



# **Redefining Neuroscience Drug Development**

**January 2025**

# Important Disclosures

This presentation contains forward-looking statements about Neumora Therapeutics, Inc. (the “Company,” “we,” “us,” or “our”) within the meaning of the federal securities laws, including statements related to: Neumora’s intention to redefine neuroscience drug development by bringing forward the next generation of novel therapies that offer improved treatment outcomes and quality of life for patients suffering from brain diseases; the timing, progress and plans for its therapeutic development programs, including the timing of initiation and data read outs for its programs and studies, program milestones and potential value-creating catalysts, as well as its clinical trial and development plans; future program guidance updates; timing and expectations related to regulatory filings and interactions; its potential to create significant value, probability of success with its proprietary approach and support for the development of its programs; the market opportunity and therapeutic potential of its pipeline; the strength, scope and timing of its intellectual property protection; the safety profiles, differentiation, rationales and suitability for evaluation of navacaprant and its other products candidates, and the probability of success of its study designs and execution; expectations and projections regarding future operating results and financial performance, including the sufficiency of its cash resources and timing of its cash runway; and other statements identified by words such as “could,” “expects,” “intends,” “may,” “plans,” “potential,” “should,” “will,” “would,” or similar expressions and the negatives of those terms. Other than statements of historical facts, all statements contained in this presentation are forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. These statements are subject to risks and uncertainties that could cause the actual results to be materially different from the information expressed or implied by these forward-looking statements, including, among others: the risks related to the inherent uncertainty of clinical drug development and unpredictability and lengthy process for obtaining regulatory approvals; risks related to the timely initiation of, enrollment in and any changes to our clinical trials, including slowing enrollment following topline KOASTAL-1 results and anticipated changes to our KOASTAL-2 and/or -3 studies; risks related to our reliance on third parties, including CROs; risks related to serious or undesirable side effects of our therapeutic candidates; risks related to our ability to utilize and protect our intellectual property rights; and other matters that could affect sufficiency of capital resources to fund operations. For a detailed discussion of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Neumora’s business in general, please refer to the risk factors identified in the Company’s filings with the Securities and Exchange Commission (SEC), including but not limited to its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 that was filed with the SEC on November 12, 2024. Forward-looking statements speak only as of the date hereof, and, except as required by law, Neumora undertakes no obligation to update or revise these forward-looking statements.





## Our Mission

We are focused on redefining neuroscience drug development by bringing forward the next generation of novel therapies that offer improved treatment outcomes and quality of life for patients suffering from brain diseases



# Redefining Neuroscience Drug Development



**Industry leading  
CNS pipeline with long-  
dated IP into the 2040s**

**Multiple value-creating  
clinical catalysts  
expected in 2025**



**Built at scale with strong  
balance sheet; \$850M  
raised since 2021**

**Cash runway into  
mid-2026 supporting  
company growth**



**World-class team with  
differentiated approach**

**Maximizing probability of  
success with team and  
proprietary approach**

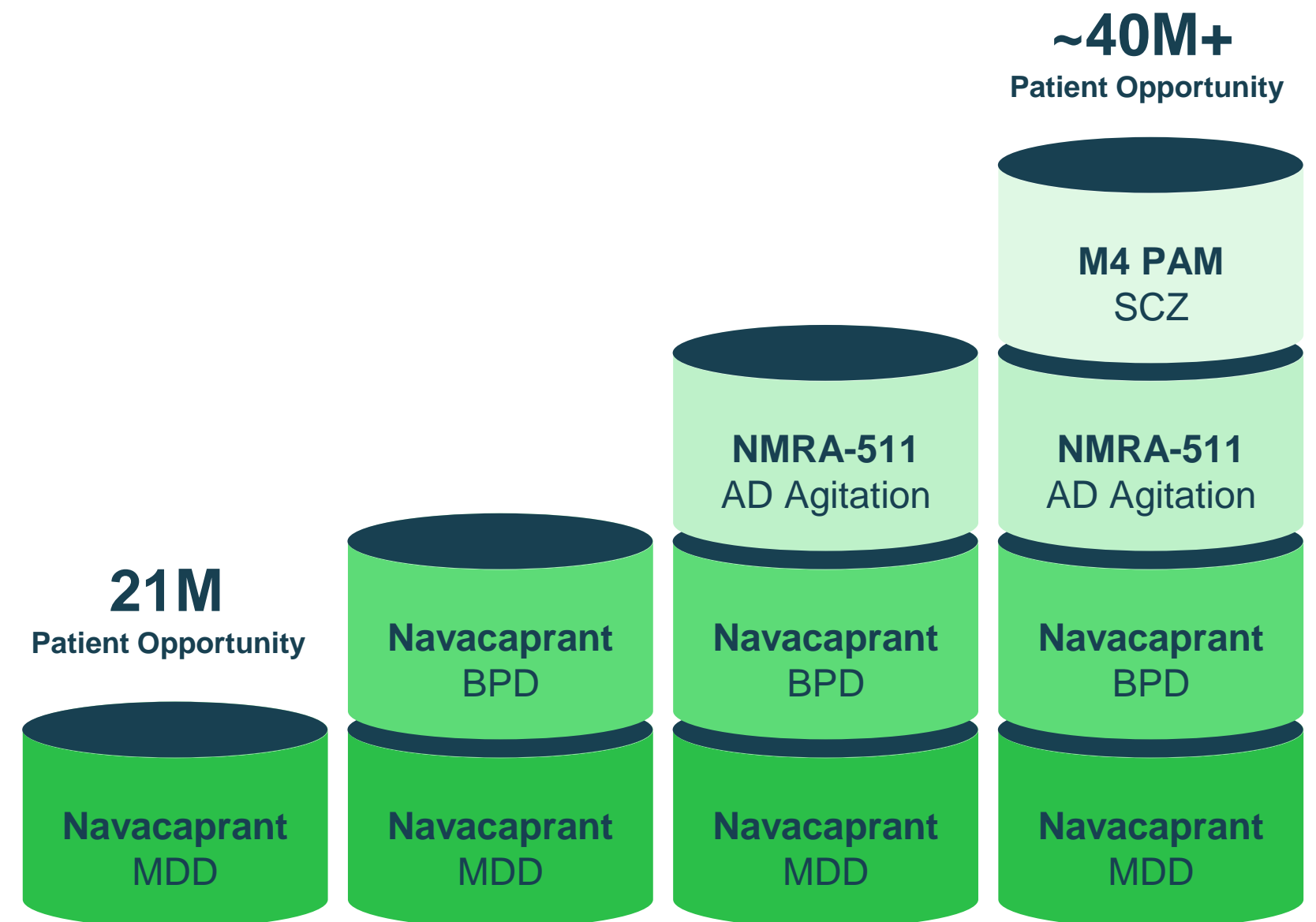
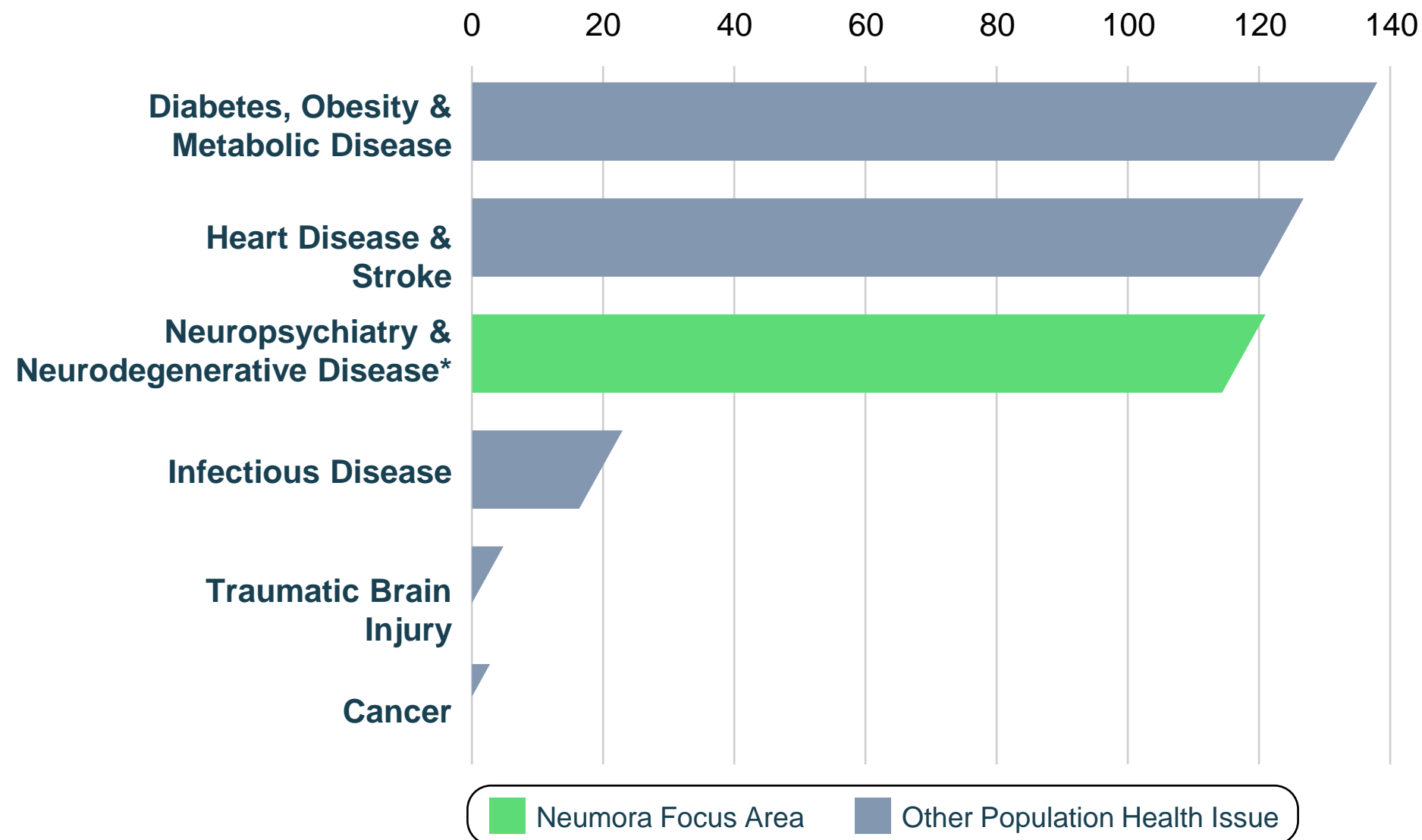


# Neumora is Tackling One of the Largest Population Health Challenges

Neumora's clinical-stage pipeline has potential to reach up to ~40M+ patients with a robust IP runway into 2041+

## Biggest Health Disorders Facing U.S.<sup>1</sup>

Patients Impacted (M)



<sup>1</sup>National Institutes of Health. Our Biggest Health Challenges. Accessed December 2023.

Note: Figure not intended as launch guidance or order. BPD = Bipolar Depression; MDD = major depressive disorder.

\*Includes: MDD, BPD, Schizophrenia, Generalized Anxiety Disorder, Post Traumatic Stress Disorder, Substance Use Disorder, Alzheimer's Disease, Parkinson's Disease, Attention-Deficit Hyperactivity Disorder

# Advancing a Leading Neuroscience Pipeline

- **Broad pipeline** addressing some of the most prevalent brain diseases
- Targeting novel mechanisms across a **broad range** of neuropsychiatric and neurodegenerative indications

PROGRAM <i>Target/Mechanism</i>	INDICATION <i>U.S. Prevalence</i>	Preclinical	Phase 1	Phase 2	Phase 3	MILESTONE <i>Guidance</i>
<b>Neuropsychiatry Programs</b>						
<b>Navacaprant (NMRA-140)</b> <i>KOR Antagonist</i>	<b>Major Depressive Disorder</b> <i>21M</i>	[Progress bar: Preclinical, Phase 1, Phase 2, Phase 3]				<b>KOASTAL-2 and -3 topline data</b> <i>To be updated in 10-K</i>
	<b>Bipolar Depression</b> <i>7M</i>	[Progress bar: Preclinical, Phase 1, Phase 2]				<b>Phase 2 data</b> <i>2H25</i>
<b>NMRA-511</b> <i>V1aR Antagonist</i>	<b>Agitation in Alzheimer's Disease</b> <i>6M</i>	[Progress bar: Preclinical, Phase 1]				<b>Phase 1b data</b> <i>2H25</i>
<b>NMRA-266*</b> <i>M4 Modulator</i>	<b>Schizophrenia</b> <i>3M</i>	[Progress bar: Preclinical, Phase 1]				<b>Provide update on clinical hold</b> <i>as available</i>
<b>NMRA-M4R</b> <i>M4 Modulator</i>	<b>Schizophrenia</b> <i>3M</i>	[Progress bar: Preclinical]				<b>Submit IND for next compound</b> <i>1H25</i>
<b>NMRA-NMDA</b> <i>NMDA Modulator</i>	<b>Schizophrenia</b> <i>3M</i>	[Progress bar: Preclinical]				
<b>Neurodegeneration Programs</b>						
<b>NMRA-CK1δ</b> <i>CK1δ Inhibitor</i>	<b>ALS/Alzheimer's Disease</b> <i>25K/6M</i>	[Progress bar: Preclinical]				
<b>NMRA-NLRP3</b> <i>NLRP3 Inhibitor</i>	<b>Parkinson's Disease</b> <i>1M</i>	[Progress bar: Preclinical]				
<b>NMRA-GCASE</b> <i>GCcase Activator</i>	<b>Parkinson's Disease</b> <i>1M</i>	[Progress bar: Preclinical]				

ALS = Amyotrophic lateral sclerosis; CK1 δ = Casein Kinase I Isoform delta; GCCase = Glucocerebrosidase; IP = Intellectual Property; KOR = kappa opioid receptor; M4R = Muscarinic Acetylcholine Receptor M4; NLRP3 = Nucleotide-binding Domain, Leucine-rich-containing Family, Pyrin Domain-containing-3; NMDA = N-methyl-D-aspartate; V1aR = Vasopressin 1a Receptor.

\*Neumora announced on 4/15/24 that NMRA-266 is currently on clinical hold

\*\*All dates are approximate / estimates / projections only



# MDD Represents a Major Population Health Challenge

MDD is the leading cause of disability worldwide<sup>1</sup>

**280M**

people worldwide have MDD<sup>1</sup>

**21M**

adults in the U.S. have MDD<sup>2</sup>; the median onset is ~32.5 years of age

**30 years**

since a novel mechanism of action was approved for MDD

Many people have inadequate response to medication and experience tolerability issues

**85%**

of patients either don't receive pharmacological treatment or fail to achieve remission with first-line treatment<sup>3-7</sup>

**>70%**

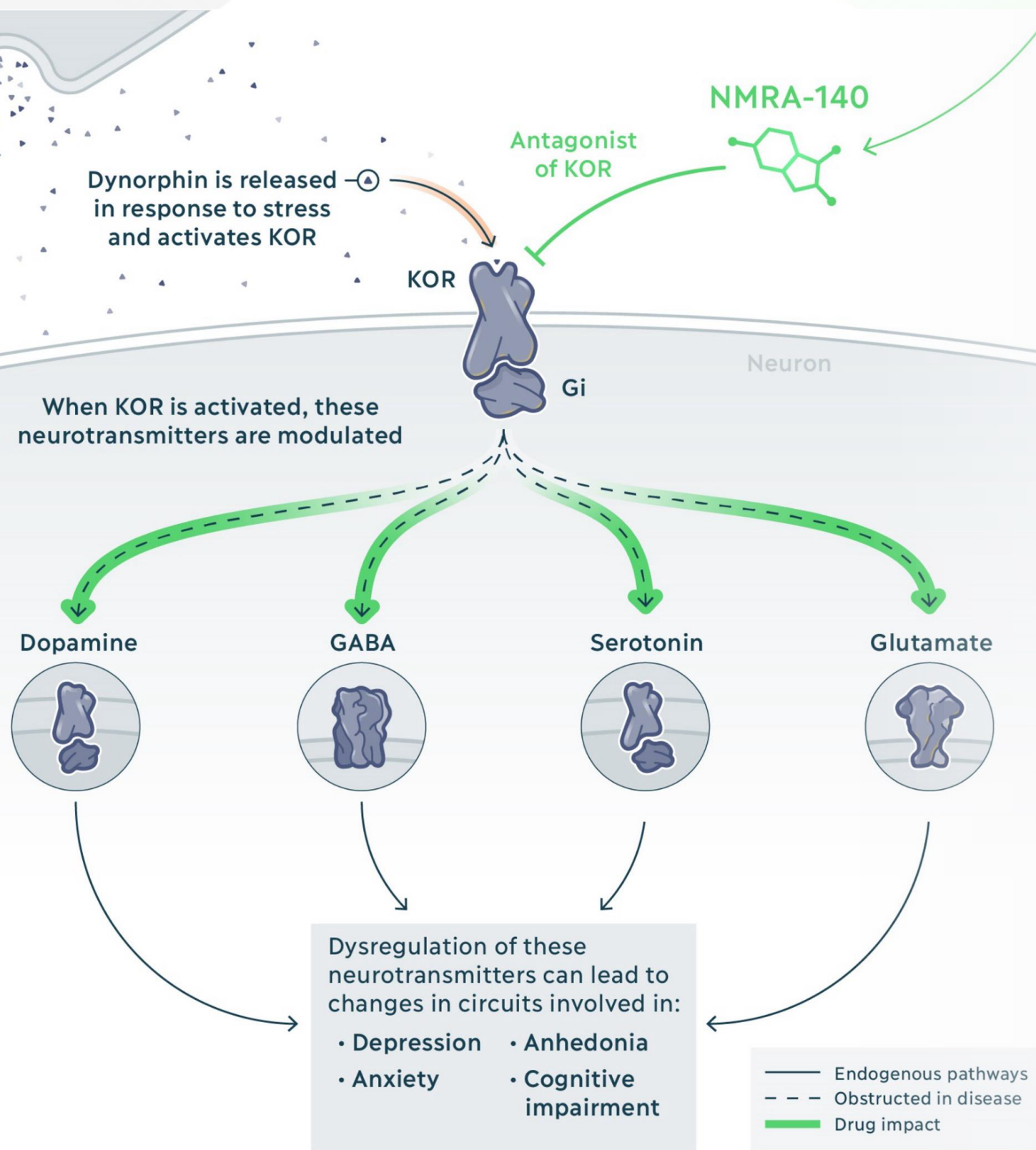
of people with MDD experience anhedonia<sup>8</sup>

**60–85%**

of patients treated with monotherapy<sup>9</sup>



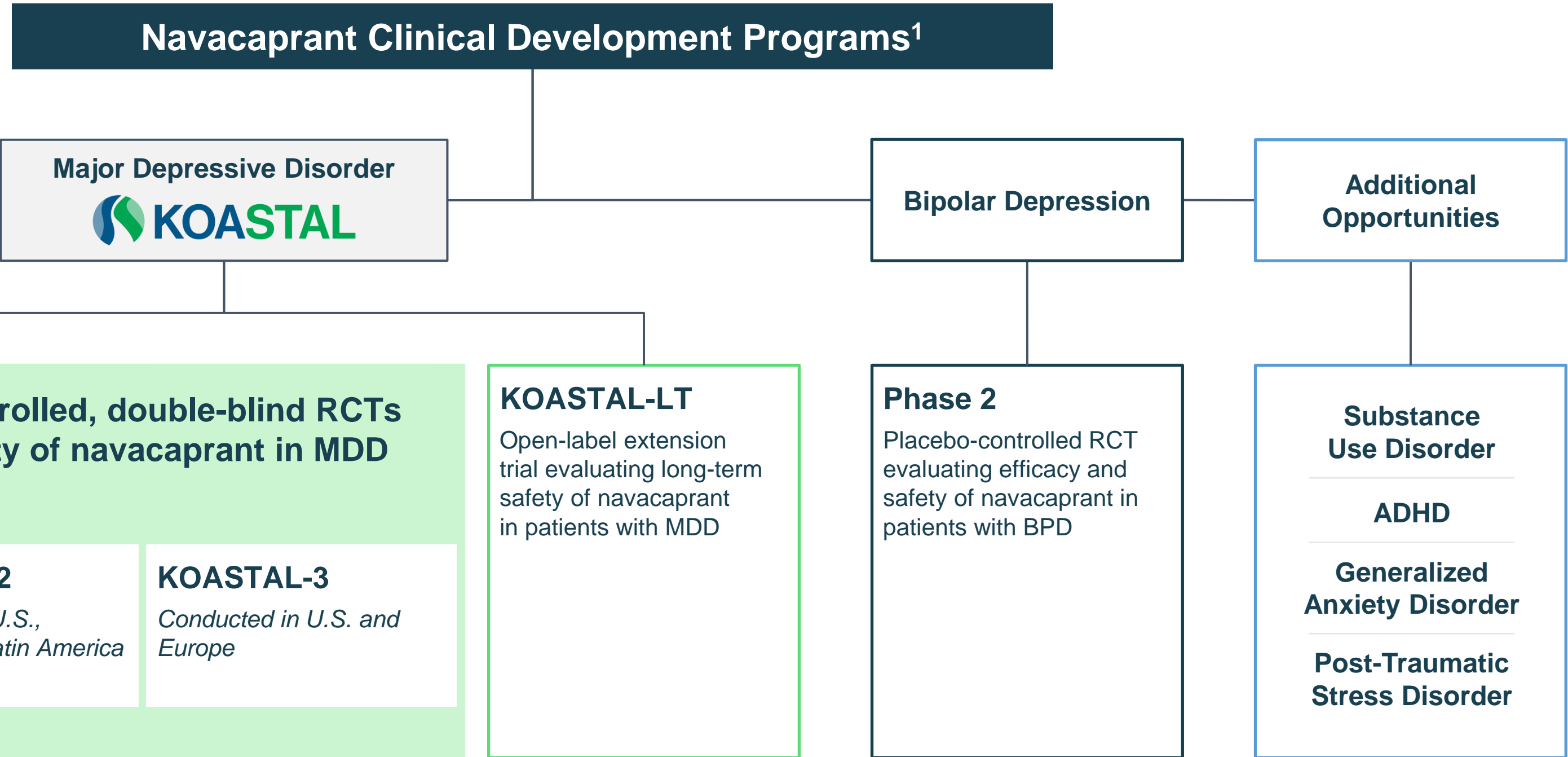
# The Role of Kappa Opioid Receptor Antagonism in MDD



- The **kappa opioid receptor (KOR)** / dynorphin system is a well-characterized pathway, and results from preclinical studies support its potential to modulate depression, anhedonia, and anxiety
- KOR system overactivation in response to stress and mediation of depressive-like symptoms including anhedonia
- KOR antagonism may allow DA and 5HT release to return to adaptive levels during reward processing



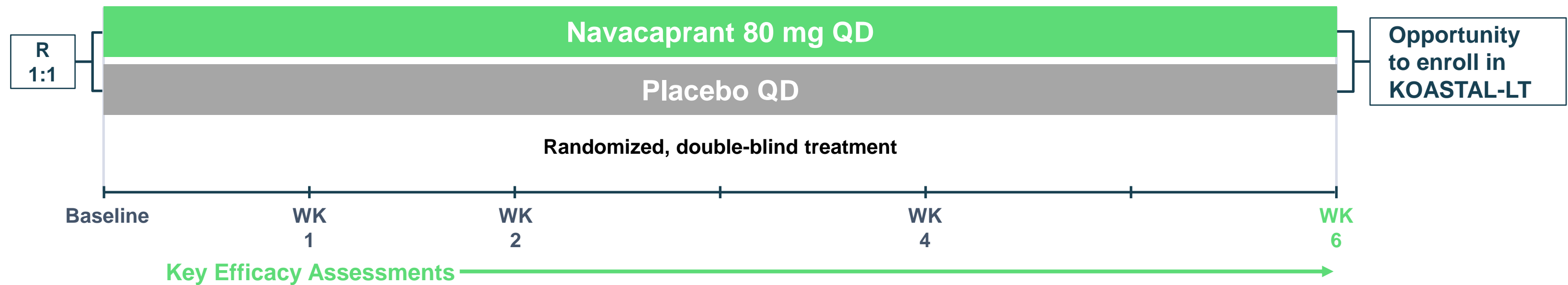
# Near-term Clinical Development Plan Focused on MDD and Bipolar Depression with Opportunity for Further Expansion



# KOASTAL Pivotal Study Design



## KOASTAL Pivotal Efficacy Studies



### KOASTAL-1, KOASTAL-2, KOASTAL-3 Summary

<b>Inclusion Criteria:</b>	<ul style="list-style-type: none"> <li>• Adults ages 18 – 65 diagnosed with MDD</li> <li>• MADRS <math>\geq</math> 25 at baseline</li> </ul>	Other Secondary Endpoints Include: <ul style="list-style-type: none"> <li>• PHQ-9</li> <li>• HAM-A</li> <li>• SDS</li> </ul>	$\Delta$ from baseline to each timepoint in: <ul style="list-style-type: none"> <li>• CGI-S and CGI-I</li> </ul>
<b>Primary Endpoint:</b>	<ul style="list-style-type: none"> <li>• <math>\Delta</math> from baseline to Week 6 in MADRS total score</li> </ul>		
<b>Key Secondary Endpoint:</b>	<ul style="list-style-type: none"> <li>• <math>\Delta</math> from baseline to Week 6 in SHAPS total score</li> </ul>	Key Exploratory Endpoints*: <ul style="list-style-type: none"> <li>• EQ-5D 5L</li> <li>• WPAI-GH</li> </ul>	$\Delta$ from baseline to each timepoint in: <ul style="list-style-type: none"> <li>• EQ-5D 5L</li> <li>• WPAI-GH</li> </ul>

\*Safety Assessments include Change in Sexual Functioning Questionnaire (CSFQ-14)

$\Delta$  = Change; CGI-I = Clinical Global Impression-Improvement scale; CGI-S = Clinical Global Impression-Severity scale; EQ-5D 5L = EuroQol-5D 5L; HAM-A = Hamilton Anxiety Rating Scale; MADRS = Montgomery-Åsberg Depression Rating Scale; MDD = Major Depressive Disorder; PHQ-9 = Patient Health Questionnaire-9; QD = once daily; SDS = Sheehan Disability Scale; SHAPS = Snaith-Hamilton Pleasure Scale; wk = week; WPAI-GH = Work Productivity and Activity Impairment Questionnaire – General Health.

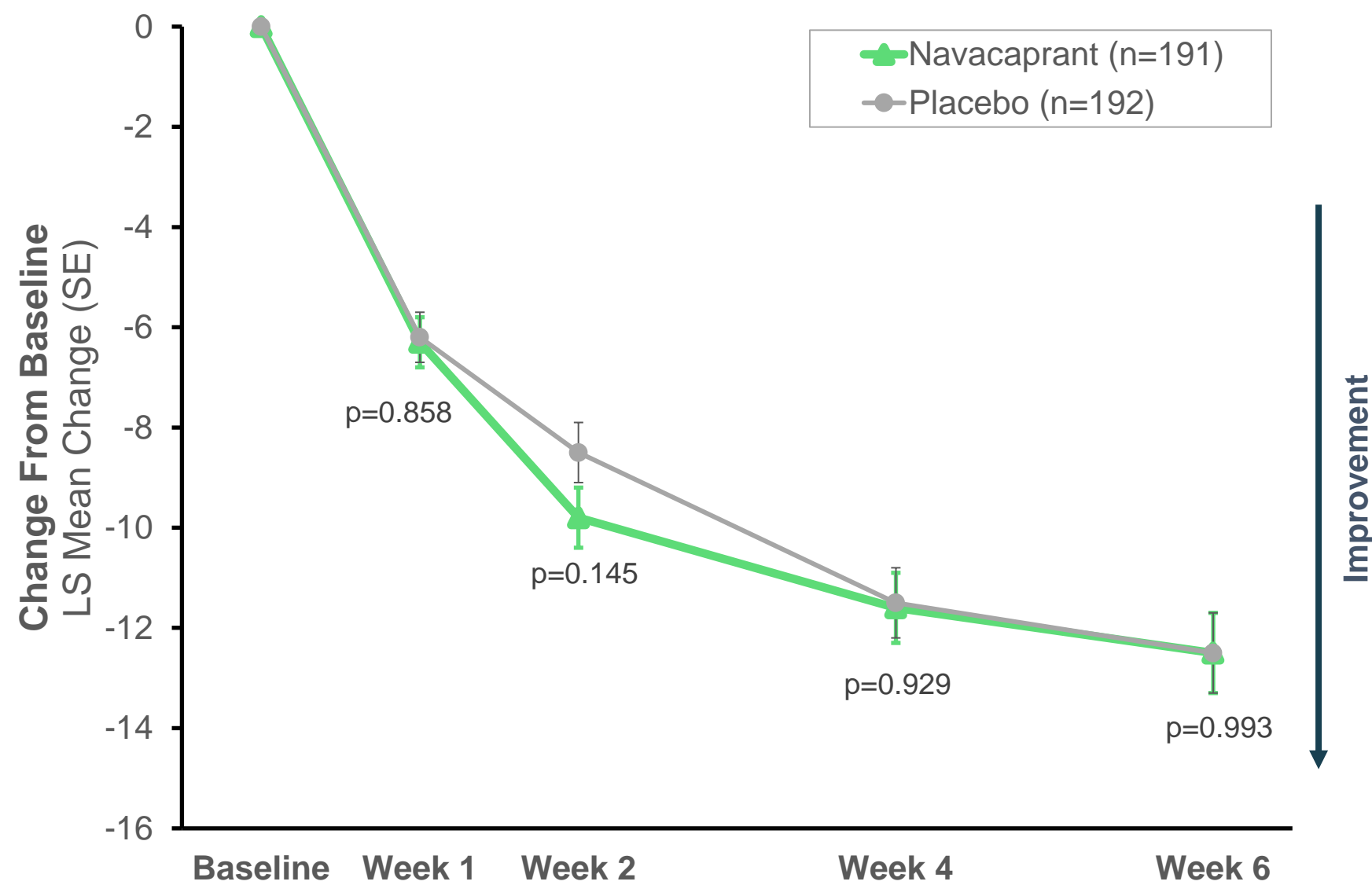
# KOASTAL-1 Topline Data: Demographics and Baseline Characteristics

Intent-to-Treat Population	Navacaprant n = 191	Placebo N = 192
<b>Age</b> , mean (SD)	40.7 (14.0)	41.1 (13.2)
<b>Sex</b> , n (%)		
Male	86 (45.0%)	86 (44.8%)
Female	105 (55.0%)	106 (55.2%)
<b>Race</b> , n (%)		
White	112 (58.6%)	127 (66.1%)
Black or African American	38 (19.9%)	31 (16.1%)
Asian	25 (13.1%)	19 (9.9%)
Other	10 (5.2%)	10 (5.2%)
Missing/Unknown	6 (3.1%)	5 (2.6%)
<b>Baseline MADRS total score</b> , mean (SD)	32.2 (4.2)	32.8 (4.7)
<b>Baseline SHAPS total score</b> , mean (SD)	36.2 (6.2)	36.5 (6.7)

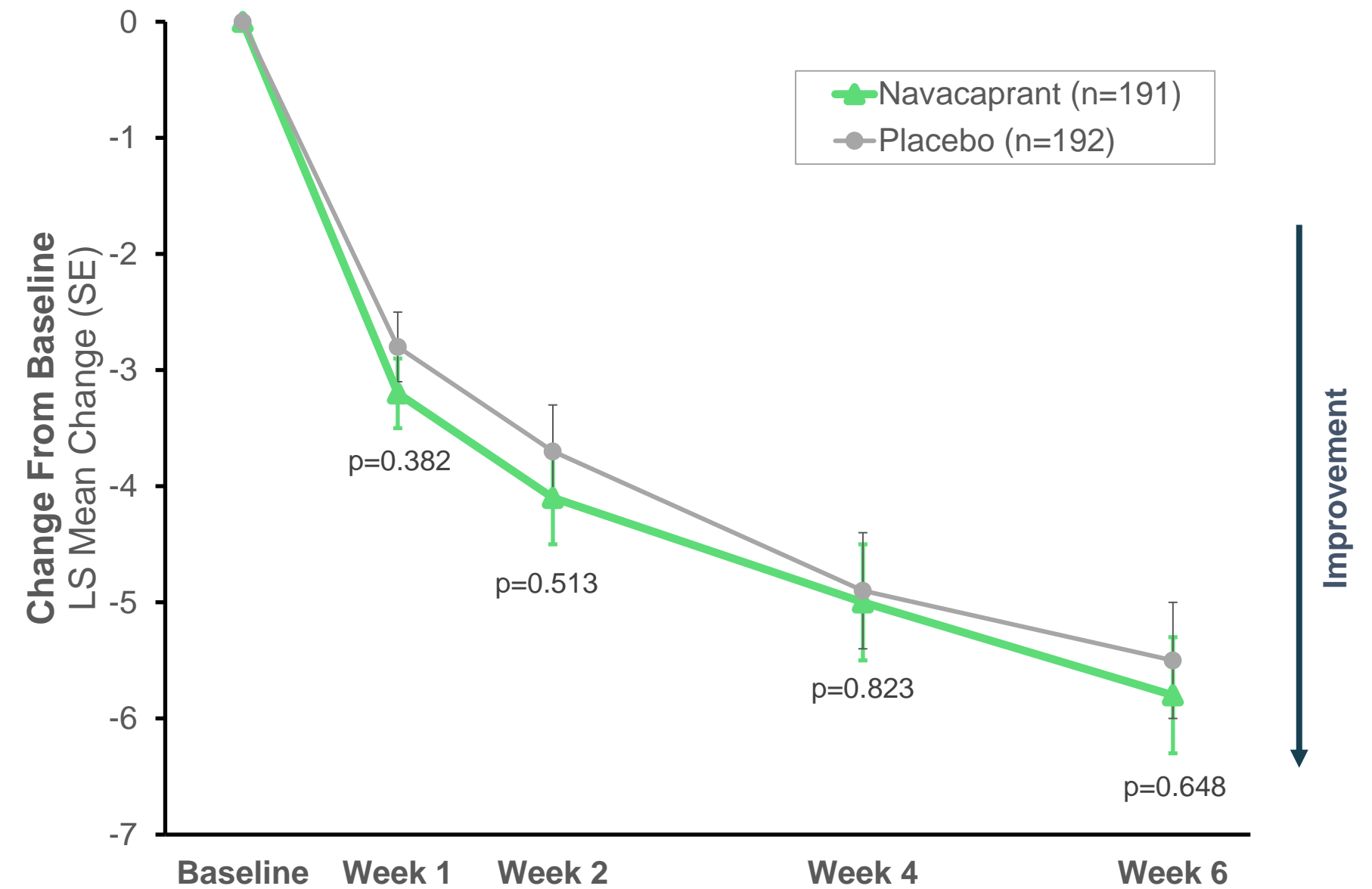


# KOASTAL-1 Topline Data: Primary & Key Secondary Endpoint

**MADRS Total Score**  
Intent-to-Treat Population



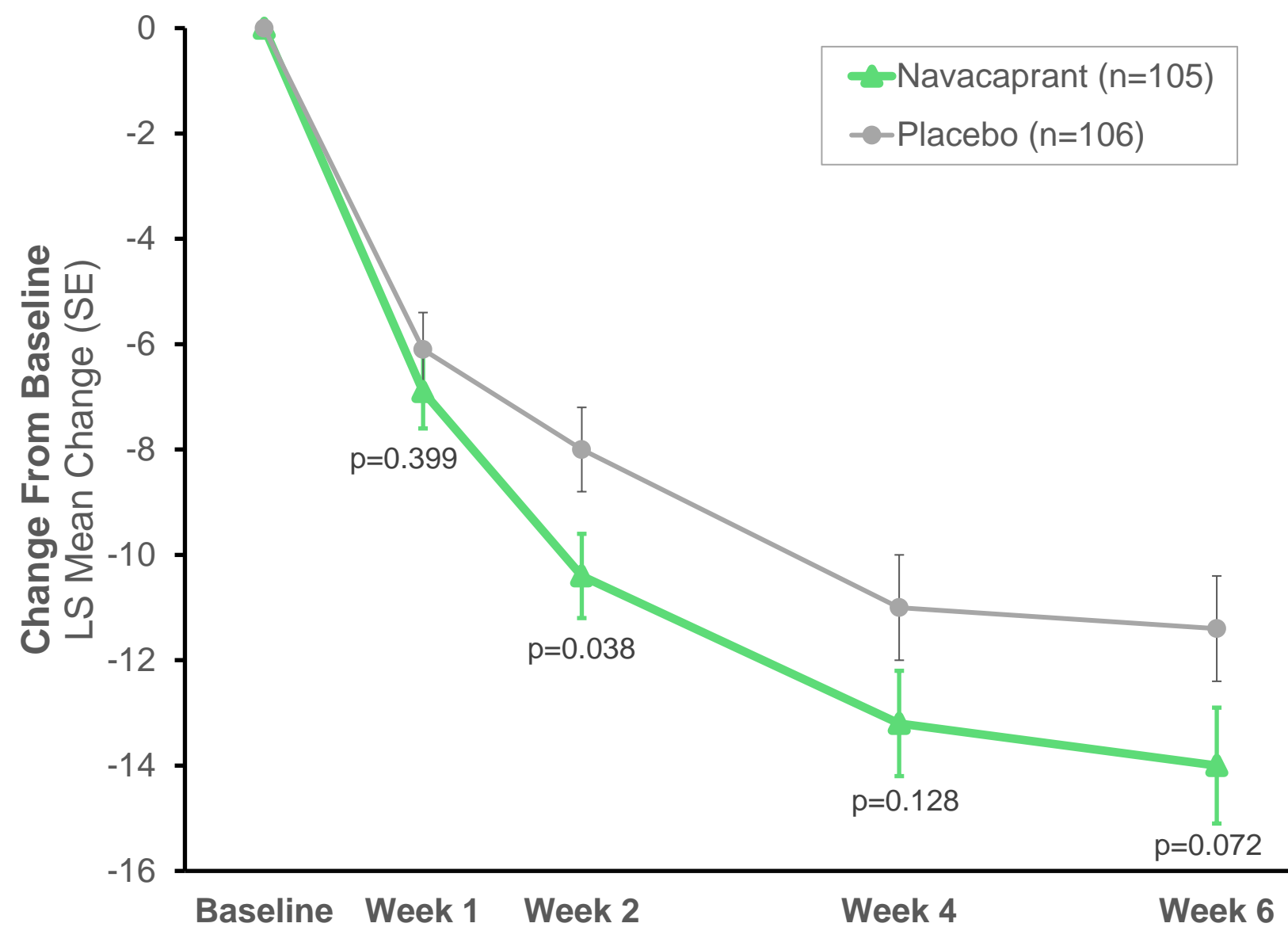
**SHAPS Total Score**  
Intent-to-Treat Population



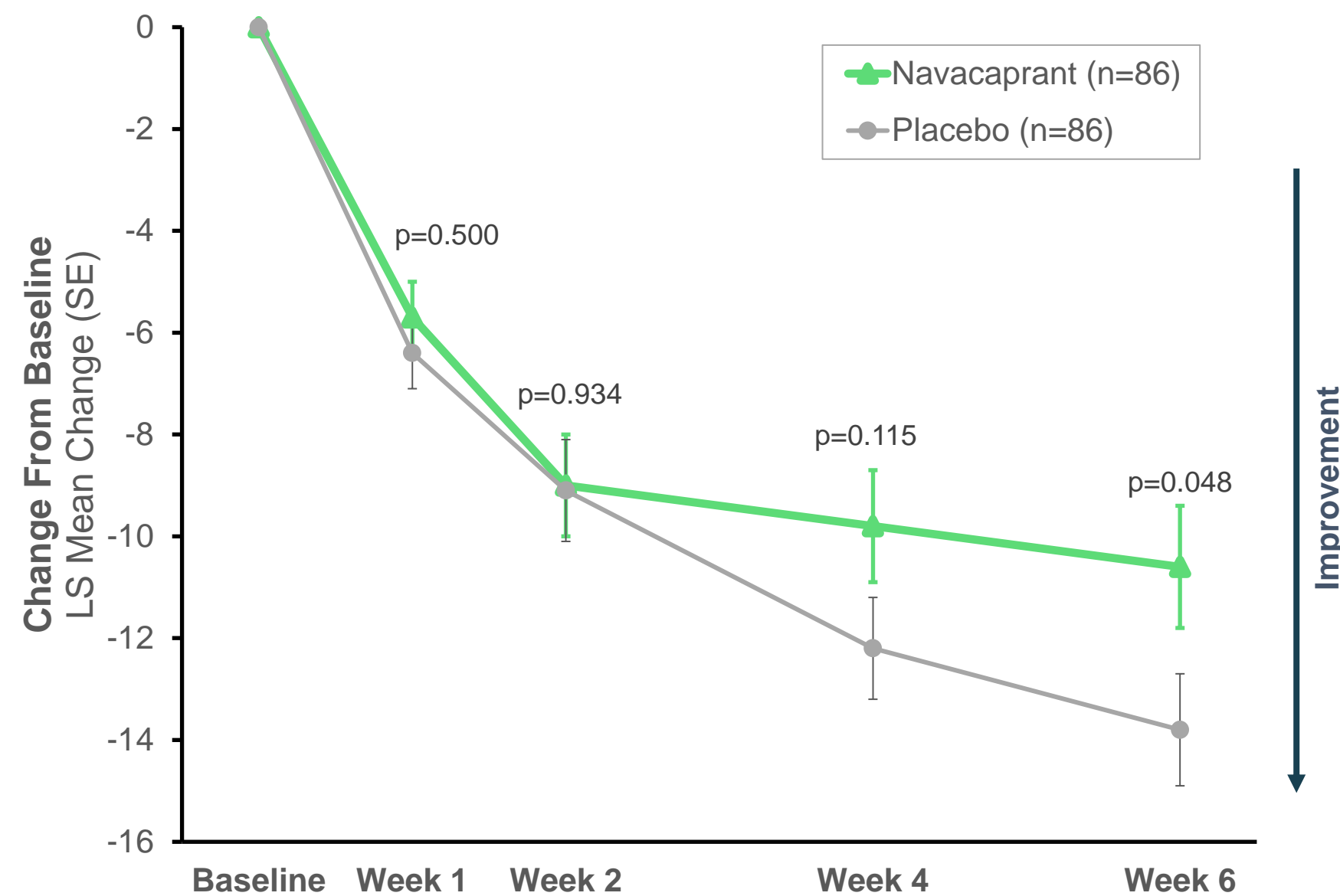
# KOASTAL-1 Topline Data

## MADRS: Efficacy Differences Observed Between Female and Male Participants

### MADRS Total Score – ITT Female



### MADRS Total Score – ITT Male

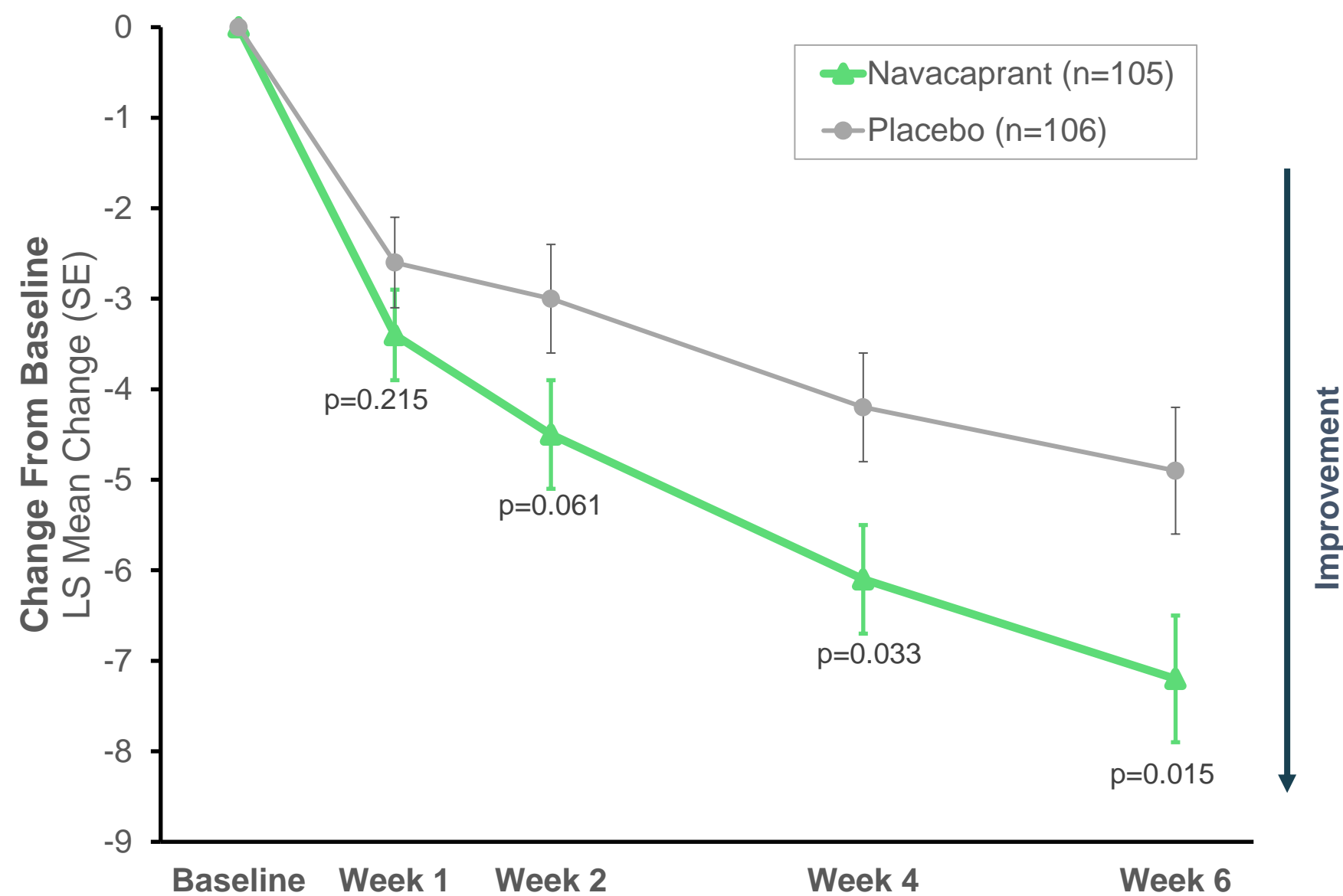


ITT = Intent-to-Treat Population  
MADRS = Montgomery-Åsberg Depression Rating Scale  
SHAPS = Snaith-Hamilton Pleasure Scale

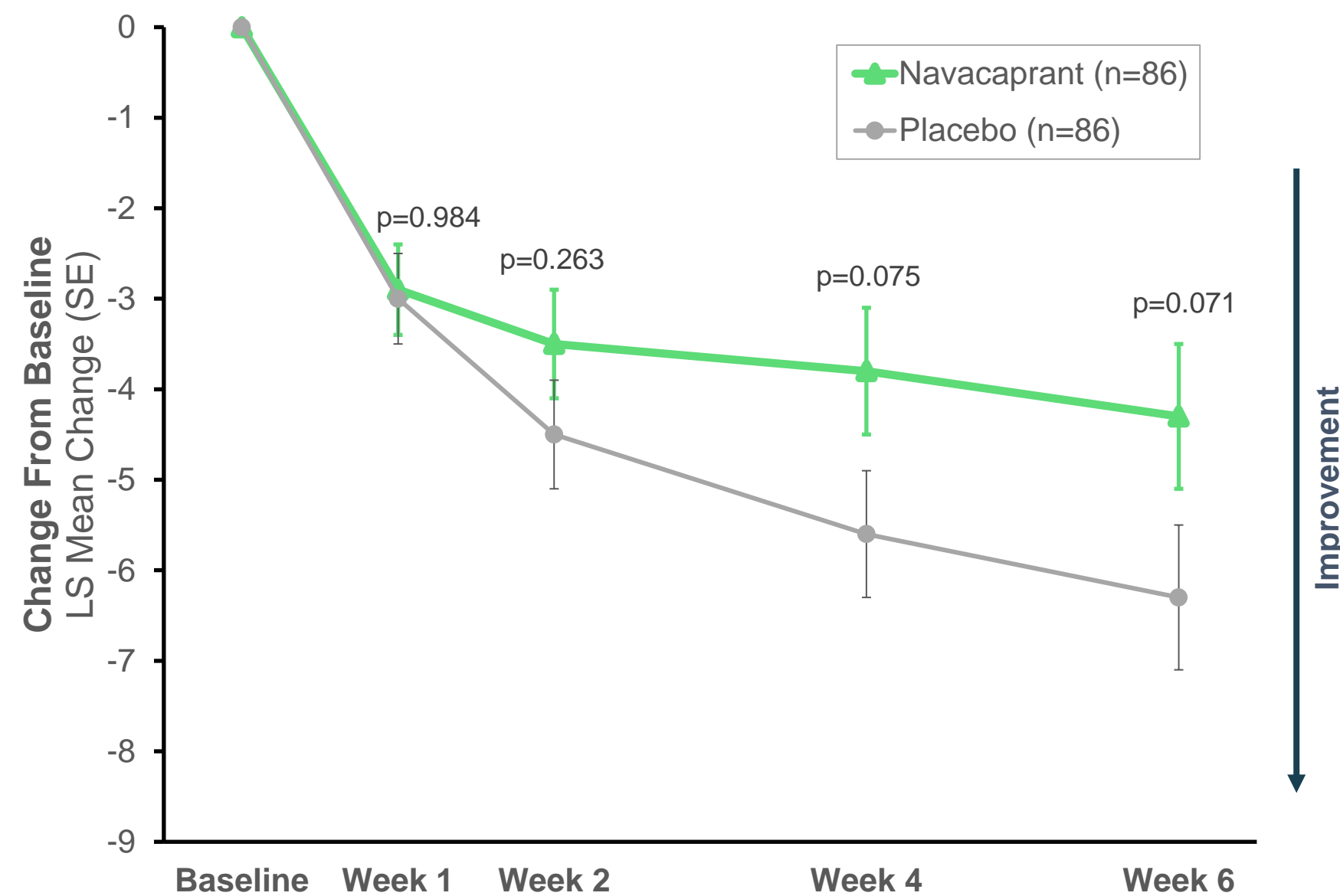
# KOASTAL-1 Topline Data

## SHAPS: Efficacy Differences Observed Between Female and Male Participants

### SHAPS Total Score – ITT Female



### SHAPS Total Score – ITT Male



ITT = Intent-to-Treat Population  
MADRS = Montgomery-Åsberg Depression Rating Scale  
SHAPS = Snaith-Hamilton Pleasure Scale

# KOASTAL-1 Topline Data: Favorable Safety Profile Demonstrated

Navacaprant was safe and generally well tolerated, with no serious adverse events reported

TEAEs Incidence (>2% in either treatment group)	Placebo n=192	Navacaprant n=191
Preferred Terms	n (%)	n (%)
Headache	14 (7.3%)	13 (6.8%)
Diarrhea	4 (2.1%)	10 (5.2%)
Nasopharyngitis	8 (4.2%)	7 (3.7%)
Pruritus	4 (2.1%)	7 (3.7%)
Nausea	6 (3.1%)	6 (3.1%)
Constipation	6 (3.1%)	5 (2.6%)
Insomnia	4 (2.1%)	3 (1.6%)
Fatigue	9 (4.7%)	2 (1.0%)
Upper respiratory tract infection	6 (3.1%)	2 (1.0%)
Dizziness	5 (2.6%)	2 (1.0%)
Dry mouth	4 (2.1%)	2 (1.0%)
Somnolence	4 (2.1%)	2 (1.0%)
Urinary tract infection	4 (2.1%)	2 (1.0%)
Back pain	5 (2.6%)	0

- No signal for increased suicidal ideation or suicidal behavior<sup>1</sup>
- Low discontinuation rate due to TEAEs (navacaprant 2.1%; placebo 3.1%)
- 83.3% of navacaprant-treated patients who completed 6 weeks' treatment elected to enroll in KOASTAL-LT



1. As measured by Columbia Suicide Severity Rating Scale (C-SSRS)

# Navacaprant Development Program Key Learnings & Next Steps

## KOASTAL-1 key learnings based on comprehensive analytics with topline data

- Higher placebo response rate than expected
- Males demonstrated especially high placebo response (14 points) and lower drug responses
- Encouraging trends in depressed mood and anhedonia in females
- Higher proportion of males in study (45%) relative to recent comparable MDD studies (~30%)
- Navacaprant was well-tolerated with notable AEs (pruritus) observed
- Full dataset, including PK data, forthcoming for analysis

## Potential adjustments to navacaprant development program

- Analyzing integrated data from Phase 2 and KOASTAL-1 (~600 patients) to inform predictors of placebo response, drug/placebo difference and potential female/male differences for near-term adjustments to KOASTAL-2 and -3
  - Optimize site selection
  - Enhance medical monitoring to identify optimal patients
- Assessing significance of sex-based differences
  - To date, KOASTAL-2 and -3 have enrolled more females than KOASTAL-1
  - Regulatory path for female-only development if warranted based on additional data
  - ~70% of MDD prescriptions are written for females according to IQVIA

**Neumora plans to provide additional information and update program guidance in 10-K**





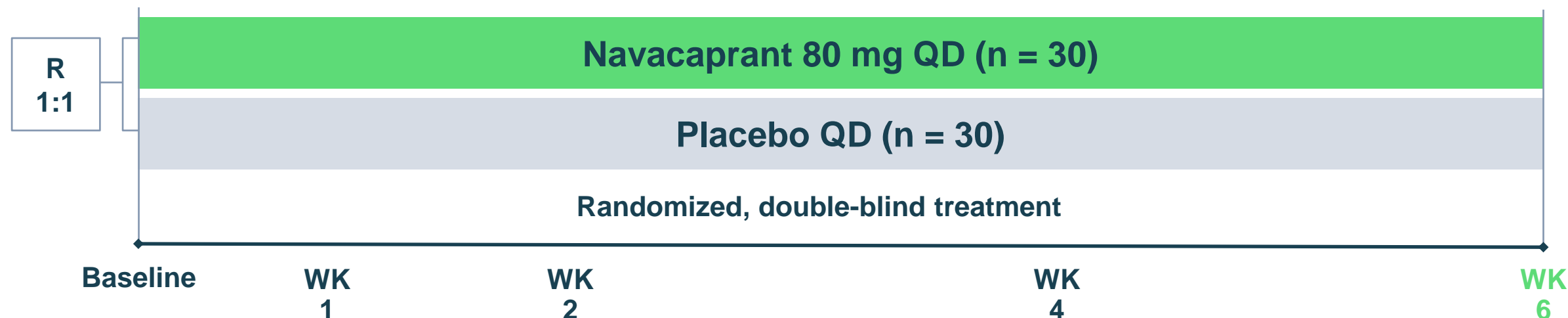
# Navacaprant Well-Suited for Evaluation in Bipolar Depression

*Signal-Seeking Study Designed to Efficiently Generate Data to Inform Development Path*

## Strong Rationale for Efficacy in Bipolar Depression

- Depressed mood and anhedonia are highly prevalent and clinically relevant symptoms in BPD<sup>1</sup>
- Navacaprant has demonstrated efficacy in treating depressed mood and anhedonia in MDD in Phase 2
- Results from this proof-of-concept study will inform further development of navacaprant in bipolar disorder
  - *Potential to develop in broader bipolar disorder populations*

## Bipolar II Depression Signal-Seeking Study



### BIPOLAR II DEPRESSION SIGNAL-SEEKING STUDY

#### Inclusion Criteria:

- Adults ages 18 – 65 experiencing an MDE associated with bipolar II depression
- MADRS  $\geq$  25 at baseline

#### Primary Endpoint:

$\Delta$  from baseline to Week 6 in MADRS total score

#### Other Endpoints Include\*:

- $\Delta$  from baseline to Week 6 in:
- SHAPS total score
  - PGIS-Anhedonia total score
  - CGI-BP-S total score

#### Statistics:

- Study not powered to demonstrate statistical significance
- Designed as a signal-seeking study; effect size will inform the potential future development of navacaprant in bipolar depression

\*Safety Assessments include Columbia-Suicide Severity Rating Scale (C-SSRS), Young Mania Rating Scale (YMRS), Change in Sexual Functioning Questionnaire (CSFQ-14)

$\Delta$  = Change; QD = once daily; MADRS = Montgomery-Åsberg Depression Rating Scale; SHAPS = Snaith-Hamilton Pleasure Scale; DARS = Dimensional Anhedonia Rating Scale; PGIS-Anhedonia = Patient Global Impression of Severity – Anhedonia; CGI-BP-S = Clinical Global Impressions Scale for Use in Bipolar Illness – Severity

<sup>1</sup>Whitton AE., et al. 2023. <sup>2</sup>Krystal, AD., et al. 2020.



# NMRA-511 is a Best-in-Class Vasopressin 1a Receptor Antagonist with Broad Potential Across Neuropsychiatric Disorders

## Rationale

Vasopressin plays a role in the regulation of aggression, affiliation, stress and anxiety response

## Indication

Agitation in Alzheimer's disease

## Status

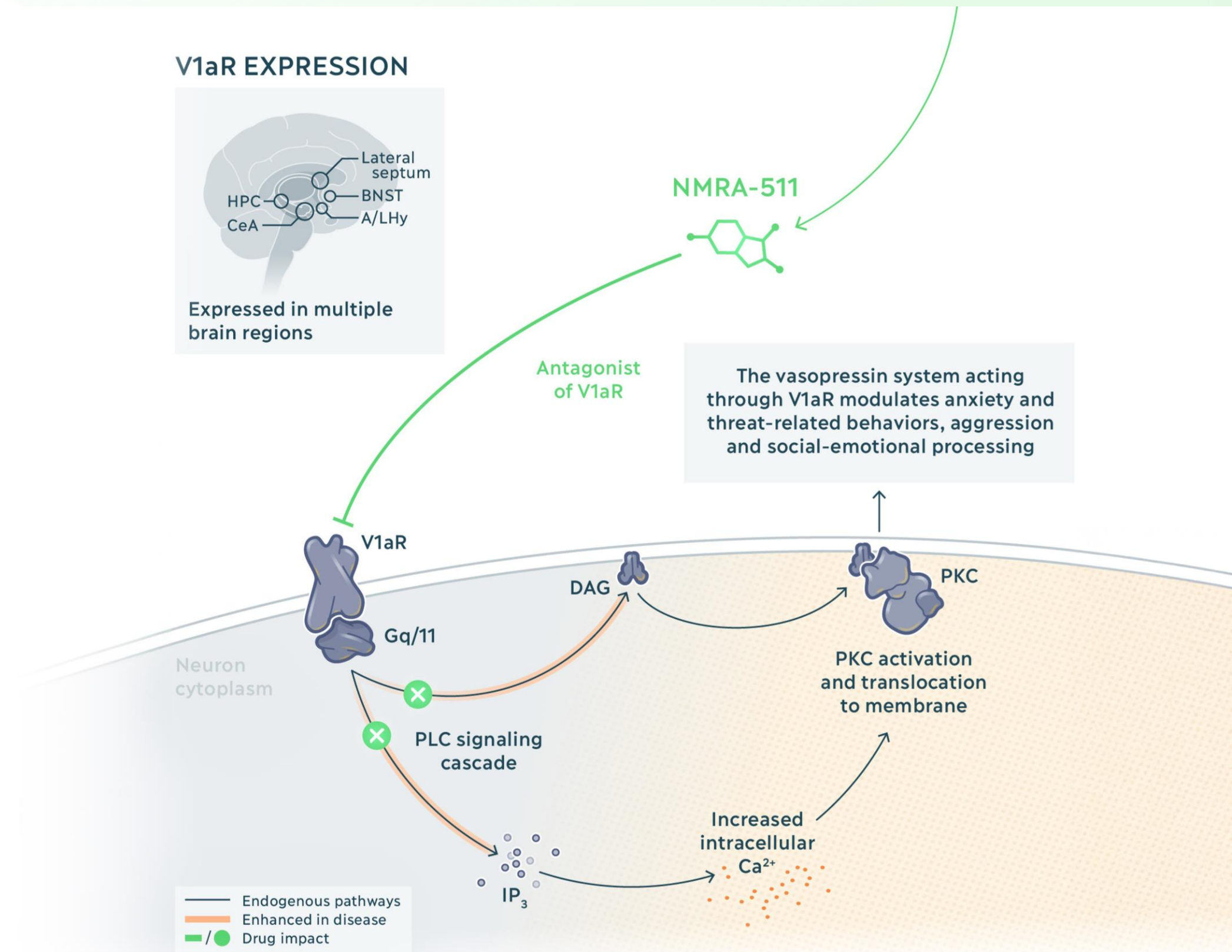
Phase 1b study underway with data anticipated in 2H25

## Drug Profile

Oral, BID dosing

## Strong IP Protection

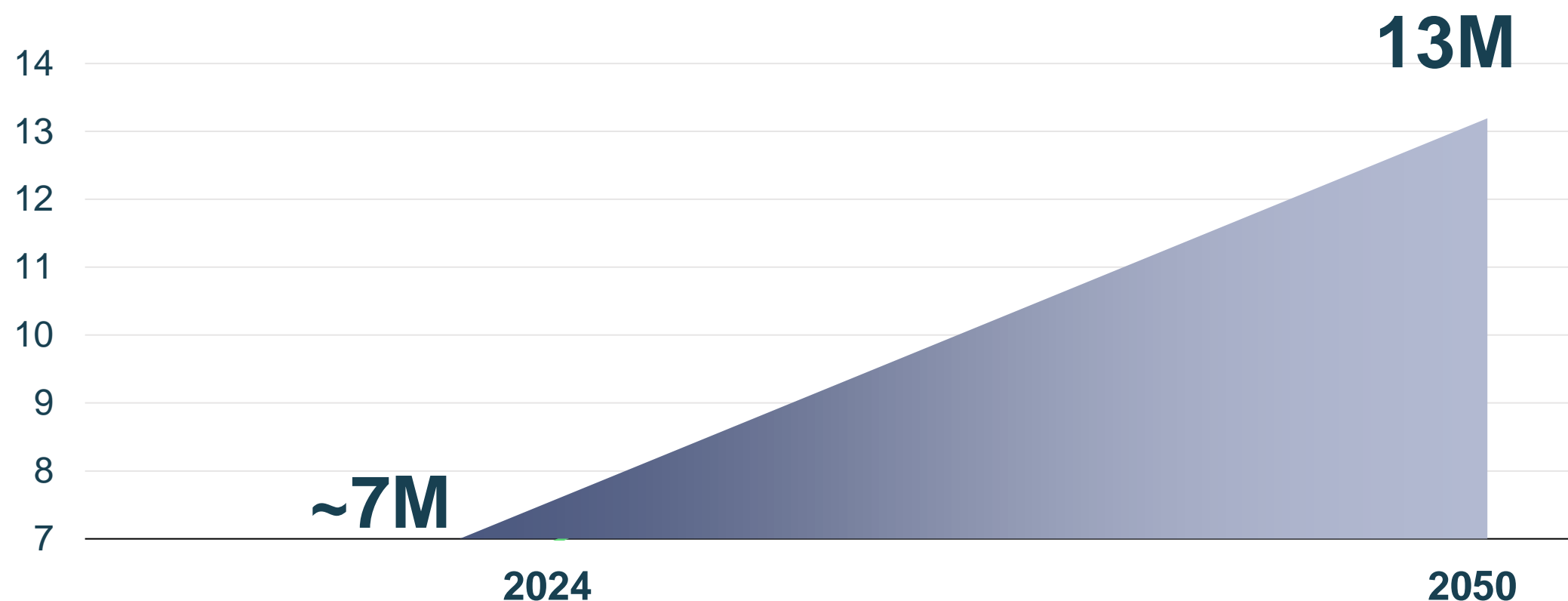
Expect exclusivity through 2042+, based on composition of matter protection and estimated patent term extension



# Alzheimer's Disease Agitation Represents in Large Market Opportunity with Significant Unmet Need

Agitation in Alzheimer's disease impacts a significant portion of the U.S. population; that number is expected to increase as the population ages<sup>1</sup>

U.S. Adults with Alzheimer's Disease (M)<sup>1</sup>



**>70%**  
of people with AD  
experience agitation at  
some point in their disease<sup>2</sup>

## Significant unmet medical need exists in this population<sup>3</sup>

Agitation is among the most disruptive symptoms of AD. It is associated with greater caregiver stress, increased morbidity and mortality and earlier placement in long-term care facilities. The only currently approved product carries a black-box warning for mortality in elderly people.

<sup>1</sup>Alzheimer's Association. Alzheimer's Disease Facts and Figures. May 2024. <sup>2</sup>Ijaopo et al., 2017., Translational Psychiatry.; <sup>3</sup>Koenig et al., 2016, Current Psychiatry.

# Several Lines of Evidence Indicate that V1a Receptor Antagonists Have Therapeutic Potential for Reducing Symptoms of Agitation



## The vasopressin system modulates social-emotional, anxiety and threat-related behaviors across species

- V1aR expression patterns critically affect social behavior<sup>1-5</sup>
- Rodent selection lines bred for aggression or anxiety show dysregulated vasopressin release and HPA axis functioning<sup>6</sup>
- Vasopressin-deficient rodents display impaired responses to threat stimuli, reduced anxiety and depressive-like behaviors, and impaired aggression toward intruders<sup>7-9</sup>

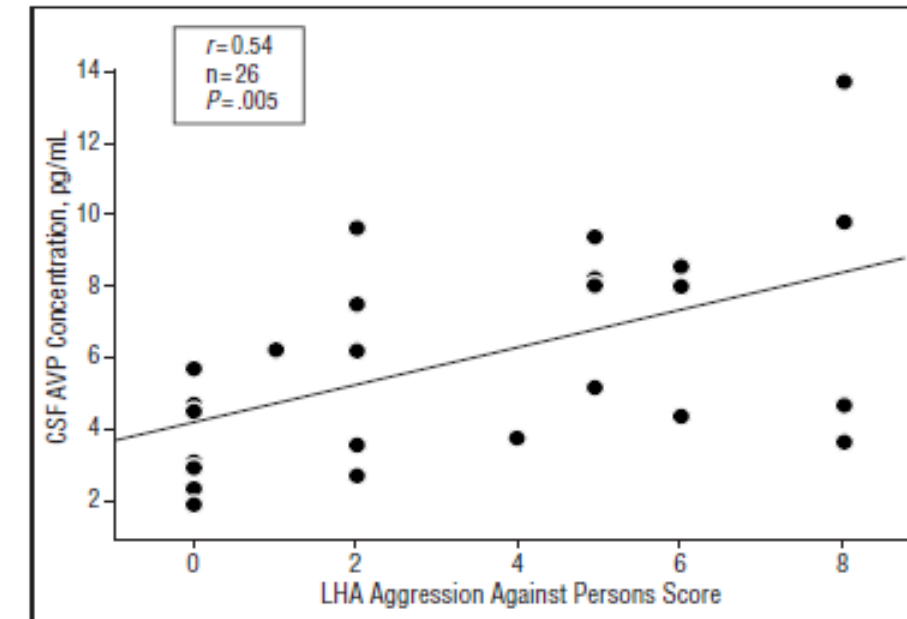


## In healthy volunteers, vasopressin enhances reactivity to threatening stimuli and disrupts emotional control<sup>1-2</sup>

- Exogenously administered vasopressin increases autonomic responsiveness to threat stimuli and increases anxiety<sup>2</sup>
- V1a antagonist administration suppresses anxiety induced by unpredictable threats<sup>10</sup>



## Positive association between vasopressin and aggression in people with personality disorders<sup>11</sup>



**Figure 1.** Correlation between Aggression Against Persons (the fighting and assault items) scores on the Life History of Aggression (LHA) assessment and cerebrospinal fluid (CSF) arginine vasopressin (AVP) concentrations in 26 individuals who met the DSM-IV criteria for personality disorder.



## In HD irritability, an investigational V1a receptor antagonist reduced an exploratory endpoint measuring aggression<sup>12</sup>

**Together, these data support the development of a V1a receptor antagonist for the treatment of symptoms of agitation, aggression, and anxiety**

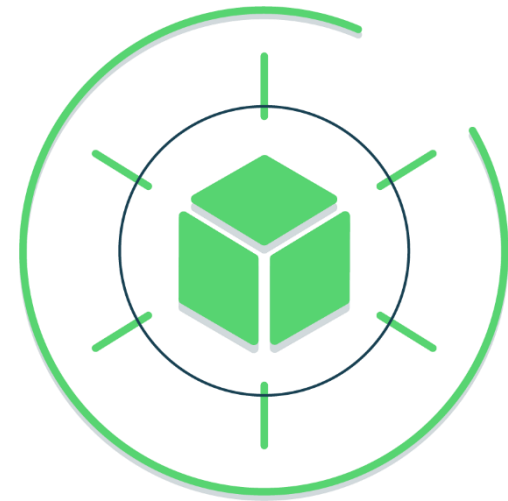
<sup>1</sup>Ebstein et al., 2009, New York Academy of Sciences.; <sup>2</sup>Thompson et al., 2006, PNAS.; <sup>3</sup>Insel et al., 2010, *Neuron Review*, PNAS; <sup>4</sup>Carter et al., 1995, *Neuroscience Biobehavioral Review*.; <sup>5</sup>Wang et al., 1994, PNAS.; <sup>6</sup>Veenema and Neumann, 2007, *Brain behavior, evolution*.; <sup>7</sup>Zelena et al., 2009, *Journal of Endocrinology*.; <sup>8</sup>Mlynarik et al., 2007, *Hormones and Behavior*.; <sup>9</sup>Fodor et al., 2014, *Psychoneuroendocrine*.; <sup>10</sup>Lago et al., 2021, *Psychopharmacology*.; <sup>11</sup>Coccaro et al., 1998., *JAMA Psychiatry*.; <sup>12</sup>Maibach et al., 2022, *Personalized Medicine*.  
HPA = hypothalamic-pituitary-adrenal

# NMRA-511 Profile Supports Advancement into Alzheimer's Disease Agitation



## Best-in-Class Pharmacology<sup>1</sup>

- Highly potent at V1a
- High selectivity over V1b, V2, and oxytocin receptors
- Excellent brain penetration



## Strong Pre-Clinical Data Translates to Humans<sup>2</sup>

- Robust pharmacodynamic (PD) effect in rodents
- Robust activity in a marmoset 'human threat test' model of stress/anxiety



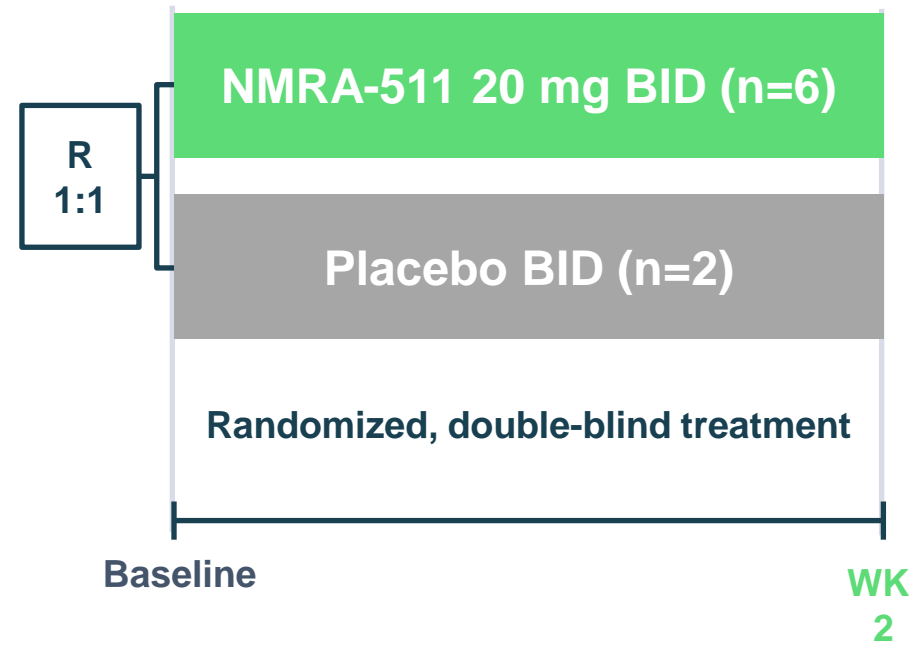
## PK and Safety Data from Phase 1 Support Advancement<sup>1</sup>

- NMRA-511 was safe and very well-tolerated in Phase 1 SAD/MAD study
- NMRA-511 was safe and well-tolerated in healthy elderly volunteers

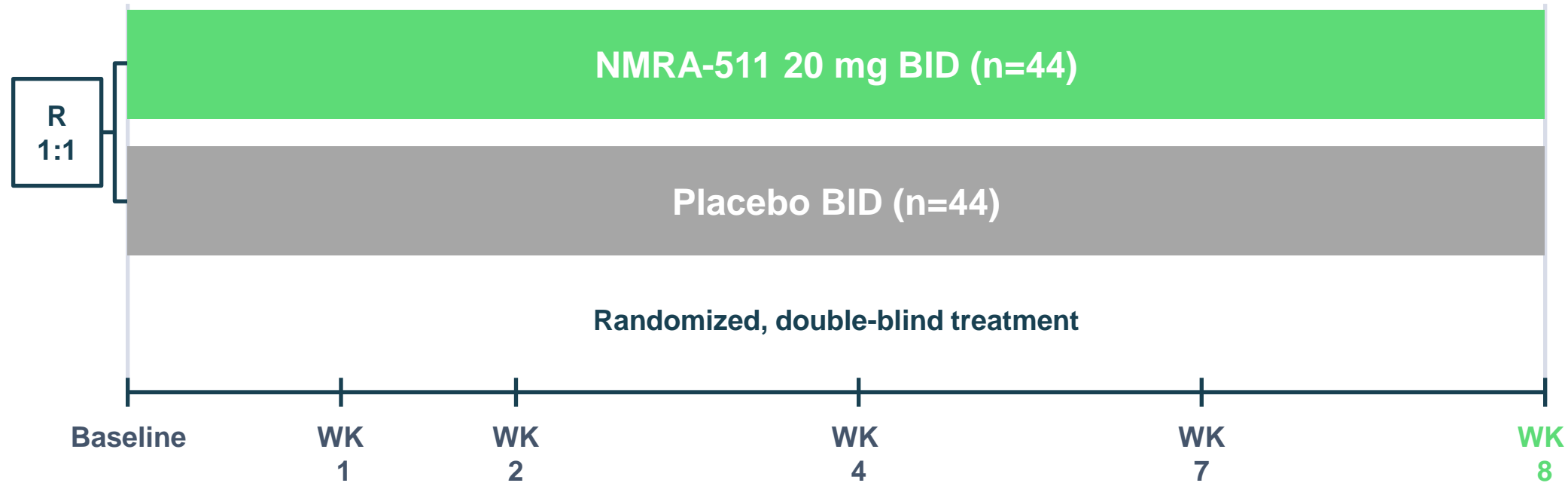


# NMRA-511 Signal Seeking Study in Alzheimer's Disease Agitation

## Part A: 2-Week Evaluation Period Enrolling Healthy Elderly Participants



## Part B: 8-Week Evaluation Period Enrolling People with Alzheimer's Disease Agitation (ADA)



### NMRA-511 Phase 1b Study

- |   |   |
|---|---|
| <b>Part A Inclusion Criteria:</b>       | <ul style="list-style-type: none"> <li>• Healthy elderly adult participants aged 65-80 years</li> </ul>   |
| <b>Part B Inclusion Criteria:</b>       | <ul style="list-style-type: none"> <li>• Adults aged 55-90 years with mild-severe dementia (MMSE score of 5-24) and clinically significant agitation (CMAI total score 45-100)</li> </ul>   |
| <b>Part B Primary Endpoint:</b>         | <ul style="list-style-type: none"> <li>• <math>\Delta</math> from baseline to Week 8 in CMAI total score</li> </ul>   |
| <b>Part B Other Endpoints Include*:</b> | <ul style="list-style-type: none"> <li><math>\Delta</math> from baseline to Week 8 in:</li> <li>• CGI-S Agitation total score</li> <li>• mADCS-CGIC total score</li> <li>• Caregiver Diary of participant agitation, aggression, and/or anxious behaviors</li> <li>• NPI total score</li> </ul> |
| <b>Statistics:</b>                      | <ul style="list-style-type: none"> <li>• Study not powered to demonstrate statistical significance</li> <li>• Designed as a signal-seeking study; effect size will inform the potential future development of NMRA-511 in ADA</li> </ul>  |

\*Safety Assessments include adverse events, clinical laboratory, vital signs, physical examination, 12-lead electrocardiogram (ECG), Columbia-Suicide Severity Rating Scale (C-SSRS).  
 $\Delta$  = Change; BID = twice daily; CMAI = Cohen-Mansfield Agitation Inventory; MMSE = Mini-Mental State Examinations; CGI = Clinical Global Impression of Change for Agitation;  
 mADCS-CGIC = mADCS-CGIC Agitation modified Alzheimer's Disease Cooperative Study – Clinical Global Impression of Change for Agitation; NPI = Neuropsychiatric Inventory.

# M4 PAM Franchise: Potentially Differentiated M4R PAMs for Schizophrenia

## M4 Franchise Target Profile

### Pharmacology

Neumora has multiple series of chemically distinct, highly selective M4 muscarinic receptor PAMs for antipsychotic-like efficacy with the potential for improved safety profile

### Indication

Schizophrenia

### Epidemiology

Estimated 3 million patients in the U.S. with schizophrenia<sup>1</sup>

### Target Drug Profile

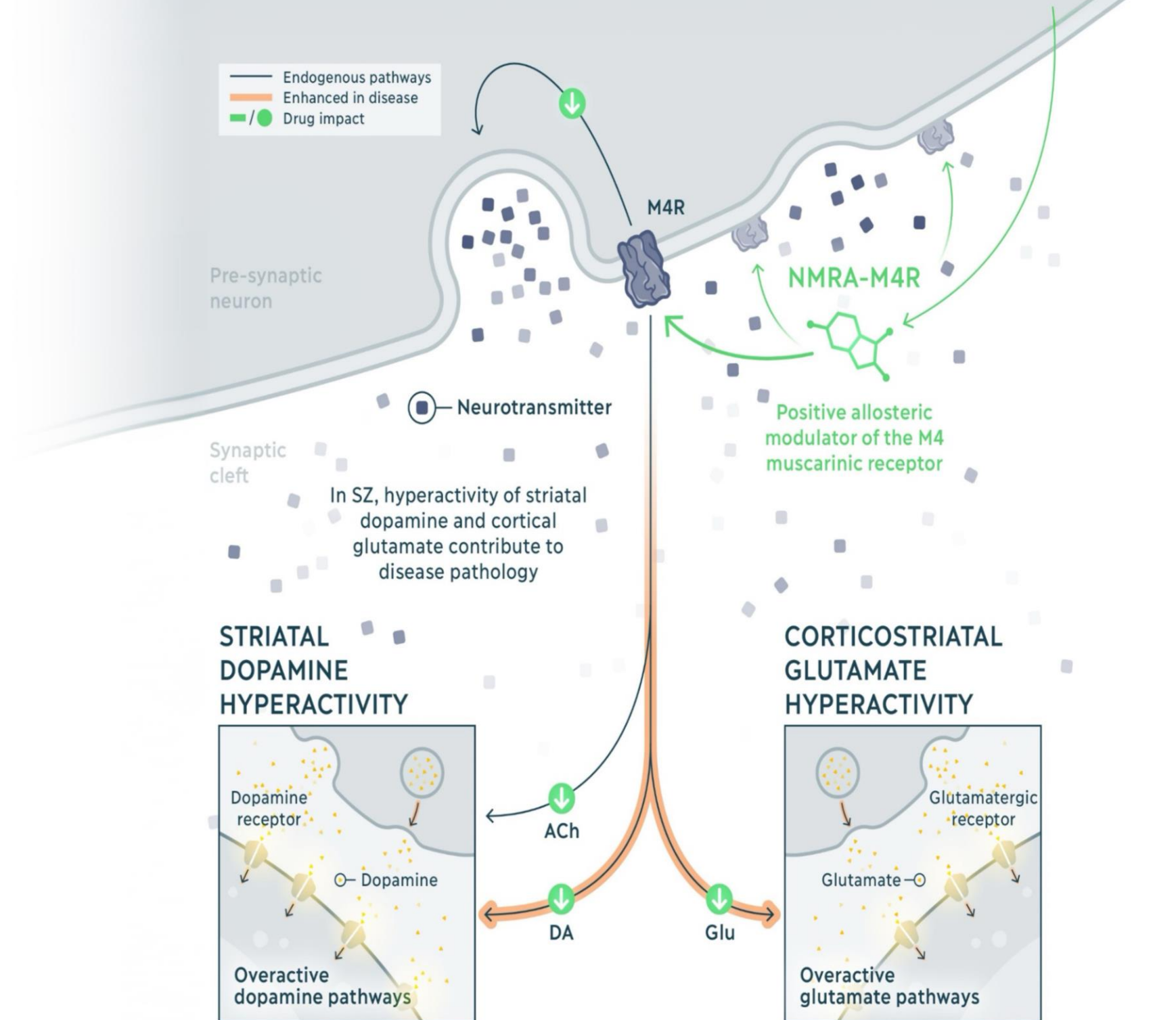
Oral, once-daily

### Strong IP Protection Across Franchise

Expect exclusivity through 2042+, based on composition of matter protection and estimated patent term extension

### Expected Milestones

- Submit IND for a NMRA-M4R compound in 1H25



<sup>1</sup>Wander, C. *Am J Manag Care*. 2020;26:S62-S68. <sup>2</sup>NMRA data on file; <sup>3</sup>CERE Company data.

Note: Data on this slide is presented for illustrative purposes only and the data for emraclidine were not derived from Neumora clinical trials or preclinical studies.

PAM = positive allosteric modulator

# Pre-Clinical Pipeline of Four Novel Programs, Each with A Strong Biological Rationale

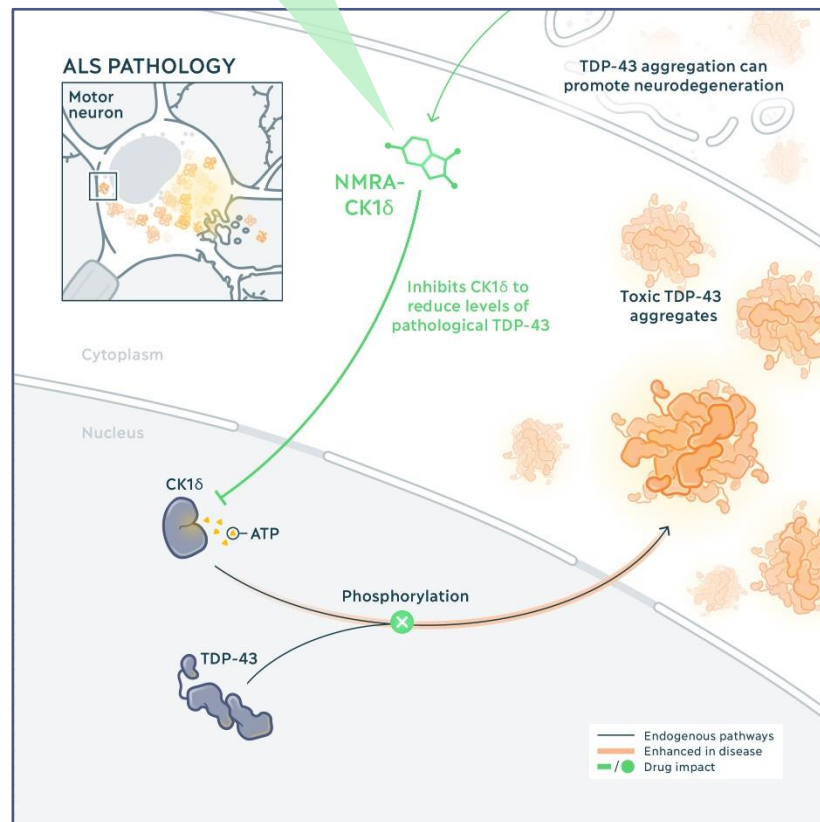
## NMRA-CK1δ

Focused on inhibiting the protein casein kinase-1δ (CK1δ) to reduce levels of the pathological form of TDP-43 and slow disease progression in ALS

### Potential Indications

ALS, Alzheimer's disease

CK1δ phosphorylates TDP-43, a key driver of TDP-43-driven pathology in ALS



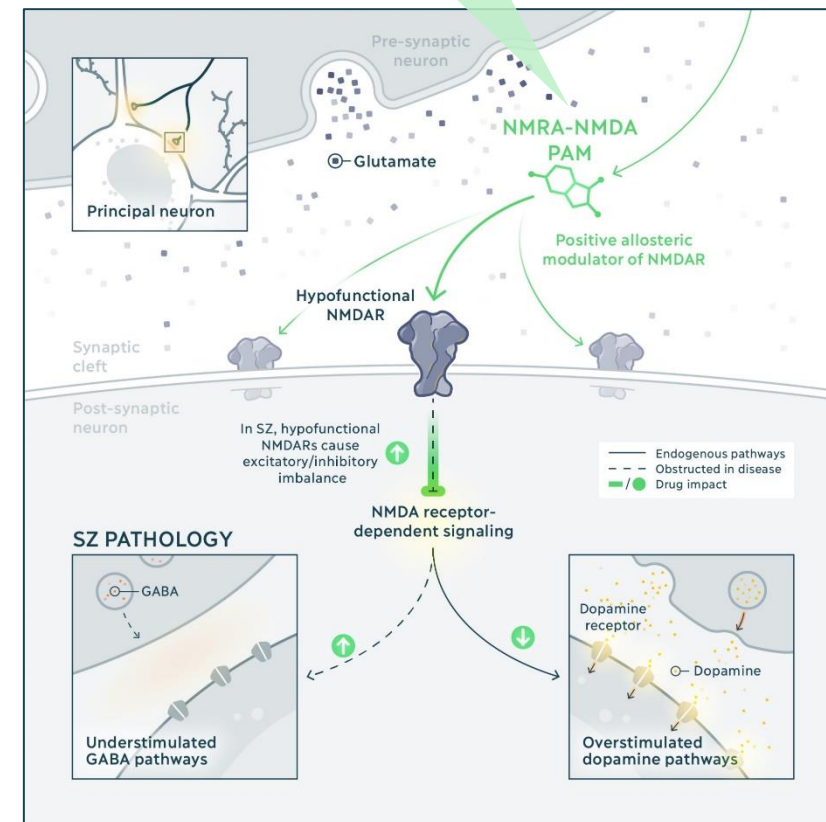
## NMRA-NMDA

NMDA receptor hypofunction is a leading hypothesis for the cause of schizophrenia.

### Potential Indications

SCZ

NMDA PAMs can selectively enhance physiological NMDAR function and decrease network hypersynchrony observed in SCZ



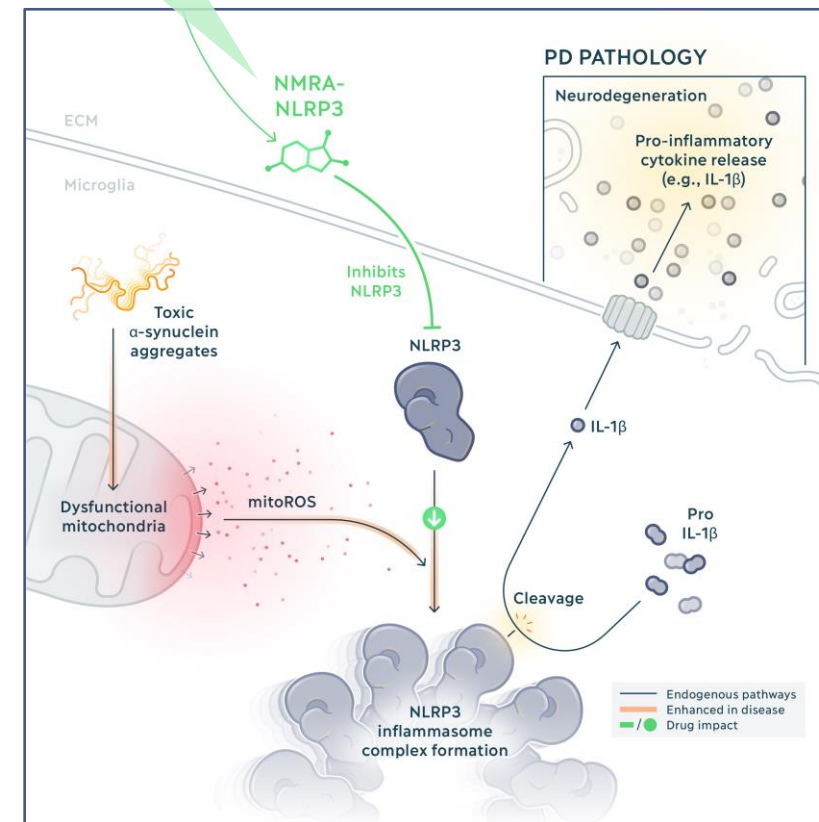
## NMRA-NLRP3

Focused on inhibiting the NLRP3 inflammasome to modulate the immune response in neurodegeneration

### Potential Indications

Parkinson's disease

NLRP3 inflammasome is activated in microglia in response to disease linked proteins such as α-synuclein, leading to proinflammatory signaling



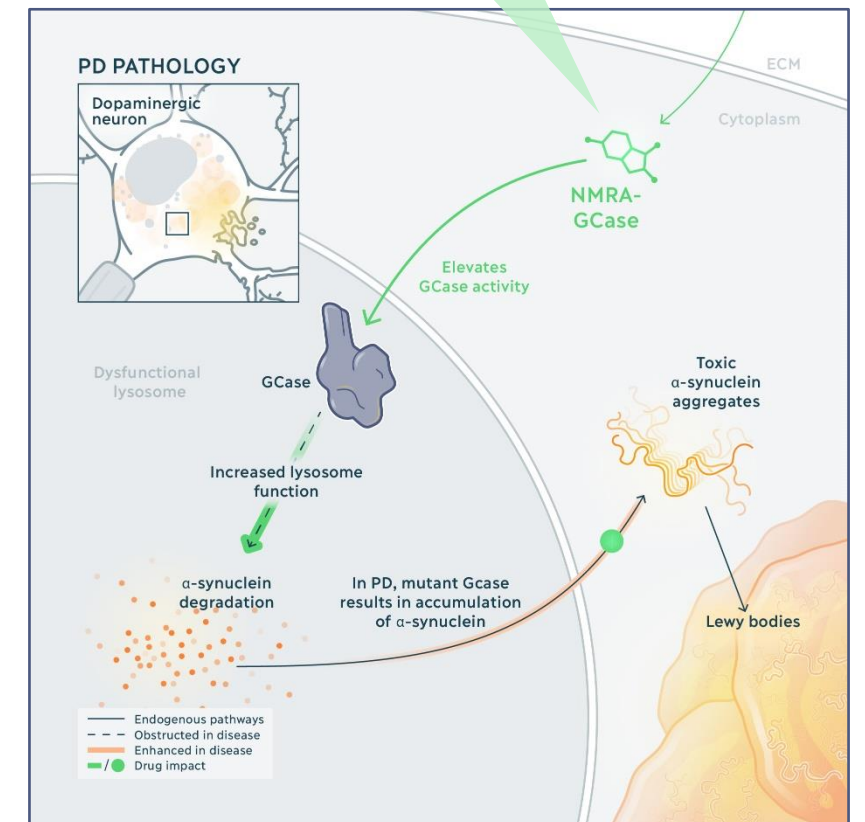
## NMRA-GCase

Focused on elevating activity of the GCase enzyme, which is encoded by the GBA1 gene, and may help to degrade toxic α-synuclein aggregates

### Potential Indications

Parkinson's disease

GCase deficiencies lead to lysosomal dysfunction and the accumulation of alpha-synuclein, a hallmark of Parkinson's





# Redefining Neuroscience Drug Development



**Industry leading  
CNS pipeline with long-  
dated IP into the 2040s**

**Multiple value-creating  
clinical catalysts  
expected in 2025**



**Built at scale with strong  
balance sheet; \$850M  
raised since 2021**

**Cash runway into  
mid-2026 supporting  
company growth**



**World-class team with  
differentiated approach**

**Maximizing probability of  
success with team and  
proprietary approach**



# Appendix



# Led by Experienced Company Builders and Leading Neuroscience Drug Developers

## Leadership



**Paul L. Berns**  
Co-Founder and Executive Chairman



**Henry Gosebruch**  
Chief Executive Officer  
abbvie J.P.Morgan  
ACELYRIN APTINYX



**Carol Suh**  
Chief Operating Officer and Co-Founder



**Joshua Pinto, Ph.D.**  
Chief Financial Officer



**Bill Aurora, Pharm.D.**  
Chief Strategy Officer



**Rob Lenz, MD, Ph.D.**  
Head of Research & Development



**Kaya Pai Panandiker**  
Chief Commercial Officer



**Nick Brandon, Ph.D.**  
Chief Scientific Officer



**Mary Chamberlain-Tharp, Ph.D.**  
Chief Business Officer



**Jason Duncan**  
Chief Legal Officer



**Lori Houle**  
Chief Quality Officer



**Raj Manchanda, Ph.D.**  
Chief Technical Operations Officer



**Amy Sullivan**  
Chief Human Resources Officer



## Board of Directors

**Paul L. Berns**  
Co-Founder, Executive Chair

**Henry Gosebruch**  
President & Chief Executive Officer

**Kristina Burow**  
Managing Director, ARCH Venture Partners

**Matthew K. Fust**  
Biotechnology Advisor


**Alaa Halawa**  
Executive Director, Mubadala Capital

**Maykin Ho, Ph.D.**  
Retired Partner, Goldman Sachs

**David Piacquad**  
Biotechnology Advisor



# Changes from Phase 2 to Phase 3 to Strengthen Navacaprant Probability of Success

	Phase 2	Phase 3 	Rationale
<b>Study Design</b>			
<b>Study Population</b>	Included Mild to Moderate MDD	Moderate to Severe MDD	FDA guidance for drug development in MDD
<b>Primary Endpoint</b>	CFB to Week 8 in HAMD-17	CFB to Week 6 in MADRS	MADRS better suited to navacaprant pharmacology
<b>Inclusion Criteria</b>	Mild-to-severe depression (HAMD-17 $\geq$ 14)	Moderate-to-severe depression (MADRS $\geq$ 25)	FDA guidance for drug development in MDD
<b>Study Execution</b>			
<b>Assessment Schedule</b>	Week 4 & 8	Week 1, 2, 4, & 6	Detect earlier onset of treatment effect
<b>Placebo-Control Reminder Script</b>	N/A	Placebo-Control Reminder Script employed	Minimize placebo effect
<b>Raters</b>	Decentralized	Centralized	Minimize rater bias and variability
<b>Rater Quality Surveillance</b>	N/A	Study Insight Analytics	Near real-time monitoring of site performance & blinded demographic and baseline scale data to ensure eligibility
<b>Medical Monitoring</b>	Adequate	Substantial	
<b>Data &amp; Analytics Approach</b>	N/A	Substantial	Near real-time oversight & quality control
<b>Site Selection</b>	Adequate: 40 sites	Stringent: 55-70 sites per study	Careful selection of sites based on objective performance data
<b>Geography</b>	US only	Global	



# KOASTAL-1 Topline Study Summary Results

The KOASTAL-1 study enrolled 383 adult patients with Major Depressive Disorder (MDD)

Outcome	MADRS Total Score			SHAPS Total Score		
	Navacaprant 80 mg	Placebo	LSMD	Navacaprant 80 mg	Placebo	LSMD
<b>ITT population CFB at Week 6 (Primary Endpoint)</b>	-12.5 (n = 191)	-12.5 (n = 192)	0.0 (p = 0.993)	-5.8 (n = 191)	-5.5 (n = 192)	-0.3 (p = 0.648)
<b>Female population CFB at Week 6</b>	-14.0 (n = 105)	-11.4 (n = 106)	-2.7 (p = 0.072)	-7.2 (n = 105)	-4.9 (n = 106)	-2.3 (p = 0.015)
<b>Male population CFB at Week 6</b>	-10.6 (n = 86)	-13.8 (n = 86)	3.2 --	-4.3 (n = 86)	-6.3 (n = 86)	2.0 --

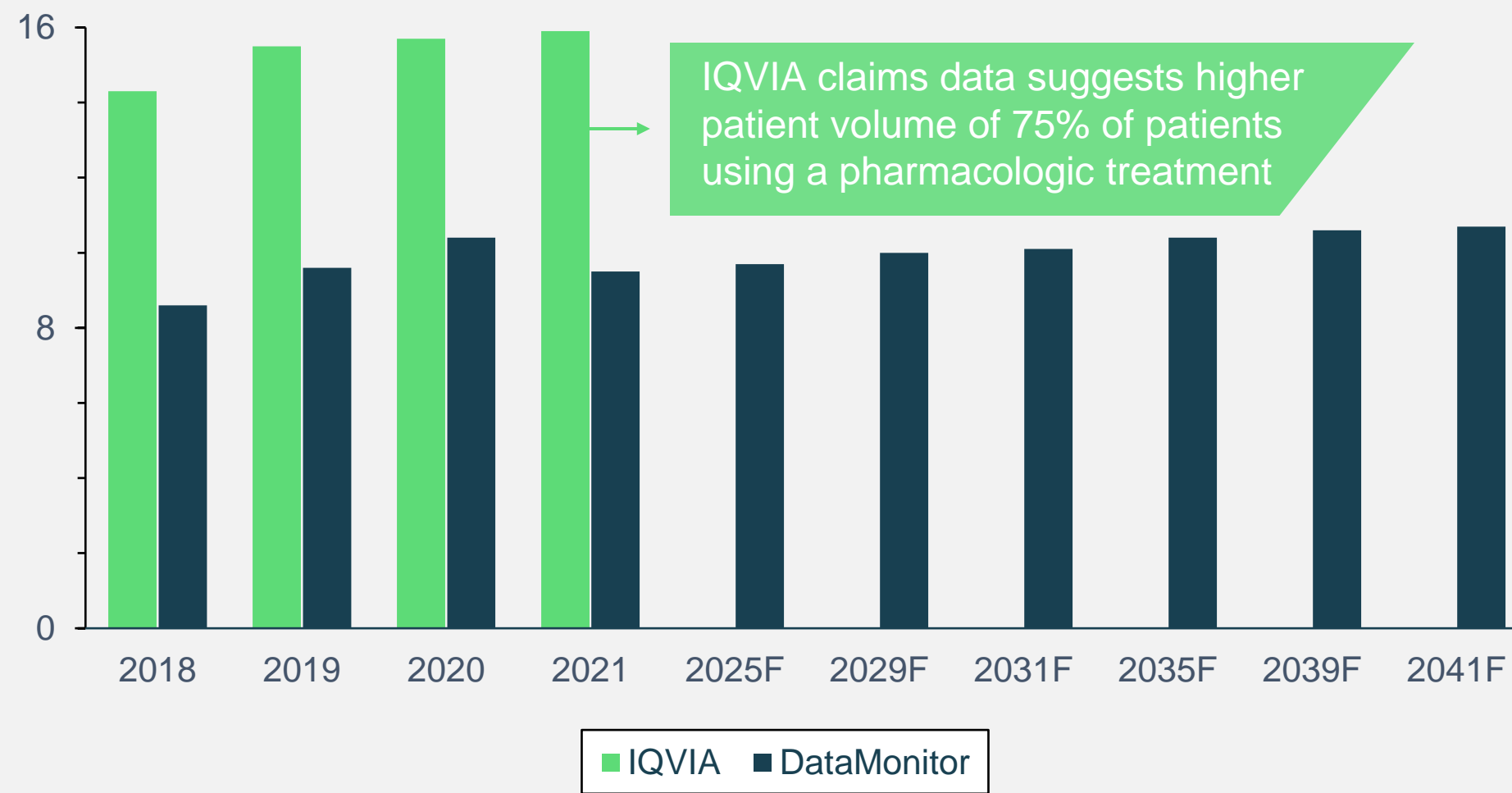
*CFB = change from baseline; LSMD = difference in LS mean change from baseline between navacaprant and placebo groups generated from mixed-effects model for repeated measures. Subgroup analysis for male or female are pre-specified.*



# Navacaprant Would Enter Large MDD Market with a Highly Differentiated Profile

## GROWTH IN ADDRESSABLE MDD MARKET EXPECTED IN-LINE WITH POPULATION GROWTH

**U.S. MDD diagnosed, pharmacologically treated prevalent population (2018-41F)** Millions of people



**60-80%** of MDD patients across lines of therapy are treated with a monotherapy agent<sup>1</sup>

**Monotherapy treatment rates across lines of therapy**

Treatment Line	CCAE	MDCD	MDCR	Optum
1 <sup>st</sup>	79.6%	82.1%	84.6%	81.7%
2 <sup>nd</sup>	67.3%	67.8%	69.3%	66.1%
3 <sup>rd</sup>	63.9%	64.9%	67.2%	62.1%
4 <sup>th</sup>	61.4%	61.4%	68.1%	60.0%

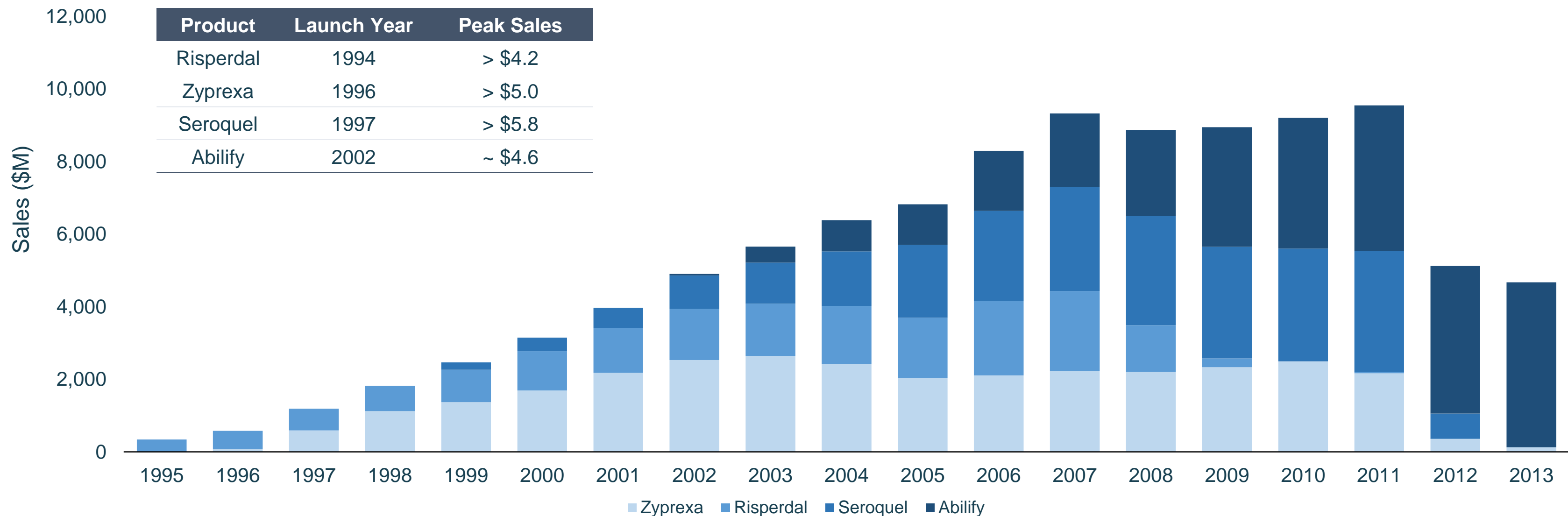
<sup>1</sup>Kern et al. Treatment patterns and sequences of pharmacotherapy for patients diagnosed with depression in the United States: 2014 through 2019. BMC Psychiatry. (2020) 20:4. U.S. Census Population Projections; DRG; Datamonitor; National Survey of Drug Use and Health 2018, 2019, 2020, 2021; Torre et al. (2021); L.E.K. research and analysis CCAE = IBM MarketScan Commercial Database; MDCD = IBM Market Scan Multi-State Database; MDCR = IBM MarketScan Medicare Supplemental Database



# Schizophrenia Market Supports Multiple Treatment Options

Historically the schizophrenia market has supported multiple branded products with similar MOAs, with new entrants driving higher overall market sales volume

Sales of Branded 5-HT<sub>2</sub> to D<sub>2</sub> Receptor Antagonists (1995 – 2013)



Sources: EvaluatePharma, L.E.K. interviews, research, and analysis; GK associates "The order of entry effect in prescription (Rx) and over the counter (OTC) pharmaceutical drugs", International Journal of Pharmaceutical and Healthcare, Marketing Vol. 2 No. 1, 2008 pp. 35-46. MOA = Mechanism of Action.

