

#### 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. Forwardlooking 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 guarter ended September 30, 2019, filed with the Securities and Exchange Commission on November 4, 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> <li>5-HT<sub>2A</sub> antagonist</li> <li>Sigma<sub>2</sub> antagonist</li> <li>α<sub>1A</sub>-adrenergic antagonist</li> <li>α<sub>1B</sub>-adrenergic antagonist</li> </ul>	Phase 3 (MIN-10	<b>1C07) Top Line Re</b>	adout H1'20	<b></b>
Seltorexant MIN-202	Primary insomnia  Major depressive	Selective orexin-2     antagonist	Phase 2b (MDD2	completed		
	disorder, as adjunctive therapy		Phase 2b (ISM20 Phase 2 (MDD20	completed completed		
MIN-117	Major depressive disorder and anxiety, as monotherapy	<ul> <li>5-HT<sub>1A</sub> antagonist</li> <li>5HT transporter</li> <li>α<sub>1A</sub>-adrenergic antagonist</li> <li>α<sub>1B</sub>-adrenergic antagonist</li> <li>Dopamine transporter</li> <li>5-HT<sub>2A</sub> antagonist</li> </ul>	Phase 2b (MIN-11	17C03) Top Line Re	eadout Q4'19	
MIN-301	Parkinson's disease	• Neuregulin-1β1 activating ErbB4	Pre-clinical			



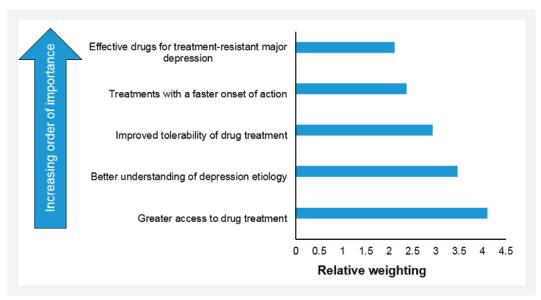
# MIN-117

An investigational molecule to address unmet needs in the MDD patient population



#### Depression is a large market with substantial unmet needs

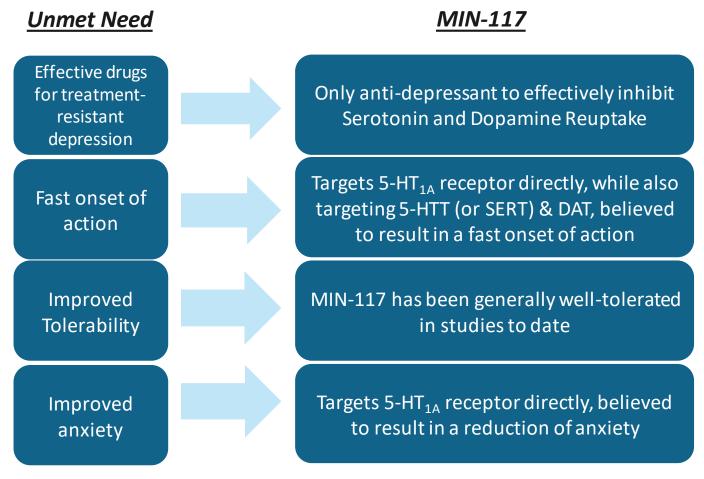
- Depression is a common psychiatric disorder (>350 million people of all ages worldwide)
  - More than 17% of U.S. population had at least one major depressive episode in the past year
  - Leading cause of disability worldwide
- Despite large number of treatment options in a broad set of treatment classes, many patients fail to achieve remission and considerable unmet needs remain, particularly in:
  - Treatment-resistant major depression
  - Onset of action
  - Tolerability
  - Anxio-depression





#### MIN-117 could potentially addresses four of the most critical unmet needs in depression

■ MIN-117 has potential to be the first of a new class of Serotonin-Dopamine Reuptake Inhibitors (SDRI) that addresses critical unmet needs in depression





What do we already know?

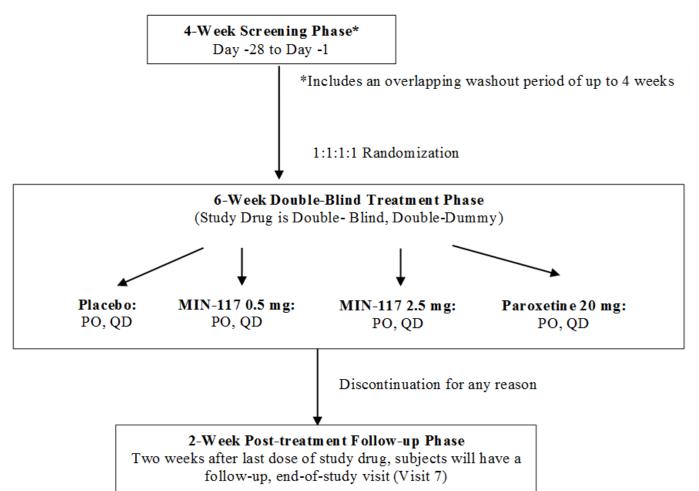


# MIN-117C01: Phase 2a

A Randomized, Double-Blind, Parallel-Group, Placebo- and Active-Controlled Study to Evaluate the Efficacy and Safety of 2 Doses of MIN-117 in Adult Subjects with Major Depressive Disorder

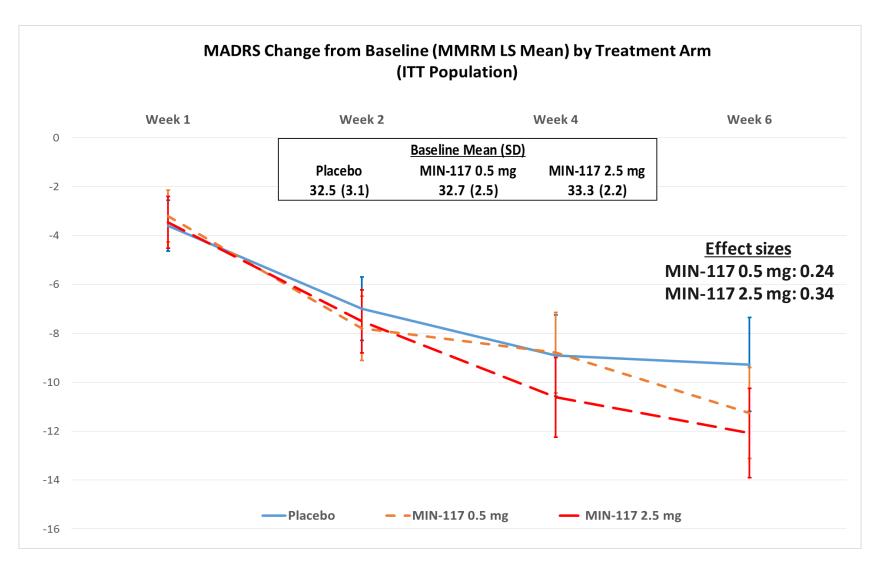


Figure 1: Study Design Diagram (Timelines not to scale)



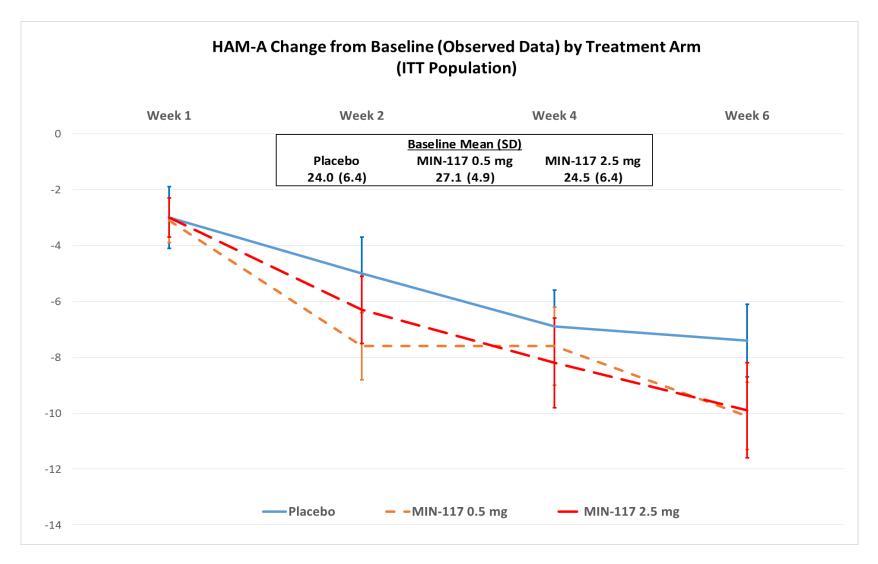


# MIN-117CO1: Efficacy – MADRS (ITT population)



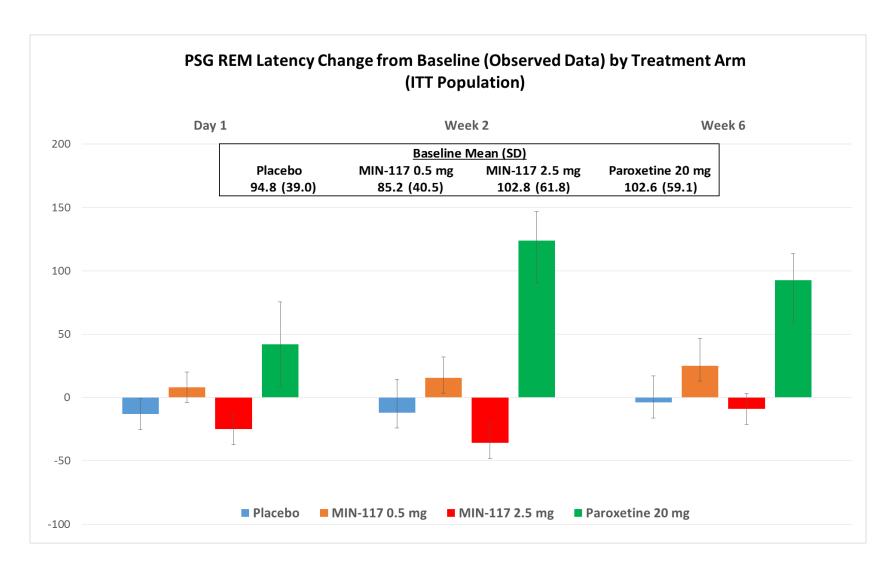


#### MIN-117C01: HAM-A





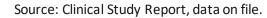
## MIN-117CO1: Sleep polysomnography – REM latency





# MIN-117CO1: Effect sizes

		MIN-117 versus Placebo		Paroxetine versus Placebo	Favorable Finding
	Endpoint	0.5 mg	2.5 mg	20 mg	
Primary Objective	,				
	Montgomery-Asberg Depression Rating Scale Total Score	-0.24	-0.34	-0.54	<b>V</b>
Secondary Objectives					
	Clinical Global Impression of Severity	0.05	-0.04	-0.13	$\downarrow$
	Clinical Global Impression of Improvement	-0.02	-0.26	-0.38	$\downarrow$
	Hamilton Anxiety	-0.49	-0.46	-0.31	<b>1</b>
	Arizona Sexual Experiences Scale	-0.45	-0.36	0.00	$\downarrow$
	Digit-Symbol Substitution Test	-0.18	0.15	-0.20	$\uparrow$
	Digit Span Backwards task	0.61	0.13	0.63	$\uparrow$
	Initiation Time	-0.01	-0.81	-0.23	<b>\</b>
	Execution Time	0.15	-0.28	0.05	$\downarrow$
	Move Count	0.07	-0.41	-0.15	<b>1</b>
	Correct Score	-0.26	0.37	-0.16	$\uparrow$

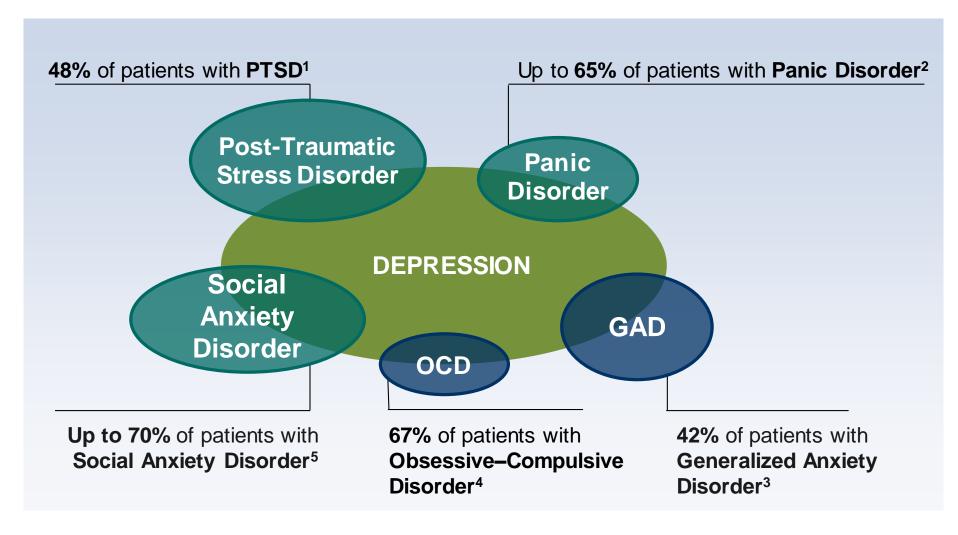




#### MIN-117C01: Summary of results

- Paroxetine differentiated from placebo, confirming assay sensitivity
- A dose-dependent superiority of MIN-117 over placebo as measured by change on the MADRS was demonstrated already at 2 weeks
- 24% of the patients treated with MIN-117 2.5 mg achieved remission as prospectively defined
- Compared to placebo, the number of patients who achieved remission based on a MADRS score of < 12, on the 2.5 mg dose had an odds ratio (OR) by Week 4 of 2.1 (0.5 for paroxetine), and by Week 6 of 3.1 (1.1 for paroxetine)
- The 2.5 mg was superior to paroxetine when evaluating the rate of response base on the definition of reduction in the baseline MADRS score by  $\geq 50\%$
- MIN-117 preserved sleep continuity and architecture and therefore is not expected to have detrimental effects on REM distribution and duration
- Both doses of MIN-117 demonstrated a favorable tolerability profile, and the incidence and types of side effects were comparable to placebo
- Treatment with MIN-117 was not associated with cognitive impairment, sexual dysfunction, suicidal ideation or weight gain
- Both doses showed improvement of anxiety measured by HAM-A scale, with ES of 0.49 and 0.45 for 0.5 mg and 2.5 mg, respectively

#### Lifetime co-morbidity of depression and anxiety disorders is common



<sup>1</sup>Kessler et al. Arch Gen Psychiatry 1995; 52 (12): 1048–1060; <sup>2</sup>DSM-IV-TR™ 2000; <sup>3</sup>Brawman-Mintzer et al. Am J Psychiatry 1993; 150 (8): 1216–1218; <sup>4</sup>Rasmussen et al. J Clin Psychiatry 1992; Suppl 4–10; <sup>5</sup>Dunner. Depression and Anxiety 2001; 13 (2): 57–71



What will we learn from the Phase 2b study?



# MIN-117C03: Phase 2b

A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of 2 Fixed Doses (5.0 mg or 2.5 mg) of MIN-117 in Adult Subjects with Major Depressive Disorder



#### MIN-117C03: Objectives

#### Primary:

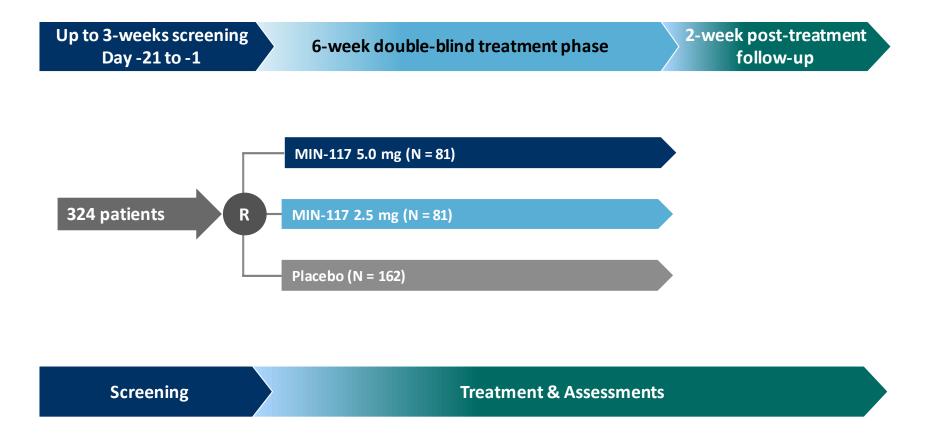
■ To evaluate the efficacy of 5.0 mg or 2.5 mg of MIN-117 compared with placebo in reducing the symptoms of MDD measured by the change from baseline in MADRS score over 6 weeks of treatment

#### Secondary:

- Reduction in symptoms of anxiety as measured by HAM-A
- Severity of illness and improvement using the CGI-S and CGI-I
- To evaluate the safety of MIN-117 over 6 weeks of treatment



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





## MIN-117

# An investigational molecule to address unmet needs in the MDD patient population

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

- Quicker onset
- More sustained and complete effects on mood
- Fewer side effects than currently available therapies for MDD
- Preserved cognition and sexual function
- Potential to address the unmet need of partial responders and non-responders
- Associated anxiety symptoms

Significant potential opportunity for MIN-117 in patients who are not adequately responding to SSRI/SNRI and prior to use of classes/products with high side effect burden

**Initial Treatment** 

SSRIs, SNRIs, mirtazapine, or bupropion

# **Potential Opportunity for MIN-117**

First-Line

If response is partial or none at 4-8 weeks, **Increase dose or switch** to a different antidepressant

Refractory Treatment Second-Line If trial of 2 antidepressants from the same class are ineffective, <a href="mailto:switch to another class or switch to">switch to</a> another class or switch to nonselective MAOI

Third-Line Combination use of antidepressant with non-MAOI antidepressant of another class or with <u>anticonvulsant</u>, atypical antipsychotic, lithium, even tricyclics



#### Summary

Lead product in Phase 3

► Roluperidone TLR expected first half 2020

Three Phase 2b TLR readouts in 2019 support Phase 3 design

- ► Seltorexant aMDD (two trials)
- ► Seltorexant insomnia

One Phase 2b study ongoing

► MIN-117 MDD enrollment completed, TLR expected Q4 2019

Well capitalized through multiple potential data readouts in 2019/H1 2020

- ▶ \$60m cash balance on September 30, 2019
- ► Cash runway to mid-2021

Experienced management team

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

