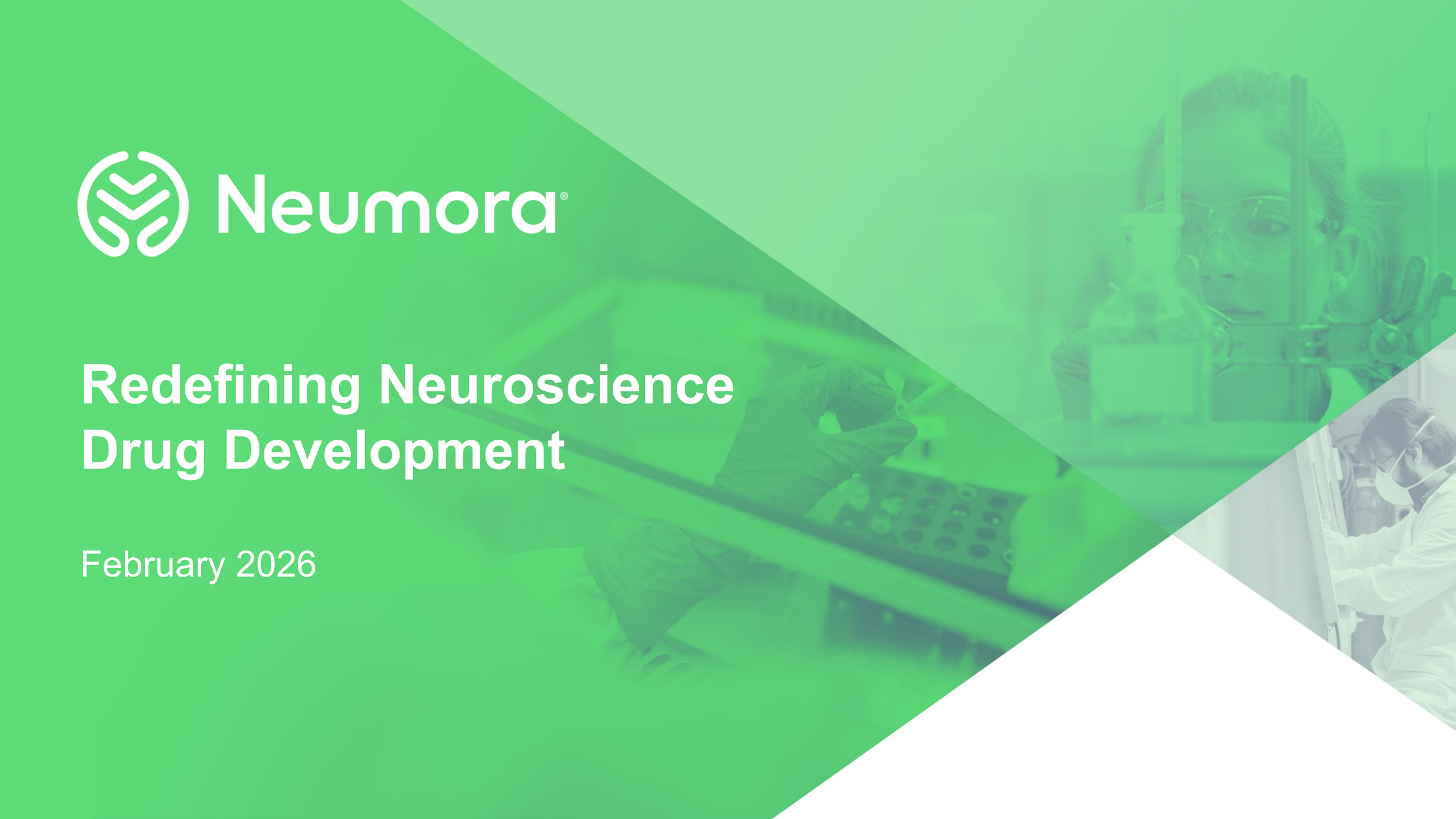
Neumora®

Redefining Neuroscience Drug Development

February 2026



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; the timing, progress and plans for its therapeutic development programs, including the timing of clinical trial initiation and data readouts and upcoming milestones and catalysts; expectations and projections regarding future operating results and financial performance, including the sufficiency of its cash resources, intellectual property protection, and expectation of the 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 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 September 30, 2025 which was filed with the SEC on November 6, 2025. 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 September 30, 2025 are also not necessarily indicative of our operating results for any future periods.

Neumora™

Our Mission

We are focused on bringing forward the next generation of novel therapies with brain-penetrant chemistry that offer improved treatment outcomes and quality of life for patients

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

Jason Duncan
Chief Legal & Administrative Officer

Nick Brandon, Ph.D.
Chief Scientific Officer

Amy Sullivan
Chief Human Resources Officer

Carol Suh
Chief Strategy Officer & Co-Founder

Lori Houle
Chief Technical Operations & Quality Officer

Michael Milligan
Chief Financial 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

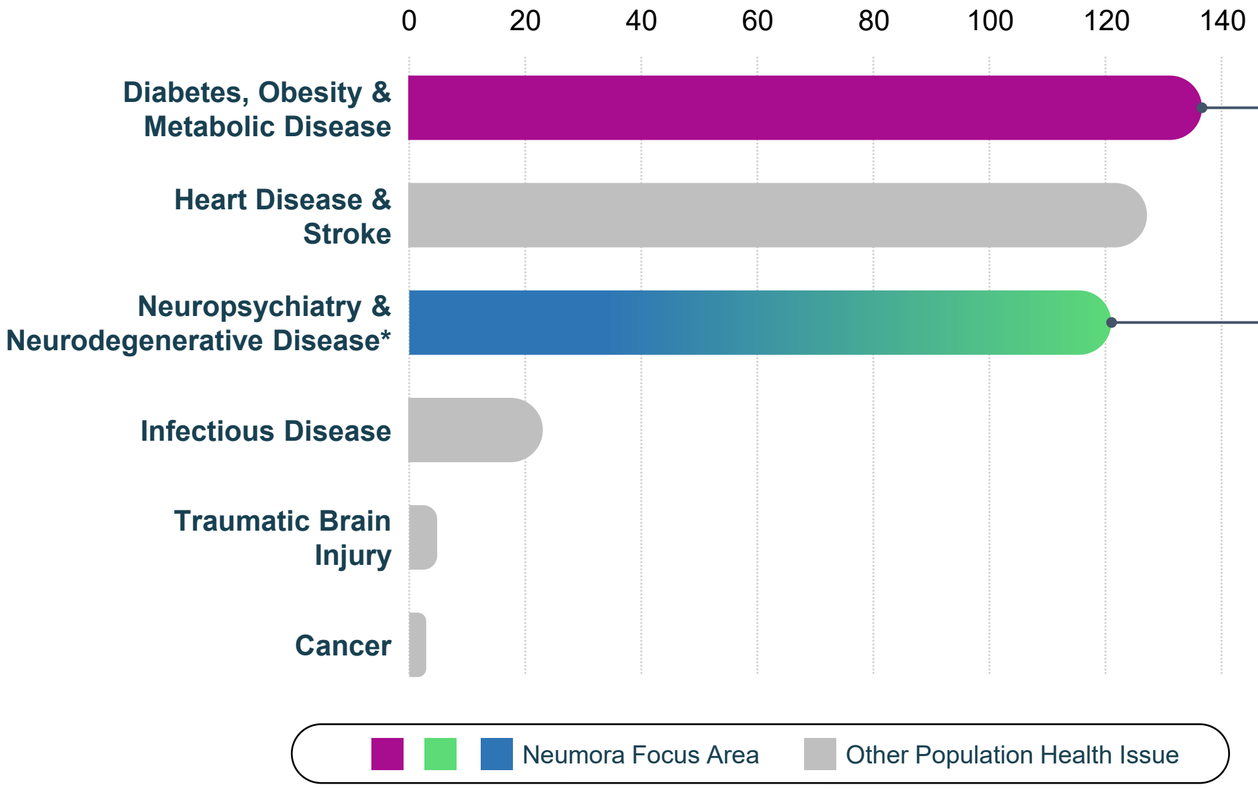
Maykin Ho, Ph.D.
Retired Partner, Goldman Sachs

David Piacquad
Biotechnology Advisor

Goal to address unmet needs across large markets

Biggest Health Disorders Facing U.S.[1]

Patients Impacted (M)



Goal To Address Unmet Needs

Metabolic Disease

- Expanded oral treatment options
- Improved tolerability profile
- Novel MoAs with potential for higher quality weight loss and maintenance

Neurogenerative Disease

- Improved tolerability and safety, particularly in elderly and high-risk populations
- Novel MoAs with greater brain penetration/efficacy
- Easy-to-maintain treatments that reduce caregiver burden

Neuropsychiatric Disease

- Effective treatments with favorable tolerability profiles
- Novel MOAs with the potential to treat multiple elements of disease (e.g., depressive symptoms, anhedonia)

[1]Source: National Institutes of Health (NIH), “Our Biggest Health Challenges,” last reviewed January 21, 2025; CDC/NCHS, NHANES 2021–2023; The Lancet Diabetes & Endocrinology Commission, 2025; NIMH, 2025.
*Includes: major depressive disorder, bipolar depression, schizophrenia, generalized anxiety disorder, post traumatic stress disorder, substance use disorder, Alzheimer's disease, Parkinson's disease, attention-deficit hyperactivity disorder

Advancing three franchises each anchored by a potential best-in-class program

PROGRAM *Target/Mechanism*	INDICATION *U.S. Prevalence*	Preclinical	Phase 1	Phase 2	Phase 3
METABOLIC DISEASE					
NMRA-215 *NLRP3 Inhibitor*	**Obesity** *103M*				
Undisclosed	**Obesity** *103M*				
NEUROGENERATIVE DISEASE					
NMRA-511 *V1aR Antagonist*	**Agitation in Alzheimer's Disease** **7***M*				
NMRA-GCASE *GCase Activator*	**Parkinson's Disease** *1M*				
NMRA-CK1δ *CK1δ Inhibitor*	**ALS/Parkinson's Disease** *25K/1M*				
NEUROPSYCHIATRIC DISEASE					
Navacaprant *KOR Antagonist*	**Major Depressive Disorder** *21M*				
NMRA-898 *M4 Modulator*	**Schizophrenia** *3M*				
NMRA-861 *M4 Modulator*	**Schizophrenia** *3M*				

ALS = Amyotrophic lateral sclerosis; CK1δ= Casein Kinase I Isoform delta; GCase = Glucocerebrosidase; IP = Intellectual Property; KOR = kappa opioid receptor; M4 = Muscarinic Acetylcholine Receptor M4; NLRP3 = Nucleotide-binding Domain, Leucine-rich–containing Family, Pyrin Domain–containing-3; V1aR = Vasopressin 1a Receptor; DIO = diet induced obesity mouse model.

Multiple catalysts expected in 2026 across three core franchises

ANTICIPATED KEY MILESTONES		
Metabolic Disease	NMRA-215 biomarker data	3Q 2026
	NMRA-215 human weight loss data	Year end ‘26
Neurogenerative Disease	NMRA-511 MAD extension data	Year end ‘26
Neuropsychiatric Disease	KOASTAL-2 and -3 topline data (joint readout)	2Q 2026
	Provide M4 franchise update	Mid-2026

Well capitalized with a cash runway to support operations into 3Q 2027

NMRA-215: differentiated NLRP3 inhibitor for obesity and related metabolic diseases

NMRA-215 Target Profile

Rationale/Pharmacology
NLRP3-related inflammatory response via release of IL-1β, IL-18 and IL-6 cytokines is associated with obesity[1,2]

Indication
Obesity, Parkinson's Disease

Target Administration
Oral, once-daily

IP
Composition of matter patent extending to 2043+*

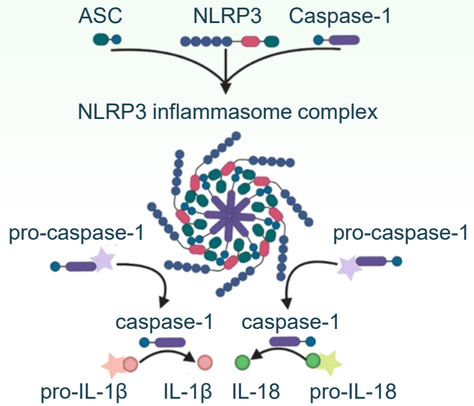
Epidemiology
~1.13 billion patients in the world with obesity by 2030[3]

Expected Milestones
- Progress NMRA-215 into the clinic in 1H 2026
- Report biomarker data (hsCRP, IC90) in 3Q 2026
- Report human proof-of-concept data around end of 2026

Multiple factors drive NLRP3-mediated inflammation resulting in disease

DRIVERS
- Diet (e.g., lipids)
- Environment
- Genetics
- Aging

NLRP3 Activation



DISEASES
- Neurodegeneration (Parkinson's)
- Cardio-metabolic (obesity)
- Monogenic / autoimmune (CAPS)

*Excluding any patent term adjustment or extension

1. O'Brian et al. *J Neuroinflammation.* 2020;17(1):104. 2. Wani K et al. *Int J Environ Res Public Health.* 2021;18(2):511. 3. World Obesity Federation. World Obesity Atlas 2024. London: World Obesity Federation, 2024. https://data.worldobesity.org/publications/?cat=22.
2. AdipoGen Life Sciences. https://adipogen.com/inflammasomes/rce

Obesity represents one of the greatest public health challenges

By 2030,

1.13 BILLION
people worldwide will be living with obesity[1]

Driving a significant market for obesity treatments

$130 - $170 BILLION
estimated obesity market size in 2030

And yet,

Significant opportunity remains

Approved incretin therapies offer weight loss, but come with challenges:

- Significant AEs, such as nausea, vomiting, constipation and diarrhea
- High discontinuation rates
- Weight regain following discontinuation
- Cold chain storage required

Emerging oral treatments produce less weight loss and are burdened by the same intolerable side effects

NLRP3 inhibition

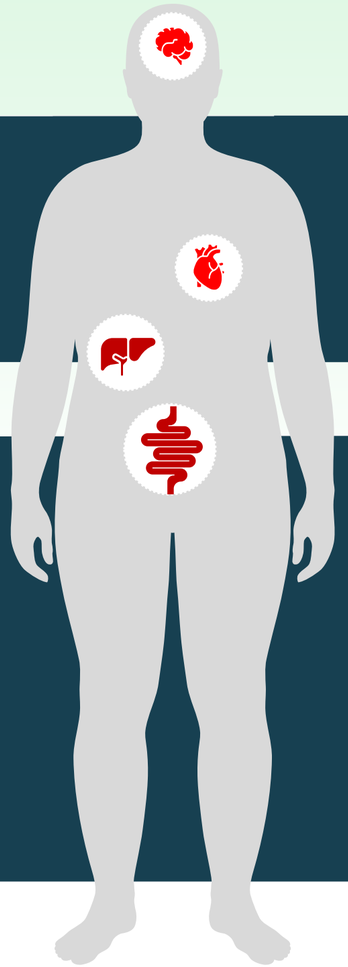
May address unmet needs

NLRP3 inhibition may offer benefit across monotherapy, combination therapy and maintenance paradigms:

- Incretin-like weight loss
- Increased response rates
- Better tolerability
- Convenience with no cold chain storage
- Lower COGS with oral small molecule

[1]World Obesity Federation. World Obesity Atlas 2025. London: World Obesity Federation, 2025. https://data.worldobesity.org/publications/world-obesity-atlas-2025-v7.pdf

CNS penetrant NLRP3 inhibition provides broad benefit



System	Drug Impact	Outcome
CNS	Reduce neuroinflammation in the brain	Reduced appetite and drive body weight loss
Periphery	Protect organ and vascular system from inflammation-related damage	Reduce the risk of comorbidities. • Reduces heart disease: improved CV outcomes • Improves type II diabetes: reduced insulin resistance in mice

Potential treatment benefits driven by both CNS and peripheral inhibition of NLRP3

NMRA-215 has an optimized pharmacological profile including best-in-class CNS exposure

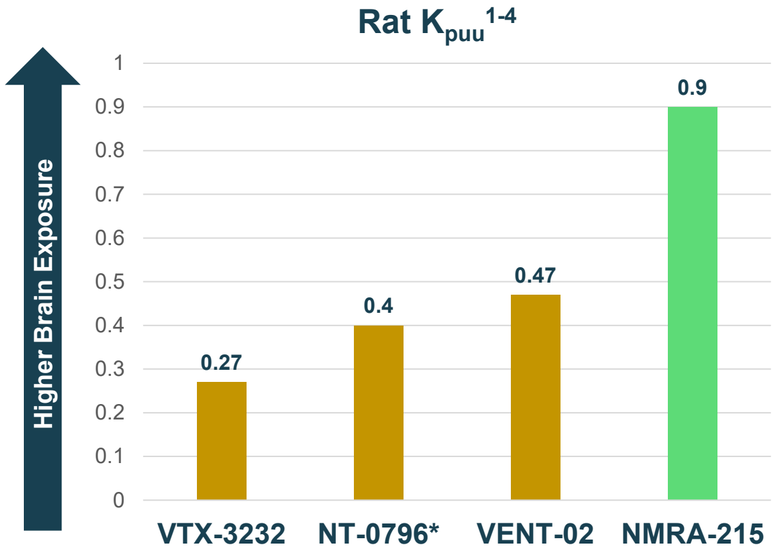
NMRA-215 is highly potent with low nM potency across a range of assays

NMRA-215 Assay Format	IC_{50}
THP-1 (IL-1β)	3 nM
Target engagement (Nanobret)	5 nM
iMicroglia (IL-1β)	8 nM
Human whole blood (IL-1β)	16 nM

NMRA-215 is highly selective for NLRP3

- NMRA-215 is highly selective for NLRP3 versus other inflammasomes (NLRP1, NLRC4, AIM2)
- >250-fold selective for NLRP3 versus a broad panel of targets (Eurofins SafetyScreen87)
- Clean profile in cardiac ion channel and kinase screening panels

NMRA-215 is extensively characterized and optimized for brain exposure



MDCK permeability:	**Unknown**	**14.0**
P-gp efflux ratio:	**Unknown**	**1.1**

*NT0796 = mouse K_{puu}

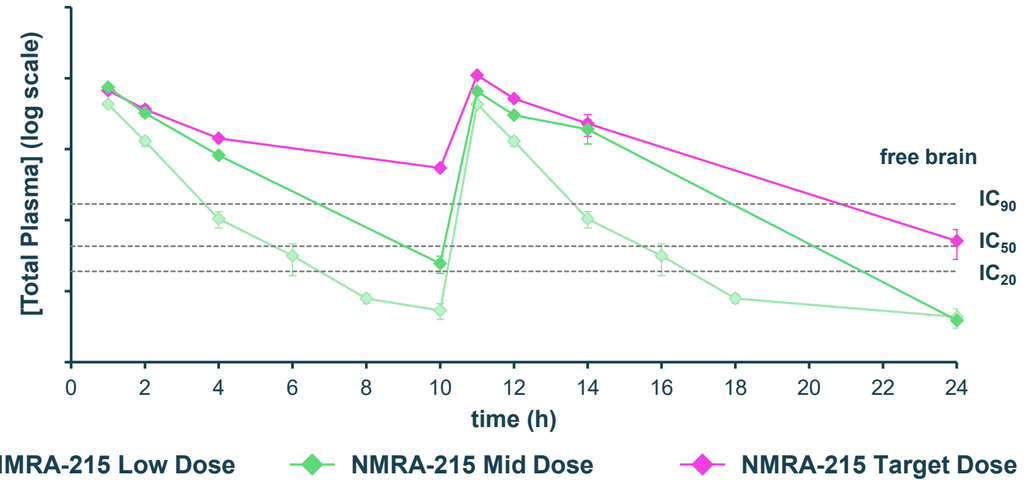
[1]Neumora data on file. [2]Thornton P, et al. *JPET*. 2024 Feb 15;388(3):813-826 . [3]Ventus Data Presented at 5th Annual Inflammasome Summit. November 28 – 30, 2023. Boston, MA. [4]Ventyx R&D Day Presentation. Published Jan 2023.

Doses selected for DIO studies to determine target coverage necessary for weight loss

NMRA-215 dose selection

Goal: Sustained IC_{90} target coverage for 24 hours

Dose (BID)	IC
Target Dose	90
Mid-Dose	50
Low Dose	20



Target dose drives IC_{90} in CNS and periphery over 24 hours based on human whole blood assay

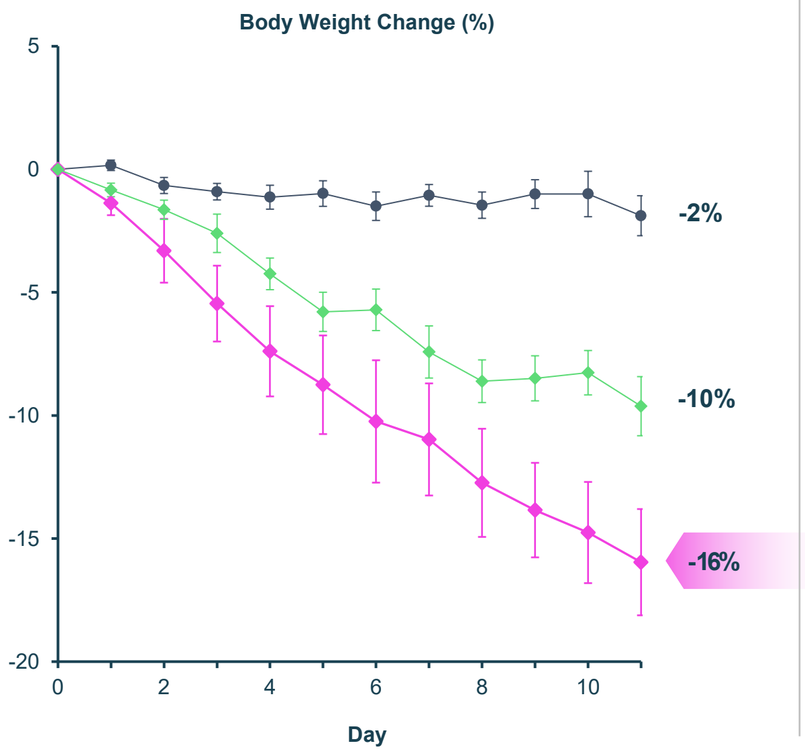
Semaglutide dose selection

Goal: Select two doses that allow for evaluation of different treatment paradigms

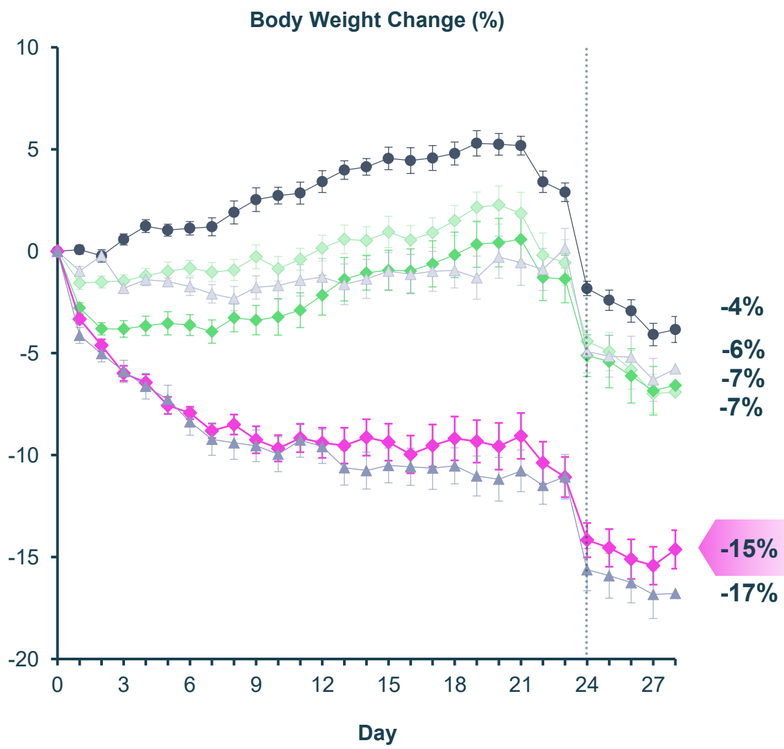
- Ability to evaluate combination and dose sparing effects of NMRA-215
  - Therapeutic dose: **3 nmol/kg**
  - Sub-therapeutic dose (incretin-sparing): **1 nmol/kg**
- Similar dosing paradigm used by other sponsors allows for comparison across studies

Monotherapy: Up to 19% weight loss with NMRA-215 with incretin-like induction

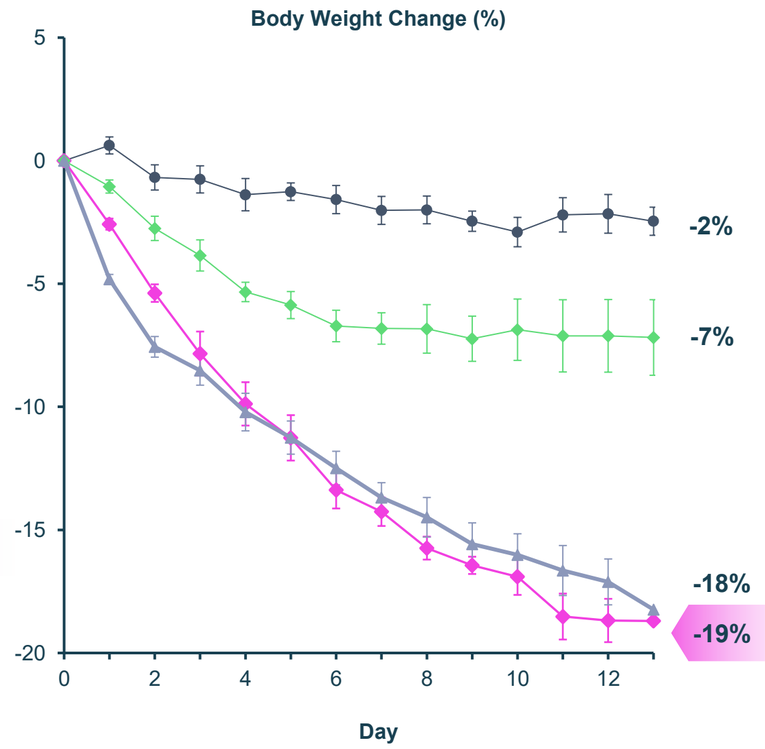
STUDY 1 Pilot Study



STUDY 2 Full DIO Study



STUDY 3 Induction Confirming Study*

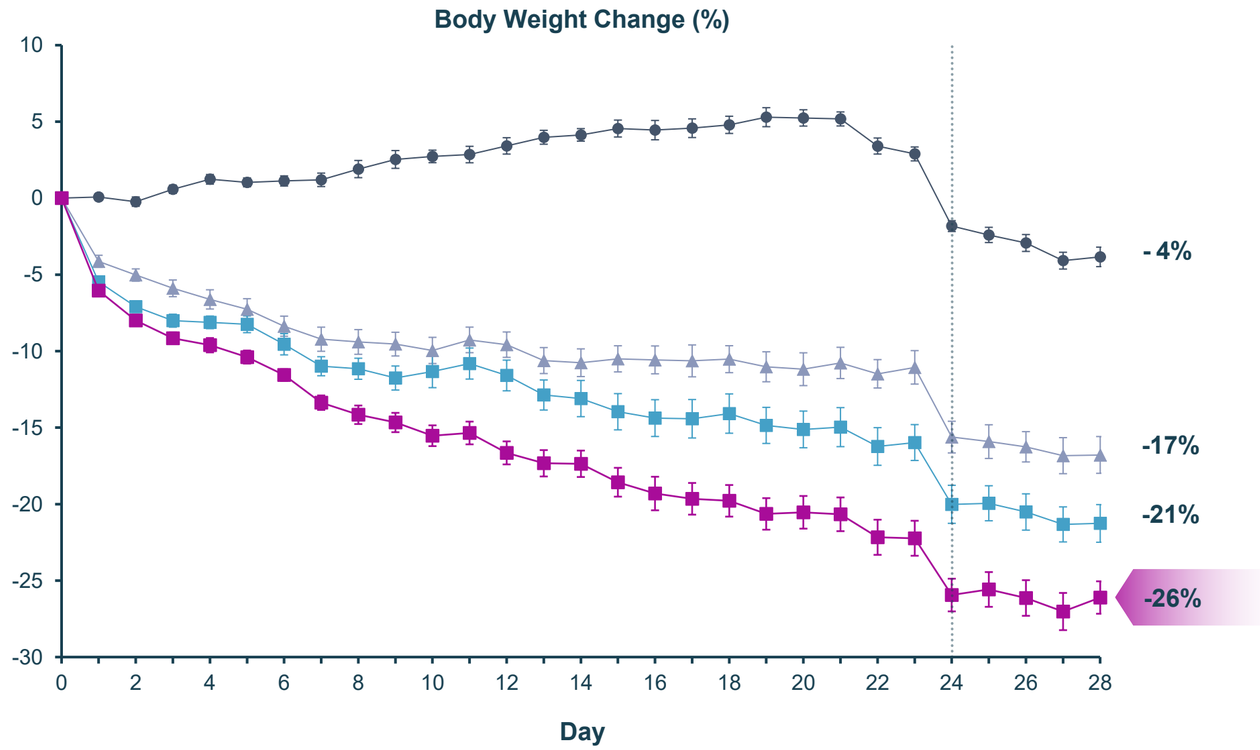


Vehicle | NMRA-215 Low Dose | NMRA-215 Mid Dose | NMRA-215 Target Dose | semaglutide 1 nmol/kg | semaglutide 3 nmol/kg

NMRA-215 administered subcutaneously in Studies 1 and 3 and administered orally in Study 2. Semaglutide administered subcutaneously in all studies. In Study 2 beginning on Day 22, mice underwent daily endpoint collections, including behavioral testing, MRI, and fasting on day 24 to support blood collection Days 25-27. *Study designed to run up to 28 days. Following achievement of study objective confirming incretin-like induction at Day 13, study was stopped due to injection site irritation, which will not be present in the clinical setting, as NMRA-215 is being developed as an oral therapy.

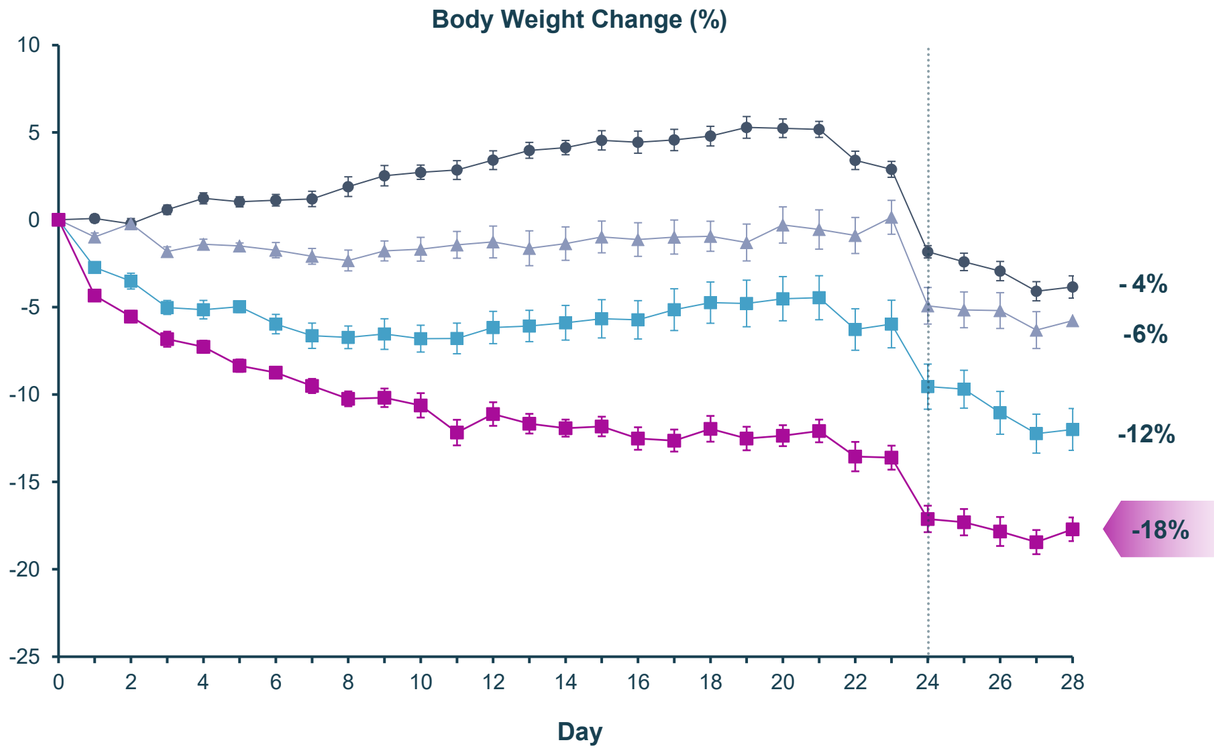
Combination therapy: Up to 26% weight loss with NMRA-215 + semaglutide

NMRA-215 + Combined with 3 nmol/kg semaglutide



Additive weight loss with therapeutically active incretin dose

NMRA-215 + Combined with 1 nmol/kg semaglutide



Potential for incretin-sparing combination with better tolerability

Vehicle | semaglutide | Combination with NMRA-215 Mid Dose | Combination with NMRA-215 Target Dose

Class-leading weight loss demonstrated with NMRA-215

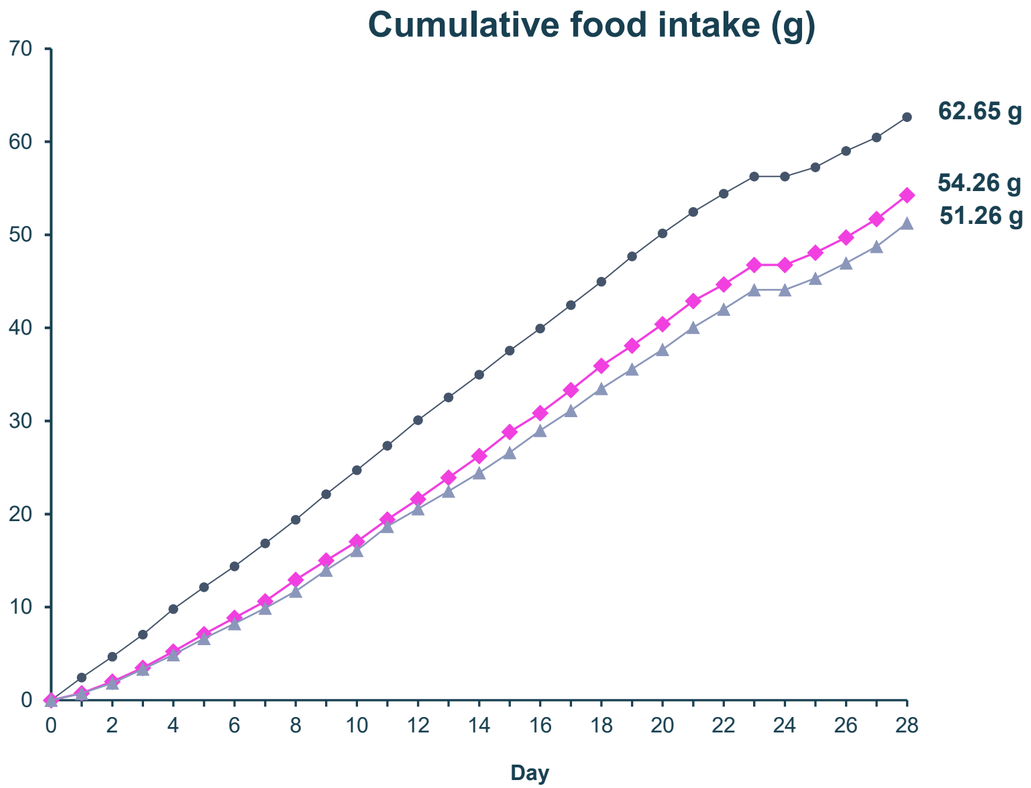
		Neumora	ventyx BIOSCIENCES	Ventus THERAPEUTICS	BIOAGE	nodthera
		NMRA-215	**VTX3232**	**VENT-02**	**BGE-102**	NT-0796
NMRA-215 monotherapy demonstrates best-in-class weight loss	**NLRP3i** (end of study)	**15%–19%**	2%	11%	6 %	*17%*
	semaglutide (end of study)	**17%–19%**	12%	21%^	5%	*21%*
NMRA-215 monotherapy matches semaglutide induction	**NLRP3i** (Day 7)	**9% / 14%** (Study 2) (Study 3)	3%	8%	6%	*7%*
	semaglutide (Day 7)	**9% / 14%** (Study 2) (Study 3)	9%	15%^	11%	*11%*
Combination demonstrates additive effects of NMRA-215	**NLRP3i + semaglutide** (Day 28)	**26%**	19%	29%^	21%	*24%#*

Studies in humanized transgenic obese mice are not directly comparable to other DIO studies

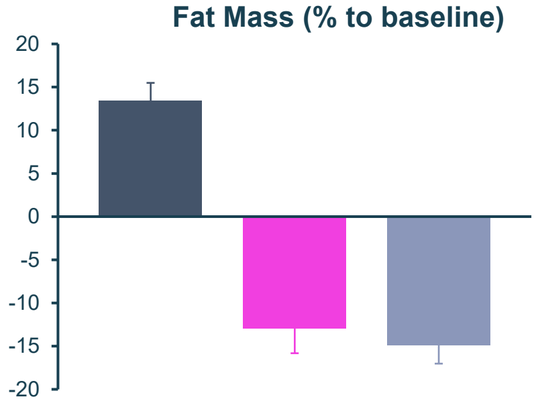
^Ventus semaglutide dose = 10 nmol/kg. #Nodthera combination study semaglutide dose = 5 µg/kg. Other market participant data obtained through company, scientific and Wall Street research publications

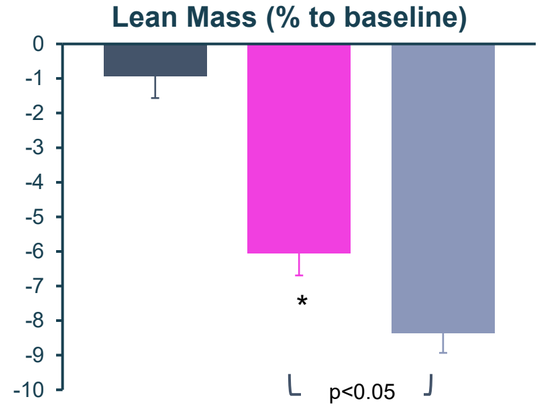
NMRA-215 matches semaglutide weight loss with higher-quality outcomes

Reduced food intake equivalent to semaglutide



Matches semaglutide weight loss, while preserving lean mass



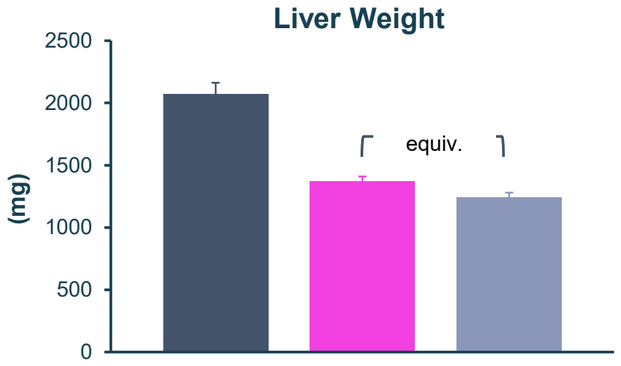


Vehicle | NMRA-215 Target Dose | semaglutide 3 nmol/kg

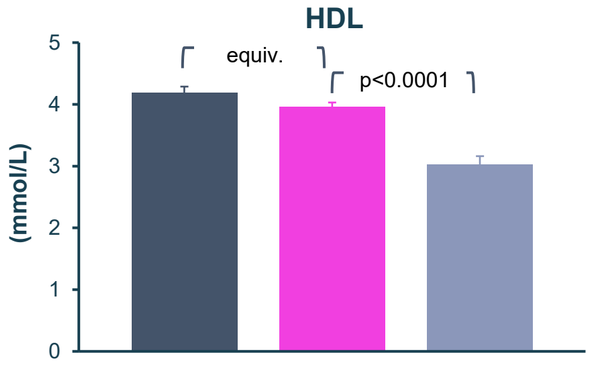
Neumora data on file. *Unpaired t-test, semaglutide 3 nmol/kg compared with NMRA-215 Target Dose

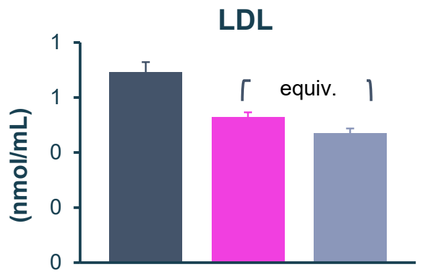
NMRA-215 drove positive results across key biomarkers

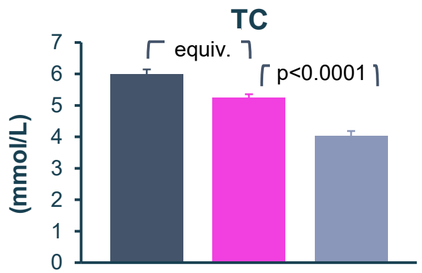
Improved liver health similar to semaglutide



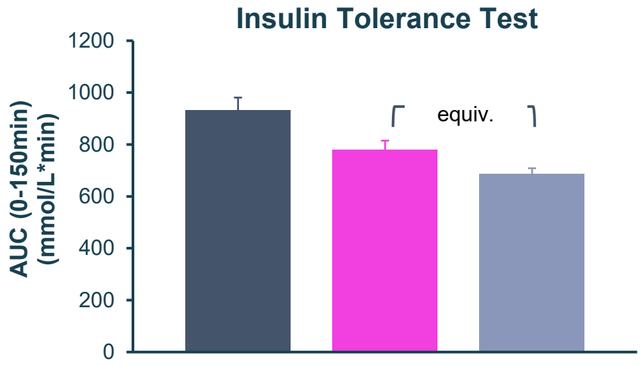
Improved cardiovascular/lipid profile relative to semaglutide







Improved insulin sensitivity



Additional Data

Cytokine data from 28-day study available in early 2026

Vehicle | NMRA-215 Target Dose | semaglutide 3 nmol/kg

Equiv. = equivalent. Neumora Data on File.

Data supports utility of NMRA-215 as monotherapy and combination therapy

Upcoming 12-week DIO data to evaluate maintenance paradigm

1 NMRA-215 as weight loss monotherapy

- Up to 19% body weight loss with semaglutide-like induction
- Dose-dependent body weight loss confirmed
- Preserved lean mass and improved metabolic biomarkers

2 NMRA-215 as add-on to a GLP-1

- Up to 26% body weight loss; additive to semaglutide alone
- Potential for incretin-sparing combination with better tolerability

3 NMRA-215 as weight maintenance treatment

- Report 12-week DIO mouse data in 1Q26

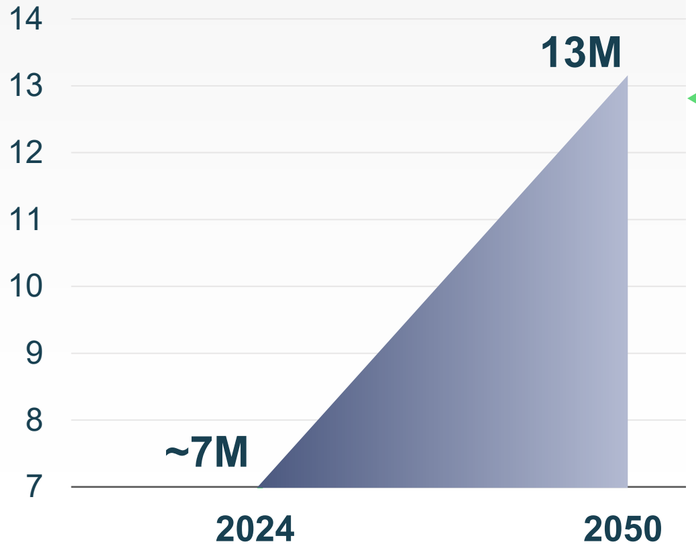
Next Step Initiate clinical program with NMRA-215 in monotherapy and combination settings in 1H 2026 and deliver proof of concept weight loss data around the end of 2026

Alzheimer’s disease agitation represents large market opportunity with significant unmet need

Alzheimer’s disease agitation is a large and growing health burden

Millions currently living with AD; prevalence expected to increase as the population ages[1]

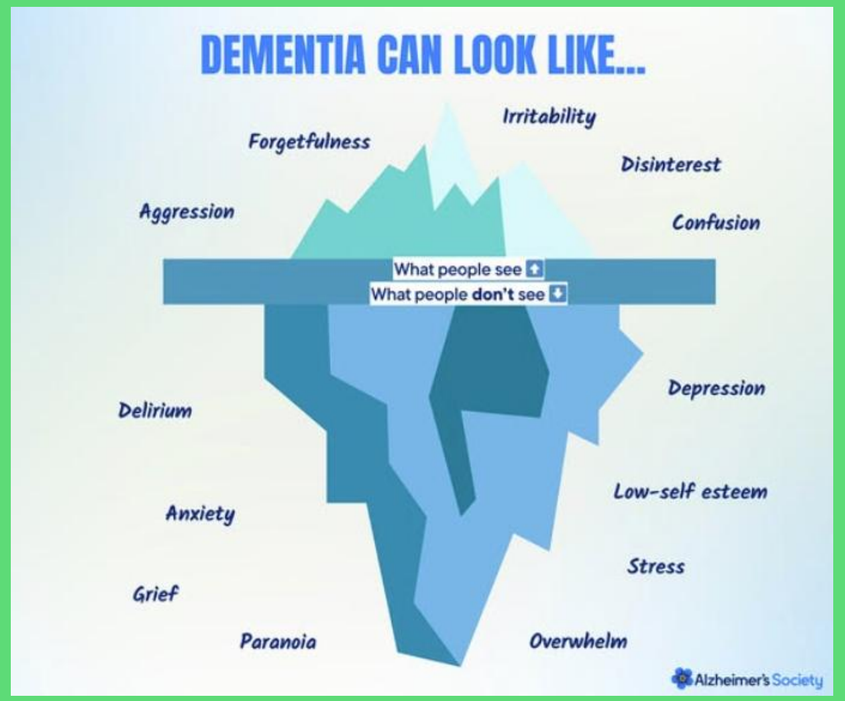
U.S. Adults with Alzheimer’s Disease (M)[1]



>70%

of people with AD experience agitation at some point in their disease[2]

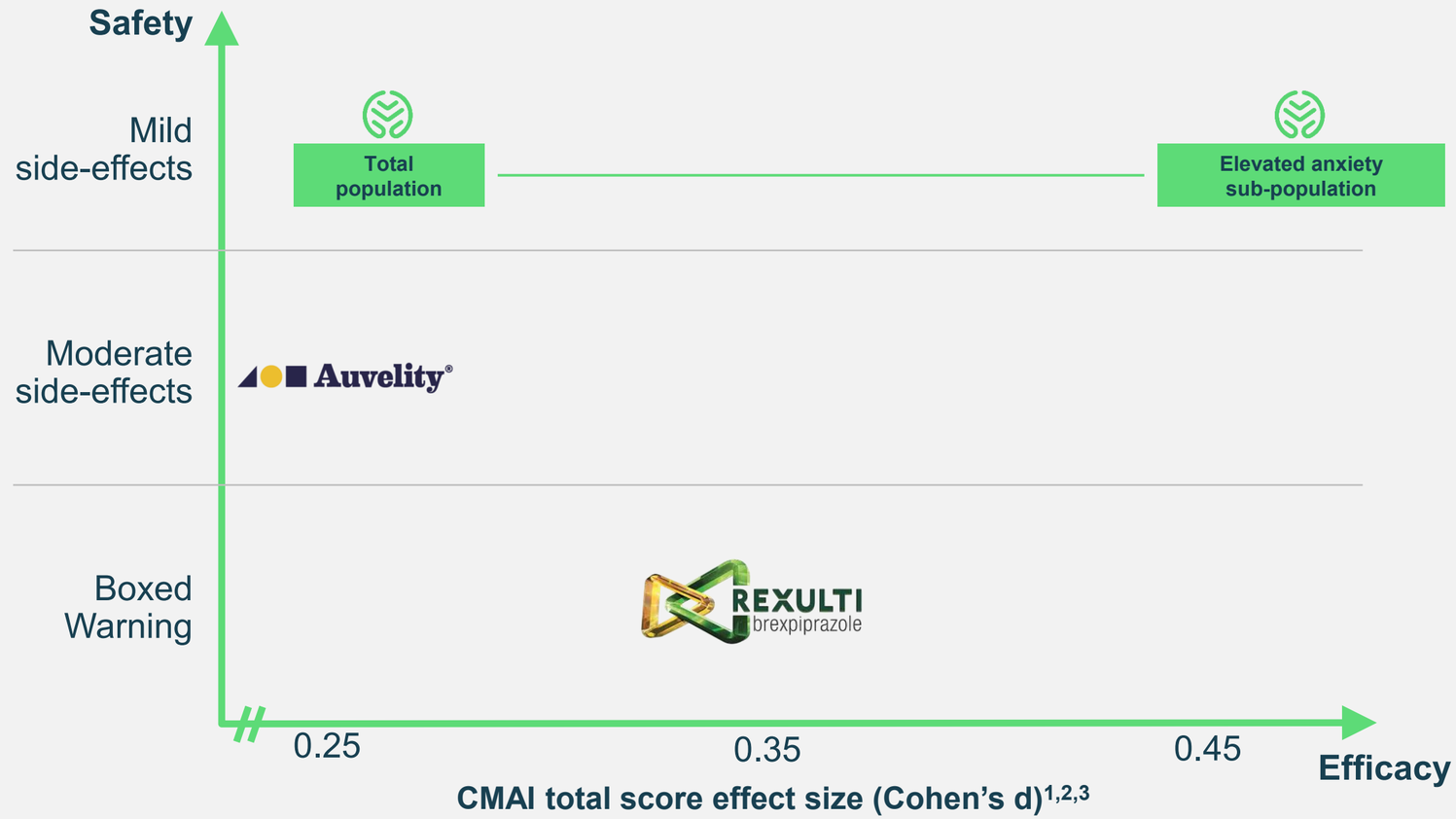
Anxiety is a key underlying driver of aggression and irritability in dementia[3]



[1]Alzheimer's Association. 2025 Alzheimer's Disease Facts and Figures. Alzheimer's Dementia 2025;21(5). [2]Van der Mussele S, et al. Aging Ment Health 2015;19(3):247-257. [3]Image from Alzheimer’s Society

NMRA-511 demonstrated unsurpassed efficacy in patients with AD agitation

Simplified market segmentation and opportunities



NMRA-511 Phase 1b key takeaways

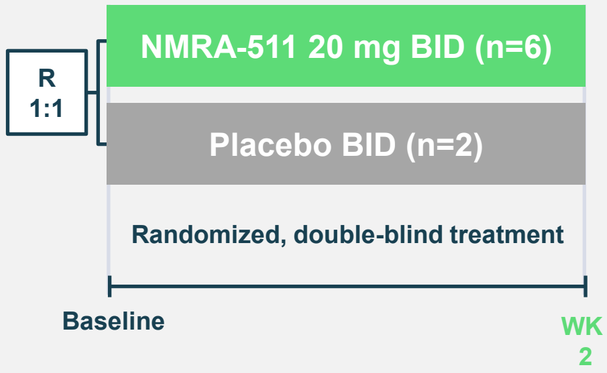
- Well tolerated, with potential for higher dosing
- CMAI effect size similar to Auvelity in total population
- Unsurpassed CMAI effect size in patients with elevated anxiety

For illustrative purposes only. NMRA-511 has not been studied in head-to-head trials against Auvelity or Rexulti, and there are differences in compounds, trial designs and other factors which must be considered.

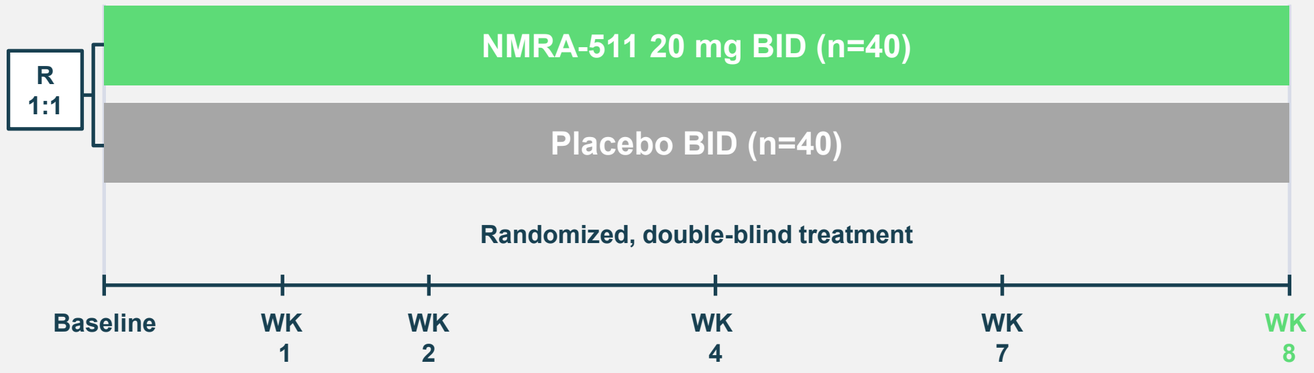
[1]Calculated from data: Addressing Dementia Via Agitation-Centered Evaluation (ADVANCE). https://clinicaltrials.gov/study/NCT03226522?intr=AXS-05&page=1&rank=9&tab=results. [2]Lee D, Slomkowski M, Hefting N, et al. Brexpiprazole for the Treatment of Agitation in Alzheimer Dementia: A Randomized Clinical Trial. JAMA Neurol. 2023;80(12):1307–1316. doi:10.1001/jamaneurol.2023.3810. [3]NMRA data on file. CMAI = Cohen-Mansfield Agitation Inventory.
Rexulti and Auvelity studies were enriched with an NPI-AA domain cutoff ≥4 at baseline. NMRA-511 Phase 1b study included no enrichment. Baseline NPI-AA scores; NMRA-511: 5.1; Rexulti: 7.7 (Study 2); Auvelity: 7.2 (Advance-1)

Study to evaluate the effects of NMRA-511 among healthy elderly and adults with agitation associated with dementia due to Alzheimer's disease

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	
Part A Inclusion Criteria:	• Healthy elderly adult participants aged 65-80 years
Part B Inclusion Criteria:	• Adults aged 55-90 years with mild-severe dementia (MMSE score of 5-24) and clinically significant agitation (CMAI total score 45-100)
Part B Primary Endpoint:	• Δ from baseline to Week 8 in CMAI total score
Part B Other Endpoints Include*:	Δ from baseline to Week 8 in: • CGI-S • NPI total score
Prespecified Sub-Populations:	• Elevated anxiety (RAID)
Statistics:	• **Study not powered to demonstrate statistical significance** • Designed as a signal-seeking study; effect size will inform the potential future development of NMRA-511 in ADA

*Safety Assessments include adverse events, clinical laboratory, vital signs, physical examination, 12-lead electocardiogram (ECG), Columbia-Suicide Severity Rating Scale (C-SSRS). Δ = Change; BID = twice daily; CMAI = Cohen-Mansfield Agitation Inventory; MMSE =Mini-Mental State Examinations; CGI = Clinical Global Impression of Change for Agitation; NPI = Neuropsychiatric Inventory.

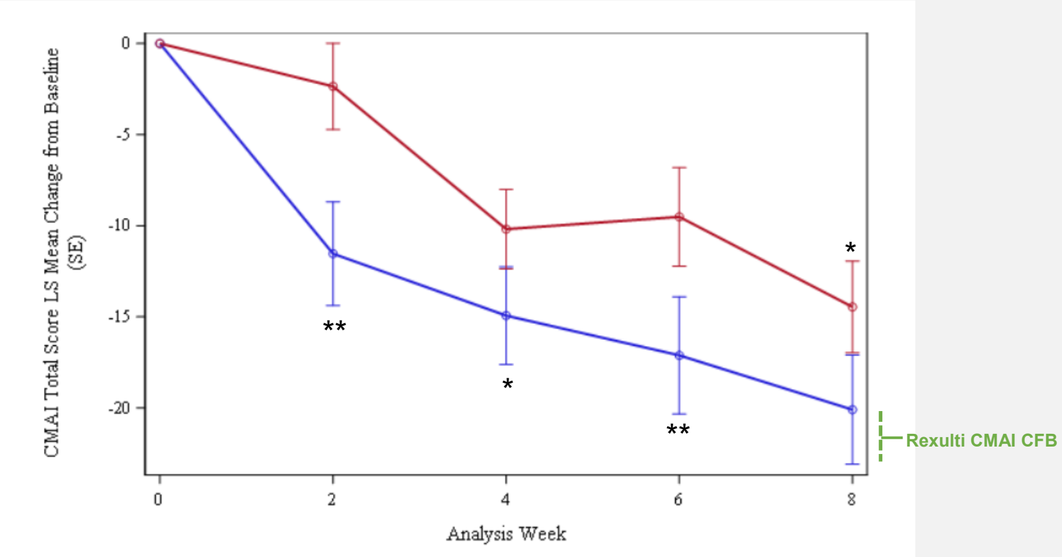
Demographics and baseline characteristics

	Total Population		Pre-specified elevated anxiety population	
	NMRA-511 n=40	Placebo n=40	NMRA-511 n=16	Placebo n=21
Mean age	71.8	72.7	66.8	71.6
Sex, n (%) Male Female	 18 (45.0%) 22 (55.0%)	 15 (37.5%) 25 (62.5%)	 7 (43.8%) 9 (56.3%)	 9 (42.9%) 12 (57.1%)
Race, n (%) White Black Asian Other	 27 (67.5%) 10 (25.0%) 2 (5.0%) 1 (2.5%)	 30 (75.0%) 9 (22.5%) 0 1 (2.5%)	 11 (68.8%) 3 (18.8%) 1 (6.3%) 1 (6.3%)	 14 (66.7%) 6 (28.6%) 0 1 (4.8%)
CMAI Total Score Mean (SD)	68.2 (14.7)	68 (14.3)	69.3 (15.6)	67.7 (14.9)
CGI-S (Agitation) Mean (SD)	4.3 (0.7)	4.2 (0.6)	4.4 (0.8)	4.3 (0.6)
NPI-AA Mean (SD)	5.1 (2.5)	5.9 (2.6)	4.8 (2.7)	5.8 (2.8)
MMSE Mean (SD)	19.0 (3.2)	19.5 (2.8)	19.2 (2.9)	19.4 (2.9)
Baseline anxiety as measured by RAID score (SD)	11.8 (6.4)	14.3 (8.6)	18.3 (4.2)	18.7 (6.5)
Protocol-Defined Medication Non-Adherence[1]	7 (17.5%)	0	N/A	
Modified Analysis Set (n)[2]	33	38		

[1]70% medication compliance required per protocol
[2]2 placebo patients excluded based on rater change driving outlier data (>3 standard deviations from the mean)
[3]Defined as Rating Anxiety In Dementia (RAID) score ≥12

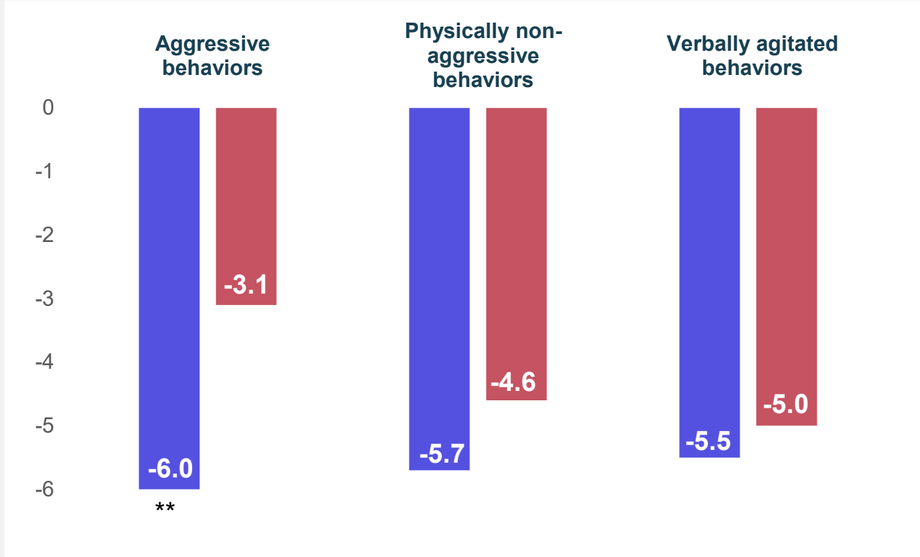
NMRA-511 demonstrated unsurpassed clinical effect size on CMAI total score in patients with elevated anxiety

CMAI Total Score Change from Baseline (pre-specified elevated anxiety sub-population)



	Week 6	Week 8
LSMD (SE)	-7.6 (4.1)	-5.6 (3.8)
Effect size range (Cohen's d)	0.64	0.51

Mean Change in CMAI Sub-Scores at Week 8 (pre-specified elevated anxiety sub-population)

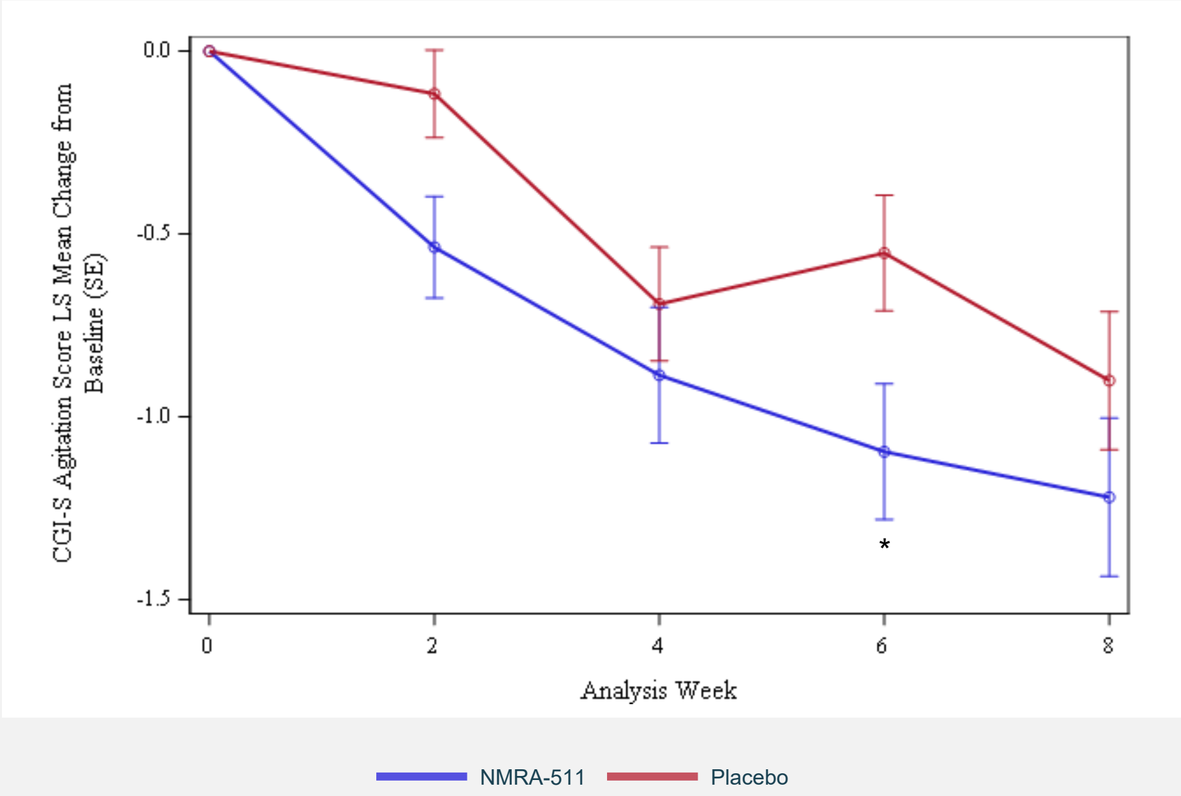


	Aggressive behaviors	Physically non-aggressive behaviors	Verbally agitated behaviors
Effect size (Cohen's d)	0.82	0.37	0.12

NMRA-511 n=16, placebo n=21
Nominal p-values: **p<0.05, *p<0.1
Cohen's d effect size range for patients with RAID ≥11: 0.45 – 0.54

NMRA-511 drove unsurpassed reductions in CGI-S agitation scores in patients with elevated anxiety at baseline

CGI-S Agitation Change from Baseline
(pre-specified elevated anxiety sub-population)

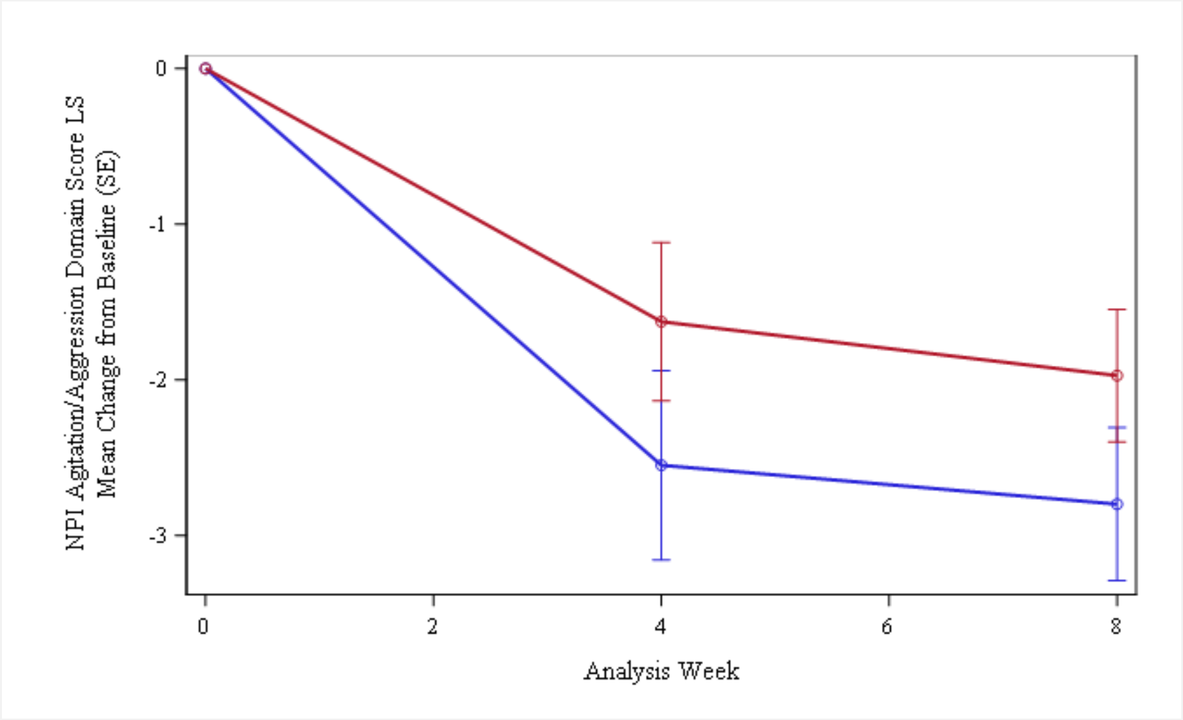


	Week 6	Week 8
LSMD (SE)	-0.5 (0.2)	-0.3 (0.3)
Effect size range (Cohen's d)	0.78	0.38

NMRA-511 n=16, placebo n=21
Nominal p-values: **p<0.05, *p<0.1

Strong clinical effect demonstrated on NPI agitation/aggression domain in patients with elevated anxiety at baseline

NPI Agitation/Aggression (NPI-AA) Change from Baseline (pre-specified elevated anxiety sub-population)



	Week 4	Week 8
LSMD (SE)	-0.9 (0.8)	-0.8 (0.6)
Effect size range (Cohen's d)	0.42	0.46

NMRA-511 n=16, placebo n=21
Nominal p-values: **p<0.05, *p<0.1

Favorable tolerability and safety profile demonstrated

NMRA-511 was safe and generally well tolerated

TEAEs Incidence (≥5% in either treatment group)	Placebo n=40	NMRA-511 n=40
Preferred Terms	n (%)	n (%)
Nasopharyngitis	3 (7.5%)	4 (10.0%)
Urinary tract infection	1 (2.5%)	4 (10.0%)
Anemia	1 (2.5%)	2 (5.0%)
Arthralgia	0	2 (5.0%)
Diarrhea	4 (10.0%)	2 (5.0%)
Dizziness	2 (5.0%)	2 (5.0%)
Headache	5 (12.5%)	2 (5.0%)
Hyponatremia	0	2 (5.0%)
Myalgia	1 (2.5%)	2 (5.0%)
Nausea	1 (2.5%)	2 (5.0%)
Vomiting	1 (2.5%)	2 (5.0%)
Abdominal pain	2 (5.0%)	1 (2.5%)

- TEAEs were typically mild to moderate in severity
- Low treatment discontinuations due to TEAEs (2.5%)
- Opportunity to evaluate higher doses of NMRA-511 based on tolerability

One serious adverse event of asthenia (general weakness) reported; resolved by time of discharge from an overnight hospitalization and resolution was maintained at study follow up after treatment discontinuation

NMRA-511 demonstrated consistent unsurpassed efficacy across measures

	CMAI Total Score	CMAI Aggressive Behaviors Score	CGI-S Agitation	NPI
NMRA-511 elevated anxiety population	0.51 – 0.64	0.82 – 1.1	0.38 – 0.78	0.42 – 0.46*
NMRA-511 total population	0.20 – 0.23	0.31 – 0.33	0.25 – 0.35	0.09 – 0.20*
REXULTI brexpiprazole	0.35	0.33	0.31	0.39^
Auvelity®	~0.2 – 0.25	Not Reported	Not Reported	Not Reported

NMRA-511 in AD agitation

- Well tolerated safety-profile, with potential for higher dosing
- Unsurpassed and consistent treatment effect across a range of measures
- Opportunity for convenient dosing with XR formulation
- Opportunity to enrich future studies for elevated anxiety (Phase 1b not enriched)

For illustrative purposes only. NMRA-511 has not been studied in head-to-head trials against Auvelity or Rexulti, and there are differences in compounds, trial designs and other factors which must be considered.

Data presented as Cohen's d effect size; elevated anxiety = RAID ≥12. *NPI-AA ^NPI-nursing home

1. Neumora data on file. 2. Lee D, Slomkowski M, Hefting N, et al. Brexpiprazole for the Treatment of Agitation in Alzheimer Dementia: A Randomized Clinical Trial. JAMA Neurol. 2023;80(12):1307–1316. doi:10.1001/jamaneurol.2023.3810.
3. Axsome Therapeutics corporate materials.

Rexulti and Auvelity studies were enriched with an NPI-AA domain cutoff ≥4 at baseline. NMRA-511 Phase 1b study included no enrichment. Baseline NPI-AA scores; NMRA-511: 5.1; Rexulti: 7.7 (Study 2); Auvelity: 7.2 (Advance-1)

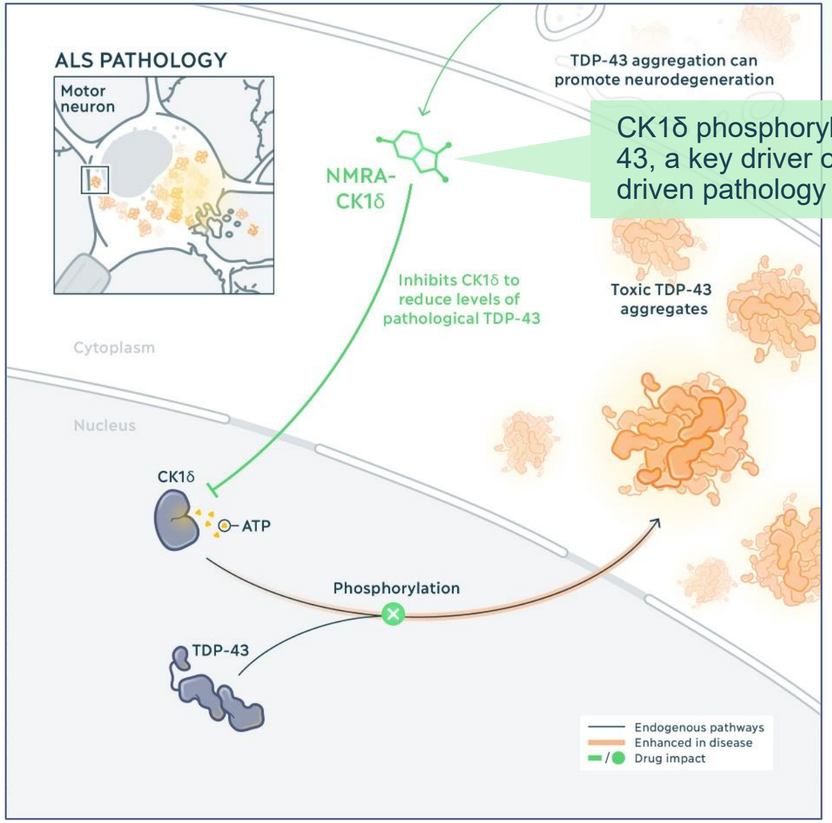
Pre-clinical neurodegeneration programs each have a strong biological rationale

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, Parkinson's disease



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

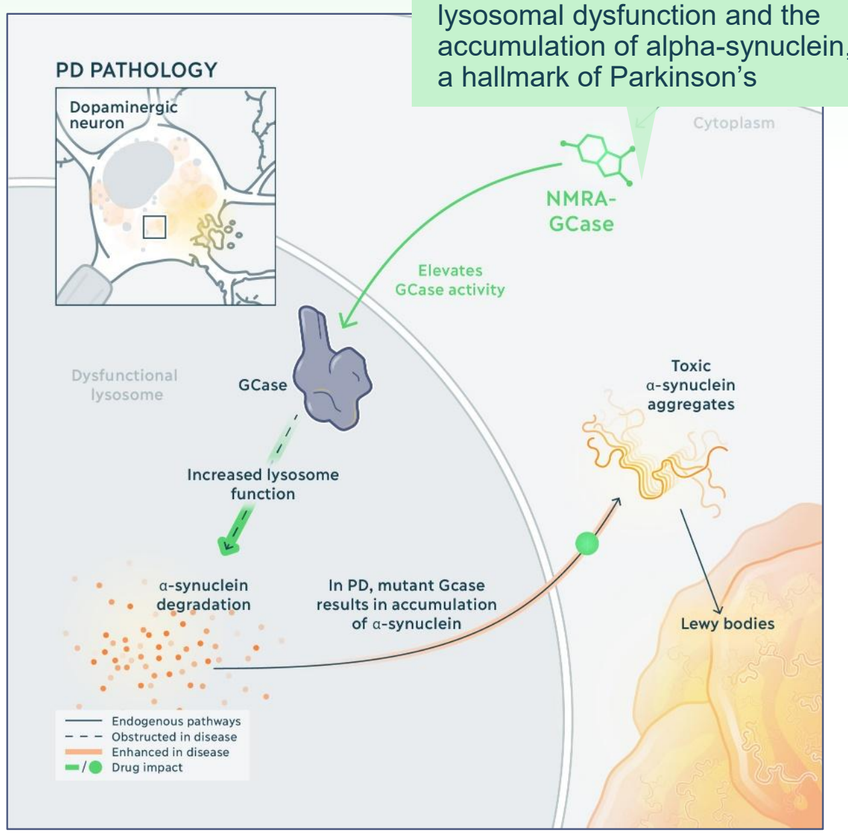
NMRA-GCASE

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

Potential Indications

Parkinson's disease

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



PAM = positive allosteric modulator; SCZ = schizophrenia; ALS = Amyotrophic lateral sclerosis; CK1 δ = Casein Kinase

MDD represents a major population health challenge

MDD is the leading cause of disability worldwide[1]

280M
people worldwide have MDD[1]

21M
adults in the U.S. have MDD[2]; 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

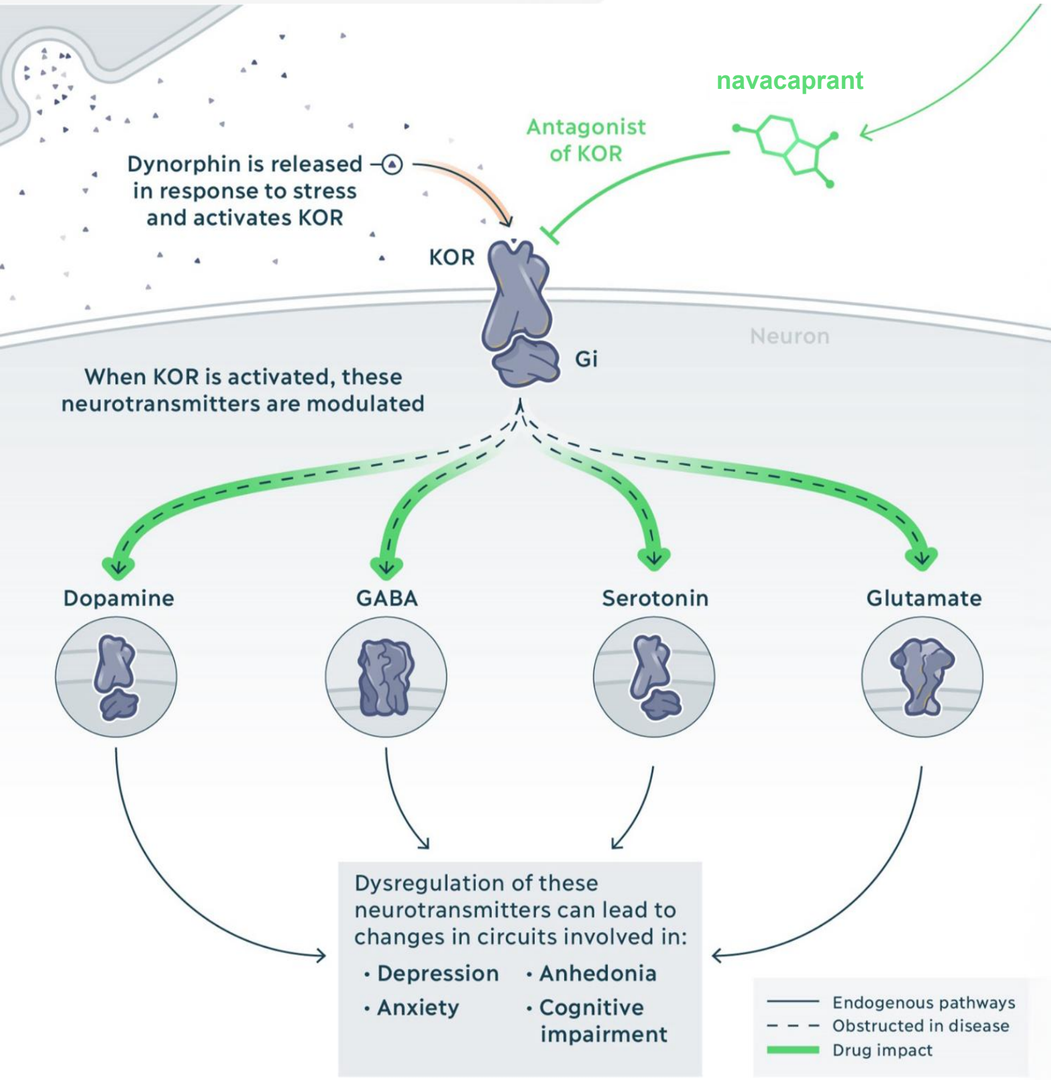
85%
of patients either don’t receive pharmacological treatment or fail to achieve remission with first-line treatment[3–7]

70%
of people with MDD experience anhedonia[8]

60–85%
of patients treated with monotherapy[9]

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). 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:l835. 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

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

KOASTAL

PHASE 3 DEVELOPMENT PROGRAM IN MDD

KOASTAL-1
Conducted in U.S.
Topline data announced 01/25

KOASTAL-2
Conducted in U.S., Canada and Latin America

KOASTAL-3
Conducted in U.S. and Europe

Placebo-controlled, double-blind RCTs evaluating efficacy and safety of navacaprant in MDD

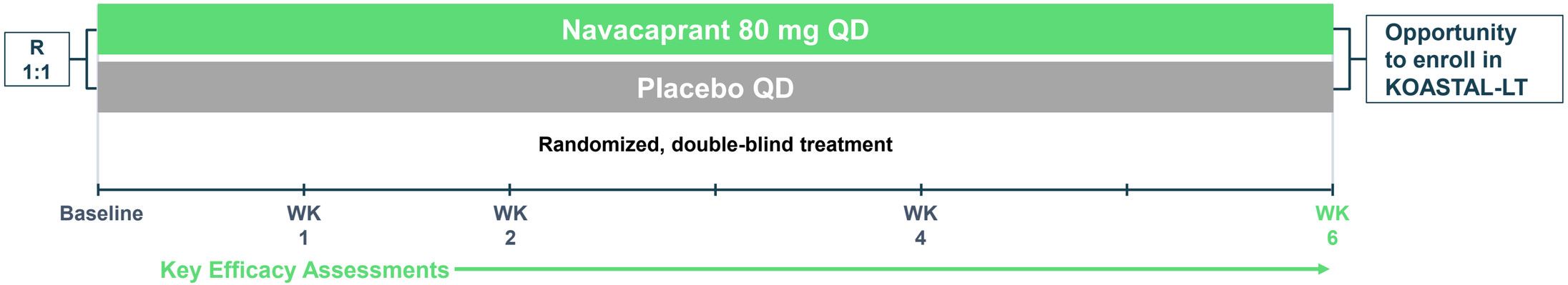
KOASTAL-LT
Open-label extension trial evaluating long-term safety of navacaprant in patients with MDD

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

MDD = Major Depressive Disorder; RCT = Randomized Controlled Trial; ADHD = Attention-Deficit Hyperactivity Disorder

KOASTAL pivotal study design

KOASTAL Pivotal Efficacy Studies



KOASTAL-1, KOASTAL-2, KOASTAL-3 Summary			
Inclusion Criteria:	• Adults ages 18 – 65 diagnosed with MDD • MADRS ≥ 25 at baseline	Other Secondary Endpoints Include:	Δ from baseline to each timepoint in: • CGI-S and CGI-I • PHQ-9 • HAM-A • SDS
Primary Endpoint:	• Δ from baseline to Week 6 in MADRS total score		
Key Secondary Endpoint:	• Δ from baseline to Week 6 in SHAPS total score	Key Exploratory Endpoints*:	Δ from baseline to each timepoint in: • EQ-5D 5L • WPAI-GH

*Safety Assessments include Change in Sexual Functioning Questionnaire (CSFQ-14)
Δ = 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.

Optimizing KOASTAL-2 and -3 Phase 3 trials

Joint topline data readout expected 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%

MDD = major depressive disorder

M4 PAM franchise: differentiated M4R PAMs for schizophrenia

M4 Franchise Target Profile

Pharmacology

Neumora has multiple series of chemically distinct, highly selective M4 muscarinic receptor PAMs, including NMRA-861 and NMRA-898, designed for antipsychotic-like efficacy with the potential for improved tolerability profile

Indication

Schizophrenia

Target Administration

Oral, once-daily

IP

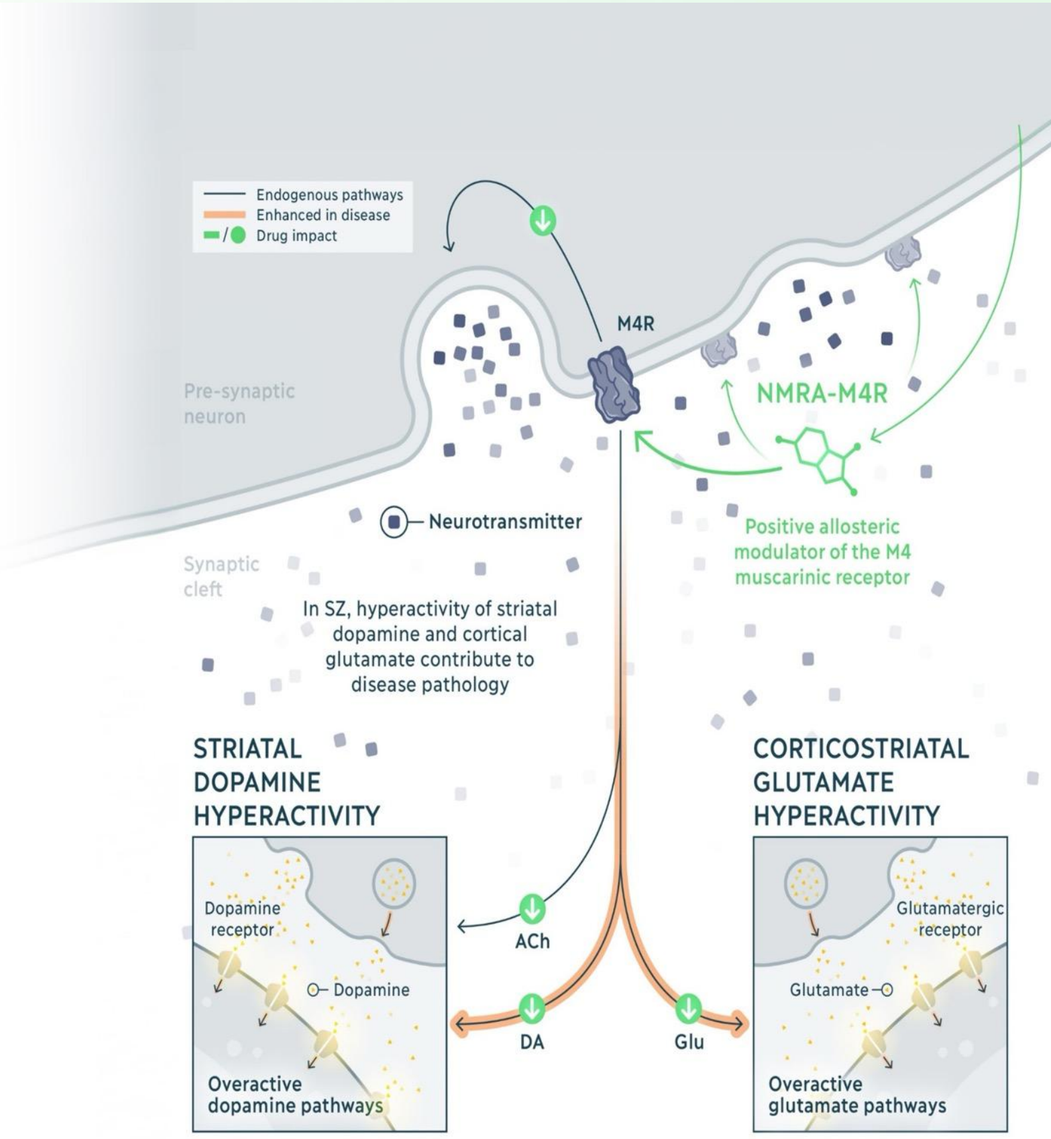
Composition of matter patent extending to 2044+*

Epidemiology

Estimated 3 million patients in the U.S. with schizophrenia[1]

Expected Milestones

Provide M4 franchise update by mid-2026

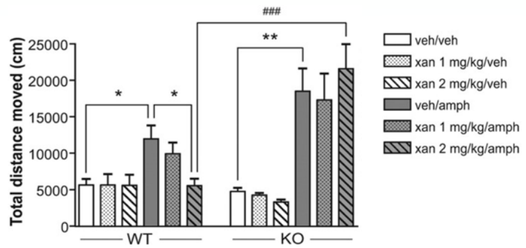


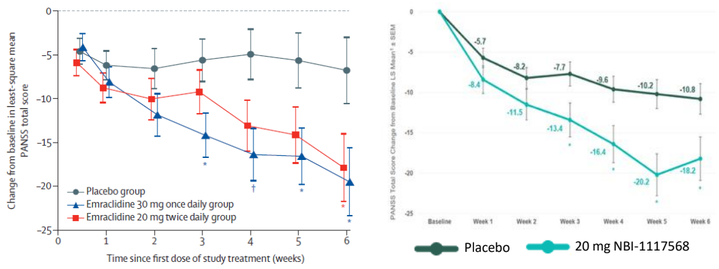
[1]Wander, C. *Am J Manag Care*. 2020;26:S62-S68.
*Excluding any patent term adjustment or extension
PAM = positive allosteric modulator

An optimized muscarinic drug profile would include selectivity and potency in the CNS

Preclinical data and clinical data in acute schizophrenia supports M4 as a driver of antipsychotic activity

Activity of xanomeline (active component of Cobenfy™) is dependent on M4R in mice





Non-selective muscarinic agents are associated with a range of peripheral AEs

M4

Cardiovascular

Transient increased BP & heart rate

M1, M2, M3

GI Tract

Increased gastric secretion & gastric motility

M1, M2, M3

Cardiovascular

Direct effect on cardiac function – increased BP & heart rate

M1, M3

Glands

Increased salivation
Increased lacrimation
Increased sweating

PAMs offer the benefits of greater selectivity

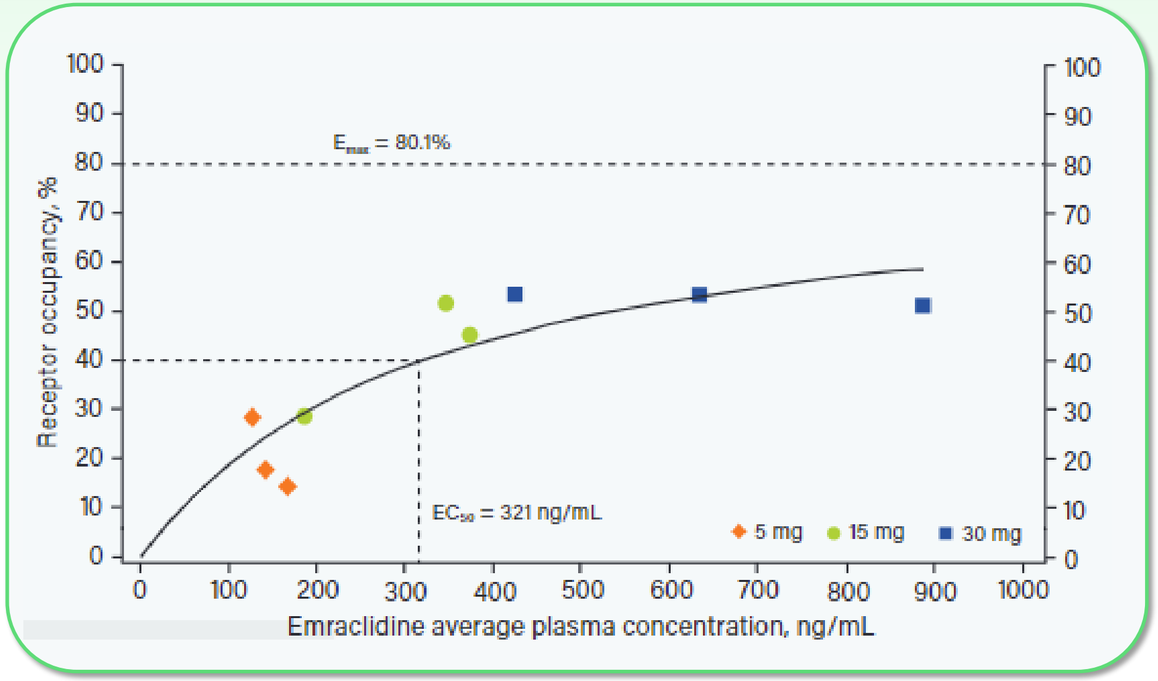
- Targeting the allosteric site specifically allows for greater selectivity for M4 over other muscarinic sub-types than if targeting the orthosteric site due to binding site conservation
- To date the pharmacology of agonists targeting the orthosteric site are often thought to display ‘partial’ agonism which could contribute to variable clinical responses
- PAMs allow for more precise potentiation of M4, maintaining the spatial and temporal signaling dynamics of ACh

1. Digby GJ, et al. *J Neurosci*. 2012;32(25):8532-44. 2. Dencker D, et al. *J Neurosci*. 2011 April 20;31(16):5905-8. 3. Krystal JH, et al. *Lancet*. 2022 Dec 17;400(10369):2210-20. 4. Neurocrine Biosciences. Q1 Earnings Presentation. April 14, 2025. www.neurocrine.com/documents/86/NBIX_Q1_2025_Earnings_Presentation_Final_05.05.25.pdf. 5. Moran SP, et al. *Trends Pharmacol Sci*. 2019 Dec;40(12):1006-20. 6. Tobin AB. *Nat Rev Drug Discov*. 2024 Oct,23(10);743-58. 7. Paul SM, et al. *Biol Psychiatry*. 2024 Oct 15;96(8):627-37.

Emraclidine receptor occupancy disconnected from plasma exposures

Receptor Occupancy for Emraclidine in Humans Suggests the Compound has Limited Brain Exposure

- In a human PET study, peripheral concentration of emraclidine shows dose linear response
- However, CNS receptor occupancy unchanged when dose doubled from 15 to 30 mg
- Data suggests emraclidine may have limitations in engaging the M4 receptor in the brain



Low CNS exposure could limit efficacy

CNS = central nervous system; PET = positron emission tomography

Duvvuri S, et al. *Evaluation of M4 Muscarinic Receptor Occupancy by Emraclidine Using [^{11}C]MK-6884 PET in Healthy Volunteers*. Poster M206. Presented at the 62nd Annual Meeting of the American College of Neuropsychopharmacology, Tampa, FL: December 3 – 6, 2023.

NMRA-861 & NMRA-898 have potential best-in-class potency and optimized brain penetration

NMRA-861 and –898 potentially more potent than emraclidine across multiple assays

NMRA-861 and –898 are selective for M4 over other muscarinic receptor subtypes

Neumora M4 PAMs are optimized for high CNS exposure

Neumora M4 PAMs are optimized for once daily dosing

Convulsions have not been observed with NMRA-861 or –898

	NMRA-861[1]	NMRA-898[1]	Emraclidine
M4 EC_{50} *(human; cAMP)*[1]	6 nM	13 nM	26 nM
M4 EC_{50} *(human; Ca^{2+})*[1]	2 nM	8 nM	180 nM
Selectivity at other muscarinic receptor subtypes *(EC_{50})*[1]	M1, M3, M5 > 10 µM, M2 0.7 µM	M1, M2, M3, M5 > 10 µM	M1, M3, M5 > 10 µM, M2 5.7 µM
Brain exposure *MDCK permeability (target >10)* *P-gp efflux ratio (target <2)*[1,2]	High 45.5 1.26	High 36.7 0.93	Moderate 9.5 3, 6.02[1,2]
Human half-life[3]	Pending Phase 1 Study	Pending Phase 1 Study	9 – 12 hr
Preclinical convulsions	Not observed in rat, dog or rabbit	Not observed in rat, dog or rabbit	Unknown

NMRA-861 and NMRA-898 have potential best-in-class pharmacology and clinical differentiation

Note: Data on this slide is presented for illustrative purposes only. These molecules have not been studied in head-to-head clinical trials.

cAMP = cyclic adenosine monophosphate; CNS = central nervous system; PAM = positive allosteric modulator

1. Data generated by The Warren Center for Neuroscience Drug Discovery at Vanderbilt University on behalf of Neumora across NMRA-861, NMRA-898 and emraclidine. 2. Butler CR, et al. *J Med Chem*. 2024 Jul 11;67(13):10831-47. 3. Krystal JH, et al. *Lancet*. 2022 Dec 17;400(10369):2210-20.

SAD/MAD studies evaluating NMRA-861 and NMRA-898 in healthy adults and people with stable schizophrenia

Study Objectives

- Confirm once-daily dosing – based on PK profile in humans
- Evaluate tolerable doses in people with stable schizophrenia
- Establish CNS penetration – based on CSF exposure

SAD – Part 1 CSP

	Dose Cohorts	Participants	Randomization
Part 1A	Dose 1, Dose 2, Dose 3, etc.	Healthy adults	6:2 active:placebo
Part 1B (Fed-Fasted cohort)	Dose to be determined	Healthy adults	12 active

MAD – Part 2 CSP

	Dose	Participants	Randomization
Cohort 1	Dose to be determined	Healthy adults	6:2 active:placebo
Cohort 2	Dose to be determined	Healthy adults	
Cohort 3	Dose to be determined	Healthy adults OR with stable schizophrenia	
Cohort 4	Dose to be determined	Healthy adults OR with stable schizophrenia	
Cohort 5	Dose to be determined	Adults with stable schizophrenia	

Healthy adults Adults with stable schizophrenia

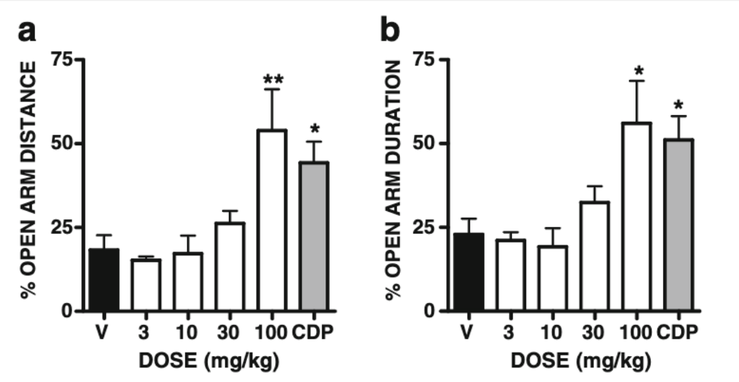
Appendix

Vasopressin/V1a receptor (V1aR) mediates anxiety-related behaviors

Robust preclinical data supports V1aR inhibition for treating anxiety in rodents

- V1a knock-out[1] or reduction by siRNA[2] drives reduced anxiety behaviors
- V1aR antagonists reduce anxiety and aggressive behaviors across models[3]
- Lines bred for aggression or anxiety show dysregulated AVP release and HPA axis functioning[4, 5, 6, 7]

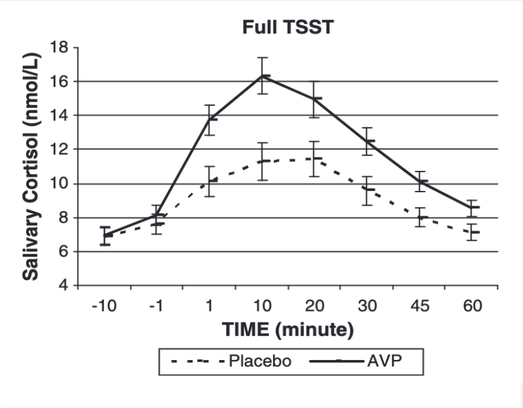
V1a receptor antagonist (JNJ-17308616) reduces anxiety behavior in rat

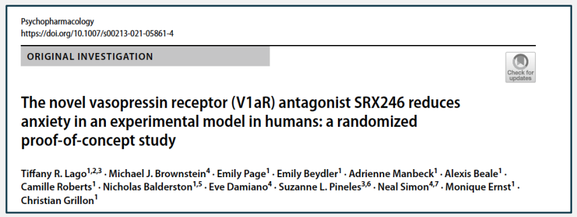


V1a antagonists and vasopressin modulate anxiety and stress related behaviors in humans

- Vasopressin administration exacerbates stress/anxiety behaviors in HVs[1, 2, 3]
- V1a receptor antagonist reduced experimentally-induced anxiety in humans and attenuated aggression in Huntington's disease

AVP increases cortisol response to social stressors (TSST)[1]




Psychopharmacology
https://doi.org/10.1007/s00213-021-05861-4

ORIGINAL INVESTIGATION

The novel vasopressin receptor (V1aR) antagonist SRX246 reduces anxiety in an experimental model in humans: a randomized proof-of-concept study

Tiffany R. Lago[1,2,3] · Michael J. Brownstein[4] · Emily Page[1] · Emily Beydler[1] · Adrienne Manbeck[1] · Alexis Beale[1] · Camille Roberts[1] · Nicholas Balderston[1,5] · Eve Damiano[4] · Suzanne L. Pineles[3,6] · Neal Simon[4,7] · Monique Ernst[1] · Christian Grillon[1]


Journal of Personalized Medicine

MDPI

Article

The Vasopressin 1a Receptor Antagonist SRX246 Reduces Aggressive Behavior in Huntington's Disease

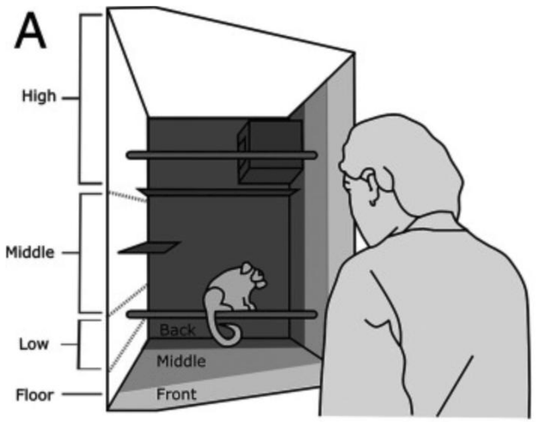
Hilda T. Maibach [1,†], Michael J. Brownstein [1,†], Steven M. Hersch [2,3], Karen E. Anderson [4], Debra E. Itzkowitz [1], Eve M. Damiano [1] and Neal G. Simon [1,5,*]

[1]Bielsky et al., 2004, NPP; [2]Barrett et al., 2013, *Horm. Behav.;* [3] Bleickardt et a., 2009, Psychopharmacology; [4]Veenema and Neumann, 2007, Brain behavior, evolution; [5]Zelena et al., 2009 J. Endo; [6]Mlynarik et al., 2007; [7]Fodor et al., 2014, Psychoneuroendocrin.

[1]Shalev et al., 2011, Hormones and Behavior; [2]Thompson et al., 2006, PNAS; [3]Kawada et al., 2019, Sci. Reports;

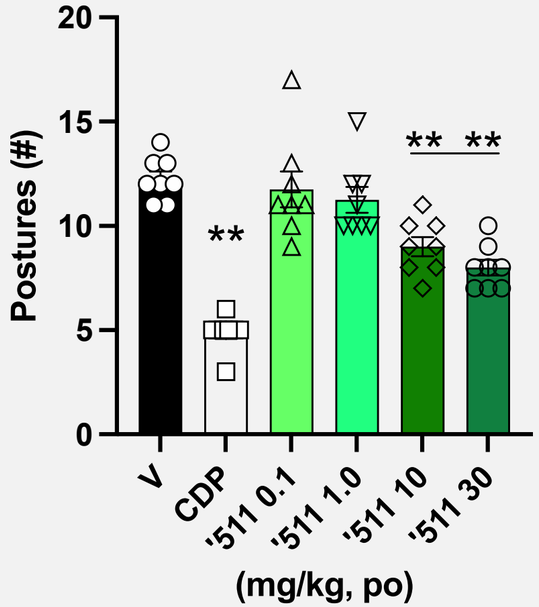
NMRA-511 reduced anxiety-related behaviors in a preclinical human threat test

Human threat test induces anxiety in marmosets[1]

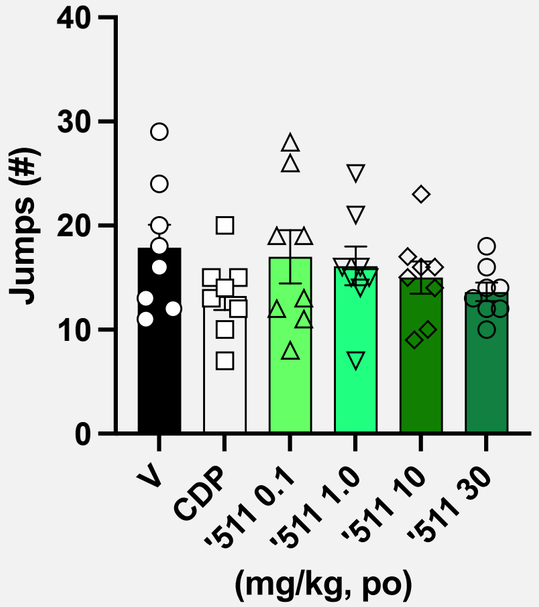


- Based on marmoset's behavioral response to situations of stress/uncertainty
- Set of characteristic postures are elicited
- Clinically effective anxiolytic drugs reduce the number of postures
- Locomotor activity is measured to control for sedative/stimulant effects of drugs

NMRA-511 reduces behavioral response to threat



NMRA-511 does not reduce locomotor activity



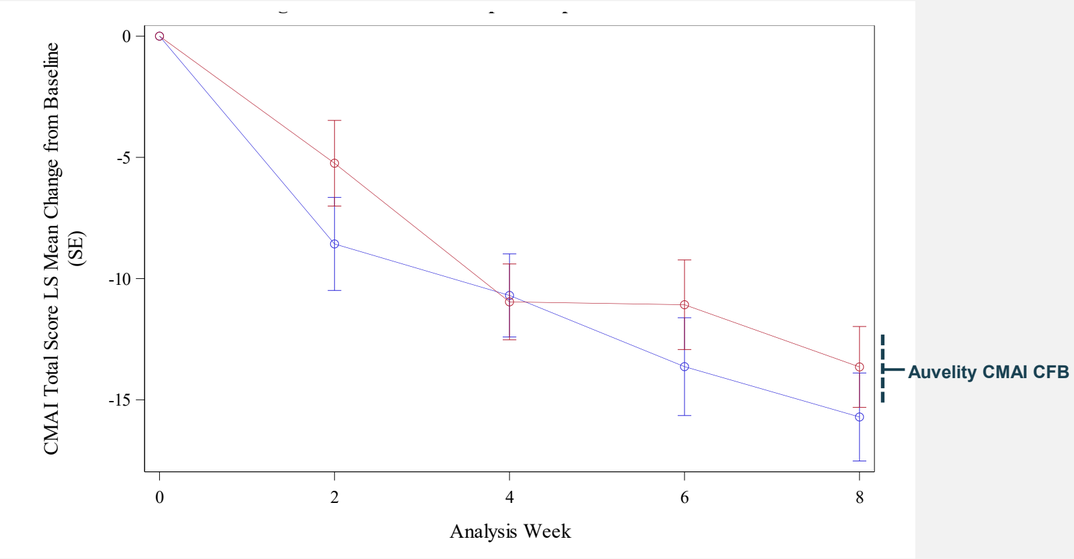
Orally administered NMRA-511 (10 and 30 mg/kg) and chlordiazepoxide (CDP, 2 mg/kg, SC) significantly reduced anxiety-related behaviors in marmosets (n=8) as measured by a decrease in the number of threat-elicited postures observed in the HTT without affecting locomotor activity or causing sedation. Testing occurred 90 mins after treatment to coincide with NMRA-511 maximal concentrations. *p<0.05 versus vehicle. Data plotted are mean± SE.

[1]Stawicka *et al*. PNAS 2020 Sep 21;117(40): 25116-25127 [2]Wallace et al., 2022. American College of Neuropsychopharmacology Annual Meeting Poster.

NMRA-511 demonstrated clinically meaningful reduction in CMAI total score and CMAI aggression sub-score

NMRA-511 demonstrated a 15.7-point reduction in CMAI total score at Week 8

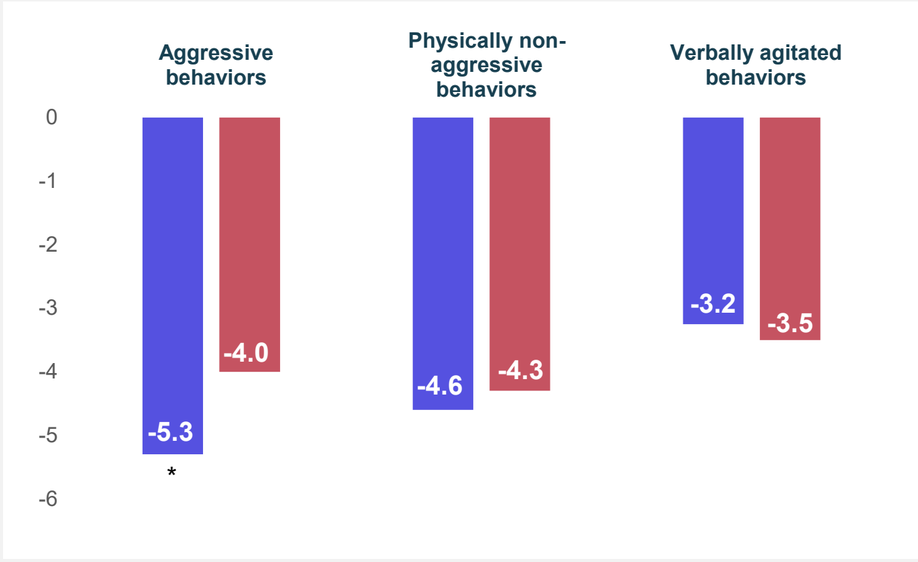
CMAI Total Score Change from Baseline (Modified Analysis Set)



	Week 6	Week 8
LSMD (SE)	-2.6 (2.7)	-2.1 (2.5)
Effect size range (Cohen's d)	0.23	0.20

CMAI aggression sub-score results suggest improvement on clinically relevant symptoms of AD agitation

Mean Change in CMAI Sub-Scores at Week 8 (Modified Analysis Set)



NMRA-511 n=33, placebo n=38
Nominal p-values: **p<0.05, *p<0.1

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