Innovative CNS therapies to address unmet medical needs

Positive TLRs from four studies with MIN-101, MIN-202 and MIN-117 since the beginning of 2016

JEFFERIES HEALTHCARE CONFERENCE
June 2016
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.
Building a portfolio of innovative therapies

<table>
<thead>
<tr>
<th>Program</th>
<th>Origin</th>
<th>Primary Indications</th>
<th>Mechanisms of Action</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Status</th>
</tr>
</thead>
</table>
| MIN-101 | Mitsubishi Tanabe | Schizophrenia | ● 5-HT2A antagonist  
● Sigma2 antagonist | **Phase IIb completed**  
Extension phase ongoing |         |         |         | Positive TLR announced May 2016 |
| MIN-117 | Mitsubishi Tanabe | Major Depressive Disorder | ● 5-HT1A  
● 5HT transporter  
● Alpha-1a, b  
● Dopamine transporter  
● 5-HT2A antagonist |         |         | **Phase IIa completed** | Positive TLR announced May 2016 |
| MIN-202 | Janssen (under co-development) | Primary Insomnia  
Major Depressive Disorder | ● Selective Orexin2 antagonist | **Phase IIa completed**  
**Phase Ib completed** |         |         | Positive TLR January 2016  
Positive TLR March 2016 |
| MIN-301 | Mind-NRG | Parkinson’s Disease | ● Neuregulin 1β1 activating ErbB4 | **Pre-clinical** |         |         | IND or IMPD; Phase 1 expected to initiate thereafter |
MIN-101

A new drug with the potential to address unmet needs in schizophrenia
MIN-101 Phase IIb study design: monotherapy, double-blind, placebo controlled in schizophrenic patients with negative symptoms

- Screening
- Treatment and Assessments

© Randomization

MIN-101 64 mg (N=78)

MIN-101 32 mg (N=78)

Placebo (N=78)

Crossover to MIN-101

MIN-101 64 mg

MIN-101 32 mg

≤ 4 Weeks

12 Weeks DB Phase

24 Weeks Open-label Extension Phase
MIN-101 Phase IIb: Primary and secondary objectives

Primary:
To evaluate the efficacy of MIN-101 compared to placebo in improving the negative symptoms of schizophrenia as measured by the change from Baseline in the Positive and Negative Syndrome Scale (PANSS) negative subscale score of the pentagonal model over 12 weeks of treatment.

Secondary:
- To evaluate the efficacy of MIN-101 compared to placebo in improving other symptoms of schizophrenia as measured by the change from Baseline in the PANSS total score, positive symptoms score, dysphoric mood, activation, and autistic preoccupation sub-scores of the pentagonal model over 12 weeks of double-blind treatment.
- To evaluate the efficacy of MIN-101 compared to placebo in improving symptoms of schizophrenia as measured by changes from Baseline in the PANSS total score and sub-scores according to the 3 factors analysis over 12 weeks of double-blind treatment.
- To evaluate the efficacy of MIN-101 compared to placebo in improving negative symptoms of schizophrenia as measured by the change from Baseline in the Brief Negative Symptoms Scale (BNSS) total score over 12 weeks of double-blind treatment.
- To assess the effects of MIN-101 compared to placebo on the Clinical Global Impression of Severity (CGI-S) and Clinical Global Impression of Improvement (CGI-I) over 12 weeks of double-blind treatment.
- To assess the effects versus placebo of MIN-101 on cognitive function as measured by the Brief Assessment of Cognition in Schizophrenia (BACS) battery over 12 weeks of double-blind treatment.
- To evaluate the safety and tolerability of MIN-101 compared to placebo.
- To assess the pharmacokinetics (PK) profile of MIN-101 and its metabolites using population PK models.
- To assess the persistence of efficacy, and the safety and tolerability of MIN-101 during the 24-week, open-label extension phase.
Primary endpoint analysis:

- Efficacy analyses are based on the Intent to Treat (ITT) population
- Mixed-effects model for repeated measures (MMRM) is applied
- Changes from baseline to week 12 in PANSS negative subscale score using the pentagonal structured model is the primary endpoint
- The Hochberg procedure is applied in order to maintain the Type I error rate due to multiple comparisons of the primary endpoint results at or below 0.050%
Efficacy: Primary endpoint
PANSS negative subscale (pentagonal structure)

PANSS Negative Symptoms Score (Pentagonal Structure) Change from Baseline (MMRM) (ITT Population)

<table>
<thead>
<tr>
<th>WEEK</th>
<th>Placebo</th>
<th>MIN-101 32 mg</th>
<th>MIN-101 64 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>31.5 (4.7)</td>
<td>31.7 (4.2)</td>
<td>31.4 (4.3)</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
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<td></td>
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<td>8</td>
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<td>10</td>
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<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline Mean (SD)

Onset of effect observed after 2 weeks (measured at first visit)

Effect size
32 mg: 0.45
64 mg: 0.58

p-value: * ≤ 0.05; ** ≤ 0.01 versus placebo
Efficacy: Secondary endpoint (1)
PANSS negative symptom score (3 Factors)

Onset of effect observed after 2 weeks (measured at first visit)

Baseline Mean (SD)
Placebo  MIN-101 32 mg  MIN-101 64 mg
26.5 (3.8)  27.0 (3.7)  26.8 (3.8)

p-value: * ≤ 0.05; ** ≤ 0.01 versus placebo
Efficacy: Secondary endpoint (2)

PANSS total score

PANSS Total Score - Change from Baseline (MMRM)
(ITT Population)

Baseline Mean (SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>MIN-101 32 mg</th>
<th>MIN-101 64 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>80.2 (10.7)</td>
<td>81.2 (9.8)</td>
<td>79.7 (11.1)</td>
</tr>
</tbody>
</table>

WEEK

<table>
<thead>
<tr>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>80.2 (10.7)</td>
<td>81.2 (9.8)</td>
<td>79.7 (11.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LS Mean ± SEM Change from Baseline

p-value: * ≤ 0.05; ** ≤ 0.01 versus placebo
Efficacy: Secondary endpoint (3)  
PANSS positive symptom score (3 Factors)

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

**WEEK**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>MIN-101 32 mg</th>
<th>MIN-101 64 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Mean (SD)</td>
<td>14.2 (3.0)</td>
<td>14.6 (3.3)</td>
<td>13.9 (3.3)</td>
</tr>
</tbody>
</table>

**LS Mean ± SEM Change from Baseline**

* p-value: * ≤ 0.05; ** ≤ 0.01 versus placebo
### Efficacy: Primary and Secondary endpoints

#### Summary table of statistically significant results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>MIN-101 versus Placebo (32 mg)</th>
<th>Effect Size (MIN-101 versus Placebo)</th>
<th>MIN-101 versus Placebo (64 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Objective</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS Negative Subscale Score (Pentagonal Structure Model)</td>
<td>0.0213 0.0030</td>
<td>0.45 0.58</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary Objectives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANSS Total Score</td>
<td>0.0714 0.0027</td>
<td>0.35 0.59</td>
<td></td>
</tr>
<tr>
<td>PANSS Positive Subscale Score (Pentagonal Structure Model)</td>
<td>0.5933 0.1926</td>
<td>-0.10 0.25</td>
<td></td>
</tr>
<tr>
<td>Dysphoric Mood Subscale Score (Pentagonal Structure Model)</td>
<td>0.5156 0.0238</td>
<td>0.12 0.43</td>
<td></td>
</tr>
<tr>
<td>Activation Subscale Score (Pentagonal Structure Model)</td>
<td>0.0213 0.0111</td>
<td>0.45 0.49</td>
<td></td>
</tr>
<tr>
<td>Autistic Preoccupation Subscale Score (Pentagonal Structure Model)</td>
<td>0.7004 0.2586</td>
<td>0.08 0.22</td>
<td></td>
</tr>
<tr>
<td>PANSS Negative Subscale Score</td>
<td>0.0058 0.0015</td>
<td>0.55 0.70</td>
<td></td>
</tr>
<tr>
<td>PANSS Positive Subscale Score</td>
<td>0.3388 0.2832</td>
<td>0.18 0.21</td>
<td></td>
</tr>
<tr>
<td>PANSS General Psychopathology Subscale Score</td>
<td>0.2270 0.0032</td>
<td>0.23 0.57</td>
<td></td>
</tr>
<tr>
<td>Brief Negative Symptoms Scale</td>
<td>0.0934 0.0044</td>
<td>0.33 0.56</td>
<td></td>
</tr>
<tr>
<td>Clinical Global Impression of Severity</td>
<td>0.0964 0.0266</td>
<td>0.28 0.28</td>
<td></td>
</tr>
<tr>
<td>Clinical Global Impression of Improvement</td>
<td>0.2345 0.0042</td>
<td>0.41 0.69</td>
<td></td>
</tr>
<tr>
<td>Brief Assessment of Cognition in Schizophrenia</td>
<td>0.0388 0.5947</td>
<td>0.40 0.10</td>
<td></td>
</tr>
<tr>
<td><strong>Exploratory Objectives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calgary Depression Scale for Schizophrenia</td>
<td>0.2315 0.0090</td>
<td>0.23 0.50</td>
<td></td>
</tr>
<tr>
<td>Personal and Social Performance</td>
<td>0.2193 0.0021</td>
<td>0.24 0.59</td>
<td></td>
</tr>
</tbody>
</table>
Safety:
QTcF (msec) – LS Mean (Upper 90% CI) of change from baseline

QTcF (msec) - LS Mean (Upper 90% CI) of Change from Baseline (ANCOVA)
(ITT Population)

- 32 mg versus Placebo
- 64 mg versus Placebo
- 10 ms Reference Line
## Safety: Summary of other safety parameters

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Phase IIb results showed</th>
<th>Relative to current generation of atypical antipsychotics (not included in Minerva’s IIb study)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs and SAEs</td>
<td>Limited and comparable to placebo</td>
<td>Improved</td>
</tr>
<tr>
<td>Weight Gain, Waist Circumference</td>
<td>No increase</td>
<td>Improved</td>
</tr>
<tr>
<td>Laboratory Tests, including Prolactin</td>
<td>No increase</td>
<td>Improved</td>
</tr>
<tr>
<td>Extra-pyramidal Symptoms</td>
<td>No effect on AIMS scale</td>
<td>Improved</td>
</tr>
<tr>
<td>Vigilance</td>
<td>No sedation</td>
<td>Improved</td>
</tr>
</tbody>
</table>

*In the Phase IIb study MIN-101 showed a differentiated safety profile versus commonly observed side effects of current treatments for schizophrenia*
MIN-101 Phase IIb study conclusions and next steps

- Demonstrated efficacy on negative symptoms
- Onset observed as early as 2 weeks
- Efficacy shown on overall psychopathology
- Efficacy also observed on most of the secondary endpoints including cognition and social functioning
- Study showed that MIN-101 was well tolerated

U.S. Investigational New Drug Application (IND) accepted by FDA in December 2015
MIN-117

Our objective is to develop a new drug to address unmet needs in major depressive disorder (MDD)
Phase IIa study design

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

4-Week Screening Phase*
Day -28 to Day -1

*Includes an overlapping washout period of up to 4 weeks

1:1:1:1 Randomization

6-Week Double-Blind Treatment Phase
(Study Drug is Double-Blind, Double-Dummy)

- Placebo: PO, QD
- MIN-117 0.5 mg: PO, QD
- MIN-117 2.5 mg: PO, QD
- Paroxetine 20 mg: PO, QD

Discontinuation for any reason

2-Week Post-treatment Follow-up Phase
Two weeks after last dose of study drug, subjects will have a follow-up, end-of-study visit (Visit 7)
Efficacy: MADRS primary endpoint (ITT population)

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

Week 1  Week 2  Week 4  Week 6

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>MIN-117 0.5 mg</th>
<th>MIN-117 2.5 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Mean (SD)</td>
<td>32.5 (3.1)</td>
<td>32.7 (2.5)</td>
<td>33.3 (2.2)</td>
</tr>
</tbody>
</table>

Effect size
MIN-117 0.5 mg: 0.24
MIN-117 2.5 mg: 0.34
Efficacy: HAM-A secondary endpoint (ITT population)

HAM-A Change from Baseline (Observed Data) by Treatment Arm (ITT Population)

<table>
<thead>
<tr>
<th></th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>24.0 (6.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIN-117 0.5 mg</td>
<td>27.1 (4.9)</td>
<td>27.1 (4.9)</td>
<td>24.5 (6.4)</td>
<td>24.5 (6.4)</td>
</tr>
<tr>
<td>MIN-117 2.5 mg</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Effect size**
- MIN-117 0.5 mg: 0.49
- MIN-117 2.5 mg: 0.45
### PSG REM Latency Change from Baseline (Observed Data) by Treatment Arm (ITT Population)

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Week 2</th>
<th>Week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>94.8 (39.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIN-117 0.5 mg</td>
<td>85.2 (40.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIN-117 2.5 mg</td>
<td>102.8 (61.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine 20 mg</td>
<td>102.6 (59.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![Graph showing PSG REM latency change from baseline by treatment arm](image-url)
MIN-117 phase IIa study demonstrated:

- Efficacy on depressive symptoms
- Onset evident as early as 2 weeks
- Efficacy on anxiety symptoms
- Both doses of MIN-117 are well tolerated

- Pharmacodynamics
  - No impairment in cognition
  - No impairment in sexual function
  - Preservation of sleep architecture and continuity
MIN-202 (JNJ-42847922)

Insomnia Disorder and Major Depressive Disorder (MDD)

A co-development & commercialization program
Phase IIa in primary insomnia: Primary endpoint
Sleep efficiency on days 1/2 and 5/6

Sleep Efficiency (%)
LSMean (SE)

Day 1/2
Day 5/6

placebo (n=28)
40mg JNJ-42847922 (n=27)

Δ 5.77 %
p < 0.001

Δ 8.12 %
p < 0.001

Sleep Efficiency  = (Total Sleep Time/480) * 100%
PSG recording = 480 min
MIN-202: observed efficacy on depressive symptoms is independent of effects on sleep

**DAY 11, N=47**

**Mean Change HDRS\textsubscript{17}**

- **Placebo**
- **JNJ-7922**
- **DPH**

**Mean Change Adjusted HDRS\textsubscript{17}**

- **Placebo**
- **JNJ-7922**
- **DPH**

\textit{HDRS\textsubscript{17}} = Hamilton Depression Rating Scale
\textit{Adjusted HDRS\textsubscript{17}} = Hamilton Depression Rating Scale with 3 sleep items removed
MIN-202 studies to date have demonstrated:

- Efficacy in insomnia
  - Primary insomnia
  - MDD patients with comorbid insomnia

- Efficacy in MDD patients on depressive symptoms
Financial Summary

- ~$44.6 M cash balance (cash, cash equivalents and marketable securities) at 3/31/16
- ~$17.5 million received from warrants exercised at $5.772 in Q1 2016
- $1.0 million received from purchase of common stock at $5.51/share by Company Director, David Kupfer, in March 2016
- Current resources estimated to fund operations into Q2 2017
- $15M credit facility with Oxford and SVB entered into January 2015
  - $10M drawn down at 12/31/15
  - 40,790 warrants issued with an exercise price of $5.516 in connection with credit facility
- PIPE completed in March 2015, yielding $31M in gross proceeds
  - 6.3 million shares sold at $4.81/share
  - 6.3 million warrants issued with an exercise price of $5.772 (~3.2 million warrants remain outstanding)
- ~27.9 million shares outstanding at 3/31/2016
- ~3.4M options outstanding 3/31/16
Thank You

Minerva Neurosciences, Inc.
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