



Clinical Expertise and Patient Focus

August, 2019

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 June 30, 2019, filed with the Securities and Exchange Commission on August 5, 2019. 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.

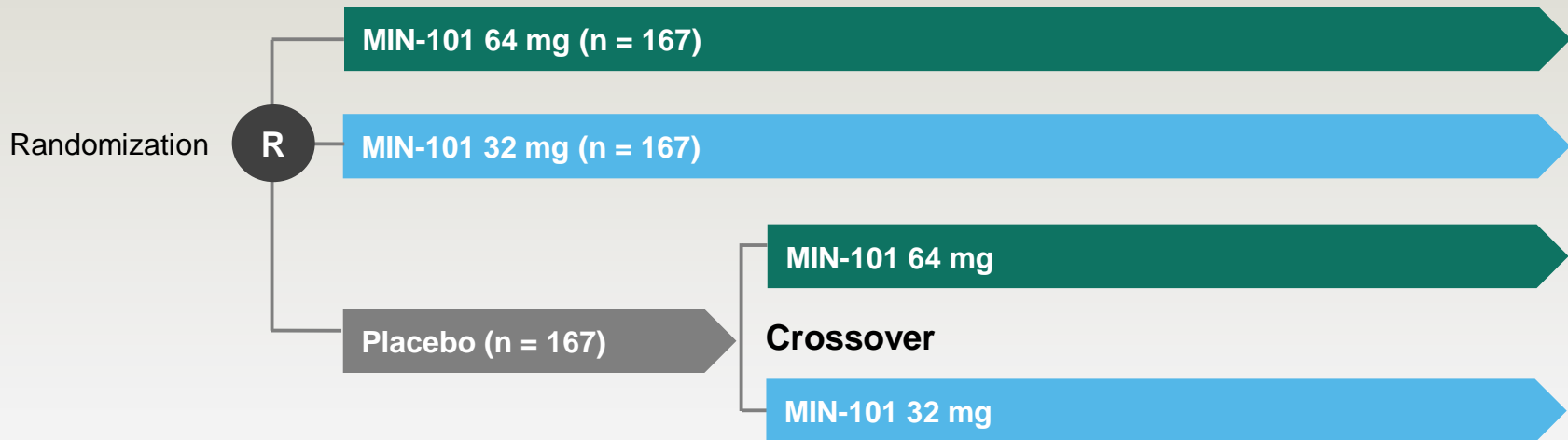
Advanced pipeline of CNS programs in indications with high unmet need

Program	Primary Indications	Mechanism of Action	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 	P3 initiated Dec 2017 (MIN-101C07) Top Line Readout Q4 '19			
Seltorexant MIN-202	Primary insomnia Major depressive disorder, as adjunctive therapy	<ul style="list-style-type: none"> • Selective orexin-₂ antagonist 	Phase 2b Top Line Readout Q2 '19 (aMDD2001) Phase 2b Top Line Readout Q2 '19 (ISM2005) Phase 2b Top Line Readout Q3 '19 (aMDD2002)			
MIN-117	Major depressive disorder and anxiety, as monotherapy	<ul style="list-style-type: none"> • 5-HT_{1A} • 5HT transporter • Alpha-1a, b • Dopamine transporter • 5-HT_{2A} 	P2b initiated Apr 2018 (MIN-117C03) Top Line Readout Q4'19			
MIN-301	Parkinson's disease	<ul style="list-style-type: none"> • Neuregulin-1β1 activating ErbB4 	Pre-clinical			

Roluperidone: Minerva's lead program is in Phase 3

- Designed to replicate successful Phase 2b
- Reviewed with FDA at end-of-Phase 2 meeting
- Phase 3 initiated December 2017
- Top line results expected Q4 2019
- 12 month safety data mid-2020

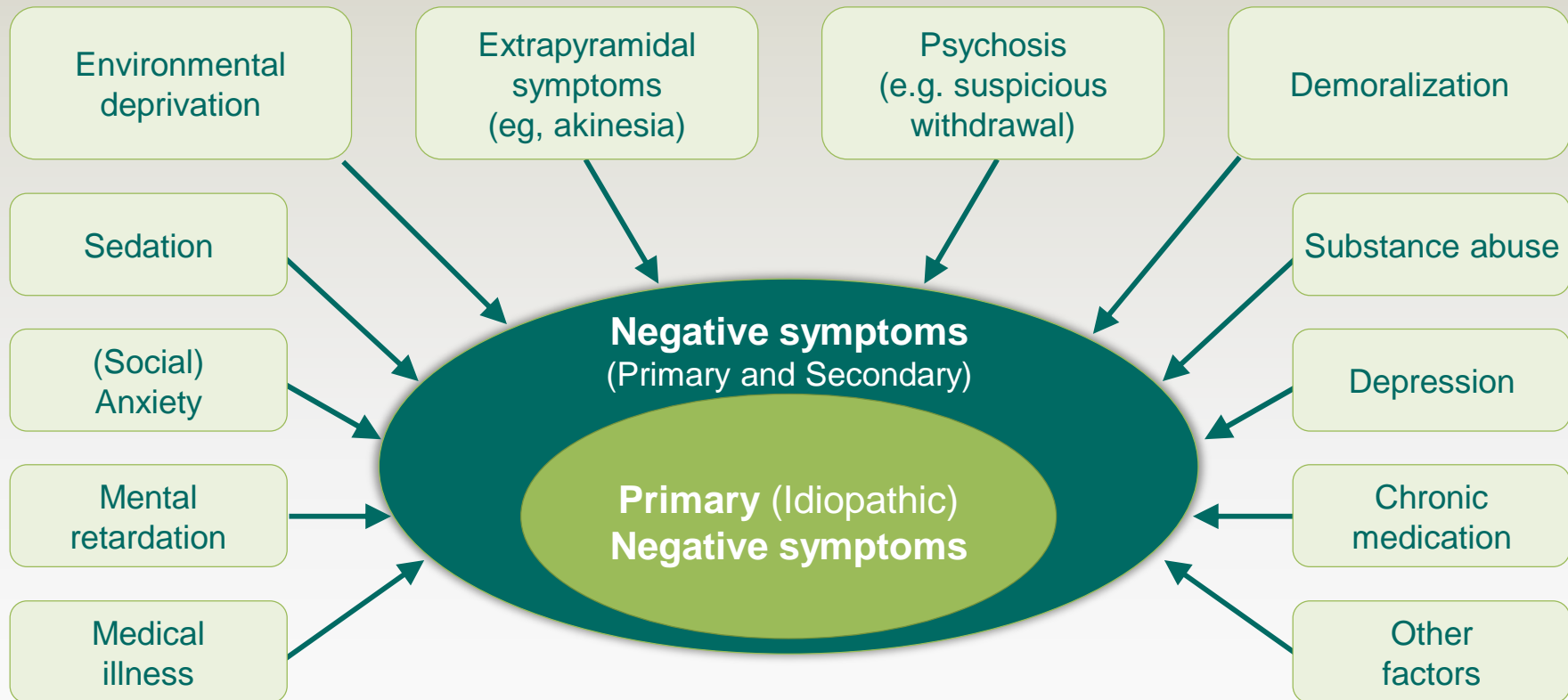
Roluperidone Phase 3 study design: monotherapy, double-blind, placebo-controlled in schizophrenic patients with negative symptoms



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.

Why monotherapy & placebo controlled?

- Demonstrate specific effect on negative symptoms
- No approved positive control
- Avoids unblinding of the study



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 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

Main inclusion criteria for Roluperidone trial

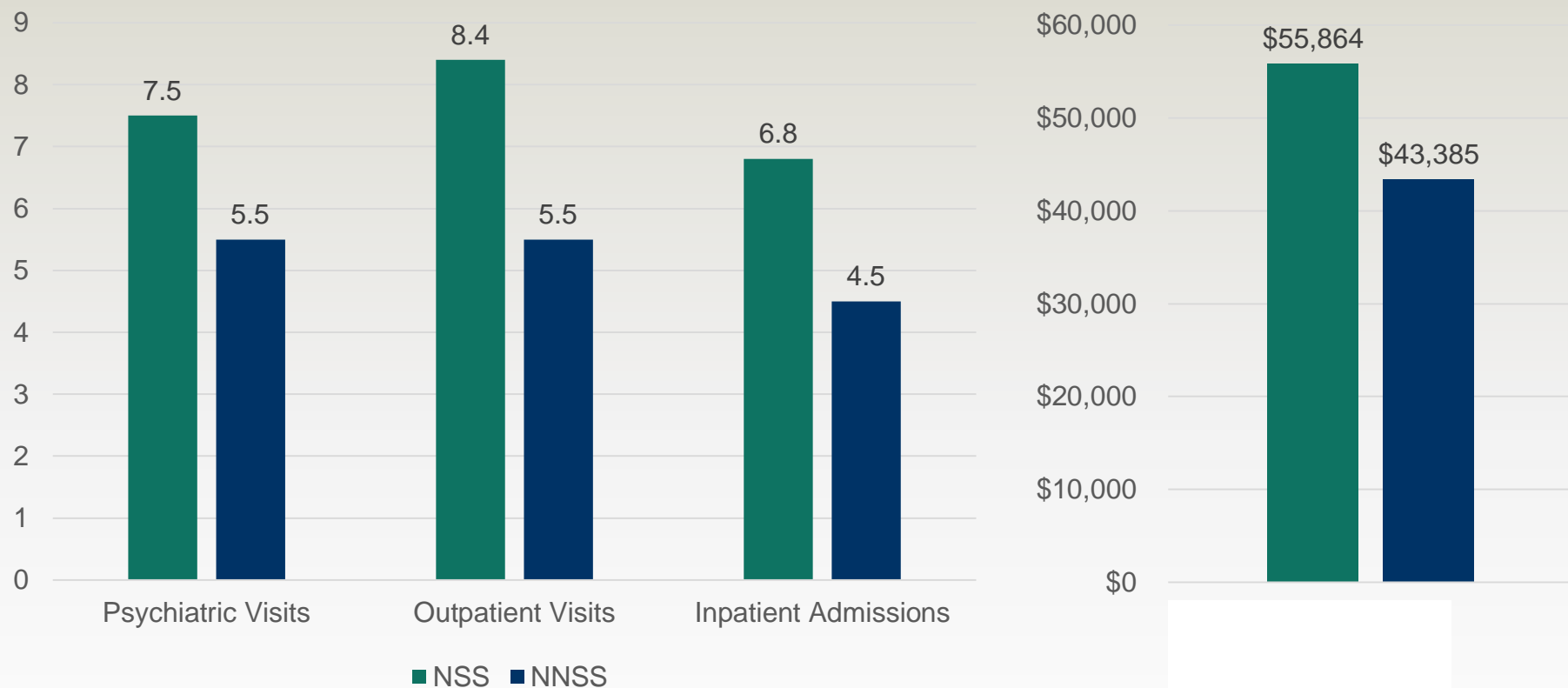
- DSM-5 schizophrenia
- Baseline score > 20 on the 7 PANSS “N” items
- Symptomatically stable and manifesting negative symptoms for 6 months as judged by the PI
- Age 18-55

Ongoing work in parallel to Phase 3

- DDI studies
- CMC work for commercialization
- NDA filing preparation
- Commercial launch plan
- KOL and prescribers meetings
- Evaluation of other therapeutic indications

Increased economic burden of patients with negative symptoms

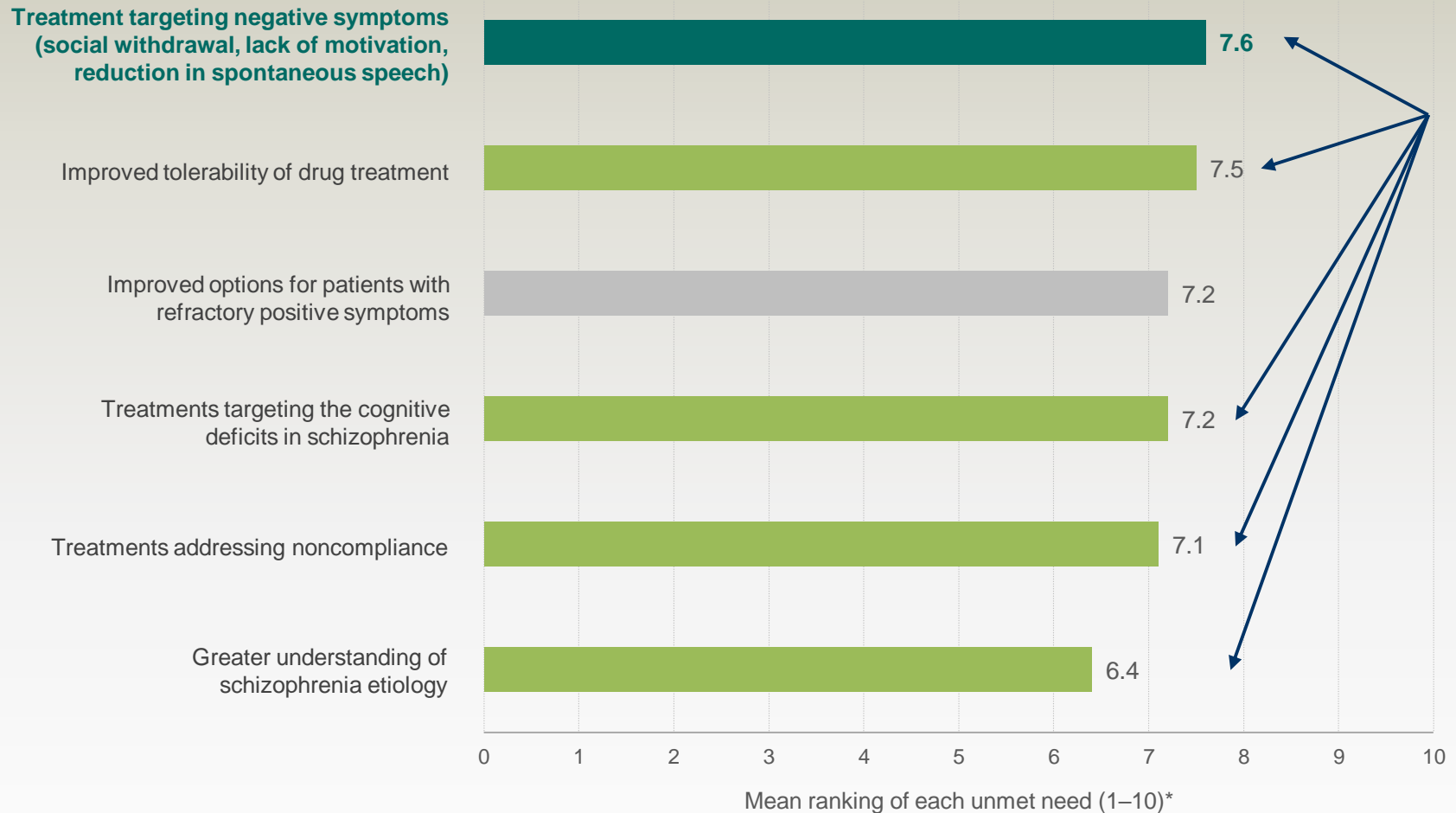
- Study demonstrated increased healthcare utilization and cost burden among patients with negative symptoms of schizophrenia compared to patients with schizophrenia and without negative symptoms



NSS: Negative Symptoms of Schizophrenia
NNSS: Non-Negative Symptoms of Schizophrenia

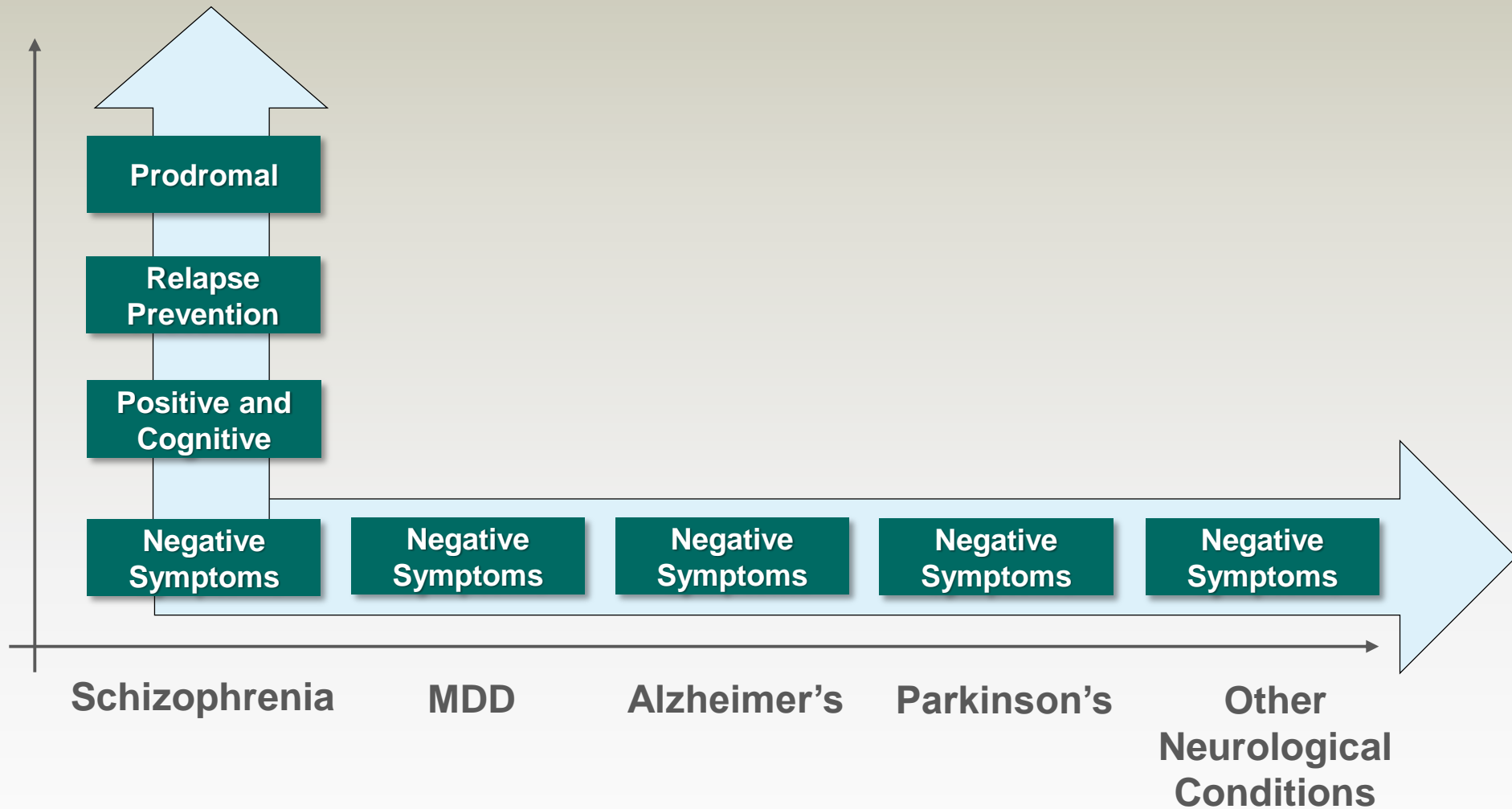
Roluperidone has the potential to specifically address negative symptoms and other unmet medical needs in schizophrenia

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

Potential for label expansion further into schizophrenia and to other conditions where negative symptoms are present



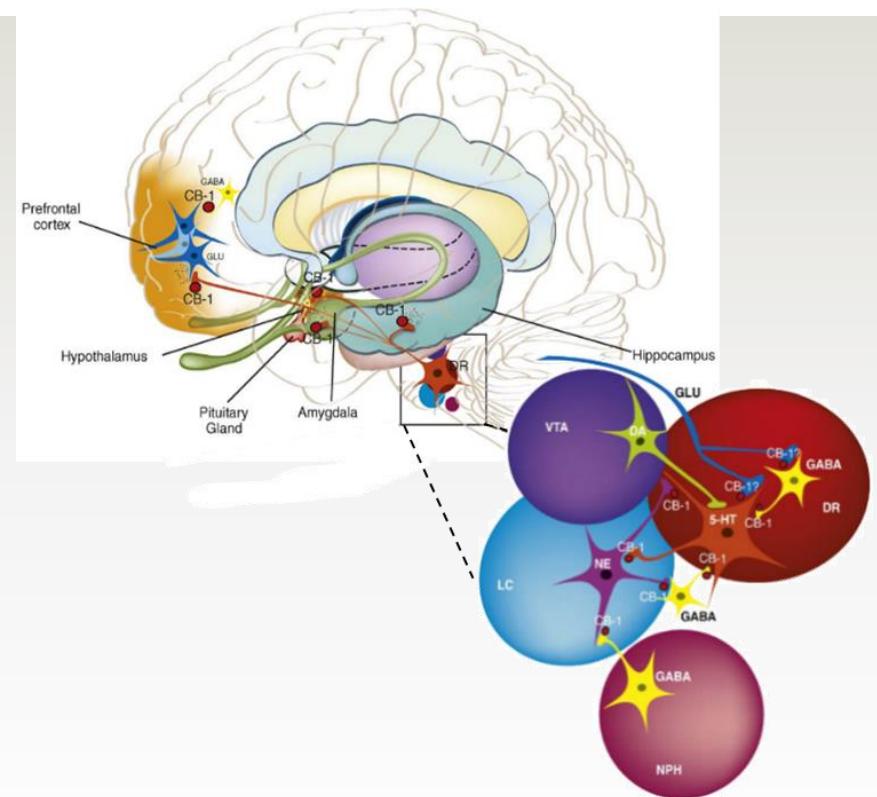
Roluperidone commercial potential

- Negative symptoms remain a debilitating symptom of schizophrenia, with no approved treatments
- Negative symptoms are identified as the leading unmet need in schizophrenia by treating physicians
- Significant market opportunity already exists for a product to treat negative symptoms across multiple indications
- Stakeholders express desperate need for solution
- Roluperidone is poised to become the first and only FDA-approved treatment for negative symptoms in schizophrenia
- Opportunity to expand profile in schizophrenia and other conditions with significant burden from negative symptoms

Seltorexant (MIN-202)

A first-in-class selective Orexin-₂ antagonist for MDD and insomnia, targeting circuits in the orexin system that mediate hyper-arousal

- Highly selective for Orexin-₂ (relative to Orexin-₁)
- Short Tmax (30 minutes) – produces rapid onset of effect
- Short half-life (2 hours) – minimizes daytime “hangover”



A co-development/co-commercialization program with



- Art: Hill, M.N., et al., *Trends in Pharmacological Sciences*, 2009;06.006.

Seltorexant Phase 2b aMDD2001 trial: positive TLR

FOR IMMEDIATE RELEASE

May 13, 2019

MINERVA NEUROSCIENCES ANNOUNCES POSITIVE TOP LINE RESULTS IN PHASE 2B CLINICAL TRIAL WITH SELTOREXANT (MIN-202) IN TREATMENT OF DEPRESSED PATIENTS WITH AN INADEQUATE RESPONSE TO SSRIS AND SNRIS

- *Potential first-in-class, oral specific orexin-₂ inhibitor demonstrates statistically significant improvement in MADRS scores at 6 weeks compared to placebo*
- *Well tolerated, with adverse events similar to or lower than the rate observed in the placebo group*
- *Improves depressive symptoms and sleep function, thus differentiating seltorexant from current therapies*
- *Demonstrates improvement in symptoms of MDD patients not adequately treated by SSRIs and/or SNRIs, a significant unmet need*
- *Data support ongoing development of seltorexant in MDD*

Seltorexant Phase 2b aMDD2001: trial design and summary results

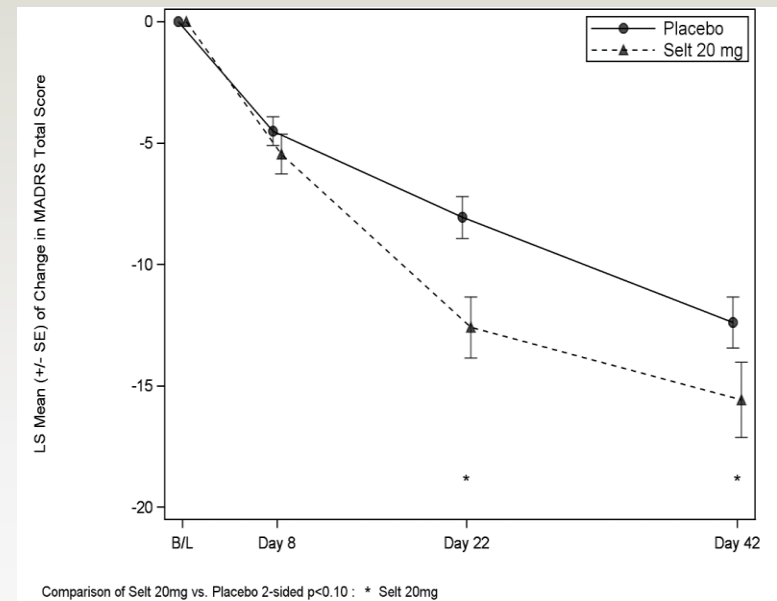
- **First aMDD trial initiated Sep 2017** ([clinicaltrials.gov: NCT03227224](https://clinicaltrials.gov/ct2/show/study/NCT03227224))
 - Double-blind, randomized, parallel-group, placebo-controlled adaptive dose-finding study
 - 4-week screening, 6-week double-blind treatment, and 2-week follow-up
 - 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 (10mg, 20mg & 40mg)

- **At the 20 mg dose patients showed a greater and statistically significant improvement in the MADRS total score compared to placebo at the end of weeks 3 and 6.**
 - The least squares mean (LS mean) difference from placebo of the change in MADRS total score at the end of week 6 was 3.1 for the 20 mg dose of seltorexant, and the 2-sided p-value was 0.083 (which is below the pre-specified 2-sided type I error level of 0.1)
- A key secondary outcome measure based on patient stratification according to baseline insomnia severity index (ISI), showed an even greater difference from placebo for the seltorexant 20 mg arm in patients with clinically significant insomnia ($ISI \geq 15$) with LS mean difference versus placebo of 4.9 on the MADRS total score and a 2-sided p-value of 0.050 compared to the overall patient population in this trial.
- The 40 mg dose, to which further enrollment was stopped following the interim analysis, showed an improvement in the MADRS total score versus placebo at the end of week 6 but did not reach statistical significance. Results for the 10 mg dose were not interpretable due to the small sample size of patients assigned to this dose.
- Seltorexant was well tolerated, and adverse events recorded were similar to those observed in previous studies and similar to or lower than the rate observed in the placebo group.

Seltorexant improves symptoms of MDD patients with inadequate response to SSRIs/SNRIs in Phase 2b Study

- In a six-week Phase 2 placebo-controlled study, seltorexant 20mg showed a statistically significant improvement in the MADRS score compared to placebo ($p=0.083$, less than the pre-specified 2 sided value of 0.1).
- PBO-subtracted difference on MADRS was 3.1 points for the entire population and 4.9 points in subjects with moderate to severe insomnia ($ISI \geq 15$)
- Seltorexant was well tolerated with an adverse events rate similar to that of placebo

Phase 2b Study top-line results Seltorexant 20mg vs. Placebo¹



MADRS: Montgomery-Asberg Depression Rating Scale

¹ Minerva Neurosciences Phase 2 Top Line Results (MIN-202) Press Release (May 13, 2019).



Seltorexant Phase 2b ISM2005 trial: positive TLR

FOR IMMEDIATE RELEASE

June 24, 2019

MINERVA NEUROSCIENCES ANNOUNCES ACHIEVEMENT OF PRIMARY AND KEY SECONDARY OBJECTIVES IN PHASE 2B CLINICAL TRIAL OF SELTOREXANT (MIN-202) IN INSOMNIA

- ***Primary endpoint, defined as Latency to Persistent Sleep (LPS) at Night 1, showed improvement with a p-value ≤ 0.001 after treatment with 10 and 20 mg doses of seltorexant***
- ***Key secondary endpoint, defined as Wake After Sleep Onset over first 6 hours (WASO-6) at Night 1, showed improvement with a p-value ≤ 0.005 after treatment with 10 and 20 mg doses of seltorexant***
- ***Treatment with 10 and 20 mg doses of seltorexant showed greater improvement compared to zolpidem in LPS and WASO-6***
- ***Beneficial effects maintained over time***
- ***Effects consistent in both adult and elderly patients***
- ***Safety and tolerability profile comparable to placebo in both adults and elderly***
- ***Potential first-in-class specific orexin-₂ receptor antagonist for the treatment of insomnia***

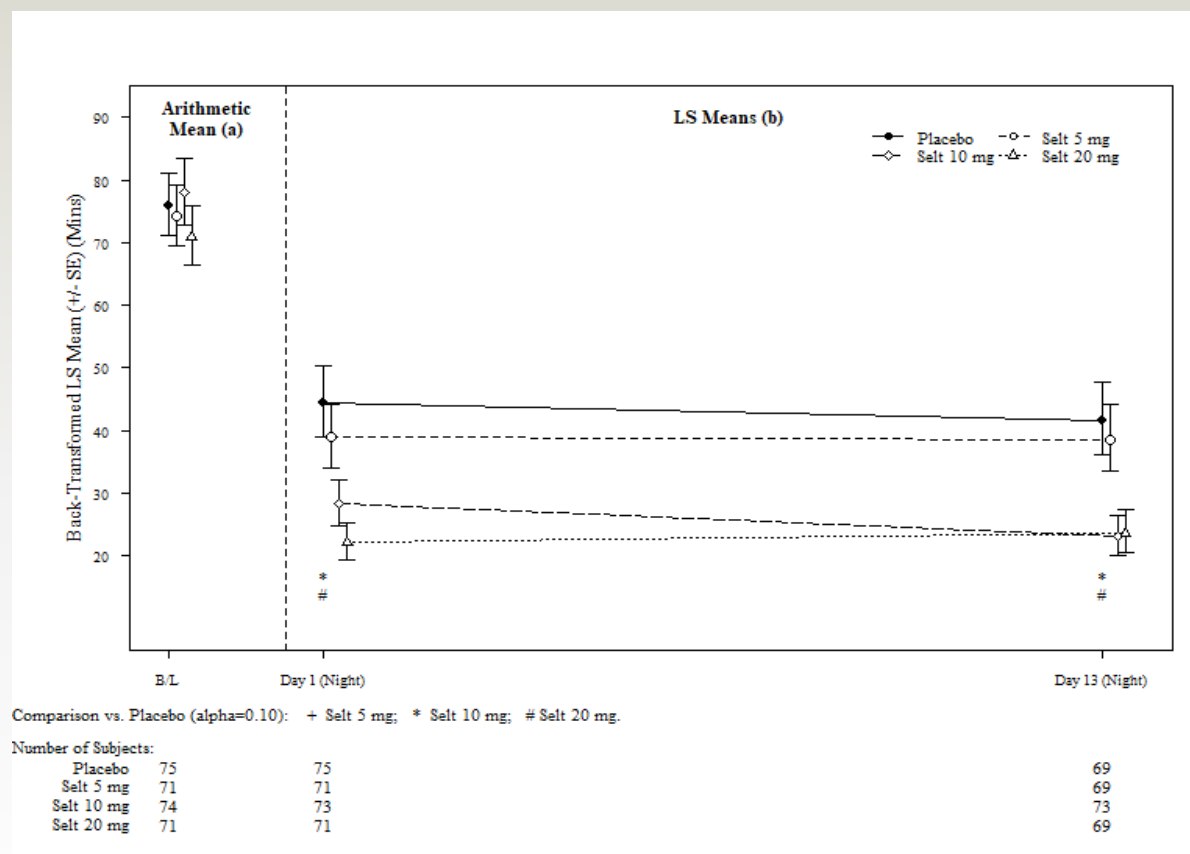
Seltorexant Phase 2b ISM2005: trial design and summary results

- **Insomnia trial initiated Dec 2017** ([clinicaltrials.gov: NCT03375203](https://clinicaltrials.gov/ct2/show/study/NCT03375203))
 - Double-blind, randomized, parallel-group, active- and placebo-controlled adaptive dose-finding study
 - Up to 61-day duration, including screening and follow-up
 - 365 patients enrolled at 56 clinical sites in the US, Europe and Japan
 - Efficacy and safety analyzed in both adults and elderly subjects randomized to receive placebo, seltorexant (5 mg, 10 mg and 20 mg), and zolpidem (available under Ambien brand name)

- **All 4 pre-specified dose-response models showed a significant dose-response relationship in the primary endpoint, Latency to Persistent Sleep (LPS) at Night one, with adjusted 1-sided p-values <0.001.**
 - Mean decreases from baseline at Night 1 in LPS were 15 minutes for placebo, 30 minutes for seltorexant 5 mg, 43 minutes for seltorexant 10 mg, and 45 minutes for seltorexant 20 mg.
- A key secondary endpoint, Wake After Sleep Onset over first 6 hours (WASO-6) at Night 1, showed improvement with a p-value ≤ 0.005 after treatment with 10 and 20 mg doses of seltorexant.
- Analyses of LPS and WASO-6 were performed by subgroups, including age (adults and elderly), and overall results were consistent with primary analysis.
- Seltorexant showed superior and more sustained efficacy compared to zolpidem.
- Seltorexant showed a good safety and tolerability profile in both adult and elderly patients.

Primary efficacy endpoint: LPS night 1 compared to placebo

- Significant separation of the 10 mg and 20 mg dose groups from placebo, indicating a 36% and 49% improvement in LPS at Night 1
- 43% and 42% improvement in LPS at Night 13 compared to placebo



Seltorexant Phase 2b program: 1 further trial with TLR expected in near future

- **Second aMDD trial (aMDD2002) 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
- **TLR Q3 2019**

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

Significant unmet needs remain in the treatment of MDD

- **MDD affects 17.3 million adults in the US^{1,2}**
 - (7.1% of the population over age 18 and over)
- **Substantial burden of illness for many patients**
 - Cognitive difficulties
 - Sleep issues
 - Apathy/Lack of energy
- **Nearly 60% of MDD patients have co-morbid anxiety disorders³**
- **Approximately 60%-70% of patients diagnosed and treated with first-line therapies, including SSRIs and/or SNRIs, do not experience adequate treatment response⁴**
 - Currently available options (such as atypical antipsychotics and mood stabilizers) have a high side effect burden (weight gain, sedations)

¹ The National Institute of Mental Health Information Resource Center Major Depression accessed May 6 2019

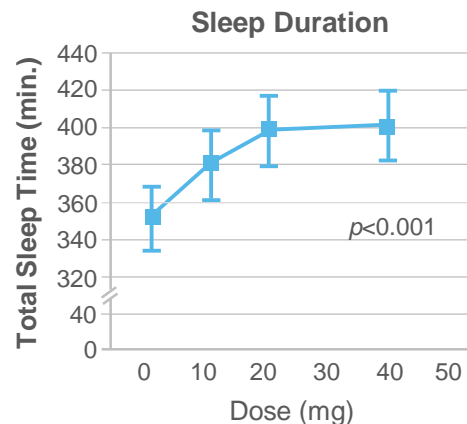
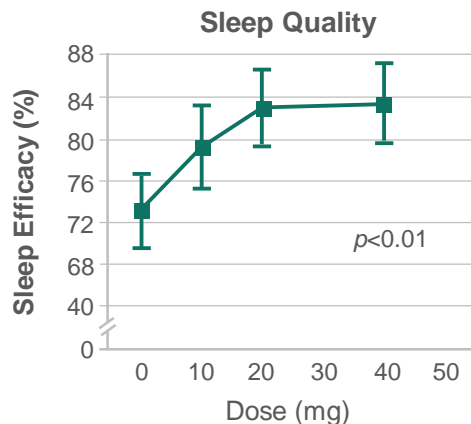
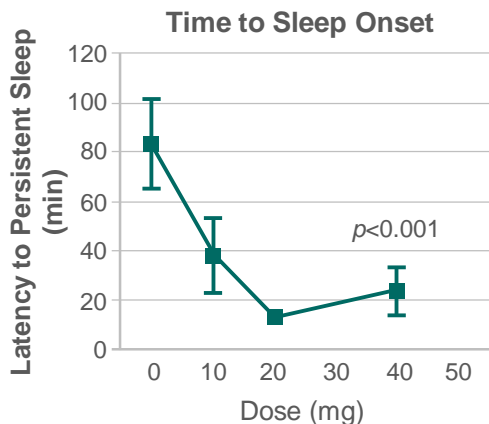
² Soverly P, Papakostas GI, Trivedi MH, Treatment-resistant depression, J Clin Psych 2006; 67(Suppl 6)16-22

³ Kessler, RC, et al. The Epidemiology of Major Depressive Disorder, JAMA, June 18, 2003 – Vol 289, No. 3

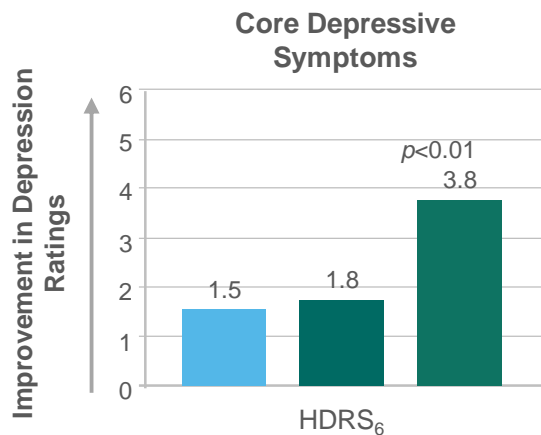
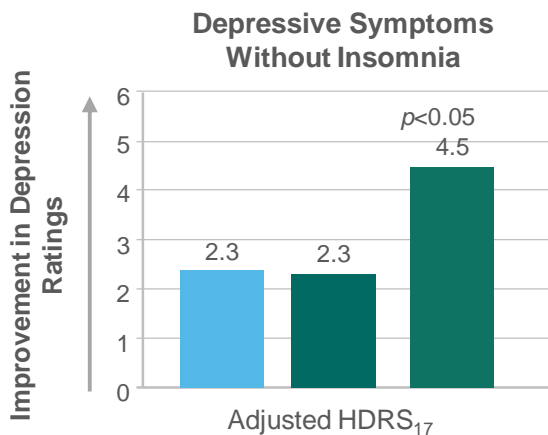
⁴ Rush, AJ, et al. (2007) Am J Psychiatry 163:11, pp. 1905-1917 (STAR*D Study)

Seltorexant study in MDD with comorbid insomnia shows improvements in insomnia and depressive symptoms (Ph1a)

Exploratory Phase 1a study in patients with major depressive disorder and insomnia (N = 20)



Minerva Neurosciences, internal data, study 42847922ED1002; disclosed Q1 2015.



■ Placebo
 ■ Diphenhydramine²
 ■ Orexin-₂ Antagonist³

Phase 1b study
 Day 11, N = 47

HDRS₁₇=17-item Hamilton Depression Rating Scale; adjusted HDRS₁₇=HDRS with the 3 items related to sleep subtracted; HDRS₆=6-item subscale encompassing the core symptoms of depression.

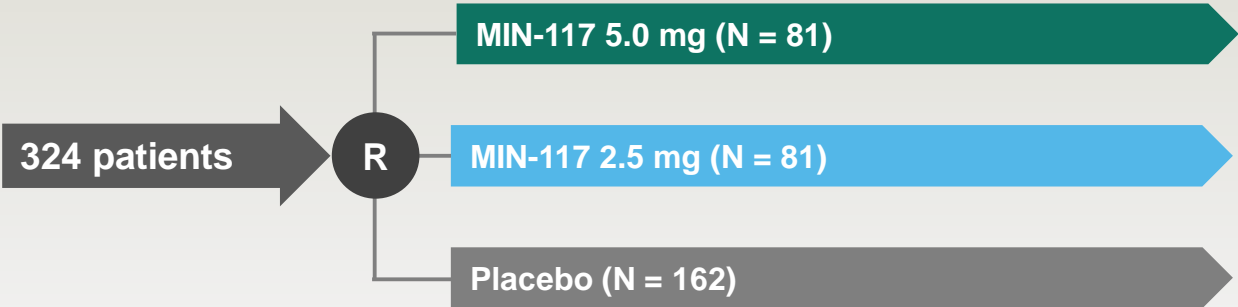
¹ ACNP. 2016; ClinicalTrials.gov NCT02476058; ² Diphenhydramine (Benadryl), included as a nocebo; ³ JNJ-7922.

MIN-117

A molecule for unmet needs in MDD patients targeting limitations of existing therapies, including:

- Quicker onset
- More sustained effect
- Fewer side effects
- Preserved cognition
- Partial responders
- Anxio-depressive patients

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



Minerva summary

Lead product in pivotal Phase 3 trial

- ▶ Enrollment completion expected H2 2019, TLR anticipated Q4 2019

Two positive Phase 2b TLR readouts in Q2 2019

- ▶ Seltorexant aMDD
- ▶ Seltorexant insomnia

Two Phase 2b studies ongoing

- ▶ Seltorexant aMDD TLR Q3 2019
- ▶ MIN-117 aMDD TLR Q4 2019

Well capitalized through multiple potential data read-outs in 2019

- ▶ \$69.4m cash balance at June 30, 2019
- ▶ Cash runway to early 2021

Experienced management team

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