



MINERVA
NEUROSCIENCES, INC.

Innovation to treat unmet medical needs in CNS disorders

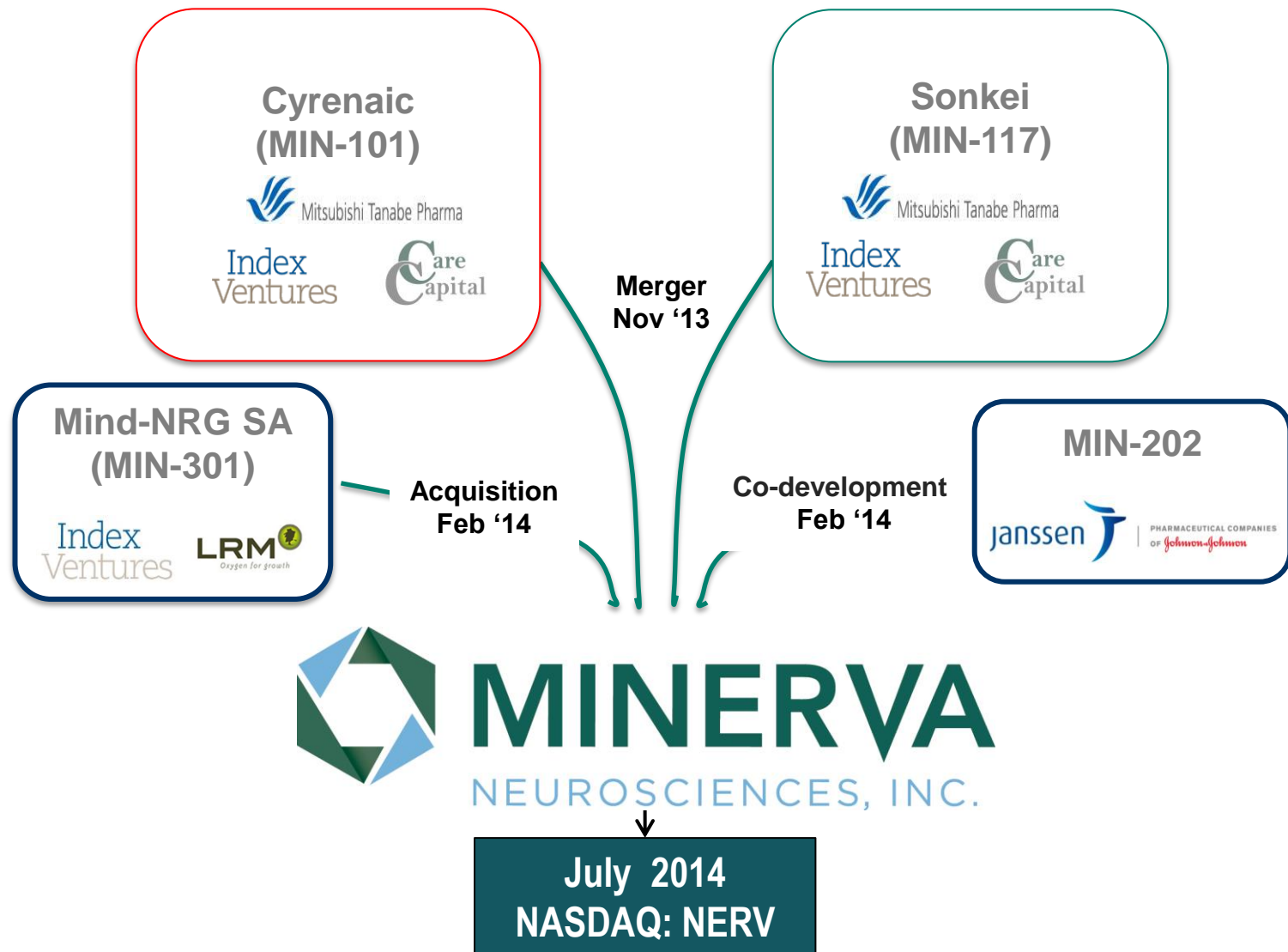
February, 2017

Nasdaq: NERV

This presentation contains certain forward-looking statements about Minerva Neurosciences that are intended to be covered by the safe harbor for “forward-looking statements” provided by the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. Words such as “expect(s),” “feel(s),” “believe(s),” “will,” “may,” “anticipate(s)” and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to: the benefits, efficacy and safety of our new formulations; whether studies performed on analogs or backups of our compounds are a good predictor of the clinical efficacy of our compounds; the timing and results of future clinical milestones; the timing of future clinical trials and results of such clinical trials; statements regarding our ability to successfully develop and commercialize our therapeutic products; our ability to expand our long-term business opportunities; our expectations regarding approval for our products by the U.S. Food and Drug Administration or equivalent foreign regulatory agencies; estimates regarding the market potential for our products; financial projections and estimates and their underlying assumptions; and future performance. All of such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond the control of the Company, that could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking statements. These risks and uncertainties include, but are not limited to: the benefits, efficacy and safety of our new formulations; whether analogs or backups of our compounds are a good predictor of the clinical efficacy of our compounds; the timing and results of future clinical milestones; the timing of future clinical trials and results of such clinical trials; whether any of our therapeutic candidates will advance further in the clinical trials process and whether and when, if at all, they will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; whether any of our therapeutic candidates will be successfully marketed if approved; whether our therapeutic product discovery and development efforts will be successful; our ability to achieve the results contemplated by our collaboration agreements; the strength and enforceability of our intellectual property rights; competition from pharmaceutical and biotechnology companies; the development of and our ability to take advantage of the market for our therapeutic products; our ability to raise additional capital to fund our operations on terms acceptable to us; general economic conditions; and the other risk factors contained in our periodic and interim reports filed with the Securities and Exchange Commission which are available on the SEC website at www.sec.gov. Our audience is cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.

A CNS company targeting schizophrenia, major depressive disorder, insomnia and Parkinson's disease

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Investment highlights

- Broad late-stage pipeline
- Lead asset, MIN-101, has differentiated MoA with specific effect on negative symptoms and is planned to initiate pivotal Phase III trials for treatment of schizophrenia in Q3 2017
- Compelling efficacy and safety data generated in randomized, double-blind, placebo-controlled Phase 2 clinical trials
- Significant unmet needs and market opportunities in schizophrenia, MDD and insomnia
- Strong cash position
- Experienced CNS-focused management team

A portfolio of innovative product candidates to treat various CNS diseases

Program	Origin	Primary Indications	Mechanisms of Action	Pre-clinical	Phase I	Phase II	Status
MIN-101	Mitsubishi Tanabe	Schizophrenia	<ul style="list-style-type: none"> • 5-HT_{2A} antagonist • Sigma₂ antagonist 	Phase IIb completed			Positive results announced May & October 2016
MIN-202	Janssen (under co-development)	Primary Insomnia	<ul style="list-style-type: none"> • Selective Orexin₂ antagonist 	Phase IIa completed			Positive results Announced January 2016
		Major Depressive Disorder		Phase Ib completed			Positive results announced March 2016
MIN-117	Mitsubishi Tanabe	Major Depressive Disorder	<ul style="list-style-type: none"> • 5-HT_{1A} • 5HT transporter • Alpha-1a, b • Dopamine transporter • 5-HT_{2A} antagonist 	Phase IIa completed			Positive results announced May 2016
MIN-301	Mind-NRG	Parkinson's Disease	<ul style="list-style-type: none"> • Neuregulin 1β₁ activating ErbB4 	Pre-clinical			Next steps: IND or IMPD filing, with Phase 1 expected to initiate thereafter

- Extensive knowledge of the pathology, course and impact of CNS diseases
- Focus on desired outcomes that address unmet patient needs
- Understanding of the impact of novel MOAs
- Insights into CNS clinical trial design and conduct based on extensive hands-on experience
- Ability to characterize and validate patient populations who will benefit from treatment with our compounds



Summary of Partnerships

MIN-101: In-licensed from Mitsubishi Tanabe Pharmaceutical Company (MTPC)

- Minerva: exclusive worldwide license includes rights to develop, commercialize and sub-license MIN-101 (and back-ups) outside of certain Asian countries
- MTPC: retains rights to commercialize and sell MIN-101 in certain Asian countries including China, Japan, India and South Korea (MTPC Territory)
- Milestones upon launch and commercialization goals could total up to \$47.5 million payable
- Royalties payable on net sales range from high single digits to low teens

MIN-117: In-licensed from Mitsubishi Tanabe Pharmaceutical Company (MTPC)

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- MTPC: retains rights to commercialize and sell MIN-117 in certain Asian countries including China, Japan, India and South Korea (MTPC Territory)
- Milestones upon launch and commercialization goals could total up to \$47.5 million payable
- Royalties payable on net sales range from high single digits to low teens

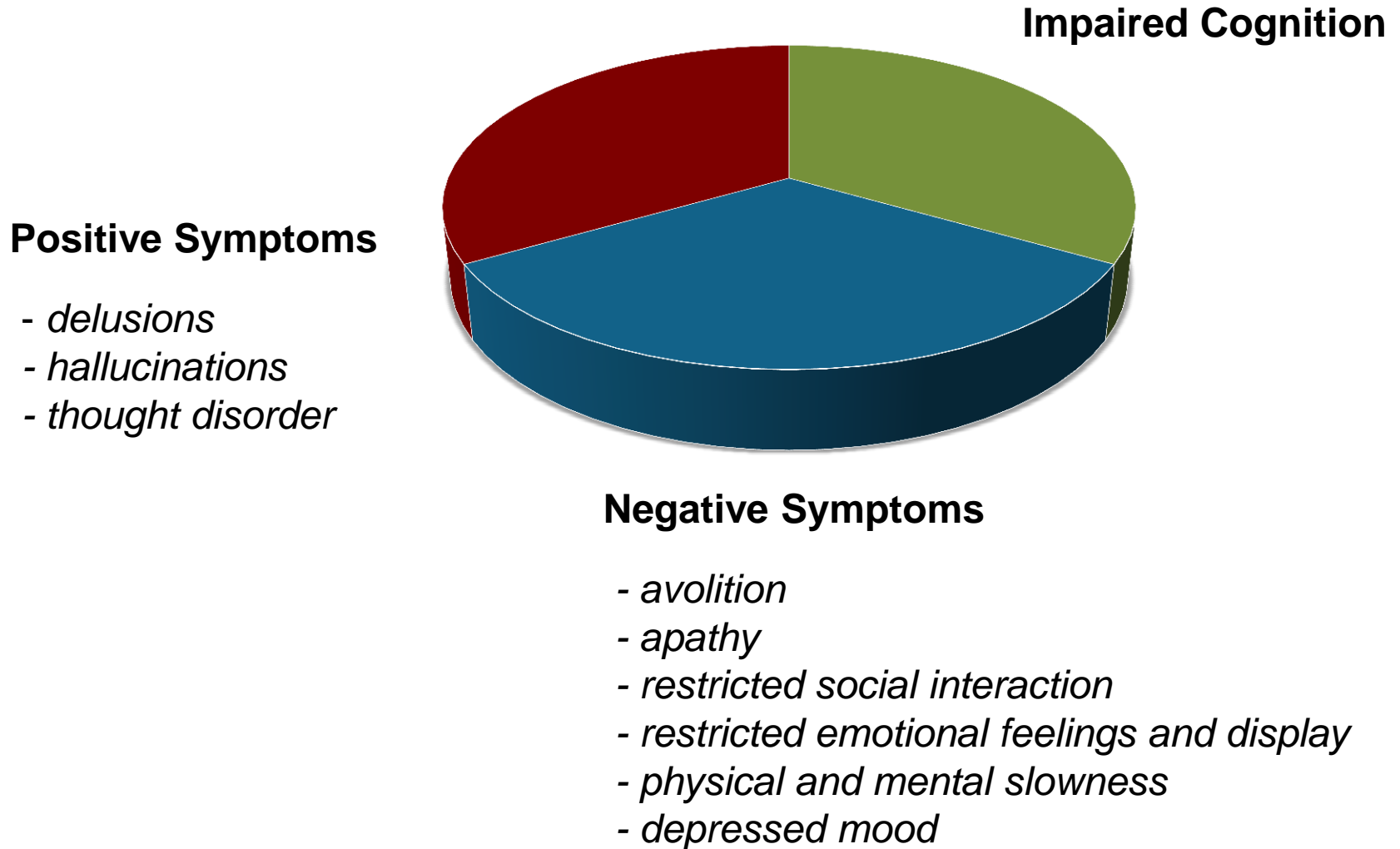
MIN-202: Co-development and license agreement with Janssen Pharmaceutica NV (Janssen)

- Minerva has commercialization rights for EU, Switzerland, Liechtenstein, Iceland & Norway (Minerva Territory) with rights to sub-license
 - Minerva pays quarterly high single digit % royalty to Janssen on Minerva Territory net sales
- Janssen has commercialization rights in all territories outside of the Minerva Territory
 - Janssen pays high single digit % royalty to Minerva on all sales outside of Minerva Territory
- Minerva contributes 40% of development cost subject to ceiling caps at various points in the clinical development plan

MIN-101

A paradigm shift in the treatment of schizophrenia

Schizophrenia: three symptom domains



Current standard of care: ‘Major tranquilizers’ or atypical antipsychotics (block dopamine D2 receptors) – *Significant unmet needs exist*

- Reduce agitation and therefore the need for physical restraint and seclusion
- Ameliorate severity of acute positive symptoms in about 60% of the patients
- Once positive symptoms ameliorated, chronic administration could impair functional improvement
- Induce adverse effects such as:
 - body stiffness and involuntary movements
 - diabetes, weight gain, and cardiovascular diseases
 - a sense of mental slowness, heaviness, and apathy

75% patients are non-adherent to existing therapies within 2 years of being discharged from hospital¹

BUT

- **No effect on negative symptoms**
- **No effect on cognitive functioning**
- **No real-life effect on social and vocational re-integration**
- Patients who do not respond to the first Rx with an antipsychotic would probably not respond to anything (*maybe with the exception of clozapine*)
- The main difference between currently marketed antipsychotics lies in their side effect profiles (*except for clozapine*)
- Relative improvement in certain aspects of a side effect profile does not constitute efficacy on negative symptoms (“pseudo-specificity”)

Unique combination of pharmacological targets without any direct binding to dopaminergic (DA) receptors

Receptor subtypes	Materials	Ki values, nmol/L
Serotonin 5-HT _{2a}	Rat, cerebral cortex	7.5
	Human recombinant	5.2
Sigma ₂	Guinea pig, brain	8.2
Sigma ₁	Guinea pig, brain	253.8
A ₁ adrenergic	Rat, brain	14.4

- Specific affinity for σ_2 , 5-HT_{2A} and α_1 -adrenergic receptors
- No affinity (>1000 nM) for other receptors including dopaminergic, muscarinic, cholinergic and histaminergic receptors
- No direct dopamine binding, unlike most (or all) available antipsychotics
- The behavioral pharmacology package is consistent with an antagonistic effect for σ_2 and 5-HT_{2A} receptors

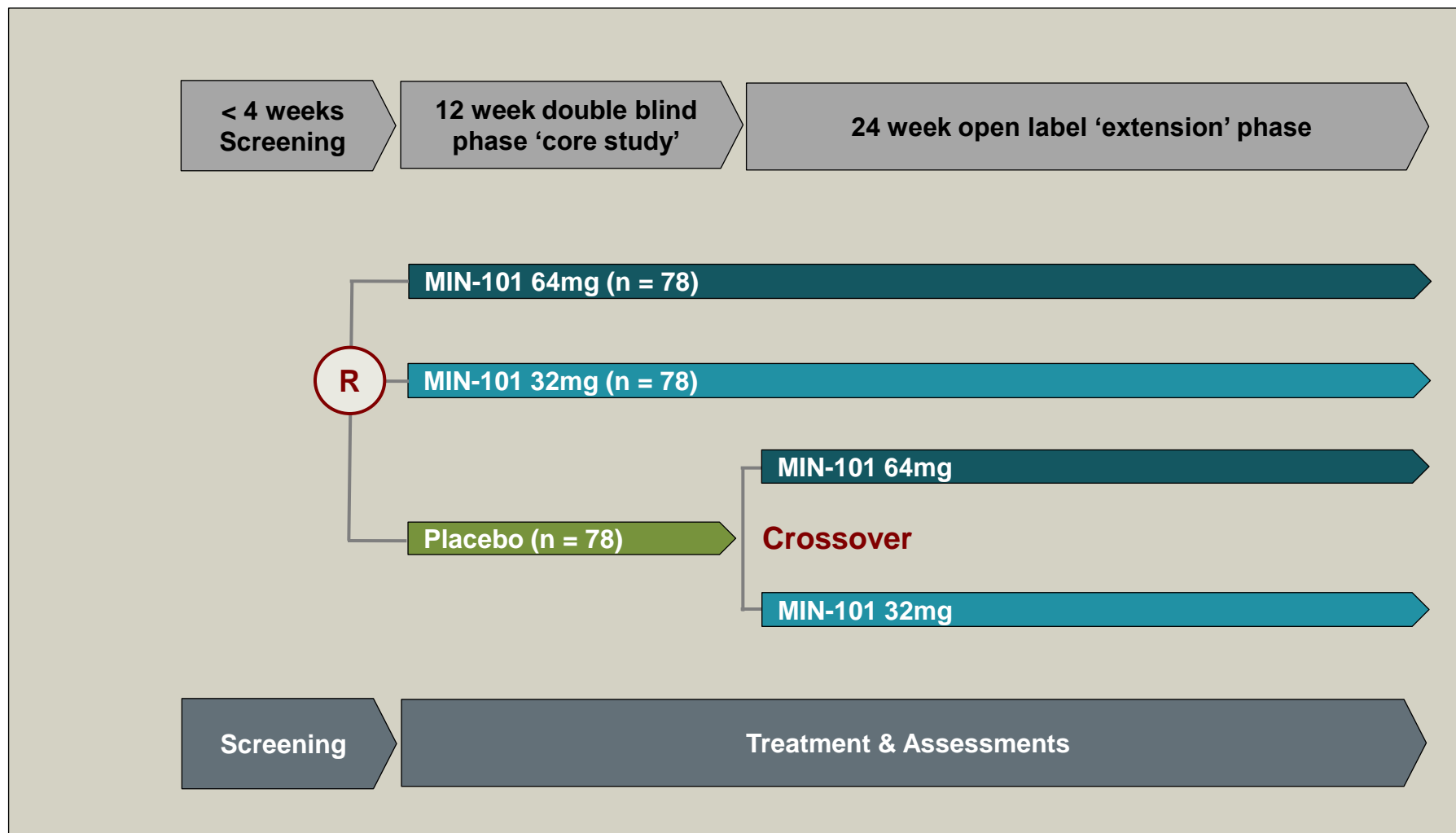


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Phase IIb in schizophrenic patients (MIN-101C03)

**Core study results published in May 2016
&
6 months extension results published in October 2016**

MIN-101 Phase IIb study design: monotherapy, double-blind, placebo-controlled in schizophrenic patients with negative symptoms



(R) = Randomization

Summary findings from Phase IIb trial with MIN-101

- MIN-101 treatment resulted in statistically significant improvement in PANSS negative symptoms and total PANSS scores
- MIN-101 also shown to be statistically superior to placebo on multiple key secondary endpoints
- Effect of MIN-101 demonstrated to be specific for negative symptoms and not secondary to improvement in other symptoms
- MIN-101 well tolerated, with incidence and types of side effects not differing significantly from placebo; two patients out of 162 who received MIN-101 discontinued based on QT prolongation (both at higher dose)

Final results of MIN-101 Phase IIb efficacy analyses

		p-value (MIN-101 vs placebo)		Effect size (MIN-101 vs placebo)	
	Endpoint at 12 weeks	32mg	64mg	32mg	64mg
Primary objective	5-Factor Negative Score (i.e., Negative Symptoms, Pentagonal Structure):	0.0240	0.0036	0.45	0.57
Secondary objectives	PANSS total score	0.0819	0.0031	0.34	0.57
	3-Factor Negative Score	0.0064	0.0004	0.54	0.70
	3-Factor Positive Score	0.4018	0.3067	0.16	0.20
	3-Factor General Psychopathology Score	0.2359	0.0034	0.23	0.56
	5-Factor Positive Score	0.5045	0.2146	-0.13	0.24
	5-Factor Dysphoric Mood Score	0.5644	0.0266	0.11	0.43
	5-Factor Activation Score	0.0240	0.0118	0.44	0.49
	5-Factor Autistic Preoccupation Score	0.6700	0.2408	0.08	0.22
	CGI-S* (severity)	0.0982	0.0234	0.35	0.43
	CGI-I** (improvement)	0.2378	0.0032	0.33	0.57
	BNSS (Brief Negative Symptom Scale)	0.0869	0.0040	0.33	0.56
	Brief Assessment of Cognition in Schizophrenia (Total Score)	0.0388	0.5947	0.40	0.10
	BACS cognition assessment (Composite T Score)	0.2737	0.8253	0.21	-0.04
	- Token Motor Test	0.0306	0.0493	0.42	0.38
	- Motor Function: Symbol Coding Task	0.6310	0.0781	0.09	0.33
	- Verbal Fluency: Semantic Fluency	0.0299	0.1838	0.42	0.25
	- Verbal Fluency: Letter Fluency	0.0328	0.0878	0.41	0.32
	- Total Verbal Fluency	0.0076	0.0554	0.51	0.36
	- Verbal Memory	0.1544	0.3158	0.27	0.19
	Executive Function: Tower of London	0.3988	0.1952	0.16	0.25
Exploratory objectives	CDSS depression scale	0.1756	0.0091	0.25	0.46
	PSP personal and social performance				
	- Socially Useful Activities	0.4775	0.0601	0.14	0.38
	- Personal & Social Relationships	0.9174	0.0129	0.02	0.53
	- Self-care	0.1736	0.0210	0.27	0.46
	- Disturbing & Aggressive Behavior	0.0532	0.0057	0.36	0.51

Bold red text indicates p-value < 0.05

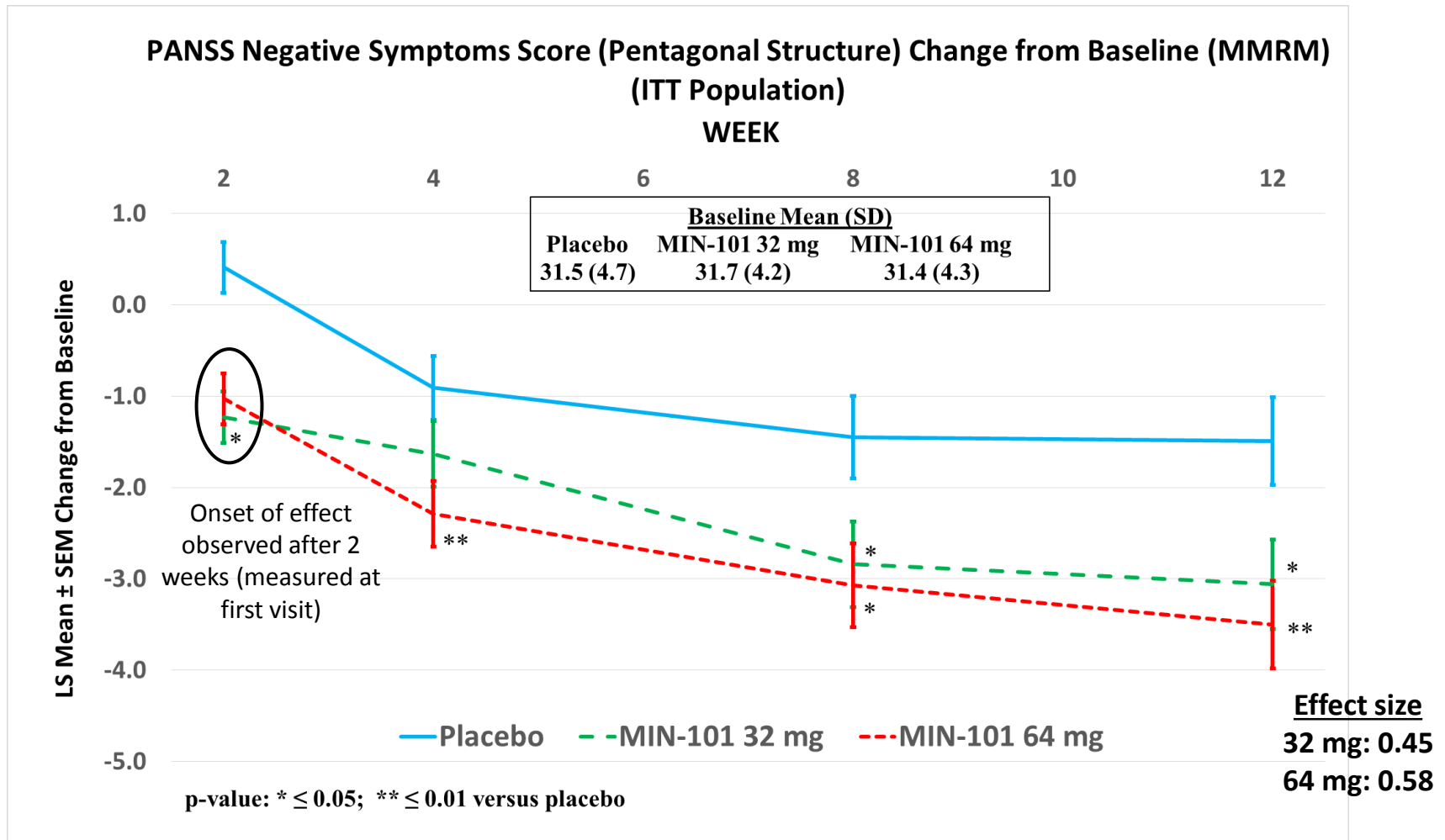
* Analyzed using ranked data: change from Baseline and ES are based on observed change from baseline data

** Analyzed using ranked data; ES is based on observed data



Efficacy: Primary endpoint

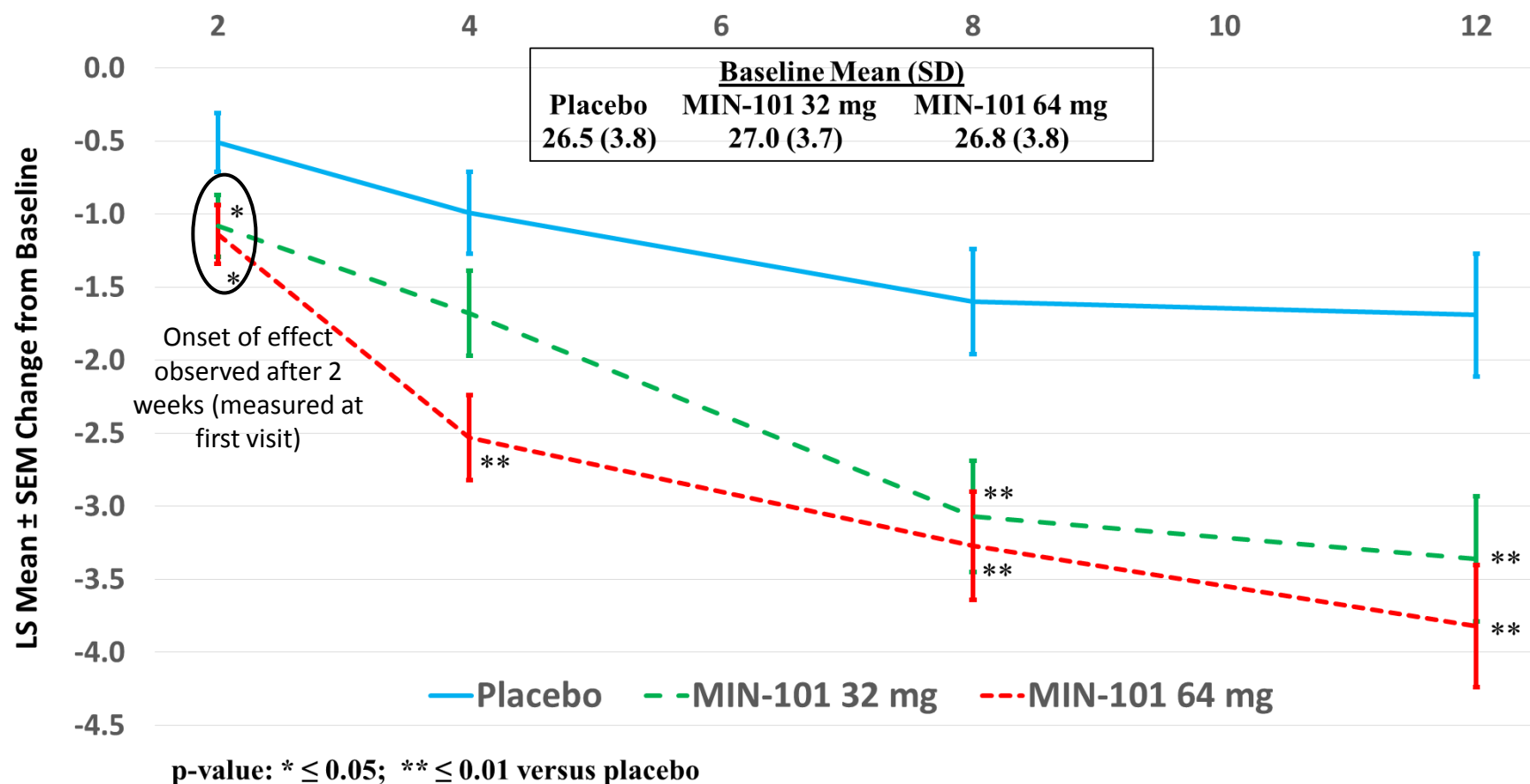
PANSS negative subscale (pentagonal structure)



Efficacy: Secondary endpoint (1)

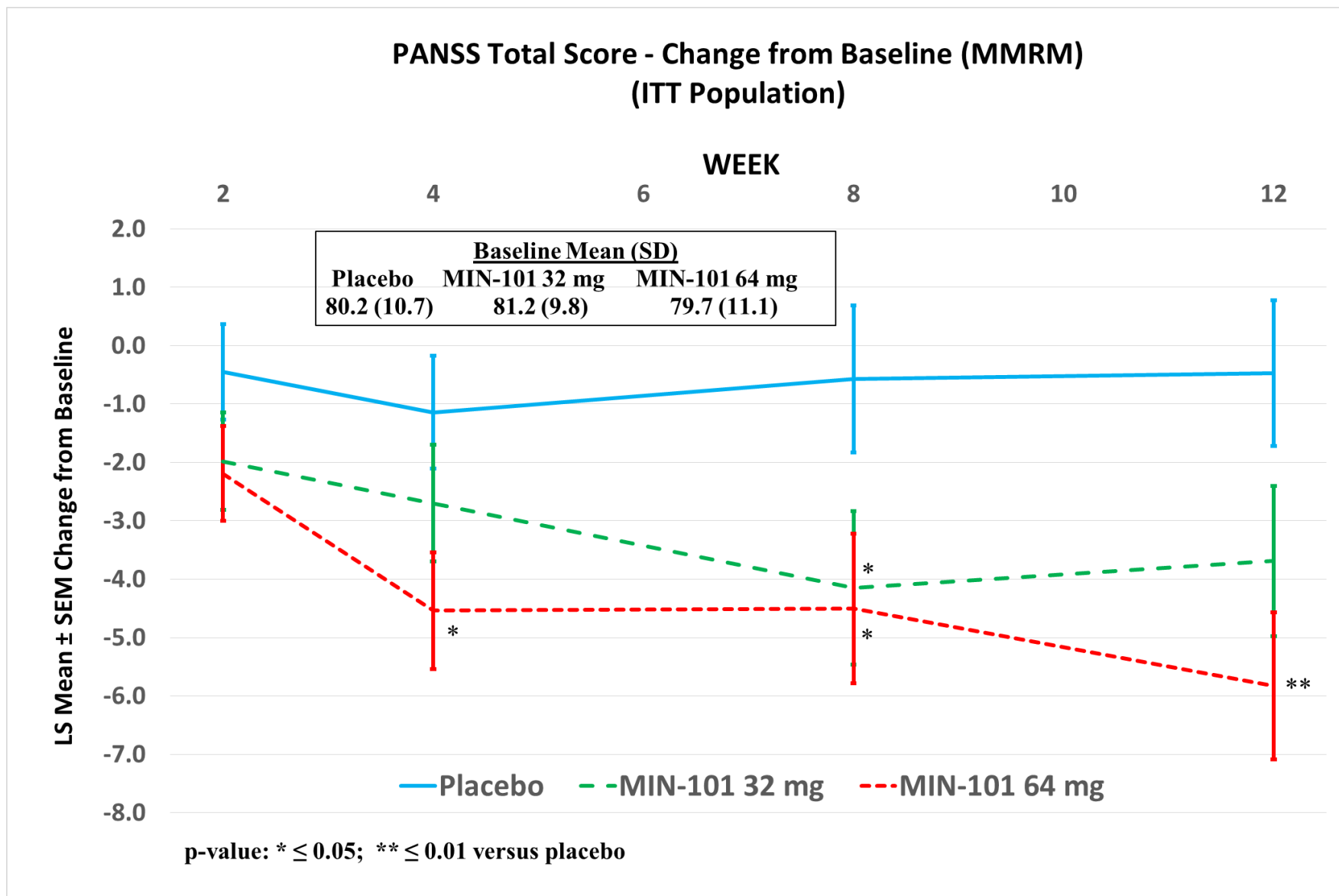
PANSS negative symptom score (3 Factors)

PANSS Negative Symptom Score (3 Factors) - Change from Baseline (MMRM)
(ITT Population)
WEEK



Efficacy: Secondary endpoint (2)

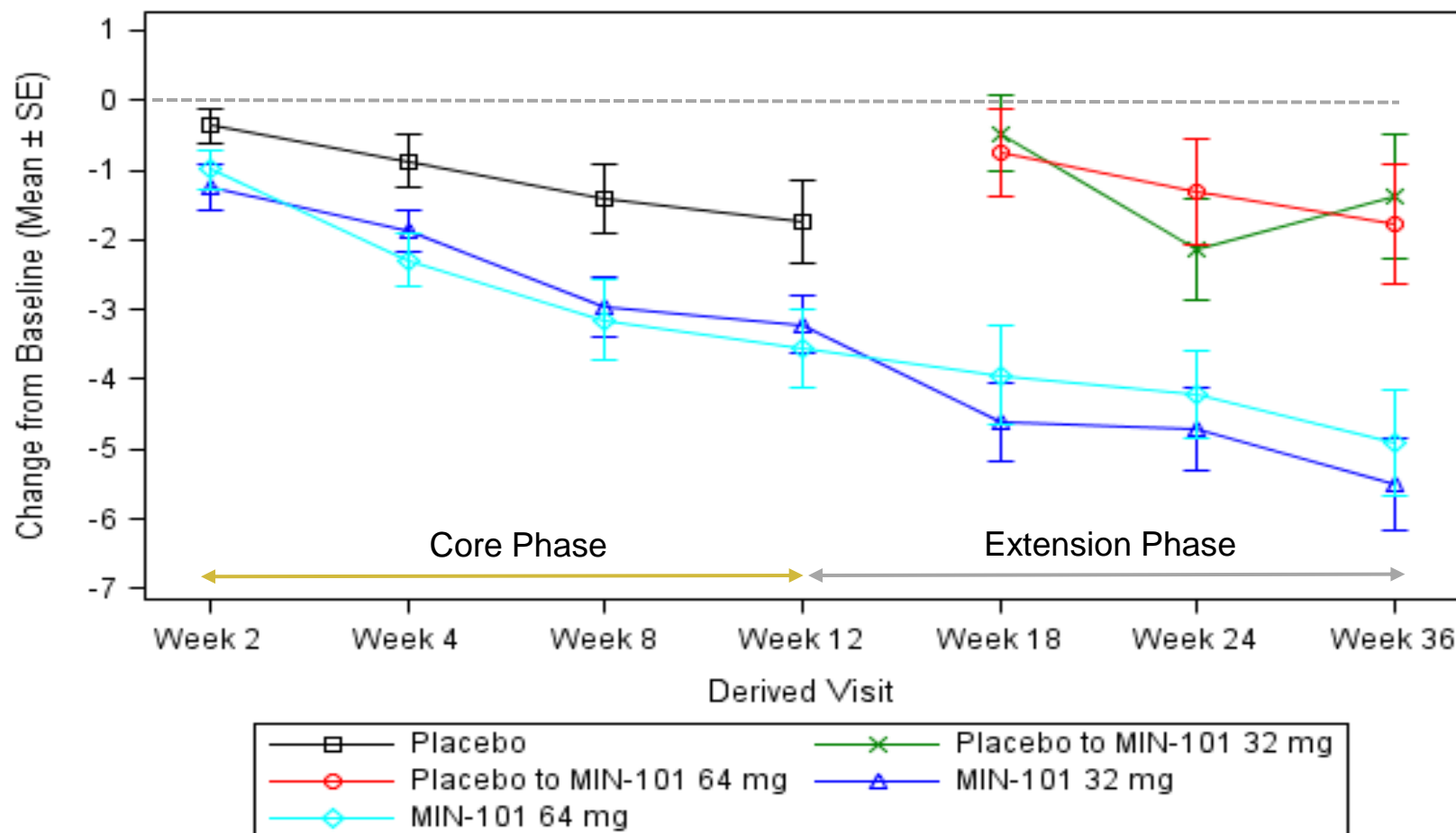
PANSS total score



Extension Phase

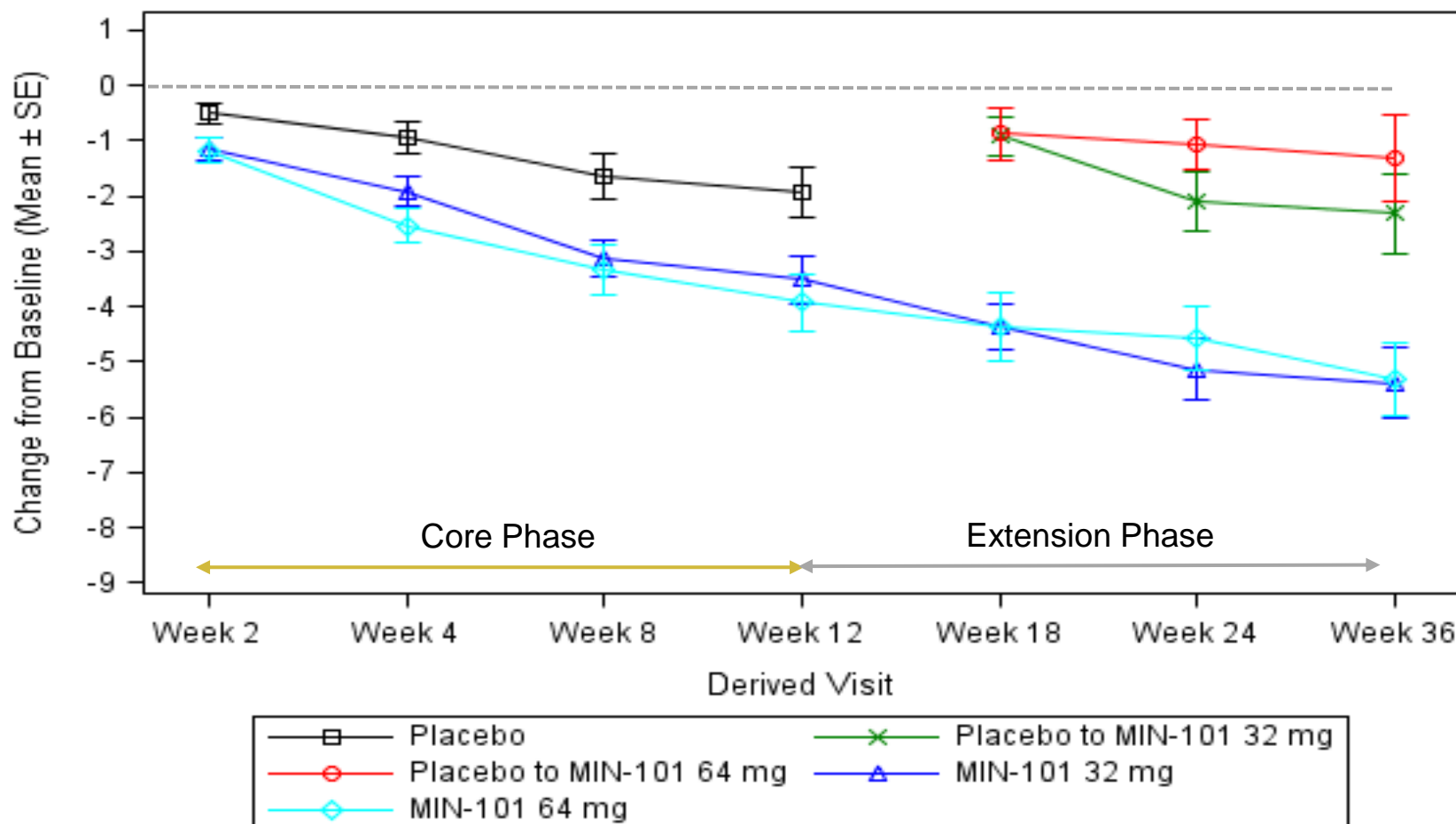
Baseline for patients who crossed from placebo to MIN-101 is start of open label (Week 12)

MIN-101C03: Negative Symptoms (Pentagonal Structure)



Baseline for Placebo-to-MIN-101 is From Start of Open Label (Week 12)

MIN-101C03: Negative Symptoms (3-Factors)



Baseline for Placebo-to-MIN-101 is From Start of Open Label (Week 12)

Safety

(complete study)

MIN-101C03: Common Adverse Events (≥ 5% of Patients)

System Organ Class Preferred Term	Placebo ¹ (N = 83)	MIN-101 ²			Overall (N = 244)
		32 mg (N = 103)	64 mg (N = 102)	Total (N = 205)	
Subjects with Any Common TEAE	20 (24.1%)	24 (23.3%)	29 (28.4%)	53 (25.9%)	69 (28.3%)
Investigations	0 (0.0%)	0 (0.0%)	6 (5.9%)	6 (2.9%)	6 (2.5%)
Electrocardiogram QT prolonged	0 (0.0%)	0 (0.0%)	6 (5.9%)	6 (2.9%)	6 (2.5%)
Nervous system disorders	3 (3.6%)	9 (8.7%)	8 (7.8%)	17 (8.3%)	19 (7.8%)
Headache	3 (3.6%)	9 (8.7%)	8 (7.8%)	17 (8.3%)	19 (7.8%)
Psychiatric disorders	18 (21.7%)	17 (16.5%)	18 (17.6%)	35 (17.1%)	50 (20.5%)
Anxiety	5 (6.0%)	8 (7.8%)	7 (6.9%)	15 (7.3%)	19 (7.8%)
Insomnia	8 (9.6%)	7 (6.8%)	8 (7.8%)	15 (7.3%)	22 (9.0%)
Schizophrenia	9 (10.8%)	4 (3.9%)	7 (6.9%)	11 (5.4%)	19 (7.8%)

¹ Patients treated with placebo during double-blind phase for 3-Month

² All patients treated with MIN-101 including patients previously treated with placebo during double-blind phase and crossed-over to MIN-101 in open-label extension part of the study

The negative symptom hypothesis

- “D2 blocking drugs should only be prescribed for acute episodes of psychosis/positive symptoms.”
- Data indicate that for the majority of young individuals the first episode of psychosis would ameliorate and occasionally disappear within 2-6 weeks without continuous DA blocking.

However

- In the majority of patients, negative symptoms persist and worsen.
- Negative symptoms are in part primary negative symptoms, which are a core component (trait markers) of schizophrenic illness and in part secondary negative symptoms, which are adverse effects of antipsychotic drugs that block DA receptors.

Once psychotic/agitation symptoms ameliorate, DA blocking drugs should be gradually discontinued and replaced by drugs that specifically target the negative residual symptoms and cognitive impairment.

This hypothesis is confirmed by our data from the Phase IIb study.



MIN-202

(JNJ42847922)

**A drug to treat insomnia &
depressive disorders by restoring
physiological sleep**

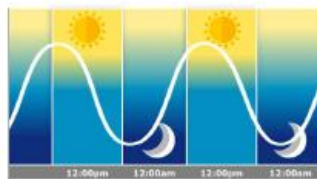
A co-development/co-commercialisation program with;



PHARMACEUTICAL COMPANIES
OF *Johnson & Johnson*

Insomnia affects about 10% of adults and the majority of people with depression

- ~85% of patients with major depressive disorder have symptoms of insomnia, which often persists despite treatment with currently available sleep medications
 - ~13.6 million Americans have major depression and insomnia
- Most existing treatments “force” sleep, rather than physiologically attenuating the “wake drive”
- The Orexin system regulates the wake drive



Circadian Rhythm

CNS Spectr. 2010 Jun;15(6):394-404.
Insomnia in patients with depression: a STAR*D report.
NIMH

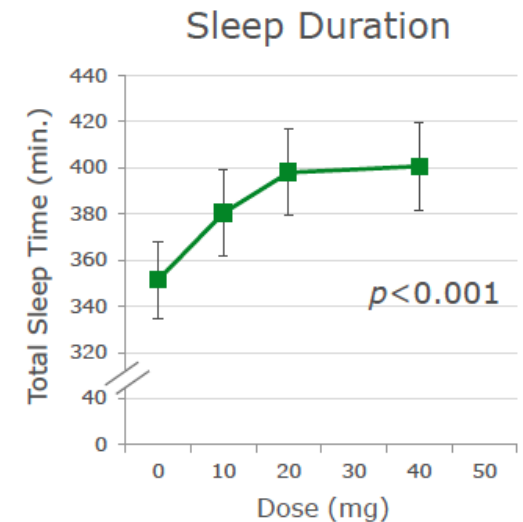
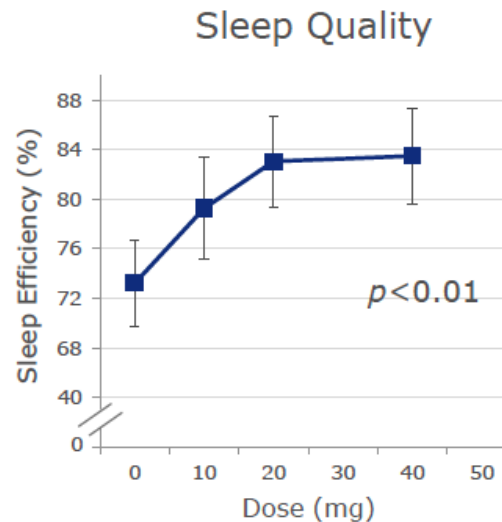
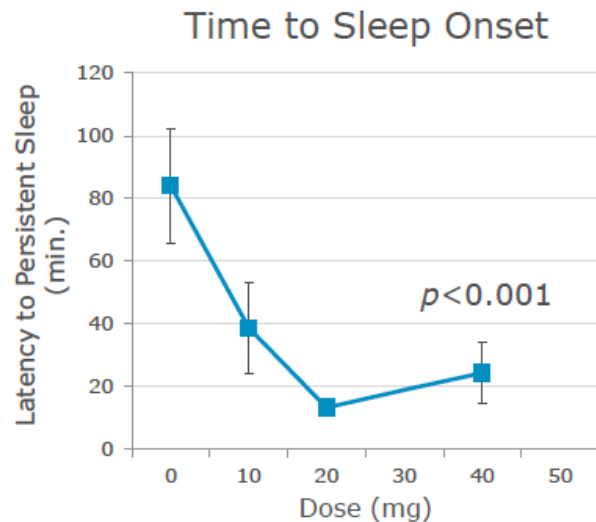


What Do We Need?

Therapies that provide:

- A more physiological approach to treat insomnia
- Rapid onset of action
- Preservation of deep, restful sleep
- Minimal residual daytime sleepiness or cognitive impairment

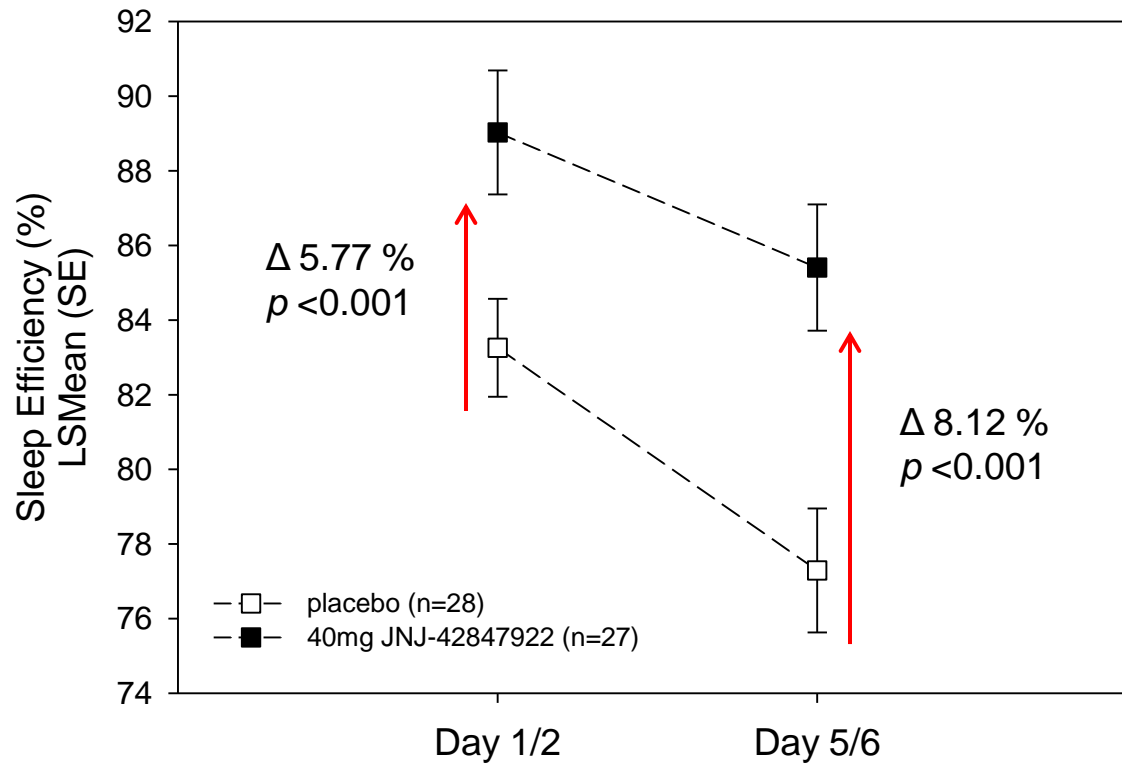
MIN-202: Exploratory study in patients with MDD and comorbid insomnia (n=20)



Reference: Internal data, study 42847922ED1002, disclosed by Minerva Neurosciences, Q1 2015.

Phase IIa in primary insomnia: primary endpoint of sleep efficiency on days 1/2 and 5/6

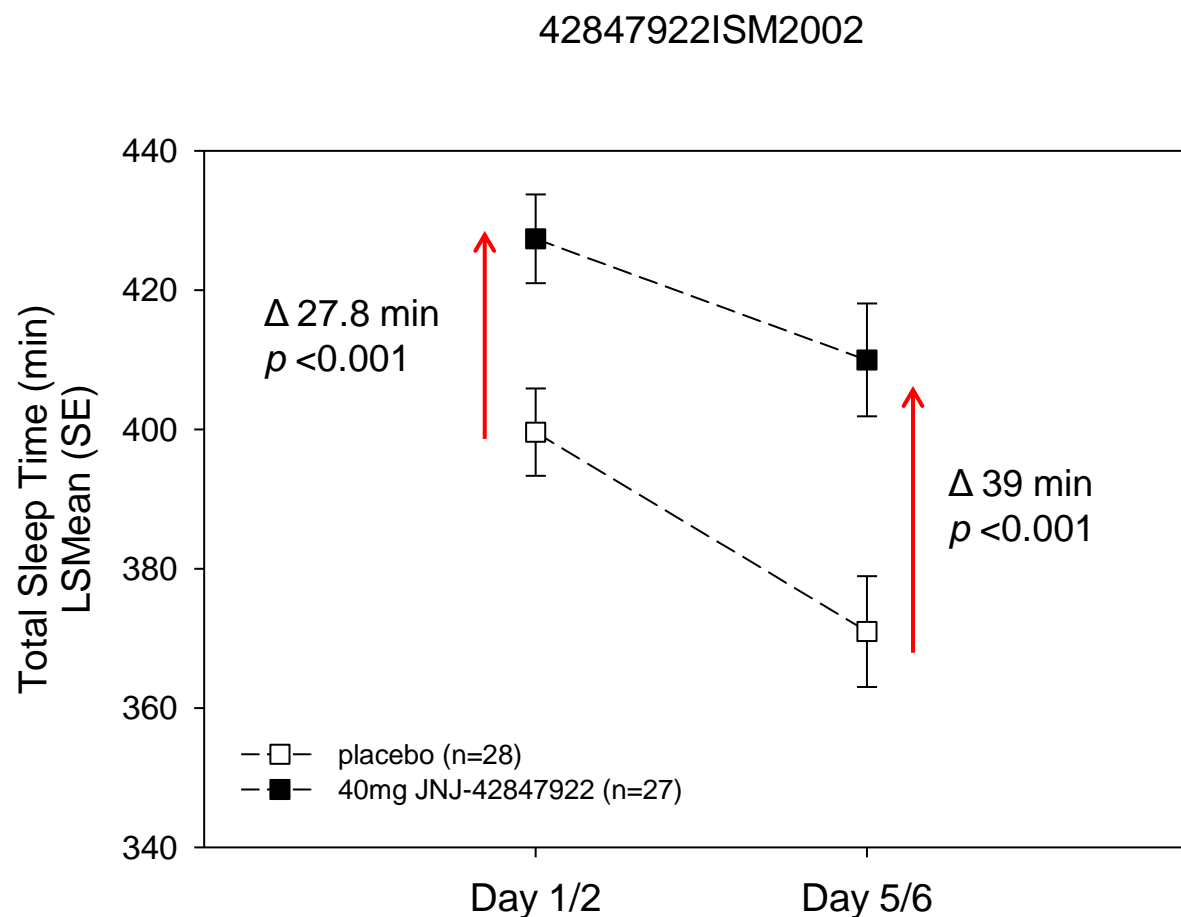
42847922ISM2002



Sleep Efficiency = (Total Sleep Time/480) * 100%

PSG recording = 480 min

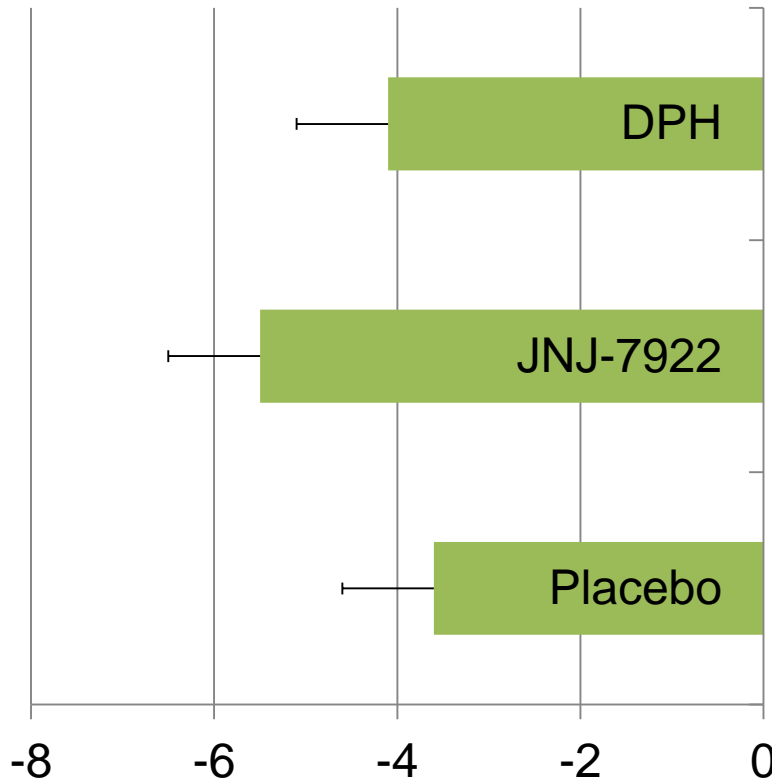
Phase IIa in primary insomnia: total sleep time is observed to increase



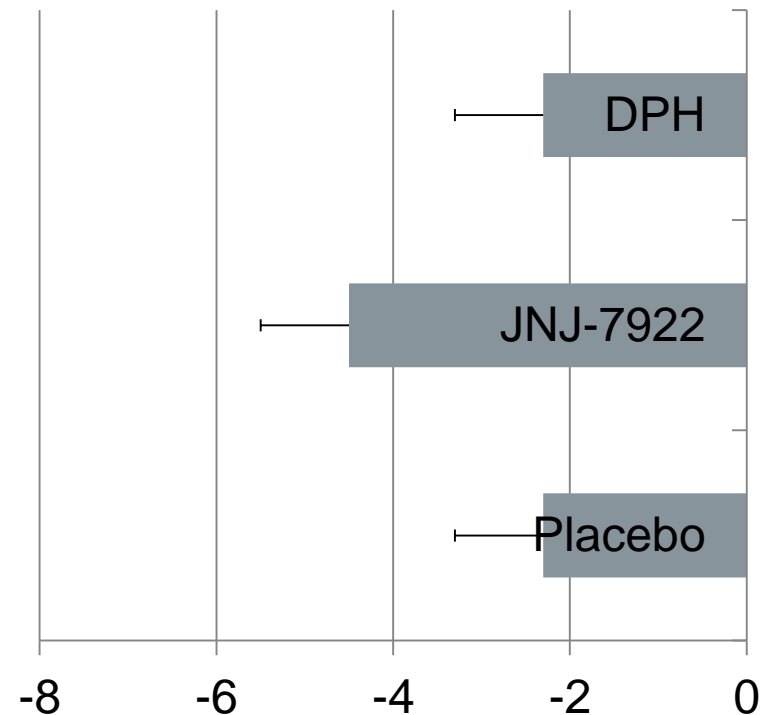
Phase Ib: observed efficacy on depressive symptoms is independent of effects on sleep

DAY 11, N=47

Mean Change HDRS₁₇

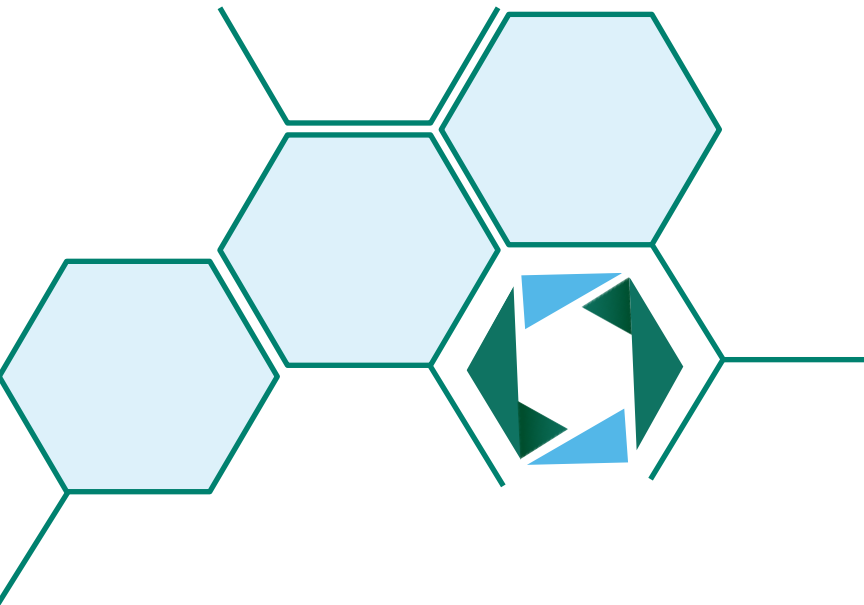


**Mean Change
Adjusted HDRS₁₇**



HDRS₁₇ = Hamilton Depression Rating Scale

Adjusted HDRS₁₇ = Hamilton Depression Rating Scale with 3 sleep items removed



MIN-117

Potential for a more effective and safer treatment to address the unmet medical needs of Major Depressive Disorder patients

Major Depressive Disorder: treatments with faster onset and better response, without side effects, are critically needed

- **Major depression: primary cause of disability worldwide by 2030¹**
- **~6 million patients in US with treatment-resistant depression²**
- **Only ~30% of patients achieve remission using current treatments³**
- **Current therapies have slow onset of effect; typically 4 – 8 weeks**



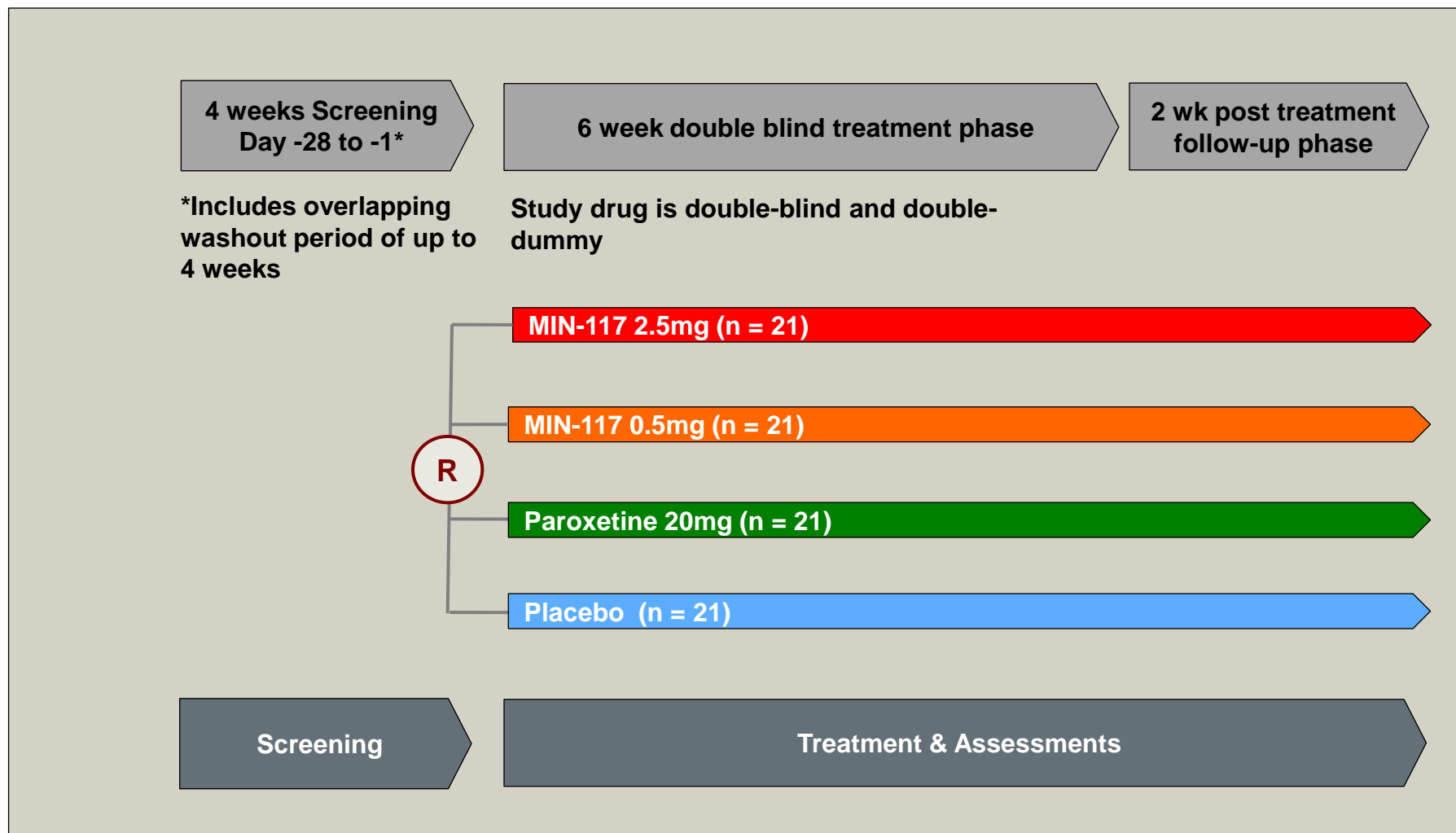
What do we need?

Treatments that:

- Act rapidly
- Are effective in patients who do not respond to or receive only partial benefit from existing medicines
- Do not impair cognition or sexual function
- Free patients from debilitating side-effects
- Improve sleep

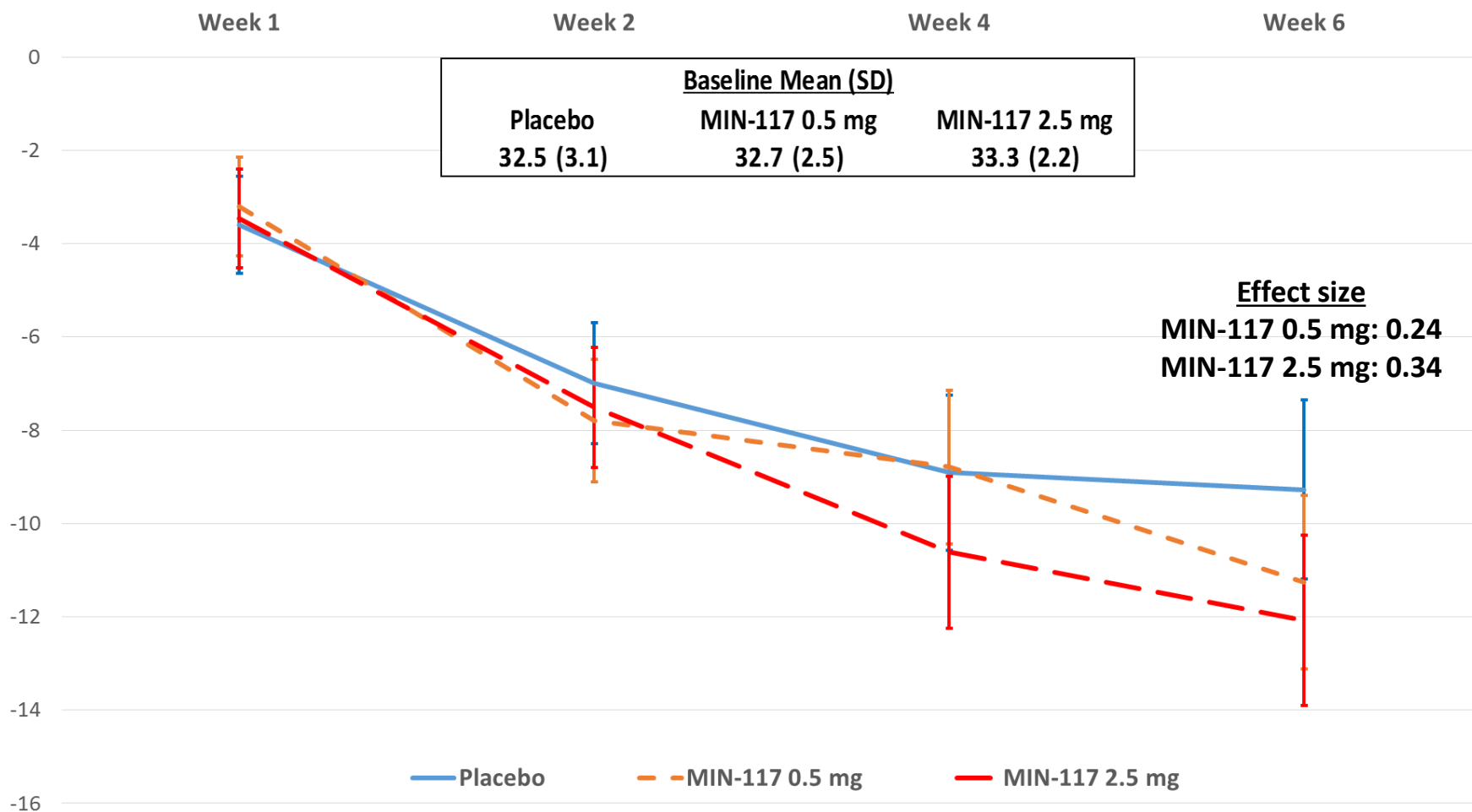
1. World Health Organisation, "Global Burden of Mental Disorders," 2011
2. IMS and Truven Health
3. Cleveland Clinic Journal of Medicine Volume 75. Number 1 January 2008

MIN-117C01: Phase IIa study design

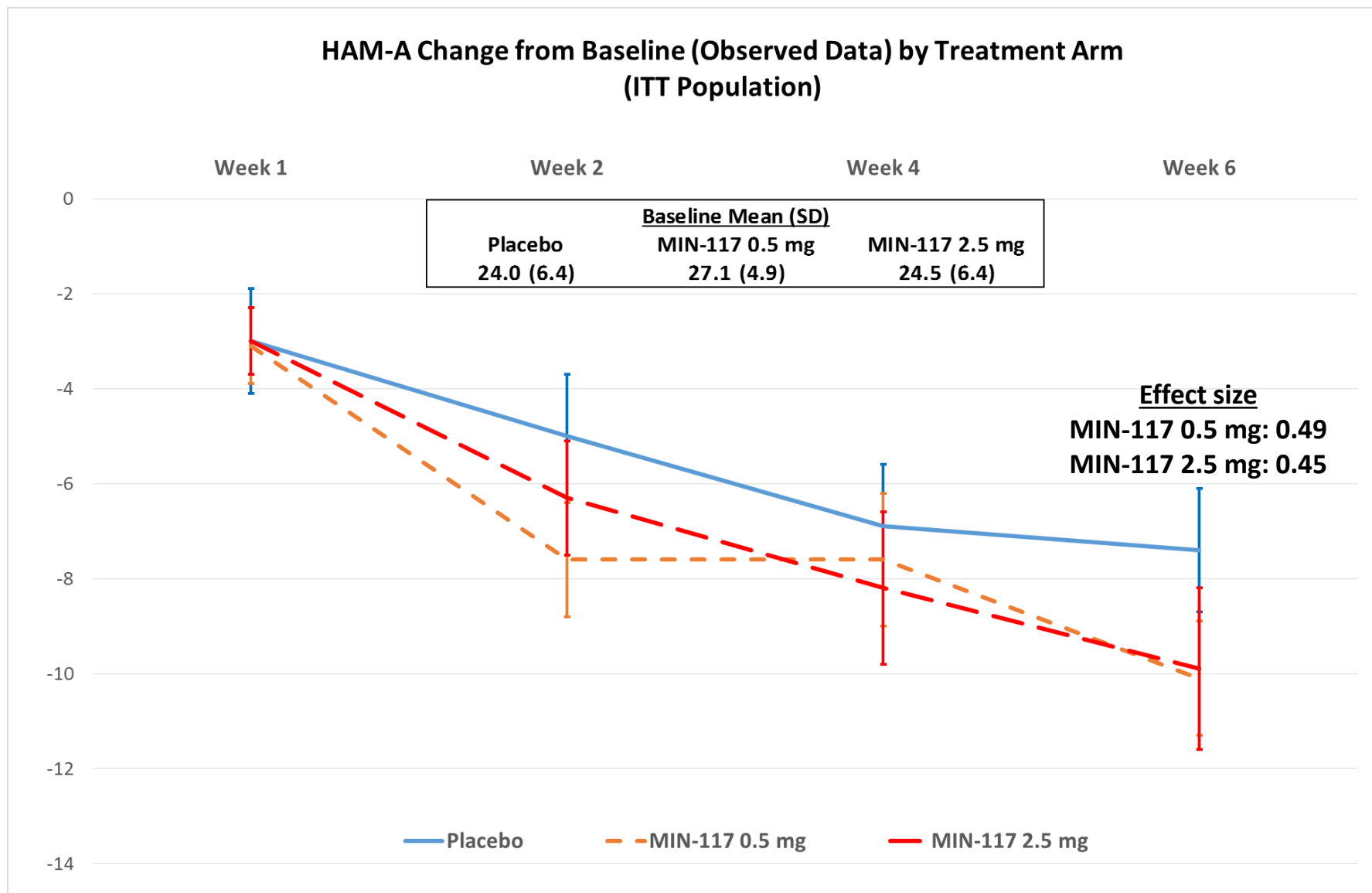


Efficacy: MADRS primary endpoint (ITT pop) in Phase IIa

**MADRS Change from Baseline (MMRM LS Mean) by Treatment Arm
(ITT Population)**



Efficacy: HAM-A secondary endpoint in Phase IIa



Next steps

Program	Primary Indication	Status
MIN-101	Schizophrenia	<ul style="list-style-type: none">• End of Phase II meeting with FDA planned to be scheduled in Q1 2017• Initiation of pivotal Phase III trials planned in Q3 2017
MIN-202	Primary Insomnia and Major Depressive Disorder	<ul style="list-style-type: none">• Phase II trial preparation underway• Next trials in insomnia disorder and MDD planned in early 2017
MIN-117	Major Depressive Disorder	<ul style="list-style-type: none">• Planning underway for next phase of clinical trials expected to begin in 2017
MIN-301	Parkinson's Disease	<ul style="list-style-type: none">• IND or IMPD, with Phase I expected to initiate thereafter

Financial update

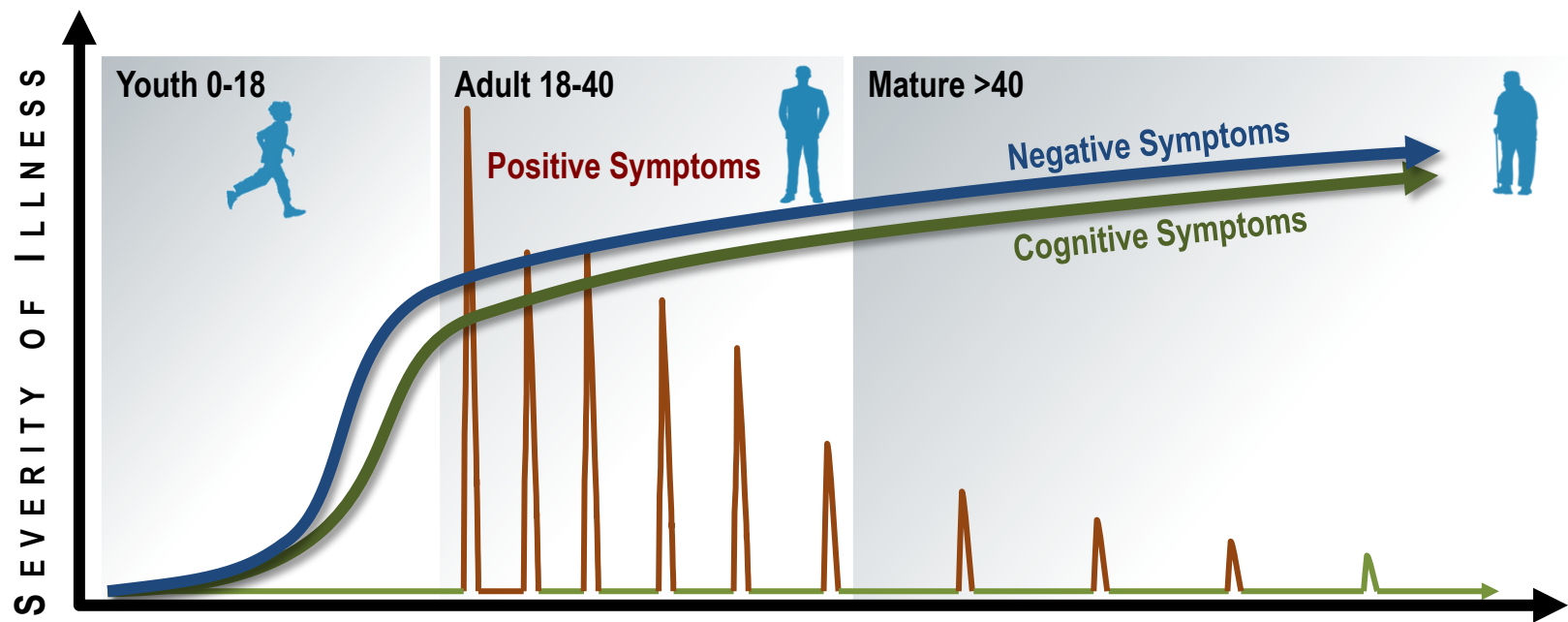
- ~\$91.9 million cash balance (cash, cash equivalents and marketable securities) at September 30, 2016 expected to fund operations into 2018
- ~\$57.5 million (before fees) received from follow-on stock offering in June 2016 (~6 million shares sold at \$9.50/share)
- Outstanding shares at October 28, 2016: ~34.8 million
- Fully diluted shares at October 28, 2016: ~40.8 million

Investment highlights

- Broad late-stage pipeline
- Lead asset, MIN-101, has differentiated MoA with specific effect on negative symptoms and is planned to initiate pivotal Phase III trials for treatment of schizophrenia in Q3 2017
- Compelling efficacy and safety data generated in randomized, double-blind, placebo-controlled Phase 2 clinical trials
- Significant unmet needs and market opportunities in schizophrenia, MDD and insomnia
- Strong cash position
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Appendix

Schizophrenia is a dynamic chronic disease -
prevalence of symptoms changes over the lifetime of
the patient

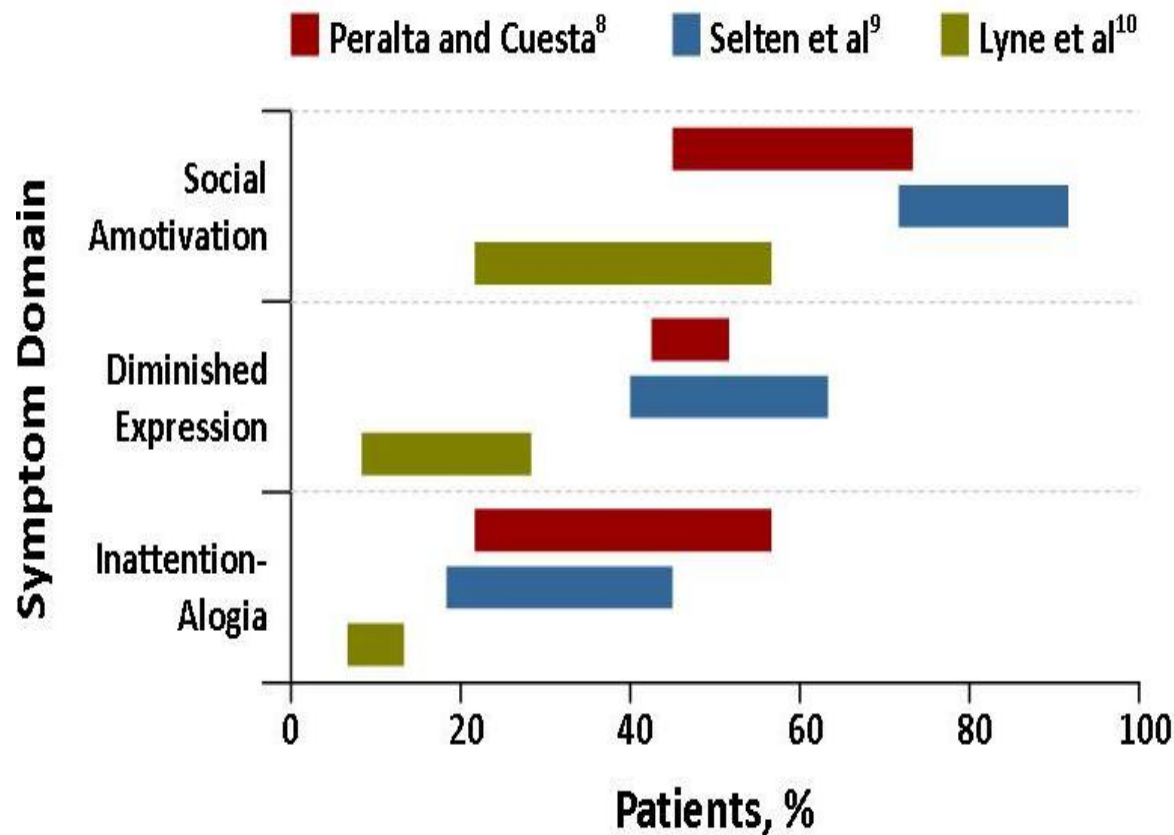


Are negative symptoms, apathy and mild cognitive impairment specific to schizophrenia?

■ Idiopathic Parkinson	0.3%	} ~10 % of the general population?
■ Major depression	3%	
■ Alzheimer's Disease	1%	
■ Frontal dementia	0.01%	
■ Mental retardation	0.5%	
■ Post-brain trauma	0.01%	
■ Post-CVA	0.3%	
■ Autism spectrum	1.2%	
■ Schizophrenia	0.7%	
■ Schizophrenia spectrum	1%	
■ Drug abuse	0.3%	

** About 20% of the healthy general population has mild manifestation of negative symptoms Werbeloff et al PLOS 2015

What percentage of people diagnosed with schizophrenia have negative symptoms?



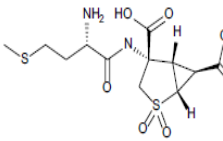
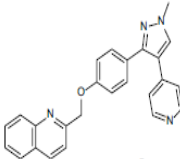
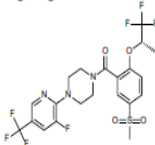
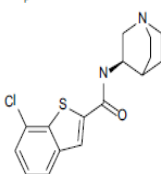
Depending on the population surveyed and on the criteria, between 60% and 95%.

⁸ <https://www.ncbi.nlm.nih.gov/pubmed/10427607>

⁹ <http://schizophreniabulletin.oxfordjournals.org/content/26/3/737.full.pdf>

¹⁰ <https://www.ncbi.nlm.nih.gov/pubmed/23523737/>

The pharma industry is not blind to the need for a drug to treat negative symptoms – but there is currently no drug approved for this indication

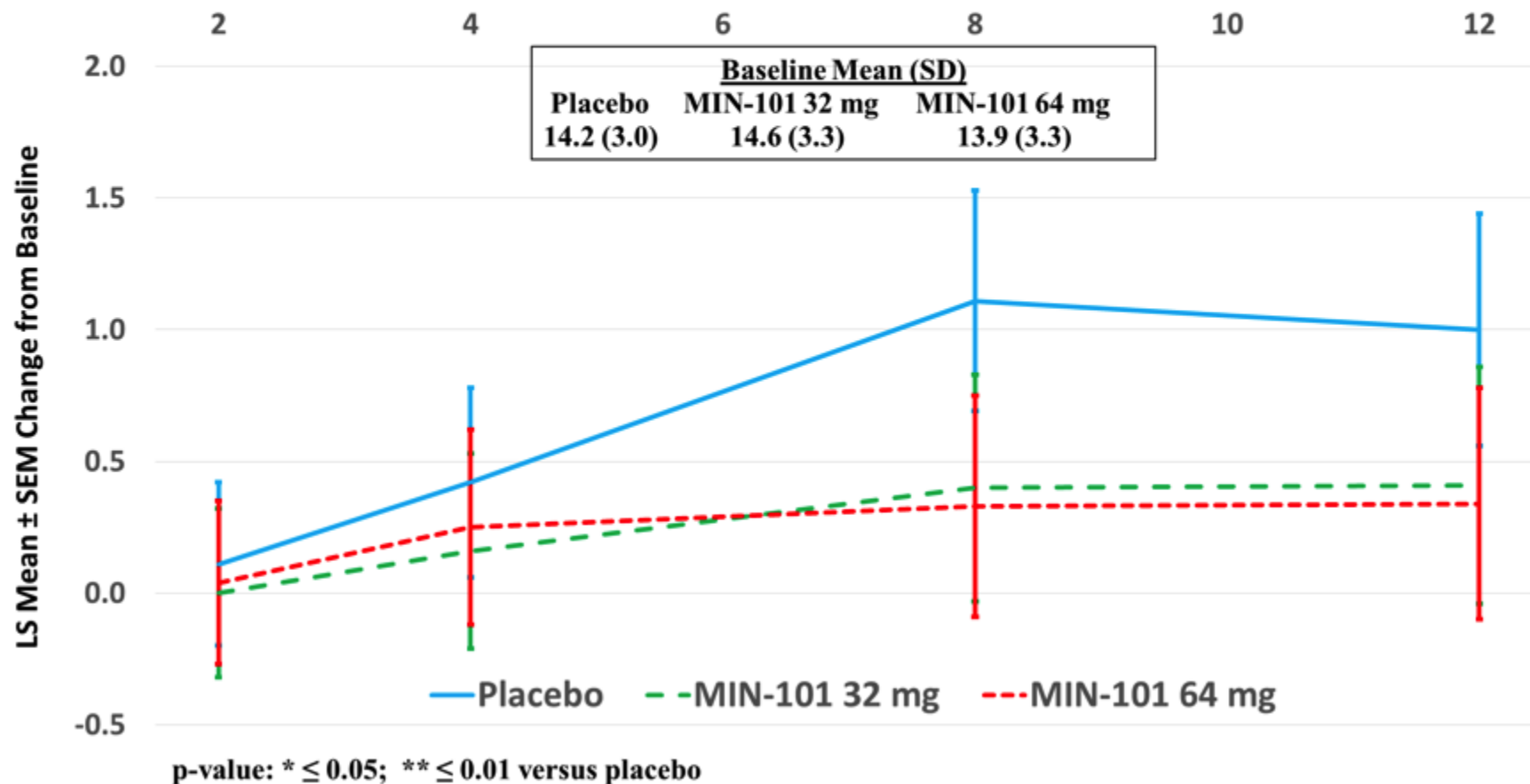
Mechanism of action	Compound number	Compound name	Structure
mGlu2/3 agonist	LY2140023	Pomaglumedad methionil	
PDE10 inhibitor	PF-02545920	MP-10	
GlyT1 inhibitor	RG1678	Bitopertin	
$\alpha 7$ Nicotinic agonist	EVP-6124	Encenicline	

244 patients

1. Patient or patient's legal representative has provided informed consent.
2. Male or female patient, 18 to 60 years of age, inclusive.
3. Patient meets the diagnostic criteria for schizophrenia as defined in the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-V), as established by a full psychiatric interview in conjunction with the Mini International Neuropsychiatric Interview (MINI).
4. Patient is stable in terms of positive symptoms of schizophrenia over the last 3 months according to his or her treating psychiatrist
5. Patient presents with negative symptoms of schizophrenia over the last 3 months according to his or her treating psychiatrist
6. Patient with PANSS negative subscore of at least 20 (as measured by PANSS 3 factors).
7. Patient with PANSS item score of <4 on:
 - P4 Excitement, hyperactivity
 - P7 Hostility
 - P6 Suspiciousness
 - G8 Uncooperativeness
 - G14 Poor impulse control

Efficacy: Secondary endpoint (3) PANSS positive symptom score (3 Factors)

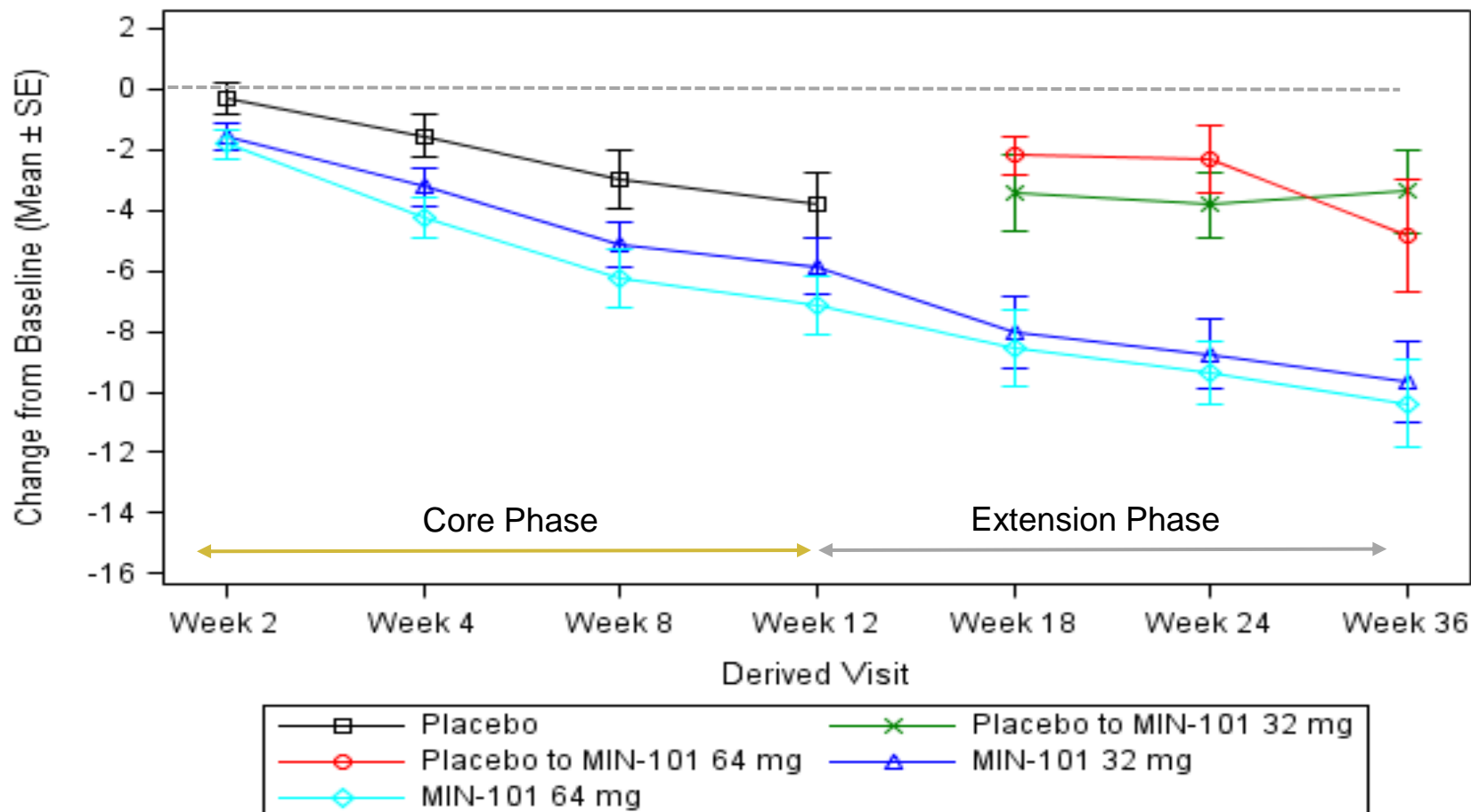
**PANSS Positive Symptom Score (3 Factors) - Change from Baseline (MMRM)
(ITT Population)**
WEEK



Extension Phase

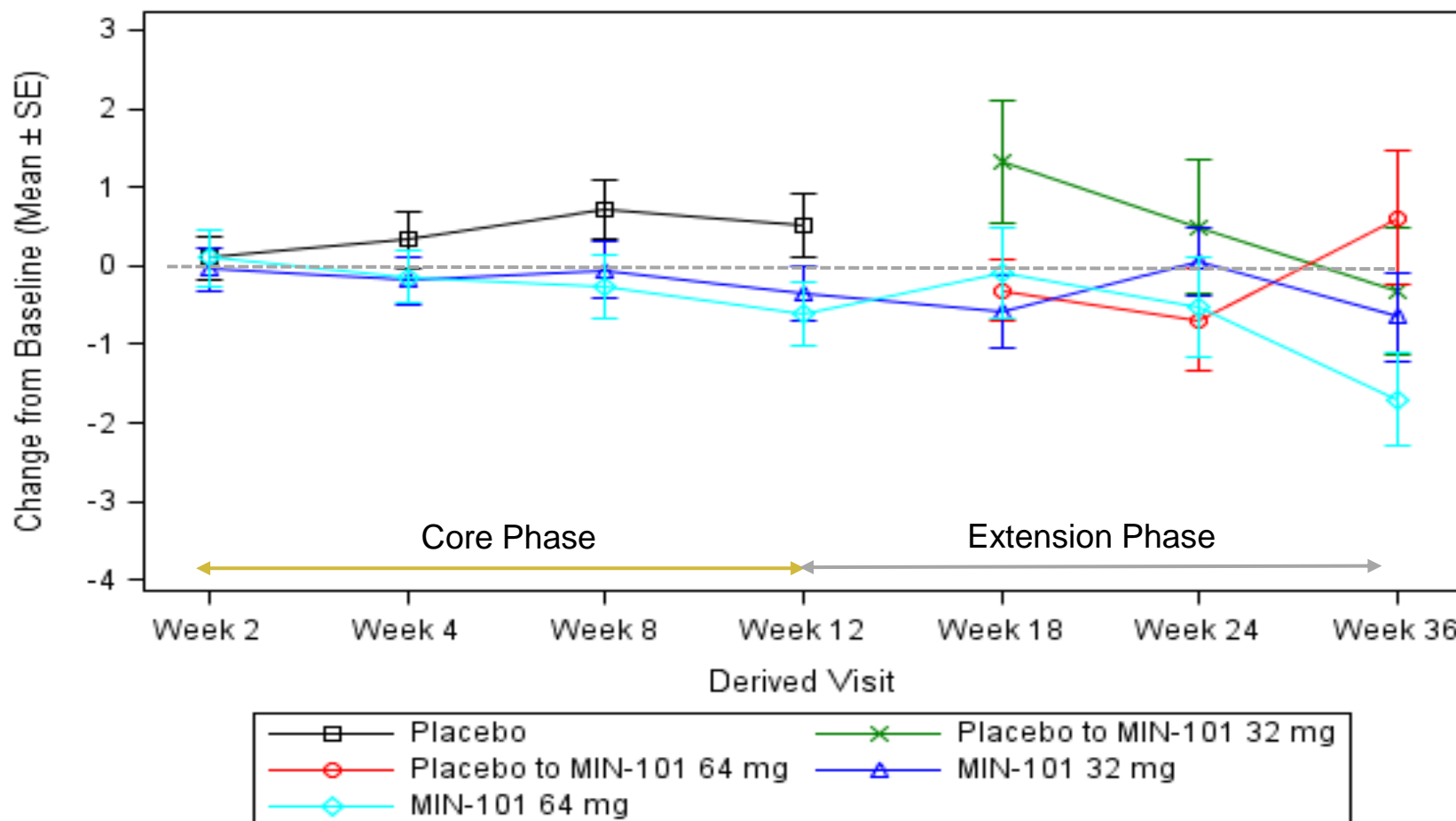
Baseline for patients who crossed from placebo to MIN-101 is start of open label (Week 12)

MIN-101C03: Brief Negative Symptom Score



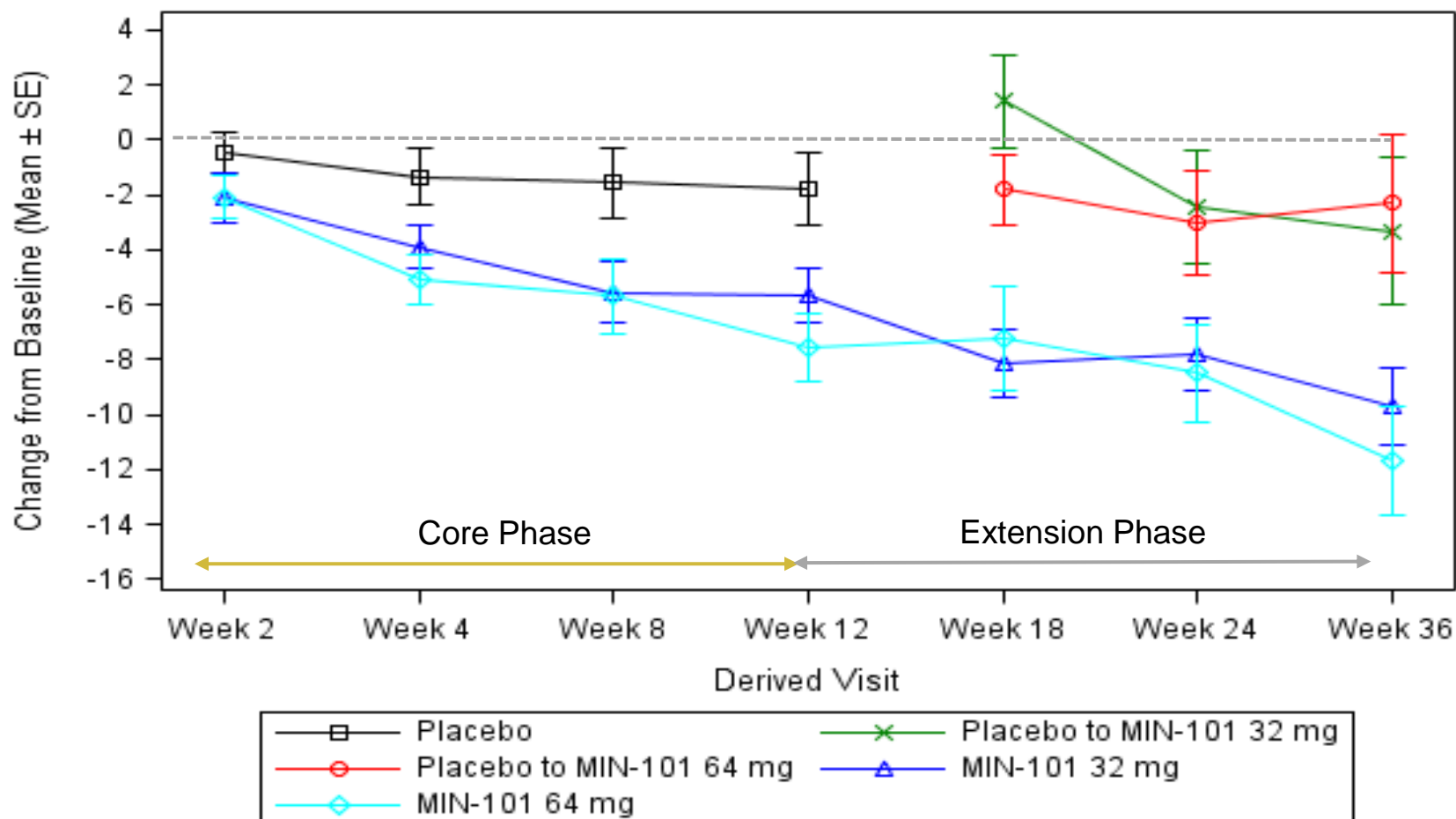
Baseline for Placebo-to-MIN-101 is From Start of Open Label (Week 12)

MIN-101C03: Positive Symptoms (3-Factors)



Baseline for Placebo-to-MIN-101 is From Start of Open Label (Week 12)

MIN-101C03: Total PANSS



Baseline for Placebo-to-MIN-101 is From Start of Open Label (Week 12)

Sleep polysomnography: REM latency in Phase IIa

PSG REM Latency Change from Baseline (Observed Data) by Treatment Arm (ITT Population)

