



# **Redefining Neuroscience Drug Development**

**May 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 patient enrollment, initiation and data read outs for its programs and studies, including for the KOASTAL-2 and -3 studies, and the Phase 1b signal seeking study evaluating NMRA-511, as well as its clinical trial and development plans; timing and expectations related to regulatory filings; expectations and projections regarding future operating results and financial performance, including the sufficiency of its cash resources and expectation of the timing of its cash runway; changes to and optimization of the KOASTAL-2 and -3 studies; the potential for Neumora to advance other compounds in its M4 portfolio; expectations regarding appropriate patients being enrolled in the KOASTAL program; 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 or 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 and enrollment in our clinical trials; risks related to our reliance on third parties, including contract research organizations; 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 March 31, 2025 which was filed with the SEC on or about the date hereof. 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 results for the quarter ended, March 31, 2025 are not necessarily indicative of our operating results for any future periods.





## **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  
on the horizon**



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

**Cash runway into  
2027 supporting  
company growth**



**World-class team with  
differentiated approach**

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

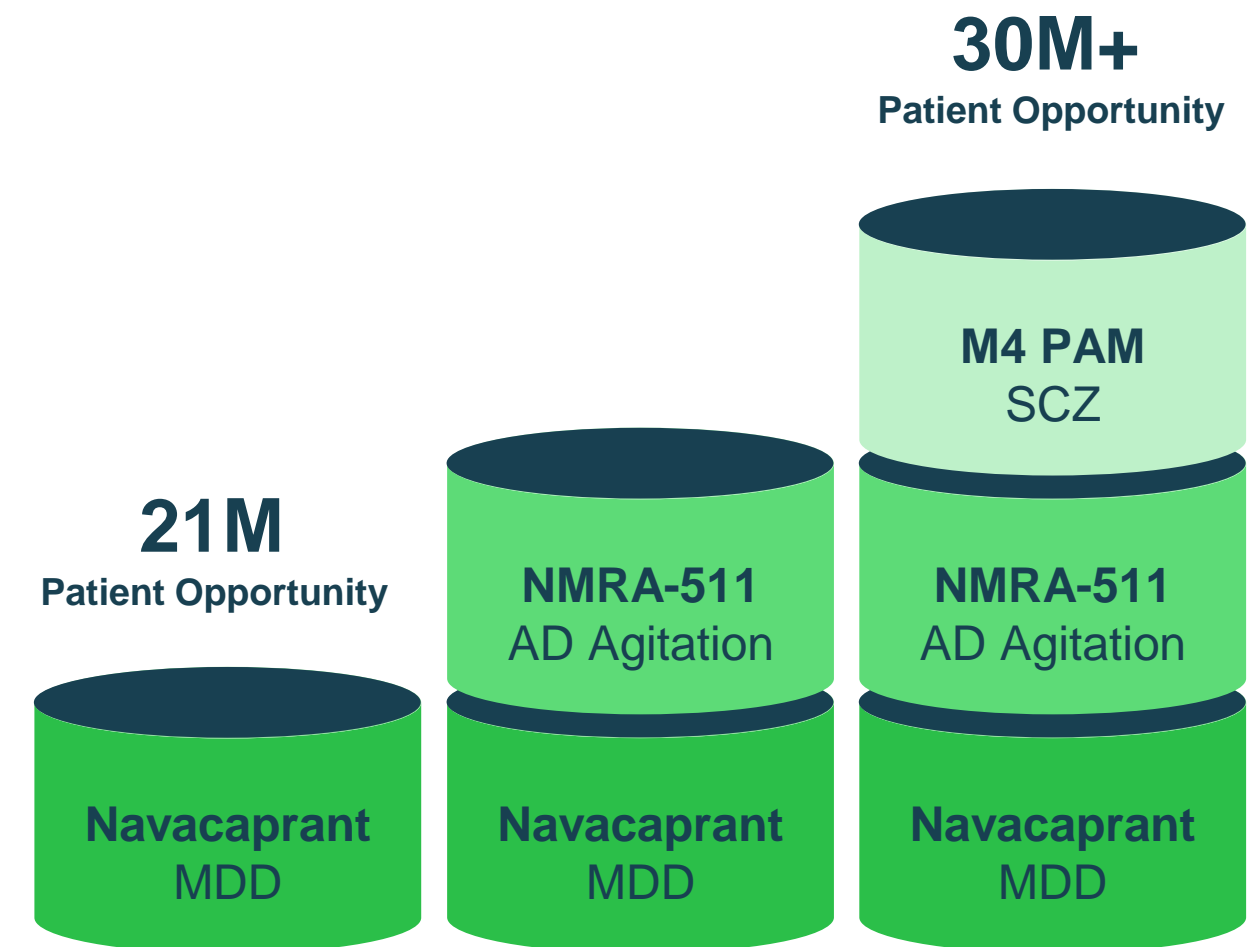
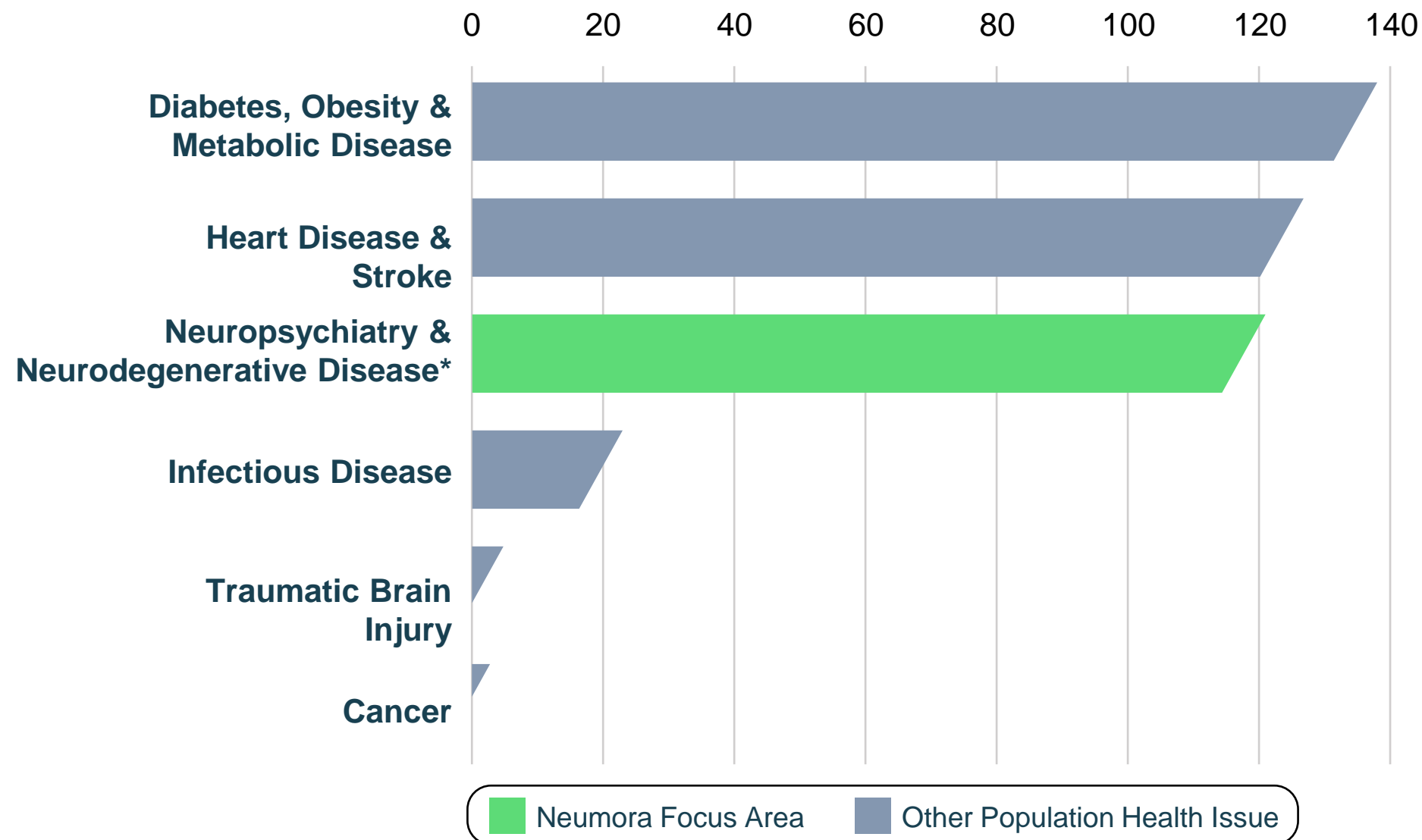


# Neumora is Tackling One of the Largest Population Health Challenges

Neumora's clinical-stage pipeline has potential to reach up to ~30M+ 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<br><i>Target/Mechanism</i>                     | INDICATION<br><i>U.S. Prevalence</i>                 | Preclinical | Phase 1 | Phase 2 | Phase 3 | MILESTONE<br><i>Guidance</i>   |
|--|--|-------------|---------|---------|---------|--|
| <b>Neuropsychiatry Programs</b>                        |  |             |         |         |         |  |
| <b>Navacaprant (NMRA-140)</b><br><i>KOR Antagonist</i> | <b>Major Depressive Disorder</b><br><i>21M</i>       |             |         |         |         | <b>KOASTAL-3 topline data</b><br><i>1Q26</i><br><b>KOASTAL-2 topline data</b><br><i>2Q26</i> |
| <b>NMRA-511</b><br><i>V1aR Antagonist</i>              | <b>Agitation in Alzheimer's Disease</b><br><i>6M</i> |             |         |         |         | <b>Phase 1b data</b><br><i>around year-end 2025</i>  |
| <b>NMRA-M4R</b><br><i>M4 Modulator</i>                 | <b>Schizophrenia</b><br><i>3M</i>                    |             |         |         |         | <b>Progress next M4 compound into the clinic</b><br><i>mid-2025</i>                          |
| <b>NMRA-NMDA</b><br><i>NMDA Modulator</i>              | <b>Schizophrenia</b><br><i>3M</i>                    |             |         |         |         |  |
| <b>Neurodegeneration Programs</b>                      |  |             |         |         |         |  |
| <b>NMRA-CK1δ</b><br><i>CK1δ Inhibitor</i>              | <b>ALS/Alzheimer's Disease</b><br><i>25K/6M</i>      |             |         |         |         |  |
| <b>NMRA-NLRP3</b><br><i>NLRP3 Inhibitor</i>            | <b>Parkinson's Disease</b><br><i>1M</i>              |             |         |         |         |  |
| <b>NMRA-GCASE</b><br><i>GCase Activator</i>            | <b>Parkinson's Disease</b><br><i>1M</i>              |             |         |         |         |  |

ALS = Amyotrophic lateral sclerosis; CK1  $\delta$  = Casein Kinase I Isoform delta; GCase = 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.  
 \*\*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%**

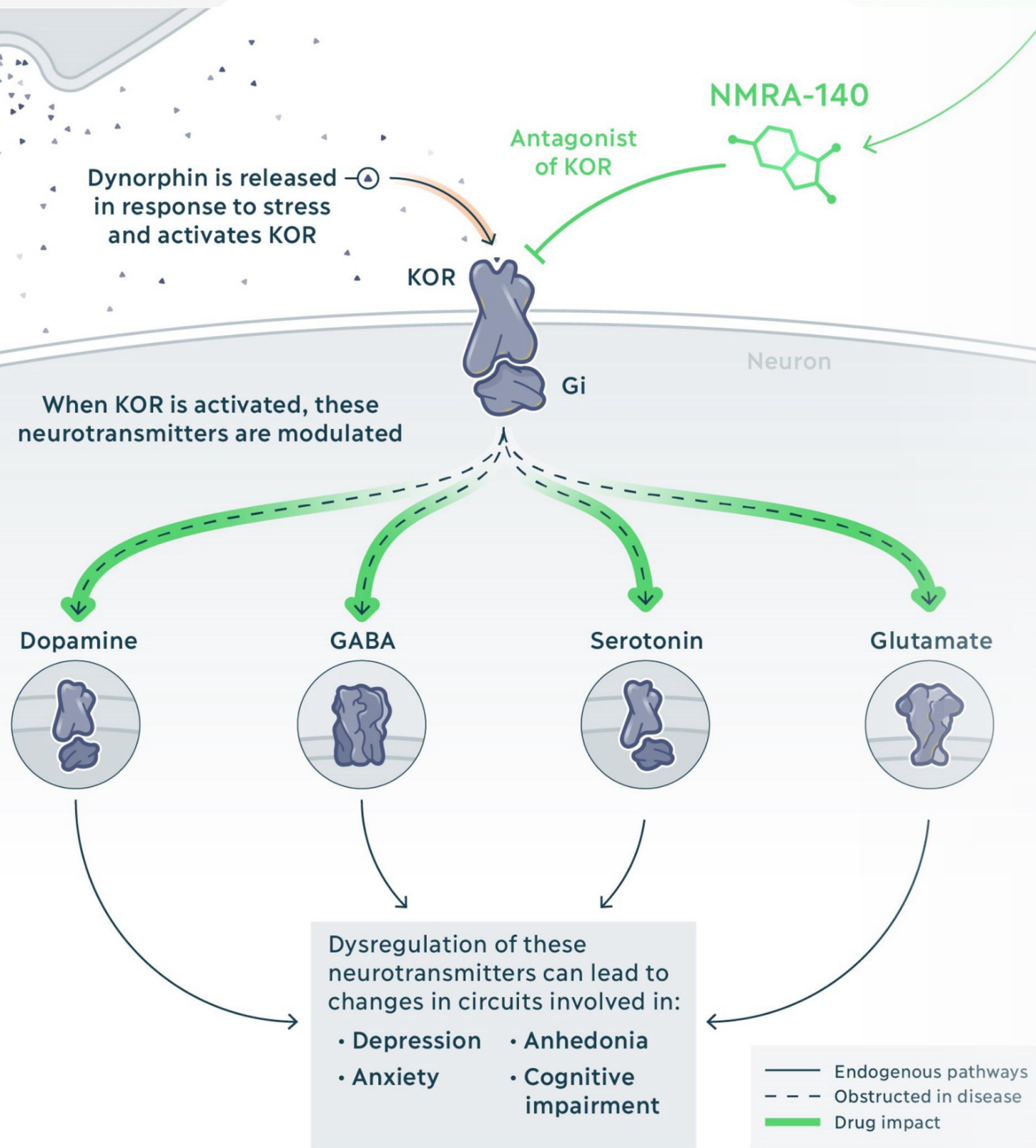
of people with MDD experience anhedonia<sup>8</sup>

**60–85%**

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

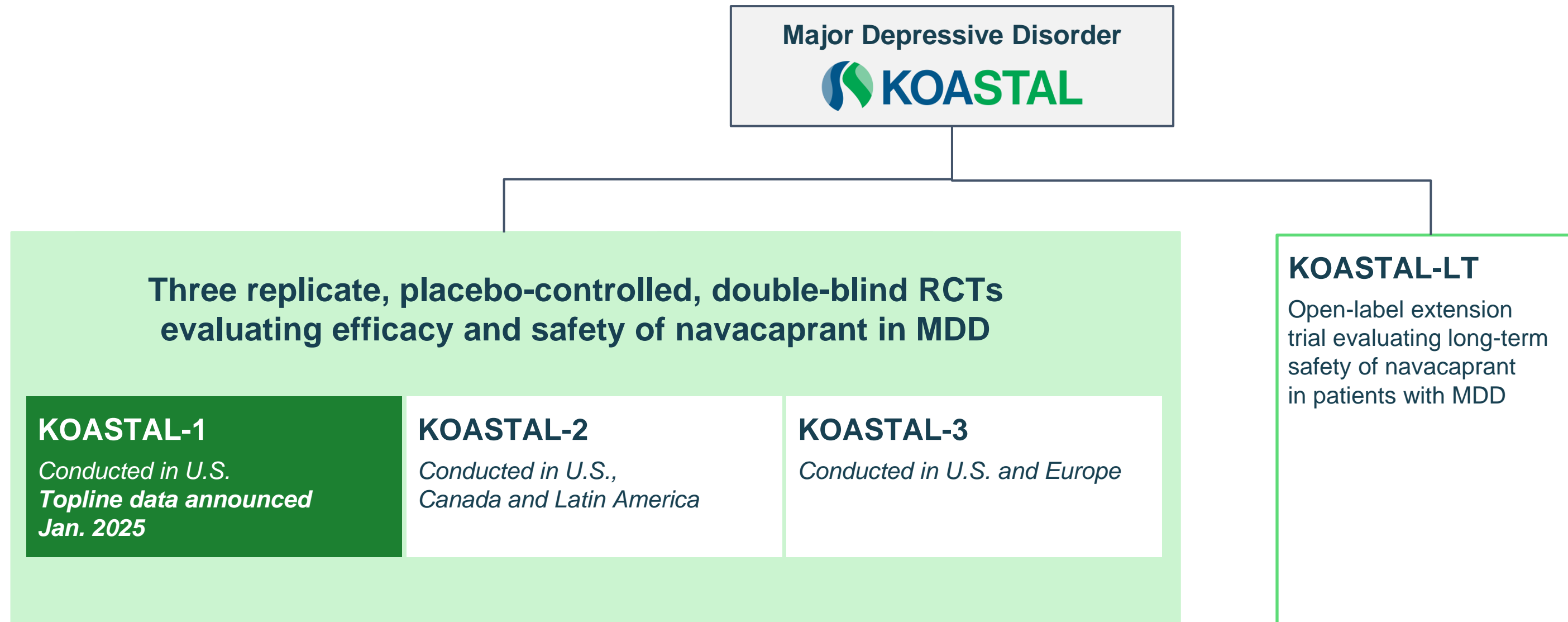


# The Role of Kappa Opioid Receptor Antagonism in MDD



- 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 with Opportunity for Further Expansion



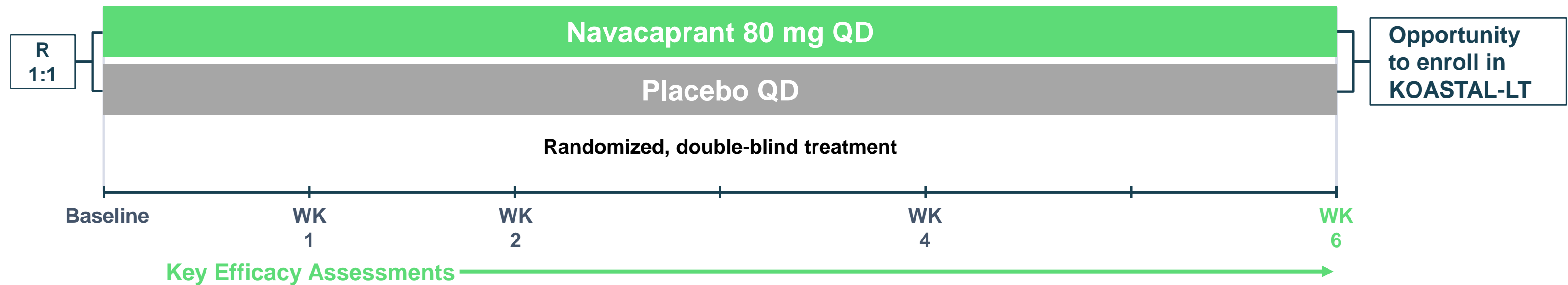
Additional indication opportunities include bipolar depression, substance use disorder, ADHD, Generalize Anxiety Disorder and Post-Traumatic Stress Disorder



# 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.

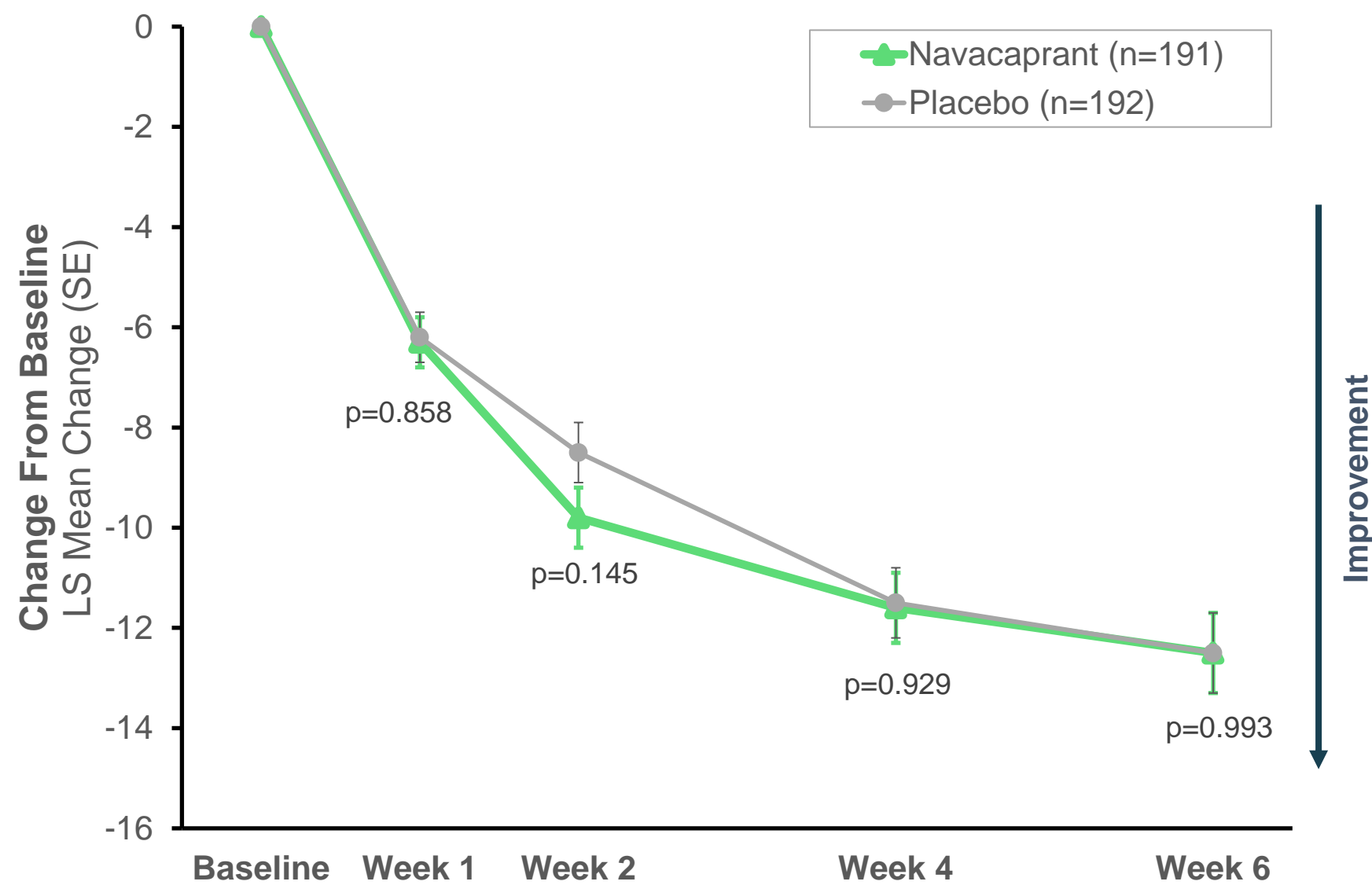
# KOASTAL-1 Topline Data: Demographics and Baseline Characteristics

| Intent-to-Treat Population                    | Navacaprant<br>n = 191 | Placebo<br>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)         |

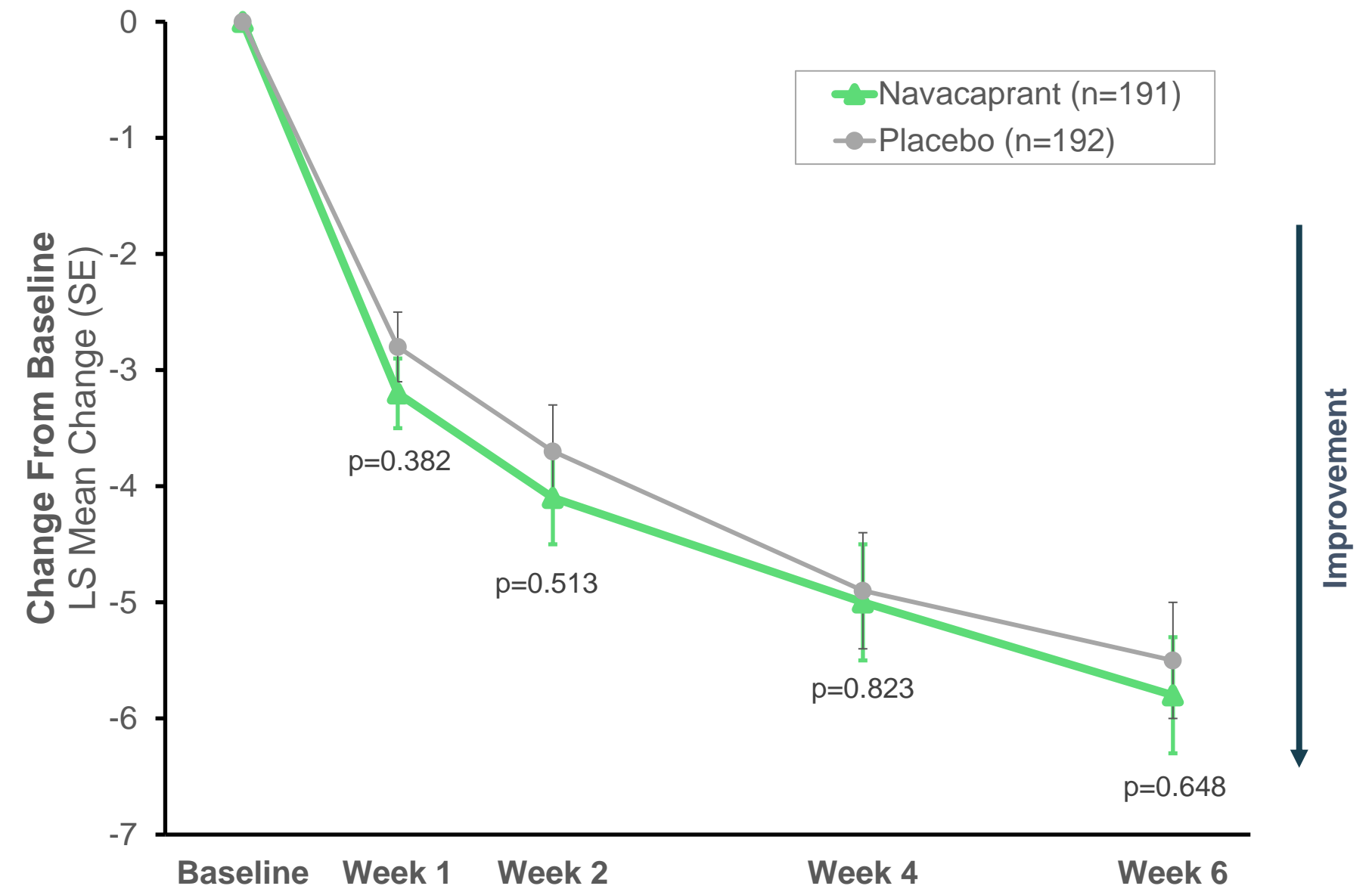


# KOASTAL-1 Topline Data: Primary & Key Secondary Endpoint

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



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



# KOASTAL-1 Topline Data: Favorable Safety Profile Demonstrated

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

| TEAEs Incidence<br>(>2% in either treatment group) | Placebo<br>n=192 | Navacaprant<br>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)

# Optimizing KOASTAL-2 and -3 Phase 3 Trials

Topline data from KOASTAL-3 in the first quarter of 2026 and -2 in the second quarter of 2026



## Site Selection

Adjusted clinical sites included in studies, with goal of including sites with demonstrated expertise in conducting MDD studies



## Medical Monitoring

Using clinician-rated Massachusetts General Hospital Clinical Trials Network and Institute SAFER approach to verify the diagnosis and appropriateness of patient population



## Screening Tools

Verified Clinical Trial (VCT) screening database complements the Clinical Trial Subject (CTS) database to screen for people who participate in multiple clinical trials



## Target Enrollment

Option included in KOASTAL-2 and -3 protocols to overenroll the studies up to 25%



# 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 around the end of 2025

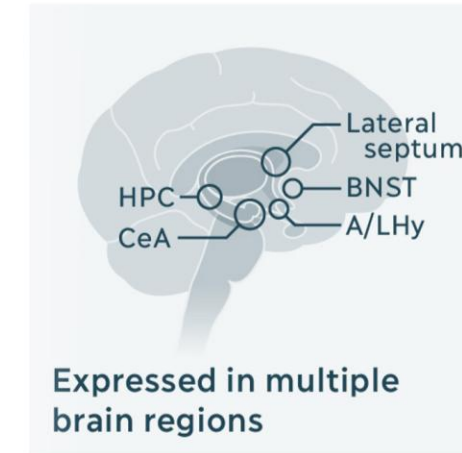
## Drug Profile

Oral, BID dosing

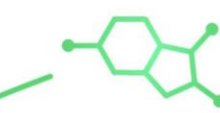
## Strong IP Protection

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

### V1aR EXPRESSION

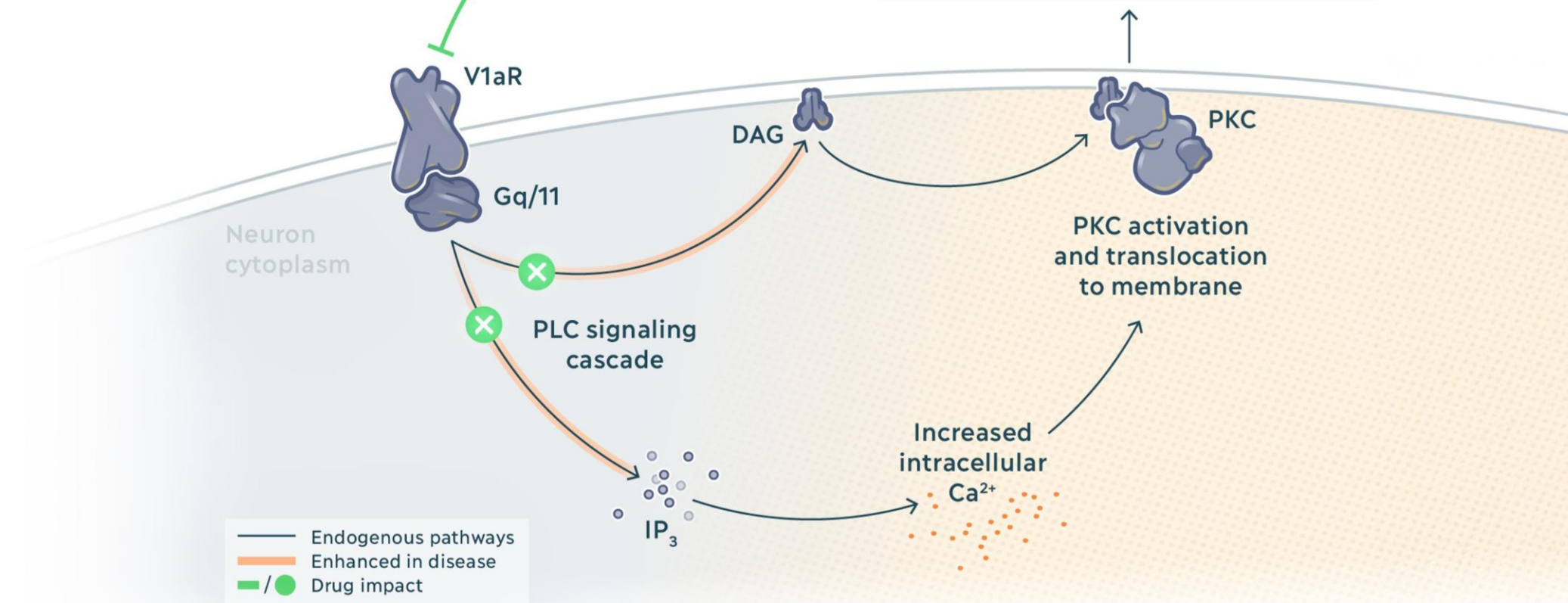


### NMRA-511



Antagonist of V1aR

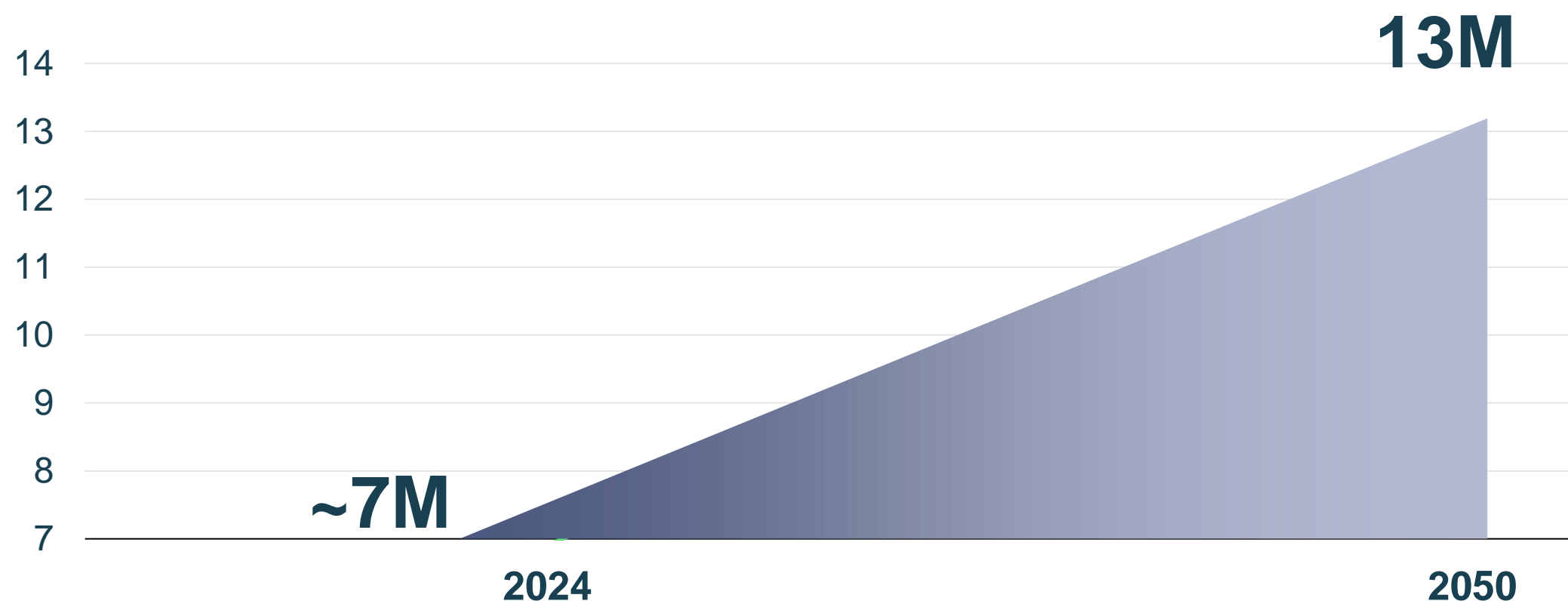
The vasopressin system acting through V1aR modulates anxiety and threat-related behaviors, aggression and social-emotional processing



# Alzheimer's Disease Agitation Represents 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>

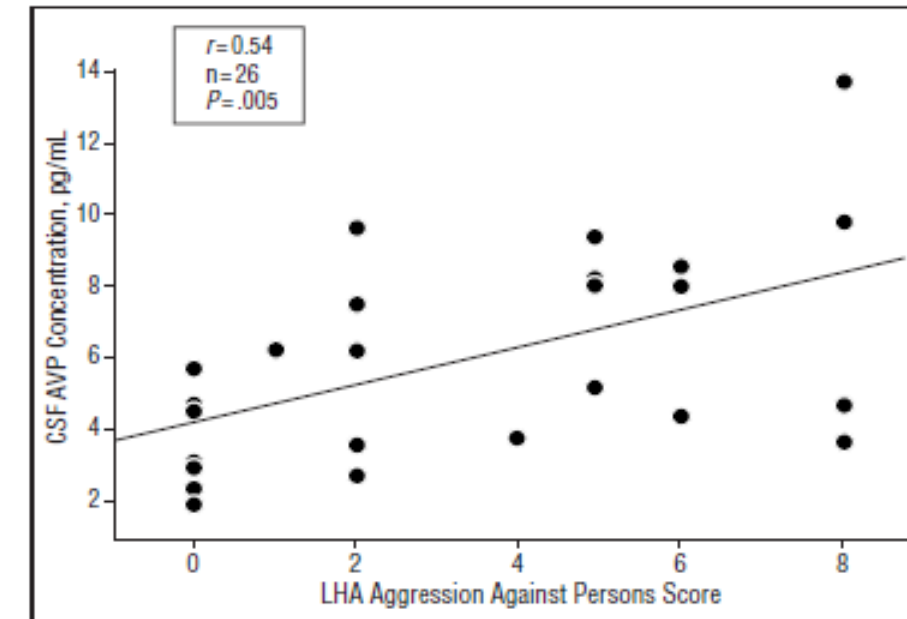


## In healthy volunteers, vasopressin enhances reactivity to threatening stimuli and disrupts emotional control<sup>1-2</sup>

- 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**

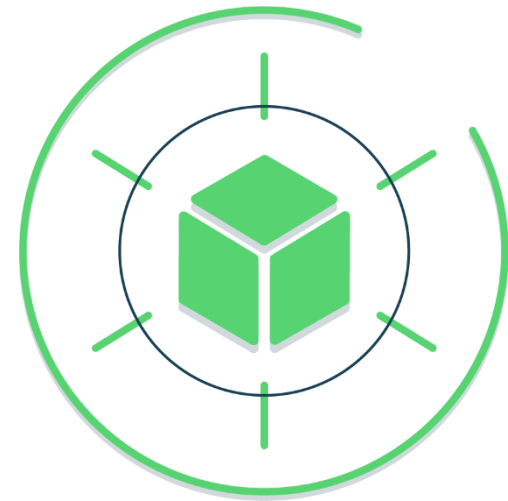
<sup>1</sup>Ebstein et al., 2009, New York Academy of Sciences.; <sup>2</sup>Thompson et al., 2006, PNAS.; <sup>3</sup>Insel et al., 2010, *Neuron Review*, PNAS; <sup>4</sup>Carter et al., 1995, *Neuroscience Biobehavioral Review*.; <sup>5</sup>Wang et al., 1994, PNAS.; <sup>6</sup>Veenema and Neumann, 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<sup>2</sup>

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



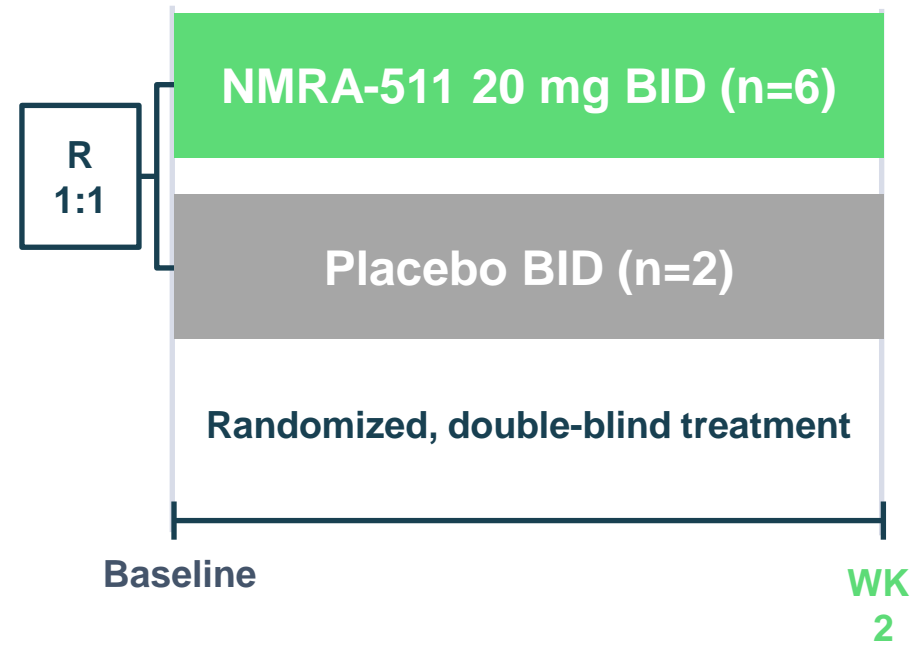
## PK and Safety Data from Phase 1 Support Advancement<sup>1</sup>

- 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

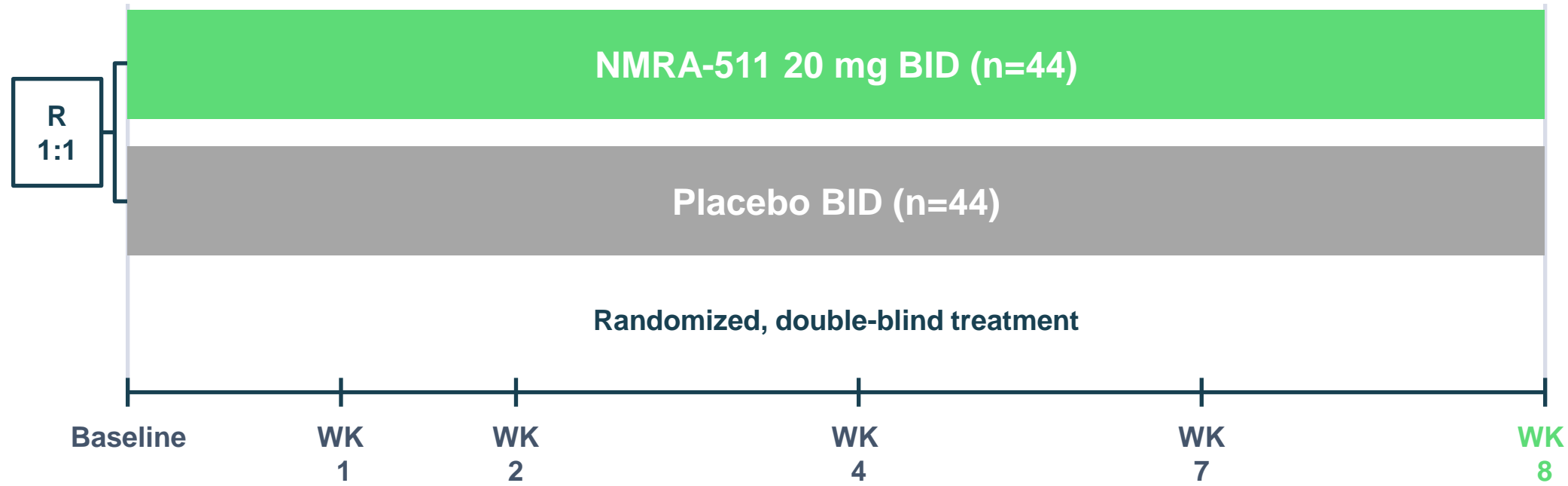


# NMRA-511 Signal Seeking Study in Alzheimer's Disease Agitation

## 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:             <ul style="list-style-type: none"> <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> </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

### Target Drug Profile

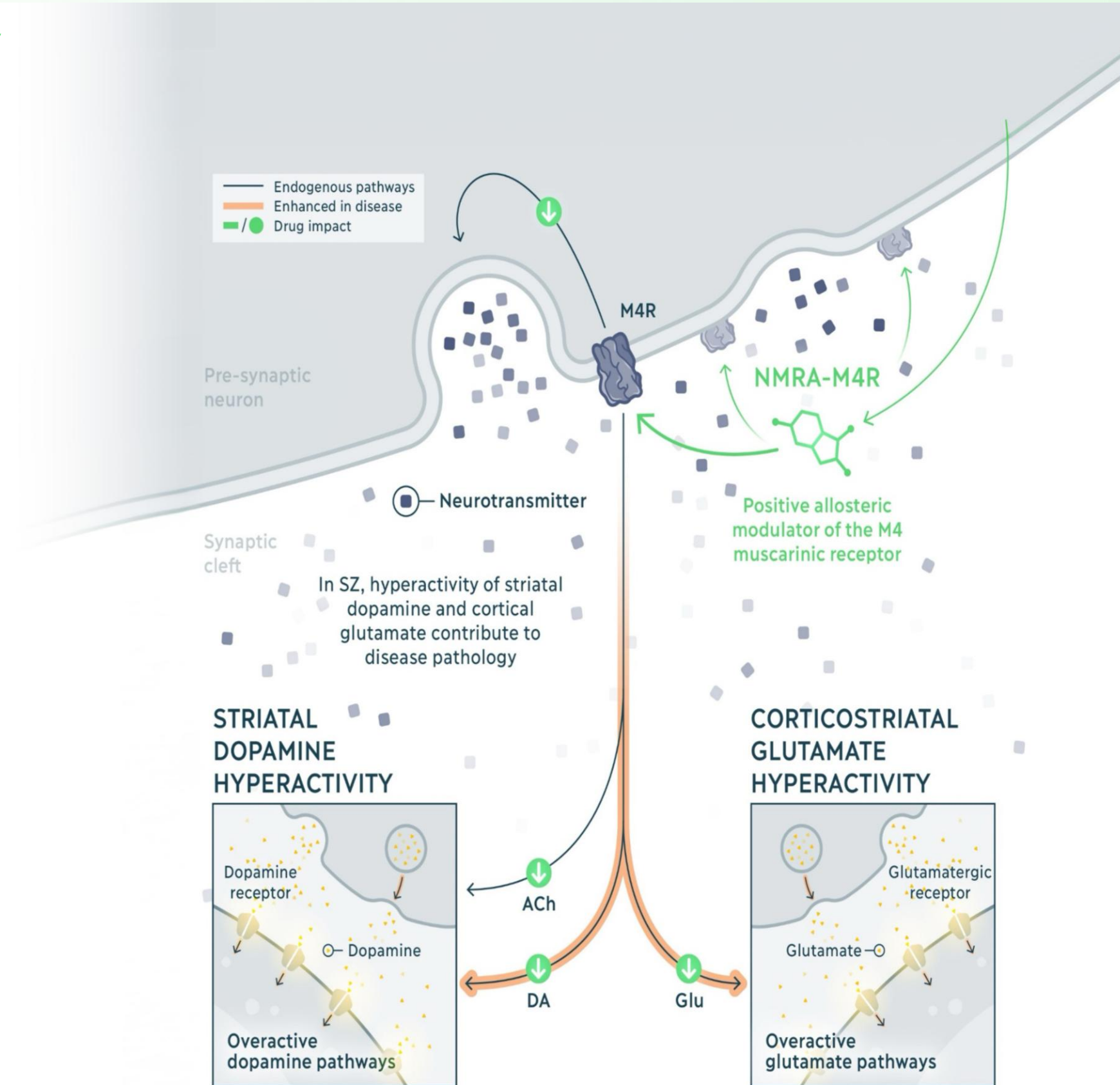
Oral, once-daily

### Epidemiology

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

### Expected Milestones

Progress an M4 PAM program into the clinic in mid-2025



<sup>1</sup>Wander, C. *Am J Manag Care*. 2020;26:S62-S68.  
PAM = positive allosteric modulator

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

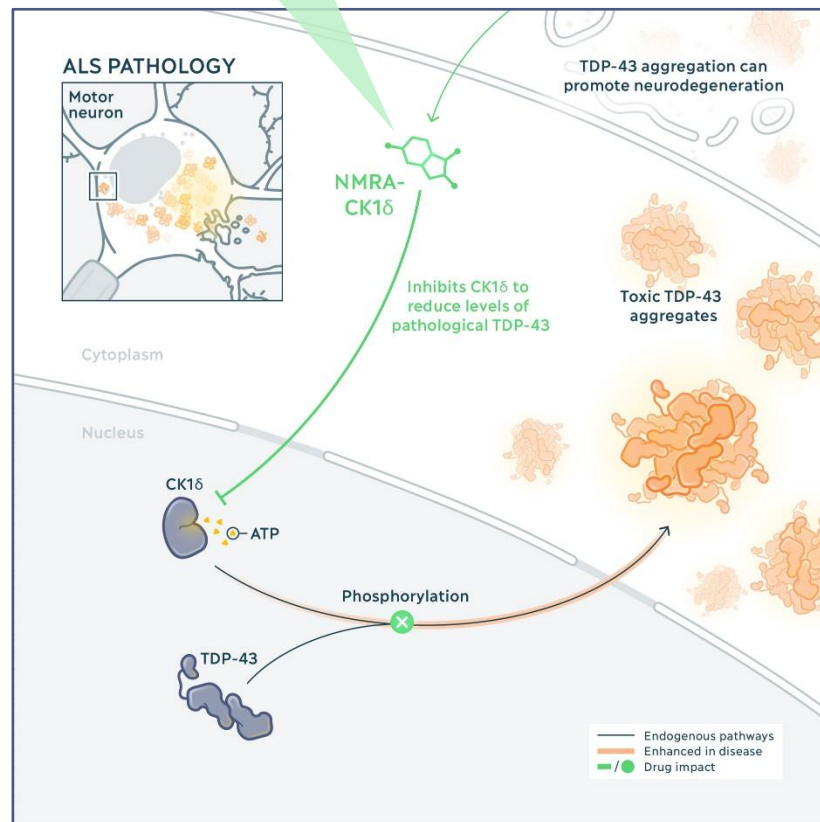
## NMRA-CK1δ

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



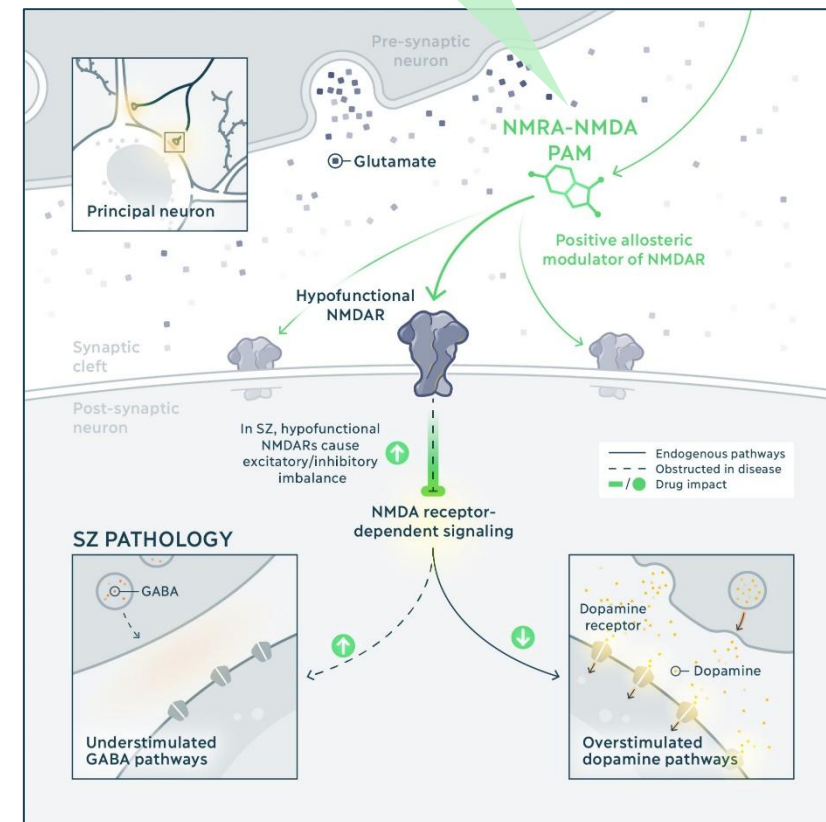
## NMRA-NMDA

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



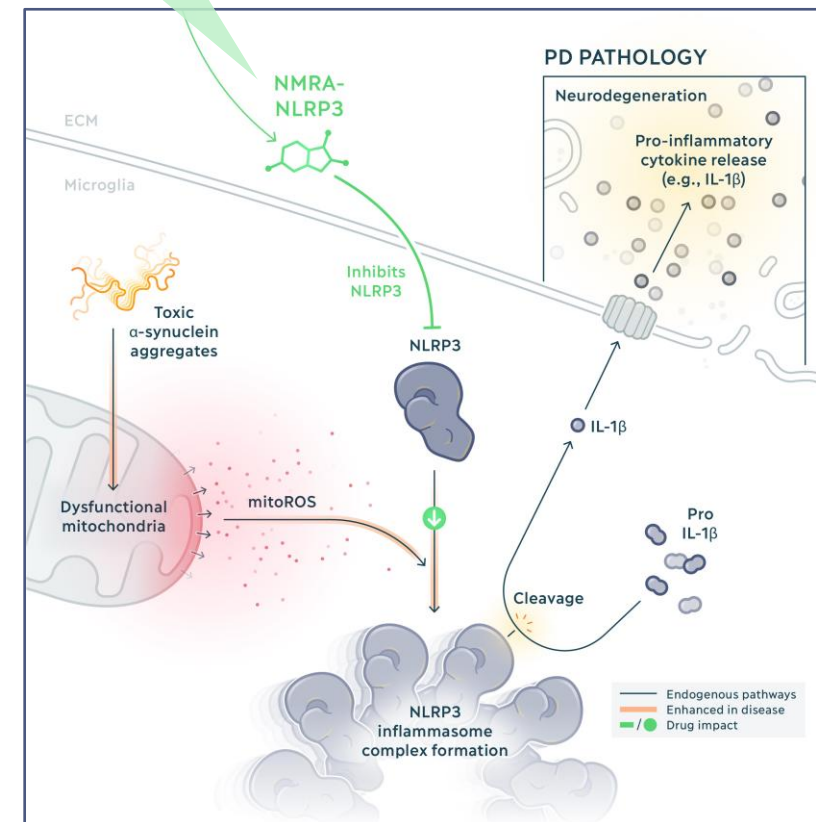
## NMRA-NLRP3

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



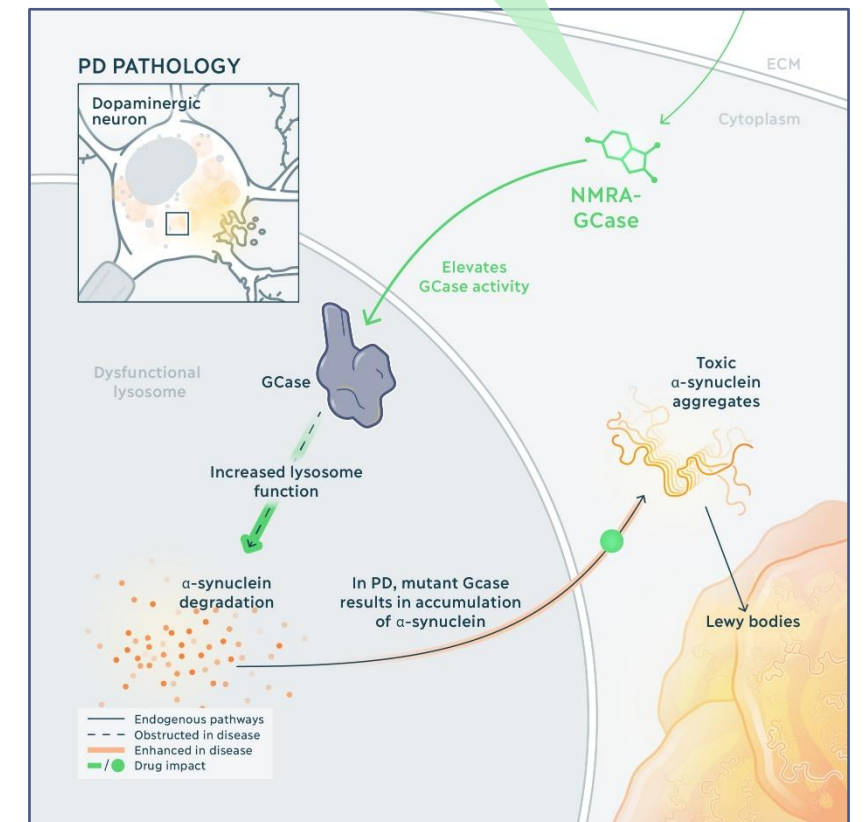
## NMRA-GCase

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  
on the horizon**



**Built at scale with strong  
balance sheet; \$850M  
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**World-class team with  
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success with team and  
proprietary approach**



# Appendix



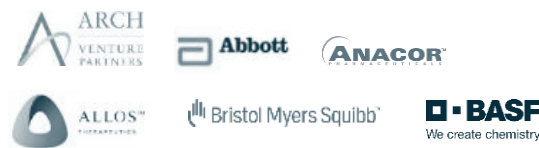
# Led by Experienced Company Builders and Leading Neuroscience Drug Developers

## Leadership



**Paul L. Berns**

Co-Founder, Chief Executive Officer & Chairman of Board of Directors



**Joshua Pinto, Ph.D.**

President



**Bill Aurora, Pharm.D.**

Chief Operating & Development Officer



**Carol Suh**

Chief Strategy Officer & Co-Founder



**Jason Duncan**

Chief Legal & Administrative Officer



**Nick Brandon, Ph.D.**

Chief Scientific Officer



**Michael Milligan**

Chief Financial Officer



**Lori Houle**

Chief Technical Operations & Quality Officer



**Mary Chamberlain-Tharp, Ph.D.**

Chief Business Officer



**Amy Sullivan**

Chief Human Resources Officer



**Pablo Gersberg**

Chief Information Officer



## Board of Directors

**Paul L. Berns**

Co-Founder, Chief Executive Officer, Chairman

**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



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

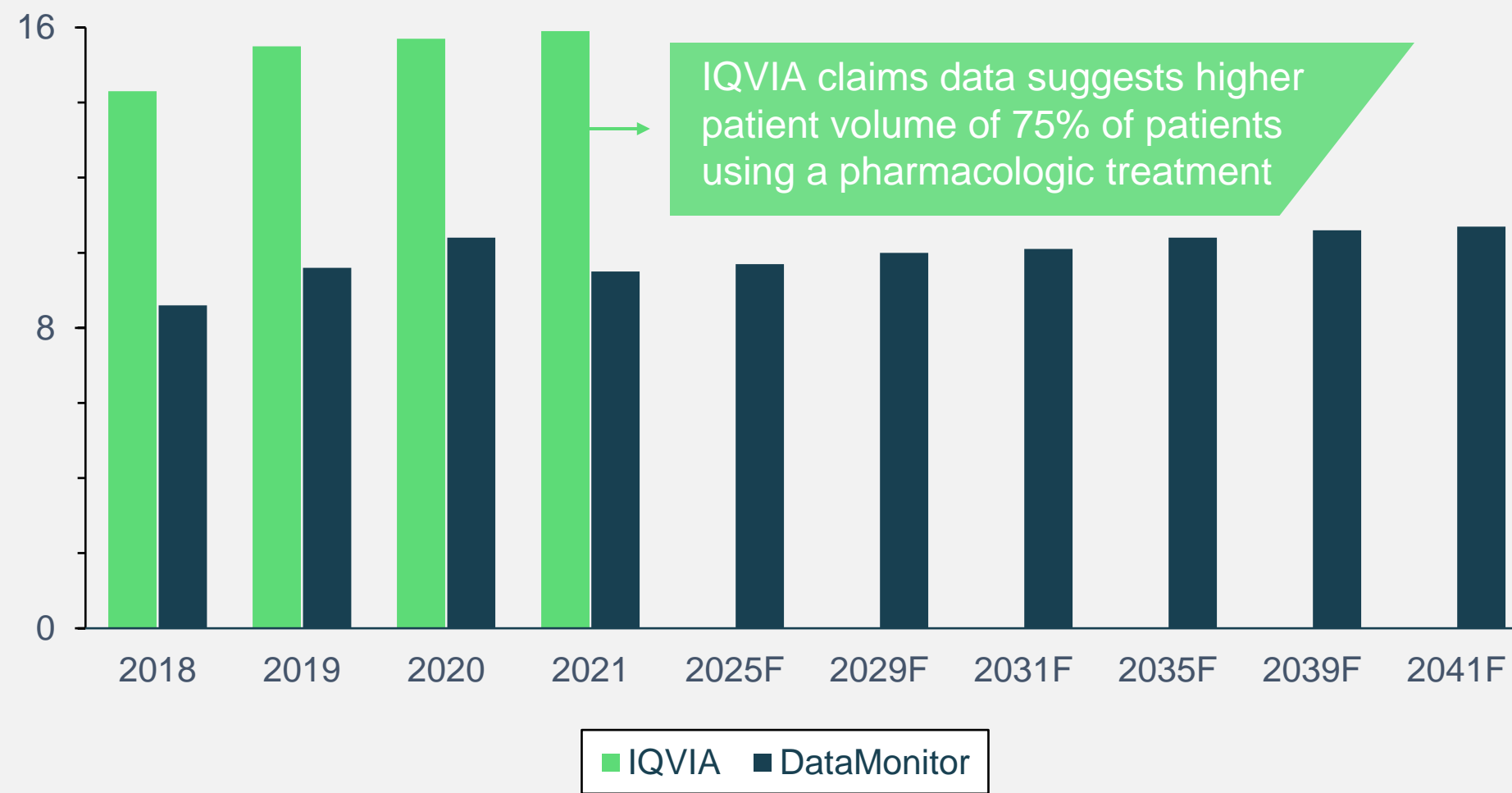
*CFB = change from baseline; LSMD = difference in LS mean change from baseline between navacaprant and placebo groups generated from mixed-effects model for repeated measures. Subgroup analysis for male or female are pre-specified.*



# 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  | CCAIE | 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% |

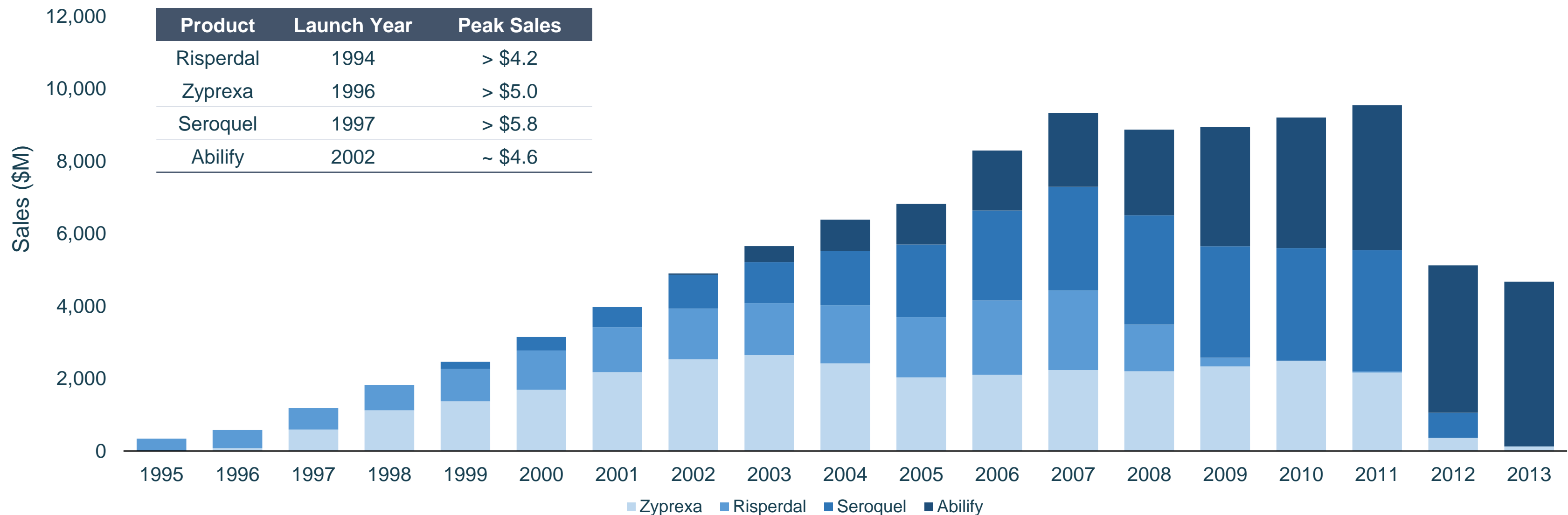
<sup>1</sup>Kern et al. Treatment patterns and sequences of pharmacotherapy for patients diagnosed with depression in the United States: 2014 through 2019. BMC Psychiatry. (2020) 20:4. U.S. Census Population Projections; DRG; Datamonitor; National Survey of Drug Use and Health 2018, 2019, 2020, 2021; Torre et al. (2021); L.E.K. research and analysis CCAIE = 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.

# Opportunity to Build a Leading Neuropsych Product Franchise

Potential for **broad indication expansion** in poorly served disorders with a **novel mechanism**

