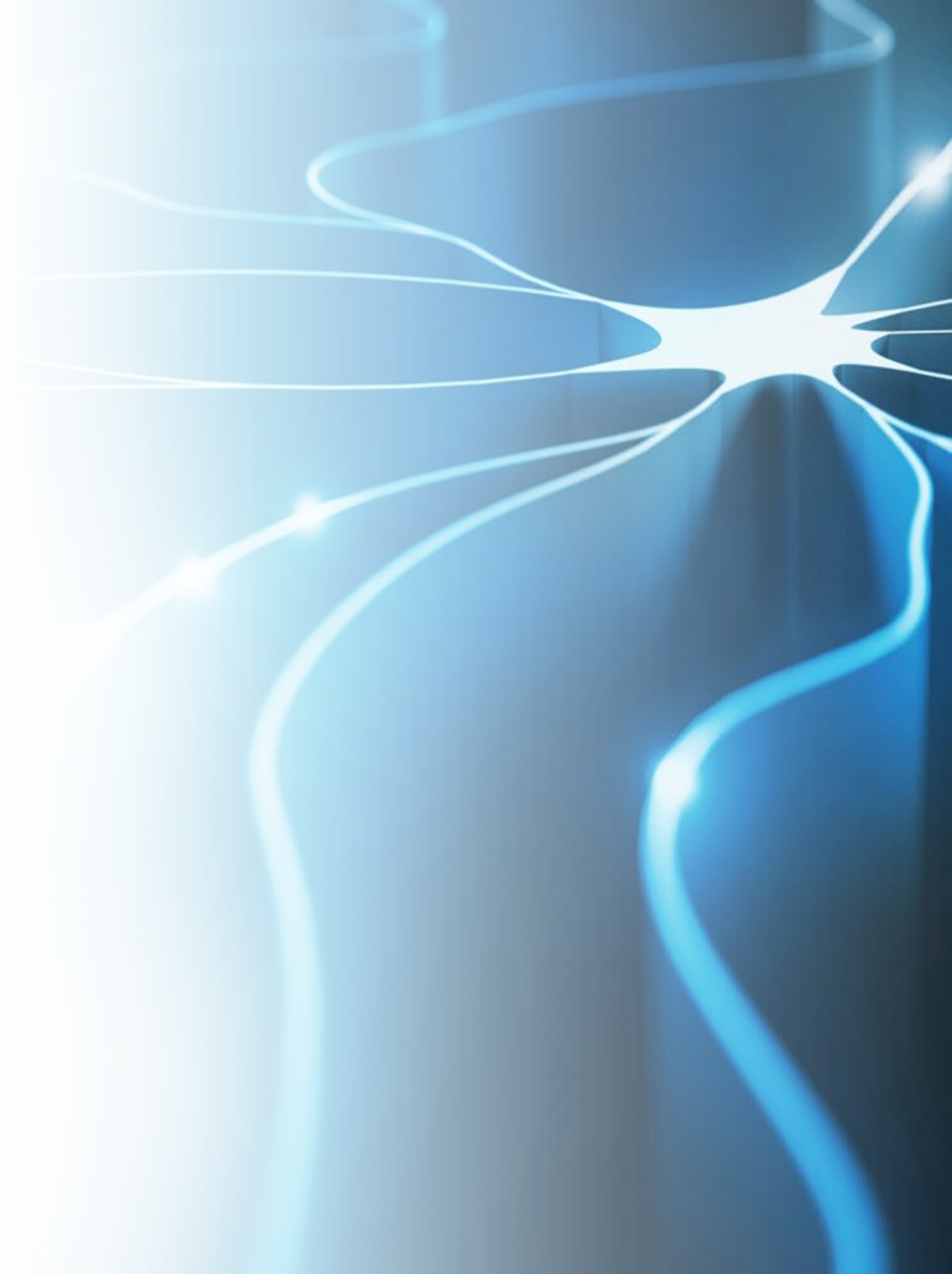
APTINYX

Innovative Therapies for Disorders of the Brain and Nervous System

Corporate Presentation

May 2022 | NASDAQ: APTX

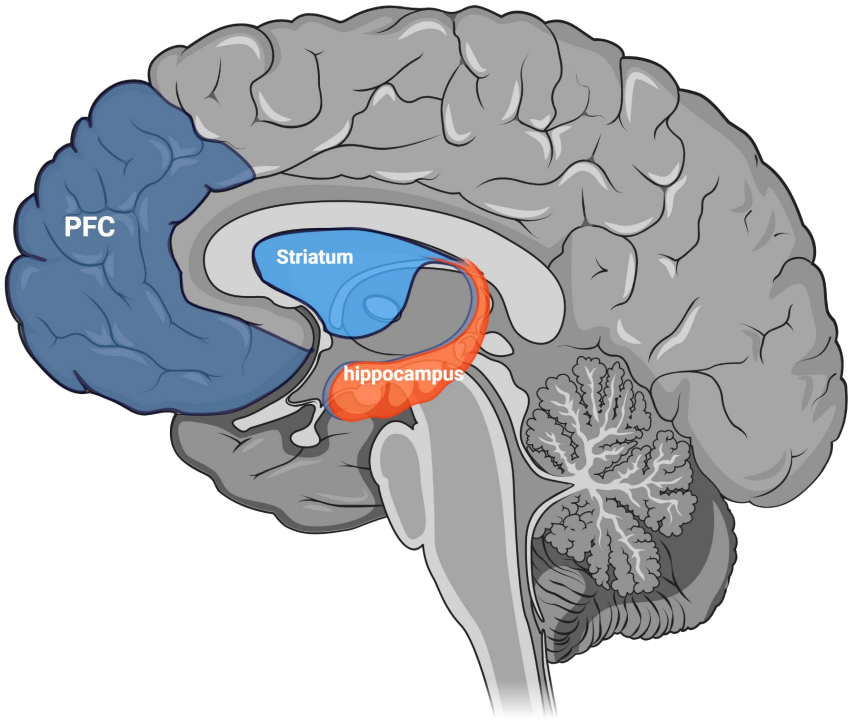


Forward-looking statements

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 relating to business, operations, and financial conditions of Aptinyx, including, but not limited to, Aptinyx’s belief in the potential benefit and profile of its product candidates, plans for preclinical and clinical development of Aptinyx’s product candidates, the timing and reporting of results from preclinical and clinical studies, the ability to replicate or apply results achieved in preclinical studies, the timing and outcome of discussions with FDA and other regulatory agencies, expectations regarding Aptinyx's uses and sufficiency of capital, including the operational runway of its current cash balance, and the impact of the COVID-19 pandemic on Aptinyx’s business and ongoing and planned preclinical and clinical studies. Words such as, but not limited to, “look forward to,” “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “would,” “should” and “could,” and similar expressions or words, identify forward-looking statements. Although Aptinyx believes the expectations reflected in such forward-looking statements are based upon reasonable assumptions, there can be no assurance that its expectations will be realized. Actual results could differ materially from those projected in Aptinyx’s forward-looking statements due to numerous known and unknown risks and uncertainties. All forward-looking statements speak only as of the date of this presentation and are qualified in their entirety by this cautionary statement. Aptinyx undertakes no obligation to revise or update this presentation to reflect events or circumstances after the date hereof.

APTINYX

Learning, memory, executive function, and the cognitive control of pain and emotion are directly regulated by NMDAr function in key brain regions



Prefrontal Cortex Hippocampus Striatum

FIBROMYALGIA
(Centralized Pain)

PTSD

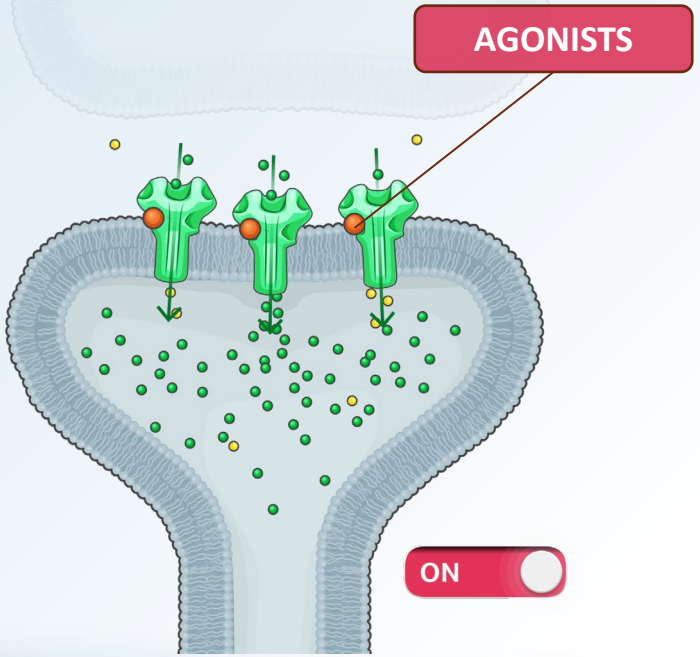
COGNITIVE IMPAIRMENT

NMDA receptor *hypofunction* in certain brain regions is implicated in a range of neurological and neuropsychiatric disorders

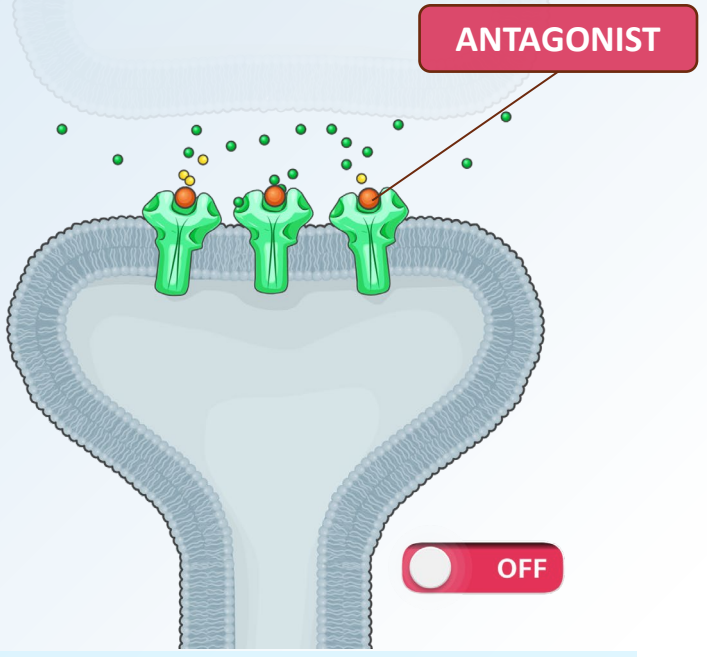
APTINYX

Unlike other NMDAr mechanisms, Aptinyx compounds are designed to target NMDAr hypofunction to retore normal CNS activity

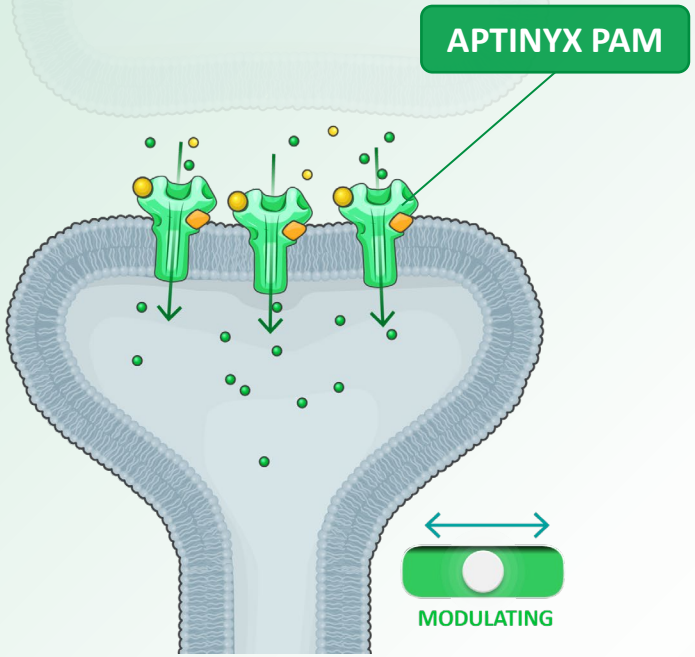
Excitotoxicity
(Broad-based activity)

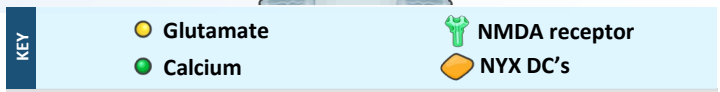


Disassociation & Abuse Risk
(Broad-based activity)



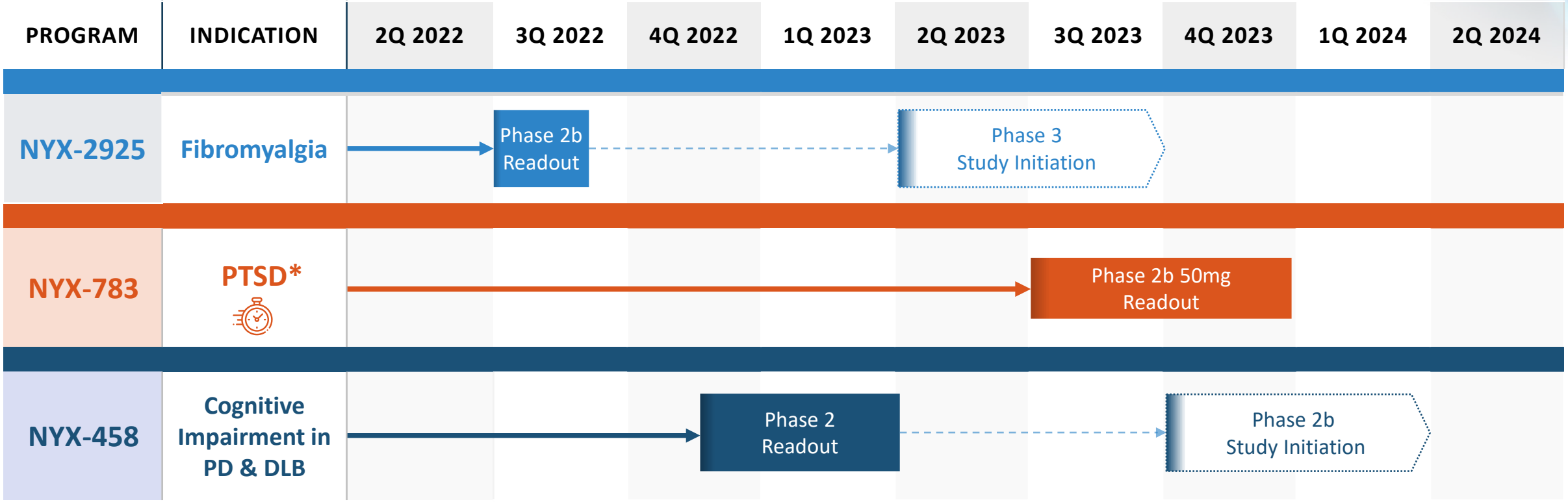
Normal Balance
(Targeted activity)





APTINYX

Pipeline primed for late-stage development with multiple ongoing Phase 2 studies across indications of high unmet need



*Temporary pause to initiation of Phase 2b study of NYX-783 150mg in PTSD

Fast track designation by FDA

APTINYX

NYX-2925

NMDA receptor positive allosteric modulator in Phase 2b development for the treatment of fibromyalgia

APTINYX

Fibromyalgia – A centralized disorder characterized by widespread musculoskeletal pain

One of the most common chronic pain conditions affecting **approximately 8+ million people in the U.S.**

- Defined by the American College of Rheumatology as a **Central Pain Amplification disorder**
- Symptoms include, **pain, tenderness, fatigue, sleep, memory, and mood** issues

Current treatments include **antiepileptics**, **antidepressants**, and **opioids**

- Current treatments have limited efficacy and **substantial side effects**, including the risk of abuse/addiction
- **Multi-billion market opportunity** at pricing consistent with previous branded therapies

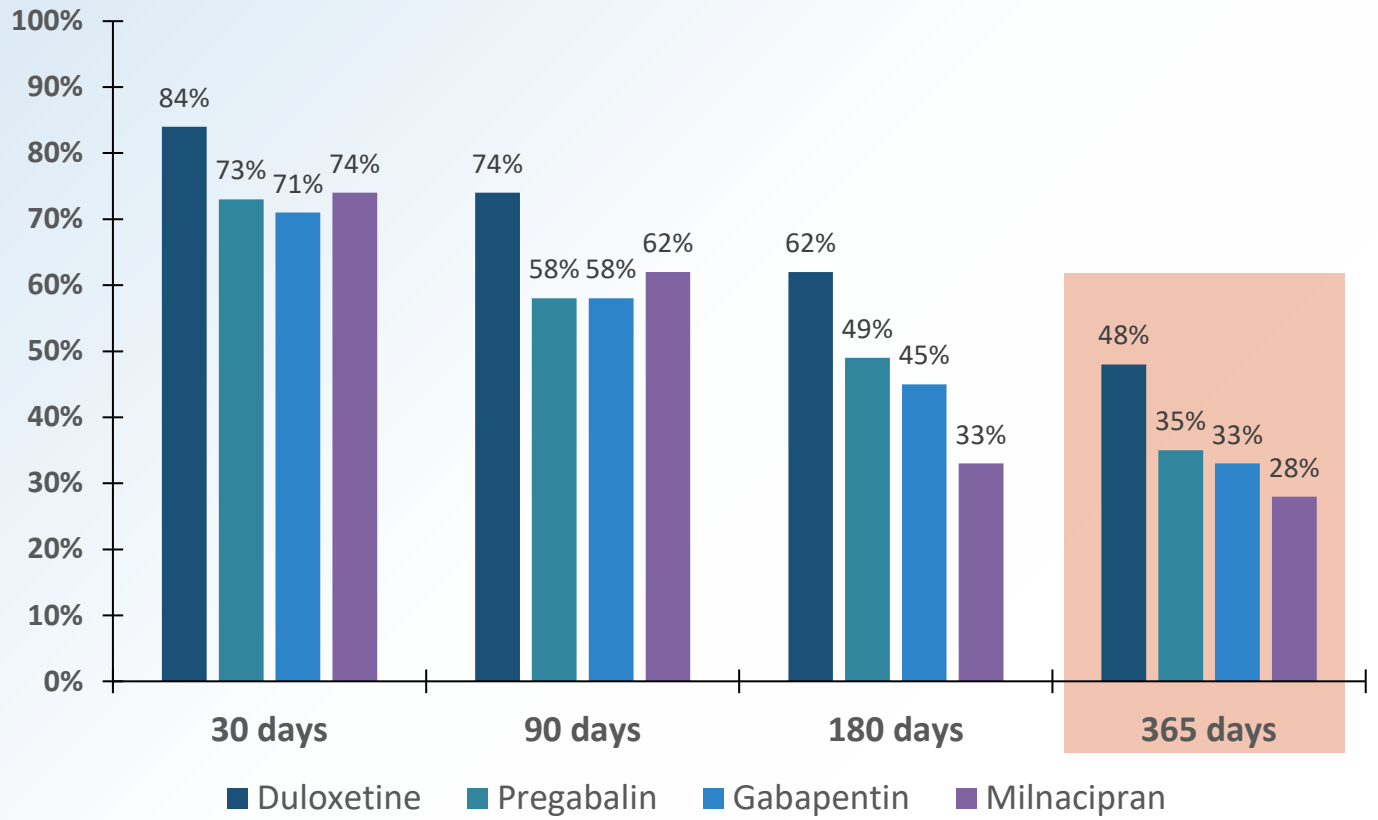
APTINYX

High rate of discontinuation among first line therapies in patients being treated for fibromyalgia

~50-70% ***of patients***

discontinue treatment after 1 year

- Significant tolerability issues
- Lack of broad-based, sustained efficacy
- Majority do not switch after discontinuing
- Often incomplete pain relief, even for those continuing with therapy
- Potential for abuse liability

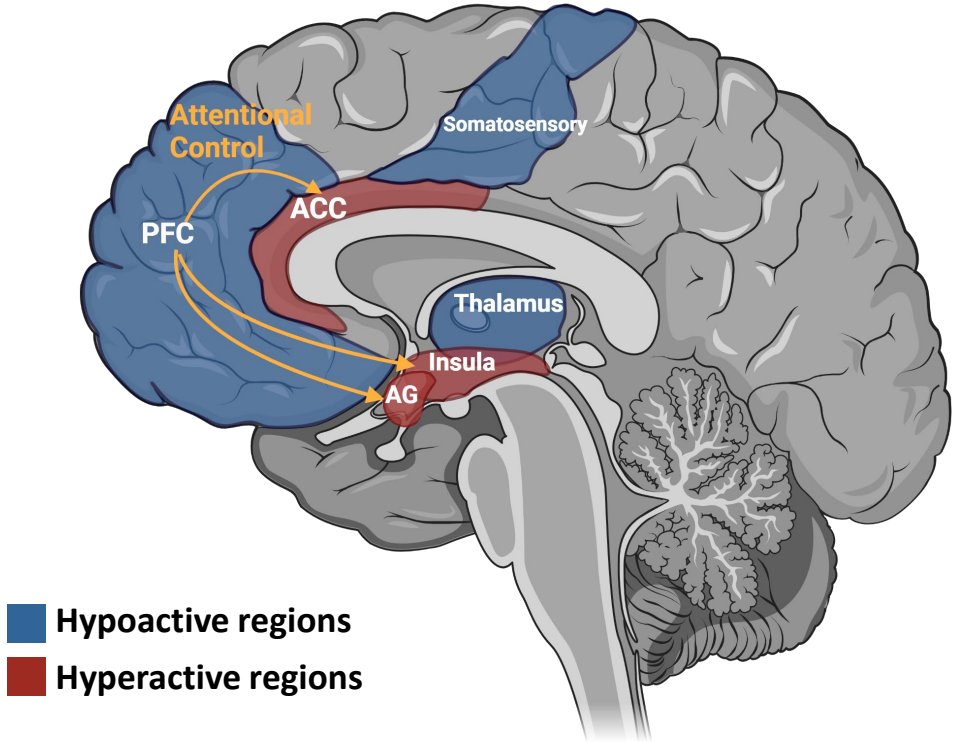


Manag Care Spec Pharm. 2016

APTINYX

NYX-2925 targets aberrant centralized pain processing resulting from NMDA receptor hypofunction in the PFC

HYPOACTIVE REGIONS REGULATE COGNITIVE CONTROL OF PAIN AND EMOTION



GLUTAMATERGIC DYSREGULATION AND PFC HYPOFUNCTION

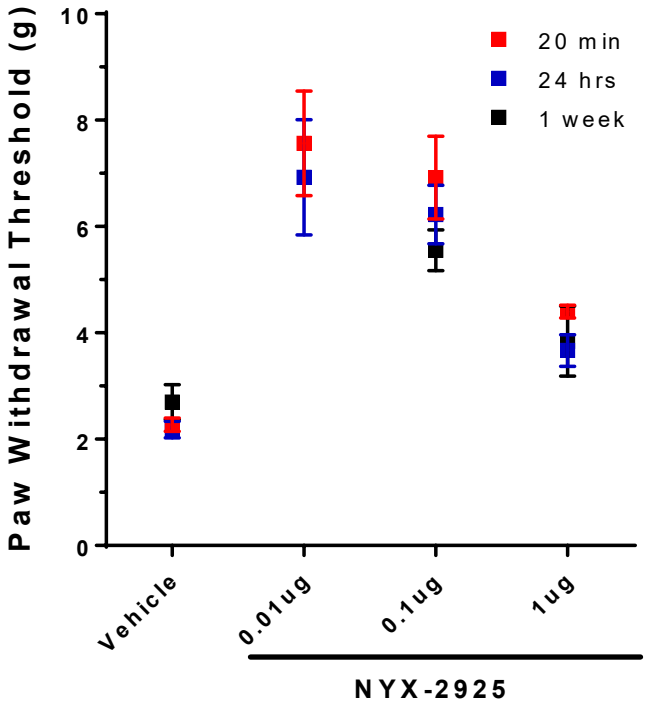
- The prefrontal cortex (PFC) plays a critical role in regulating the emotional and cognitive aspects of centralized pain processing
- Centralized pain can arise from altered brain circuitry caused by glutamatergic hypofunction in the PFC
- Modulation and normalization of NMDA receptors may lead to increased activity in the PFC and alleviate centralized pain
- Direct infusion of NYX-2925 in the mPFC (not intrathecal) is analgesic—demonstrating central, non-spinal mediated action

NYX-2925 demonstrates analgesic effects in a range of animal models, effect has shown to be localized in the PFC, and is NMDA receptor-dependent

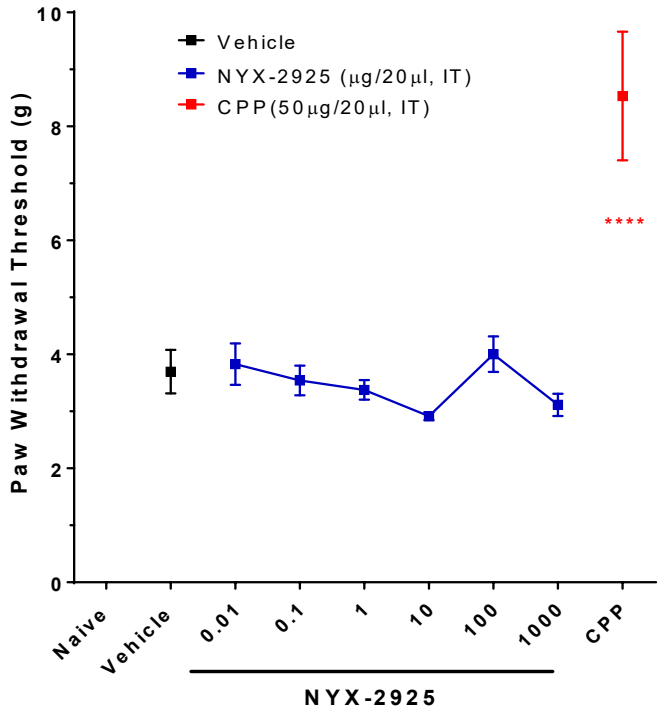
APTINYX

Direct mPFC, but not intrathecal, infusion of NYX-2925 is analgesic in CCI model — demonstrating central, non-spinal mediated action

CCI - mPFC ADMINISTRATION



CCI - INTRATHECAL ADMINISTRATION

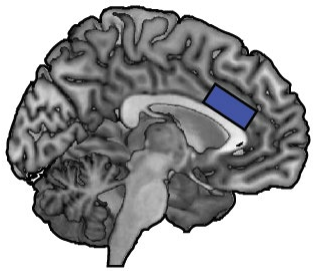


The mechanism of NYX-2925 in centralized pain is distinct from that of NMDAr antagonists

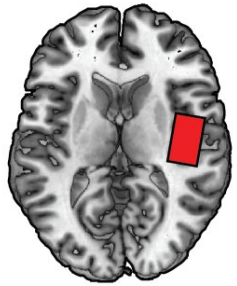
APTINYX

In exploratory Phase 2a fibromyalgia study, NYX-2925 affected imaging biomarkers of pain perception and improved patient-reported symptoms

NYX-2925 MODIFIES PAIN-INDUCED BRAIN ACTIVITY IN KEY BRAIN REGIONS



Dorsal Anterior Cingulate Cortex (dACC)



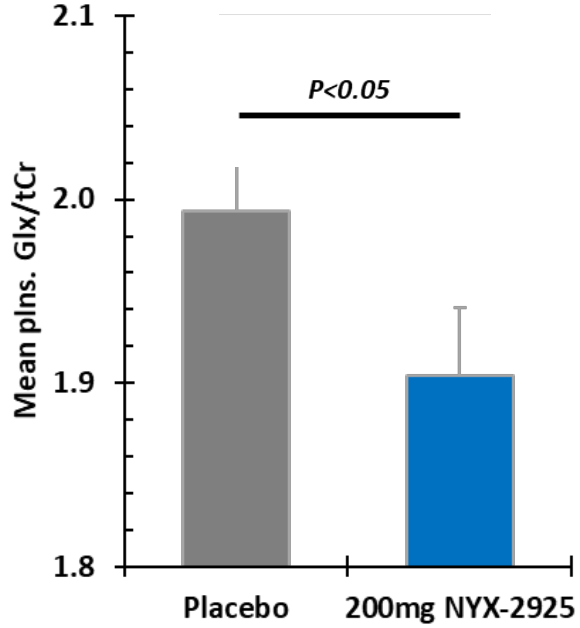
Posterior Insula (pINS)

- NYX-2925 produced statistically significant reductions of glutamate and glutamine in key pain-regulating brain regions vs. PBO
- Also observed reduced functional connectivity with NYX-2925 in certain brain regions vs. PBO
- Greater concentrations of pain-evoked glutamine in posterior insula at baseline was associated with greater reductions in pain sensitivity following treatment

NYX-2925 REDUCED GLX LEVELS, LEADING TO PAIN ALLEVIATION

pINS Glx Levels

(Post-Evoked Pain)



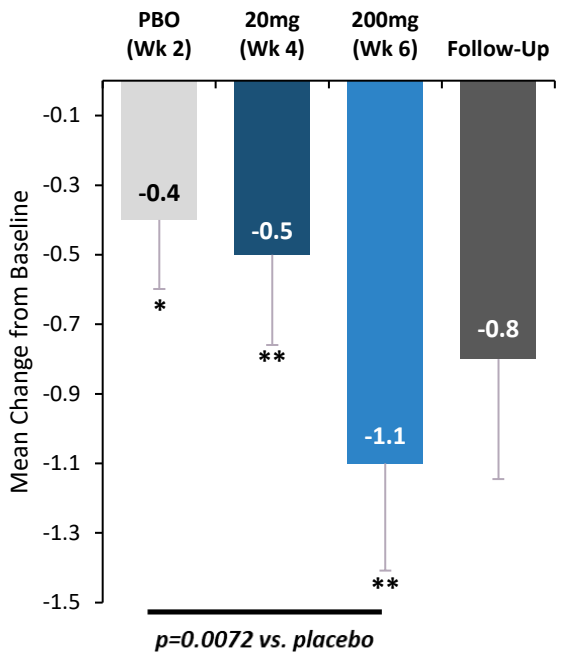
- Increased Glx levels are associated with higher pain perception

APTINYX

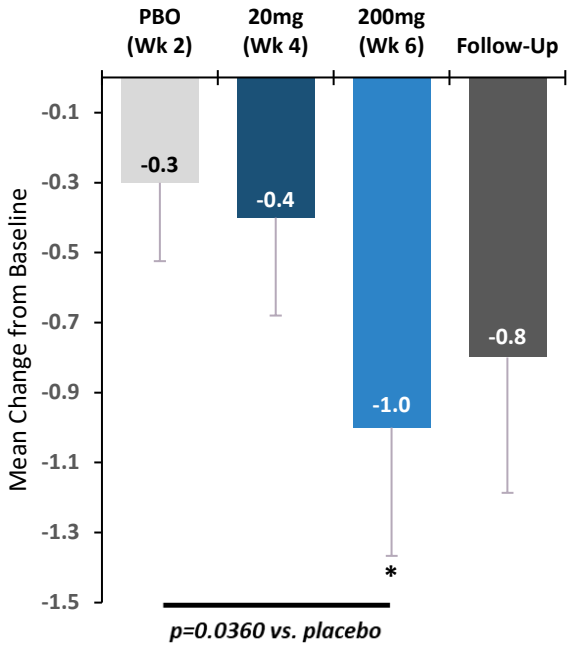
NYX-2925 demonstrated statistically significant, meaningful improvements in patient-reported measures of fibromyalgia

PAIN ENDPOINTS

Average Daily Pain



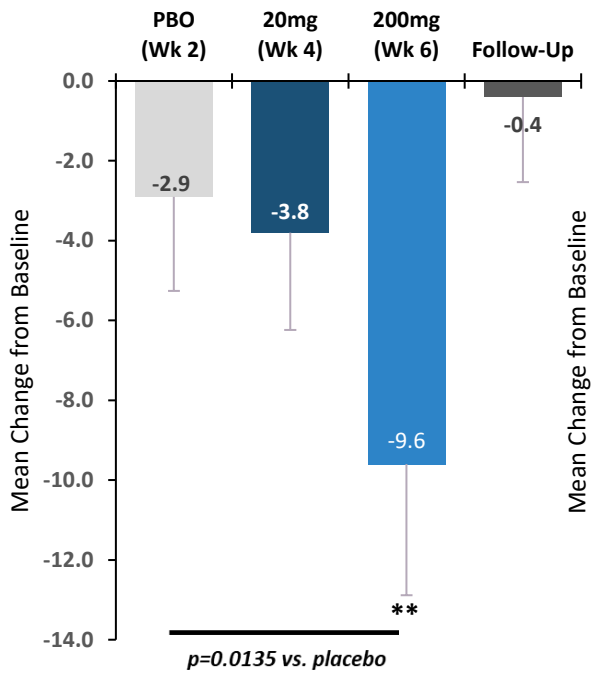
Worst Daily Pain



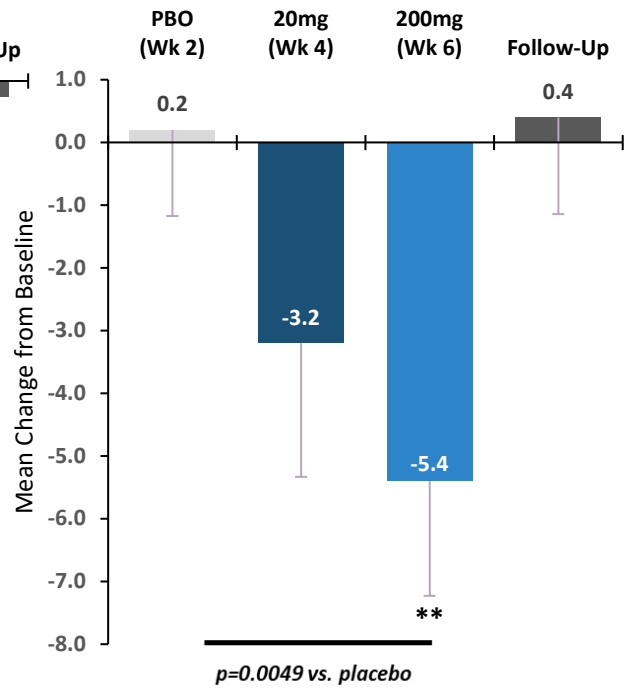
* = p<0.05 vs. baseline ** = p<0.01 vs. baseline

KEY QOL/FUNCTION ENDPOINTS

Total FIQR Score



PROMIS$_{FM}$ Total Fatigue Profile Score

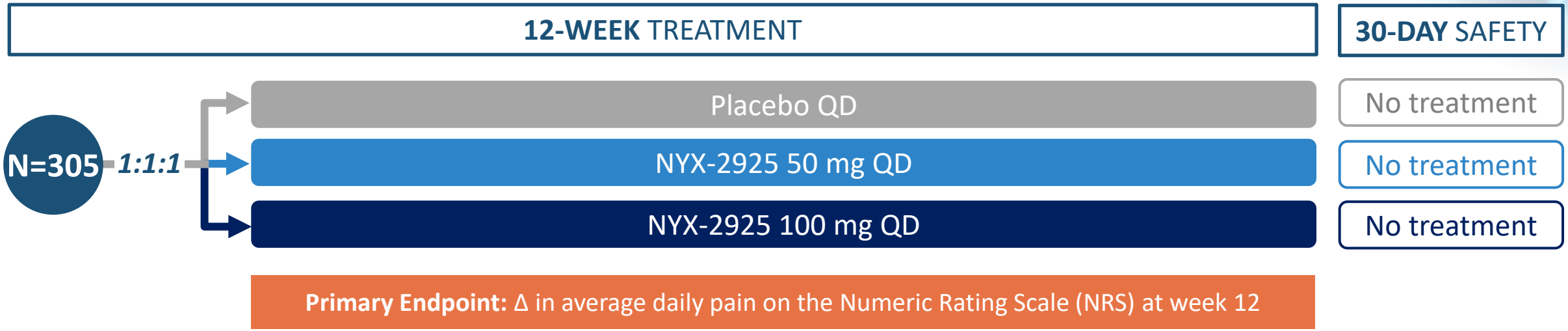


N=22

Promising activity on patient-reported measures informs ongoing larger Phase 2b study

APTINYX

Key learnings from previous Phase 2a neuroimaging study de-risk ongoing Phase 2b study in fibromyalgia



DESIGN OF PHASE 2b STUDY OF NYX-2925 IN FIBROMYALGIA

- 12-week treatment period
- No concomitant analgesics
- Primary endpoint: Change in average daily pain on the Numeric Rating Scale (NRS)
- Other endpoints: Worst daily pain, daily sleep interference, FIQR, PROMIS

OTHER NOTABLE INCLUSION CRITERIA

- Meets the 2016 American College of Rheumatology criteria for fibromyalgia
- Fibromyalgia diagnosed >1 year prior to Screening

APTINYX

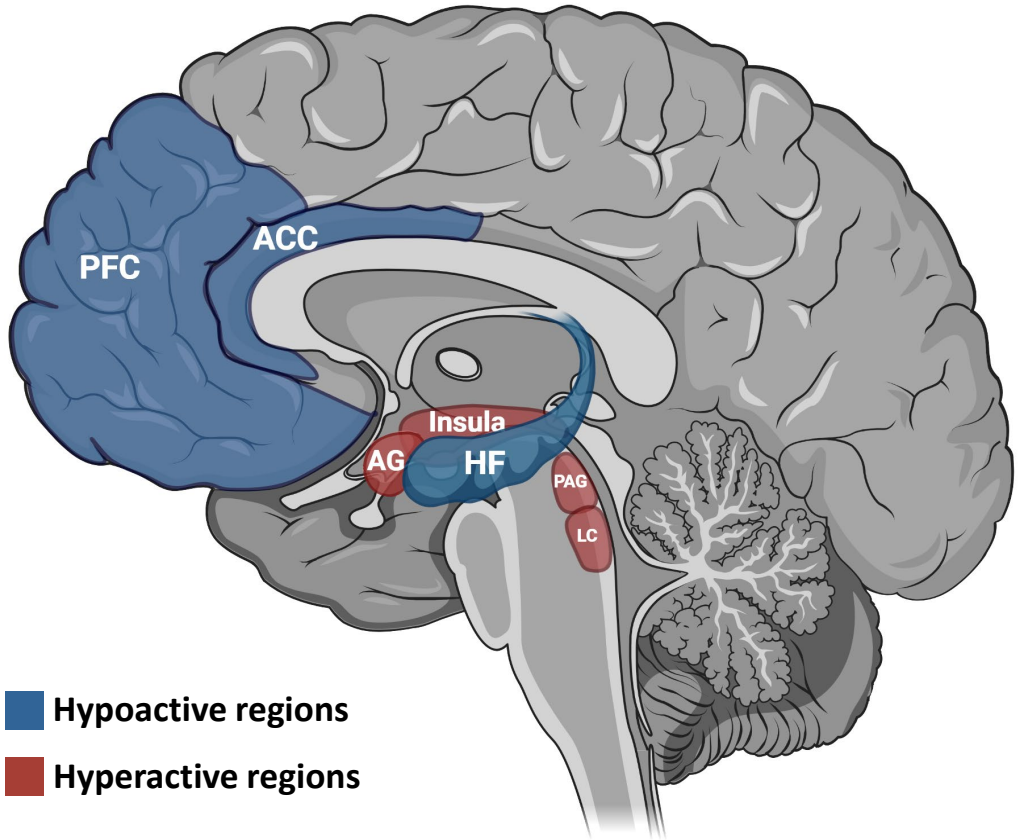
NYX-783

NMDA receptor positive allosteric modulator in Phase 2b development for the treatment of post-traumatic stress disorder

APTINYX

Targeting NMDA receptor hypofunction in key brain regions supports therapeutic development in PTSD

HYPOACTIVE REGIONS REGULATE FEAR EXTINCTION LEARNING AND COGNITIVE CONTROL OF EMOTION

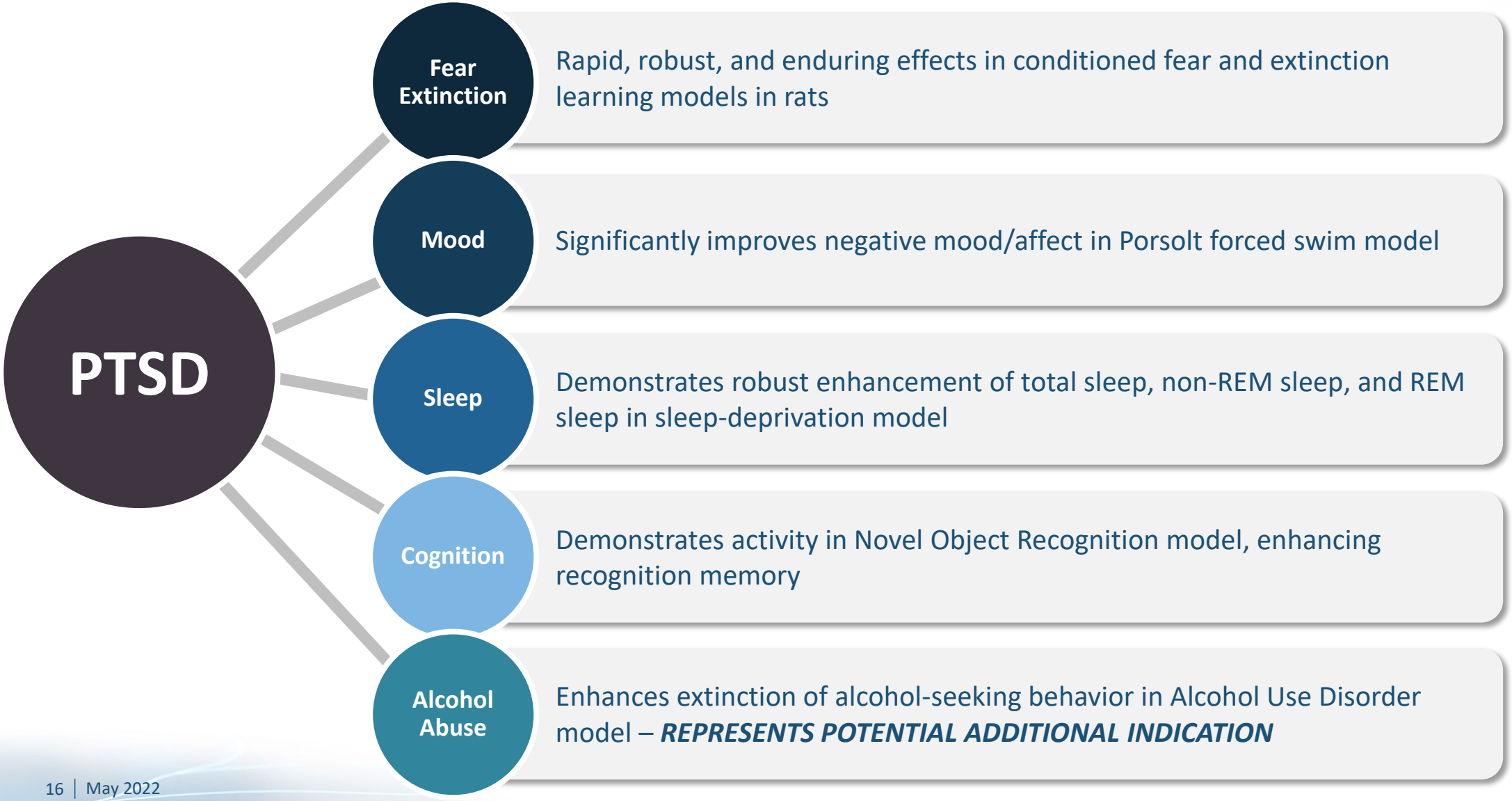


GLUTAMATERGIC DYSREGULATION AND PFC HYPOFUNCTION

- Activation of prelimbic and infralimbic regions of the mPFC are associated with extinction learning in animal models
- PTSD patients show reduced activity of the mPFC involving glutamatergic dysregulation
- Long-term extinction of PTSD symptoms requires cognitive reappraisal and reprocessing of traumatic memories

APTINYX

Preclinical work demonstrates that NYX-783 has the potential to address the diverse symptomatology of PTSD



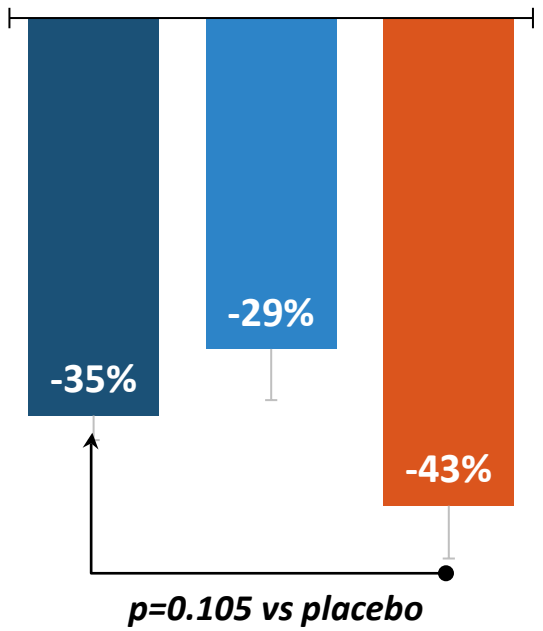
APTINYX

In exploratory Phase 2a study, NYX-783 exhibited clinically meaningful improvement of PTSD symptoms after 4 weeks of treatment

CAPS-5 TOTAL SCORE

WEEK 4

MMRM LSM % Change from Baseline

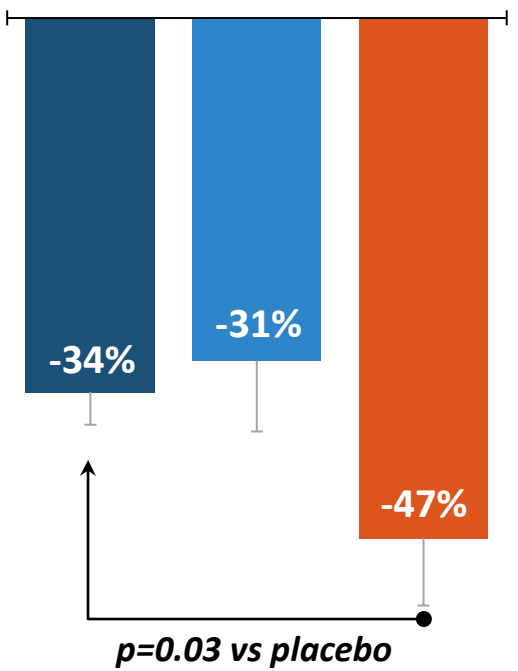


- Placebo (n=103)
- 10 mg NYX-783(n=24)
- 50 mg NYX-783(n=26)

CAPS-5 TOTAL SCORE (Corrected time since trauma imbalance)

WEEK 4

ANCOVA LSM % Change from Baseline

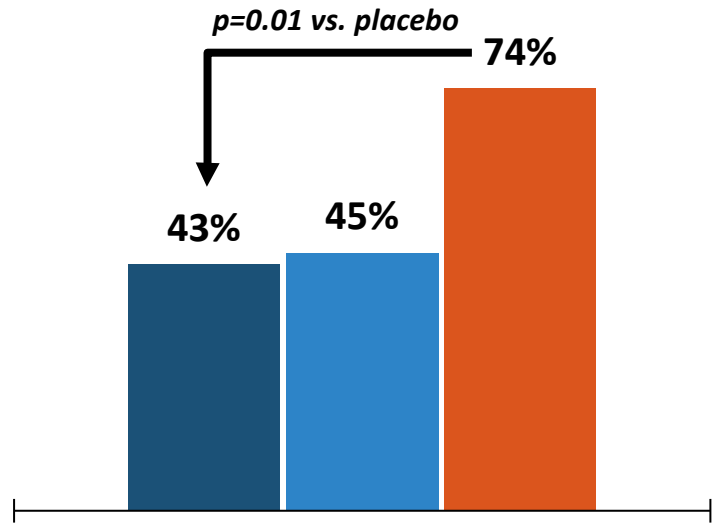


- Placebo (n=86)
- 10mg NYX-783 (n=20)
- 50mg NYX-783 (n=19)

CAPS-5 TOTAL SCORE – "Clinically Reliable Change"

WEEK 4

Proportion of Patients Achieving a ≥ 13-Point Improvement on CAPS-5 Total from Baseline



Placebo (n=86) 10mg NYX-783 (n=20) 50mg NYX-783 (n=19)

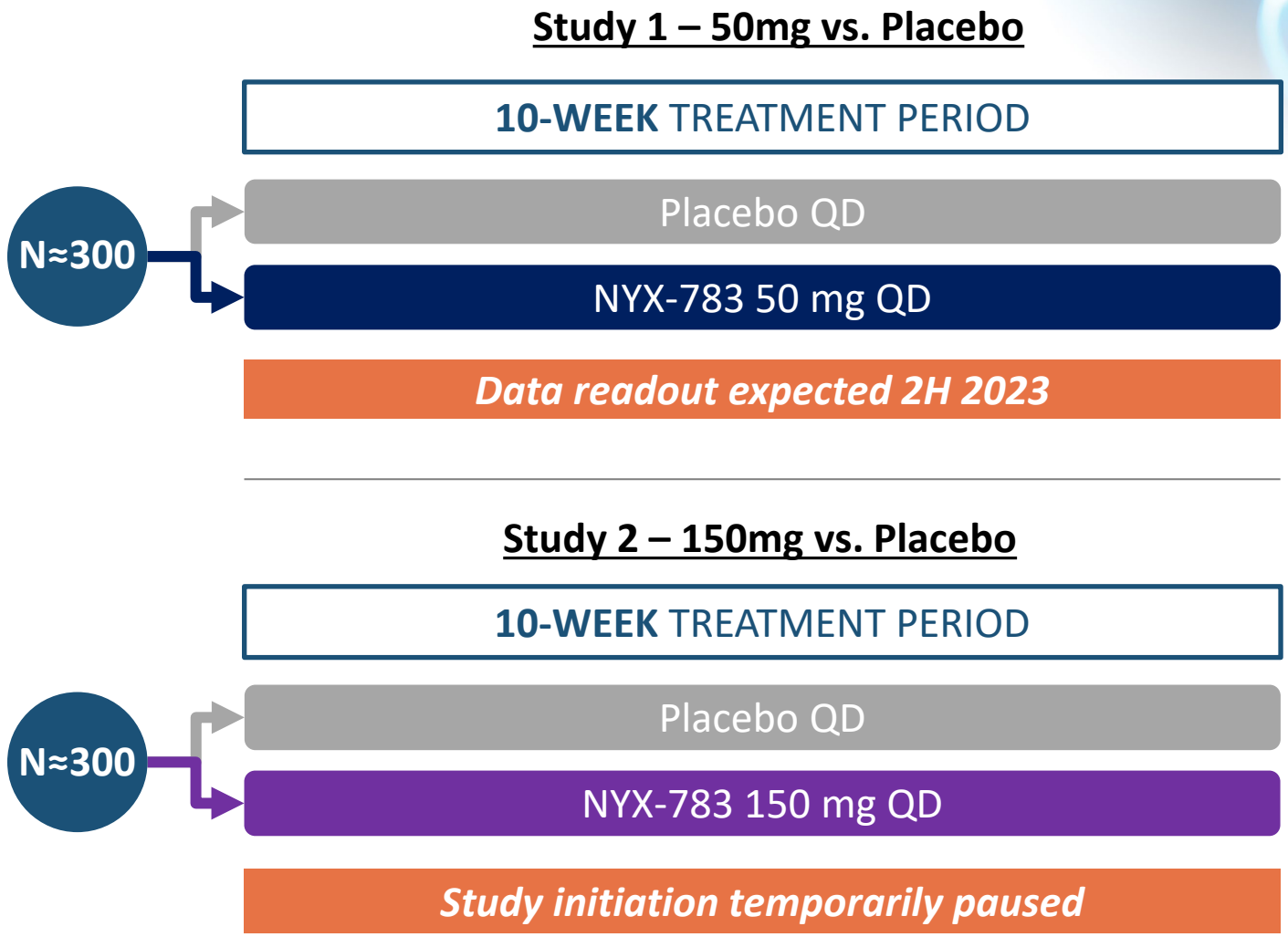
CAPS-5 (Clinician Administered PTSD Scale – DSM 5th Edition) | All statistical analyses represent 1-sided analysis

APTINYX

Design of Phase 2b program following Type C meeting with FDA

KEY STUDY ELEMENTS – BOTH STUDIES

- ~300 patients – civilian and military PTSD
- 10 weeks of daily treatment
- Randomized, parallel, double-blind design
- No concomitant PTSD pharmacotherapies (SSRIs)
- Primary endpoint: CAPS-5 Total score
- Series of tactics being utilized to mitigate placebo and patient variability



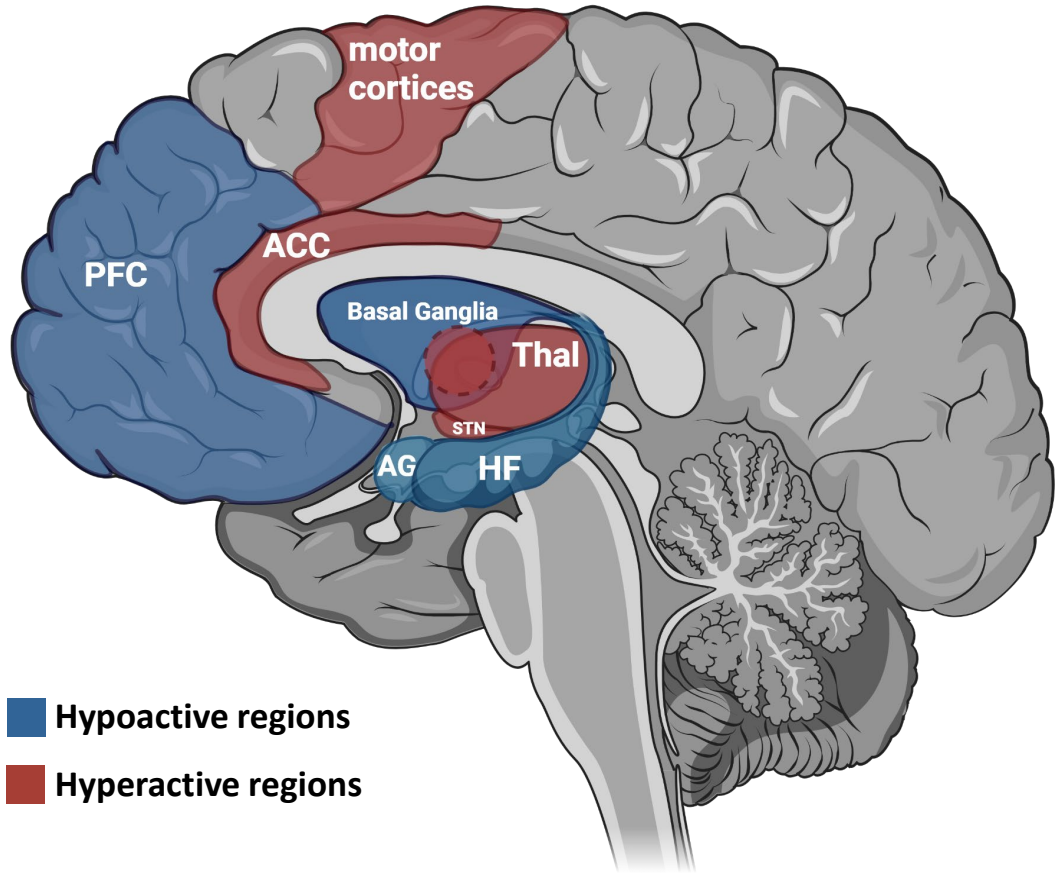
APTINYX

NYX-458

NMDA positive allosteric modulator in Phase 2 development for cognitive impairment associated with Parkinson's Disease and Dementia with Lewy Bodies

Targeting NMDA receptor hypofunction supports therapeutic development in cognitive impairment in PD and Dementia with Lewy Bodies

HYPOACTIVE REGIONS IN PARKINSON'S DISEASE REGULATE EXECUTIVE FUNCTION, WORKING MEMORY, AND ATTENTION



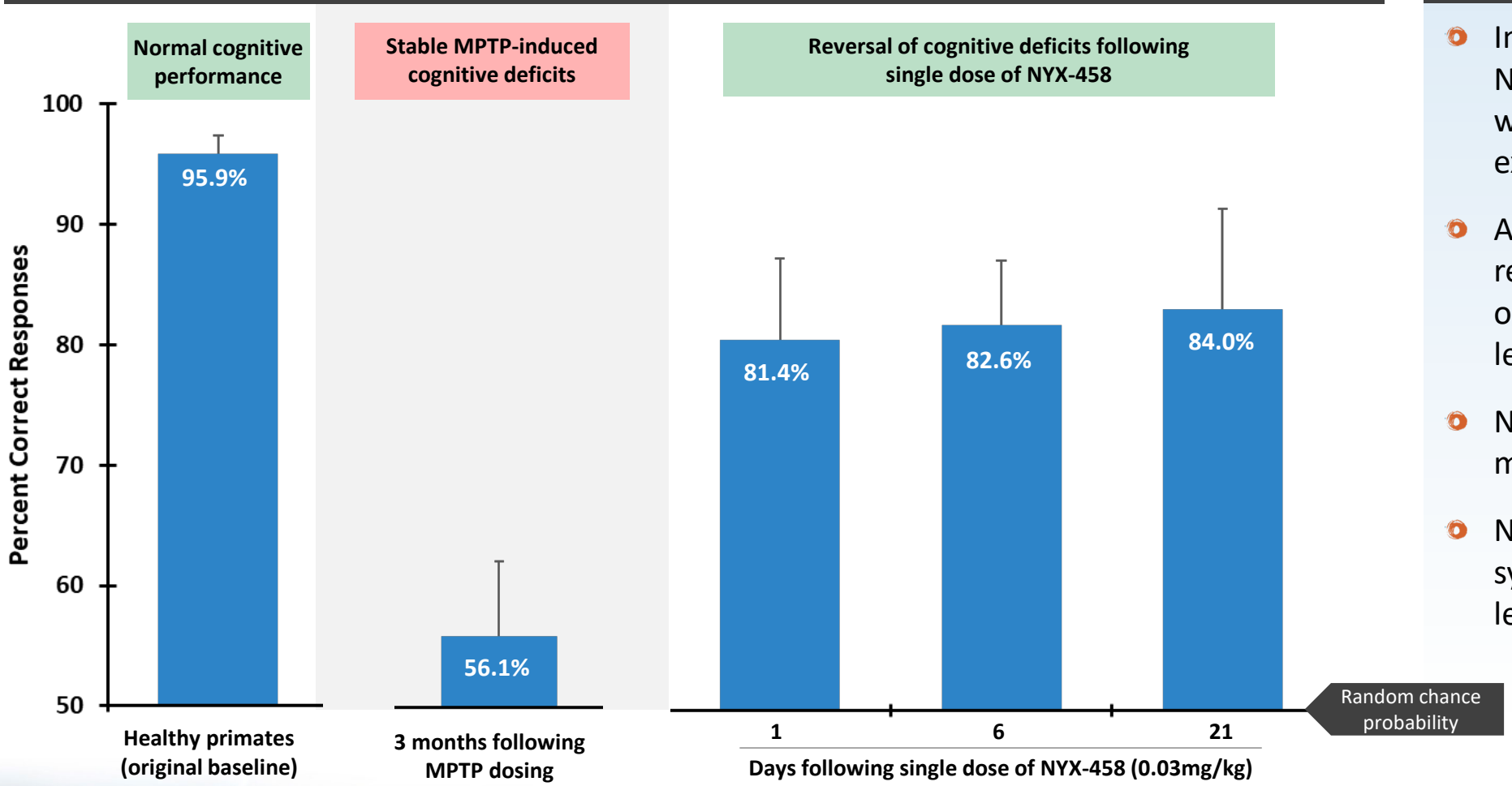
GLUTAMATERGIC DYSREGULATION IN PARKINSON'S DISEASE

- Glutamatergic hypofunction plays a key role in the development of PD-CI, especially in the prefrontal cortex and hippocampus.
- Dopaminergic cell loss and the dysregulation of dopamine transmission affects glutamatergic signaling in the brain.
- Modulating glutamatergic activity within these circuits with an NMDAR PAM may act to treat cognitive decline in PD

APTINYX

NYX-458 reverses cognitive impairment in preclinical models, including translatable non-human primate model of Parkinson's disease

VARIABLE DELAYED RESPONSE (VDR) – 10-SECOND DELAY LENGTH



STUDY HIGHLIGHTS

- Improvements observed with NYX-458 across attention, working memory, and executive function
- After re-induced impairment, replication of NYX-458 effects observed across multiple dose levels and with repeat dosing
- NYX-458 effects lasted ~3 months after final dose
- NYX-458 did not worsen motor symptoms or interfere with levodopa

APTINYX

Exploratory Phase 2 study of NYX-458 in cognitive impairment associated with Parkinson's disease and dementia with Lewy bodies

KEY STUDY ELEMENTS

- Randomized, 12-week, double-blind, parallel-design study evaluating NYX-458 against placebo
- Primary objective is to evaluate the safety, tolerability, and cognitive benefits of NYX-458
- Cognitive benefits assessed with battery of neurocognitive tests:

Groton Maze Learning	Executive function
Identification	Attention/working memory
One Back	Executive function
Two Back	Attention/working memory
International Shopping List	Memory
Continuous Paired Associate Learning	Memory

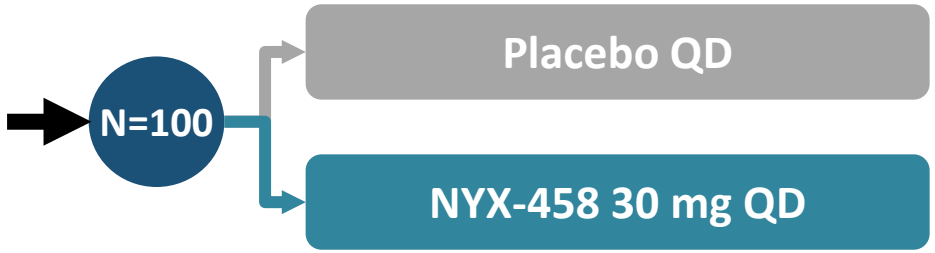
STUDY ELIGIBILITY EVALUATION

SCREENING & BASELINE *(UP TO 4 WEEKS)*

- 50-85 years of age
- PD-MCI, PDD, DLB, MCI-LB
- CGI-S at least 3 (mildly impaired)
- Subjective cognitive complaints
- MOCA 15-25

PLACEBO-CONTROLLED, DOUBLE-BLIND, RANDOMIZED TREATMENT

12-WEEK TREATMENT PERIOD



Data from exploratory Phase 2 study expected late 4Q 2022 / 1Q 2023

APTINYX

Strong balance sheet funds Phase 2 data catalysts across all pipeline programs and operations into 2024

$100M

Cash & equivalents
as of March 31, 2022

$25M

Remaining capital credit facility
(K2 HealthVentures)

~67M

Total shares outstanding

APTINYX

Experienced management team and highly regarded board

Norbert Riedel, PhD
Executive Chairman

Andy Kidd, MD
President & CEO

Ashish Khanna
Chief Financial Officer & Chief Business Officer

Kathryn King, PhD
SVP, Clinical and CMC Operations

Harald Murck, MD, PhD
VP, Clinical and Medical Affairs

naurex INC A NEUROPHARMACEUTICAL COMPANY · Takeda · Baxter · Johnson & Johnson · BCG BOSTON CONSULTING GROUP · abbvie · janssen · VANDA PHARMACEUTICALS INC. · Hoechst · BOSTON UNIVERSITY SCHOOL of Medicine · levō · MIT · Veeva

BOARD OF DIRECTORS

Norbert Riedel, PhD (Exec. Chairman)
Former CEO, Aptinyx

Patrick Enright
Founder & Managing Director

Henry Gosebruch
EVP, Chief Strategy Officer, AbbVie

Terry Gould
Partner & Head of Venture & Growth Equity

Robert Hombach
Retired CFO, Baxter and Baxalta

Andy Kidd, MD
President & CEO, Aptinyx

Adam Koppel, MD, PhD
Managing Director

Joan W. Miller, MD
David Glendenning Cogan Professor & Chair of the Dept. of Ophthalmology, Harvard Medical School

Gilmore O'Neill, MB, MMSC
Former CMO, Sarepta and senior development executive, Biogen

Rachel Sherman, MD, MPH
Former FDA Principal Deputy Commissioner

APTINYX · Longitude CAPITAL · abbvie · J.P.Morgan · ADAMS STREET PARTNERS · Baxalta · Baxter · APTINYX · BainCapital Life Sciences · HARVARD MEDICAL SCHOOL · MGH 1811 · Biogen · Rachel Sherman Partners