May 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 March 31, 2019, filed with the Securities and Exchange Commission on May 6, 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.

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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	• 5-HT_{2A} antagonist • $Sigma_2$ antagonist	**P3 initiated Dec 2017 (MIN-101C07) Top Line Readout Q4 '19**			
Seltorexant MIN-202	Primary insomnia Major depressive disorder, as adjunctive therapy	• 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	• 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	• Neuregulin-1β1 activating ErbB4	**Pre-clinical**			

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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

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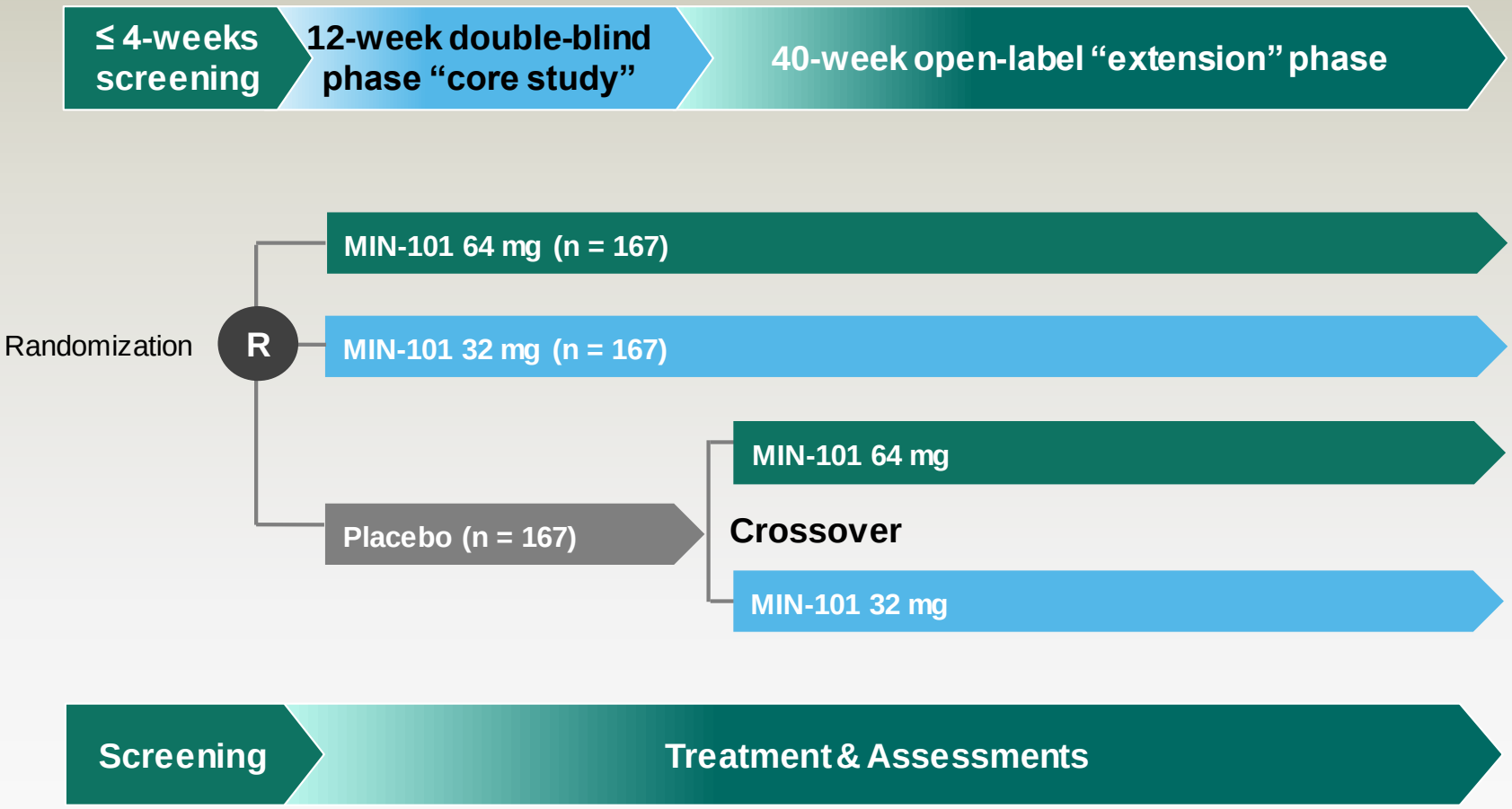
Roluperidone Phase 3 study design: monotherapy, double-blind, placebo-controlled in schizophrenic patients with negative symptoms



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.

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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

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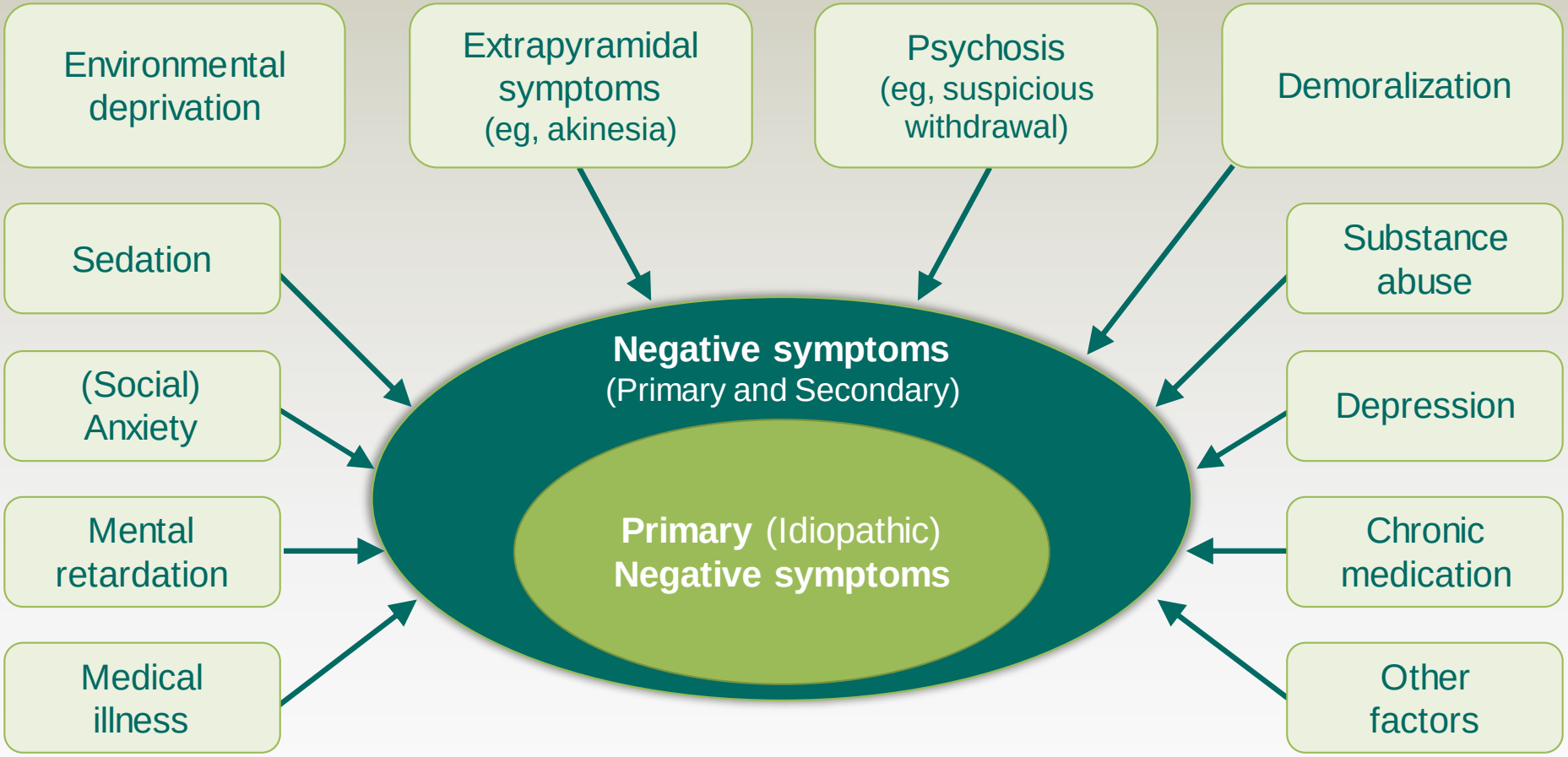
Main inclusion criteria Roluperidone trial

- 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

Why monotherapy & placebo controlled?

1. Demonstrate specific effect on negative symptoms
2. There is no approved positive control
3. Avoid unblinding of the study



Fervaha et al, European Psychiatry 2014

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Ongoing work in parallel to the Phase 3

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

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Planned work post-approval

- Pediatric population/adolescents at ultra-risk
- “Relapse” study
- Study in patients with CIAS*
- “Acute relapse prevention” study
- Efficacy studies in other therapeutic indications

* Cognitive Impairment Associated With Schizophrenia

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Target patient populations

Patients with the diagnosis of schizophrenia and not functioning well due to impairing negative symptoms

and

for future development, several other neuropsychiatric diseases

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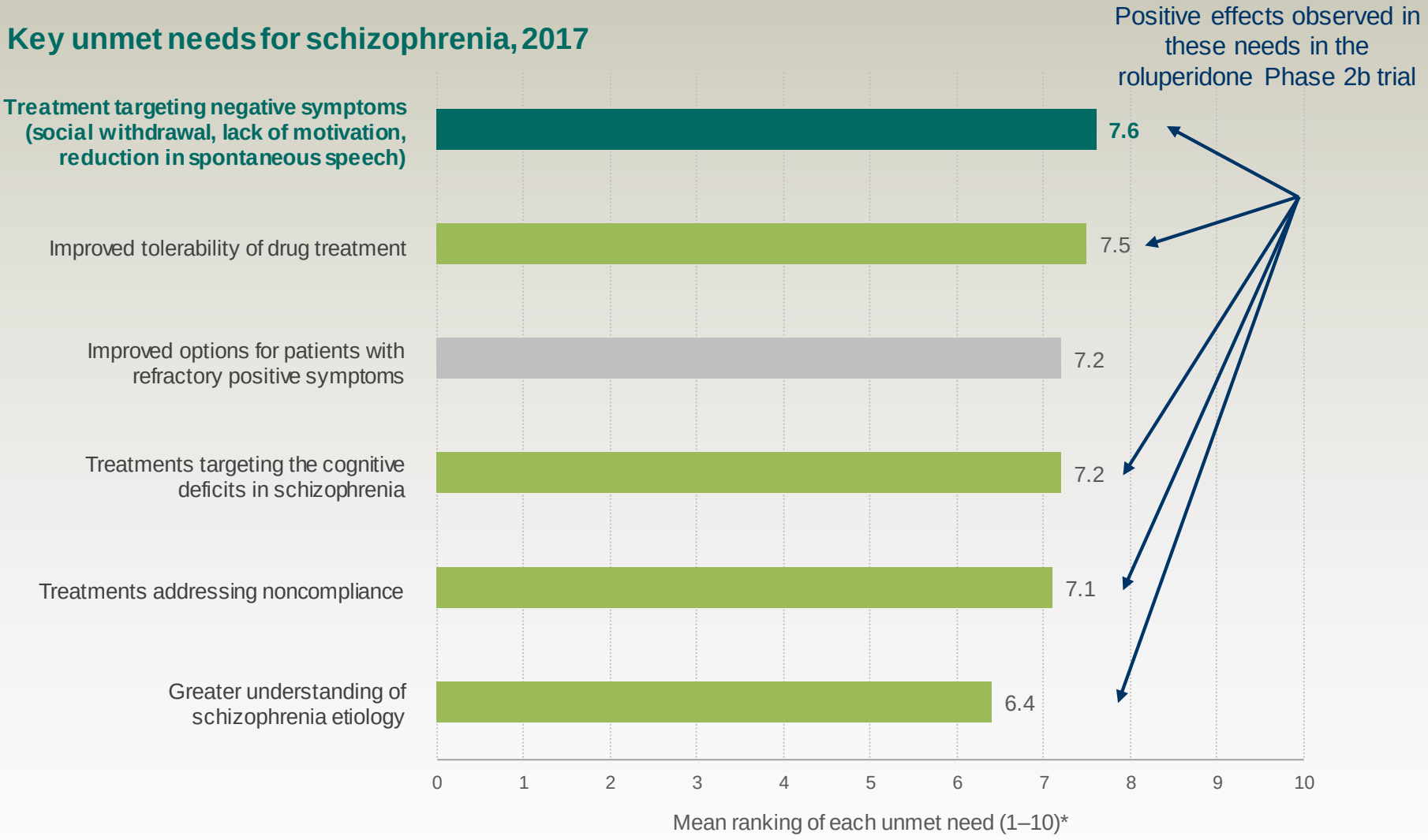
Roluperidone has the potential to specifically address negative symptoms and other unmet medical needs in schizophrenia

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

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Phase 2b:

Roluperidone observed to specifically improve negative symptoms and secondary and exploratory endpoints

Efficacy: Primary and Secondary Endpoints

Summary Table of Statistically Significant Results

	P-Value		Effect Size	
	MIN-101 versus Placebo		MIN-101 versus Placebo	
Endpoint	32 mg	64 mg	32 mg	64 mg
Primary Objective				
PANSS Negative Subscale Score (Pentagonal Structure Model)	0.0213	0.0030	0.45	0.58
Secondary Objectives				
PANSS Total Score	0.0714	0.0027	0.35	0.59
PANSS Positive Subscale Score (Pentagonal Structure Model)	0.5933	0.1926	-0.10	0.25
Dysphoric Mood Subscale Score (Pentagonal Structure Model)	0.5156	0.0238	0.12	0.43
Activation Subscale Score (Pentagonal Structure Model)	0.0213	0.0111	0.45	0.49
Autistic Preoccupation Subscale Score (Pentagonal Structure Model)	0.7004	0.2586	0.08	0.22
PANSS Negative Subscale Score	0.0058	0.0004	0.55	0.70
PANSS Positive Subscale Score	0.3388	0.2832	0.18	0.21
PANSS General Psychopathology Subscale Score	0.2270	0.0032	0.23	0.57
Brief Negative Symptoms Scale	0.0934	0.0044	0.33	0.56
Clinical Global Impression of Severity	0.0964	0.0266	0.28	0.28
Clinical Global Impression of Improvement	0.2345	0.0042	0.41	0.69
Brief Assessment of Cognition in Schizophrenia	0.0388	0.5947	0.40	0.10
Exploratory Objectives				
Calgary Depression Scale for Schizophrenia	0.2315	0.0090	0.23	0.50
Personal and Social Performance	0.2193	0.0021	0.24	0.59

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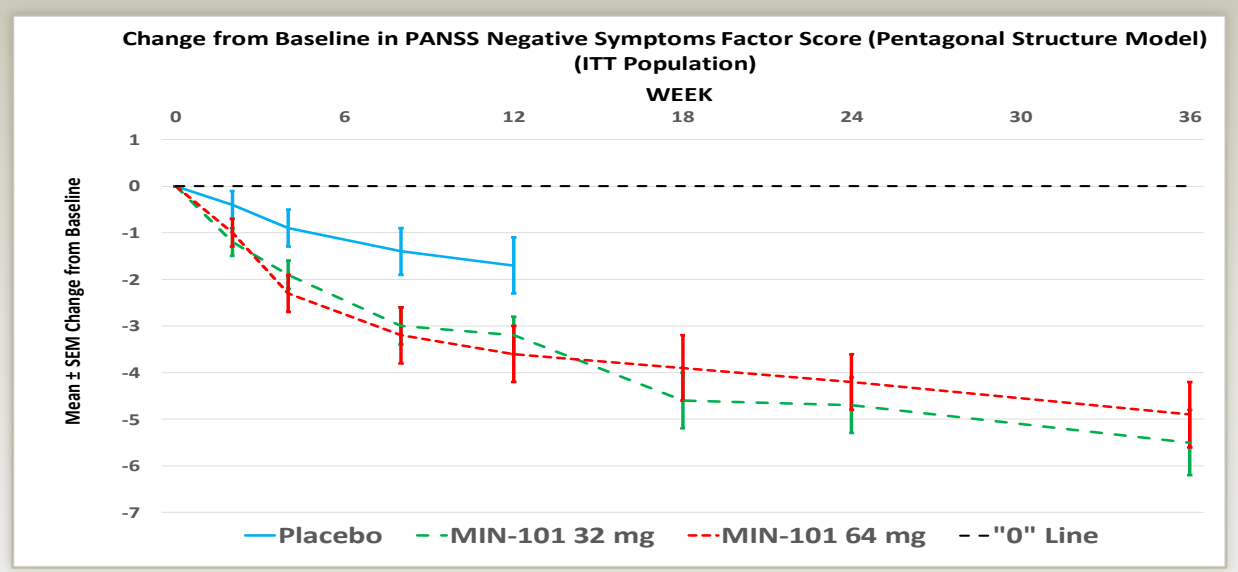
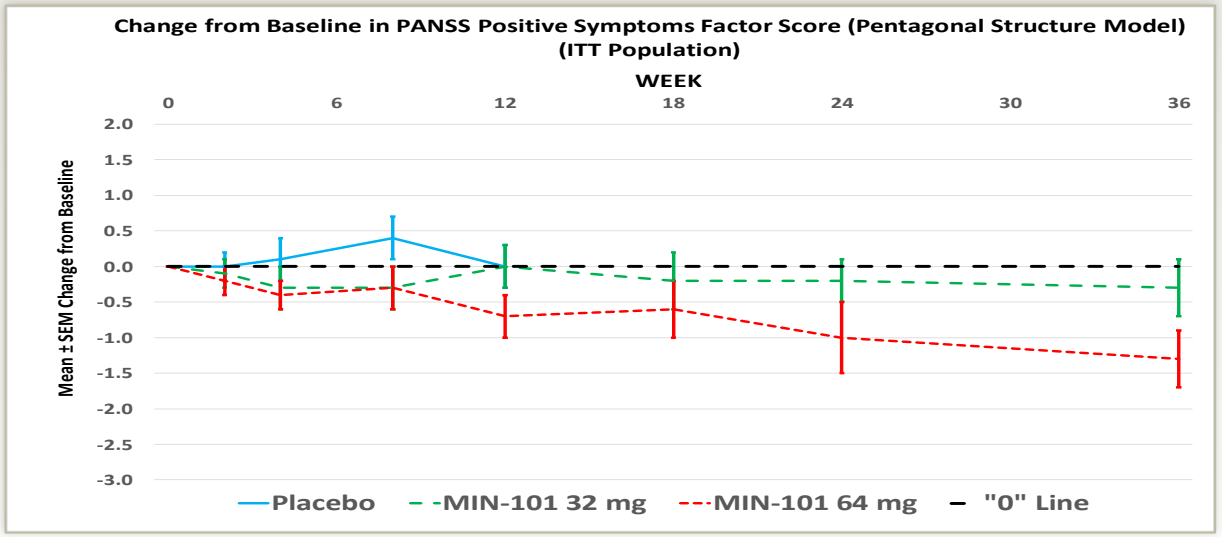
Phase 2b:
Continuous improvements in negative symptoms observed over 36 weeks

Negative symptoms



Positive symptoms



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Roluperidone: Phase 2b published data on negative symptoms and cognition

Peer-reviewed data publications

1. **Overall study results:**
   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

2. **CIAS-cognition:**
   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

3. **Negative symptoms:**
   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

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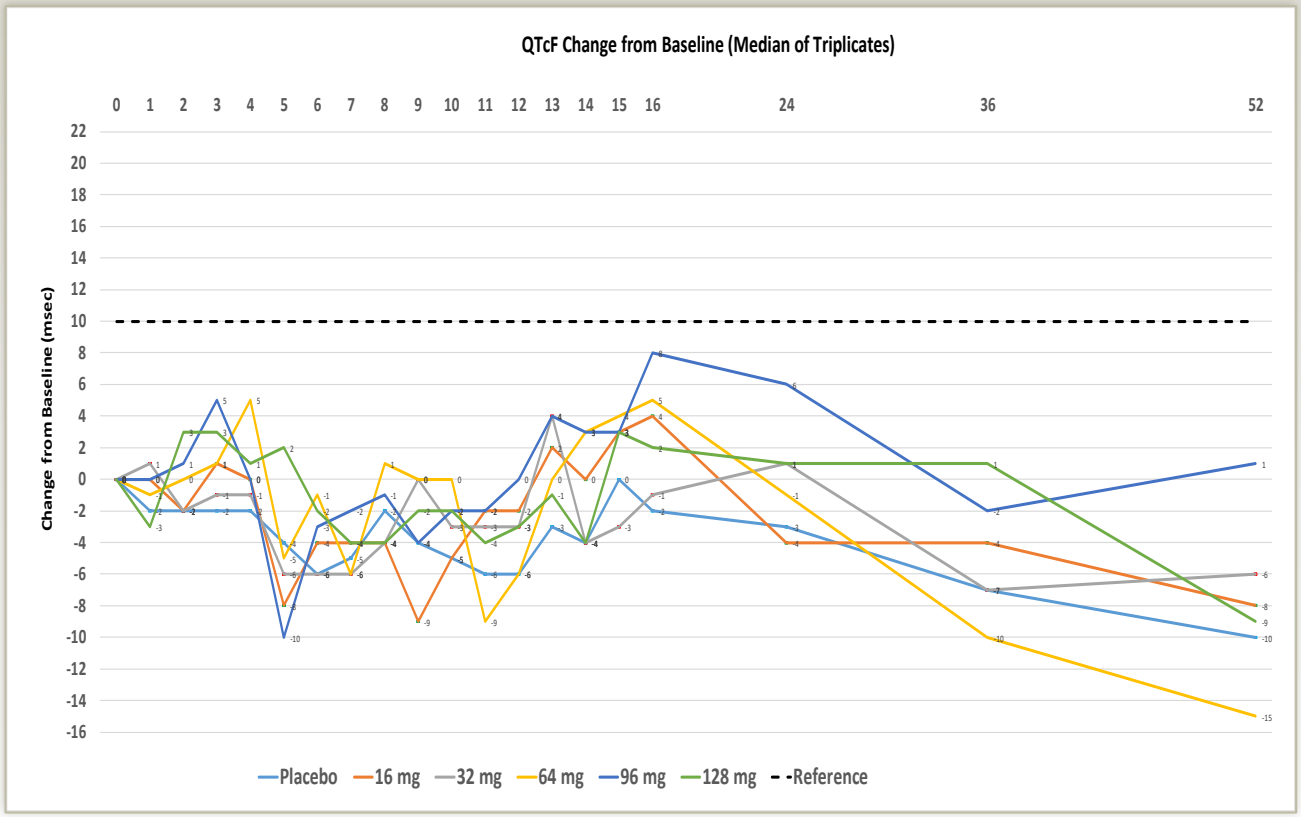
Roluperidone:

Safety profile observed to differ from atypical antipsychotics

- No weight gain
- No sedation
- No prolactin increase
- No significant QtcF increase at 2x high dose (128mg)



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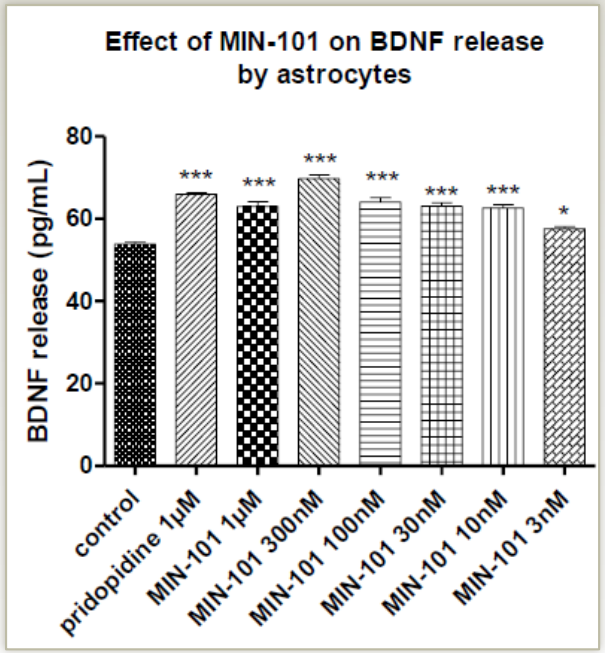
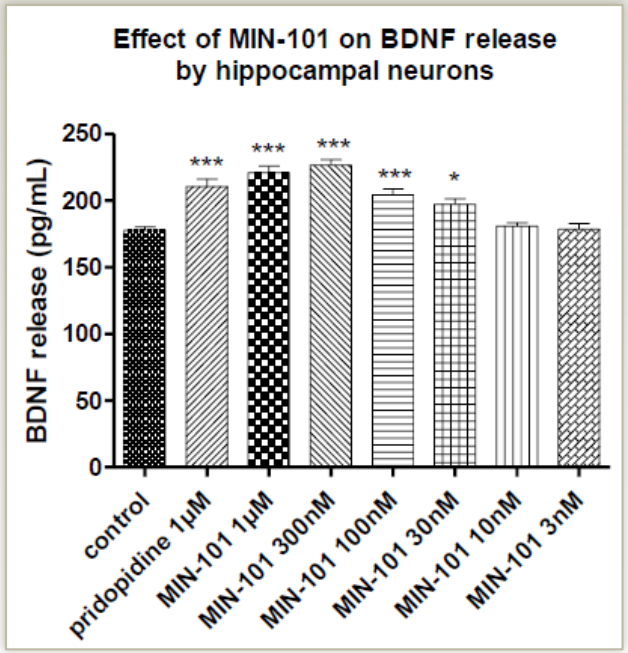
Elucidating MoA further:
Roluperidone increases BDNF release

- Evaluation of MIN-101 effect (6 concentrations)
  - *In-situ* ELISA for BDNF detection
  - Rat primary astrocytes (5 days of incubation)
  - Rat primary hippocampal neurons (3 days of incubation)





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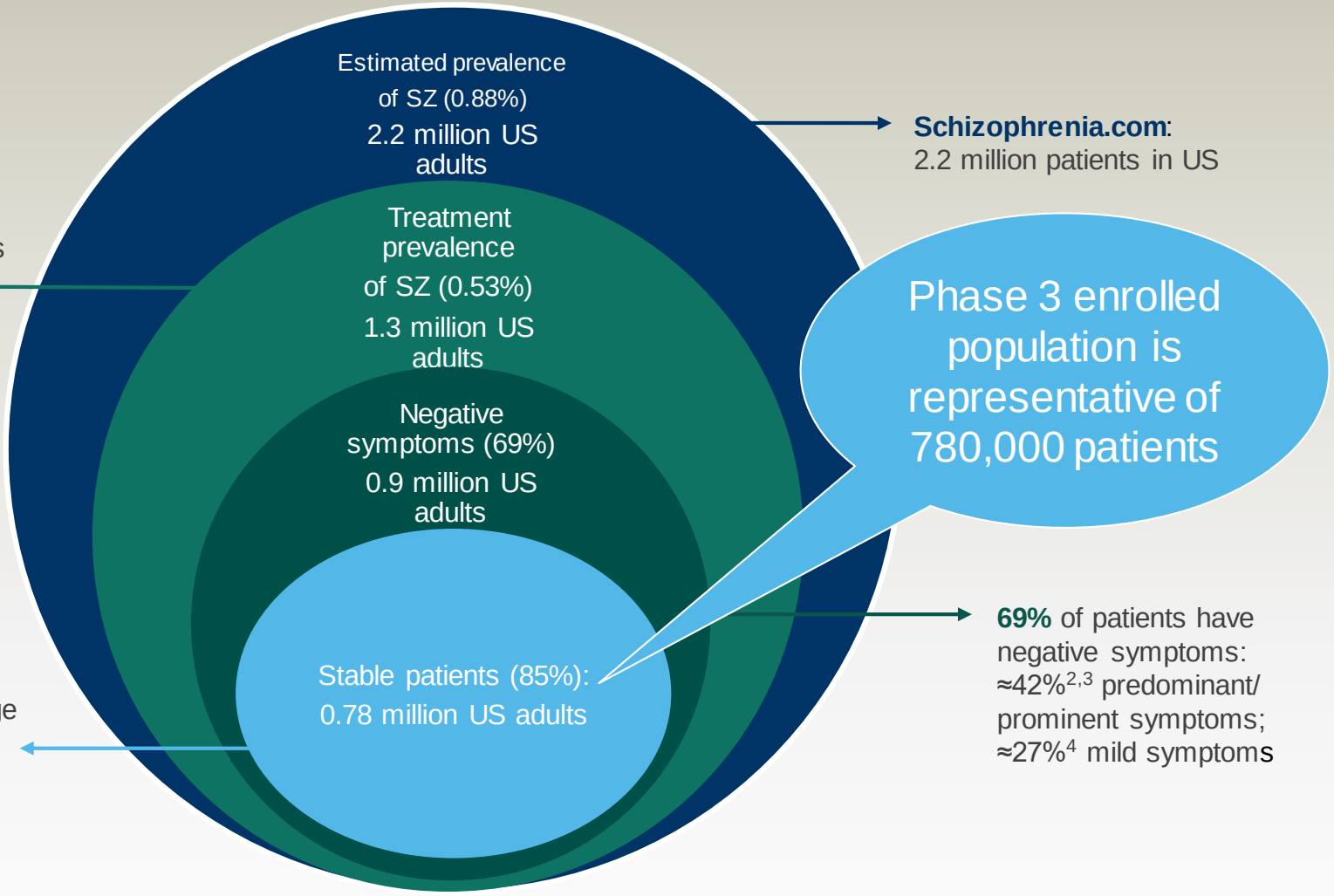
≈ 60% of adult patients with schizophrenia who are treated have negative symptoms and are relapse free over 6 months



SZ=schizophrenia.

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

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Potential of Roluperidone is becoming independently recognized

Landscape & Forecast

Schizophrenia

Disease Landscape & Forecast

If roluperidone is *"approved for the treatment of negative symptoms—an indication of high unmet need and commercial potential— it will achieve blockbuster sales in this market (approximately $1,740 million in 2027)* ***and will be the main driver for the schizophrenia market during the forecast period."***

*"**The most notable impact on the schizophrenia market will be from the availability of roluperidone**, a 5-HT2A and sigma2 receptor antagonist, for patients with the negative symptoms of schizophrenia—an area of high unmet need—in the United States and Europe."* DRG anticipates that "*Roluperidone will launch in these markets nearly halfway through the forecast period and will achieve blockbuster sales during this period."*

www.DecisionResourcesGroup.com

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Expected prescribing patterns for Roluperidone after launch

- **Initially, patients similar to clinical study subject population:**
  - Manifest life-long predominately negative symptoms with mild to moderate positive symptoms (Bobes et al 2010; Buchanan 2007; Sauve et al 2019)
  - Are considered Rx refractory because of persistent negative symptoms (Iasevoli F 2018; Downs J et al 2018)
  - Poorly tolerate antipsychotics (Morrison 2012; Murray et at 2015)
  - Refuse to take antipsychotics or agree but do not adhere (Czobar et al 2015; Dufort A Zipursky R 2019)
  - Recent onset but remitted psychosis (first episode) or young patients with equivocal positive but clear negative symptoms (Chang et al 2013; Alvarez-Jimenez et al 2016; Bowtell at 2017)
- **Eventually, other schizophrenic patients who have negative symptoms, including those on antipsychotic or DA blockers**
  - Expected label at launch to include DDI data showing such use will not adversely affect safety profile of Roluperidone

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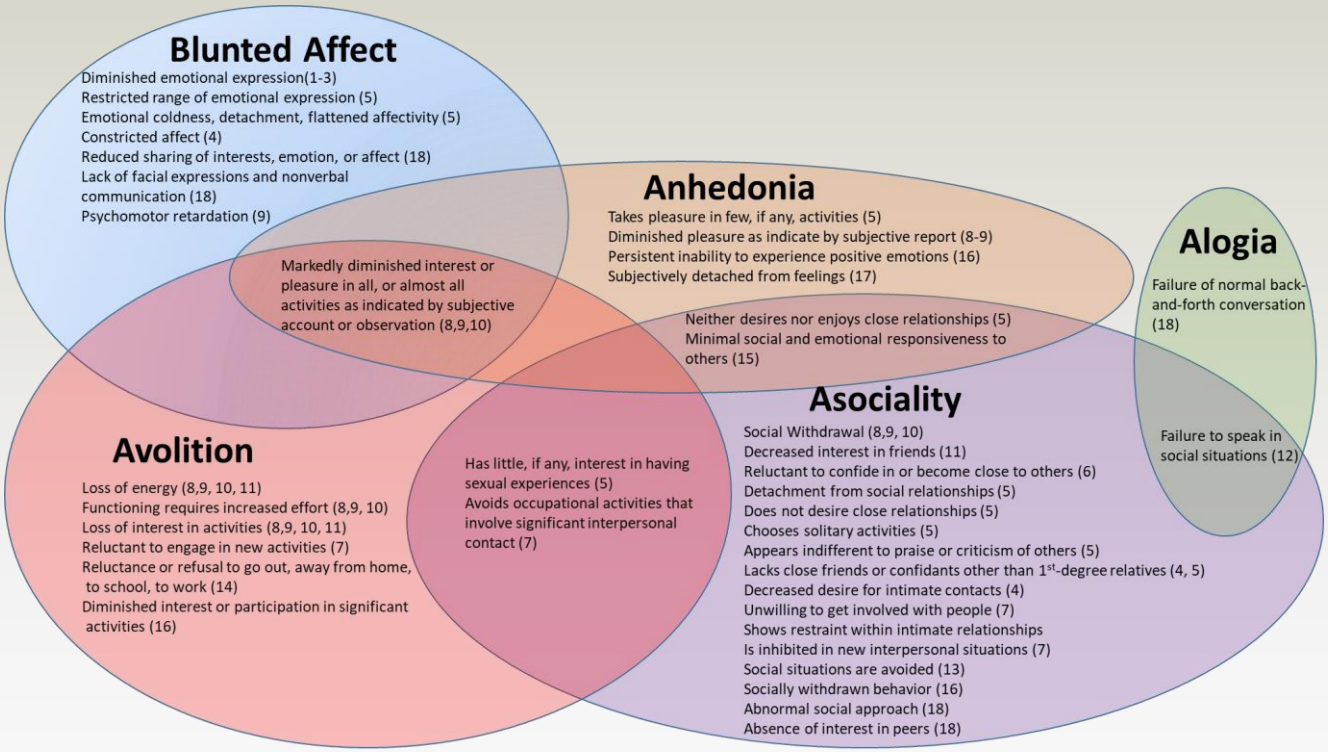
Relapse rates of patients who discontinue antipsychotic treatment

- In RCT and in clinical practice, DA blocking antipsychotic drugs improve agitation and psychosis in acutely exacerbated patients and, reduce risk of worsening in these who achieved improvement (Hasan et al 2012; Leucht et al 2012)
- However, depending on the population and on the length of follow-up, up to 45% of patients maintain symptomatic improvement without antipsychotic treatment while many other exacerbate despite treatment (Kishi et al 2018;Davidson 2018; Gøtzsche et al 2015; Morganet al 2014; Wunderink et al 2013)
- In RTC of antipsychotic drugs versus placebo, between 40% and 75% of the patients drop-out, mostly during the first 3 months of the trial (Rabinowitz et al 2008; Gueorguieva and Rosenhaek 2012)

Negative symptoms occur outside of schizophrenia – we just don't call them that



1.Schizophrenia
2. Schizoaffective Disorder
3. Schizophreniform Disorder
4. Schizotypal Personality Disorder
5. Schizoid Personality Disorder
6. Paranoid Personality Disorder
7. Avoidant Personality Disorder
8. Bipolar Disorder (I and II)
9. Major Depressive Disorder
10. Persistent Depressive Disorder (Dysthymia)
11. Premenstrual Dysphoric Disorder
12. Selective Mutism
13. Social Anxiety Disorder
14. Separation Anxiety Disorder
15. Reactive Attachment Disorder
16. Posttraumatic Stress Disorder
17. Depersonalization/Derealization Disorder
18. Autism Spectrum Disorder
19. Neurocognitive Disorders

Strauss, G. P., & Cohen, A. S. (2017). A transdiagnostic review of negative symptom phenomenology and etiology. *Schizophrenia bulletin*, *43*(4), 712-719.

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Seltorexant (MIN-202)

A differentiated Orexin antagonist for MDD and insomnia

A co-development/co-commercialization program with

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Seltorexant Phase 2b program: 2 trials in aMDD and 1 in insomnia ongoing with data read-outs 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.

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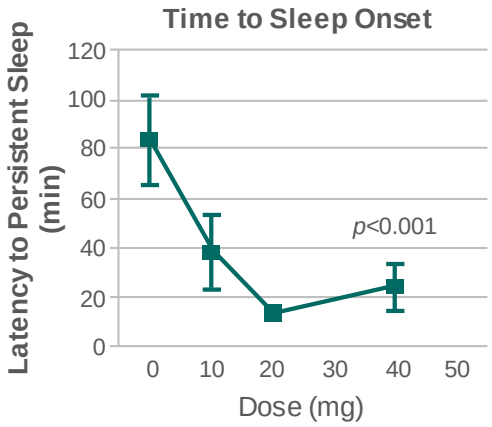
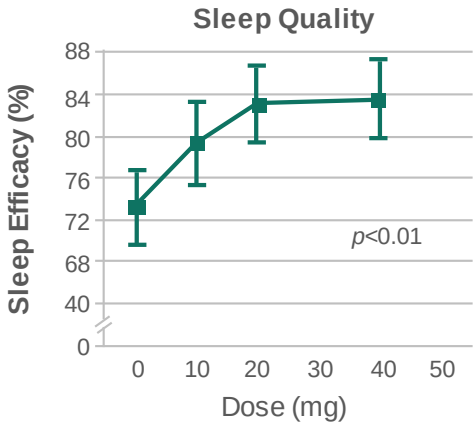
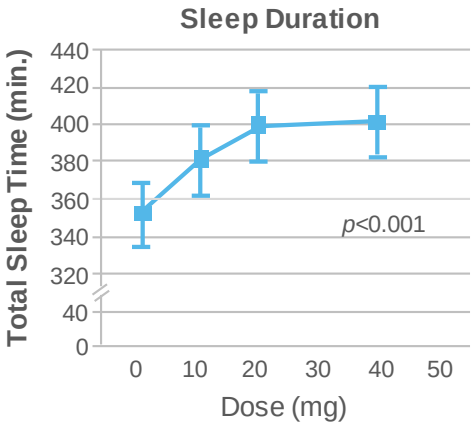
Seltorexant study in MDD with comorbid insomnia shows improvements in insomnia and depressive symptoms

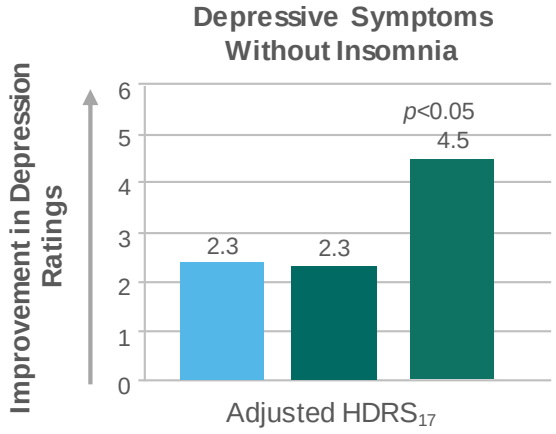
Exploratory Phase 1a study in patients with major depressive disorder and insomnia (N = 20)

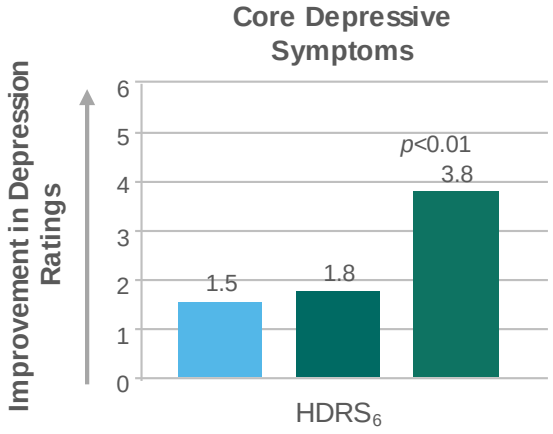


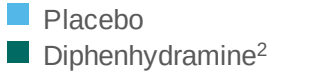




Minerva Neurosciences, internal data, study 42847922ED1002; disclosed Q1 2015.







Phase 1b study
Day 11, N = 47

$HDRS_{17}$=17-item Hamilton Depression Rating Scale; adjusted $HDRS_{17}$=HDRS with the 3 items related to sleep subtracted; $HDRS_6$=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.

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Seltorexant: Published data

Peer-reviewed data publications

1. Insomnia in patients with MDD:

Brooks et al., The selective orexin-2 receptor antagonist seltorexant improves sleep: An exploratory double-blind, placebo controlled, crossover study in antidepressant-treat major depressive disorder patients with persistent insomnia, Journal of Psychopharmacology, sagepub.com/journals-permissions
https://doi.org/10.1177/0269881118822258

2. Insomnia without comorbid psychiatric disorders:

De Boer, P. et al., A randomized Phase 2 study to evaluate the orexin-2 receptor antagonist seltorexant in individuals with insomnia without psychiatric comorbidity, Psychopharmacol. 2018 Jun; 32(6): 668-677,
https://doi.org/10.1177/0269881118773745

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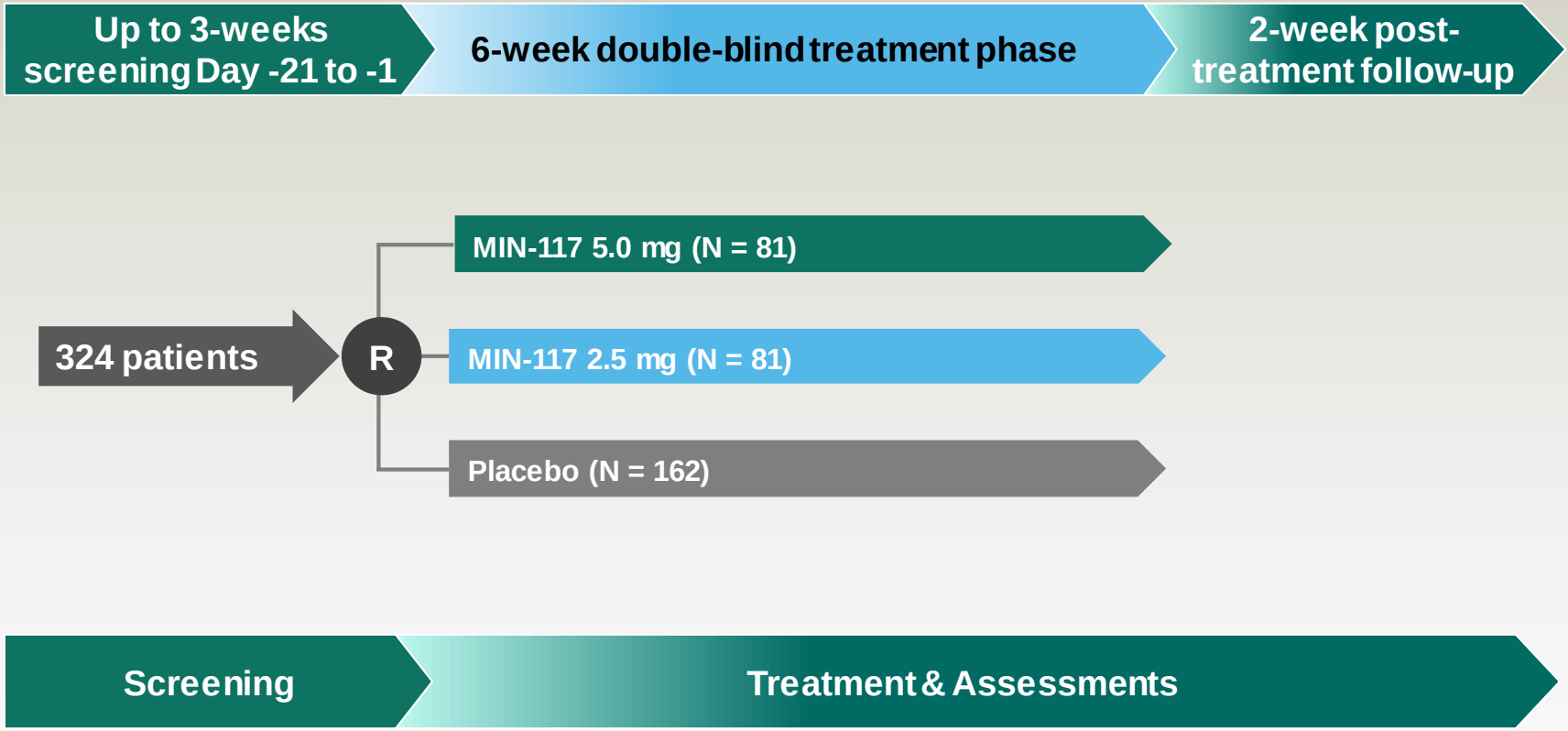
MIN-117

A molecule being studied with the goal of addressing unmet needs in MDD patients and the 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



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Minerva summary

Lead product in pivotal Phase 3 trial	▶ Enrollment completion expected H2 2019, TLR anticipated Q4 2019
Four Phase 2b studies ongoing	▶ Seltorexant aMDD and insomnia — TLR Q2 2019 ▶ Seltorexant aMDD — TLR Q3 2019 ▶ MIN-117 aMDD — TLR Q4 2019
Well capitalized through multiple data read-outs in 2019	▶ $79.3m cash balance at March 31, 2019 ▶ Cash runway to early 2021
Experienced management team	▶ Decades of combined experience in clinical practice and CNS drug discovery and development

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