



# **Redefining Neuroscience Drug Development**

**November 2024**

# 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, as well as its clinical trial and development plans; timing and expectations related to regulatory filings and interactions; its potential to create significant value; the market potential and oral-once daily nature of its compounds; 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; its ability to create significant value 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 and enrollment in our clinical trials; 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

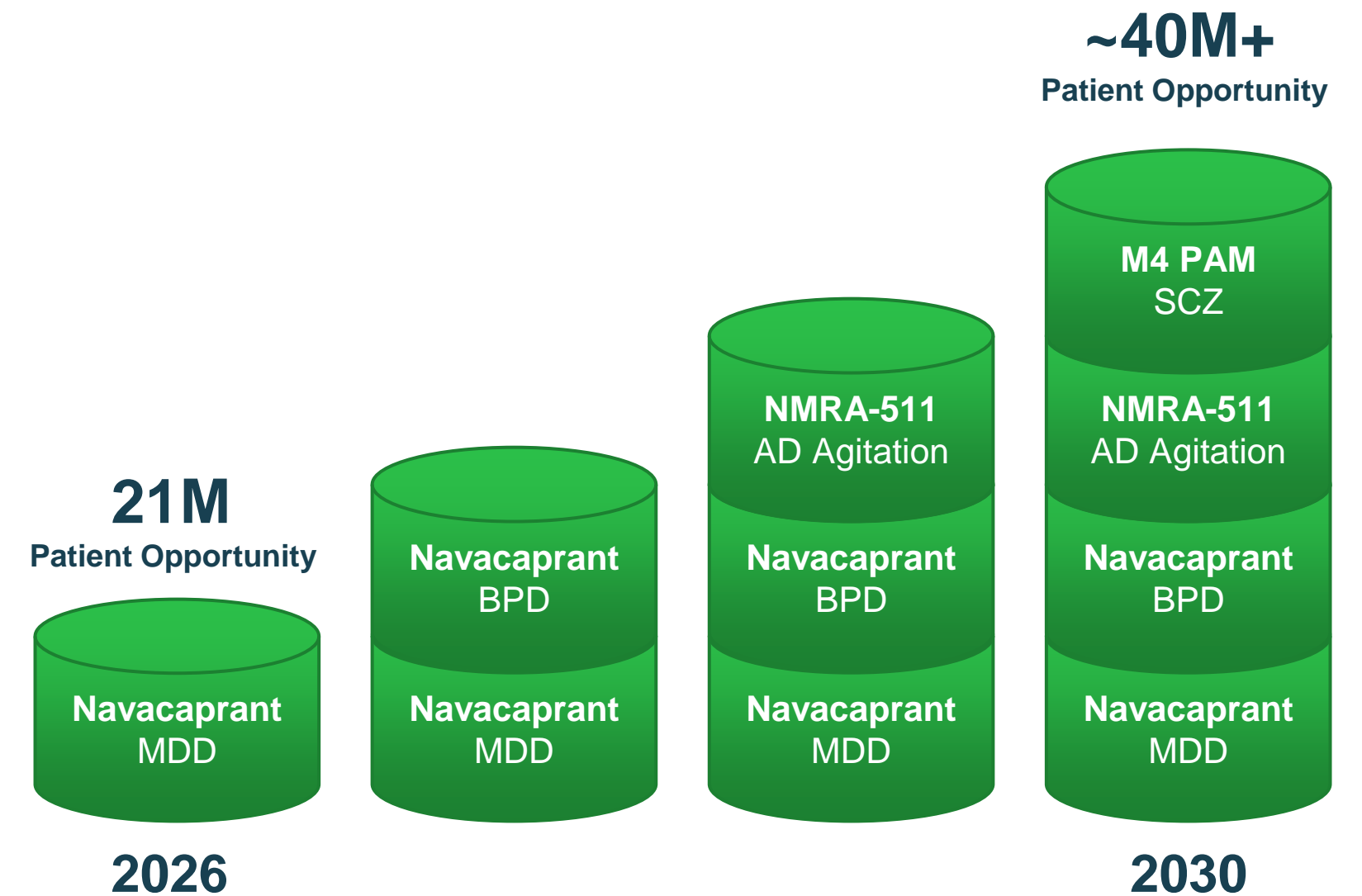
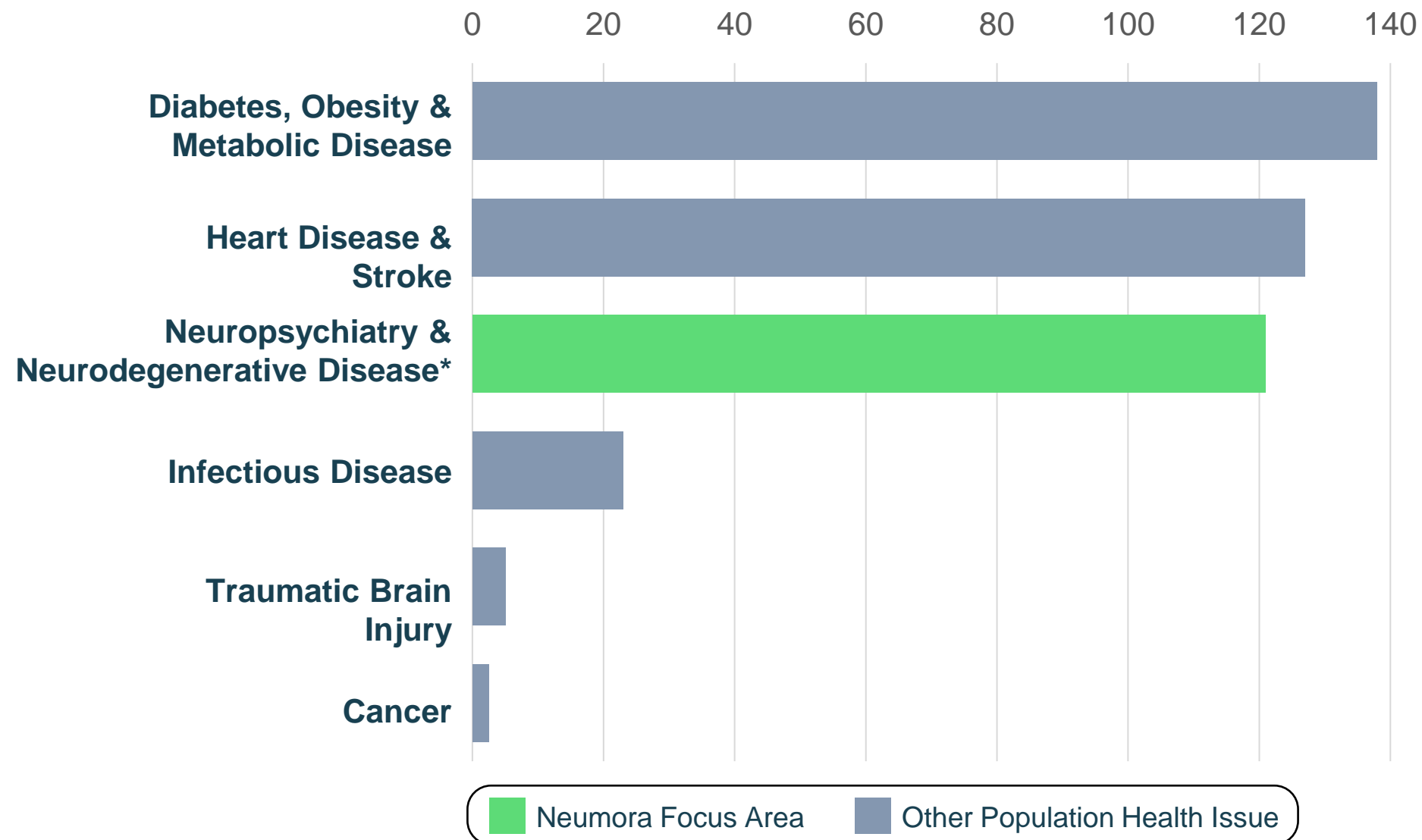


# Neumora is Tackling One of the Largest Population Health Challenges

Neumora's clinical-stage pipeline has potential to reach up to ~40M+ patients starting in 2026 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

# Redefining Neuroscience Drug Development



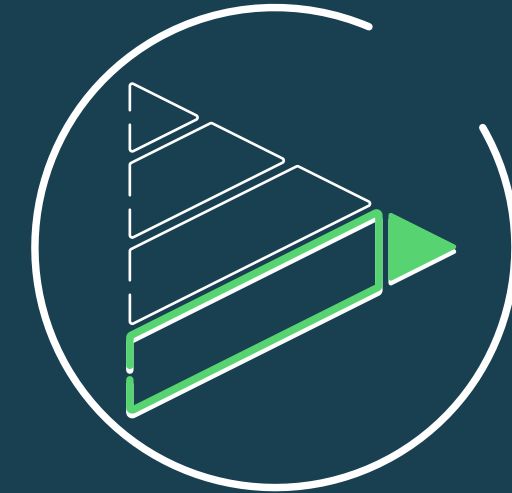
**World-class team with differentiated approach**

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



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

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



**Industry leading CNS pipeline**

**Five value-creating clinical catalysts through 2025**



# 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
- **Scaling** pipeline through internal discovery efforts and business development activities
- **Strong IP** with **worldwide rights** to all programs into the 2040s

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> 21M					<b>KOASTAL-1 topline data</b> <i>Around year-end</i>
	<b>Bipolar Depression</b> 7M					<b>KOASTAL-2, -3 topline data</b> 1H25
<b>NMRA-511</b> <i>V1aR Antagonist</i>	<b>Agitation in Alzheimer's Disease</b> 6M					<b>Phase 2 topline data</b> 2H25
<b>NMRA-266*</b> <i>M4 Modulator</i>	<b>Schizophrenia</b> 3M					<b>Phase 1b data</b> 2H25
<b>NMRA-M4R</b> <i>M4 Modulator</i>	<b>Schizophrenia</b> 3M					<b>Provide update on clinical hold</b> <i>as available</i>
<b>NMRA-NMDA</b> <i>NMDA Modulator</i>	<b>Schizophrenia</b> 3M					<b>Submit IND for next compound</b> 1H25
<b>Neurodegeneration Programs</b>						
<b>NMRA-CK1δ</b> <i>CK1δ Inhibitor</i>	<b>ALS/Alzheimer's Disease</b> 25K/6M					
<b>NMRA-NLRP3</b> <i>NLRP3 Inhibitor</i>	<b>Parkinson's Disease</b> 1M					
<b>NMRA-GCASE</b> <i>GCCase Activator</i>	<b>Parkinson's Disease</b> 1M					

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



# Navacaprant is a Kappa Opioid Receptor Antagonist with a Differentiated, Best-in-Class Clinical Profile

**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>  
median onset is ~32.5 years

**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>

**Navacaprant has the potential to reshape the treatment of depression; pivotal data expected around the end of 2024**

**Favorable safety and tolerability profile**

no weight gain, sexual dysfunction or other AEs commonly associated with ADT seen in Phase 2

**Potential to treat depressed mood and anhedonia**

designed to be easy-to-use as an oral, once-daily 80 mg dose without titration required

**Prescribers Prefer Profile in Market Research**

due to novel mechanism, dosing and side effect profile\*

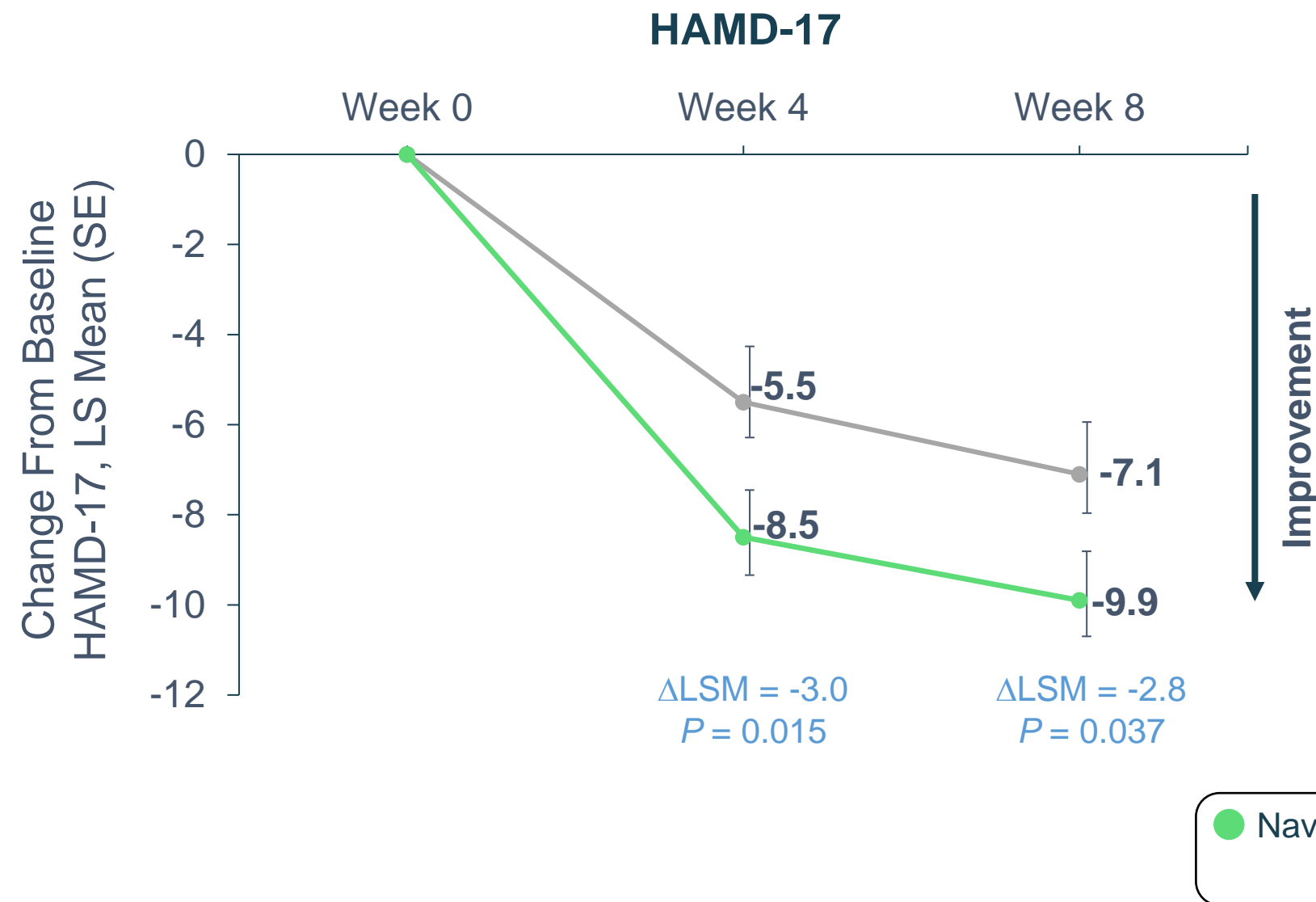
\*Independent market research, interviews, and analysis using anticipated navacaprant profile based on Phase 2 data conducted by L.E.K. Consulting, March 2023.

1. World Health Organization. Depressive disorder (depression). Published March 31, 2023. Accessed June 5, 2024. [https://www.who.int/news-room/fact-sheets/detail/depression#:~:text=An%20estimated%203.8%25%20of%20the,world%20have%20depression%20\(1\)](https://www.who.int/news-room/fact-sheets/detail/depression#:~:text=An%20estimated%203.8%25%20of%20the,world%20have%20depression%20(1)). 2. National Institute of Mental Health. Major depression. Published January 2022. Accessed May 9, 2022. <https://www.nimh.nih.gov/health/statistics/major-depression>. 3. Gaynes BN, et al. Cleve Clin J Med. 2008;75:57-66. 4. Corey-Lisle PK, et al. Arch Intern Med. 2004;164:1197-1204. 5. Cartwright C, et al. Patient Prefer Adherence. 2016;10:1401-1407. 6. Ramanuj P, et al. BMJ. 2019;365:1835. 7. Moret C, et al. J Psychopharmacol. 2009;23:967-974. 8. Khazanov GK, et al. Behav Res Ther. 2020;125:103507. 9. 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. ADT = antidepressant therapy; AE = adverse events

# First Program to Demonstrate Improvement in Both Symptoms of Depressed Mood and Anhedonia

*Anhedonia is the lack of interest, enjoyment or pleasure*

## Robust Phase 2 Data in Moderate to Severe Patients



Navacaprant improved depressed mood with results in-line with approved agents



Navacaprant improved anhedonia, a symptom not addressed by approved agents

Note: Graphs depict prespecified statistical sensitivity analysis for moderate-to-severe patients (n=100; baseline HAMD-17  $\geq$  22). HAMD-17 = 17-Item Hamilton Rating Scale for Depression; MDD = Major Depressive Disorder; SHAPS= Snaith-Hamilton Pleasure Scale. Study included 40 sites in the U.S., and enrolled 204 patients; 100 patients included in pre-specified moderate-to-severe population.



# Favorable Safety Profile Demonstrated in Phase 2

**Navacaprant was well tolerated and was not associated with weight gain or sexual dysfunction**

<b>TEAEs Incidence</b> (≥2% in either treatment group)	<b>Placebo</b> n=102	<b>Navacaprant</b> n=102
<b>Preferred Terms</b>	<b>n (%)</b>	<b>n (%)</b>
Headache	5 (4.9)	5 (4.9)
COVID-19	3 (2.9)	4 (3.9)
Nausea	1 (1.0)	5 (4.9)
Diarrhea	3 (2.9)	2 (2.0)
Upper respiratory tract infection	1 (1.0)	3 (2.9)

**Navacaprant was not associated with side effects that cause discontinuation of approved treatments**



# Navacaprant is a Differentiated Kappa Opioid Receptor Antagonist

1

## Development Approach

navacaprant is being developed as a monotherapy

2

## Pharmacology

navacaprant is more selective for KOR over MOR and demonstrated greater RO over 24 hrs

3

## Efficacy

navacaprant demonstrated robust effect on HAMD and SHAPS in Ph 2

4

## Safety

navacaprant was not associated with MOR-related AEs

**Navacaprant is investigational and has not been evaluated in a head-to-head clinical trial against any other kappa opioid receptor antagonist.**

eITT = enriched population; consists of randomized lead-in PBO non-responders receiving  $\geq 1$  dose of study medication & having  $\geq 1$  post-treatment baseline efficacy measurement; non responders:  $< 30\%$  decrease in MADRS during PBO lead-in  
fITT = full intention-to-treat analysis set; consists of all randomized subjects receiving  $\geq 1$  dose of study medication & having  $\geq 1$  post-treatment baseline efficacy measurement

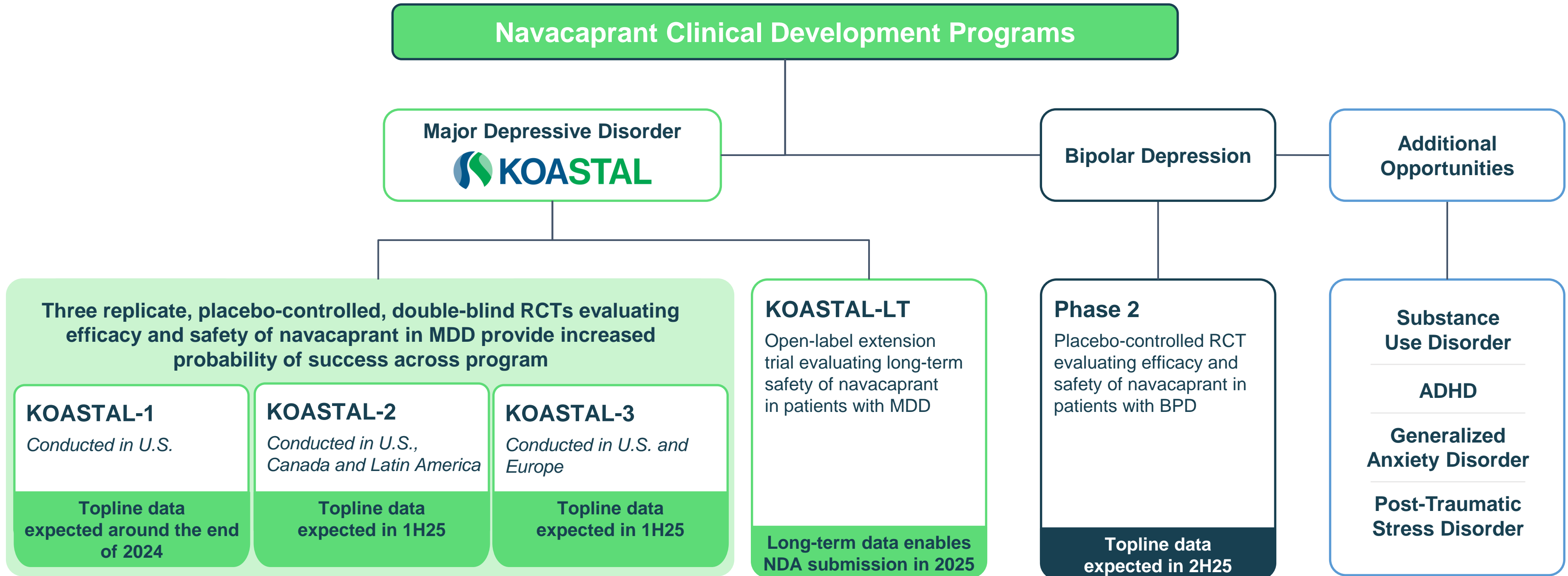
KOR, kappa opioid receptor; MOR, mu opioid receptor;  $t_{1/2}$ , half-life; NHP, non-human primate; RO, receptor occupancy; MDD, Major Depressive Disorder

1. Guerrero M, et al. *J Med Chem*. 2019;62(4):1761-1780. 2. Neumora Data on File. 3. Rorick-Kehn LM, et al. *Neuropharmacology*. 2014;77:131-144. 4. Lowe SL, et al. *J Clin Pharmacol*. 2014;54(9):968-978. 5. [www.clinicaltrials.gov](https://www.clinicaltrials.gov) accessed 28 JAN 24

6. Schmidt ME, et al. Efficacy and safety of aticaprant, a kappa opioid receptor antagonist, adjunctive to oral SSRI/SNRI antidepressant in major depressive disorder: Results of a phase 2a randomized, double-blind, placebo-controlled study.

Presented at: American Society of Clinical Psychopharmacology; May 29-June 2, 2023; Miami Beach., <sup>7</sup>EU Clinical Trials Register; <sup>8</sup>US Patent Document.

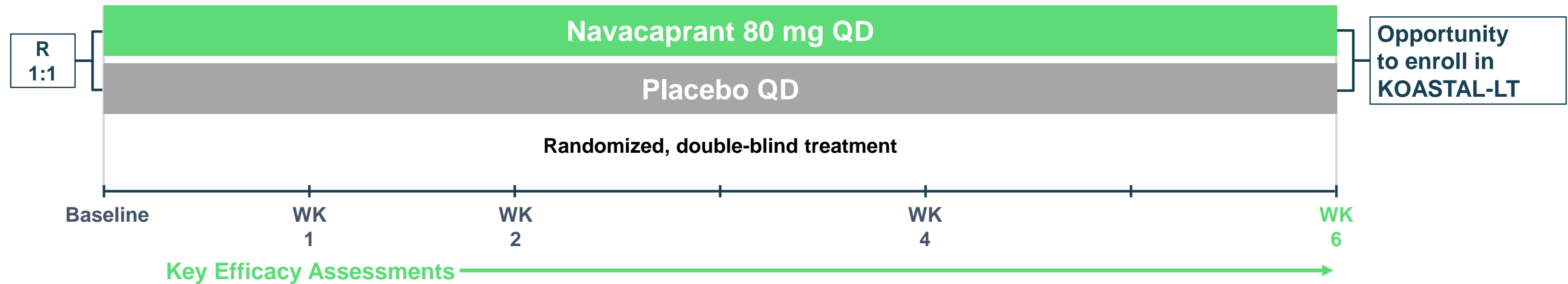
# Near-term Clinical Development Plan Focused on MDD and Bipolar Depression with Opportunity for Further Expansion



# KOASTAL Pivotal Study Design Well Suited for Navacaprant Pharmacology



## 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>		
<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>	Other Secondary Endpoints Include:	<ul style="list-style-type: none"> <li><math>\Delta</math> from baseline to each timepoint in:                             <ul style="list-style-type: none"> <li>CGI-S and CGI-I</li> <li>PHQ-9</li> <li>HAM-A</li> <li>SDS</li> </ul> </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><math>\Delta</math> from baseline to each timepoint in:                             <ul style="list-style-type: none"> <li>EQ-5D 5L</li> <li>WPAI-GH</li> </ul> </li> </ul>



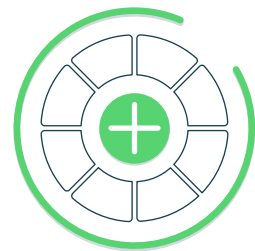
\*Safety Assessments include Change in Sexual Functioning Questionnaire (CSFQ-14)  
 $\Delta$  = Change; CGI-I = Clinical Global Impression-Improvement scale; CGI-S = Clinical Global Impression-Severity scale; EQ-5D 5L = EuroQol-5D 5L; HAM-A = Hamilton Anxiety Rating Scale; MADRS = Montgomery-Åsberg 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.

# 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 ≥ 14)	Moderate-to-severe depression (MADRS ≥ 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	

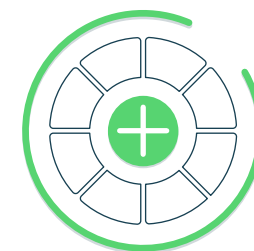


# Enhancing KOASTAL with Digital Applications



## Track

Automatically compiles site-level and patient-level data across each KOASTAL Study and calculates site-level metrics of site activity



## Project

Utilizes data from KOASTAL tracker to simulate future screening and enrollment predictions



## Explore

Visualizes blinded clinical data from baseline and follow-up visits for data quality-control purposes

Leveraging data-driven applications developed in-house to enhance accuracy of KOASTAL program

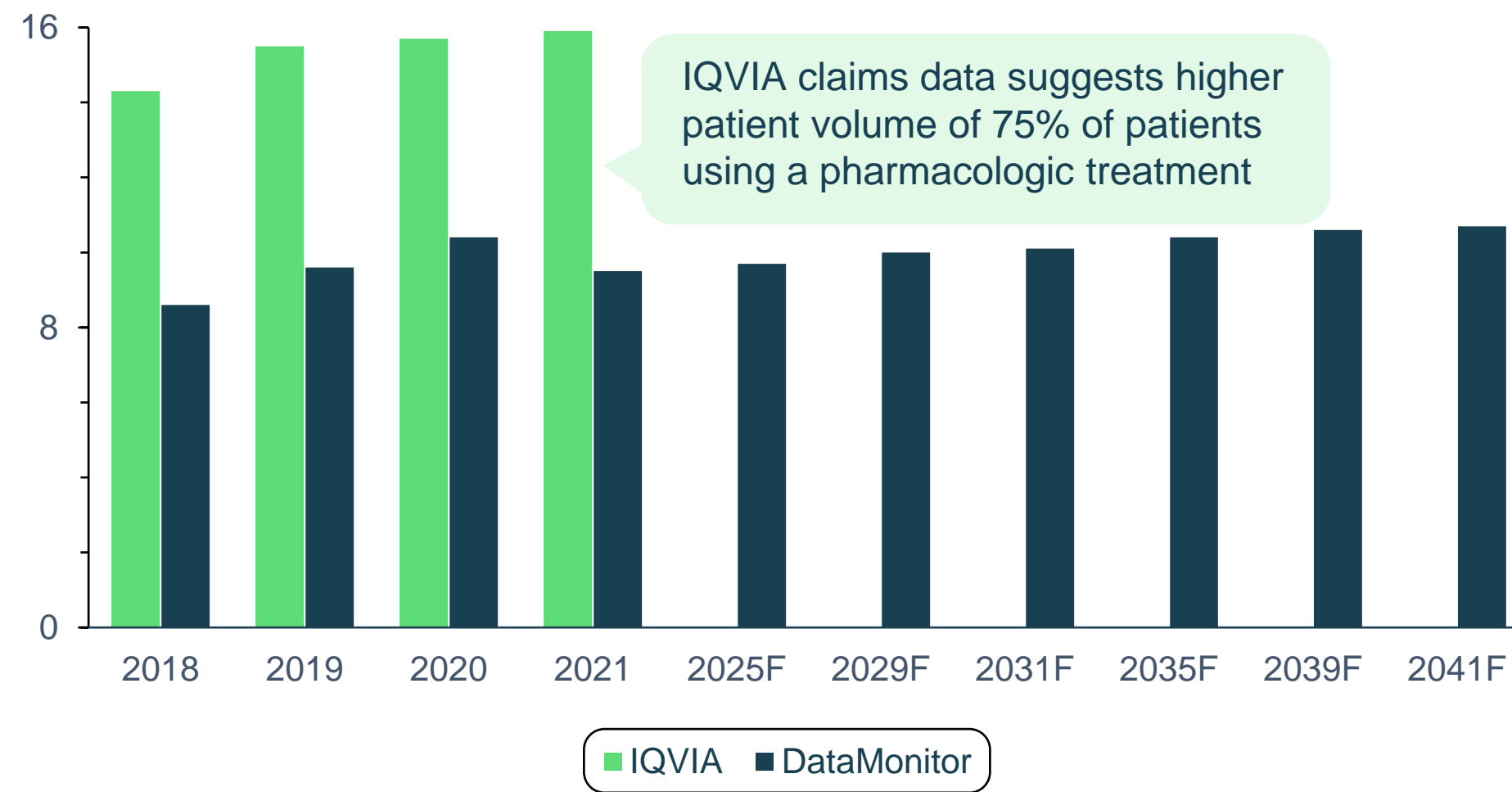


# Navacaprant Would Enter Large MDD Market with a Highly Differentiated Profile

## 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>

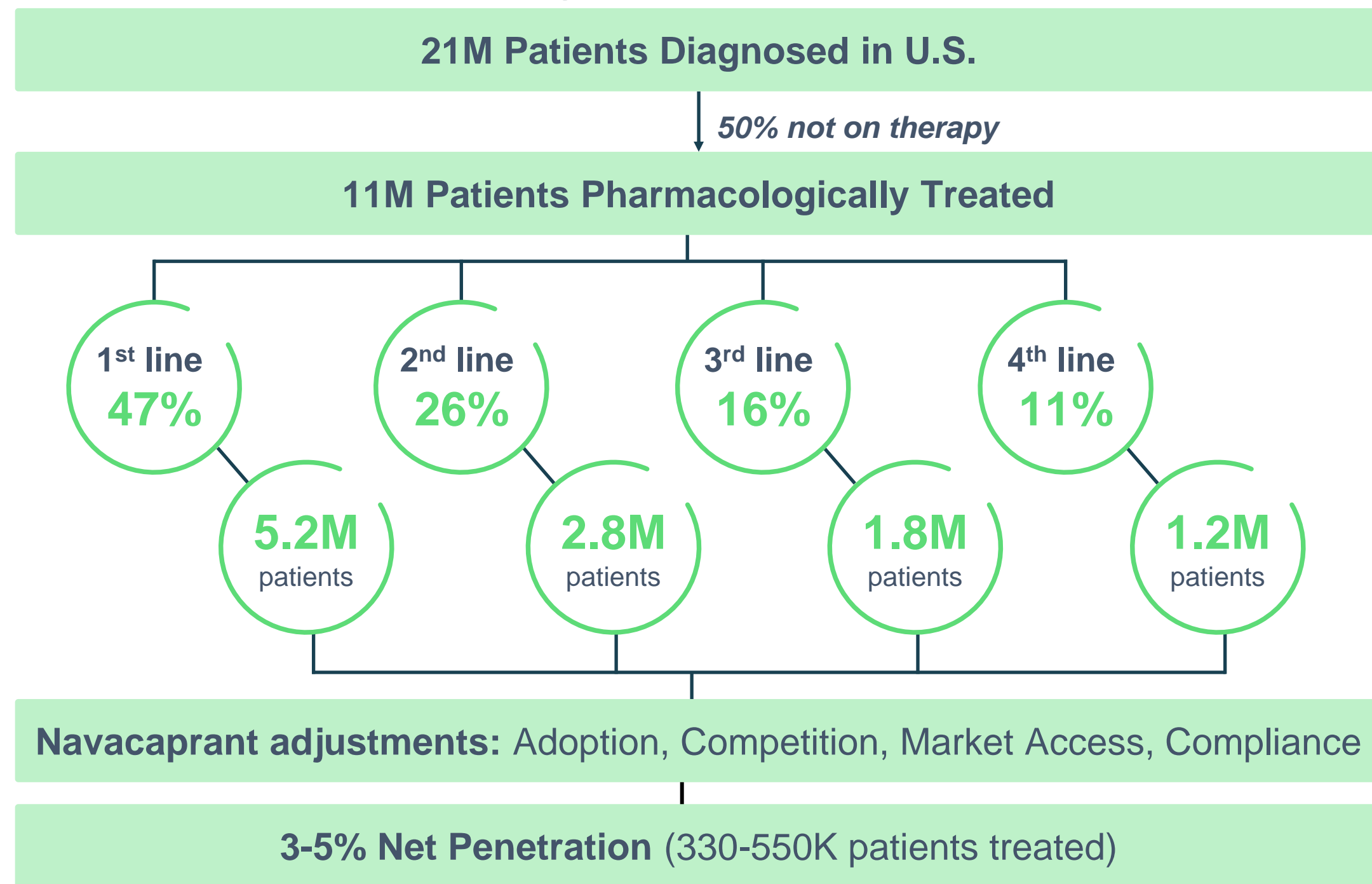
### Monotherapy treatment rates across lines of therapy

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

# Navacaprant: MDD Market in U.S. Provides Potential Large Blockbuster Opportunity for Differentiated Product with Novel Mechanism of Action

## MDD Market Represents Large Patient Opportunity



### Upside drivers



Safer agent drives treatment seeking



Patients fast fail 1<sup>st</sup> line



Safer agent drives compliance



Inflation adjusted pricing

## Neuropsychology Pricing Catalogues

	WAC (per month)	GTN discount
Rexulti	\$1,419	~36%
Vraylar	\$1,378	~32%
Nuplazid	\$4,565	~20%
Auvelity	\$1,080	~50%

“...is a combo of two products that exist; I would expect a pretty steep discount, for example 50-60% is going to be what it takes ... [navacaprant] is a lower discount since it is a unique MOA ...”

– Executive, Magellan

“... 15-25% or up to 30% are reasonable discounts [for navacaprant] a few years after launch, given it's a new MoA as an antidepressant, that's a big benefit ...”

– Pharmacy Director, Anthem BCBS OH





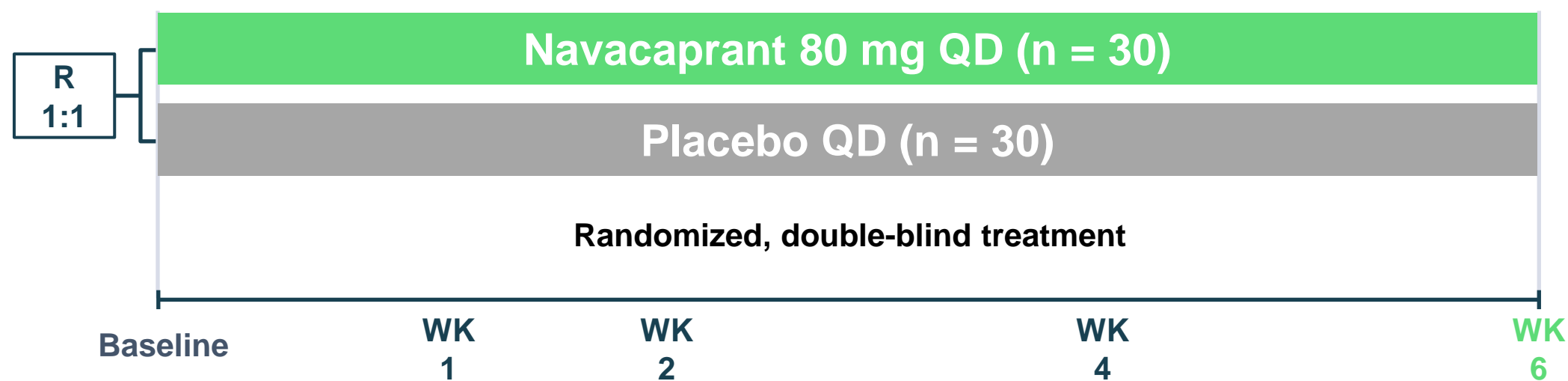
# Navacaprant Well-Suited for Evaluation in Bipolar Depression

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
- 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

<b>Inclusion Criteria:</b>	<ul style="list-style-type: none"><li>• Adults ages 18 – 65 experiencing an MDE associated with bipolar II depression</li><li>• MADRS <math>\geq</math> 25 at baseline</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>Other Endpoints Include*:</b>	<p><math>\Delta</math> from baseline to Week 6 in:</p> <ul style="list-style-type: none"><li>• SHAPS total score</li><li>• PGIS-Anhedonia total score</li><li>• CGI-BP-S 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 navacaprant in bipolar depression</li></ul>

\*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

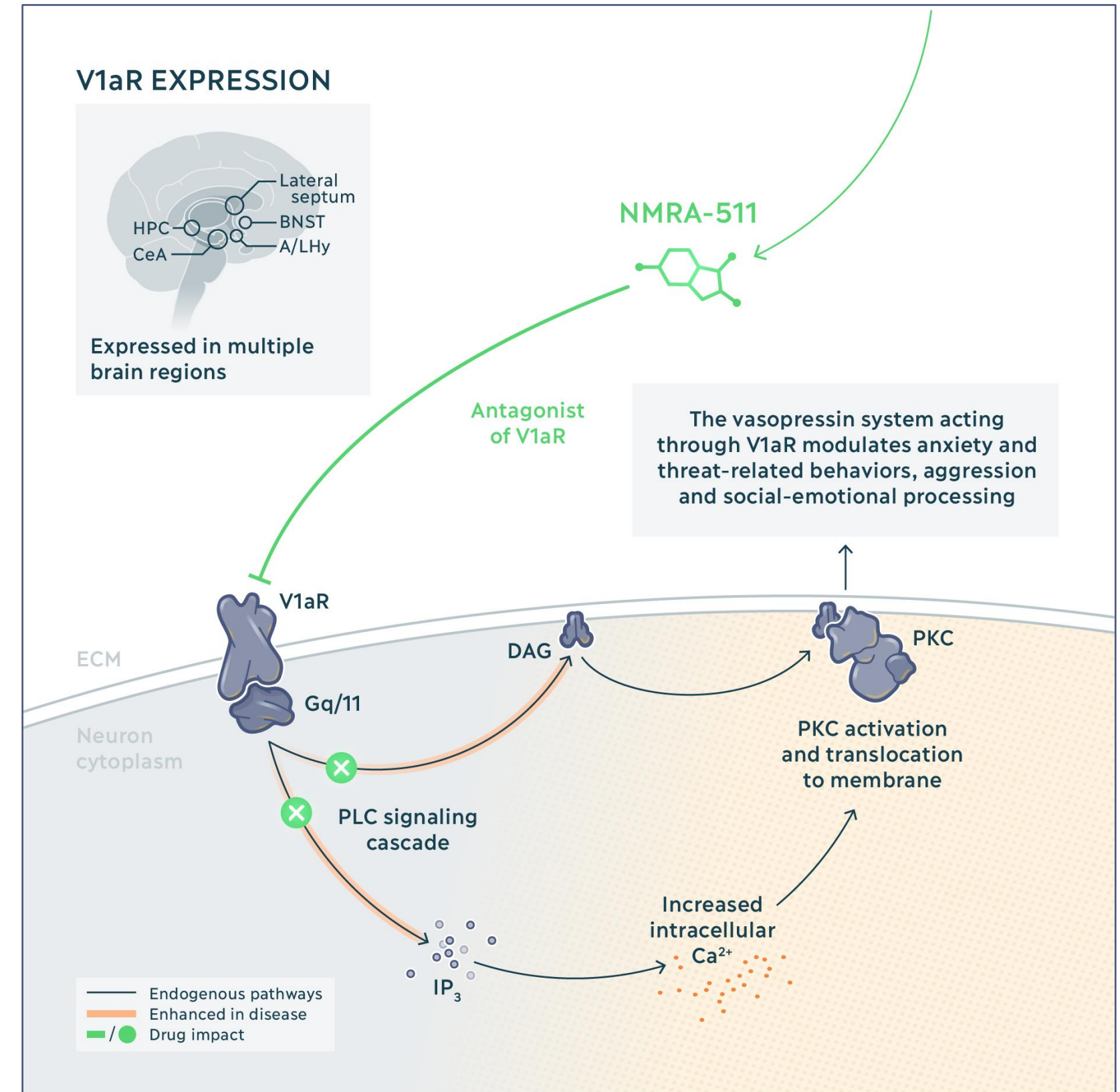
Phase 1b study underway with data anticipated in 2H25

## Drug Profile

Oral, BID dosing

## Strong IP Protection

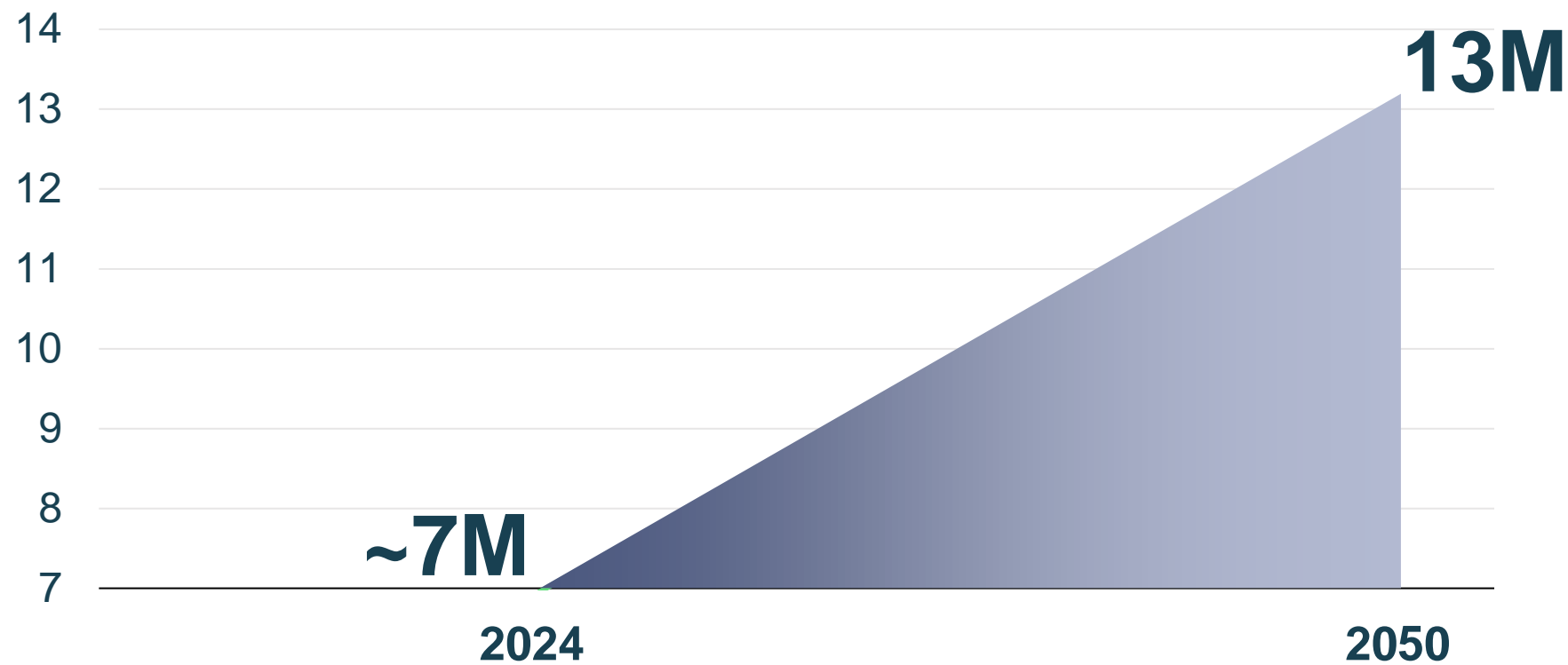
Expect exclusivity through 2042+, based on composition of matter protection and estimated patent term extension



# 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>

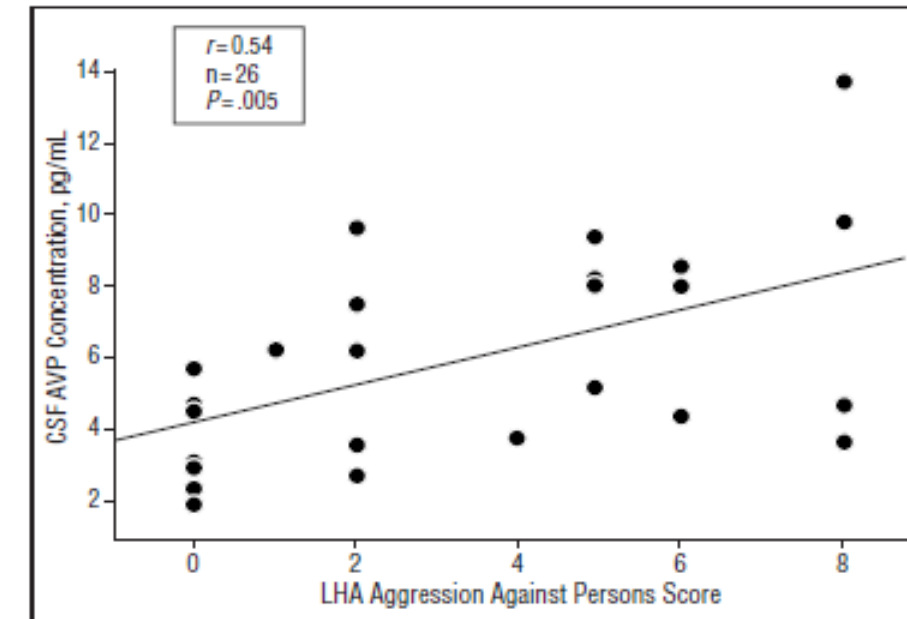


## In healthy volunteers, vasopressin enhances reactivity to threatening stimuli and disrupts emotional control<sup>1-2</sup>

- 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

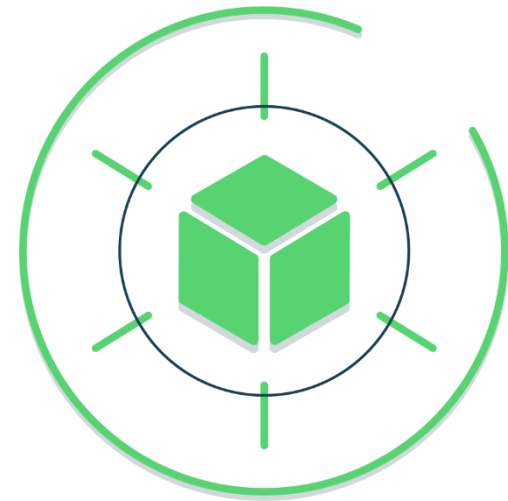
<sup>1</sup>Ebstein et al., 2009, New York Academy of Sciences.; <sup>2</sup>Thompson et al., 2006, PNAS.; <sup>3</sup>Insel et al., 2010, *Neuron Review*, PNAS; <sup>4</sup>Carter et al., 1995, *Neuroscience Biobehavioral Review*.; <sup>5</sup>Wang et al., 1994, PNAS.; <sup>6</sup>Veenema and Neumann, 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
- EEG signature in marmoset translated to humans in a Phase 1 study



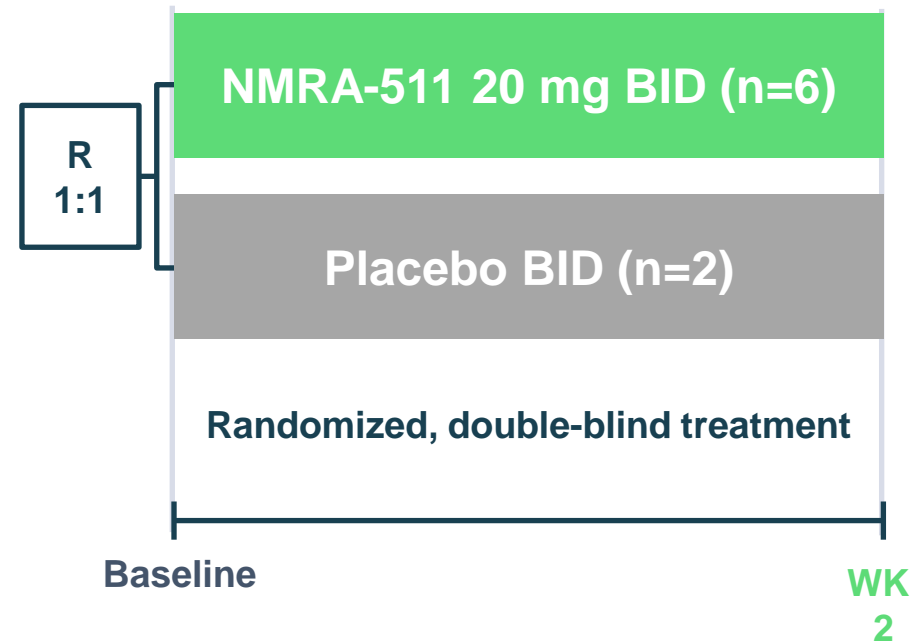
## PK and Safety Data from Phase 1 Support Advancement<sup>1</sup>

- NMRA-511 was safe and very well-tolerated in Phase 1 SAD/MAD study
- Pilot EEG collection in Phase 1 was consistent with marmoset data suggestive of a central PD effect

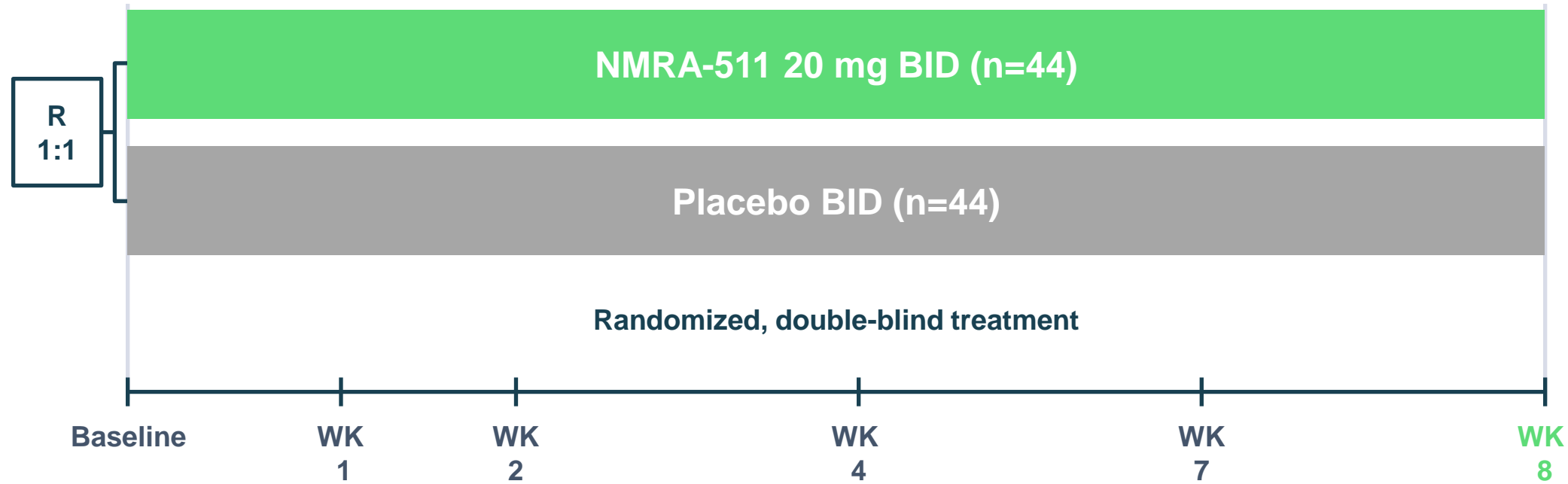


# NMRA-511 Signal Seeking Study in Alzheimer's Disease Agitation

## 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

### Epidemiology

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

### Target Drug Profile

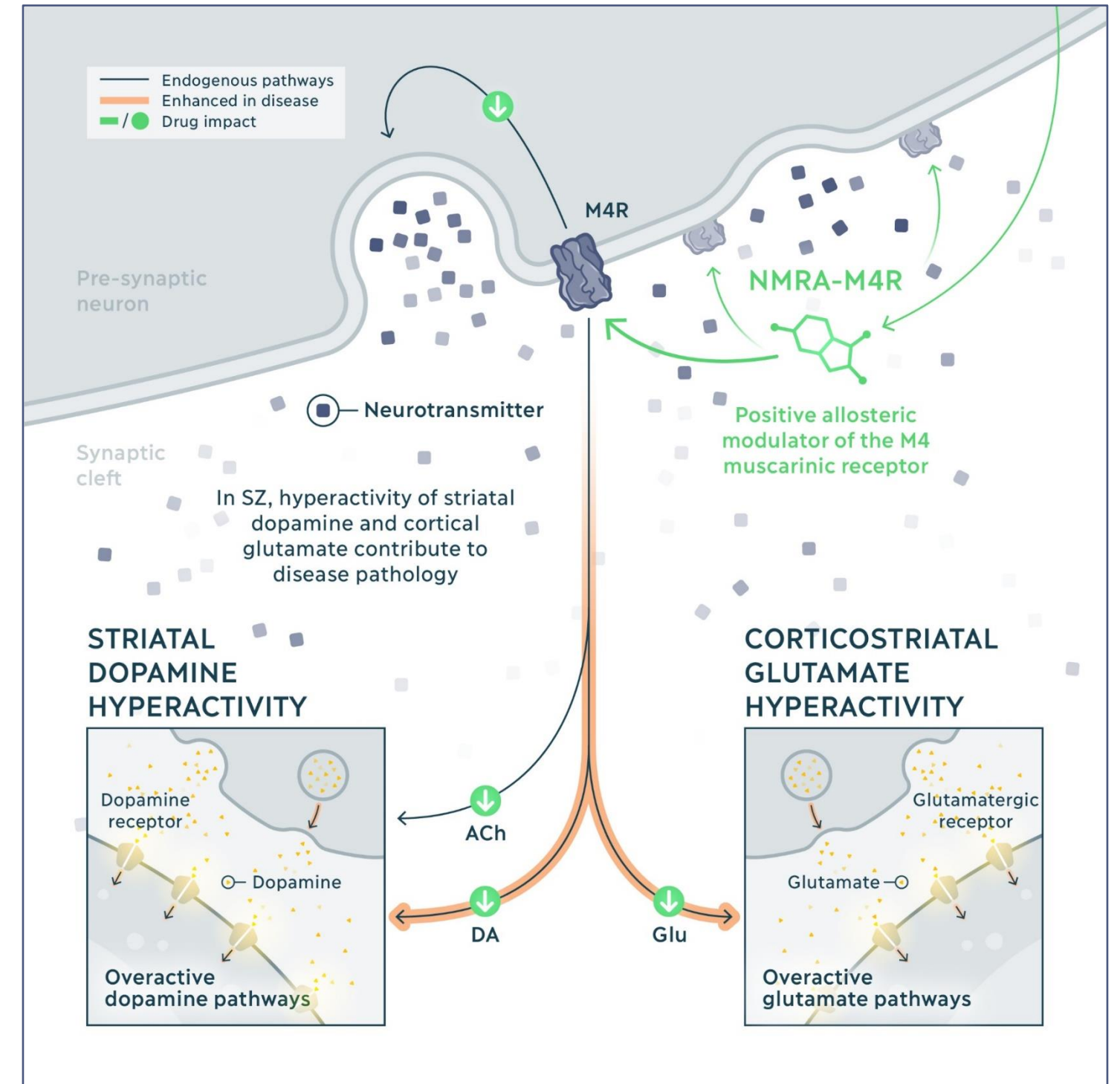
Oral, once-daily

### 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

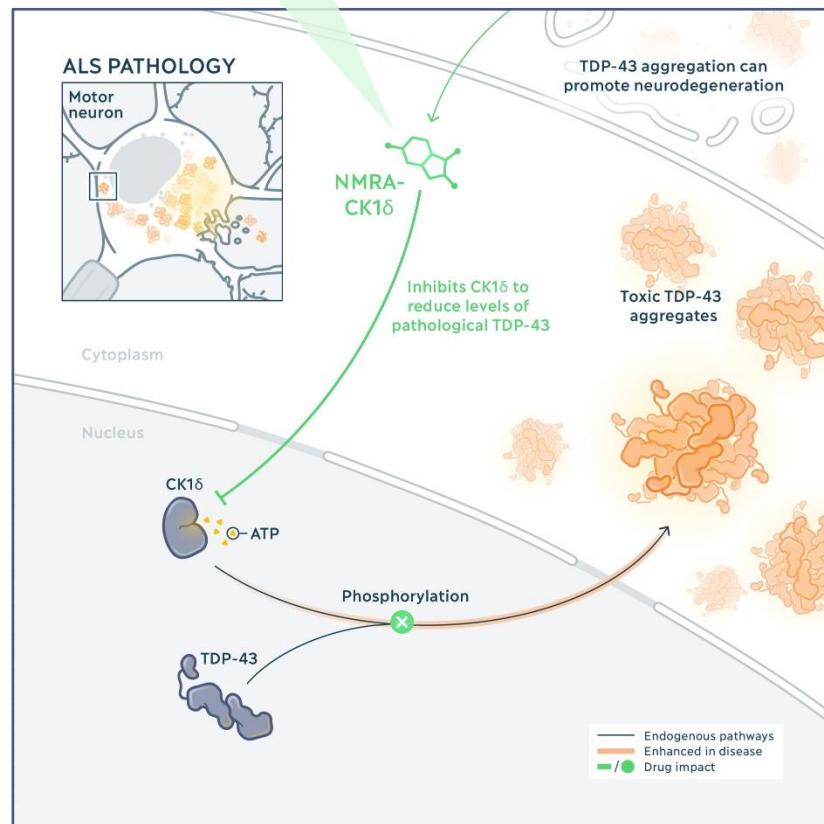
## NMRA-CK1δ

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



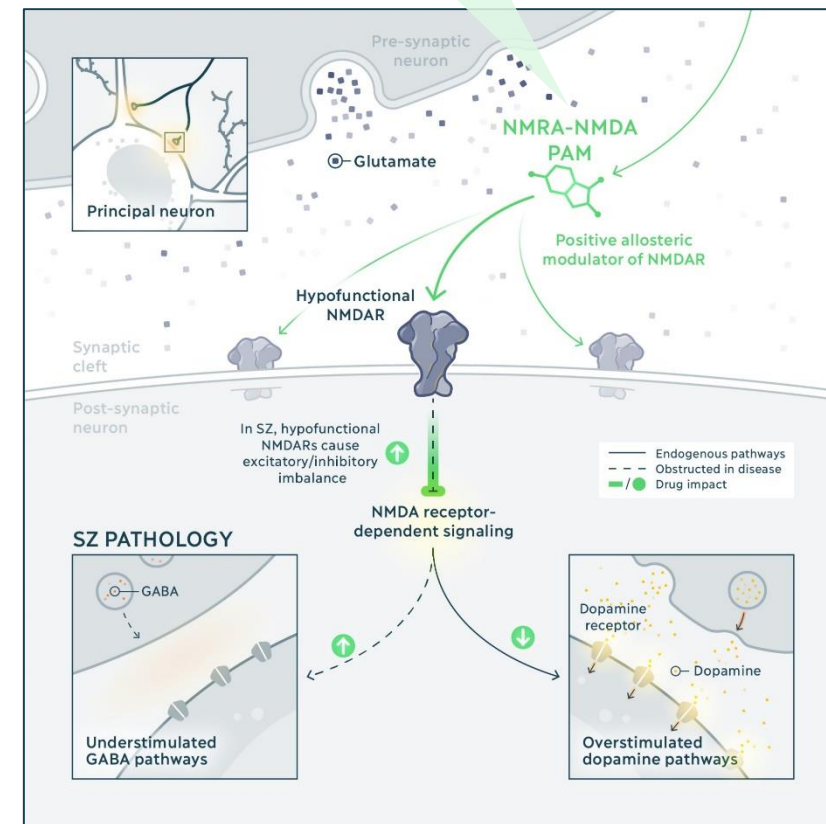
## NMRA-NMDA

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



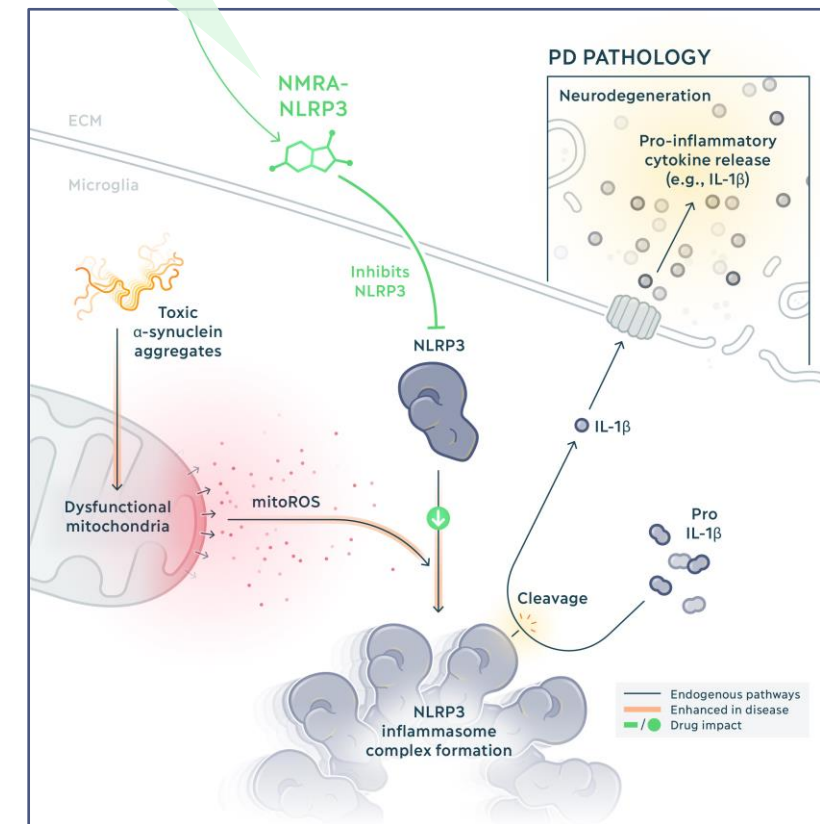
## NMRA-NLRP3

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



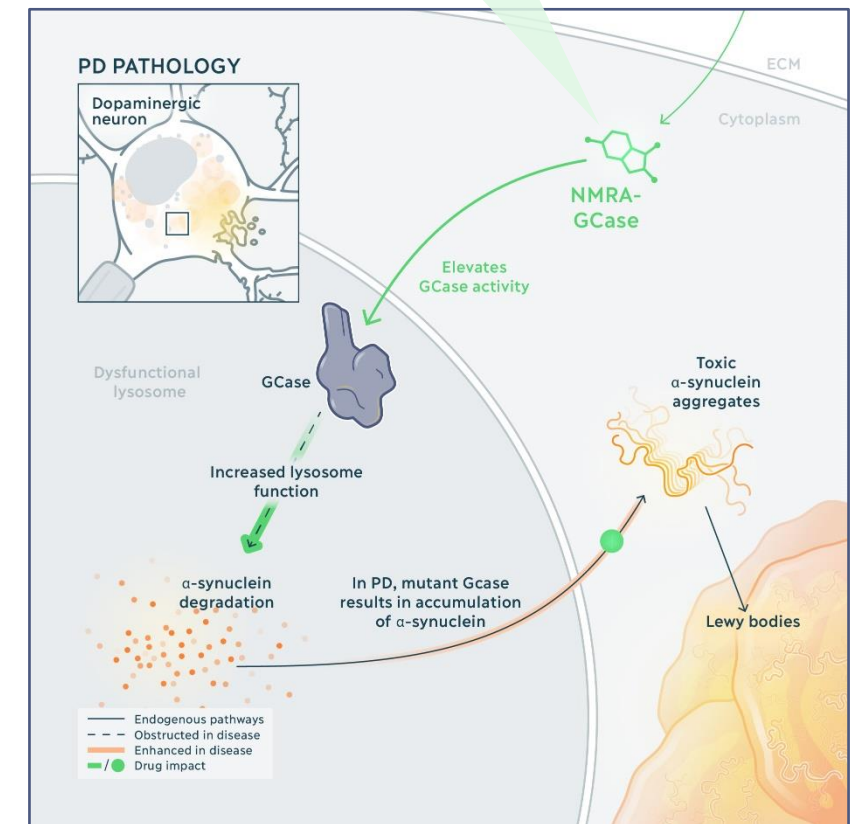
## NMRA-GCase

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





# 2024 and 2025 Are Catalyst Rich Years for Neumora

## INDUSTRY-LEADING CNS PIPELINE

Five value-creating clinical catalysts through 2025

## BUILT AT SCALE

Cash runway into 2026 supporting company growth

## WORLD CLASS TEAM & APPROACH

Maximizing probability of success with team and proprietary approach

2024

### Navacaprant

- Topline data readout from KOASTAL-1 study in MDD (around the end of 2024) ①
- ✓ Initiate Phase 2 clinical study in BPD (study initiated in May)

### NMRA-511

- ✓ Initiate study in Alzheimer's disease agitation (study initiated in June)

2025

### Navacaprant

- Data readout from KOASTAL-2 in MDD (1H25) ②
- Data readout from KOASTAL-3 study in MDD (1H25) ③
- NDA submission in MDD (2025)
- Topline data readout from Phase 2 in BPD (2H25) ④

### NMRA-511

- Topline data readout in Alzheimer's disease agitation (2025) ⑤

### M4 PAM Franchise

- IND submission for a NMRA-M4R compound (1H25)



# Appendix



# Led by Experienced Company Builders and Leading Neuroscience Drug Developers

## Leadership



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

ARCH VENTURE PARTNERS  
Abbott ANACOR  
ALLOS<sup>®</sup> Bristol Myers Squibb<sup>®</sup> BASF



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

CREDIT SUISSE Lilly  
PIPER SANDLER



**Kaya Pai Panandiker**  
Chief Commercial Officer

cerevel Lundbeck



**Jason Duncan**  
Chief Legal Officer

Albireo<sup>®</sup> STALLERGENES GREER  
sobi



**Amy Sullivan**  
Chief Human Resources Officer

sobi Takeda  
Shire



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

ACELYRIN<sup>®</sup> APTINYX<sup>®</sup>



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

Dermira<sup>®</sup> NEUROCRINE  
MERCCK AMGEN



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

MERCCK jnana  
Pfizer AstraZeneca



**Lori Houle**  
Chief Quality Officer

NIR SAREPTA  
Dermira



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

ARCH VENTURE PARTNERS ORBITAL BOUNDLESS BIO  
Sana Autobahn esk



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

AMGEN Abbott



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

abbvie Lilly



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

ANOKION FREQUENCY THERAPEUTICS  
Biogen

## 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



# Clinical Stage Neuropsychiatry Portfolio Pursuing Large Markets with Clinically Validated Targets

Differentiated programs with broad potential



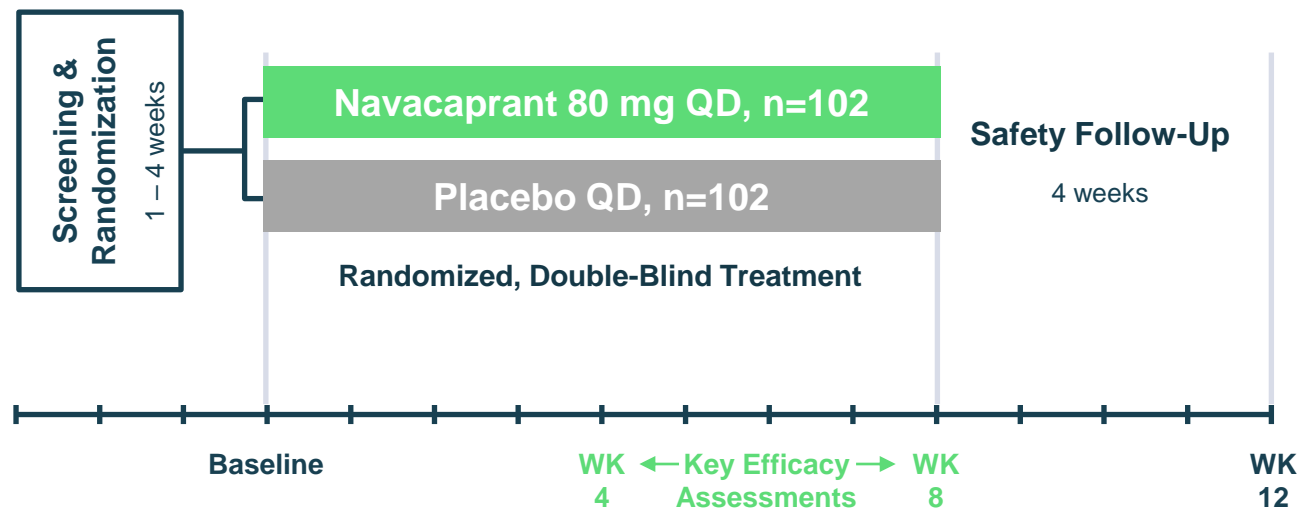
	Navacaprant	NMRA-511	M4 PAM Franchise
Mechanism	Kappa Opioid Receptor Antagonist	V1a Receptor Antagonist	M4 Receptor Positive Allosteric Modulator
Stage	Phase 3	Phase 1b	Phase 1, Preclinical
Best-in-Class Pharmacology	✓	✓	✓
First-in-Class Mechanism	✓	✓	
Market Opportunity	75M+ patients	20M+ patients	25M+ patients
IP Protection	Composition of Matter into 2041+	Composition of Matter into 2043+	Composition of Matter into 2042+
Clinical Validation	✓		✓
Market Participants	 		 
Multi-Billion Sales Potential	✓	✓	✓



# Navacaprant Phase 2a Trial Design Amended by Neumora after Acquisition of BlackThorn

Amendments included expanding enrollment criteria to allow patients with moderate-to-severe MDD

## Inherited from BlackThorn



## Initial Study Inclusion (pre-Neumora)

- Enrollment focused on mild-to-moderate patients (baseline HAMD-17 range 14-22)
- Target enrollment of 120 (20 sites)
- Efficacy assessments at week 4 and week 8



## Neumora Amended to Fit With MDD Studies

Product Candidate	MDD Severity Criteria
SAGE-217	HAMD-17 $\geq$ 24
PRAX-114	HAMD-17 $\geq$ 23
Aticaprant	MADRS $\geq$ 25
MD-120	HAMD-17 $\geq$ 20
Lumateperone	MADRS $\geq$ 24

*Phase 3 trials posted to clinicaltrials.gov after Jan 1, 2020, and have been completed or currently enrolling, excludes trials without disclosed criteria*

## Neumora Amendments to Optimize Trial

- Increased HAMD-17 inclusion to focus on moderate-to-severe patients (baseline HAMD-17 range 22-30)
- Increased target enrollment to 204 (40 sites)

## Study Endpoints

### Primary Endpoint:

- $\Delta$  from Baseline to WK 8 on the HAMD-17 (depression)

### NMRA Prespecified Subgroup Analysis of Primary Endpoint

- $\Delta$  from Baseline to WK 8 on the HAMD-17  $\geq$  22 at baseline

### Secondary Endpoints:

- % of HAMD-17 responders ( $\geq$ 50%  $\downarrow$ )
- $\Delta$  from Baseline in SHAPS (anhedonia)
- $\Delta$  from Baseline in HAM-A (anxiety)

### Final Efficacy Population:

- N=171 patients<sup>1</sup>
- N=100 moderate-to-severe MDD<sup>2</sup>

1) Patients with a baseline HAMD-17 total score that received at least one dose of study drug and had at least one post-baseline HAMD-17 assessment

2) Baseline HAMD-17 score  $\geq$  22

# Navacaprant Demonstrated Efficacy Across Broad Range of Treatment Outcome Measures in Moderate-to-Severe Population

	Week 4 Difference (p-value)	Week 8 Difference (p-value)
<b>Depressive Symptom Improvement</b>		
HAMD-17 Total Score Change from Baseline	-3.0 (0.015)	-2.8 (0.037)
HAMD-17 Response Rate % ≥50% Reduction in HAMD-17 from Baseline	21.4% (0.010)	25.9% (0.007)
Remission HAMD-17 Score ≤7	14.9% (0.014)	20.3% (0.005)
HAMD-6 Score (Core Symptoms) Change from Baseline in HAMD-6	-2.4 ( $<0.001$ )	-1.9 (0.013)
CGI-I % of Patients with Very Much / Much Improvement	12.4% (0.178)	19.0% (0.056)
CGI-S Change from Baseline	NA	-0.5 (0.041)
<b>Anhedonia Symptom Improvement</b>		
SHAPS Total Score Change from Baseline	-2.4 (0.071)	-4.8 ( $<0.001$ )
<b>Anxiety Symptom Improvement</b>		
HAM-A Total Score Change from Baseline	-2.4 (0.035)	-1.6 (0.197)
<b>Functional Improvement</b>		
SDS Total Score Change from Baseline	-2.5 (0.146)	-4.0 (0.013)

Note: Prespecified statistical sensitivity analysis for moderate-to-severe patients (HAMD-17  $\geq$  22)



# Navacaprant is Differentiated from Aticaprant

## Key Areas of Differentiation from Aticaprant:

- 1 Development Approach:** navacaprant is being developed as a monotherapy
- 2 Pharmacology:** navacaprant is more selective for KOR over MOR and demonstrated greater RO over 24 hrs
- 3 Efficacy:** navacaprant demonstrated robust effect on HAMD and SHAPS in Phase 2
- 4 Safety:** navacaprant was not associated with MOR-related AEs

	Navacaprant <sup>1,2</sup>	Aticaprant <sup>3-8</sup>
<b>Target Indication/s</b> <b>1</b>	Monotherapy for Major Depressive Disorder & Bipolar Depression at 80 mg	Adjunctive therapy for MDD at 10mg
<b>Development Status</b>	Three MDD Phase 3 studies (KOSTAL-1, -2 and -3) underway Initiation of BPD Phase 2 planned for 2Q24	Phase 3 studies underway
<b>Pharmacology:</b> •Binding Selectivity (KOR/MOR) •KOR RO at Therapeutic Dose •Human t <sub>1/2</sub> <b>2</b>	<ul style="list-style-type: none"> <li>• ~310x</li> <li>• 95-87% coverage for ~24 hrs</li> <li>• &gt;30 hrs</li> </ul>	<ul style="list-style-type: none"> <li>• ~30x</li> <li>• 94-73% coverage for ~24 hrs</li> <li>• 30 – 40 hrs</li> </ul>
<b>Phase 2 Efficacy</b> <b>3</b>	In mod/severe population (n = 100)  Change from Baseline at 8 wks vs. placebo: <b>HAMD-17:</b> LOCF Δ LSM -2.8; p = 0.037 <b>SHAPS:</b> LOCF Δ LSM -4.8; p = 0.006	In full intent to treat population (fITT) (n = 166)  Change from Baseline at 6 wks vs. placebo: <b>MADRS:</b> Δ LSM -3.1; p = 0.0017 <b>SHAPS:</b> Δ LSM -0.8; p = 0.251  In Enriched Intent to Treat (eITT) (n = 121): <b>MADRS:</b> Δ LSM -2.1; p = 0.0443 <b>SHAPS:</b> Δ LSM -0.7; p = 0.419
<b>Phase 2 Safety and Tolerability</b> <b>4</b>	<b>Most frequent AEs ≥ 2% and higher than PBO, Safety Population</b> (active vs. placebo): Headache: 4.9% vs 4.9% Nausea: 4.9% vs 1.0% COVID-19: 3.9% vs 2.9% Upper resp. infection: 2.9% vs 1.0% Diarrhea: 2.0% vs 2.9%	<b>AEs &gt; 5% incidence and higher than PBO, fITT</b> (active vs. placebo): Headache: 11.8 % vs 7.1% Diarrhea: 8.2% vs 2.4% Pruritus: 5.9% vs 0% Nasopharyngitis: 5.9% vs 2.4%

Navacaprant and aticaprant are investigational and have not been evaluated in a head-to-head clinical trial. No comparisons of safety or efficacy between the products should be drawn from the above differentiators.

eITT = enriched population; consists of randomized lead-in PBO non-responders receiving ≥ 1 dose of study medication & having ≥ 1 post-treatment baseline efficacy measurement; non responders: < 30% decrease in MADRS during PBO lead-in  
fITT = full intention-to-treat analysis set; consists of all randomized subjects receiving ≥ 1 dose of study medication & having ≥ 1 post-treatment baseline efficacy measurement

KOR, kappa opioid receptor; MOR, mu opioid receptor; t<sub>1/2</sub>, half-life; NHP, non-human primate; RO, receptor occupancy; MDD, Major Depressive Disorder

1. Guerrero M, et al. *J Med Chem.* 2019;62(4):1761-1780. 2. Neumora Data on File. 3. Rorick-Kehn LM, et al. *Neuropharmacology.* 2014;77:131-144. 4. Lowe SL, et al. *J Clin Pharmacol.* 2014;54(9):968-978. 5. [www.clinicaltrials.gov](http://www.clinicaltrials.gov) accessed 28JAN24

6. Schmidt ME, et al. Efficacy and safety of aticaprant, a kappa opioid receptor antagonist, adjunctive to oral SSRI/SNRI antidepressant in major depressive disorder: Results of a phase 2a randomized, double-blind, placebo-controlled study.

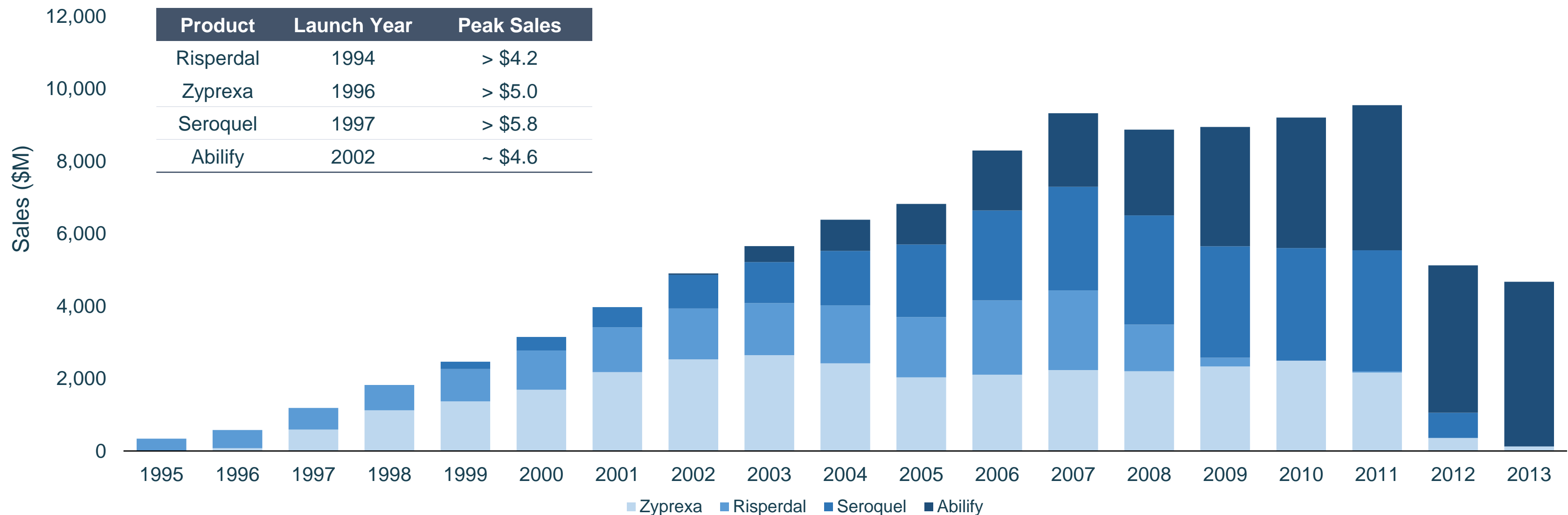
Presented at: American Society of Clinical Psychopharmacology; May 29-June 2, 2023; Miami Beach., <sup>7</sup>EU Clinical Trials Register; <sup>8</sup>US Patent Document.



# 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

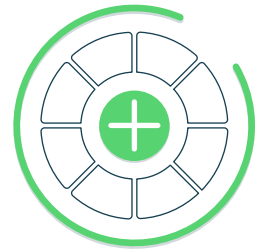
Sales of Branded 5-HT<sub>2</sub> to D<sub>2</sub> Receptor Antagonists (1995 – 2013)



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.

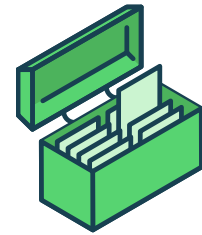


# Neumora's Precision Medicine Approach Can Be Leveraged to Maximize the Value of Our Programs



## Challenge: Match Right Drug to the Right Patient

- How do we gain further confidence in a selected target?
- How do we identify indications for a given target?
- How do we identify likely responders / treatment non-responders?



## Neumora's Precision Toolbox

Proprietary analytical capabilities with one petabyte of data onboarded

**Molecular, Translational, and Clinical Tools**  
(e.g., genomics, proteomics, EEG, Imaging, Digital, Clinical measures)

**Multimodal Methods**  
(e.g., AI/ML, analytic capabilities)

**Longitudinal, Multi-modal patient datasets** (includes multiple disorders)

**Exclusive partnership with deCODE Genetics** (through Amgen relationship)



## Maximize Value: Improve Probability of Success & Expand Indications

- Gain confidence in target and/or indication
- Characterize more homogeneous, targeted patient populations
- Inform inclusion / exclusion criteria
- Increase indication expansion opportunities
- Identify placebo responders
- Identify biomarkers

Neumora's precision toolbox provides a key competitive advantage in our development approach



