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From Unmet Need to Reality

Roluperidone is Potentially the First Treatment for Negative Symptoms of Schizophrenia

KOL Event | February 3, 2026

Forward-Looking Statement

This presentation contains forward-looking statements 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. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this presentation include, but are not limited to, statements with respect to Minerva's expectations regarding the potential of roluperidone to treat negative symptoms of schizophrenia and address unmet clinical and market needs; the design, timing conduct and anticipated results of the confirmatory Phase 3 trial of roluperidone; potential regulatory outcomes regulatory outcomes related to the Phase 3 trial and the development of roluperidone more broadly; and the anticipated financial resources to fund the planned Phase 3 trial and support Minerva's corporate objectives. 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, trials and studies may be delayed and may not have satisfactory outcomes, and earlier trials and studies may not be predictive of later trials and studies; the design and rate of enrollment for clinical trials, including the current design of the Phase 3 confirmatory trial evaluating roluperidone may not enable successful completion of the trial(s); the commercial opportunity for roluperidone in negative symptoms of schizophrenia may be smaller than anticipated; Minerva may be unable to obtain and maintain regulatory approvals; Minerva may experience uncertainties inherent in the initiation and completion of clinical trials and clinical development; the need to align with collaborators or partners may hamper or delay development and regulatory efforts or increase costs; uncertainties of patent protection and litigation; and general economic conditions. Other factors that may cause our actual results to differ from those expressed or implied in the forward-looking statements in this presentation are identified under the caption "Risk Factors" in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2024, filed with the Securities and Exchange Commission on February 25, 2025, as updated by our Quarterly Report on Form 10-Q for the period ended September 30, 2025. Copies of reports filed with the SEC are posted on our website at www.minervaneurosciences.com. The forward-looking statements in this presentation are based on information available to us as of the date hereof, and we expressly disclaim any obligation to update any forward-looking statements, except as required by law.

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Welcome to Today's Presentation: Introductions

Professor Gregory Strauss, PhD	
	Franklin Professor of Psychology
	Department of Psychology
	University of Georgia
Professor Brian Kirkpatrick, MD, MSPH	
	Peters Professor of Psychiatry
	University of Arkansas for Medical Sciences (UAMS)
	Department of Psychiatry
	Co-chaired the National Institute of Mental Health (NIMH)-sponsored
	Consensus Development Conference on Negative Symptoms
Remy Luthringer, PhD	
	Executive Chairman
	Chief Executive Officer
	Minerva Neurosciences, Inc.

Agenda

01 Defining Negative Symptoms of Schizophrenia and how they Impact Patients and their Families
Professor Gregory Strauss

02 The Challenge of Assessing Negative Symptoms of Schizophrenia in Clinical Trials
Professor Brian Kirkpatrick

03 Roluperidone: Proposed Phase 3 Confirmatory Trial Design and Execution
Dr. Remy Luthringer, CEO Minerva

04 Q&A

February 2026: The Minerva Confluence

FDA guidance on Phase 3 trial design following Public Meeting

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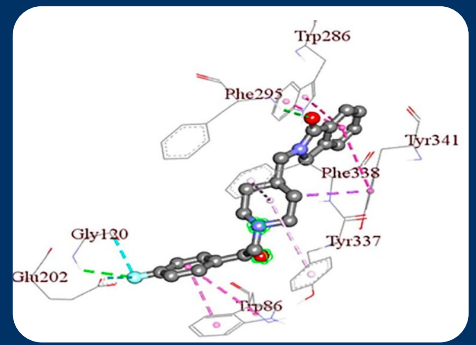
$200m raised
Top Tier Investors

General alignment on FDA guidance, broad awareness in the psychiatry community, promising MOA and financial factors all combine to enable the confirmatory Phase 3 trial and a potential paradigm shift in the treatment of negative symptoms of schizophrenia



Roluperidone

Broad understanding of unmet medical need

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General Alignment with FDA on Phase 3 Trial Design

General alignment reached on proposed design of a confirmatory Phase 3 study following extensive collaborative discussions with FDA throughout 2023-2024 and the findings of an FDA Public Meeting in August 2024:

Evaluating the Negative Symptoms of Schizophrenia in Clinical Trials[1]

Excerpts from FDA Meeting Minutes

- ***FDA acknowledges Minerva's position*** *that a population of people with schizophrenia can be identified* ***with high negative symptoms and a low risk of relapses*** *who can safely be withdrawn from antipsychotic treatment.*
- *The Division is willing to discuss an additional study that provides robust, controlled data about the efficacy and safety of long-term* ***monotherapy*** *with roluperidone in* ***subjects with negative symptoms of schizophrenia****.*
- *The Division agreed that it would consider a resubmission that included a double-blind, placebo- or active-controlled trial of roluperidone with a duration of at least 52 weeks.*
- *The Division does not object to a 12-week primary efficacy endpoint for negative symptom.*
- *To support a* ***monotherapy indication,*** *a comparison of relapse rates between patients on roluperidone monotherapy and similar patients maintained on antipsychotics would be important for regulatory decision making.*
- ***Would represent a new treatment paradigm.***

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[1] *FDA Meeting August 16, 2024*

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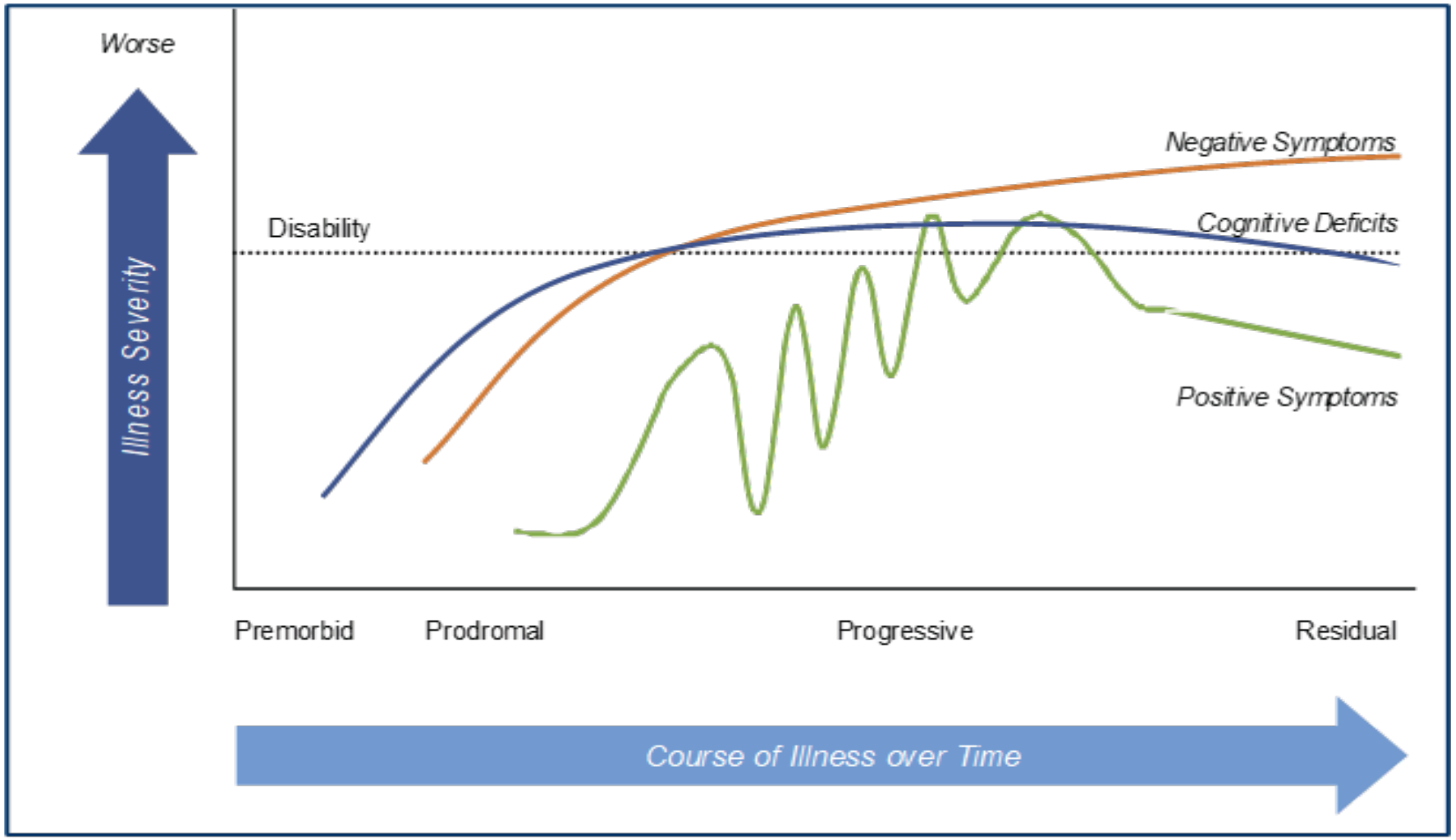
Defining Negative Symptoms of Schizophrenia and How They Impact Patients and Their Families

Dr. Gregory Strauss

Positive Symptoms Often Ameliorate with Antipsychotic Treatment But Negative Symptoms Can Persist for Life and Drive Functional Impairment and Long-term Disability[1]

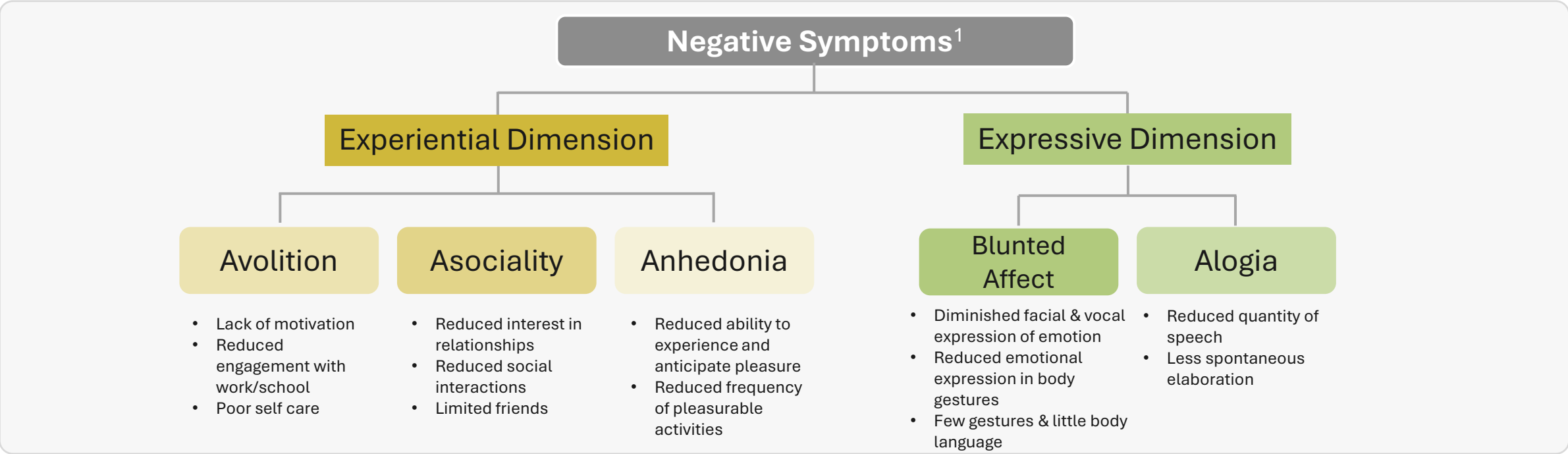


Source: Correll and Schooler, 2020

1 Fervaha G, et.al. *Impact of primary negative symptoms on functional outcomes in schizophrenia. Eur Psychiatry. 2014 Sep;29(7):449-55*

Negative Symptoms of Schizophrenia are Underdiagnosed and Undertreated

- KOL consensus that negative symptoms:
  - May have profound impact on patients' quality of life (QOL)
  - Often present significant challenges for treatment
  - Antipsychotic treatment might worsen negative symptoms in some of the patients
- Clinical practice and drug development have largely focused on treating the positive symptoms
- No FDA approved therapies in the US for negative symptoms of schizophrenia



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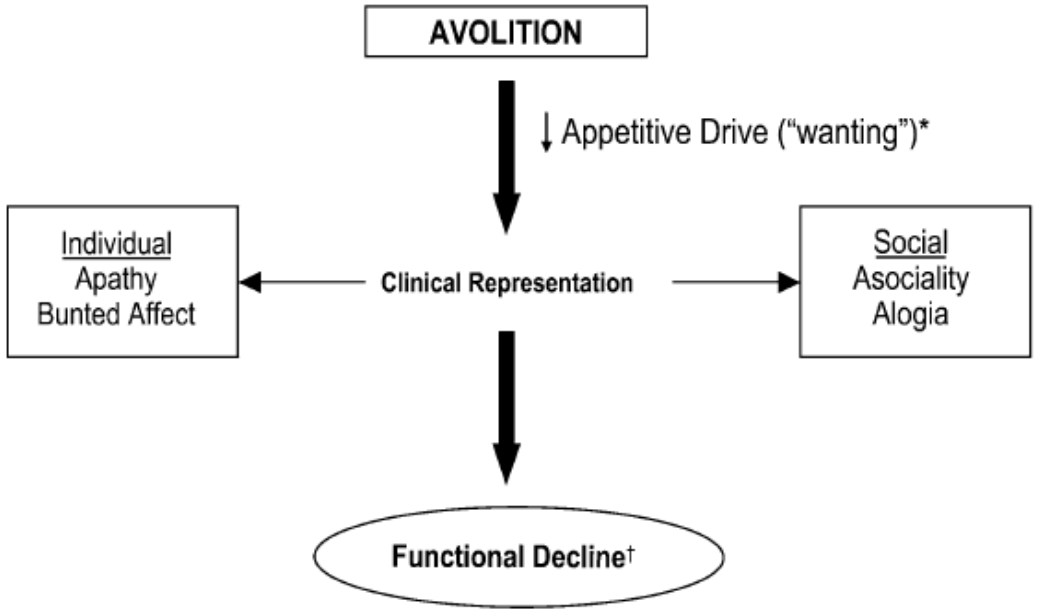
1 Kirkpatrick B, Fenton WS, Carpenter Jr WT, Marder SR. The NIMH-MATRICS consensus statement on negative symptoms. Schizophrenia bulletin. 2006 Apr 1;32(2):214-9.

All Domains are Not Created Equal: Avolition Acts as a Central Hub

- Avolition (lack of motivation) acts as a central hub in schizophrenia's negative symptoms
  - Significantly impacts other domains of anhedonia (pleasure loss), asociality (social withdrawal), blunted affect (reduced emotional expression), and alogia (poverty of speech)
- Disrupts goal-directed behavior and reward processing
- Targeting avolition improves the entire constellation of symptoms & functional outcomes

Avolition is a determinant of poor functional outcome

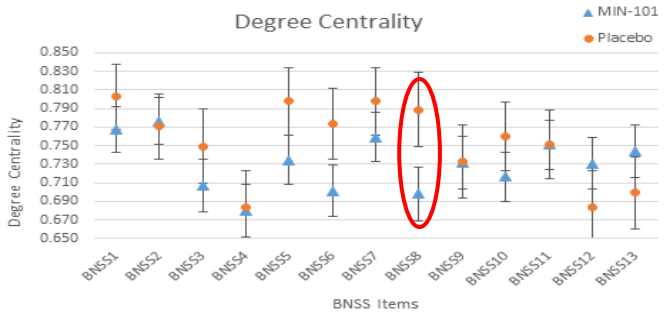


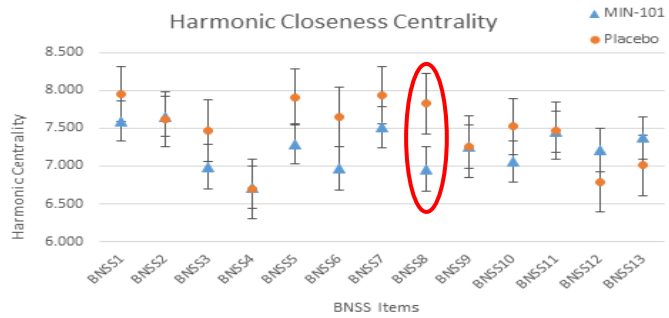
Foussias & Remington, Schizophr Bulletin 2010

Roluperidone Shows Pronounced Improvement in Avolition

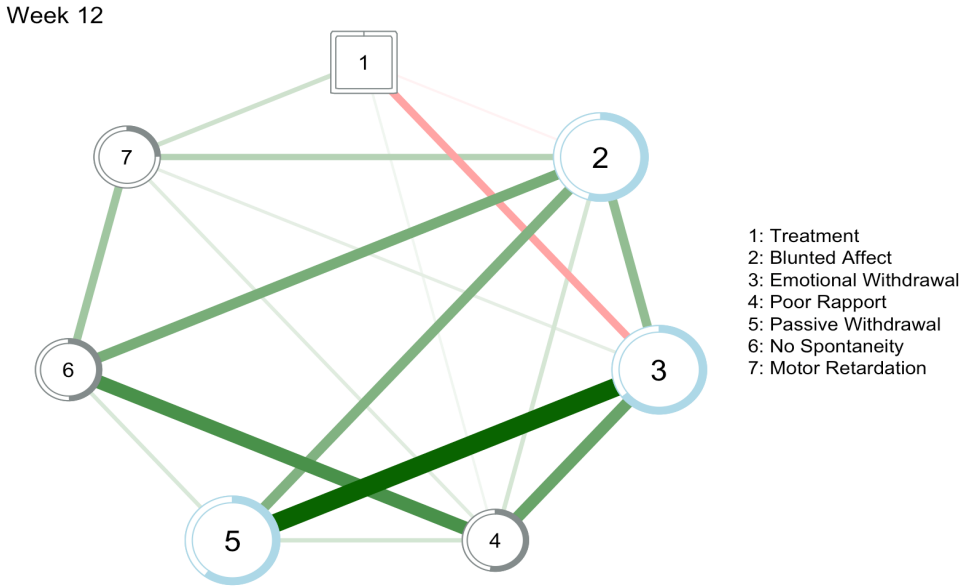
- Roluperidone targets key cortico-striatal circuits related to motivational deficits
- Cascading improvement on other domains once motivation (avolition) improves

Roluperidone Phase 2b: Avolition is most central for improvement
(Strauss et al., 2020b)





Roluperidone Phase 3 Replicated: Avolition is most central for improvement
(James et al., 2024)



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Clinical Relevance: Improvement of Negative Symptoms with Roluperidone in Phase 2b Correlates to What Patients and Caregivers Deem Most Important

- **Self-perceptions study to determine clinical relevance**[1]
  - Patients and caregivers rated the magnitude of change in BNSS they believed was necessary for life to be meaningfully improved
- **Comparison to roluperidone Phase 2b data**[2]
  - Right two columns reflect the BNSS score that clinicians rated patients' improvement - equated to a 1 or 2-point improvement on CGI
  - Tight correlation of actual roluperidone results[5,6] to self perception study "clinically relevant"[3,4]
  - Compelling evidence that roluperidone improves negative symptoms to a level that is meaningful to patients, caregivers and physicians

	Self-Perceptions Study[1]		Roluperidone Phase 2b Data	
BNSS Domain	Clin Rate – Self Ideal[3]	Clin Rate – Rel/Car Ideal[4]	ROL CGI-1[5]	ROL CGI-2[6]
MAP	-0.65	-0.17	-0.72	-1.40
Anhedonia	-0.38	-0.07	-0.67	-1.61
Asociality	-0.53	-0.06	-0.71	-0.83
Avolition	-1.10	-0.48	-0.69	-1.75
EXP	-0.23	-0.33	-0.59	-1.68
Blunted Affect	-0.87	-0.79	-0.59	-1.44
Alogia	+0.46	+0.15	-0.60	-1.92

MAP: motivation-pleasure; EXP: emotional expressivity

1,2. GP Strauss; New Initiatives for Assessing Negative Symptoms: BNSS and Digital Phenotyping; presented at FDA public meeting 2024
3. Patient assessment of clinically meaningful; 4. clinician assessment of clinical meaningful; 5. 1-point improvement in CGI; 6. 2-point improvement in CGI

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The Challenge of Assessing Negative Symptoms of Schizophrenia in Clinical Trials

Dr. Brian Kirkpatrick

Why do Negative Symptom Trials Fail? Three Hurdles

Placebo response (the noise)

- Increased clinical attention by the research staff creates an expectation after previous positive trials & other supportive care (“nursing effect”) during the trial increase the placebo response rate
- A widespread problem in all psychiatric trials – not just in schizophrenia studies

Add-on to antipsychotics (the graveyard):

- Antipsychotics interfere with dopaminergic neurotransmission, which in turn inhibits the brain’s reward system
- Blocking dopamine receptors counteracts the effect of a therapy intended to improve negative symptoms
- Hence trials as add-on therapy to antipsychotics are extremely challenging to show improvement in negative symptoms

Pseudo-specificity (the false signal):

- Improvement of a psychotic delusion by treatment with an antipsychotic changes the external perception of the patient, creating a misleading change in negative symptom ratings
- However, this is not a true improvement in the primary illness-related negative symptoms

Critical to Distinguish Between Primary and Secondary Negative Symptoms and Then Treat the Primary Negative Symptoms

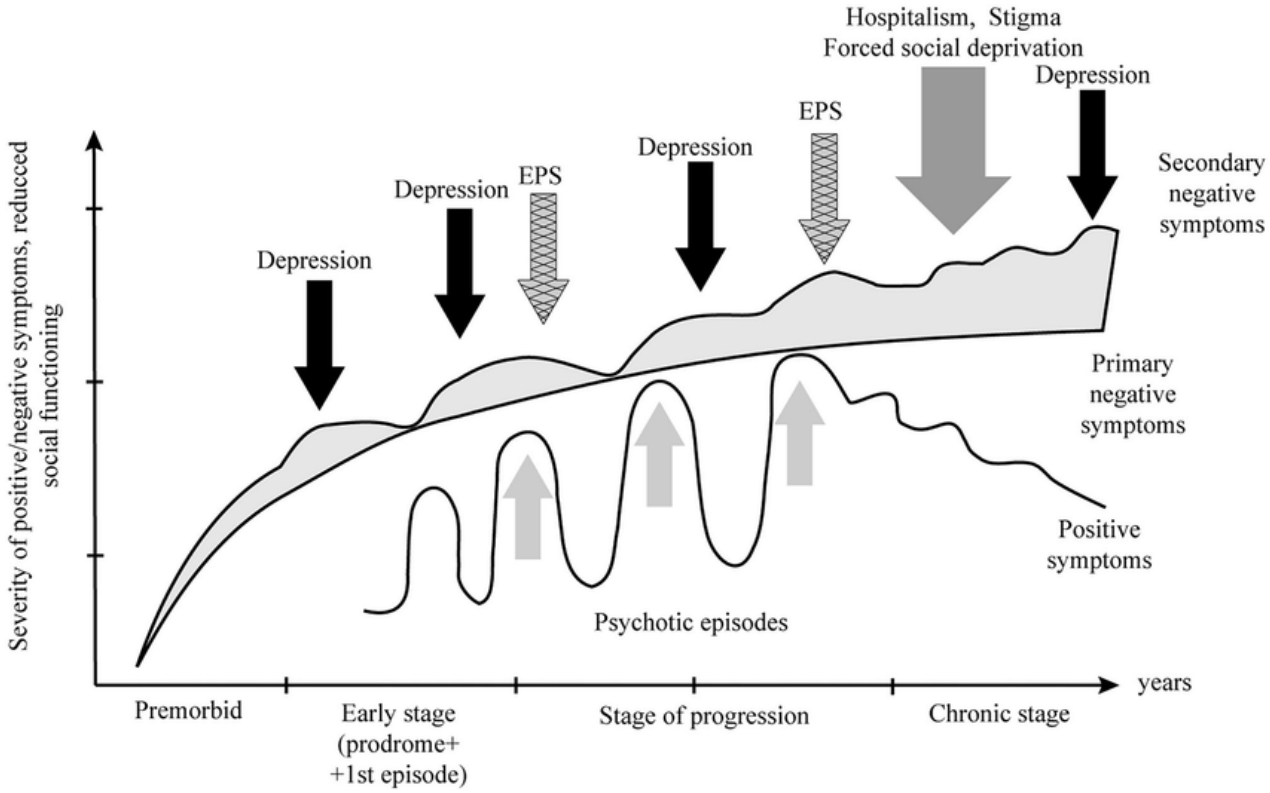
Primary vs secondary distinction

(Kirkpatrick et al., 2001)

Primary negative symptoms are a key factor in schizophrenia, often present prodromally, and may persist or even worsen throughout the patient's lifetime

Secondary negative symptoms result from intrinsic and environmental factors affecting patients with schizophrenia:

- Positive symptoms (e.g. social withdrawal due to paranoia and delusions)
- Depression
- Side effects of antipsychotic treatment
- Substance abuse
- Social deprivation due to hospitalization or breakdown of family and social relationships



Mosolov et al., 2022

Prior Trials not Designed nor Sufficient for Negative Symptom Indication

FDA recently commented on Cobenfy marketing which claimed to show an "*improvement across a range of symptoms*" including negative symptoms

FDA: *"The pivotal trials supporting the schizophrenia indication for Cobenfy were not designed to capture changes in positive or negative symptoms as distinct groups…Additionally, the pivotal trials for Cobenfy were not designed to evaluate the efficacy of the drug in negative symptoms because the patients in the studies were experiencing acute exacerbations of schizophrenia, which can confound the assessment of improvement of negative symptoms."*[1]

How to Best Evaluate Negative Symptoms of Schizophrenia in Clinical Trials?[2]

- Therapies in trials in patients with acute positive symptoms cannot demonstrate an effect on primary negative symptoms
- **Trial design as add-on to antipsychotics (blocking dopamine receptors) is not the solution because:**
  - Signal obscured by 'noise' associated with antipsychotic-induced sedation, avolition, movement disorder
  - Blocking dopamine receptors in limbic structures involved in emotions and NS may be counterproductive
  - Not possible to discriminate between improvement of primary and/or secondary negative symptoms
- **Advantage of monotherapy trial design**
  - Ideal to isolate the drug effect on primary negative symptoms
  - Include patients with stable positive schizophrenia symptoms and stable anxiety/depression symptoms

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1. FDA letter, December 15, 2025; 2. Schizophrenia Bulletin Open, Volume 1, Issue 1, January 2020

Importance of Function – Assessed by Personal and Social Performance Scale (PSP)

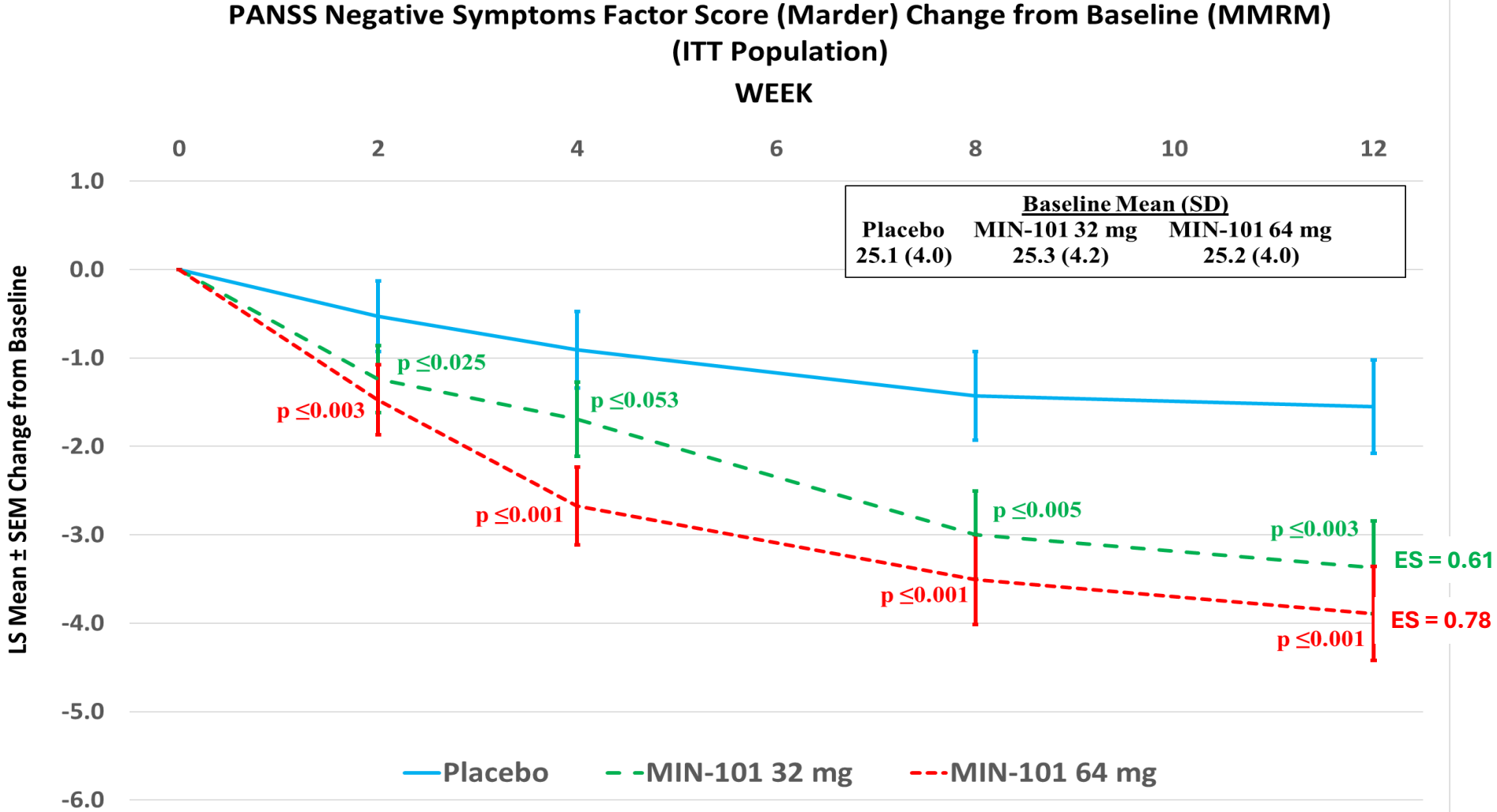
Improving function

- Regulators, payers and patients care about function and quality of life (QOL)
- Improvement in functioning is a “lagging indicator”
  - Patients have often lived for years with negative symptoms, leading to diminished social networks, poor social skills, decreased opportunities, poor confidence

Personal and Social Performance Scale (PSP)

- A clinician-rated scale widely accepted as a measure of function in schizophrenia.
- Four subscales:
  - Socially useful activities (including work and study).
  - Personal and social relationships.
  - Self-care.
  - Disturbing and aggressive behaviors.

Phase 2b: Study Hit Primary Endpoint At Week 12
Roluperidone Separated from Placebo Throughout The Trial



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

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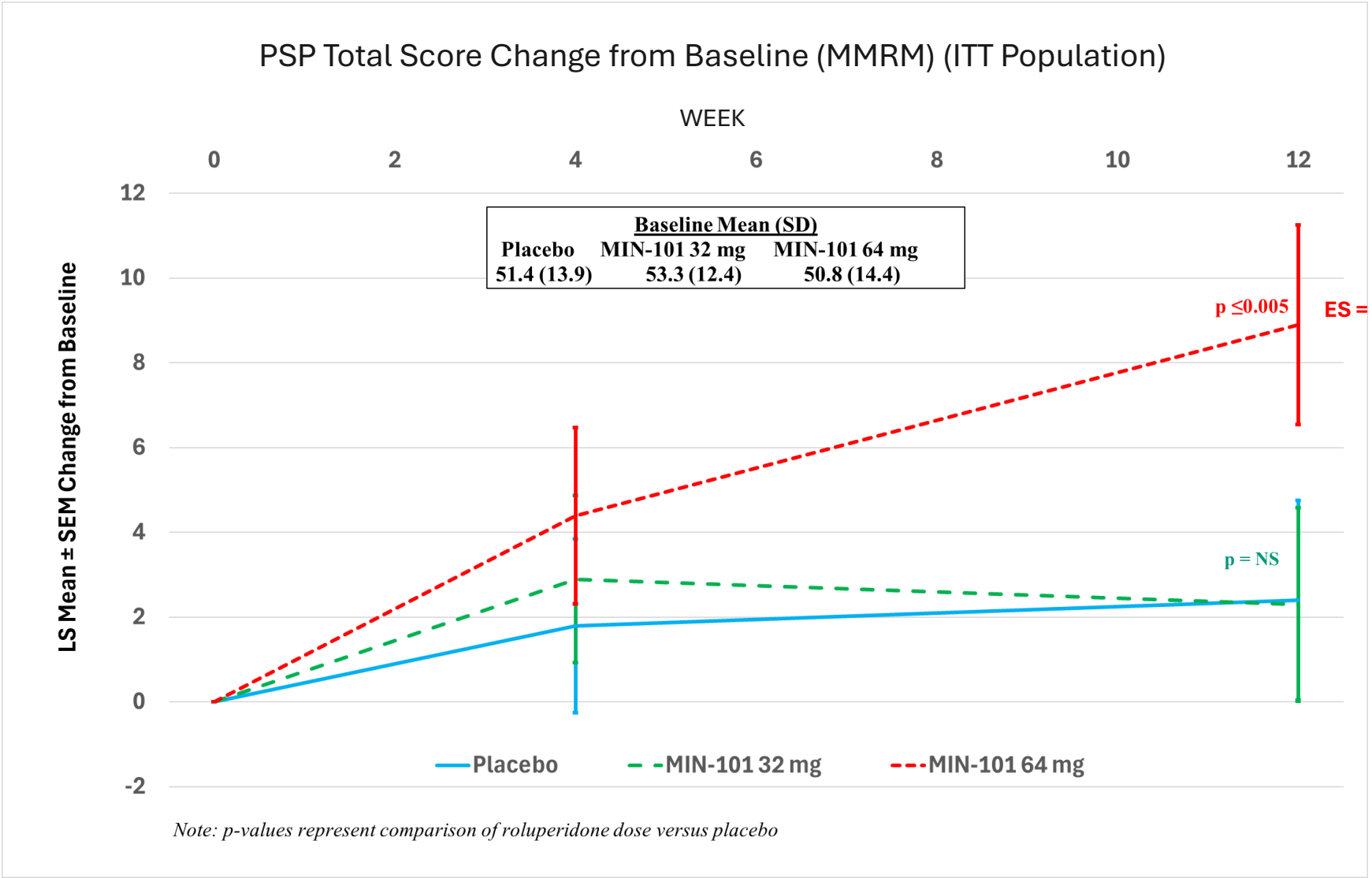
Phase 2b: Significant Improvement in PSP Total Score (Function) at 64 mg Dose



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

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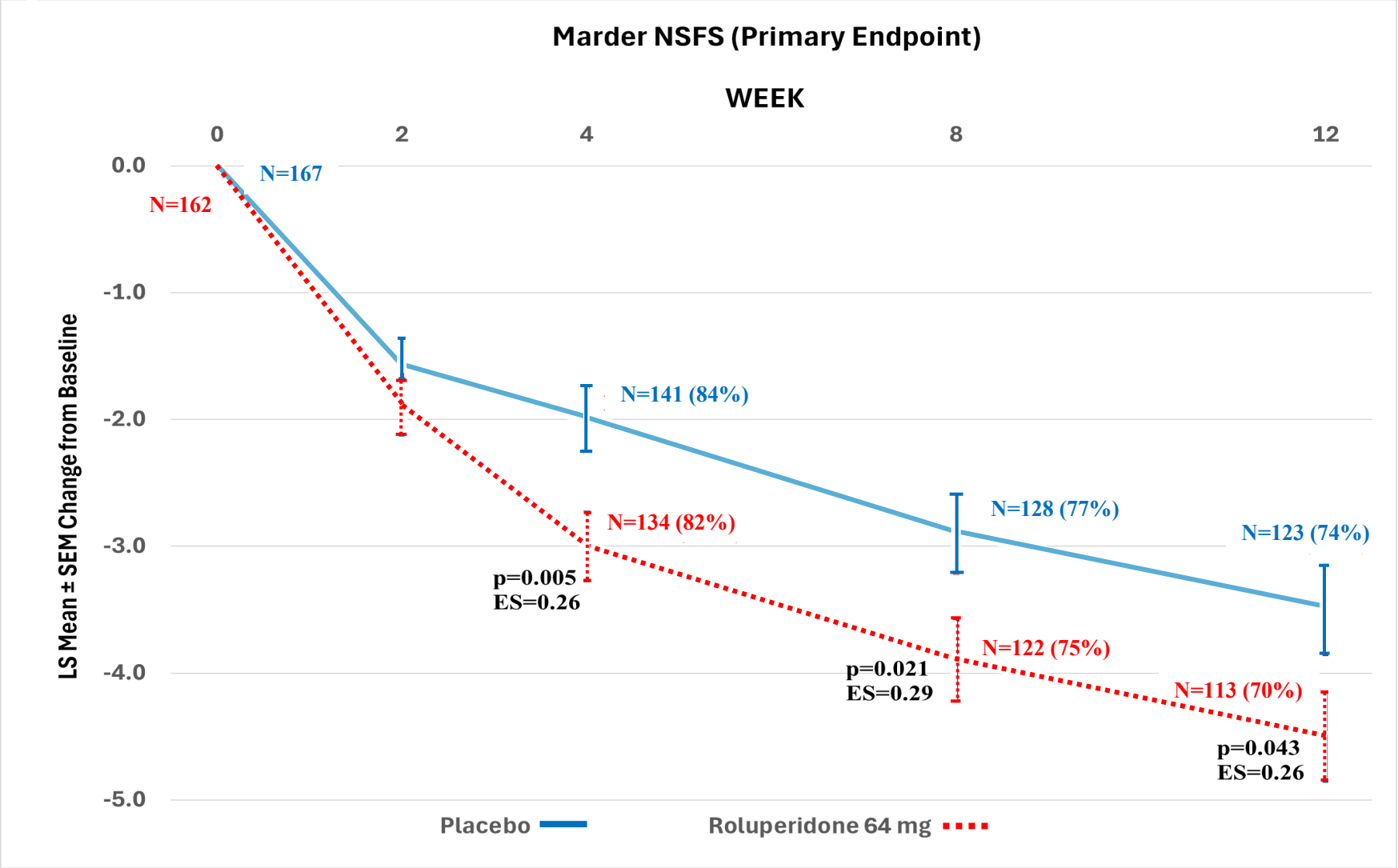
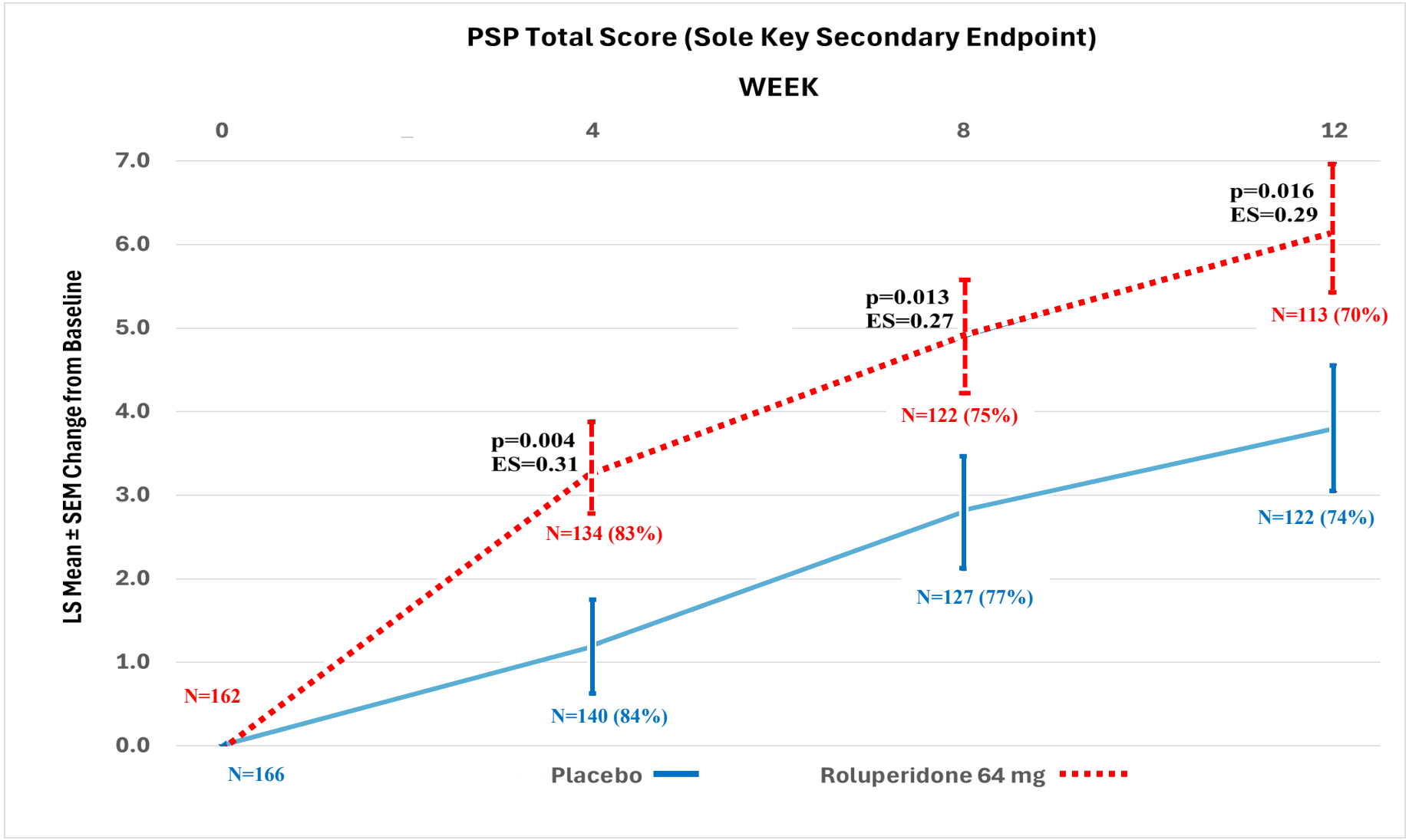
Phase 3: 64 mg Dose Meets Primary Endpoint NSFS (Negative Symptoms)*



*mITT population (excludes 1 site for reasons of implausible data)

Phase 3: Significant Improvement in PSP Total Score (Function) at 64 mg Dose*

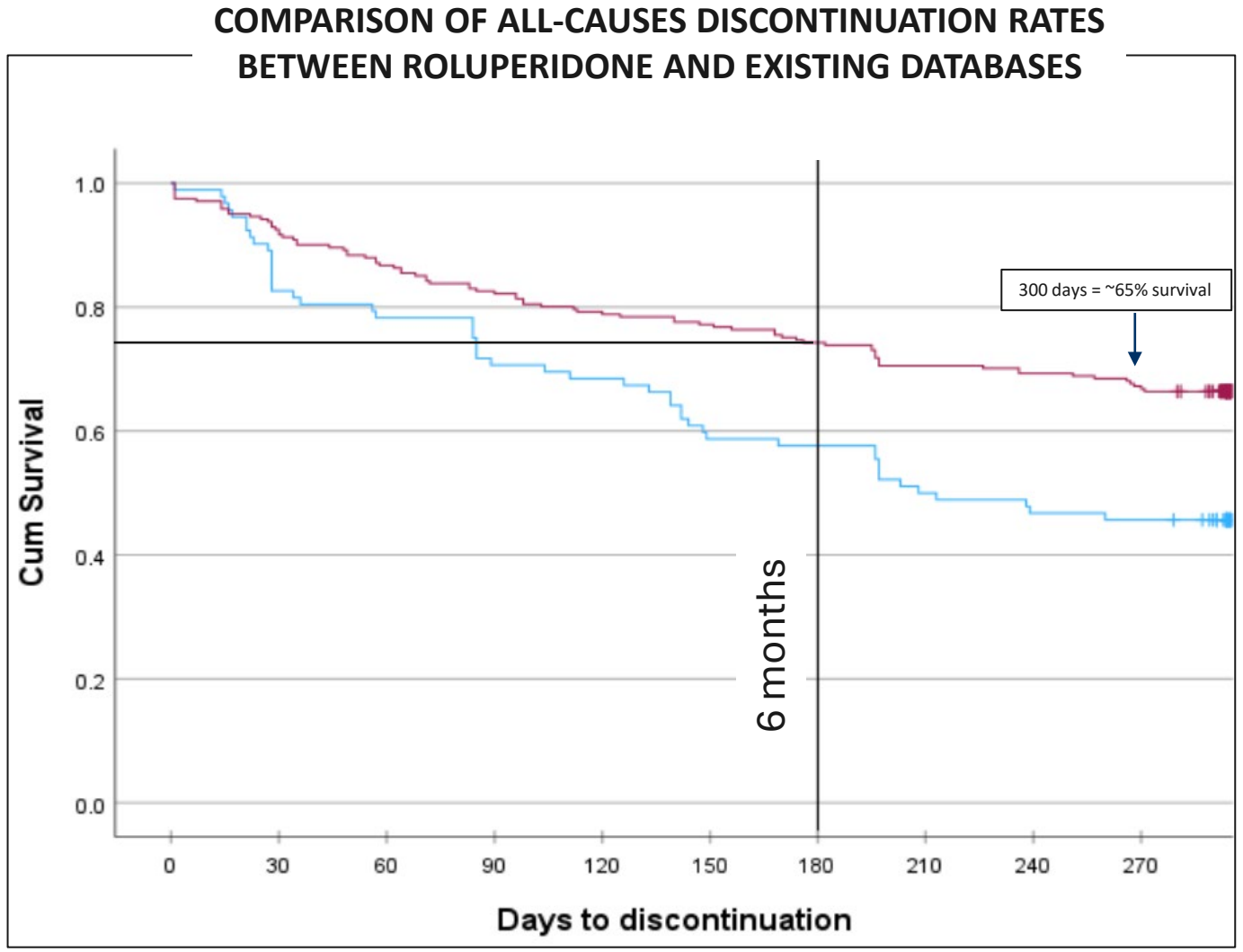


*mITT population (excludes 1 site for reasons of implausible data)

Discontinuation Rates in Combined Roluperidone Studies Outperforms Case-Matched Historical Database Controls

Red line:
Roluperidone

Blue line:
CATIE[1] & EULAST[2] patients that met Minerva inclusion criteria



1. Lieberman JA, Stroup TS, McEvoy JP, et al: Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. NEJM 353:1209–1223, 2005
2. Winter-van Rossum, I., Weiser, M., Galderisi, S., et al. (2023). "Efficacy of oral versus long-acting antipsychotic treatment in patients with early-phase schizophrenia in Europe and Israel: a large-scale, open-label, randomised trial (EULAST)." The Lancet Psychiatry, 10(3), 197–208

Conclusions from Phase 2b and Phase 3* Trials

- Roluperidone demonstrated clear statistical significance on multiple efficacy endpoints
  - ✓ Improves primary negative symptoms
  - ✓ Improves functioning
  - ✓ Improves avolition
  - ✓ No increase in positive symptoms or anxiety/depression
  - ✓ Monotherapy was associated with a low relapse rate
- No evidence of the well-known disabling side-effects regularly observed with atypical antipsychotic treatment
  - ✓ Metabolic syndrome
  - ✓ Sedation
  - ✓ Motor symptoms (extra pyramidal symptoms; EPS)
  - ✓ Prolactin elevation
  - ✓ Nausea (for muscarinic antipsychotics)
- Novel pharmacological profile that drives differentiated clinical benefit in all Minerva's previous clinical trials

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**mITT population (excludes 1 site for reasons of implausible data)*

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Roluperidone Proposed Phase 3 Confirmatory Trial Design and Execution

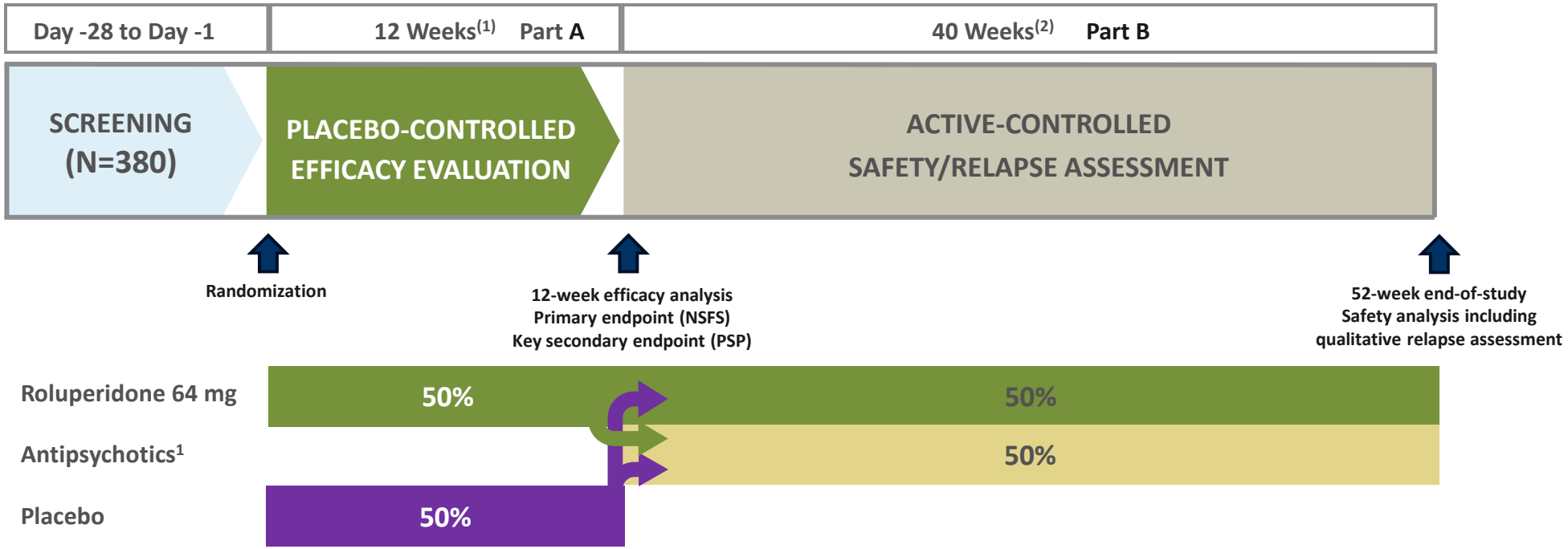
Dr. Remy Luthringer

Proposed Phase 3 Confirmatory Trial Design

Screening (28 days) – to ensure patients meet eligibility criteria for stable symptoms prior to randomization

Efficacy Assessment (12 weeks):
Two parallel treatment arms randomized (1:1) to roluperidone or placebo using a double-blind study design

Safety/Relapse Assessment (40 weeks following first 12 weeks):
Two parallel treatment arms re-randomized (1:1) to roluperidone or one of three antipsychotics using a double-dummy study design



[1] Patients re-randomized to either one of three atypical antipsychotics or roluperidone

Subject to ongoing feedback from the FDA

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Proposed Phase 3 Trial Design – Efficacy Endpoints for Part A

Part A – 64 mg roluperidone vs. placebo for 12 weeks

- N=380 randomized – following 28-day screening to ensure only patients with stable symptoms are enrolled
- Primary endpoint: change from baseline in **NSFS** (Marder Negative Symptoms Factor Score)
  - Avolition drives negative symptoms and all prior studies show roluperidone has strong effect on avolition[1]
- Sole key secondary endpoint:
  - Change from baseline in **PSP** (Personal and Social Performance) total score – functional assessment
  - Avolition also closely correlated to function and daily performance
- Statistical analysis: Mixed-effect Model Repeated Measurement (MMRM)

1. Strauss GP, Bartolomeo LA, Harvey PD. Avolition as the core negative symptom in schizophrenia: relevance to pharmacological treatment development. NPJ Schizophr. 2021 Feb 26;7(1):16. doi: 10.1038/s41537-021-00145-4. PMID: 33637748; PMCID: PMC7910596.

Proposed Phase 3 Trial Design – Part B Safety/Relapse Assessment

Part B: safety/relapse assessment to evaluate relapse rate in patients on roluperidone vs. SOC

- Following 12-week efficacy endpoint, patients re-randomized to roluperidone or antipsychotics
- 40-week treatment (52 weeks total)
- Addresses FDA request to evaluate longer-term data on relapse rates in this population
- Qualitative analyses of relapse rates as part of longer-term safety assessment

Proposed Confirmatory Phase 3 Trial – Execution is Highest Priority

380 patients recruited from ~40 sites

- US (target 25-30%) and 4 European countries
- Rigorous inclusion/exclusion criteria to ensure correct patients
- Reduces potential for variability to optimize statistical integrity

Site selection based on quality performance metrics

- Only working with the best sites with ability to recruit patients that meet inclusion criteria
- Performance in Minerva's previous negative symptoms trials and in other similar trials
- Qualified training in PANSS rating, staff stability and access to high volume of appropriate patients

Minimize potential placebo effect/maintain roluperidone improvement observed in two previous trials

- Fewer assessment visits reduces the well-known "nursing effect" from enhanced clinical attention
- Intensive PANSS rater training
- Only one active drug dose (1:1 with placebo) reduces expectation bias that the patient was randomized to active drug
- Careful attention to patient selection based on consensus of site and sponsor
- Real time monitoring of rating quality by an independent expert service provider, with Minerva oversight from in-house personnel
- Data collection using software on e-tablets with built in prompts to reduce rating errors
- Single dose comparison to placebo obviating need for Type I correction (previous Phase 3 trial had two dose arms and Hochberg Type I correction)

Subject to ongoing feedback from the FDA

Proposed Confirmatory Phase 3 Trial – Status and Timelines

- Syneos appointed as CRO
- Topline results from 12-week primary efficacy endpoint expected 2H 2027
- Multiple sites activated
- Relapse assessment expected 2H 2028
- First patient in (FPI) expected Q2 2026
- NDA resubmission strategy

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Subject to ongoing feedback from the FDA

Up to $200 Million Financing Announced October 21, 2025

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Federated Hermes

B SQUARED CAPITAL

Janus Henderson INVESTORS

FORESITE CAPITAL

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Ally Bridge Group

TRAILS EDGE CAPITAL PARTNERS

SPRUCE STREET CAPITAL

Balyasny

FARALLON ESTABLISHED 1986

COASTLANDS CAPITAL

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Minerva Neurosciences Announces Financing of up to $200 Million to Advance Roluperidone for the Treatment of Negative Symptoms in Patients with Schizophrenia Through a Phase 3 Confirmatory Trial and Resubmission of its New Drug Application and Preparation for US Commercial Launch, if Approved

- Minerva secures $80 million up front and up to an additional $80 million subject to the full exercise of Tranche A warrants.
- Minerva and the FDA have defined a path forward for roluperidone's clinical development and NDA resubmission.
- Further $40 million proceeds may be received in connection with cash exercise of Tranche B warrants contingent upon achievement of milestone event. With the proceeds of the financing and alignment with the FDA, Minerva is expected to be sufficiently funded through the confirmatory Phase 3 trial for roluperidone and the resubmission of its New Drug Application (NDA) to the FDA.

Summary: The Minerva Confluence

Right Pharmacology and MOA

Only drug to date to demonstrate a significant and clinically relevant specific improvement on *primary* negative symptoms of schizophrenia

Right Phase 3 Trial Design

Previous experience with two statistically significant (one nominally) trials + upcoming ‘high touch’ confirmatory Phase 3 trial improves probability of success

Right Moment

FDA guidance on Phase 3 trial design + broad awareness of the unmet need in the psychiatry community + $200m investment from top tier investors

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Q&A

A new approach to treating the unmet needs of schizophrenia patients