



November 2018

Forward-Looking Statement Safe-Harbor

This presentation contains forward-looking statements about Minerva Neurosciences which are subject to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts, reflect management's expectations as of the date of this presentation, and involve certain risks and uncertainties. Forward-looking statements include, but are not limited to: the benefits, efficacy and safety of our new formulations; the potential of the diagnosis and treatment of negative symptoms of schizophrenia and other diseases; whether studies performed on analogs or backups of our compounds are a good predictor of the clinical efficacy of our compounds; statements with respect to the timing and results of future clinical milestones with roluperidone (MIN-101), seltorexant (MIN-202) and MIN-117, including the Phase 3 trial of roluperidone, the Phase 2b trials of seltorexant and the Phase 2b trial of MIN-117; statements regarding our ability to successfully develop and commercialize our therapeutic products; 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; 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 forward-looking statements are based on our current expectations and may differ materially from actual results due to a variety of factors including, without limitation, whether any of our therapeutic products 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 the results of future clinical trials of roluperidone, seltorexant, MIN-117 and MIN-301, if any, will be consistent with the results of past clinical trials; whether roluperidone, seltorexant, MIN-117 and MIN-301 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 co-development 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; and general economic conditions. These and other potential risks and uncertainties that could cause actual results to differ from the results predicted are more fully detailed under the caption "Risk Factors" in our filings with the Securities and Exchange Commission, including our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, filed with the Securities and Exchange Commission on November 5, 2018, as well as our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the Securities and Exchange Commission on March 12, 2018. Copies of reports filed with the SEC are posted on our website at www.minervaneurosciences.com. Our audience is cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we disclaim any obligation to update any forward-looking statements, except as required by law.

Minerva - snapshot

Late Stage Clinical Pipeline

▶ Three molecules with innovative mechanisms of action to treat significant unmet medical needs in the CNS area in late stage clinical studies

Lead product in pivotal Phase 3 trial

▶ Topline data read-out anticipated mid-year 2019

Four Phase 2b studies ongoing

▶ Multiple data read-outs anticipated in 2019

Well capitalized through multiple data read-outs in 2019

▶ \$97.7m cash balance at Sept 30, 2018

Experienced management team

▶ Decades of combined experience in clinical practice and CNS drug discovery & development

Pipeline of four innovative programs

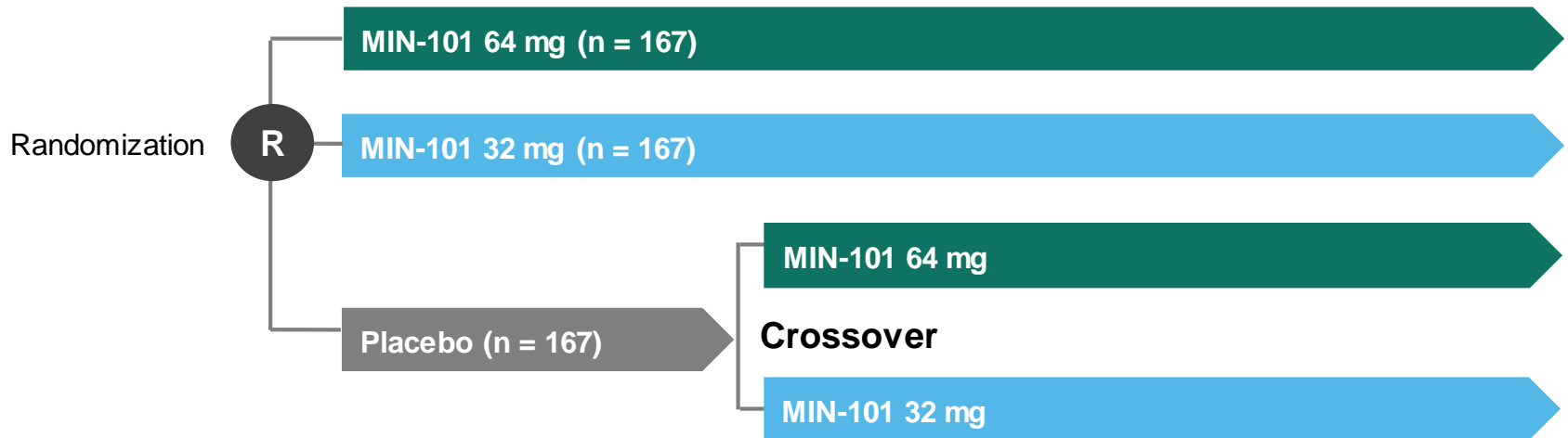
Program	Primary Indications	MoA	Preclinical	Phase 1	Phase 2	Phase 3
Roluperidone MIN-101	Negative symptoms in schizophrenia	<ul style="list-style-type: none"> • 5-HT_{2A} antagonist • Sigma₂ antagonist 	<p>Phase 3 initiated Dec 2017 (MIN-101C07)</p>			
Seltorexant MIN-202	Primary insomnia Major depressive disorder, as adjunctive therapy	<ul style="list-style-type: none"> • Selective orexin2 antagonist 	<p>Phase 2b initiated Dec 2017 (ISM2005)</p> <p>Phase 2b initiated Sep 2017 (aMDD2001)</p> <p>Phase 2b initiated Dec 2017 (aMDD2002)</p>			
MIN-117	Major depressive disorder, as monotherapy	<ul style="list-style-type: none"> • 5-HT_{1A} • 5HT transporter • Alpha-1a, b • Dopamine transporter • 5-HT_{2A} 	<p>Phase 2b initiated Apr 2018 (MIN-117C03)</p>			
MIN-301	Parkinson's disease	<ul style="list-style-type: none"> • Neuregulin-1β1 activating ErbB4 	<p>Pre-clinical</p>			

Roluperidone (MIN-101)

Phase 3

- Designed to replicate successful Phase 2b
- Reviewed with FDA at end-of-Phase 2 meeting
- Phase 3 initiated December 2017
- Data read-out expected mid-year 2019

Roluperidone Phase 3 study design: monotherapy, double-blind, placebo-controlled in schizophrenic patients with negative symptoms



Phase 3 compared to Phase 2b: same patient population; same double-blind duration; same doses; PANSS NSFS primary endpoint; CGI-S and PSP secondary endpoints; 40-week extension allows 1 year safety coverage.

Phase 3 efficacy study: confirmatory study design guided by insights from Phase 2b and dialogue with FDA

Design

- 501 patients randomized 1:1:1 to 32 mg and 64 mg doses of MIN-101 vs placebo
 - Symptomatically stable patients for several months with moderate to severe negative symptoms (>20 PANSS NSFS) and stable positive symptoms
- If patients are on antipsychotic medication, switch to MIN-101 without long wash-out periods so as to mimic clinical practice
- Study carried out in US (approximately 30% of patients) and Europe

Primary endpoint

- PANSS Negative Symptoms Factor Score (NSFS) according to Marder after 12 weeks' administration

Secondary endpoints

- Personal and Social Performance scale (PSP)
- Clinical Global Impression of Severity (CGI-S)
- 40 weeks (9 months) open-label extension

Powering assumptions

- 90% powered & 40% drop-out rate

Roluperidone 2b clinical data

Peer-reviewed data publications

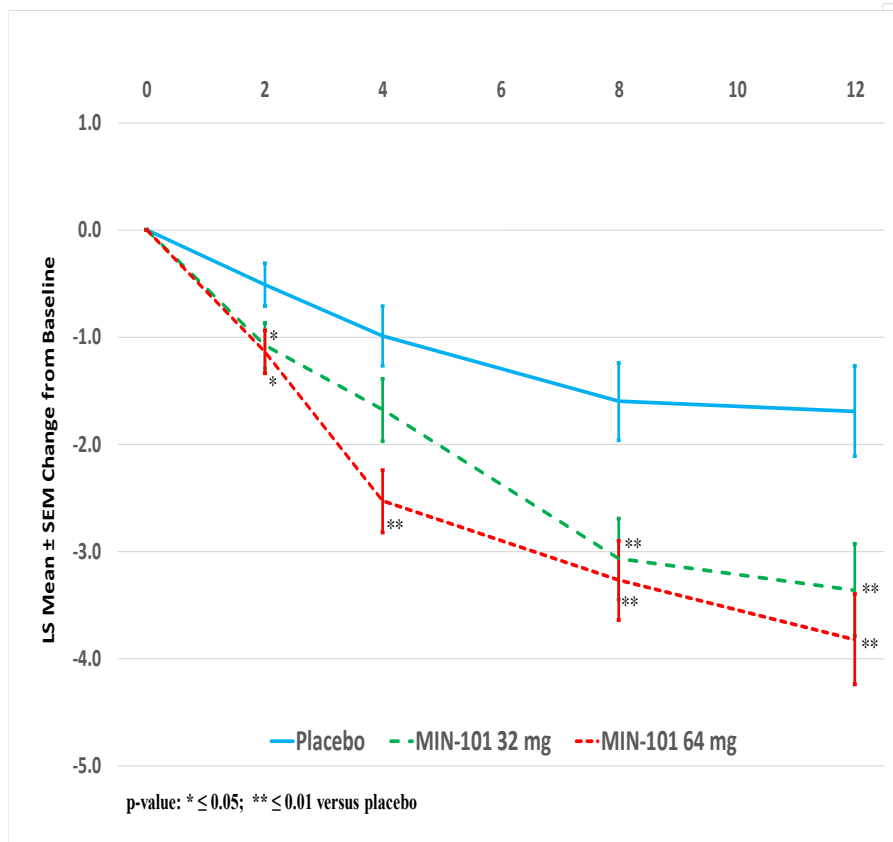
Davidson, M., et al., Efficacy and Safety of MIN-101: A 12-Week Randomized, Double-Blind, Placebo-Controlled Trial of New Drug in Development for the Treatment of Negative Symptoms in Schizophrenia, Am J Psychiatry, <http://www.medical-reprints.com/US-MN-AJP-Davidson>

Keefe, R., et al., Cognitive Effects of MIN-101 in Patients with Schizophrenia and Negative Symptoms: Results from a Randomized Controlled Trial, J Clin Psychiatry, <https://doi.org/10.4088/JCP.17m11753>

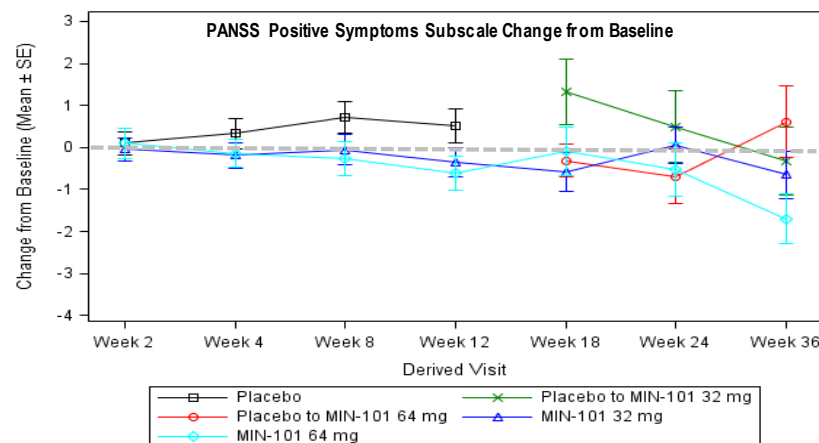
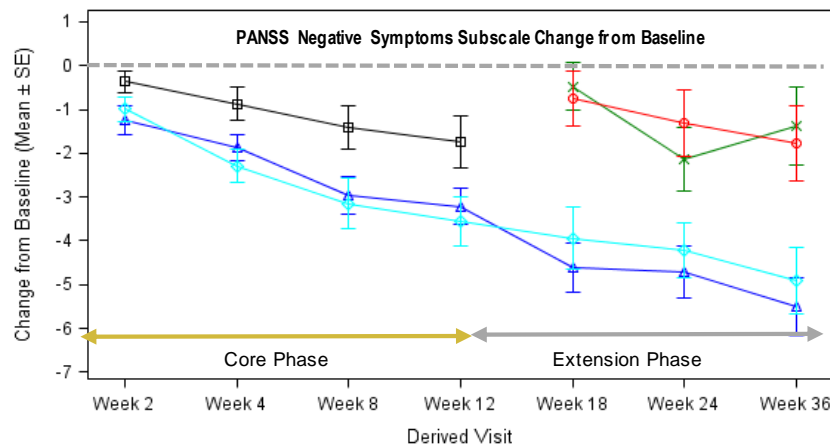
Kirkpatrick, B., et al., The brief negative symptom scale (BNSS): Sensitivity to treatment effects, Schizophr. Res. (2017), <https://doi.org/10.1016/j.schres.2017.11.031>

Phase 2b study showed specific improvements in negative symptoms over 12 weeks and 36 weeks in both doses and stable positive symptoms

Core 12-week phase: Statistically significant improvements in the primary endpoint



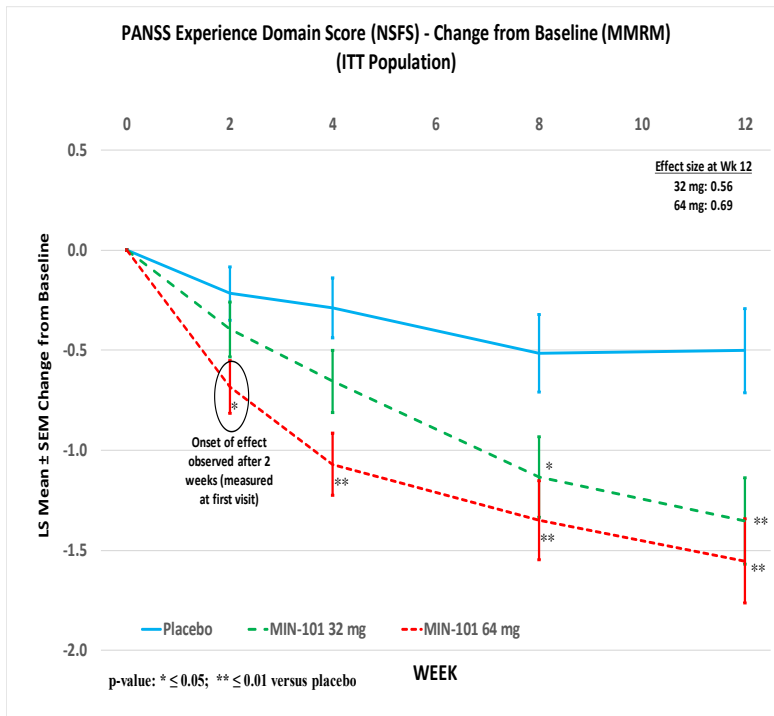
12-Week DB & 24-week extension phase



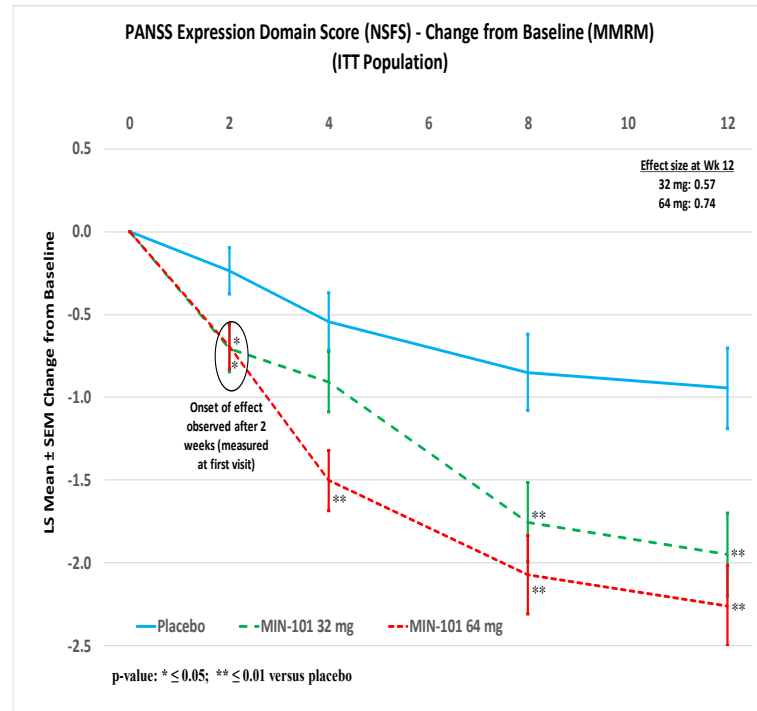
Source: Davidson et al., 2017

Roluperidone is the first drug showing improvement in both the “Experience” & “Expression” dimensions of Negative Symptoms

Experience



Expression



Negative Symptoms in Schizophrenia

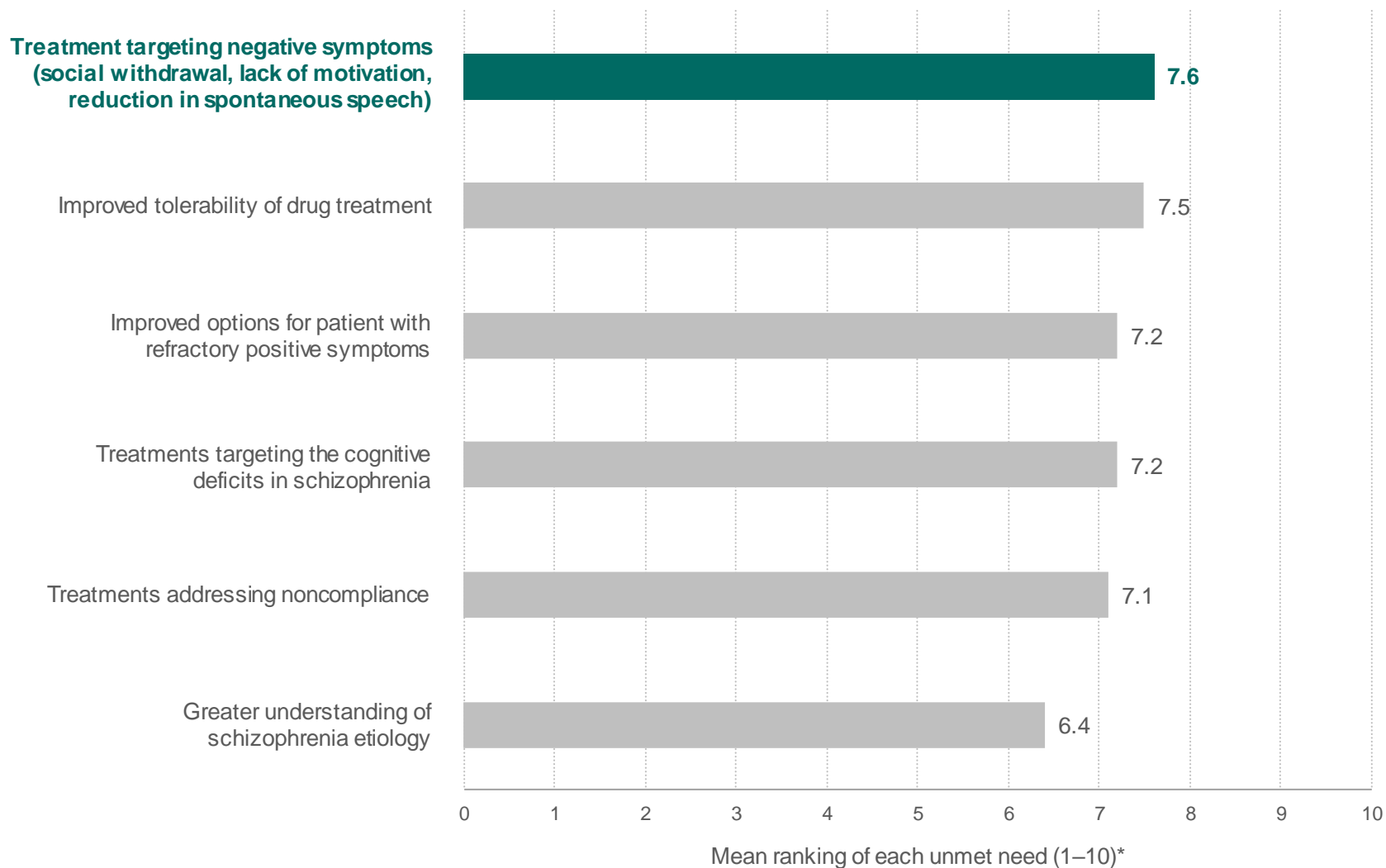
Negative vs positive symptoms in schizophrenia

- Positive symptoms reflect an excess or distortion of normal functions
 - Delusions and hallucinations
 - Disorganized speech / thought
 - Grossly disorganized behaviour
 - Agitation
- Negative symptoms reflect a diminution or loss of normal functions
 - Affect blunted / flat affect
 - Alogia, or reduced speech and short answers
 - Avolition, or lack of motivation, sense of purpose, ability to follow through on plans
 - Anhedonia, or lack of pleasure and lack of interest
 - Asociality / social withdrawal

“Negative symptoms account for a substantial portion of the morbidity associated with schizophrenia.” – DSM-5

Recent survey of psychiatrists ranks negative symptoms as the #1 unmet medical need for patients with schizophrenia

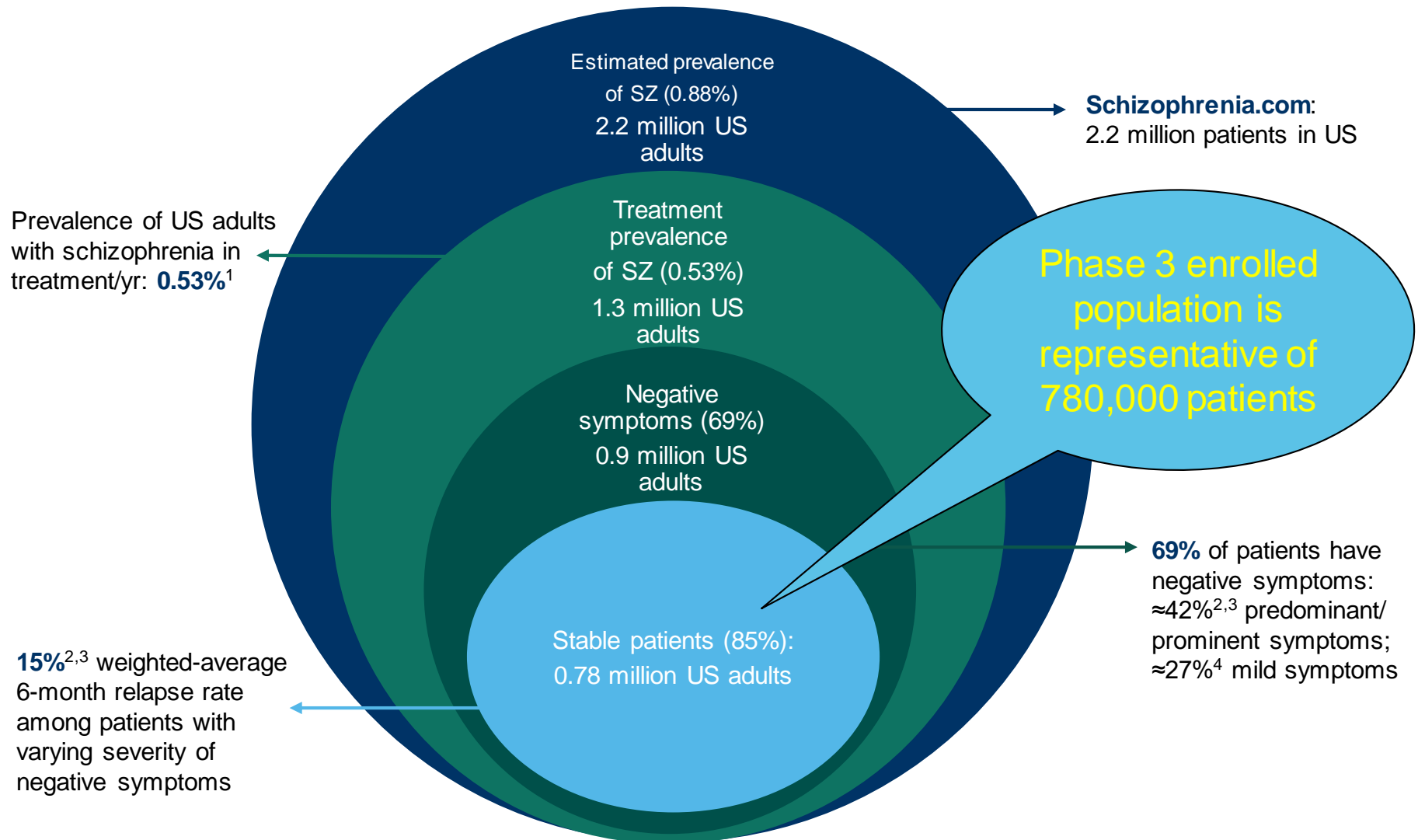
Key unmet needs for schizophrenia, 2017



*Higher scores denote greater importance assigned to the unmet need.
Source: Datamonitor Healthcare's proprietary schizophrenia survey, September 2017

Market considerations and commercial landscape

≈60% of adult patients with schizophrenia who are treated have negative symptoms and are relapse free over 6 months



SZ=schizophrenia.

1. Wu et al. *Psychol Medicine*. 2006; 2. Millier et al. *J Mark et Acc Health Policy*. 2017; 3. Haro et al. *Schizophr Research*. 2015; 4. Nordstroem et al. *J Social Psychiatry*. 2017.

Roluperidone is positioned to launch in negative symptoms without competitors - only compound in Phase 3 - only study in monotherapy

Clinical trials in negative symptoms in schizophrenia on ClinicalTrials.gov

Phase 3 in Negative Symptoms



MIN-101 (monotherapy)

5-HT_{2A} & σ_2 receptors antagonist

Phase 3 study:

- Study results anticipated **mid-year 2019**

Primary endpoint:

- Positive and Negative Symptoms Scale (PANSS)
Negative Symptoms Factor Score (NSFS)

Secondary endpoints:

- Personal and Social Performance (PSP) scale, measure of functioning
- Clinical Global Impression-Severity (CGI-S), clinician-rated overall severity of schizophrenia

Phase 2 in Negative Symptoms



AVP-786 (adjunctive use)

Fixed-dose quinidine + dextromethorphan
(weak NMDA antagonist + σ_1 R agonist)

Phase 2 completed **Aug 2017, awaiting results**



LY500307 (adjunctive use)

Selective estrogen receptor β agonist

Phase 2a anticipated to complete in **Jun 2018**



ACP-103 (adjunctive use)

5-HT_{2A} inverse agonist

Phase 2 anticipated to complete in **Jun 2019**



TAK-831 (adjunctive use)

DAAO inhibitor

Phase 2 anticipated to complete **Apr 2020**



Vraylar

Refusal to file for negative symptoms **Sep 2017**

Negative symptoms are described in 19 DSM-5 categories

...many symptoms assigned to a single disorder may occur, at varying levels of severity, in many other disorders... DSM-5

Table 2. Qualitative Comparison of 5 Core Negative Symptom Domains Across Diagnostic Categories

Negative Symptom Domain					Disorder
Asociality	Avolition	Anhedonia	Alogia	Blunted Affect	
X	X	X	X	X	1. Schizophrenia
X	X	X	X	X	2. Schizoaffective disorder
X	X	X	X	X	3. Schizophreniform disorder
X		X		X	4. Schizotypal personality disorder
X	X	X		X	5. Schizoid personality disorder
X					6. Paranoid personality disorder
X					7. Avoidant personality disorder
X	X	X		X	8. Bipolar disorder (I and II)
X	X	X		X	9. Major depressive disorder
	X			X	10. Persistent depressive disorder (dysthymia)
X	X				11. Premenstrual dysphoric disorder
X			X		12. Selective mutism
	X				13. Social anxiety disorder
X				X	14. Separation anxiety disorder
X	X				15. Reactive attachment disorder
		X			16. Posttraumatic stress disorder
		X			17. Depersonalization/derealization disorder
X			X	X	18. Autism spectrum disorder
X	X	X	X	X	19. Neurocognitive disorders

Note: We reviewed the “diagnostic criteria,” “diagnostic features,” and “associated features supporting diagnosis” sections of disorders included in the 20 DSM-5 sections and recorded terms/phrases that reflected any of the 5 NIMH negative symptom consensus domains. A total of 19 disorders were identified as having blunted affect, alogia, anhedonia, avolition, or asociality within their DSM-5 diagnostic criteria or associated features. Not considered are disorders due to general medical condition, “other specified” disorders, unspecified disorders, and substance induced disorders. Symptoms displayed in neurocognitive disorders vary based on the neurological condition in question.

Pipeline of four innovative CNS compounds

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Seltorexant (MIN-202)

A co-development/co-commercialization program with



Seltorexant Phase 2B program: 2 trials in aMDD and 1 in insomnia ongoing, with data read-outs (DP4) anticipated in 2019

- **First aMDD trial initiated Sep 2017** (clinicaltrials.gov: NCT03227224)
 - Double-blind, randomized, parallel-group, placebo-controlled adaptive dose-finding study
 - 4-week screening, 6-week double-blind treatment, and 2-week follow-up
 - 280 patients planned to be enrolled at >85 clinical sites in the US, Europe, Russia, and Japan
 - Safety and tolerability and dose-response and efficacy for up to 3 doses of seltorexant

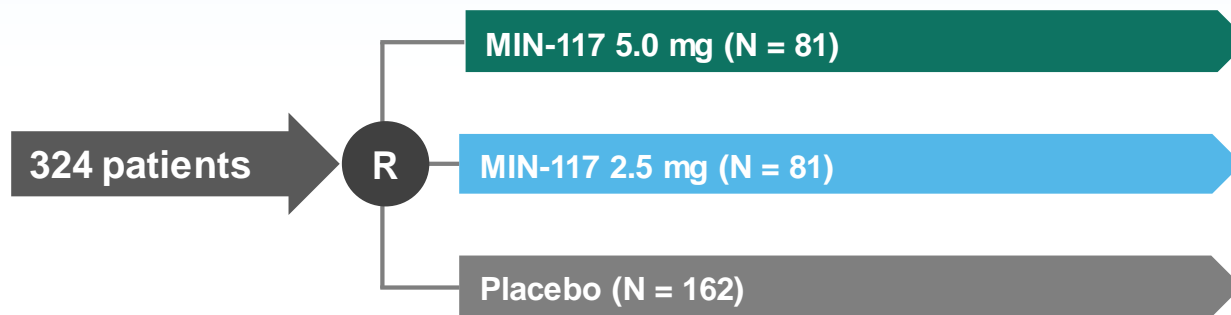
- **Second aMDD trial initiated Dec 2017** (clinicaltrials.gov: NCT03321526)
 - Double-blind, randomized, flexible-dose parallel-group study
 - 4-week screening, 6-month double-blind treatment, and 2-week follow-up
 - 100 patients planned to be enrolled at ≈34 clinical sites in the US
 - Assess the efficacy of flexibly dosed seltorexant compared with flexibly dosed quetiapine as adjunctive therapy to baseline antidepressant therapy (either an SSRI or SNRI) in delaying time to all-cause discontinuation of study drug over a 6-month treatment period

- **Insomnia trial initiated Dec 2017** (clinicaltrials.gov: NCT03375203)
 - Double-blind, randomized, parallel-group, active- and placebo-controlled dose-finding study
 - Up to 61-day duration, including screening and follow-up
 - 360 patients planned to be enrolled at clinical sites in the US, Europe, and Japan
 - Assess the dose-response of 3 doses of seltorexant compared to placebo on sleep onset as measured by latency to persistent sleep (LPS) using polysomnography (PSG)
 - Assess the dose-response of these doses compared with placebo on wake after sleep onset (WASO) over the first 6 hours using PSG
 - Compare the effects of seltorexant on sleep and cognition to those effects of zolpidem

SSRI=selective serotonin reuptake inhibitor; SNRI=serotonin and norepinephrine reuptake inhibitor.

MIN-117

Ongoing Phase 2b study designed to evaluate MIN-117 in patients with moderate to severe MDD



Minerva - summary

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- ▶ Data read-outs anticipated in 2019

Well capitalized through multiple data read-outs in 2019

- ▶ \$97.7m cash balance at Sept 30, 2018
- ▶ Cash runway to mid-2020

Experienced management team

- ▶ Decades of combined experience in clinical practice and CNS drug discovery & development