UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 8, 2021

Minerva Neurosciences, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-36517**	**26-0784194**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

1601 Trapelo Road **Suite 286** **Waltham, MA**	**02451**
(Address of principal executive offices)	**(Zip Code)**

(Registrant's telephone number, including area code): (617) 600-7373

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**NERV**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On December 8, 2021, Minerva Neurosciences, Inc., or the Company, released a presentation of the Company's product candidate roluperidone at the 60th Annual Meeting of the American College of Neuropsychopharmacology, taking place at the Puerto Rico Convention Center, San Juan, Puerto Rico.

A copy of the above-referenced presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The information furnished pursuant to Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities of that section, and shall not be deemed incorporated by reference into any of the Company's filings under the Securities Act of 1933, as amended or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific reference in such filing. The furnishing of the information in this Current Report on Form 8-K is not intended to, and does not, constitute a determination or admission by the Company that the information in this Current Report on Form 8-K is material or complete, or that investors should consider this information before making an investment decision with respect to any security of the Company.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Presentation of Minerva Neurosciences, Inc. dated December 8, 2021.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

MINERVA NEUROSCIENCES, INC.

By: /s/ Geoffrey Race
Name: Geoffrey Race
Title: President

Date: December 8, 2021

Efficacy and safety of roluperidone for the treatment of negative symptoms of schizophrenia

Authors: Michael Davidson[1,2] MD, Jay Saoud[1] PhD, Corinne Staner[3] MD, Nadine Noel[3] PhD, Sandra Werner[3] PhD, Elisabeth Luthringer[3] RN, Philip Harvey PhD, Gregory Strauss PhD, Mark Weiser[4]MD, Remy Luthringer[1] PhD

Study registration: Eudra-CT: 2017-003333-29; NCT03397134

Affiliations: (1) Minerva Neurosciences; (2) Nicosia University Medical School; (3) PPRS, (4) University of Tel Aviv School of Medicine (6) University of Miami Miller School of Medicine (7) University of Georgia

Minerva Neurosciences is the sponsor of the trials

Abstract

- **Objective:** In a previous large multi-national trial, roluperidone (MIN-101) a compound with antagonistic properties for 5-HT_{2A}, $sigma_2$ and α_{1A}-adrenergic receptors demonstrated statistically significant efficacy in reducing negative symptoms and good tolerability in stable schizophrenia patients. The objective of the current study was to confirm roluperidone's efficacy, safety, and tolerability in similar schizophrenia patients.

- **Methods:** Roluperidone 32 mg/day, roluperidone 64 mg/day, or placebo was administered for 12 weeks to 513 schizophrenia patients with moderate to severe negative symptoms. The primary endpoint was the PANSS-derived Negative Symptoms Factor Score (NSFS) (Marder negative symptoms subscore) and the key secondary endpoint was Personal and Social Performance scale (PSP) total score.

- **Results.** NSFS scores were lower (improved) for roluperidone 64 mg compared to placebo and marginally missing statistical significance for the intent-to-treat (ITT) analysis set ($p \leq 0.064$) but reaching nominal significance ($p \leq 0.044$) for the modified-ITT (mITT)* set. Change in PSP total score was significantly higher (better) on roluperidone 64 mg compared to placebo for ITT and mITT ($p \geq 0.021$ and $p \geq 0.017$, respectively).

- **Conclusions:** Results of this trial confirm roluperidone's potential for the treatment of negative symptoms of schizophrenia leading to better daily functioning.

* Modified ITT excluded 17/513 patients **before the data lock and unblinding** because of behavioural and physiologic implausible data

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Roluperidone

Receptor subtypes	Materials	Ki values, nmol/L
Serotonin 5-HT_{2a}	Rat, cerebral cortex	7.5
	Human recombinant	5.2
$Sigma_2$	Guinea pig, brain	8.2
$Sigma_1$	Guinea pig, brain	253.8
A_1 adrenergic	Rat, brain	14.4

- ✓ **Specific Affinity for 5-HT_{2A}, σ_2, and α_1-adrenergic receptors**
- ✓ **No affinity (>1000 nM) for other receptors, including dopaminergic, muscarinic, cholinergic and histaminergic receptors**
- ✓ **No direct Dopamine binding**
- ✓ **The behavioral pharmacology package is consistent with an antagonistic effect for 5-HT_{2A}, σ_2, and α_1-adrenergic receptors**

Trial design and patient population

- 12 weeks double blind 32 mg/day, 64 mg/day or placebo in 1/1/1 ratio, followed by 9 months open label phase
- DSM-5 schizophrenia
- Baseline score ≥ 20 on the PANSS negative symptoms subscale
- Symptomatically stable for 6 months
- A score <4 on the PANSS
  - P-4 excitement/hyperactivity
  - P-6 suspiciousness/persecution
  - P-7 hostility
  - G-8 uncooperativeness
  - G-14 poor impulse control

Upper threshold based on agitation/hostility rather than psychosis

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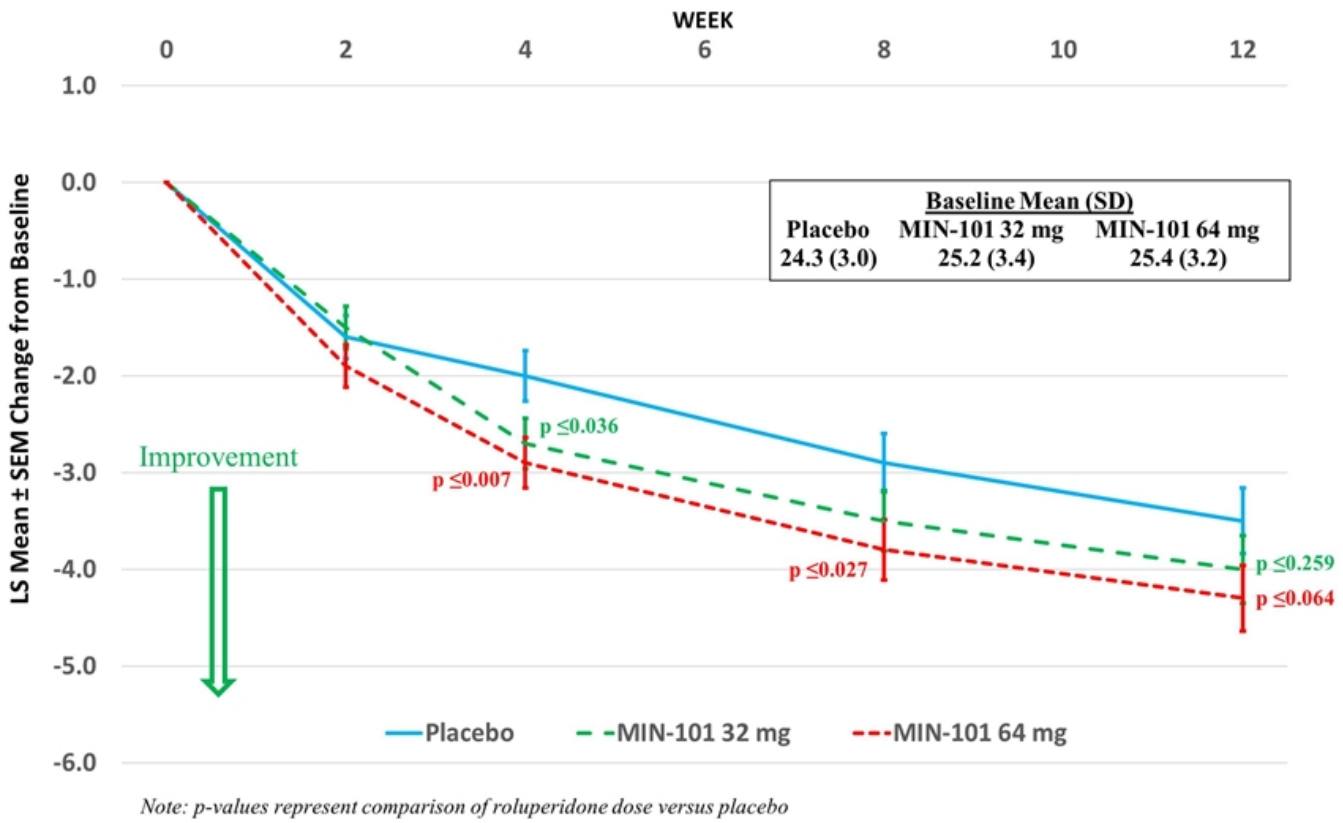
PANSS Negative Symptoms Factor Score (Marder) Change from Baseline (MMRM) (ITT Population)



Note: p-values represent comparison of roluperidone dose versus placebo

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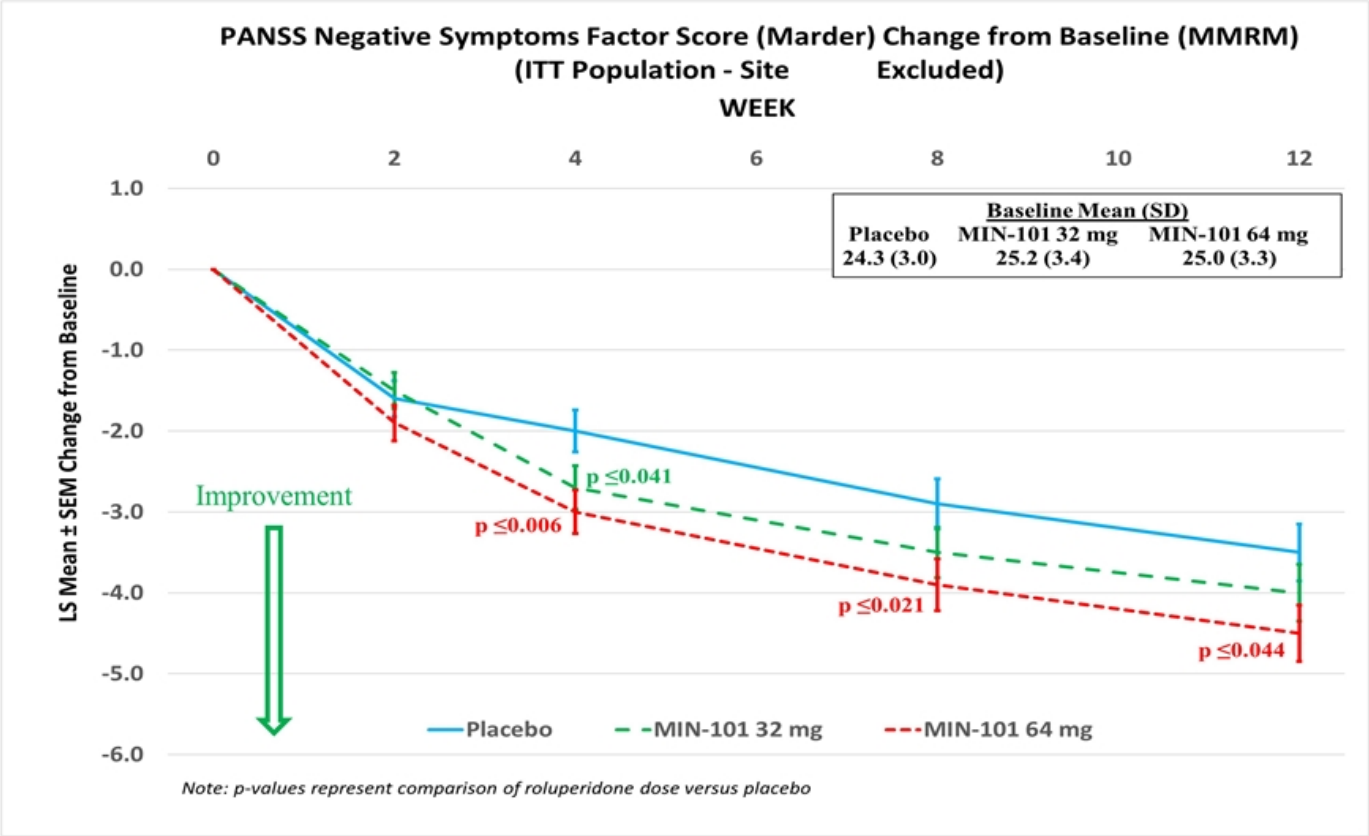
NSFS Score – Double-Blind Primary Endpoint , mITT



Decision to exclude one site because of questionable data quality was taken before the data blinding was removed

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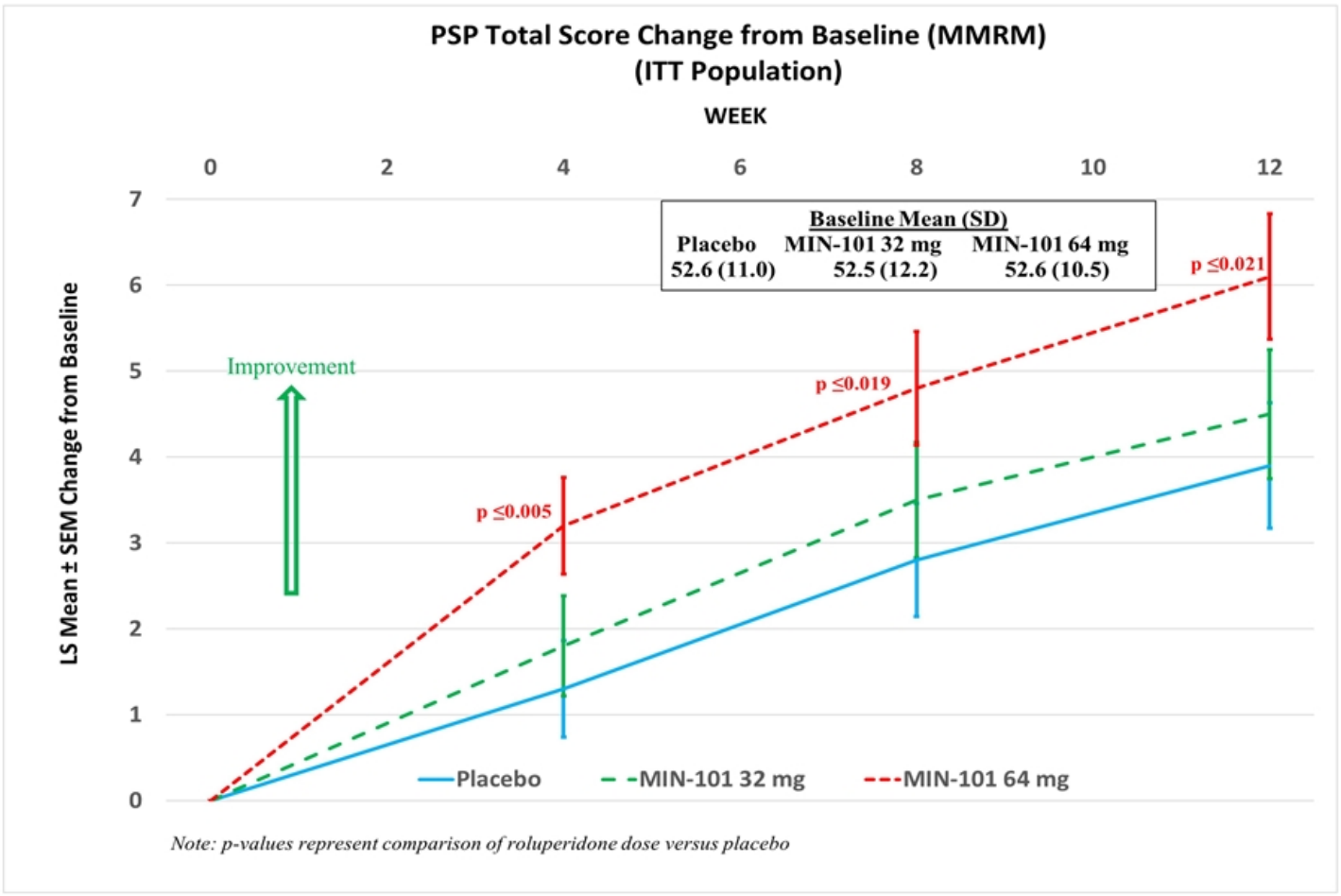
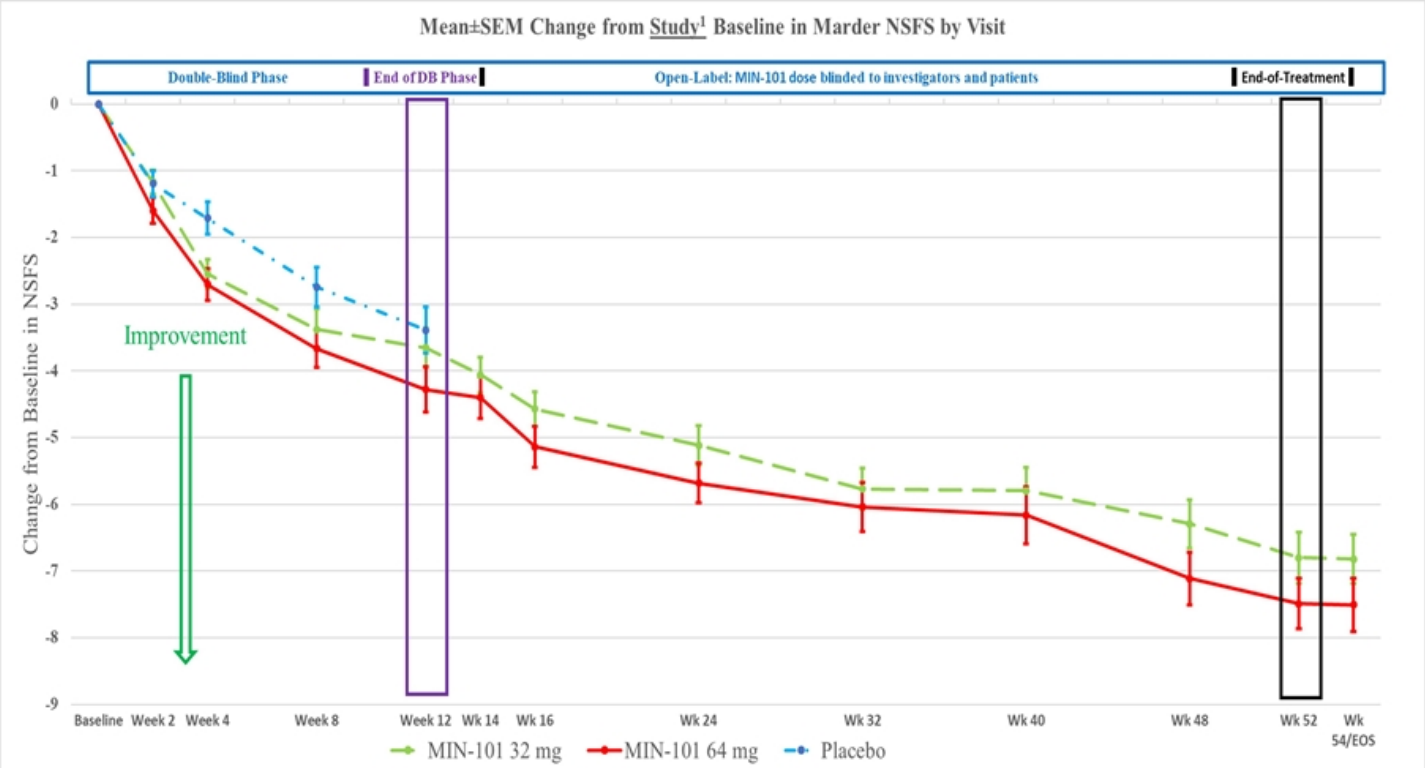

PSP Total Score Change from Baseline (MMRM)
(ITT Population)
WEEK
0
2
4
6
8
10
12
LS Mean ± SEM Change from Baseline
7
6
5
4
3
2
1
0
Baseline Mean (SD)
Placebo
52.6 (11.0)
MIN-101 32 mg
52.5 (12.2)
MIN-101 64 mg
52.6 (10.5)
Improvement
p ≤0.005
p ≤0.019
p ≤0.021
Placebo
MIN-101 32 mg
MIN-101 64 mg
Note: p-values represent comparison of roluperidone dose versus placebo



[1] *Study baseline is defined as the last valid evaluation done before the study drug administration on Day 1*

Change from Baseline				
	Double-Blind (12 Wks)		End-of-Treatment (WK 52)	
Treatment Arm	Mean	SD	Mean	SD
MIN-101 32 mg	-3.7	3.18	-6.3	4.00
MIN-101 64 mg	-4.3	3.80	-7.8	3.56
Placebo to MIN-101 32 mg	-3.4	3.91	-4.5	3.50
Placebo to Min-101 64 mg			-4.9	4.66

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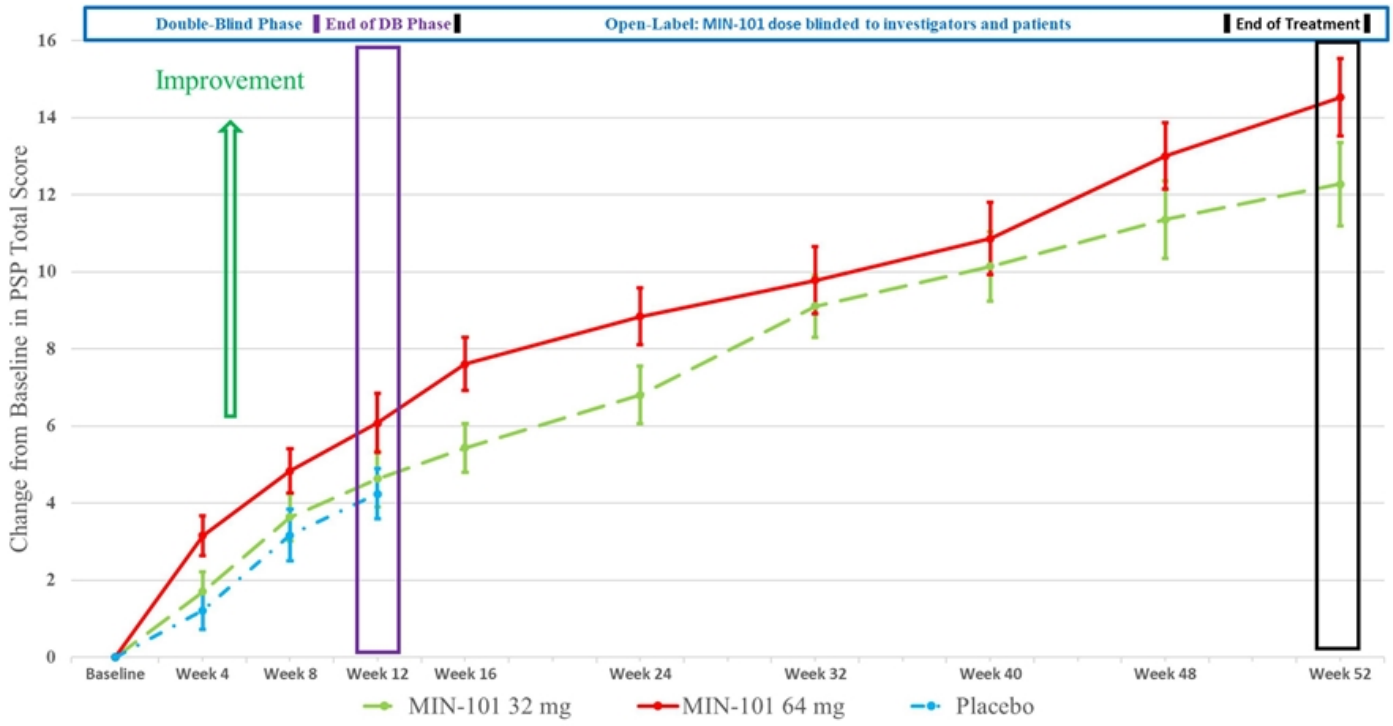
Mean±SEM Change from Study[1] Baseline in PSP Total Score by Visit



[1] Study baseline is defined as the last valid evaluation done before the study drug administration on Day 1

Change from Baseline	Double-Blind (12 Wks)		End-of-Treatment (WK 52)	
Treatment Arm	Mean	SD	Mean	SD
MIN-101 32 mg	4.6	7.88	10.6	10.87
MIN-101 64 mg	6.1	8.37	14.1	9.19
Placebo to MIN-101 32 mg	4.2	7.34	11.7	9.48
Placebo to Min-101 64 mg			11.8	9.61

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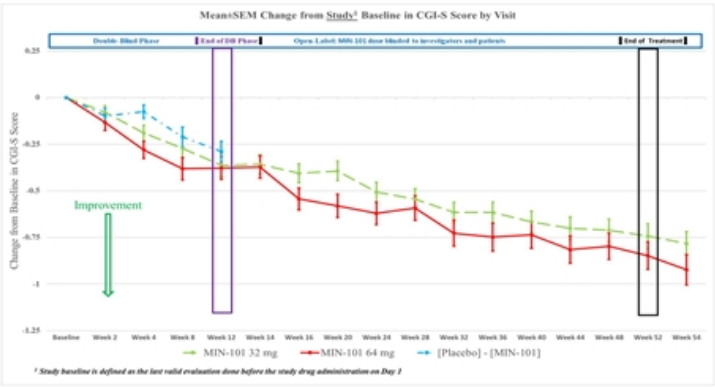
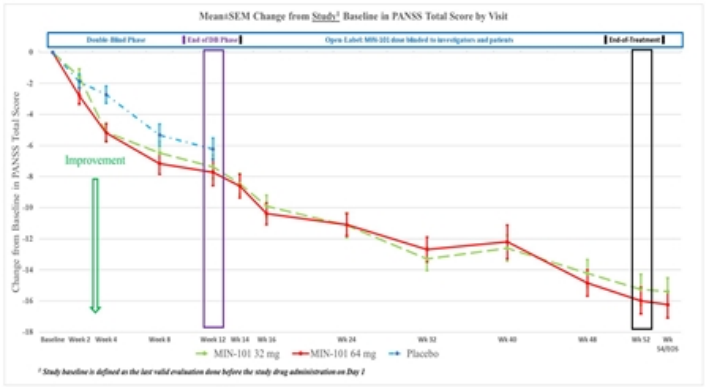
Other key efficacy parameters

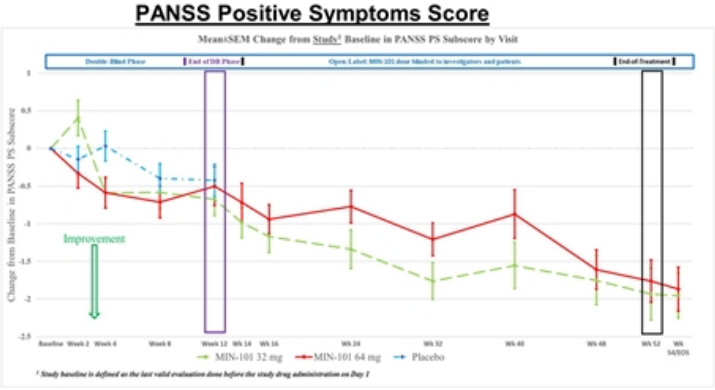
CGI-S



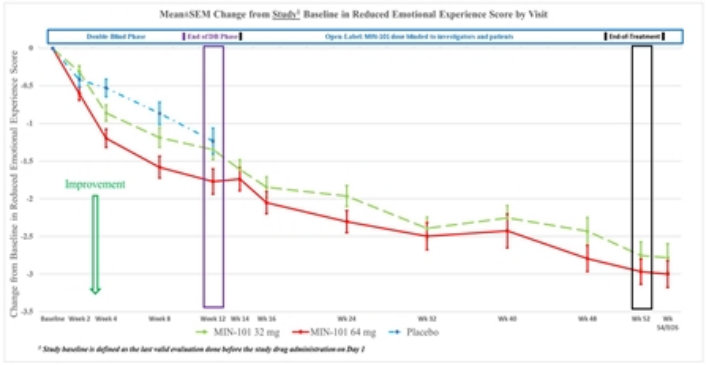
PANSS Total Score



PANSS Positive Symptoms Score



Reduced Emotional Experience Score



The relapse rate during the OLE, defined as patients being withdrawn from the trial due to worsening of symptoms of psychosis, was 15 patients out of 166 patients (9%) in the 32 mg arm and 10 patients out of 167 patients (6%) in the 64 mg arm. Over the one-year duration the relapse rate was 11.7% overall.

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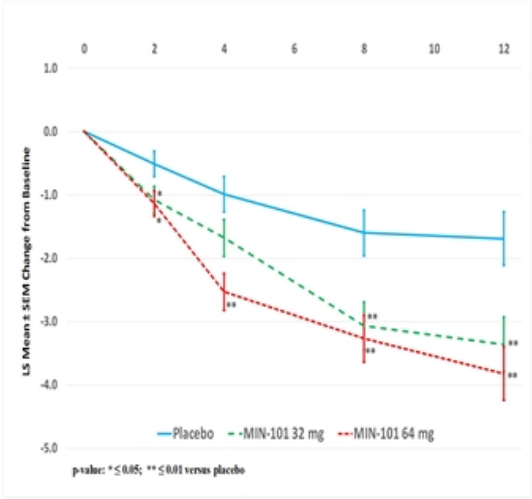
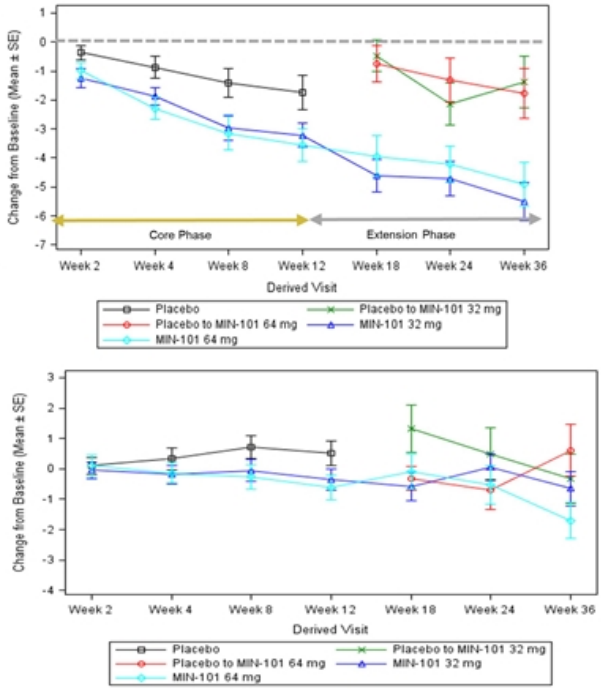
Phase 2b study showed improvements in NS over 12 weeks and 36 weeks in both doses and stable positive symptoms

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



12-Week DB & 24-week extension phase



Source: Davidson et al., 2017

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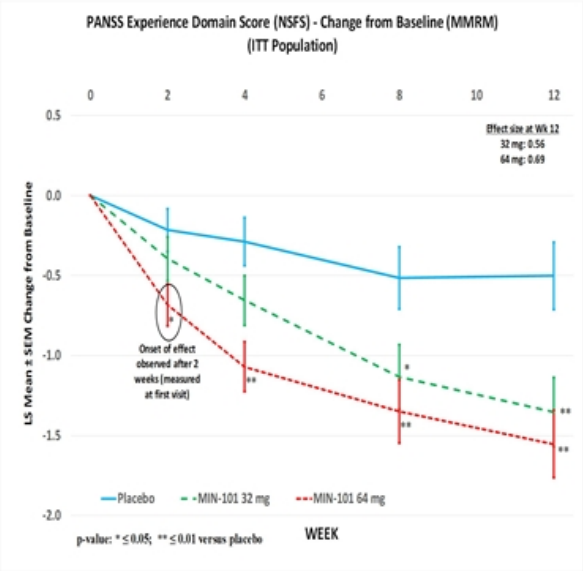
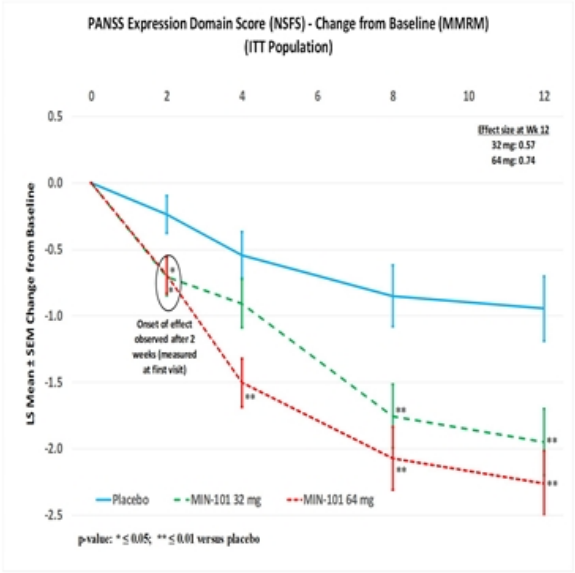
Roluperidone showing improvement in both "Experience" & "Expression" of Negative Symptoms





These results are consistent with improvements observed in other scales such as PSP (Personal & Social Performance Scale)

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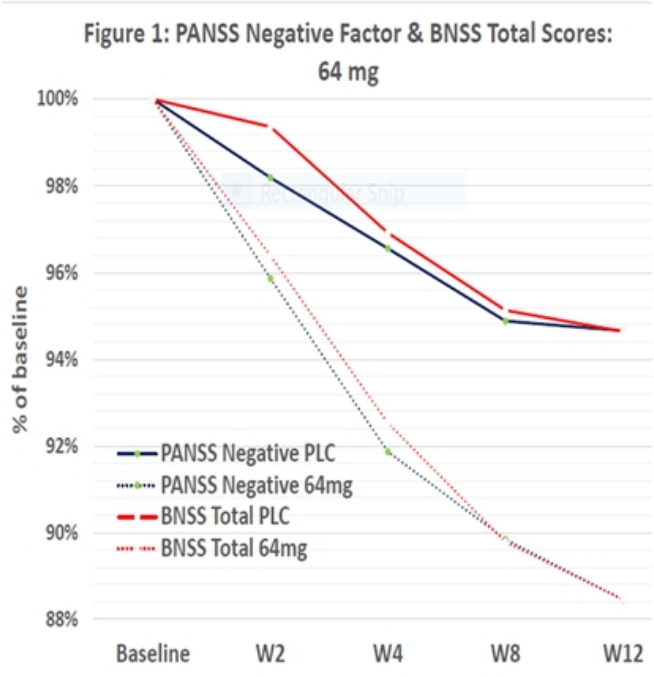
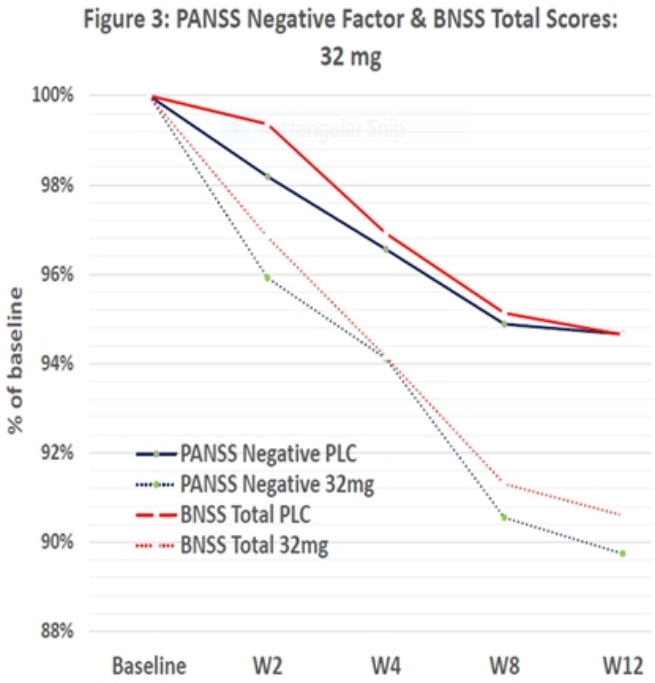
How much does the assessment instrument matter?





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Discussion

- Roluperidone **administered as monotherapy** may improve negative symptoms and social functioning in patients suffering from schizophrenia and moderate to severe negative symptoms.

- Monotherapy, rather than add-on to antipsychotics, design was selected for two trials because:
  - antipsychotics may produce secondary negative symptoms such as rigidity, akathisia and sedation hence confounding the effects of the experimental compound
  - antipsychotics by blocking DA receptors and interfering with brain reward circuits, might enhance negative symptoms

- It is possible that a subgroup of patients with stable positive symptoms, low level of symptoms related to agitation and moderate to severe negative symptoms can maintain symptomatic stability in absence of maintenance treatment with antipsychotic drugs