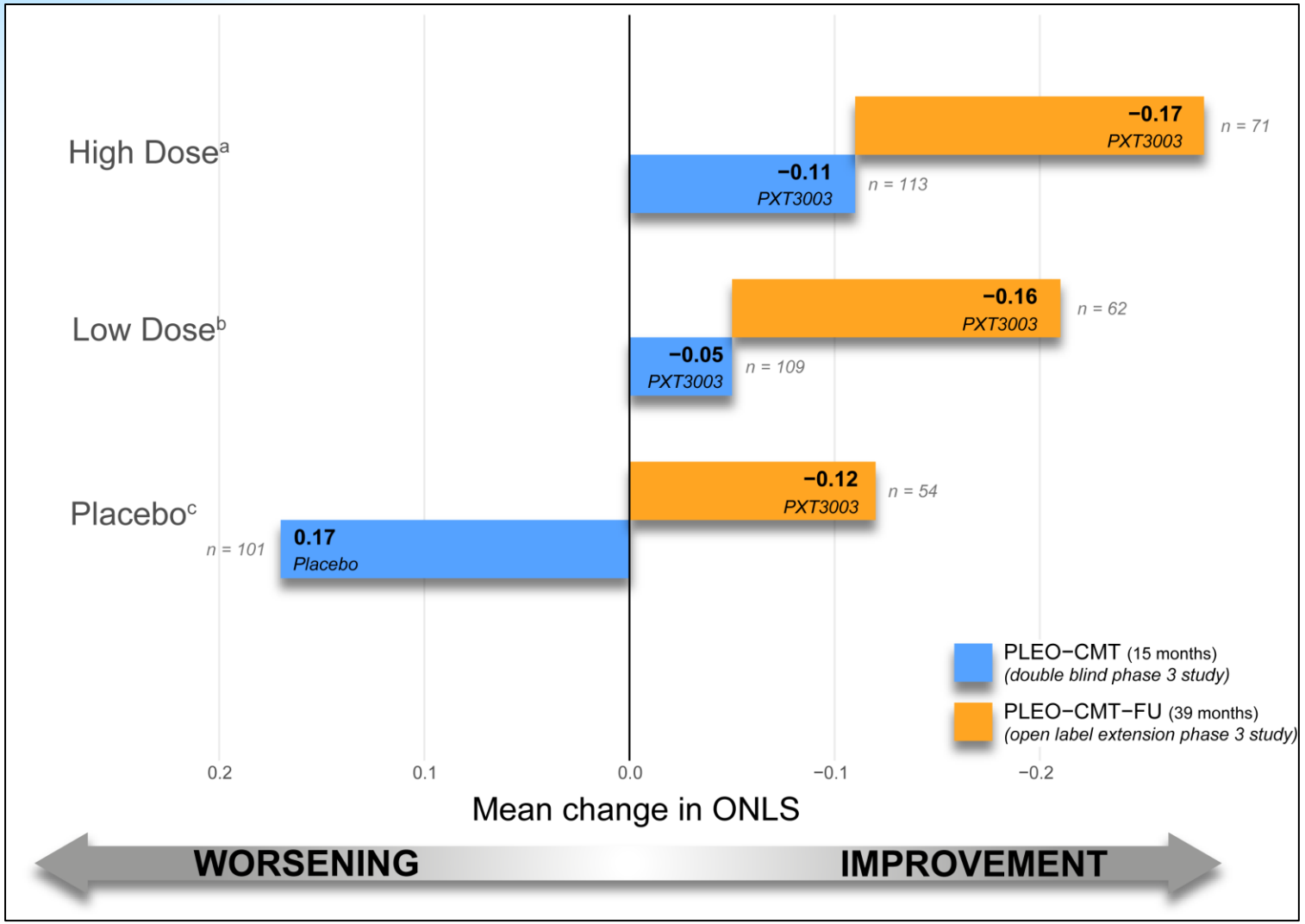
Future commercial format

Design of First Double-Blind Phase III and Open-Label Extension Studies



* PXT3003 HD given as twice the volume of PXT3003 LD formulation (2 X 5 mL b.i.d.) after PXT3003 HD arm discontinuation in September 2017

Sustained Benefits for CMT1A Patients after 4.5 Years of Total Trial Time



[a]Cohort of CMT1A patients treated with PXT3003 High Dose during PLEO-CMT and ongoing PLEO-CMT-FU trials

[b]Cohort of CMT1A patients treated with PXT3003 Low Dose during PLEO-CMT + PLEO-CMT-FU Period 1, and then switched to PXT3003 High Dose during PLEO-CMT-FU period 2

[c]Cohort of CMT1A patients treated with Placebo during PLEO-CMT, PXT3003 Low Dose or High Dose during PLEO-CMT-FU Period 1 and PXT3003 High Dose during PLEO-CMT-FU Period 2

Sustained Good Safety Profile of PXT3003 after 4.5 Years of Total Trial Time

- **In the double-blind phase III study, the majority of adverse events were mild-to-moderate, and comparable to placebo over a 15-month period.**

- **The long-term safety profile observed in the extension study is consistent with the good safety profile reported in the prior blinded study. No new safety signals have been identified over a time period of additional 39 months.**

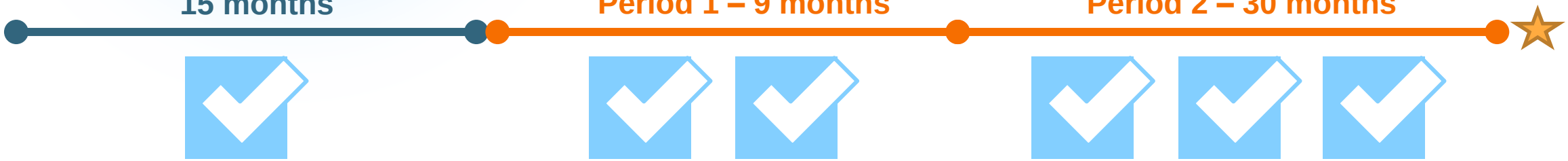
PXT3003 - Summary of Clinical Progression over 54 Months

PLEO-CMT
Double-Blind (db) Phase III
15 months

PLEO-CMT-FU
Open-Label Phase III Extension - Ongoing

Period 1 – 9 months

Period 2 – 30 months



- **Strong Safety**
- **Promising efficacy (ONLS) Positive Dose Response**
- **Placebo = Decline (ONLS)**
- **Formulation Issue (Missing Data)**

- **Strong Safety**
- **Sustained Efficacy Signal (ONLS)**
- **Placebo patients improved when switched to PXT3003 (ONLS)**
- **Data support PXT3003 disease modifier MOA***

- **Strong Safety**
- **Sustained Efficacy Signal (ONLS)**
- **Better efficacy signal with PXT3003 HD**
- **Long-term disease improvement / stabilization**

Interim analysis planned on an annual basis

* MOA = Mechanism of Action

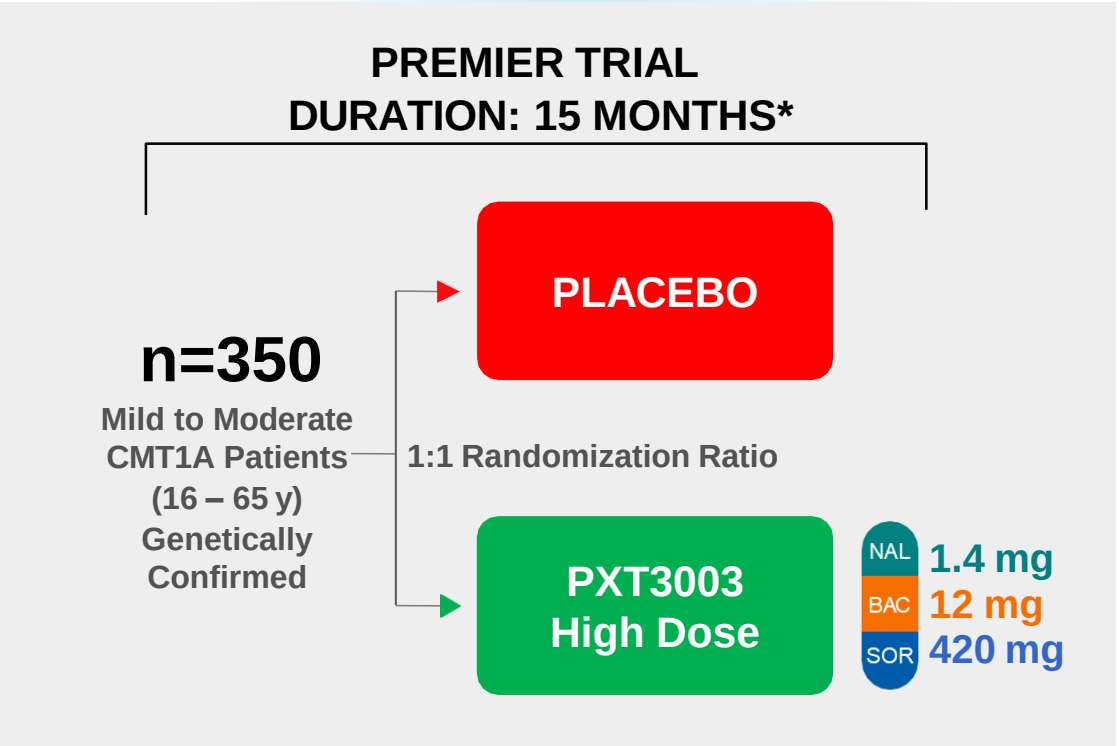
PXT3003 - Summary of Prior Studies and Path to Approval

- ☑ **Positive Phase II Study**
- ☑ **Positive Preclinical Factorial Study in Validated Disease Animal Model**
- ☑ **Promising Phase III Study (PLEO-CMT) (strong efficacy signal despite CMC interruption)**
- ☑ **Positive Phase III Extension Study (PLEO-CMT-FU)**
- ☑ **Clear FDA Guidance on Regulatory Pathway to Approval (received 2Q 2020)**
  - Clear guidance from FDA on next pivotal Phase III study
  - Clear guidance on performing pivotal factorial GLP* study in animals (in same CMT1A disease animal model as previously performed), typically required in humans
- ☐ **Execute Pivotal Phase III & GLP Factorial Studies**

*Good Laboratory Practice

Design of the Ongoing PREMIER Trial

Pivotal, international, randomized, double-blind, placebo-controlled, Phase III Study



Optimized Phase III design and incorporated FDA feedback to further de-risk the pivotal study

- **U.S, Canada, France, Germany, Spain, Italy, Belgium, the Netherlands, Denmark, Israel**
- **First-patient-in:** March 2021
- Estimated Enrollment Period: 12 months
- **Study Size: 350 patients** with approximately 175 patients per arm vs 100 patients per arm in previous Phase III (PLEO-CMT) for 90% power to detect a 0.4-point treatment effect
- **Primary efficacy endpoint: ONLS mean change from baseline**
- **Secondary efficacy endpoints:** 10-MWT, QMT (feet), PGI-S and PGI-C (ADL, QoL), CMTNS V2 based on positive efficacy endpoints from prior Phase III (PLEO-CMT), QMT (hand)
- **Exploratory endpoints:** TMPRSS5 (blood biomarker), BDI-II
- **Study drug: PXT3003 HD (12mg baclofen, 1.4mg naltrexone, 420mg sorbitol daily)** given as 10mL oral solution of PXT3003 LD formulation b.i.d. supplied in unit-dose stick packs to maximize compliance and de-risk CMC

* 15 months + 1-month safety follow-up vs 12-15-month average in previous Phase III (PLEO-CMT) to allow for increased treatment effect

ONLS = Overall Neuropathy Limitations Scale, 10-MWT = 10-Meter Walk Test , QMT = Quantified Muscular Testing (bilateral foot dorsiflexion dynamometry and handgrip), CMTNS V2 = Charcot-Marie-Tooth Neuropathy Score version 2, PGI-S = Patient Global Impression of Severity, PGI-C = Patient Global Impression of Change

PXT3003 Commercial Opportunity in CMT1A

Significant unmet need with no approved treatment

No other mid/late-clinical stage programs in active development for CMT1A

- Most advanced is in Phase I

Worldwide peak sales potential of ~$1Bn

Data from first Phase III study showed promising efficacy signal

- PXT3003 showed statistically significant improvement vs. placebo and overall improvement over baseline
- Beyond KOLs expectations

IP protection through 2030, including composition of matter

US and EU Orphan Drug Designation

- 7-year exclusivity in US
- 10-year exclusivity in EU

FDA Fast Track Designation

UK Promising Innovative Medicine Designation

Large ~ $1 Billion Revenue Opportunity in CMT1A

$1Bn Worldwide peak sales potential

- More than 100,000 adult patients with mild-to-moderate CMT1A (US and EU5*)
- 5 pricing / independent market research studies with consistent feedback on US and EU pricing

Significant portion of core target patient population already located

- ~26,000 CMT1A patients located in the US and EU5 through market research, claims data analysis, field activities and PAGs
- Several patient registries available: GRIN, INC, CMT-Net, etc.
- Plans to go beyond prior launch with MSLs and sponsored Dx campaign

Primary target treating physicians identified (cover >80% of CMT patients)

- Neurologists (NMD specialists), GPs, podiatrists, PTs

Strong relationships developed with key stakeholders

- Patient advocacy groups: HNF and CMTA in the US; and ECMTF in EU
- KOLs and scientific societies: PNS, AANEM, AAN and other national peripheral nerve societies

Generation of pharmacoeconomic data prior to launch

- CMT&Me: digital lifestyle study sponsored by Pharnext (>2,000 patients enrolled)

Continual assessment of commercial partnership options for various geographies, including US, EU, Japan and ROW; China commercialization rights are licensed to GeneNet, a JV formed by Pharnext & Tasly

GRIN: Global Registry of Inherited Neuropathies; INC: Inherited Neuropathy Consortium; PAGs: Patient Advocacy Groups; Dx: Diagnosis; HCPs: Healthcare Professionals; NMD: Neuro-Muscular Disease; GPs: General Practitioners; PTs: Physiotherapists; HNF: Hereditary Neuropathy Foundation; CMTA: CMT Association; ECMTF: EU CMT Federation; PNS: Peripheral Nerve Society; AANEM: American Association of Neuromuscular & Electrodiagnostic Medicine; AAN: American Academy of Neurology

* EU5 = France, Germany, Italy, Spain, UK

Pharnext Corporate Milestones Through 2023

- **A** **Feb 2, 2019:** FDA Fast Track Designation granted
- **B** **Jan 6, 2020:** Announced top-line results of extension study (PLEO-CMT-FU) of long-term safety and efficacy of PXT3003
- **C** **March 31, 2021:** First Patient enrolled in the second Phase III study in CMT1A (PREMIER trial)
- **D** **April 28, 2021:** Top-line data from interim analysis of ongoing long-term extension study (extension from Phase III PLEO-CMT study and 9-month PLEO-CMT-FU extension study)
- **E** **Q3 2021:** Initiation of first EU clinical site in Phase III PREMIER study
- **F** **Q4 2021:** Publication of first Phase III study manuscript in peer reviewed journal
- **G** **Q2 2022:** Additional top-line data from interim analysis of continued long-term extension study with PXT3003 in CMT1A
- **H** **Q2 2022:** Complete enrollment of Phase III PREMIER Study
- **I** **Q1 2023:** Top-line data from pivotal factorial study with PXT3003 in CMT1A animal model
- **J** **Q3 2023:** Top-line data from Phase III PREMIER study with PXT3003 in CMT1A

Any timelines may be impacted by covid (particularly delays in enrolling patients in clinical trials)

3. PXT864

Overview

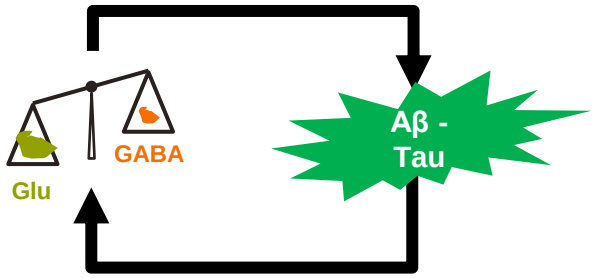
Novel AD Approach:
Correcting chemical imbalance in the diseased brain

Disease at-a-glance

Healthy brain

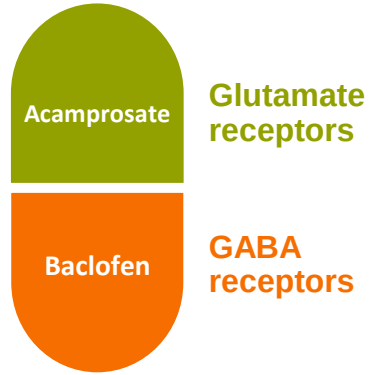
Diseased brain

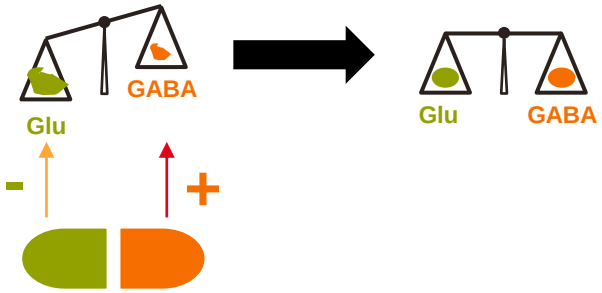
Vicious cycle occurring in AD brain



Upstream of **Aβ -Tau** imbalanced cells overproduce each

PXT864 to break vicious cycle





E/I imbalance = GLU excitation / GABA inhibition

"Therapeutics that correct the E/I imbalance in early AD may prevent neuronal dysfunction, cell loss and cognitive impairments associated with later stages of the disease"

Glu = Glutamate

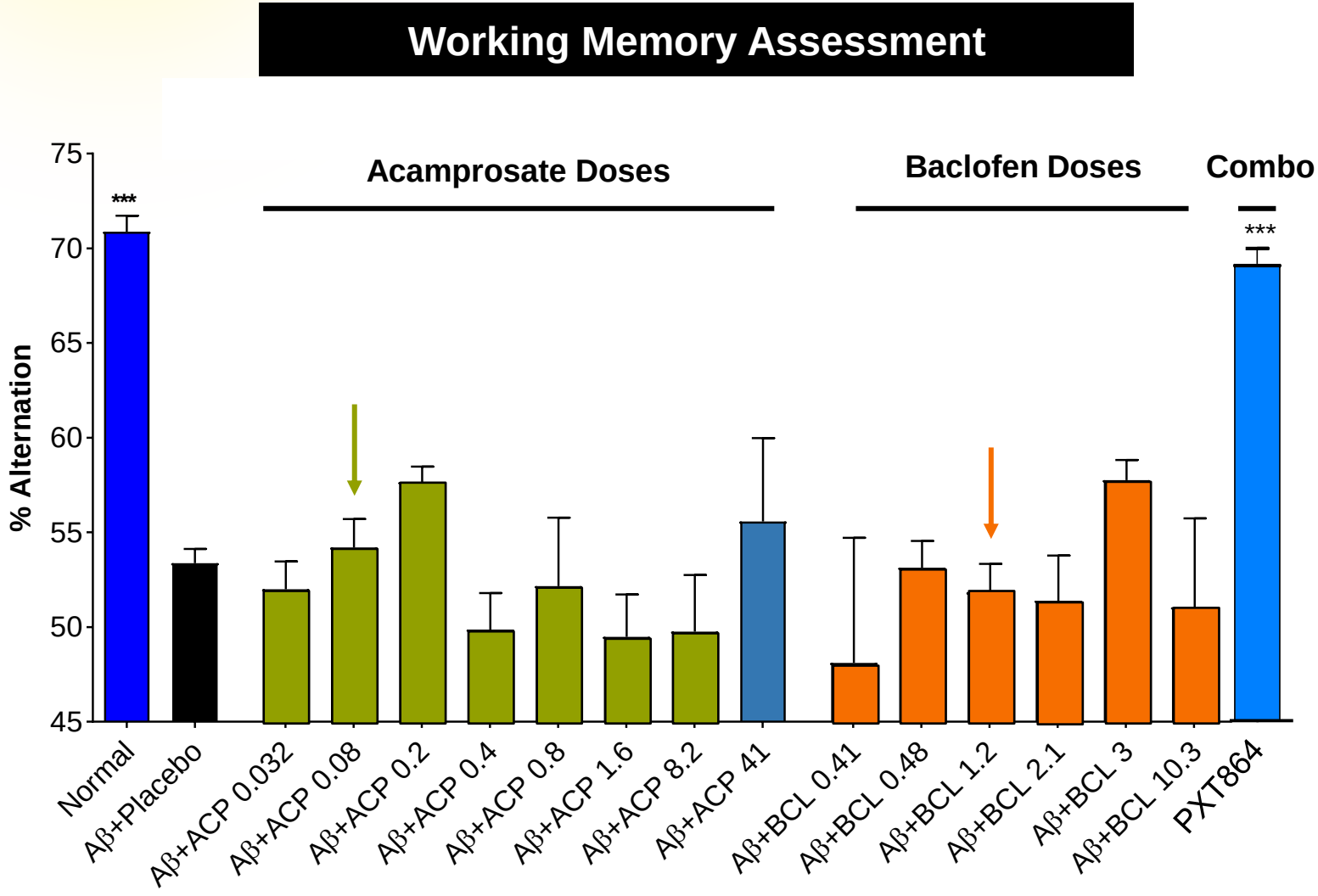
Sources: Govindpani 2017; Talantova 2013

PXT864 in Alzheimer's Disease Overview

Higher doses of PXT864 have potential to demonstrate a sustained therapeutic effect on Alzheimer's Disease, due to the following advantages:

- **Strong safety profile**
- **Can be co-administered with already approved drugs in AD**
- **Can be synergistic with other NCEs to create a powerful novel new entity**

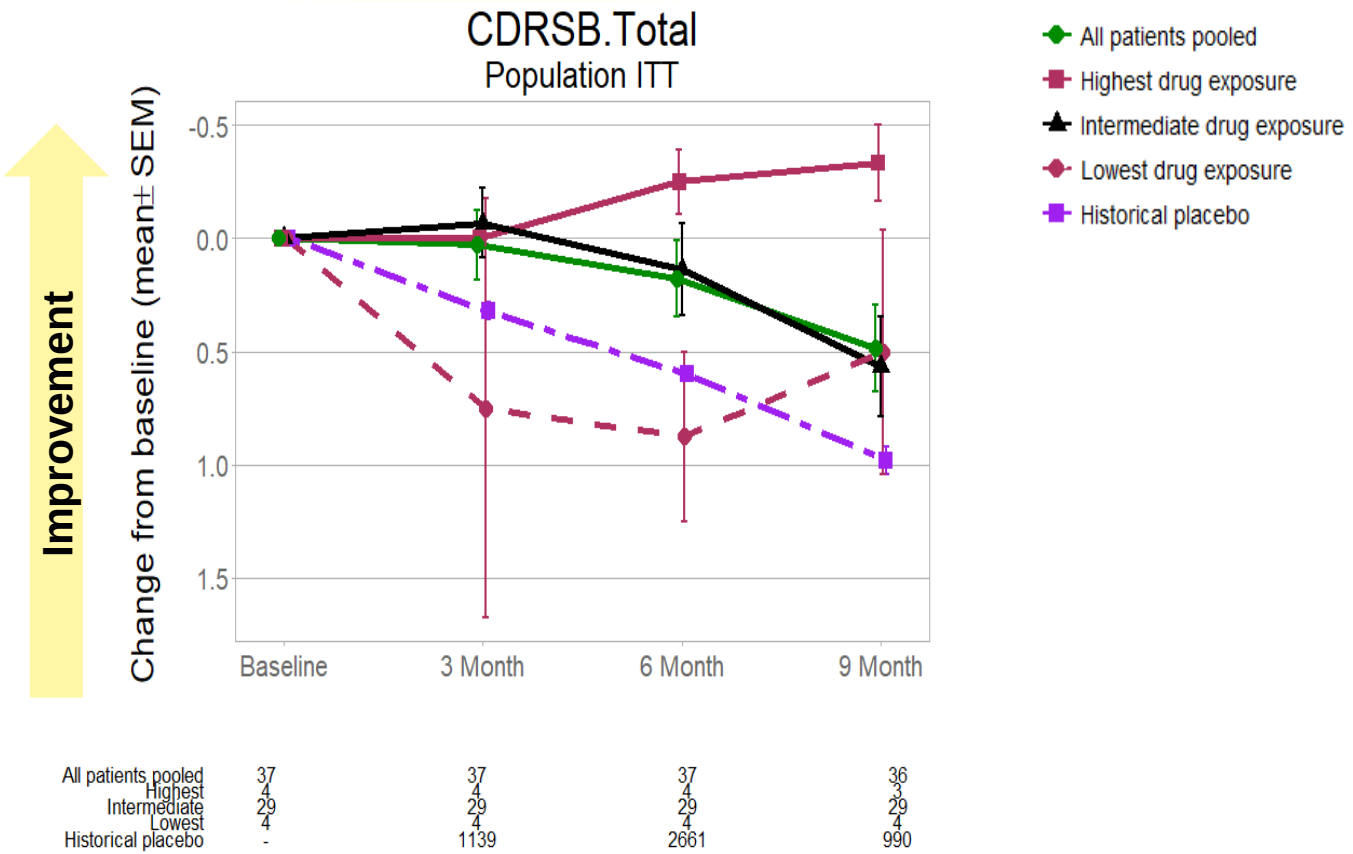
PXT864 Demonstrates Synergistic Efficacy in AD Animals



Source: Chumakov et al., 2015

PXT864: CDR-SB Analysis Based on Plasma Drug Exposure

Higher Dose Could Rapidly Generate Partial Recovery Vs Less Decline With No Safety Concerns



	Acamprosate	Baclofen
Approved dose	**2000 mg**	**80 mg**
Ingested dose 3	**40 mg**	**24 mg**

4. PLEOTHERAPY™ AI PLATFORM

Overview

Virtual Repositioning Step 1

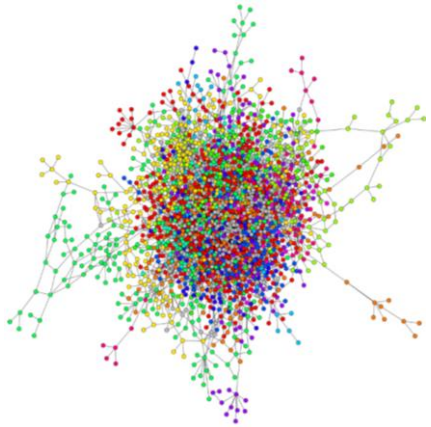
Disease Associated Molecular Network

BIG DATA

- Genome Wide Association Studies (GWAS) e.g. from AD patients
- Protein – Protein Interaction
- Literature
- Known Drug-Target relationships

AI **EXPERTS**

e.g. AD Associated Molecular Network



Virtual Repositioning Step 2

Identifying Candidate Drugs from Drug Data Base and Disease Associated Molecular Network

BIG DATA

Genome Wide Association Studies (GWAS) e.g. from AD patients

Protein – Protein Interaction

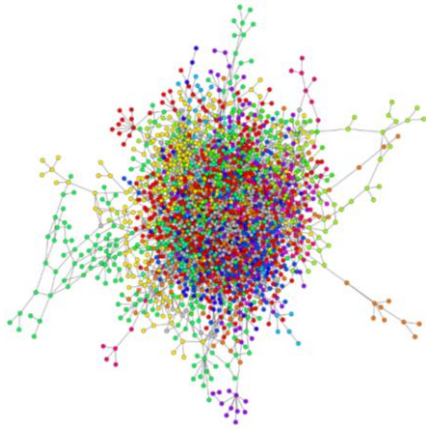
Literature

Known Drug-Target relationships

AI

EXPERTS

e.g. AD Associated Molecular Network

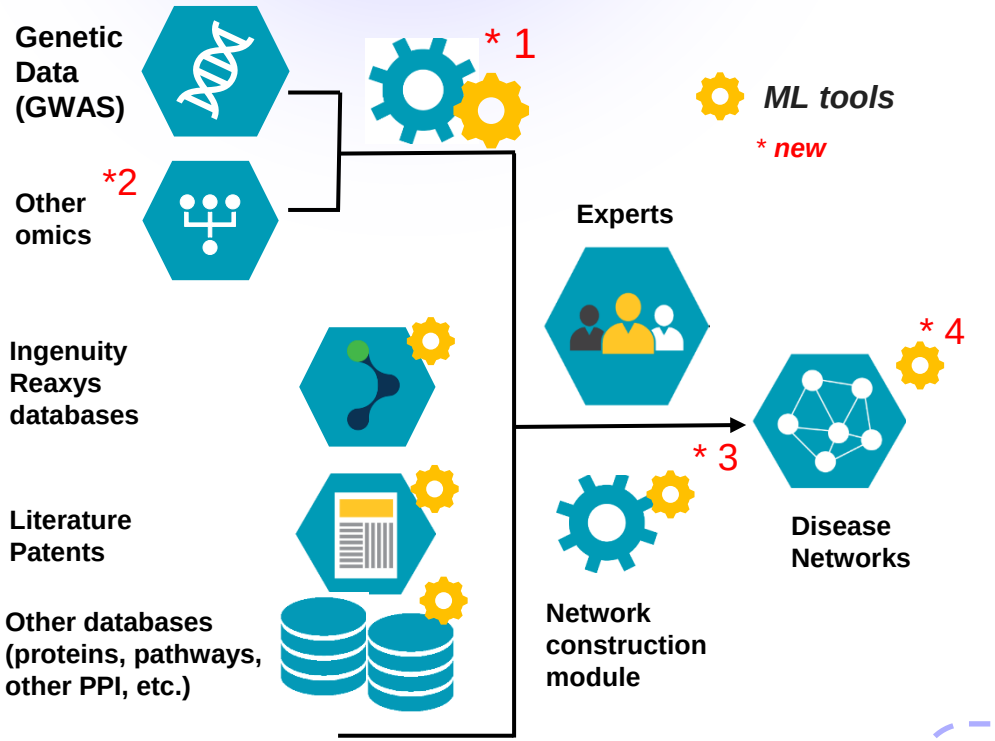


Candidate drugs

Experimental Testing

Virtual Repositioning Powered by AI and Big Data with New Machine Learning (ML) Tools

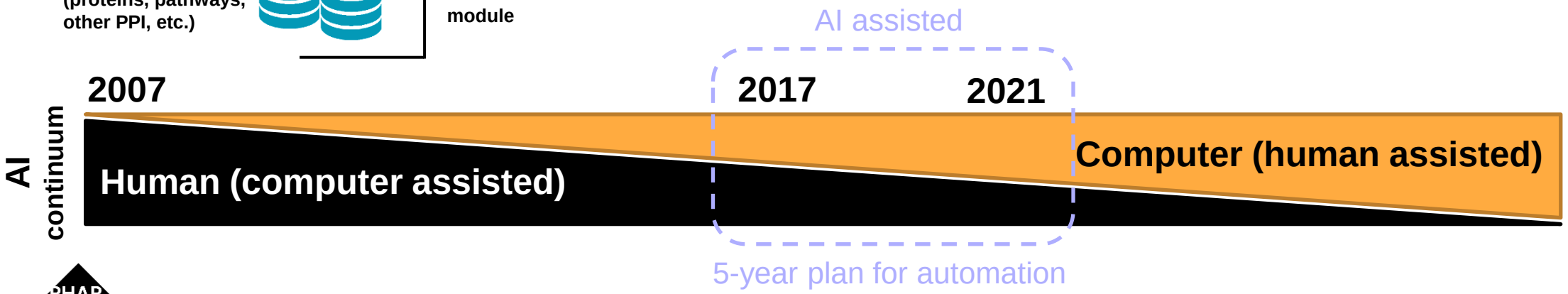
Process reduced from 1 year to 1 quarter - now aiming to reduce to only a few weeks



Platform Status 2017-2021

1. New generation GWAS module: machine learning & deep learning-based imputation (by end 2019) + disease risk prediction (projected 2020)
2. Other Omics data (Big Data)
3. Network building powered by AI, learned from Pharnext's existing networks and methods
4. Network analysis powered by AI (ex: synergy prediction)

- And other ML projects …



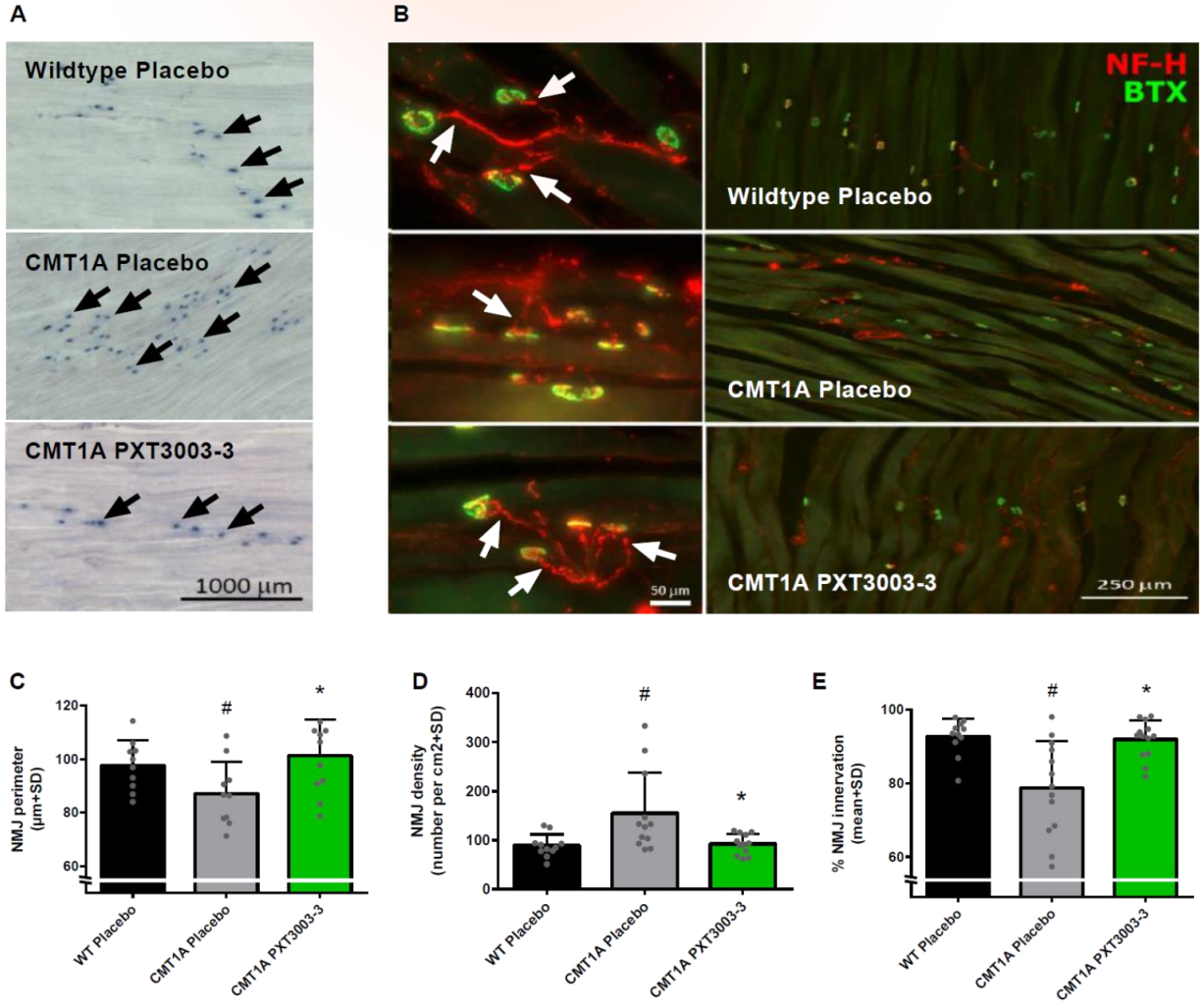
Thank you !

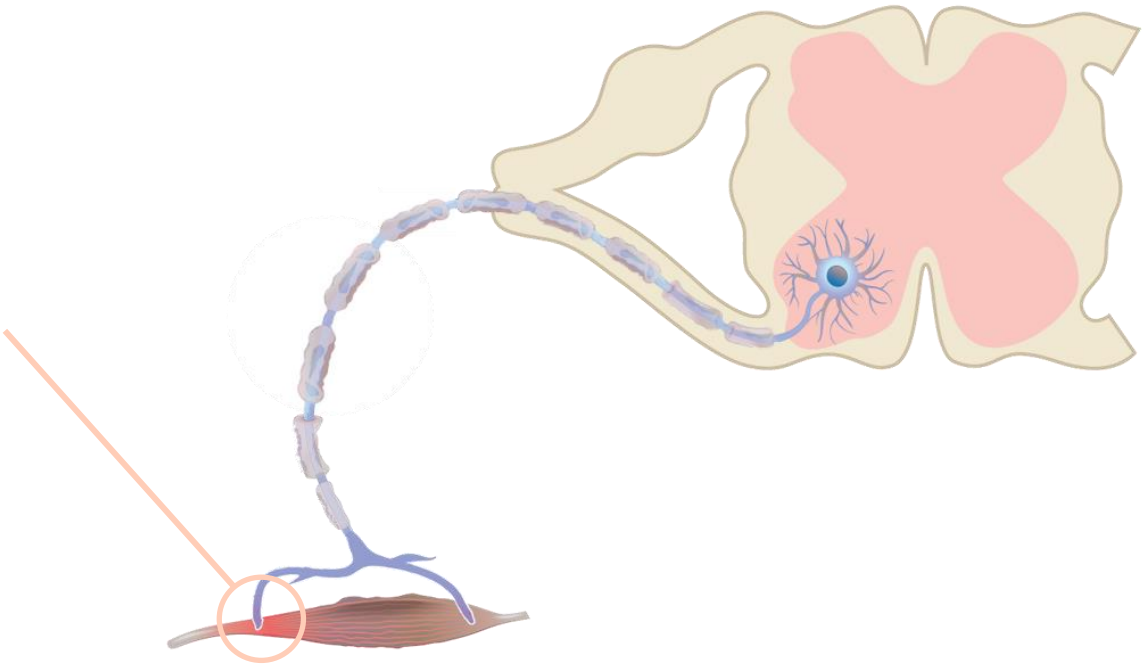
5. Appendix

Mechanism of action of PXT3003 in CMT1A

Preclinical Data Demonstrate That PXT3003 Acts On Different Cell Types Of The Motor Unit In CMT1A

Improves innervation of neuromuscular junctions



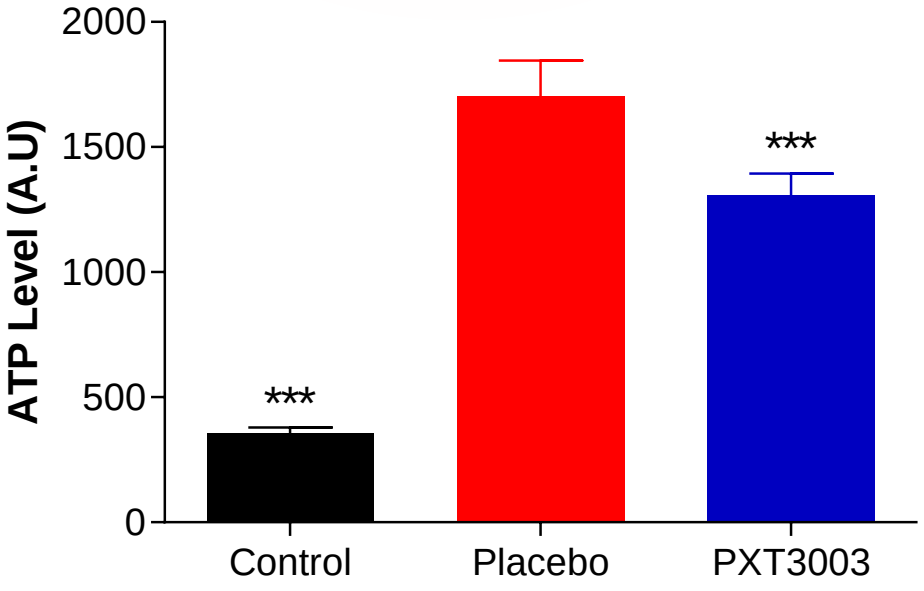


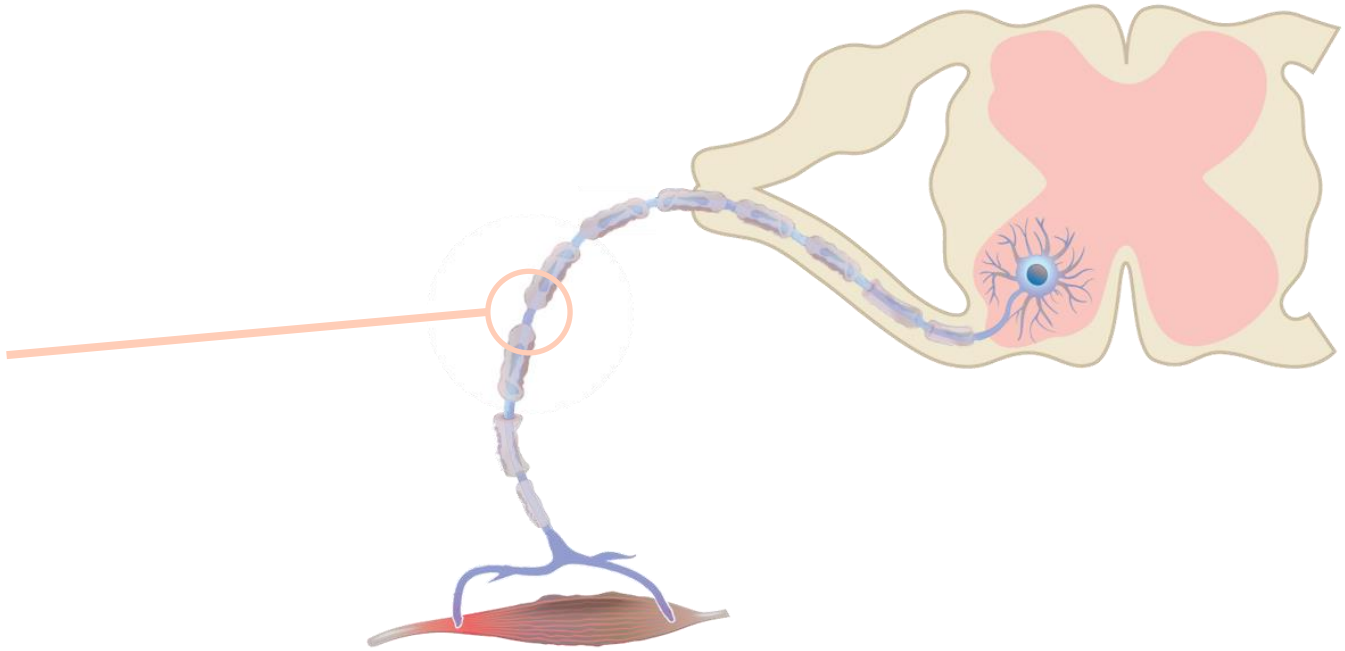
(A,C,D) Morphology and number of neuromuscular junctions (black arrows in A), (B,E) Innervation of neuromuscular junctions (white arrows in B)
***p<0.05, **p<0.01, ***p<0.001 vs placebo**

Mechanism of action of PXT3003 in CMT1A

Preclinical Data Demonstrate That PXT3003 Acts On Different Cell Types Of The Motor Unit In CMT1A

Improves global energy expenditure *in vitro*

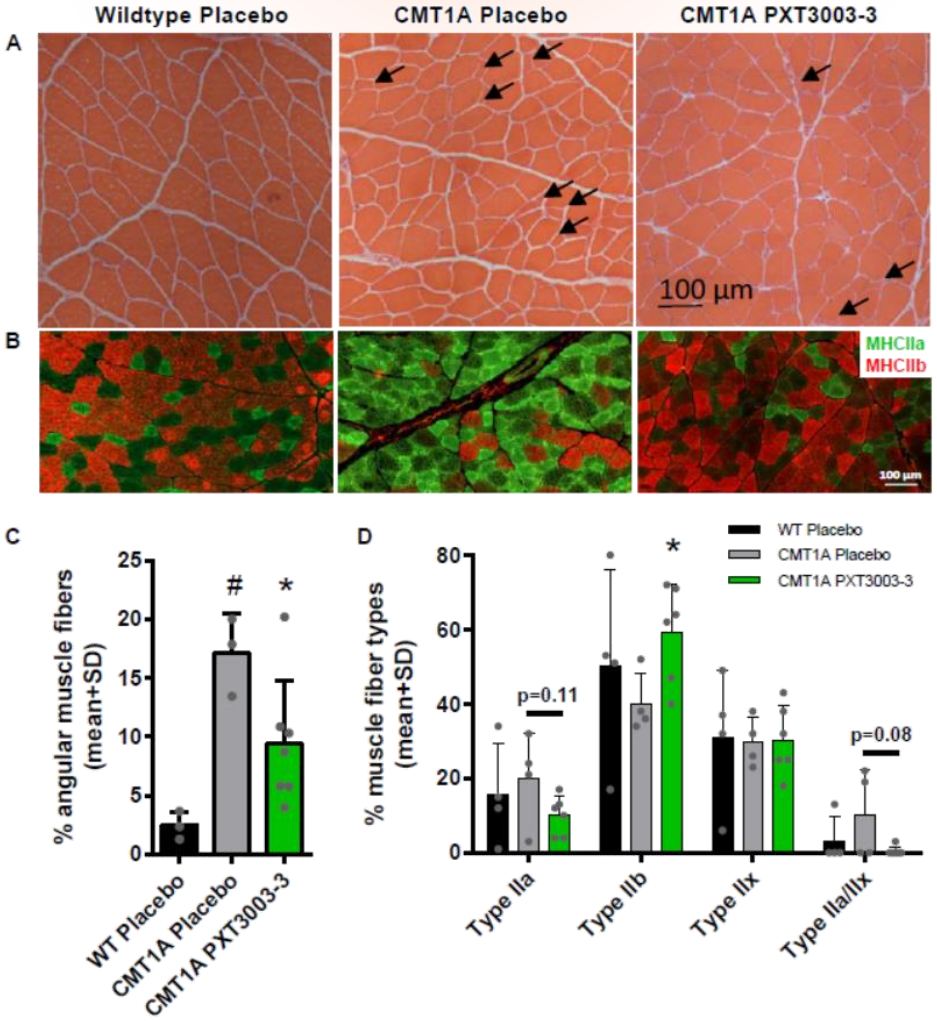




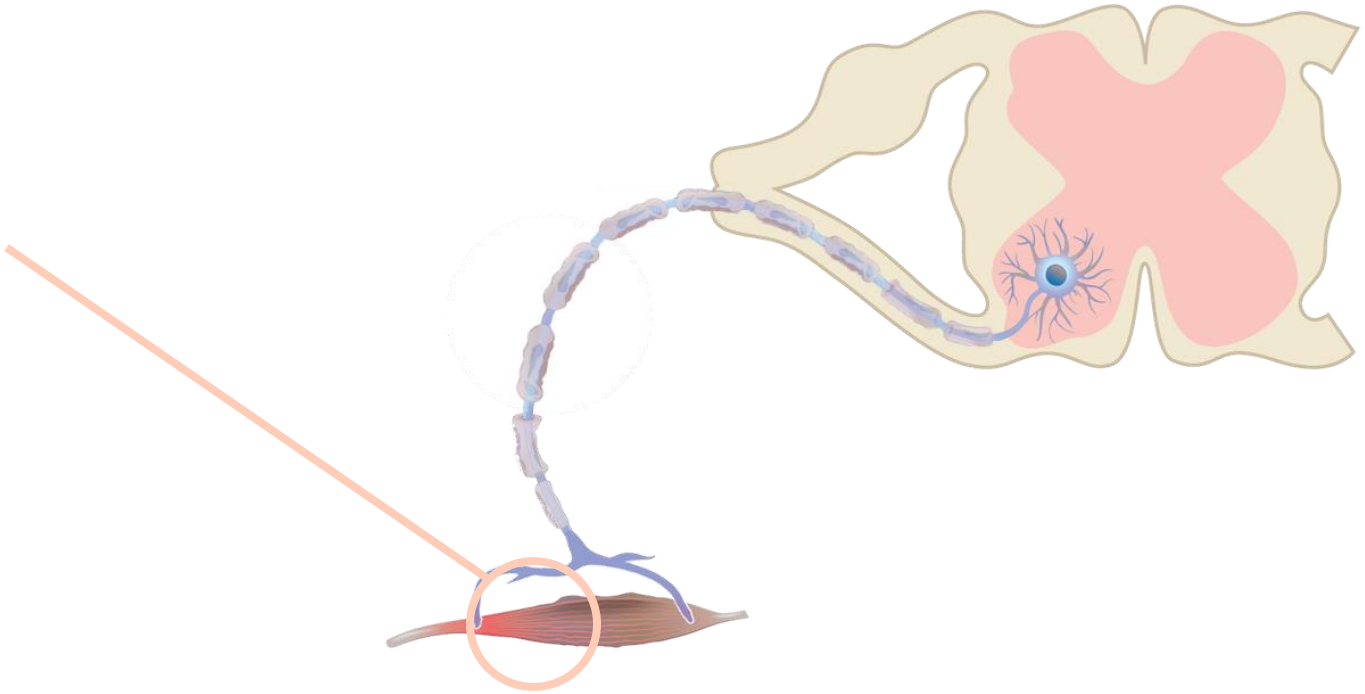
*p<0.05, **p<0.01, ***p<0.001 vs placebo

Mechanism of action of PXT3003 in CMT1A

Preclinical Data Demonstrate That PXT3003 Acts On Different Cell Types Of The Motor Unit In CMT1A



Restores muscle fibers number and types



(A,C) Angular fiber phenotype (reflecting atrophy in CMT1A) (B,D) Muscle fiber type quantification (fast type IIb vs slow type IIa)

PLEODIAL: Exploratory Phase IIa Trial Design

- 45 mild naïve AD patients treated by 3 doses:
- Clinically diagnosed but low mean Log Abeta 42/40
- 7 centers in France
- Assessed at 0,3,6,9 months
- 9 clinical endpoints, open label, single blind

(mg)	Acamprosate	Baclofen
Dose 1	0,8	12
Dose 2	2	30
Dose 3	40	24

Functions assessed by each endpoint

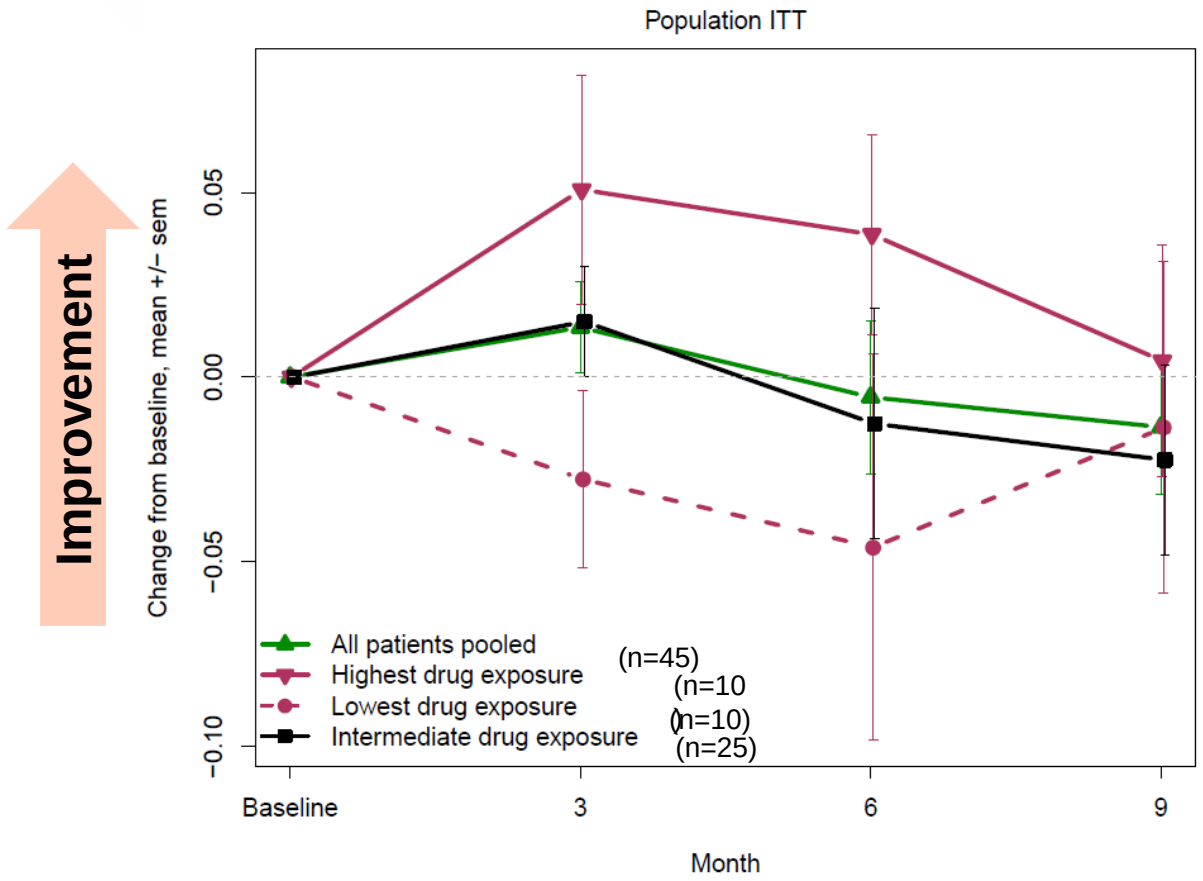
	Memory	Orientation	Language	Attention	Visuospatial	Executive function	Speed	Daily activity	Social interaction
Adas Cog	■	■	■	■	■	■			
CDRSB	■	■		■		■		■	■
IADL		■			■	■		■	
TMT A			■	■	■	■	■		
TMT B			■	■	■	■	■		
ZAZZO				■	■	■	■		
Apathy Inventory			■					■	■
DSST				■	■	■	■		
ISAAC	■		■	■		■	■		

- Biomarker: Plasma $A\beta_{42/40}$ assessed by Quanterix

Plasma $A\beta_{42/40}$ Analysis Based on Plasma Drug Exposure

Improvement at 3 and 6 Months, but a Higher Dose Could Rapidly Generate Sustained Effect

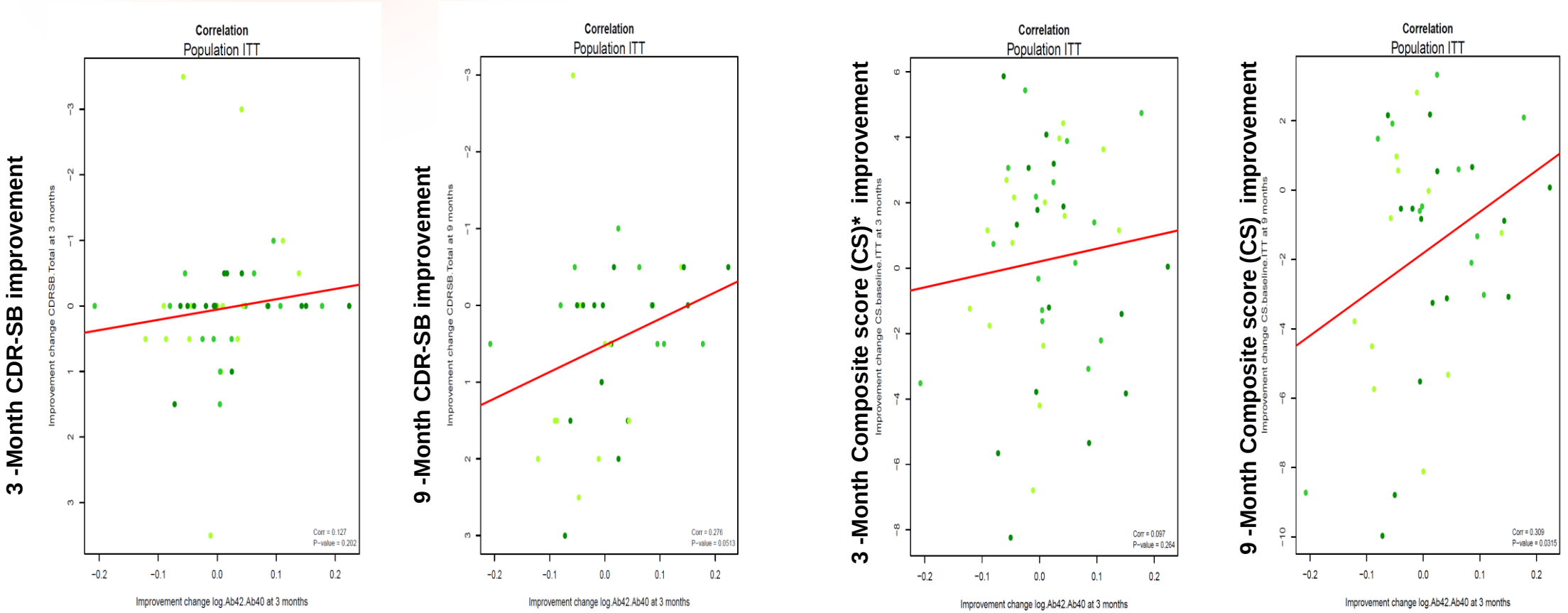
Evolution of log Ab42 Ab40 in PLEODIAL



	Acamprosate	Baclofen
Approved dose	**2000 mg**	**80 mg**
Ingested dose 3	**40 mg**	**24 mg**
Next dose to be tested	**400 mg**	**24 mg**

Drug exposure = C_{max} for both drugs

Plasma $A\beta_{42/40}$ 3-Month Improvement Correlates With Clinical Improvement at 9 Months: Suggests a Delayed Effect "From Molecular To Clinical"

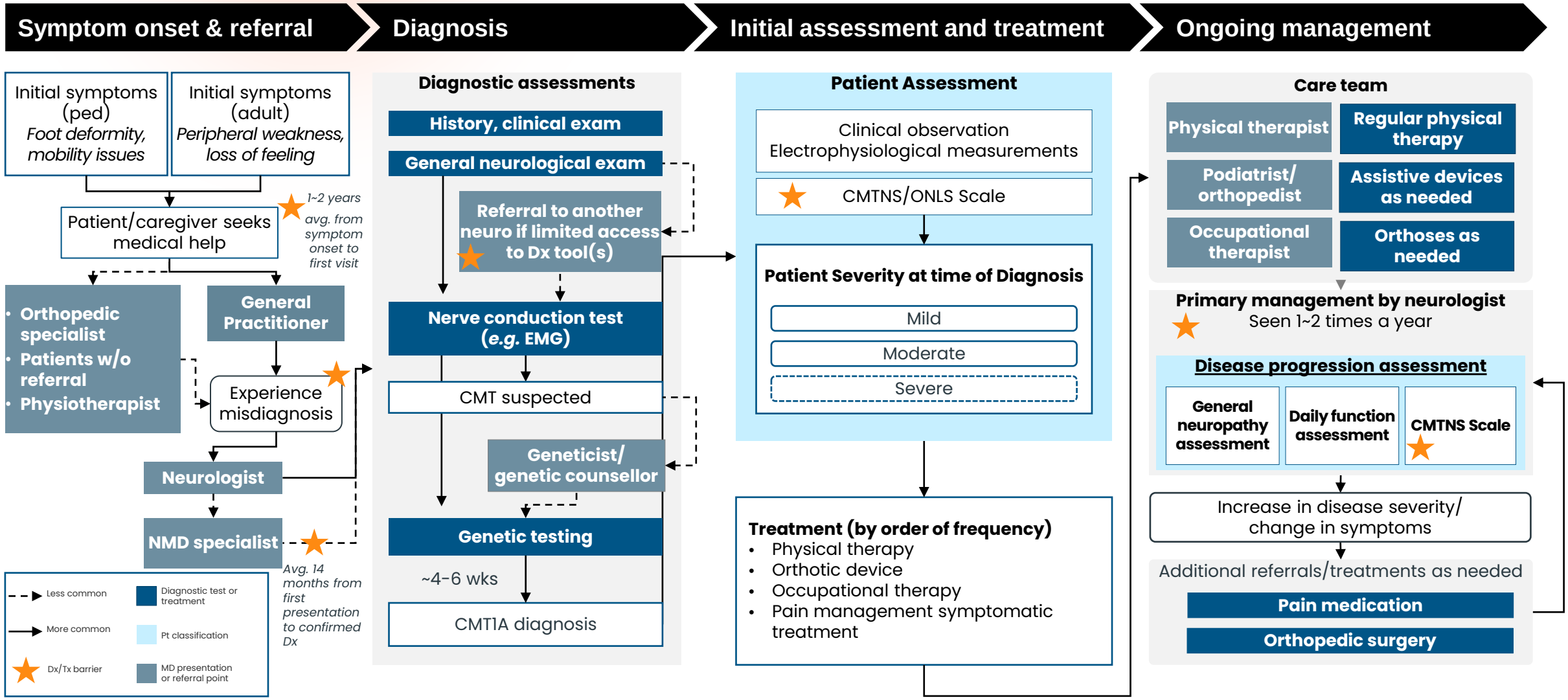


Biomarker 3-Month improvement

Biomarker 3-Month improvement

* Composite score of all clinical endpoints.

Overview of CMT1A Patients Journey



Source: Market research study conducted in the US and EU5 in 2019 with IQVIA