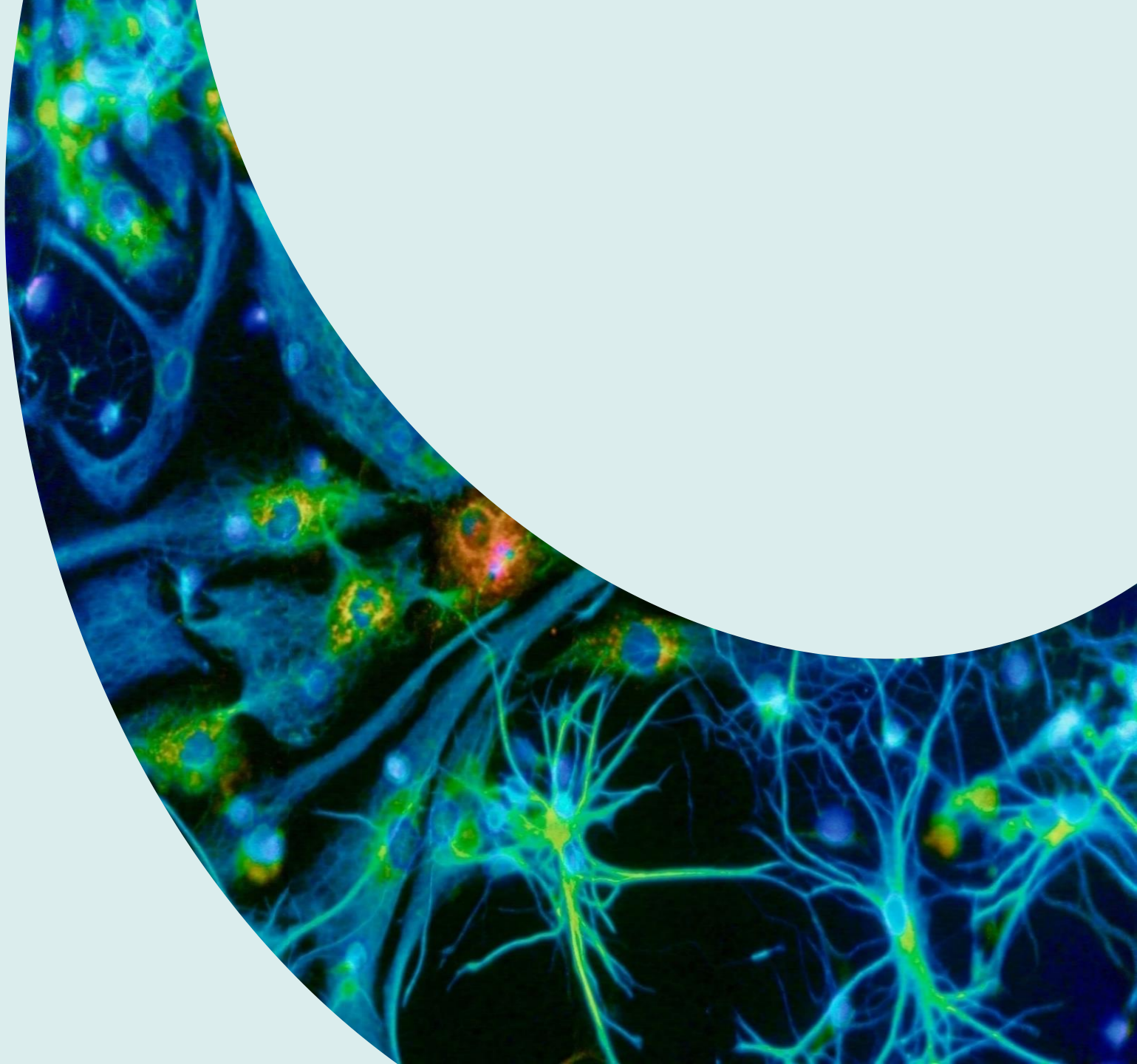
Topline Results for Phase 2 Trial of NBI-1117568 (NBI-’568) in Schizophrenia

August 28, 2024



NEUROCRINE® BIOSCIENCES

You Deserve Brave Science®

Forward Looking Statements

In addition to historical facts, this presentation contains forward-looking statements that involve a number of risks and uncertainties. These statements include, but are not limited to, statements regarding the clinical results from, and our future development plans with respect to, NBI-1117568, as well as the therapeutic potential and clinical benefits or safety profile of NBI-1117568. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: top-line data that we report may change following a more comprehensive review of the data related to the clinical study and such data may not accurately reflect the complete results of the clinical study; risks that clinical development activities may not be initiated or completed on time or at all, or may be delayed for regulatory, manufacturing, or other reasons, may not be successful or replicate previous clinical trial results, may fail to demonstrate that our product candidates are safe and effective, or may not be predictive of real-world results or of results in subsequent clinical trials; risks that regulatory submissions for our product candidates may not occur or be submitted in a timely manner; our future financial and operating performance; risks associated with our dependence on third parties for development, manufacturing, and commercialization activities for our products and product candidates, and our ability to manage these third parties; risks that the FDA or other regulatory authorities may make adverse decisions regarding our products or product candidates; risks that the potential benefits of the agreements with our collaboration partners may never be realized; risks that our products, and/or our product candidates may be precluded from commercialization by the proprietary or regulatory rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; risks associated with U.S. federal or state legislative or regulatory and/or policy efforts which may result in, among other things, an adverse impact on our revenues or potential revenue; risks associated with potential generic entrants for our products; and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission, including without limitation the Company's quarterly report on Form 10-Q for the quarter ended June 30, 2024. Neurocrine Biosciences disclaims any obligation to update the statements contained in this presentation after the date hereof other than required by law.

Agenda

1 **Introduction**

Kevin Gorman, Ph.D. | *Chief Executive Officer*

2 **Trial Design & Results**

Eiry Roberts, M.D. | *Chief Medical Officer*

3 **Q&A**

Kevin Gorman, Ph.D. | *Chief Executive Officer*
Kyle Gano, Ph.D. | *Chief Business Development and Strategy Officer*
Jude Onyia, Ph.D. | *Chief Scientific Officer*
Eiry Roberts, M.D. | *Chief Medical Officer*
Samir Siddhanti | *VP Business Development & Muscarinic Agonist Team Lead*
Jaz Singh, M.D. | *VP Clinical Development, Psychiatry*

Summary of Phase 2 Topline Results

Once-Daily 20mg Dose: Efficacy, Safety, and Tolerability Results Support Advancement to Phase 3

20mg Once-daily Demonstrated Statistically Significant and Clinically Meaningful Improvements Across Primary and Additional Endpoints

- **PANSS Total Score Change: -18.2**
- **PANSS Total Score Change vs. Placebo: -7.5 (p=0.011)**
- **Effect Size: 0.61**
- **CGI-S Change vs. Placebo: -0.7 (p<0.001)**
- **Marder Factor Score Change vs. Placebo:**
  - ***Positive:* -3.0 (p=0.004)**
  - ***Negative:* -1.9 (p=0.028)**

Generally Safe and Well-tolerated Across All Doses Tested

- Treatment discontinuation rates due to adverse events were similar between NBI-'568 and placebo
- Adverse events with the highest incidence were somnolence, dizziness, and headache
- Nausea, constipation and other gastrointestinal adverse events were low in frequency and similar to placebo
- NBI-'568 was not associated with a greater increase in weight than placebo

Efficacy, Safety and Tolerability Profile Combined With Once-daily Dosing Supports Advancement to Phase 3 Development

- NBI-'568 Phase 3 program in Schizophrenia expected to begin in early 2025
- Evaluating additional indications for NBI-'568
- Advancing follow-on compounds in muscarinic agonist portfolio

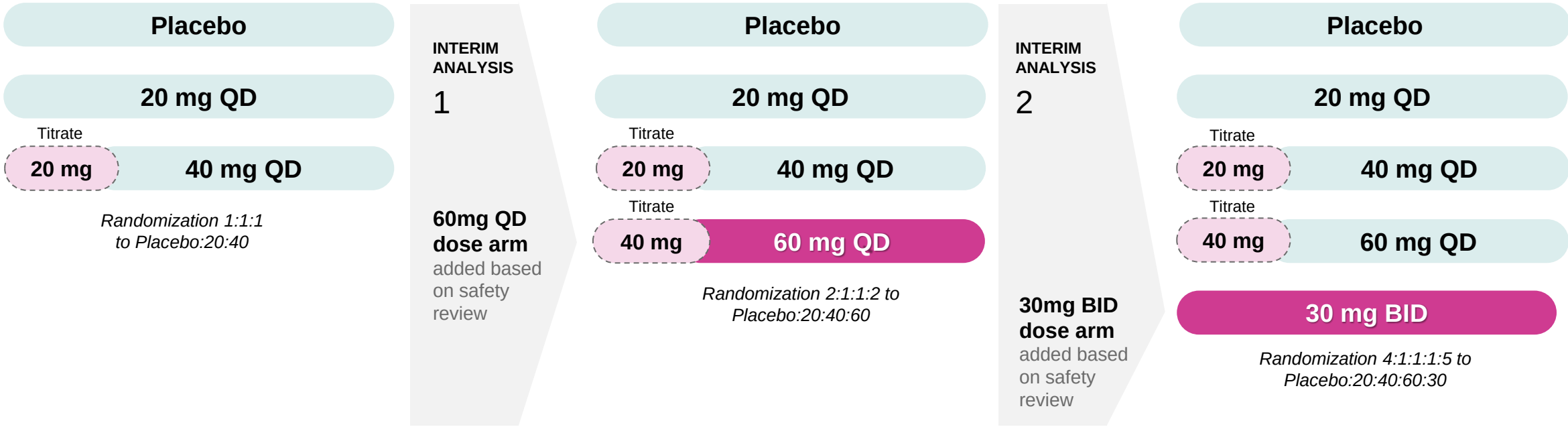
NEUROCRINE® BIOSCIENCES

PANSS = Positive & Negative Syndrome Scale; P-values are one-sided. Effect size (Cohen's D) is based on observed data.

Trial Design & Results

NBI-’568 Phase 2 Study Design

Dose-finding Study Using a First-in-Class Selective M4 Agonist



Notes:

- Adults with PANSS ≥80, Ages 18-55 enrolled at 15 US sites (inpatient)
- **Primary Endpoint:** Change in PANSS total score from baseline at Week 6
- Doses of 60mg QD and 30mg BID were added in a prespecified, blinded fashion by an independent data review committee based on safety and tolerability of previous dose levels
- Maintained 2:1 randomization ratio (all active doses: placebo) in the study overall

NEUROCRINE® BIOSCIENCES

PANSS = Positive & Negative Syndrome Scale; QD = Once-Daily Dosing; BID = Twice-Daily Dosing

Baseline Characteristics and Demographics Summary

	Placebo N=70	20mg QD N=40	40mg QD N=39	60mg QD N=34	30mg BID N=27	All Subjects N=210
Disease Characteristics At Baseline						
PANSS Total Score, mean	97	97	95	96	98	96
Demographics						
Age (years), mean	40	41	41	40	41	41
Male: n (%)	60 (85.7)	31 (77.5)	30 (76.9)	28 (82.4)	22 (81.5)	171 (81.4)
Race: n (%)						
American Indian or Alaska Native	0	0	0	0	1 (3.7)	1 (0.5)
Asian	1 (1.4)	1 (2.5)	0	0	0	2 (1.0)
Black or African American	57 (81.4)	30 (75.0)	28 (71.8)	24 (70.6)	14 (51.9)	153 (72.9)
White	11 (15.7)	9 (22.5)	10 (25.6)	7 (20.6)	11 (40.7)	48 (22.9)
Other	0	0	0	1 (2.9)	1 (3.7)	2 (1.0)
Multiple	1 (1.4)	0	1 (2.6)	2 (5.9)	0	4 (1.9)

Once-Daily 20mg Dose Met Primary Endpoint

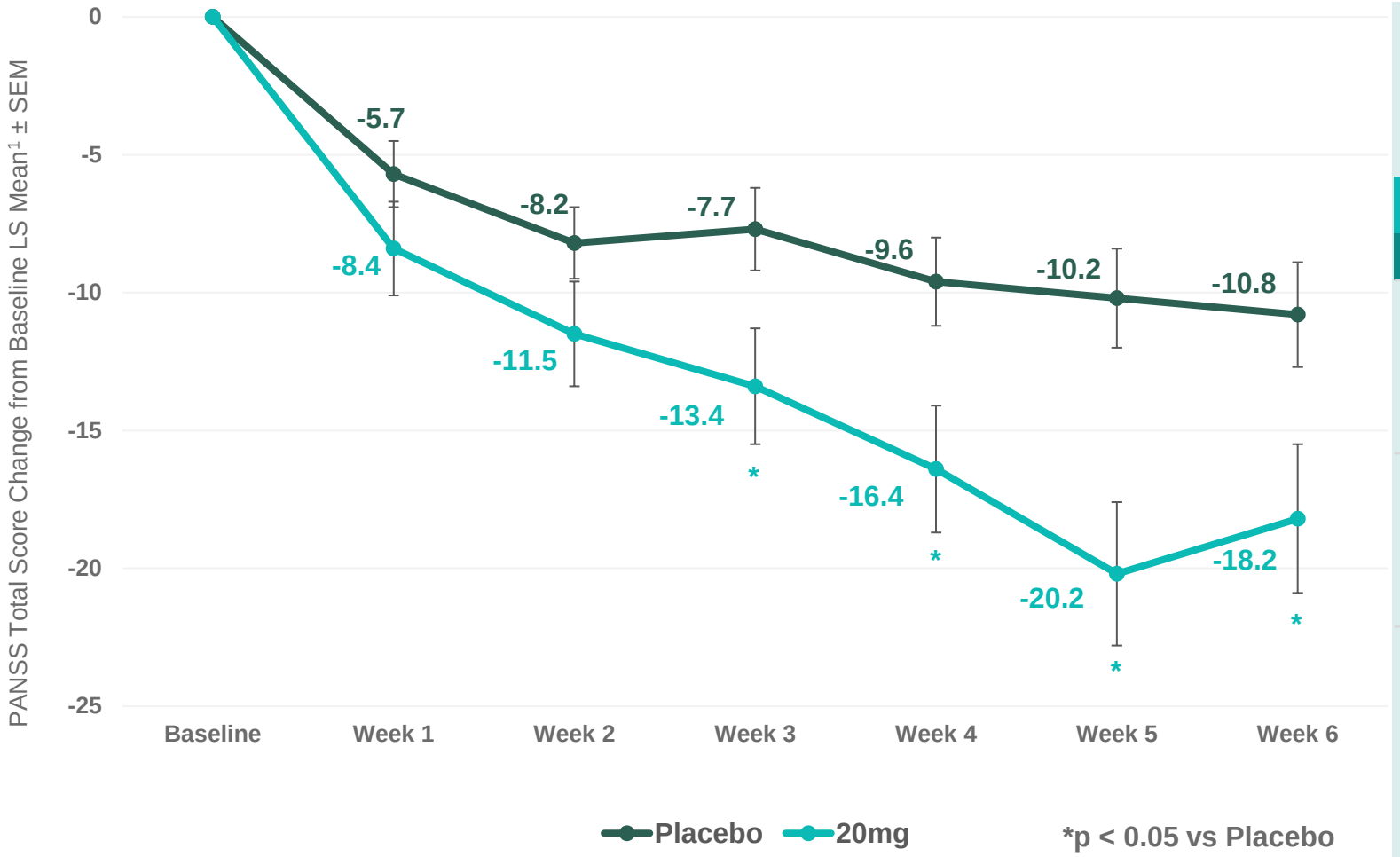
PANSS Total Score vs Placebo

Week 6	Placebo N=68	20mg QD N=35	40mg QD N=38	60mg QD N=34	30mg BID N=26
PANSS Total Score					
LS Mean Change from Baseline*	-10.8	-18.2	-12.6	-13.7	-15.8
LS Mean Difference vs. Placebo, p-value*		-7.5 p = 0.011	-1.9 p = 0.282	-2.9 p = 0.189	-5.0 p = 0.090
Effect Size**		0.61	0.27	0.39	0.23

NEUROCRINE® BIOSCIENCES

*Least-squares (LS) means are from a MMRM which includes treatment group, visit, and study period as fixed effects; treatment group-by-visit interaction; baseline PANSS total score as a covariate; and subject as a random effect.
**Effect size (Cohen's D) is based on observed data.

Once-Daily 20mg Dose Demonstrated Clinically Meaningful and Statistically Significant Efficacy at Week 3, 4, 5, and 6



20mg QD Efficacy Data
Week 4 – Week 6

Week	4	5	6**
PANSS Total Score			
LS Mean[1]	-16.4	-20.2	-18.2
LS Mean Difference vs. Placebo[1]	-6.8 p = 0.008	-10.0 p < 0.001	-7.5 p = 0.011
Effect Size[2]	0.53	0.72	0.61

*** Primary Endpoint = Week 6*

[1] Least-squares (LS) means are from a MMRM which includes treatment group, visit, and study period as fixed effects; treatment group-by-visit interaction; baseline PANSS total score as a covariate; and subject as a random effect.
[2] Effect size (Cohen's D) is based on observed data.

Once-Daily 20mg Dose Demonstrated Statistically Significant Improvement in Additional Endpoints

Week 6	CGI-S		Marder Factor — Positive		Marder Factor — Negative	
	Placebo N=68	20mg QD N=35	Placebo N=68	20mg QD N=35	Placebo N=68	20mg QD N=35
LS Mean Change from Baseline*	-0.5	-1.2	-2.8	-5.8	-1.2	-3.1
LS Mean Difference vs. Placebo*		-0.7 p < 0.001		-3.0 p = 0.004		-1.9 p = 0.028

*Least-squares (LS) means are from a MMRM which includes treatment group, visit, and study period as fixed effects; treatment group-by-visit interaction; baseline value as a covariate; and subject as a random effect.

NBI-’568 Was Generally Safe and Well Tolerated at All Doses Studied

Treatment-Emergent Adverse Events Occurring in ≥ 5% of NBI-'568 All Treated Group

	Placebo N=70	20mg QD N=40	40mg QD N=39	60mg QD N=34	30mg BID N=27	All Treated N=140
Somnolence	2 (2.9)	5 (12.5)	2 (5.1)	7 (20.6)	1 (3.7)	15 (10.7)
Dizziness	1 (1.4)	5 (12.5)	3 (7.7)	4 (11.8)	1 (3.7)	13 (9.3)
Headache	14 (20.0)	1 (2.5)	5 (12.8)	1 (2.9)	5 (18.5)	12 (8.6)
Nausea	2 (2.9)	2 (5.0)	3 (7.7)	3 (8.8)	0	8 (5.7)
Constipation	2 (2.9)	2 (5.0)	3 (7.7)	1 (2.9)	1 (3.7)	7 (5.0)

5.0% Treatment Discontinuation Rate Due to Adverse Events Across All NBI-'568 Arms vs. 4.3% For Placebo

NEUROCRINE® BIOSCIENCES

NBI-’568 is the First and Only Muscarinic M4 Selective Orthosteric Agonist in Clinical Development

Type of Muscarinic Activation	Subtype Selectivity	Requires Endogenous Ligand (Acetylcholine)
Pan Agonism	**Low** Targets M1-M5	**No**
Positive Allosteric Modulation	**High** Targets only M4	**Yes**
Selective Agonism (NBI-'568)	**High** Targets only M4 >500-fold agonist selectivity for the M4 receptor over other muscarinic receptors	**No**

Large Opportunity For NBI-'568, A Novel And Differentiated Asset

With no reliance on innate acetylcholine levels, NBI-'568 is the **first and only highly selective orthosteric M4 agonist**, potentially introducing a **new modality for treatment.**

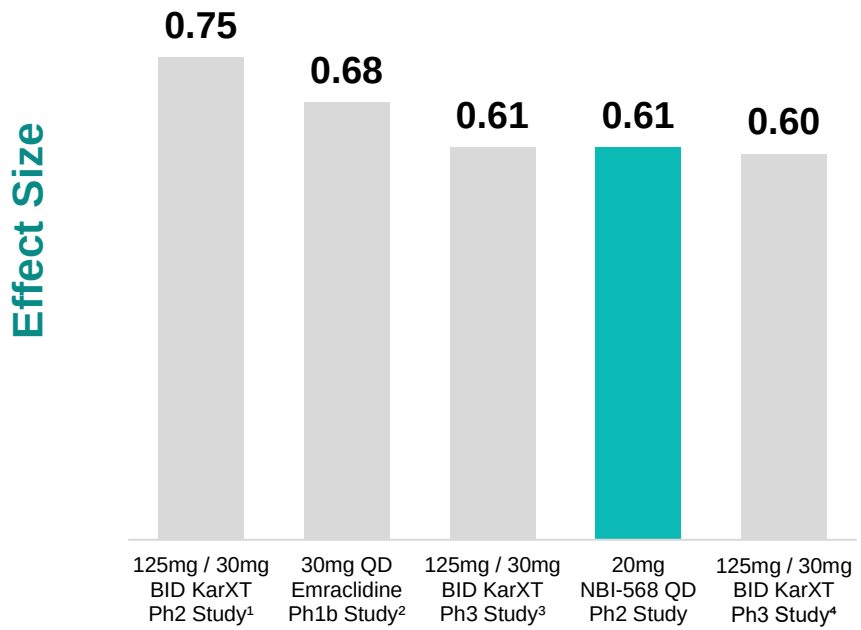
NBI-'568 potentially offers a compelling and competitive benefit-risk profile

Convenience of **once-daily dosing with or without food**

Increased conviction in **indication expansion opportunities** for NBI-'568 and Neurocrine’s muscarinic portfolio

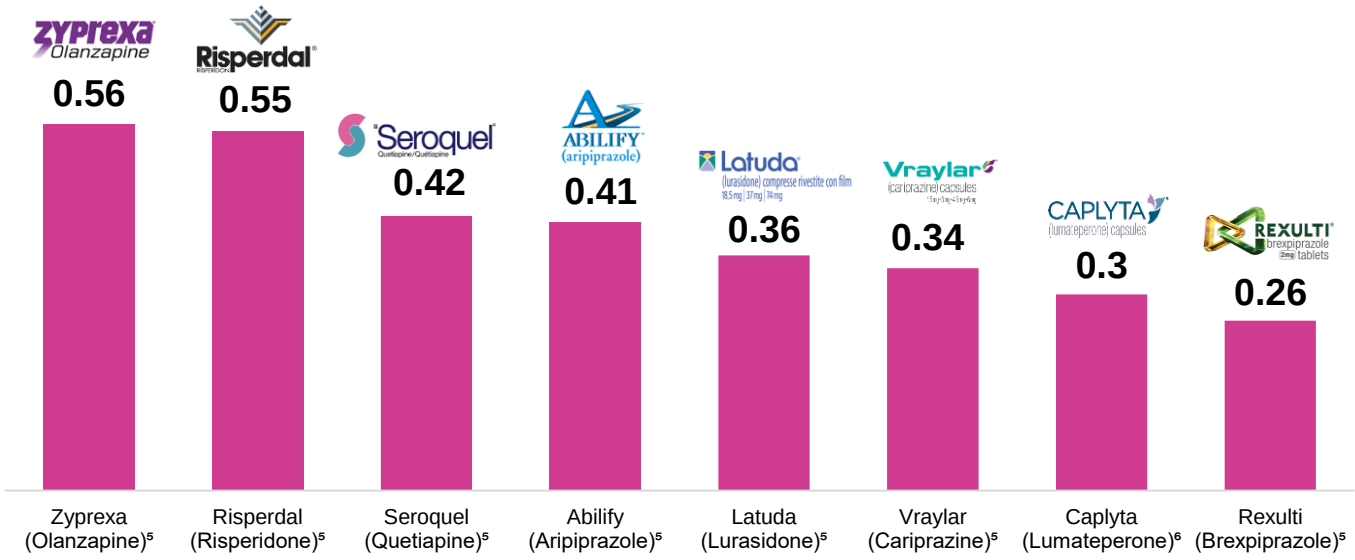
NBI-’568 Effect Size Comparable to Known Muscarinic Programs and Leading Antipsychotics

Clinical-Stage Muscarinic Programs



Sites	12	5	22	15	30
Randomization Ratio (active:placebo)	1:1	2:1	1:1	2:1	1:1
Weeks of Treatment	5	6	5	6	5
Date	Nov ‘19	Jun ’21	Aug ’22	Aug ’24	Mar ‘23

Leading Approved Treatments



Source: 1. Brannan S, et al. N Engl J Med. 2021;384(8):717-726. 2. Krystal J, et al. Lancet. 2022;400(10369):2210–2220. 3. Kaul I, et al. Lancet. 2024;403(10422):160–170. 4. Kaul I, et al. JAMA Psychiatry. 2024;81(8):749-756. 5. Huhn M, et al. Lancet. 2019;394(10202):939-951. 6. Correll CU, et al. JAMA Psychiatry. 2020;77(4):349-358.

NEUROCRINE BIOSCIENCES

Validation of Selective Orthosteric Agonist Mechanism Strengthens Conviction In Opportunities For Industry Leading Muscarinic Portfolio

	Primary Mechanism (M1-M4)	Phase	Therapeutic Areas	Potential Areas For Development
NBI-1117568	M4 agonist	2	Psychosis Cognition	Alzheimer's Disease Bipolar Disorder Lewy Body Dementia Parkinson's Disease Schizophrenia
NBI-1117567	M1 agonist	1		
NBI-1117569	M4 agonist	1		
NBI-1117570	M1/M4 dual agonist	1		
NBI-1076986	M4 antagonist	1	Movement Disorders	Dystonia Parkinson's Disease Tremor

Summary of Topline Results

NBI-'568 20mg once-daily dose demonstrated meaningful improvement in PANSS Total Score at Week 6:

- 18.2 point improvement in PANSS Total Score
- 7.5 point placebo-adjusted improvement
- Effect size of 0.61

NBI-'568 was well tolerated across all doses:

- 5.0% treatment discontinuation rate due to adverse events across all NBI-'568 active arms vs. 4.3% for placebo
- Nausea, constipation and other gastrointestinal adverse events were low in frequency and similar to placebo
- No weight gain relative to placebo

Data support advancing NBI-'568 into Phase 3 for schizophrenia

NBI-'568 Has A Differentiated Profile Vs. Other Antipsychotics:

- **Novel Mechanism of Action**
- **Simple once-daily dosing with or without food**
- **GI effects and weight gain similar to placebo**

NEUROCRINE® BIOSCIENCES

PANSS = Positive & Negative Syndrome Scale. Effect size (Cohen's D) is based on observed data.

Q&A

Kevin Gorman, Ph.D.

Chief Executive Officer

Kyle Gano, Ph.D.

Chief Business Development and Strategy Officer

Jude Onyia, Ph.D.

Chief Scientific Officer

Eiry Roberts, M.D.

Chief Medical Officer

Samir Siddhanti

VP Business Development & Muscarinic Agonist Team Lead

Jaz Singh, M.D.

VP Clinical Development, Psychiatry