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): November 12, 2026

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

Delaware	**000-36517**	**26-0784194**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

1500 District Avenue, Burlington, MA 01803
(Address of principal executive offices) (Zip Code)

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

Not Applicable
(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 Capital 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 November 12, 2026, Minerva Neurosciences, Inc. (the "Company") hosted a key opinion leader event regarding roluperidone, the Company's product candidate for the treatment of negative symptoms in patients diagnosed with schizophrenia (the "KOL Event").

Frank Sasinowski, the Company's regulatory counsel, participated in the discussion based on his experience and involvement in the Company's discussions with the U.S. Food and Drug Administration (the "FDA"). During the KOL Event, he expressed his personal views concerning the potential regulatory outcome in the event the Company receives positive results from the initial 12-week, placebo-controlled portion of the Company's ongoing C19 Phase 3 clinical trial ("Phase A"), and he characterized his view of certain FDA discussions and clinical findings.

The Company is furnishing a revised transcript of the KOL Event as Exhibit 99.1 to this Current Report on Form 8-K in order to clarify certain statements made during the KOL Event. Mr. Sasinowski's expressions of confidence regarding potential approval reflected his personal opinions and predictions and should not be understood as assurances regarding any future action or decision by the FDA. Any decision by the Company to resubmit its New Drug Application ("NDA") for roluperidone will depend on the results of the C19 trial, the complete data package and further assessment. Positive results from Phase A, if obtained, would not, by themselves, assure approval of a resubmitted NDA. The FDA has not committed to approval of roluperidone, and the acceptability of any resubmission and the ultimate regulatory outcome including the specific language of any approved labeling would remain subject to the FDA's review of the complete submission.

The Company remains committed to completing the relapse comparison portion of the C19 trial ("Phase B"). The Company maintains ongoing discussions with the FDA and plans to review the Phase A results with the FDA when topline results are available.

In addition, certain statements made during the KOL Event should not be understood as regulatory conclusions of effectiveness or safety for the potential use of roluperidone alone or in combination with any other product, or as indicating that any safety concern identified by the FDA could necessarily be resolved through product labeling. References during the KOL Event to personal relationships and escalation were intended to describe potential opportunities for additional communication with the FDA and should not be understood as suggesting preferential treatment or access or providing any assurance of a favorable regulatory decision.

To address these matters, the question-and-answer session at the end of the KOL Event, during which the statements concerning approval predictions, safety and professional relationships were made, has been removed from the revised transcript furnished as Exhibit 99.1. Investors should not rely on the statements that have been removed. The revised transcript supersedes any previously published transcript of the KOL Event.

The information in this Item 7.01 of this Current Report on Form 8-K, including the accompanying Exhibit 99.1, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

The Company is filing an updated investor presentation as Exhibit 99.2 to this Current Report on Form 8-K, which the Company may use from time to time in conversations with investors and analysts.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Revised transcript of Minerva Neurosciences, Inc. Key Opinion Leader Event held on November 12, 2026.
99.2	Corporate Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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.

Date: November 16, 2026

MINERVA NEUROSCIENCES, INC.

/s/ Fred Ahlholm
Name: Fred Ahlholm
Title: Chief Financial Officer

Minerva Neurosciences Inc – Study update *(Fast-Follow Transcript)*

∨ Call Participants

Remy Luthringer

Executive Chairman and CEO, Minerva

Gregory Strauss

Professor of Psychology and Neuroscience, University of Georgia

Brian Kirkpatrick

Professor of Psychiatric Research, University of Arkansas for Medical Sciences

Christoph Correll

Professor of Psychiatry and Molecular Medicine, Zucker School of Medicine at Hofstra/Northwell

Frank Sasinowski

Director, Hyman, Phelps & McNamara, P.C.

Mikhail Keyserman

Managing Director, LifeSci Capital

Operator

Presentation

Remy Luthringer

Executive Chairman and CEO

Good morning, everybody. It's really a pleasure and honor to have you here on behalf of the Minerva team. Most of my colleagues are here, so after these presentations, when we have something to eat afterwards, don't hesitate to go to see them, to speak with them. It's already an honor to have you here, to really, I think, present you something which is very important. As you know, since 70 years, people have tried hard in order to improve negative symptoms of patients suffering with schizophrenia. I think here today, we have now roluperidone, which is really, really creating some hope for patients. As you know, we are all here in order to come up with better treatments for patients. This is what we will go through today, to give you an update about where we are and where we are going.

If it is moving, it is moving. Because we are a public company, I have always to show this slide. I think it's just to mention that we are a public company, and if you want to know more, you have to go to our SEC filings. I have really the great pleasure to have with us three persons who have been extremely important for the space. I have the honor to have Dr. Strauss, Greg, yes, because we are working together since quite long, yes, so allow me to call you Greg, yes.

Greg, you will see, has worked on our data, has analyzed our data, and he has obviously a very broad knowledge about the space. I will not go more into the details because his CV is too long, and he will present his research when he will speak.

The second person could not make it today. It is Dr. Brian Kirkpatrick, and Brian will also speak. Brian is really, I think this is really amazing because Brian is really, really an incredible researcher, but he kept really the contact with patients. He sees patients on a daily basis, and he will tell us about how his patients are looking like, how he sees his patients. I mean, we are targeting with roluperidone in his clinical practice.

Last but not least, we have Dr. Correll, yes, and Christoph is, as you know, no need to present him. He's an amazing person, and he has really contributed a lot to the space. We will have obviously a Q&A session, so you can ask all the questions to my three colleagues here speaking. What we will address today is a quite large program, yes.

First, I will give you a refreshment about roluperidone, where we are with roluperidone. Also, a quick update on the C19 study because the study is ongoing. Afterwards, I hand over to Greg, to Dr. Strauss, who will speak about how important primary negative symptoms are. Yes. We're not going into the details about primary, secondary negative symptoms because Dr. Strauss will speak a lot about it, and he will explain how important they are in order to give some hope to patients. Dr. Kirkpatrick will speak about, again, as I said, his view on our patients, why these patients are not keen to relapse or have limited relapses, and how he sees his patients in his clinical practice.

I will go quickly through some new analysis because we continue to work on our data, just to better understand the data, to better characterize the patient population, to better characterize roluperidone. You will see we have quite exciting data. We have here in the room Jonathan Rabinowitz and Michael Davidson, who have worked on this. If you have questions, they are more than happy to answer the questions. Afterwards, I will conclude with giving you a flavor about what is a market opportunity. Afterwards, we open for Q&A.

I wanted also to mention that we have the chance to have my friend, Frank, who is here, yes, because Frank has been from the beginning of this journey. He is really guiding us through how to bring over the message to the FDA, to the regulator, of this paradigm shift, yes, because we are speaking here about a paradigm shift. I hope that at the end of the presentation, you will see that indeed what we are doing here is a paradigm shift.

As you know, when you are changing something in clinical practice, when you are coming up with new ideas, it is always a little bit challenging, but we are getting there because I think roluperidone could really be the first drug approved for negative symptoms. Very quickly, a few words about what we are doing here. Just to reemphasize the fact that negative symptoms are really central.

It is really central when we are thinking about giving a solution or treating or providing a treatment for patients with schizophrenia. I will not focus on all this primary, secondary negative symptoms because I think Greg will cover this much better than me. I wanted to focus just on the figure on the top right, by the way, published by Dr. Correll.

Just to mention that, and it is maybe obvious for everybody, but it is important, you have three types of symptoms when you are dealing with patients suffering from schizophrenia. You have the positive symptoms, materialized or shown by these green lines. You have some acute phases of positive symptoms, what we call relapses of positive symptoms. Afterwards, when the disease is aging, these positive symptoms are less bothering, are less frequent, are really no longer really a big problem.

This is what we are currently treating with antipsychotics, yes? We are really focusing on treating positive symptoms. You see that we have two types of other symptoms, the cognitive deficit, which is materialized with the blue line here. This is a type of symptoms which are present all along the life of the patient. We have negative symptoms in the brown line. Again, you will hear a lot about negative symptoms. Just what I wanted to mention on this slide, look, what Christoph put is a level where disability starts to kick in, yes? When you see when disability starts to kick in, it is really when negative symptoms are becoming a real problem.

Really, I think it is very clear now to everybody that if we want to give a chance for patients to have a decent family life, to have a small job, we need to find a solution for negative symptoms. Just to make my case here, yes? We know very well, it is very well described in the literature, and there are some references here at the bottom. It is really negative symptoms, not the positive symptoms, which are really the primary drivers of the disability in patients.

This very schematic way to present things, it is clear that if you are able to improve negative symptoms, probably you are able to improve the daily functioning of these patients. You will see that in our studies, we have really always measured the daily functioning using a scale which is called the PSP scale, and obviously the improving quality of life.

I think what speaks very well here, and I am always taking this example, it is now 70 years or so that we have antipsychotics. Again, don't take me wrong, antipsychotics are very important, yes? They are very important in our ammunition in order to help these patients. But when you are looking to how many patients have a job, nothing has changed since 70 years, yes?

When you see that 80%-90% of these patients have no job, compared to 4%, 5% to normal people, definitely, I mean, there is something which has to be done. Again, probably improving negative symptoms, but probably also improving primary negative symptoms is definitely important. Now, coming to roluperidone, yes? Slide shows up, it takes a little bit time. This is the pharmacology of roluperidone, and I wanted just to give you the rationale how we designed roluperidone.

The first objective was to get rid of direct dopamine blockade, yes? This was the first objective because we know that blocking dopamine is very important for antipsychotics to help to treat an acute episode of psychosis or positive symptoms. But we know also that by doing so, you are inducing a lot of side effects. We are always forgetting sometimes the side effects, but when, I think Michael showed me a recent study, the reason why patients are really willing to stop the treatment is because they are bothered with side effects.

Obviously, they have also the psychotropic effects, but they are really bothered with side effects. So it is really a problem. Roluperidone has no direct blocking effect on dopamine. It is definitely modulating dopamine, and I will not go into the details because it would be too long. But definitely, it is not blocking dopamine.

The three targets we have here is serotonin. We are targeting the sub-receptors, which is called the 5-HT2A receptor. It has an antagonistic activity there. The sigma-2 receptor, which is a less known pathway in the brain, but definitely, in my opinion, and based on my clinical observations, developing quite a lot of drugs in my life, the sigma activity is probably one of the key drivers of explaining why our drug is improving negative symptoms.

You will see probably primary negative symptoms, and afterwards, you have also an alpha-1 adrenergic activity. So it is always difficult to say this target is doing this, but I think the combination of the three targets is definitely explaining the uniqueness of roluperidone. Last but not least, we have done a lot of work to better understand what is going on also, for example, in terms of nerve growth factors.

For the moment, it is preclinical, but I mean, it's very, very compelling data. We can demonstrate that roluperidone is inducing a huge increase in transcription of BDNF and GDNF, and also the release of BDNF and GDNF. Think one second, I mean, these nerve growth factors are really, really important in neuroplasticity, to restore neuroplasticity. This is what is about roluperidone, and it has been designed on purpose.

Now, let's see if, I mean, all these hypotheses are translating into what we have seen in clinical practice. Here, it's very summarized, just because, I mean, the objective is not to go through all the data. It's more important that my colleagues are speaking afterwards. What you can see in terms of efficacy, so in all the two studies, we have run two studies, which one is called C03 study, the other one C07 study.

We have measured negative symptoms using the PANSS scale, which is a gold standard. When you're looking to the negative score, which has been proposed by Professor Marder, which is called the NSFS score, you see that the first study, the C03 study- No-brainer. I mean, 64 mg showed a very, very strong difference compared to placebo after 12 weeks of treatment in monotherapy. Keep in mind that here, the patients are not staying on antipsychotics. These are really treated in monotherapy for 12 months. What you can see is that in the C07 study, we still have for 64 mg, which was the highest dose we tested, a P-value, which is obviously going down because a larger study, more clinical sites, but we have still a P-value.

What we also measured, because this is important, and we `will hear a lot about functioning, we measured functioning using the PSP scale. What you can see here, again, in the two studies, we could demonstrate that indeed, looking to daily activities, because PSP is a very practical scanner, so looking to daily activity, indeed, you can see that these patients are, once they're improving the negative symptoms, they're also improving their daily functioning. Obviously, last but not least, what is important, is this drug safe in terms of relapses, when you give it in monotherapy? Because again, the paradigm shift here is to say there is a subpopulation who does not need continuous treatment with an antipsychotic. Obviously, the pharmacology of roluperidone might help, but what happens in terms of relapses?

The green boxes or the green bars, you can see, these are the results we obtained in terms of relapses in the two studies we have run, the C03 study and the C07 study. You can see this is over 12 weeks, + 24 weeks for the C03 study, and +4 0 weeks for the C07 study. Jonathan did a comparison by selecting from a database, which is called the CATIE database. I think it's familiar to everybody. It is the largest database which has been generated in the U.S. with antipsychotics. He extracted the patients who have the same eligibility criteria as the one we have in our two studies, and you can see what is the relapse rate you see in patients who are getting antipsychotics.

It's not the final say here, but I mean, it's clear that the patients we have recruited in our studies and the patients we are currently recruiting in our C19 study seem to be less keen to relapse. We'll hear much more about it, why we might think that this is the case. This is a study. I think everybody has seen the study design, but this study is really coming out of all what we learned from the previous studies with in-length and very productive discussion with the FDA. I have to say that we had really, really good interactions, good advice, and I think it's fair to say that this is somehow a consensus of what we have to do here.

The first thing we have to do, because keep in mind that this is a large patient population we are addressing, what is called Phase A of the study, the first 12 weeks, you see, this is to really confirm what we have seen in terms of efficacy with the two previous studies. The big difference here compared to the two previous studies is that we are focusing on 64 mg, which is the dose for which we are seeking an approval, and we have no longer 32 mg in this phase.

The objective here is really to demonstrate that indeed, using the NSFS endpoint, so the negative symptom endpoint we have used in the previous studies, we show a P-value between placebo and treatment at 64 mg. What we call Phase B, this is really different from what we have done in the two previous studies.

In the two previous studies, the patients were allowed to go into an open-label extension, so everybody was switched to treatment. In this case, and this is really something which has been discussed with the FDA, and I think it's very important. Also, it will be purely descriptive because the number of relapses we have does not allow you to do any formal statistical analysis. It will be purely descriptive, but it's a comparison between our patient population, the patients we have recruited in our studies, the patients we are recruiting in the C19 study, once they are receiving an antipsychotic, we will check the relapse rate, and we will compare it to the relapse rate we see with roluperidone.

This is important to reassure the patients, to reassure the prescriber, to reassure the agency that indeed, there is nothing severe which happens when you take off this patient population from antipsychotics. We will hear much more about this from Dr. Kirkpatrick. This is basically the study. I will not go into the details of where we are with the study. We are really enrolling. The study is going according to plan, and as we have disclosed, we really hope that we will have the results in the second half of next year. Today, definitely, we are on track to have the results coming out. I'm speaking obviously about the first 12 weeks, so about Phase A, during the course of second half of next year. I will be not very long on this slide, just because this is too complicated, too busy.

But it's just to say that the study design we have implemented here is not just because we wanted to do it in this way. It was really done by really thinking what we are trying to achieve here. First of all, we wanted to demonstrate that we have an effect on primary negative symptoms. So on primary, meaning disease-related negative symptoms. Here, you need to avoid patients who are fluctuating too much. We are looking to stability of these patients over the last six months before they're candidates to the studies. They need, obviously, to have negative symptoms which are impairing in order to be part of the study.

Just to mention that you go to the literature, and I'm using the word Mike is always telling me, and he knows the literature in and out, Dr. Davidson, it's a graveyard to put drugs on top of antipsychotics because you're blocking dopamine, and the things they like you to improve, negative symptoms, is difficult. I'm not saying that it is not possible, but we have decided to focus on a subpopulation where we think that there is more stability in order to really demonstrate that first, roluperidone has an effect, sorry, on primary negative symptoms. When the drug will be approved, we can really think about moving forward.

When you're looking to the conclusion of all this work, and even there was a committee at the ISCTM meeting who was working on study designs, I think it's fair to say that probably the best study design is monotherapy, a long period enough, stable patients, and because there is no approved drug in terms of negative symptoms, the comparator is placebo.

A last thing, which is coming on the last slide before I hand over to Dr. Strauss, I wanted really to make something very clear. Because I'm obviously reading all the reports, I'm reading all what is published, and a lot of people say, "Okay, I have an effect on negative symptoms." This slide, I think, is to explain that you have two things. You can improve primary negative symptoms, so this is a brown line, yes?

Basically, you're reproducing the brown line, which was also in the slide from Dr. Correll. So this is what we call, and technically, this is a trait marker. So this is a marker. These are symptoms which start very early on and are present all lifelong of the patient. Afterwards, you have what we call state markers. These are markers or symptoms when you're looking to the patient today, yes? One day, the patient can show some depressive disorders. One day, he can be bothered with extrapyramidal symptoms, his motor symptoms, because his treatment is not completely adapted. Sometimes these patients have an acute relapse of positive symptoms, which is a green light at the bottom. When you bring down from these acute episodes a patient, this is what we call a pseudo-improvement, yes?

You are improving, or you are bringing back the patients to the level of their primary negative symptoms, of their disease negative symptoms. I think the only way to claim that you have really an effect on primary negative symptoms is to do what we are doing, stable patients, long-term effect, and all the rest is hope maybe to improve negative symptoms. But to bring someone down from an acute episode is a pseudo-effect, a pseudo-improvement of negative symptoms. It is very important, so that we understand about what you are speaking. I think it is time now to hand over to Greg.

Gregory Strauss

Professor of Psychology and Neuroscience

Good morning, everyone. It is a pleasure to be here. I am Dr. Gregory Strauss. I am a Professor of Psychology and Neuroscience at the University of Georgia, and my research over the last 20 years or so has focused on negative symptoms, in particular the phenomenology or how we conceptualize them, developing new assessments for negative symptoms, understanding their mechanisms from a neurobiological perspective, and of course, working on new treatments. There is also always a beautiful irony of having negative symptoms be your scientific expertise. I am very motivated to study the lack of motivation. I enjoy studying the inability to experience pleasure, and of course, I am excited to talk to you about some of our new work on this today. As Dr. Luthringer set up so beautifully, negative symptoms are heterogeneous.

In other words, you can have two patients with the exact same score on a negative symptom clinical interview scale, like the PANSS, for very different reasons. For example, they may both have a score of 20 on the PANSS. One patient may be predominantly apathetic. We call this primary negative symptom. It is something that is assumed to be a direct manifestation of the illness of schizophrenia itself.

You can have another patient who looks identical on paper, but their negative symptoms are secondary, the result from other factors. This is not a concept specific to negative symptoms or even to psychiatry. It is known throughout medicine. Give you a brief example. Last summer, took my daughters to Orlando. We went to Disney World. They were very excited until we got home to this rental house at the end of the first night.

My younger daughter, seven years old, wanted to go downstairs and get a drink. Daddy went downstairs with no contacts in. I went one way, my ankle went the other way. Snap, snap. Later, I cannot walk for a few days. Fast-forward a couple of months, I go to the doctor and I say, "My knee is hurting." And looks at the knee, nothing is wrong with the knee. She says, "This is secondary. You need to improve your ankle. You have not rehabilitated your ankle. You went back to your normal level of exercise too quickly."

In psychiatry, it is a similar idea. The idea is that there are common secondary sources of negative symptoms. Screen went forward on me. There are several common secondary sources of negative symptoms, and two of them are depression and anxiety. For example, someone may be incredibly sad, feeling worthless. They may have sleep problems.

These may cause them to have a lack of recreational activity, goal-directed social behavior. Another person may be very worried. They may be very tense in their expression of emotion in the face and look very blunted. They may be so concerned about the things they are worrying about that they do not seek out social or goal-directed activities. This is very different from someone with true or primary negative symptoms.

These patients will not feel depressed or anxious regardless of what is happening to them, regardless of the stimulus. For example, a case where a patient's brother passed away. They were living with the brother, sharing a room with the brother. They did not feel sad. They did not feel depressed at all after losing the brother. Anxiety, same thing. Another patient with this primary negative symptom profile was held up at gunpoint. Remarkably terrifying experience for anyone.

Did not feel fear in this situation. No anxiety, right? This is a very different profile, this secondary negative symptom profile, than what happens with primary negative symptoms. Similarly, positive symptoms can induce negative symptoms as a secondary cause. For example, hallucinations. Someone may hear a voice telling them, "Don't get up off the couch or the FBI will come and chop your legs off and you will die."

They sit on the couch, they do not engage in activities, and they are behaviorally delusions. Same thing. They may be paranoid, thinking others are out to harm them, so they withdraw socially as a protective mechanism. Or they may be so disorganized in their thought that they cannot execute goal-directed activities to engage in motivated behavior. This is not a primary negative symptom. People with primary negative symptoms have very low levels of positive symptoms, low levels of hallucinations, delusions, disorganization.

Without having any of those positive symptoms at a severe level, they still have negative symptoms. They still withdraw socially. They are not interested in the social interactions. They could take it or leave it. They do not feel lonely even though they have spent the majority of their time alone during the day, right? This is a very different profile. Similarly, medication side effects. Someone might be sedated due to the effects of their antipsychotic. This may cause them to have less behavioral activation.

Someone with primary negative symptoms, they continue to show the lack of behavior even in periods where they are medication-free, right? Their negative symptoms persist even into these medication-free periods. Treating, importantly, there are a couple of very critical things to know about this primary-secondary distinction. The first one is primary and secondary phenotypes have distinct underlying mechanisms.

We have estimated that primary negative symptoms largely result from disrupted cortico-striatal circuitry that is driving this apathetic profile. Secondary negative symptoms, on the other hand, have different underlying biological factors that travel with the secondary sources. They travel with mood, anxiety, positive symptoms, et cetera. Because of these distinct underlying mechanistic profiles, point number two is really critical.

Treatments targeting secondary sources often reduce negative symptoms in patients with secondary phenotypes. In other words, if you have a patient who is depressed, treat the depression. If their negative symptoms are driven by anxiety, give them an anxiolytic. Not in every case, but a good percentage of the time, the negative symptoms will improve as these secondary sources improve. This is the pseudo-specificity that Remy was talking about a moment ago, right? The negative symptom effect is essentially a byproduct, if you will, of improving these secondary sources.

The third point is that treatments targeting secondary sources do not reduce negative symptoms in patients with primary phenotypes. Treating patients with a primary phenotype with antidepressants, anxiolytics, will not improve their negative symptoms. It is the wrong mechanism. Their mechanism is distinct and not being hit by that compound. Fourth, treatments targeting primary negative symptoms are not expected to reduce negative symptoms in patients with secondary phenotypes. Essentially, again, another mismatch between mechanism and mechanism of action of the drug and the underlying mechanism in a patient. What does this tell us? The treatment of primary negative symptoms is the Holy Grail. This is something that has not been addressed in the literature to date. There are strategies for addressing secondary negative symptoms, but not primary.

They are critical because, of course, for many reasons, but they are tied to lower rates of recovery, poorer functioning, lower well-being, greater stress on the family and caregivers. This is really, as others have termed, the holy grail of psychiatry, is to find a treatment for primary negative symptoms. Of course, the critical question becomes, is roluperidone doing that? The short answer is yes. On the screen in front of you, what you see is data from a probability calculator that estimates the extent to which someone's negative symptoms reflect primary or secondary causes. If you look at the figure on your left, primary negative symptoms are displayed. What this is an algorithm we developed called the Primary Stability Weighted Score.

What this is essentially an estimate of the severity of someone's primary negative symptoms, weighted by how persistent they are over time, from baseline to the end of the study. Here, higher values mean that the negative symptom is more primary and more persistent, right? What you see here is that placebo has higher primary and persistent scores than roluperidone. This is exactly what you would want if the drug is treating primary negative symptoms.

Placebo is going to be consistent across time. Their negative symptoms are not changing. They are primary. They do not fluctuate. They are enduring trait-like features. When given roluperidone, the patients who are responding are the ones with this primary phenotype. Their negative symptoms become both less severe, the primary negative symptoms become less severe, and less enduring. You can see that indicated by the lower scores there for roluperidone than placebo.

If you are not familiar with looking at these types of charts, a handy way to know if something is statistically significant is to not just compare the height of the bars, but also to look at the overlap in the standard error bars. You can see the error bars here have minimal, or potentially no overlap, and that is indicating a greater likelihood of statistical significance.

You can see in this particular metric, the P-value is 0.03, so less than 0.05. In contrast, the secondary score did not significantly differ. You can see here the P-value is 0.61. The secondary score is a little bit different. First thing to know is that it is on a different scale than the primary score. The figure is also very zoomed in, so it is also on a the axis is a little bit centered differently.

But what this scale score represents is essentially the likelihood that someone's negative symptoms are driven by secondary factors like anxiety, depression, paranoia, hallucinations, and how dynamic they are over time. Because remember, secondary negative symptoms are transient. They fluctuate a lot as those secondary sources vacillate across time. They're inherently unstable. So this score weights not only how secondary the patient is, but how inconsistent or unstable their scores are across time. And what we see here is that placebo and roluperidone do not differ, and that's suggesting that the drug is not having an effect on secondary negative symptoms, but of course, it is on primary. And again, this is really the holy grail of psychiatry, of showing an improvement in primary negative symptoms. Now, importantly, that's not a given.

I would argue that prior studies, if they have reported an effect on negative symptoms, many of them have, if not all, have been really driven by pseudo-specificity and these improvements in secondary factors. So this is something that is really an important finding. Now, another key thing that we have found with roluperidone is addressing what is driving the effect, and I don't mean at a neurobiological level. We know the components of the drug.

I'm talking about in terms of a symptom network level interaction. Many clinicians think of individual symptoms as being distinct entities, but that's not correct. Just like almost any other element of the environment, things interact. Symptoms can interact. For example, why would someone not show emotion in the face? Why would they not speak? Why would they not engage in social activity? Maybe they don't enjoy those things.

Maybe there's an underlying factor driving. Maybe it's a hedonic deficit. Maybe the way to treat that deficit would be to hit that component, right? And you would see a cascading effect temporally where all the other domains would improve. You could make another hypothesis that maybe it's social functioning. These are people who've been devoid of social interaction for years, and maybe the drug achieves its effect by making them more social, so then they have more opportunities to speak, become more expressive, more motivated in general.

So there are many possible interpretations. The one we hypothesized, however, was neither of those. It was that the drug achieved its effect by hitting a key mechanism of avolition, or a reduction in motivation, right? So what actually was found here using these network analytic approaches is that when the drug improved the negative symptom constellation, it first hit motivation.

Once motivation improved, there was a subsequent cascading effect across time where all of the other domains improved. So motivation is highly central to the improvement of the entire negative symptom constellation. And this was data from the C03 study. We subsequently replicated this effect in the C07 study. This is a similar but more recent network analytic approach and intervention network analysis.

These algorithms are changing, l ike, every six months, there's something new out there, so we applied one of the newer ones. And what we found is that there's actually a direct effect of the treatment on the PANSS item most similar to avolition, which is called emotional withdrawal. So in other words, the drug effect was hitting this item related to avolition, and again, it produced this cascading effect where you saw subsequent improvements in the other negative symptoms.

A replication of the Phase II C03 study findings. Now, hang with me. Why does this matter? Why do these network approaches matter? Who should care about this? I would argue that these are perhaps some of the most critical findings. Why do any of us do anything we do throughout the day? Our motivational system is functioning. Why do you change your clothes? Why do you go to work? Why do you have romantic relationships, friendships, write checks? Motivation is a critical component of this. Without it, these activities become much more difficult to activate. One reason that this network finding matters is because of this graph here. In both the C03 and C07 studies, what you see is an improvement of functioning, of role and social functioning for roluperidone compared to placebo.

It improved these aspects of daily life, such as doing chores, getting to your appointments, having friendships, romantic relationships. This is not a given, right? It is possible to change motivation but not change these critical behaviors. It may be that someone wants to do them, but they do not do them in the real world. That was not the case here. With roluperidone, you see that with this effect that happens on motivation, there is a subsequent effect on functional improvement. So motivation may be important to change because of its critical relationship with functioning. To give you an easy way to remember this, what is the importance of avolition or motivation here? Why does the entire constellation of negative symptoms improve?

You change motivation, you make people want to speak more, you make them more likely to be expressive, you make them more likely to interact socially, to engage in pleasurable recreational activities. Interestingly, you can also improve their cognition. One of the key findings previously published on roluperidone is that it also improves basic neuropsychological test performance. Motivation is also a critical aspect of cognitive impairment. You have to be motivated intrinsically to do well on these tests to have a good performance. So changing motivation may be critical. Improving cognition in tandem may actually also be critical for improving motivation. It may allow you to have better executive functioning to execute goal-directed activities better. So why is roluperidone important from a clinical perspective?

It is improving all of these aspects of negative symptoms that are critical through this effect on motivation that has the subsequent improvement on the two critical unmet needs in schizophrenia therapeutics, cognitive impairment and functional outcome, right? These are really important for improving the quality of lives that patients have and making them more likely to recover and do better in life.

Again, primary negative symptoms are really important as one take-home message, and roluperidone is indeed changing primary negative symptoms, but not secondary. It is achieving this effect through a direct improvement on motivational processes that are important for improving functioning. I will stop here and pass it back to Dr. Luthringer.

Remy Luthringer

Executive Chairman and CEO

Thank you so much, Greg. Now it's my pleasure to introduce Brian. Brian is sitting in a very nice location. Brian, the floor is yours. I don't know, do I have to change the slides? Okay. Brian, you tell me when I have to change your slide.

Brian Kirkpatrick

Professor of Psychiatric Research

Thank you. I'm Brian Kirkpatrick. I'm a professor in the Psychiatric Research Institute of the University of Arkansas for Medical Sciences, and throughout my career, I have focused on research and clinical care on people with psychosis. Next slide. I'm going to be talking about clinical issues for patients with primary negative symptoms, give you some more idea of who these patients are, then talk about whether monotherapy is safe or even beneficial for some people, and what are the consequences of treating negative symptoms.

Next slide. This is a very distinctive group of patients. There's been a lot of research on those patients whose negative symptoms don't appear to be due to anxiety, depression, hallucinations, disorganization, and so on. In Europe, the usual term is predominant negative symptoms, and in the U.S., it's more often referred to as primary or deficit schizophrenia.

In a clinic, they usually receive less attention than other outpatients. They kind of fade into the background a little bit, unfortunately, partly because their hallucinations, delusions, disorganization of speech, and agitation are mild or absent, and these are things that clinicians typically worry about and routinely assess. Plus, by definition, as a group, they simply have less motivation, avolition. They complain little. In the U.S., if they're placed in a group home, they tend to stay there. Plus, another factor for there being less, people pay less attention to them is, there's an absence of established treatment. Clinicians are pessimistic about their prognosis and pessimistic about interventions. All this is unfortunate because they have poorer function on average than do people who don't have primary negative symptoms. Next slide.

I'm going to show you some evidence of the importance of these primary negative symptoms for function. Patients in an outpatient clinic were rated for the presence or absence of primary negative symptoms, and it was a categorical rating, present or absent. Then five years later, they were assessed by other raters who were blind to the study hypothesis of function. The primary/secondary categorization that had been made five years earlier explained variance that was not accounted for by other symptoms. What you see on the P-values is that after accounting for variance from negative symptoms broadly defined, for instance, on the SANS or the PANSS, or the severity of hallucinations and delusions, and of disorganized speech, of demographic features and age of onset, primary negative symptoms still had a significant relationship to poorer function. Next slide.

So, what about monotherapy, which is the design for the roluperidone studies? Antipsychotics decrease the number of relapses and hospitalizations in people with schizophrenia. So, that raises questions about the use of roluperidone as a monotherapy, as it's not considered an antipsychotic. As a group, antipsychotics are associated, as you've been told, with increased risk of weight gain and its consequences, including hypertension and diabetes, movement, and also risk of movement side effects, tardive dyskinesia, abnormal involuntary movements, restlessness, which can really be miserable for someone, and stiffness. They may feel sleepy during the day because of antipsychotics. And there was mention before of elevated prolactin, hyperprolactinemia. This is a hormone, a normal hormone that everybody has, but when it's elevated, it has certain problems, especially for women, and other problems for men.

And antipsychotics don't improve primary negative symptoms and can worsen secondary negative symptoms, and there's direct evidence on that latter part, that latter statement. Next slide. So, people who stop taking an antipsychotic have been studied for many years, and the broad conclusions are, yes, they have more relapses. But if they are having some contact with a clinic, serious consequences are rare.

Also, some people are able to enter treatment because we'll accept that they will only take antipsychotics when they have increased symptoms. And patients also often have an increase in symptoms, such as non-specific things like depression, anxiety, sleeping more, before there's an increase in hallucinations and delusions and so on. What's interesting about this in part is that, in my experience, patients tend to have their own idiosyncratic warning signs. Some people consistently become anxious. Some people consistently simply become withdrawn.

So, they and their loved ones often notice these early changes in time to stop the worsening of psychotic symptoms. Next slide. Well, before I go on, let me just tie together a little bit more of a sense of who these folks are. The kind of thing that you might hear from family members is, "You know, my son isn't worried about the FBI anymore, and he doesn't seem to be hearing things or seeing things anymore, but he stays in his room all the time.

He says he's not depressed, he's sleeping okay, he's eating okay, but he's just not doing anything, and it doesn't seem to bother him that his life is really pretty boring." That's an example of things I've heard. So, now I'm going to give evidence that patients who meet Minerva entry criteria simply have a low risk of relapse independently of treatment.

I'm going to give you evidence from the CATIE study again, and from Minerva's C03 and C07 studies, the Phase II-B and the Phase III studies. Also, data from a meta-analysis of relapse in patients who have been in studies of stopping antipsychotics, and also what is known about baseline symptoms. We'll kind of take apart the symptom group, the symptoms that are used to define the Minerva entry criteria. We'll look at baseline symptoms and subsequent risk of relapse. Next slide. So, Dr. Luthringer mentioned that there was a difference between patients in the CATIE study who did and did not meet the Minerva entry criteria. So, the CATIE study had almost 1,500 schizophrenia patients who were recruited from 47 U.S. sites, and they were then randomly assigned to one of five antipsychotics and followed longitudinally.

What you see on the graph to the right is time to relapse. So 100% of patients at the beginning, those who met criteria and those who did not meet criteria, had not relapsed by definition. They were stable. What you see is that very quickly a difference appears. There are fewer who have remained without, I am sorry, there are more who have remained without relapse if they met the Minerva entry criteria.

Their last data point, they had about 68% or 69% who continued not to have a relapse, whereas it is more around 58% or 59% in those who did not meet the criteria, and this difference was significant. In this study that is not conducted by olanzapine, that was published in 2005, you see that there is something about this group of patients that seems to confer a lower risk of relapse.

Next slide. Now we are going to bring in data from a meta-analysis of drug discontinuation trials, and they were treated with placebo or an antipsychotic, and there were 9,000 patients in this meta-analysis. What you see here are the data. The meta-analysis presented up to three months and then up to four or six months. That is why you have those two time points.

What you see is that the two loratadine studies that are up at the top, C07, C03, and the patients who were from the CATIE study who met the Minerva entry criteria, but were all on an antipsychotic, are all up at the top. The CATIE positive folks on drug, not going to push this too hard because not necessarily all the P values are significant, but you see that they have lower relapses.

If you compare those three studies from patients on placebo from a meta-analysis, there is a very big difference. We are comparing with C07 and C03, we are comparing patients who were on monotherapy with loratadine to patients who were drug-free and on placebo. They were C03, C07, and the bottom graph, the black dashed line. None of them were on antipsychotics. The CATIE study patients were. Next slide. How about if you break it down into specific symptom groups? These are five studies from two repositories, the YODA and Vivli repository of clinical trials. The Minerva entry criteria define a group. By definition, they have low positive symptoms and high negative symptoms. What you see on the chart is that, look at the top line.

That is PANSS positive symptom factor, and compared, the greater the difference between patients with higher symptoms who are otherwise similar to other patients in the same studies, the greater the impact on risk of relapse. For positive symptoms, it increases. You have this stepwise increase the more they deviate from otherwise similar patients. Whereas with negative symptoms, the more negative symptoms they have, the less the relapse rate.

Low positive, high negative symptom profiles, which is the patient group that we have been discussing, they are less likely to relapse. Given this, patients in Minerva's clinical studies should have a low risk of relapse. It would have been surprising if they had not. Next slide. This is from a similar finding from an Italian cohort of 24 university psychiatric clinics and mental health departments. It is a four-year follow-up study.

On the graph, what you see is four groups, and the measurement there, as you can see on the axis, is PANSS negative symptom factor score. So from seven to 16, all the way up to 28- 48. Again, there's a stepwise decrease in risk of relapse over this four-year period. The higher your negative symptoms, the less the relapse. Next slide. What does this relapse evidence mean? Well, there's a consistently lower relapse risk in this population across decades, across national borders, across different studies, across various definitions of relapse, including hospitalization. This provides evidence for not only the existence, but also the validity of this group of patients with this symptom profile. For this group, roluperidone has a reasonable risk-benefit ratio. Finally, monotherapy with roluperidone is an example of precision medicine. Next slide.

You have a pharmacological treatment that decreases negative symptoms. There's an important issue to keep in mind clinically for these patients. Many of these patients have had years of relative social isolation and poor function, and they may not have much confidence or much skill with regard to self-care, relationships, and employment. Despite that, in the 12-week intervals, roluperidone patients have shown improvement in really the most widely used function scale, strongest function scale, the Personal and Social Performance scale, which is a measure of function in the C03 and C07 studies.

An important consequence, though, of successful treatment of their negative symptoms will be that they will be able to respond more to the evidence-based psychosocial treatments, which, by the way, have pretty good effect sizes. So they should have the opportunity to continue to have further improvement. Next slide. We are back to Dr. Luthringer.

Remy Luthringer

Executive Chairman and CEO

Thank you so much, Brian, for all this important data. Yes, I think what Brian is really addressing is we are more and more working on this, but we are more and more characterizing this patient population. I think this is extremely important, yes, when the drug will be available, that the prescriber will understand which patients would benefit from this treatment. So, I think we are making a lot of progress, and I have to say that at Minerva, we have put together an outstanding SAB with these people who are speaking today, but with other persons who are really bringing a lot of their knowledge in order to really be ready to better explain how this treatment should be administered when it will be available to patients.

What I will speak about just quickly, yes, before handing over to Dr. Correll to finish off, is just some analysis we have done, continuing to try to understand and to show the uniqueness of the effect of roluperidone. I will go through three different things. The first one is a Bayesian analysis we have done with our data. I will come to this in a second. The other aspect is what we call the global statistical test. Last but not least, something which is very important is afterwards to compare how many patients are responding to our drug compared to placebo. This is obviously what usually the FDA is using.

They say, "Okay, the drug is improving, I don't know, positive symptoms, and you have 30% of the patients responding with treatment versus whatever percentage under placebo." I will focus on these three things very quickly. Why do I show you the Bayesian analysis? As you know, what you usually have to do is to have two studies, which we call frequentist analysis. You are analyzing the data in a frequentist way. In the case of frequentist analysis, you are just putting each study as a standalone observation. Yes? Each study needs to show a P-value, and you don't take into account what you know already about the study, about the drug, excuse me.

Interestingly enough, I think the FDA starts to recognize that, yes, this is still the gold standard, but probably we would benefit by learning from what we have known before we run the study from the drug. This is interesting enough, the FDA put out a guidance in January 2026, in order to really explain how you could apply the Bayesian analysis. What we have done here is to, based on a very positive study, obviously the C03 study was a very positive study, we looked how much you have to borrow. This is about borrowing, about what you have learned from the previous study, in order to make the C07 study a very successful study.

What you can see very nicely for the primary efficacy endpoint, which is NSFS and PSP, what you have to borrow to really make the Bayesian analysis highly positive is extremely limited. Clearly, we discussed this in length with Frank, when the borrowing is below 20% or 30% or even 40%, you can really come to the conclusion that your drug has a real effect.

In our case, you have to borrow less than 20% to make the things highly positive. I do not take more out of this. I am just saying that, if you are applying Bayesian analysis, you can come to the conclusion very easily that the roluperidone is working. It is just another way to look to our data and to come to the conclusion that indeed, roluperidone is working not only on negative symptoms, but also on functioning.

Now, the global statistical analysis is an interesting one, yes, because global statistical analysis is, as you can see, it is to combine endpoints into a single test, while correcting for correlations. Really, I think this is what is important. Usually what you are doing when you are analyzing data, you have your primary endpoint, you are looking to your secondary endpoint, and as you know, human beings, we are not completely objective. Yes? This is a way to really demonstrate that indeed, using a very robust statistical approach, that indeed, improving negative symptoms is translating into an improvement of functioning. Obviously when you are doing GST, you have to combine something which makes sense, and here is exactly what we did in the two studies, primary efficacy endpoint and sole key secondary endpoint.

What you can see very nicely is that, for the C03 study, where you have a very, very high P-value in the GST approach, so basically combining negative symptoms and functioning. Look to the C07 study, again, highly significant. What matters at the end of the day, indeed, is that patients are functioning better, as we heard from Dr. Strauss. Clearly, I think this is a very nice demonstration that with an objective statistical tool, we are demonstrating that the two things are really correlated, not correlated, that negative symptoms are producing a very strong functional improvement. When you are integrating, obviously, the two studies, at the bottom line, the things are staying extremely significant.

I think it is a very objective way to reemphasize what Dr. Strauss was saying, that I think the uniqueness of roluperidone, it is on one hand improving primary negative symptoms, but it is also transforming into a functional improvement, which is, best of my knowledge, has never been really demonstrated. Now, coming to what usually the agency is looking at, yes, and this is what we call the responder analysis.

On the complete left side, this is a classical responder analysis. You are looking to the primary efficacy endpoint, you are looking to the patients who are improving more than 20% during the course of the treatment, and you are comparing this between the placebo group and your drug. What you can see very nicely here is that the patients are treated with roluperidone 64 mg, it is around 38%, whereas for the placebo group, you are at around 22%.

Usually also, and I am speaking under the control of Frank, when you are going above 30% of responders, I think this starts to speak positively for your study. We wanted to go further down the road in order to better understand the difference between roluperidone and placebo. What we did, and this is the middle analysis, what we did, basically Jonathan, who is here in the room, did, we did an analysis where we were anchoring the primary efficacy endpoint, so negative symptoms, NSFS.

We were anchoring this to CGI-S. It is very well described in the literature that one point improvement or more of the CGI-S is clinically meaningful. Yes? It is really telling you that something good is going on in terms of functional improvement of the patient. Look again, definitely roluperidone 64 mg is much better than when you are treating your patients with placebo.

Last but not least, we wanted to focus on functioning, yes, and we did this analysis using not the primary endpoint negative symptoms, but PSP functioning. This is on the right side of the graphs on the right side. What is known from the literature, and I think Dr. Nasrallah published this in length, is that when you have an improvement of more than seven points of the total score of PSP, this is really clinically meaningful. What we did here, because our recent publication showing that, I mean, if you are going to 10 points or more improvement, not only the patients will function better, but, I mean, the likelihood that they might relapse is also reduced. Just to continue to better understand our data.

But so when you're looking to these results, which is very challenging, yes, to reach 10 points, you see again that definitely, roluperidone 64 mg is doing a much better job than PSP. But to put this into the context, yes, so you see that another way to look to this data is to look to the number needed to treat.

So, how many patients do you need in the treated group to be better than the placebo group? And you see that the numbers for these three types of analysis are seven, eight, and nine patients. It might look a lot, yes, but when you're putting this in the context and you're looking the number of patients, and this is at the bottom right, the number of patients you need for antipsychotics and for antidepressants, we are exactly in the range.

So, just to say that it's always very difficult to say that all this is clinically meaningful, because I think it's too early, because this is the first drug really moving the needle on negative symptoms. But I think all this data really demonstrating that there is a real benefit for the patients who are treated with roluperidone compared to placebo. I have now the pleasure to hand over to Christoph Correll, who is making some emails, but Christoph, you have to speak now. Thank you, Christoph.

Christoph Correll

Professor of Psychiatry and Molecular Medicine

Great. Thanks so much, Remy. Thank you all for being here today. I hope this is on. Yes. So my name is Christoph Correll. I'm Professor of Psychiatry and Molecular Medicine at the Zucker School of Medicine at Hofstra/Northwell, where I've been for the last 29 years, and I'm also Professor and Chair of the Department of Child and Adolescent Psychiatry at the Charité University in Berlin, where I've been for the last eight years. My work for the last 30 years has focused on clinical work and research in people with mood disorders and psychosis. And we talked last night about regret, and basically, I have one professional regret. When I started medicine, I was a little naive. I thought I could cure and understand schizophrenia. I now understand this is out of reach.

But I have one personal regret, and that is that during my work and work of many others, we have not yet found a treatment for negative and cognitive symptoms in people with schizophrenia, the two drivers of disability. And that's why we're here today, to change that regret. So let's talk about the negative symptoms, but also where roluperidone, if and when it's being approved for negative symptoms, can go, because these symptoms are not owned by schizophrenia. Our brain has multiple ways of expressing something that is positive, but also something that's missing. And this missingness cuts across multiple disorders. So I see a lot of opportunity for roluperidone to help patients with other disorders where there's a lot of disability. Let's briefly revisit what Greg Strauss has been talking about, the negative symptoms.

The way we currently narrowly define them for schizophrenia, they have to do with two dimensions. One is expressive, where we understand what the patient is maybe feeling and thinking. It's very important for social interaction. That has to do with blunting of affect and also alogia, not talking much. Patients have a hard time connecting with other people if other people can't read them, if they can't express themselves.

What is even more relevant for the functionality, though, is the intrinsic experience of life, and that has to do with anhedonia, not being able to experience pleasure, but then also the expression of that motivation on the social level or other things. Asociality is central. People just sit on the couch, as we've heard. They're not interested in other people, and families beg us to bring their son and daughter back.

They feel their children, their loved ones have checked out. They're just physically there and not much more. This avolition cuts across everything. Families notice when something changes. They just want their loved one to pick up the newspaper again and show a sign of light and interest in life. That's what we're here for. We need to change that. There are different ways of cutting the pie of negative symptoms. Some have even some cognitive aspects in there, because Professor Strauss also mentioned that there's this interaction between cognition and negative symptoms. You can only use your cognitive abilities when you're motivated to do so. But when we looked at multiple studies, the frequency of different dimensions of negative symptoms might be different based on the patient population we're looking at.

But within each study, we could see that the blue is more frequent, then the red is more frequent, then the green. That means we have a lot of social amotivation, no matter what the study is. My apologies, so it has to do with the study. But you see that within the red, within the blue, and within the green, we have more social amotivation, then with diminished expression, and then inattention, alogia. This social aspect, not being able to motivate yourself to do things, is crucial that we need to address. Because negative symptoms have multiple pathways into eroding people's lives, eroding their social interactions, eroding their aspirations for job, and also for work.

Freud said, "The two things that are relevant in life is work and love." Those are the two things that are undermined by negative symptoms, even more so than by positive symptoms, which we can now treat. As you've seen in the subtype of patients that have little residual positive symptoms, that is not the issue anymore.

This type of precision psychiatry that also Brian Kirkpatrick was talking about is unique. We don't have any psychiatric treatment right now that has focused on a biological and clinical subgroup that is relevant, and that gives us much higher likelihood of success rather than blasting patients with one medication to treatment of patients that have very heterogeneous results and also underpinnings. Again, to just highlight the interaction between cognition and negative symptoms, cognition gives you the ability to do something. It's your capacity.

But without then doing something about it, you are just keeping your capacity floating freely around. You need to have performance, and functional performance has to do with executing this. The execution of your capacity has to do with motivation and seeing also value in doing it. The value has to do with hedonic drive. I can anticipate that things are going to be good. I can enjoy them. That then gives us reinforcing behaviors. We know that people with negative symptoms also have high cost that accumulates. So here, payers should be very interested in that. We know the interest by the FDA is great because you do not even need to have an extra outcome of functionality. This is a given. Not so much with cognition. With cognition, we need extra measurement of outcomes on the functional side.

But since negative symptoms and functioning are so tightly intertwined, that is not needed. Now, we have seen with the data for roluperidone that PSP was really moving even stronger than the negative symptoms. So we see an agglomeration of the effect on what patients want, what families want, and what regulators are interested in. Now, I mentioned that I am also a child psychiatrist, and I became a child psychiatrist because I wanted to prevent the illness, and that means we are looking at the so-called prodromal phase. It is the clinical high-risk phase where patients do not yet have positive symptoms, but this is loaded with negative symptoms. It is loaded with cognitive symptoms.

While we still need to collect data on that, there is at least a prospect that by treating the negative symptoms early in the illness, we might be able to avert the psychosis from evolving, because there is an interaction between the neuropsychology or neuropathology that is underlying the negative symptoms that might actually secondarily drive the positive symptoms. As we have reduction in functioning in some areas of the brain that have to do with dopamine and glutamate as the final endpoint, there are other areas in the brain that come online in order to compensate for that.

Now, this is future music. One would have to look into this, but it is obviously very, very compelling. Even if patients do not yet have the real risk for psychosis, treating negative symptoms early that are independent of depression will help them even at that stage to function better.

Now, this is a slide that I got from RexKako, like the last one and the next two ones, which really has a lot of text on there, and this should dizzy you because that is the purpose of this. How dizzying is it that the negative symptoms that were defined and we have always been talking about in the context of schizophrenia actually might occur in 18 other conditions? That has to do with the fact that what we call negative symptoms, this terminology, when you use some other words that have been used in other conditions, actually it converges on the same thing. Has to do with lack of motivation and willpower, has to do with apathy, not being able to get yourself to experience something or express yourself, and it has to do with anhedonia, not enjoying things. These aspects really cut across multiple domains.

The question then is obviously, where would one put one's emphasis the most? We will get there in a minute. First, some more data that RexKako also put together just to show you that the so-called negative symptoms, which is a group term for problems that is there is an absence of things in the brain and in people's lives, cut across not only schizophrenia, but also major depressive disorder, the ultra-high risk syndrome, which I just mentioned, the risk syndrome for psychosis, bipolar disorder, and it is much higher than in healthy controls. Now, we could say that some adolescents have a little bit of negative symptoms. They have all the capacity and just sit on the couch. That is a prodrome to adulthood, but obviously, we need to motivate everyone to do better and express themselves.

Because especially during early phases of development, when you have learned that you are not able to do certain things, that people don't read your emotions, that you are not connecting, that becomes part of your persona. You don't even expect this to change. You are not really motivated to do things about it because there is no reinforcement. This reinforcement needs to come by lighting the bulb up again and getting patients back into life.

Here you see the comparison of the so-called negative symptom domain compared to people in the general population, and you can see that it really cuts across multiple of these disorders and that there is a big problem with anhedonia and avolition. Putting all of this together, where could roluperidone fit in the clinical treatment paradigm? Now, obviously, it is being developed for schizophrenia.

That is a right path because that is where negative symptoms have been owned for so long, and we already have one very positive study and one near-positive study. When you remove some patients from sites, it was positive. Even in that study, the functionality was significantly better than from placebo. That is really very promising for the next study that we will see again, 12-week data showing significant improvement of negative symptoms without needing the dampening on the brain of the dopamine-blocking medication.

That is unique. No other company has really tried that, and it is bold, but I think it is possible when you do use this precision psychiatry approach, giving the right treatment to the right patients. Now, what other patients might be right patients? Schizophrenia and schizoaffective disorder, for the right, are very, very closely related.

They are almost siblings because you still have all of the schizophrenia side, but there are symptoms of mania or depression. These patients also frequently have negative symptoms. On the left-hand side, major depressive disorder, I think, is a number one target because we have patients where the depression is treated, they are not sad anymore, but there is residual anhedonia, apathy, and also the lack of ability to enjoy themselves and connect back with life.

They are sitting, and they are not sad anymore, but they are blank, and there is a lot of emptiness. Hopefully, for these residual symptom patients in a very frequent disorder like MDD, roluperidone could play a major role. We are all aging, I have to break the news to you, but also the population is aging, and we will have more and more Alzheimer disease patients. You know that.

And we also have two types of Alzheimer's that is really problematic for families and societies. One is obviously where there's the too muchness of psychosis and agitation, and some companies are going that route. But what we're really not focusing enough on is the apathetic subtype of Alzheimer's disease, where basically patients are disappearing from their families. They're just sitting there, and they're not interacting, and that is so painful that you're losing your loved one this way.

You want to reach them, and they're like behind a milk glass. This apathetic type of Alzheimer's disease has a very high likelihood to also respond to roluperidone. Now, looking at Parkinson's disease, where there is a lack of juice in the brain, there's too little dopamine, there's also a lot of depression, but apathy. So here, I think it's a high likelihood that this could be treated.

Similarly, in another neurological disease, multiple sclerosis, where there is a shutting down of certain neurocircuits that need to be lit up again in order to make patients more interact and enjoy their life. COVID has brought us a lot of patients who have long COVID now that somehow can't get back into life, can't light the bulb again in their life, and they are often just sitting around, lying around, and have checked out. So this long COVID post-viral syndrome that we don't fully understand yet what happens in the brain may also respond to roluperidone. And very much related to that is the myalgic encephalomyelitis or chronic fatigue syndrome, which has been around for many, many years, where we don't have anything approved to treat this kind of illness.

And then finally, traumatic brain injury is another disruption of the brain that hopefully a treatment like roluperidone that treats apathy and anhedonia and amotivation in people with schizophrenia, where the hardware is impaired. Here, we have hardware impairment after a traumatic event, and it's also a real target. And then finally, let's finish up again with neurodevelopment. What about autism spectrum disorders, where we have also, like with Alzheimer's, a too muchness of aggression and agitation, but we also have this lack of social interaction, where we have this checking out and just being in your own world. You may know that Bleuler, who coined the term schizophrenia, actually felt that one of the main features was autism for people with schizophrenia, meaning being in their own world, being shut off from others. So here, I think roluperidone, again, would have a path forward.

And since there needs to be a pediatric plan, that would be something, I think, to actually study, rather than schizophrenia, which is much rarer in children and adolescents. And other companies have done that they actually use this for agitation and aggression as their primary autism, as their primary target for fulfilling the pediatric plan. So I thank you for the opportunity to talk about this transdiagnostic opportunity for roluperidone once it's, and if it's approved for schizophrenia and negative symptoms. Thank you very much.

Remy Luthringer

Executive Chairman and CEO

Thank you, Christoph. Incredible presentation. Thank you. I think, very importantly, you see how important it is to bring roluperidone to patients, and afterwards, it might open to a lot of other disorders where there is a huge unmet medical need. I think it is our duty here to come to this. Let me just go back to the numbers, because everybody likes numbers. This is just to give you a flavor about what is the opportunity when we will have the data in hand of the C19 study. This is really focusing on the patient population we are currently targeting, and these are some data. You know that the prevalence of schizophrenia is, depending on the studies, 1%, 1.2%. This represents, and here I am focusing on the U.S. only, it is around 3.4 million in the U.S. who are definitely suffering from schizophrenia.

Interestingly enough, the number of patients who are treated or seen by the medical system are not from all the patients, but it is nevertheless 2.2 million people who are seen by the medical system in the U.S. So, a very large population. Afterwards, when you apply our criteria somehow, so patients who have negative symptoms, this is going down to 60% of this population or these patients who are seen by the medical system, and so you end up with 1.3 million people.

When you are going with patients who are stable, because this is what we are aiming for here, what our studies are recruiting, you end up with around 900,000 patients who might benefit from roluperidone in the U.S. only. Maybe people who have seen our previous data say, "Ah, they have increased the number." No, we have not increased the number.

What has changed since the last review we did is that the number of patients seen by the medical system has increased. In our last analysis, it was half of the patients. Here, it is more than half of the patients, which is explaining the difference here. It is just to be clear that we are not emphasizing or inflating the numbers. It is just because more patients are seen by the medical system. The same is true for the, how to say, the overall market for schizophrenia. It has also increased. It is now at around $7 billion. On negative symptoms, there is definitely no dollars coming because there is no approved drug for the moment.

When you apply this to our patient population by using the criteria I was showing you before, this is an opportunity for the first indication, which are negative symptoms in patients with schizophrenia. You are speaking about an opportunity of more than $2 billion. Before opening to Q&A, hopefully you have a lot of questions, because I think what we are doing here is so exciting, and when I hear my colleagues speaking about it, how important it is, it gives, I think, to the complete Minerva team the energy to move forward and to continue to work. I think Minerva is the right conference here, because we have definitely here the right pharmacology and the right mechanism of action. It is, I think, the only drug today who shows really clinically relevant improvements.

We are really showing that we are able to improve primary negative symptoms, and after presentations like the one from Christoph, I think you are all convinced that there is a label expansion which is possible with this drug. Importantly, we discussed this, and I think we have what I think we brought to the table, even broader than Minerva, to the medical and scientific community, is to think about the fact that patients with a diagnosis of schizophrenia are heterogeneous. I think we are able to really come up with a clinically relevant population who has really these impairing negative symptoms and with a low risk of relapse. I think this is coming to the notion of precision medicine, but this is extremely important, and I think this is not important only for schizophrenia. We can speak about depression, it is exactly the same, or other disorders.

But I think this is a second pillar of what we are doing here. Now we are understanding more and more data, more and more the patient, and more and more why these patients are different in terms of reacting to the drug, in terms of negative symptoms, but also why they are not relapsing. Something very important, obviously, we need to have a positive C19 study. The team is completely focused on this, but I think it is about execution. It is not about the fact do you have a drug or not. Because when you are looking to the two previous studies, we definitely show a very good discrimination between placebo and treatment for negative symptoms and functioning. It took us time.

I know that some of you were questioning me often, “Why did you not start your study immediately after the feedback from the FDA?” I think it was necessary that we open the dialogues, that we had these interactions. As I said at the beginning, we really got very, very good advice in order to come up with the C19 study.

We learned all from the two previous studies that we have implemented, and it is long to go through it, all implemented in order to really magnify the effect of roluperidone, keeping the placebo effect under control and definitely coming up with a positive study. It is also the right moment because I think the space is really moving. Patients are more aware about negative symptoms. The scientific community is working on it. The medical community is working on it.

It is important, and I wanted to highlight this very strongly. I mean, we are backed by world-class investors, which is, as you know, without having these people supporting us, nothing is possible, unfortunately, in drug development. So thank you to all the investors who are supporting us. I think when you think about the opportunity, there is an opportunity to have a big readout coming during the course of next year, hopefully confirming that the drug is working on negative symptoms and transforming into functional improvement. It is time to hand over to Q&A. So maybe Christoph and Greg and Frank, maybe you can sit. We have Brian somewhere, so can we see Brian?

Brian Kirkpatrick

Professor of Psychiatric Research

I can see you. We’re good.

Remy Luthringer

Executive Chairman and CEO

Okay. Please.

Unknown Speaker 1

The mic is coming.

Remy Luthringer

Executive Chairman and CEO

The mic is coming.

Question And Answer

Unknown Speaker 2

This is John here for Andrew Tsai from Jefferies. As we think about the real-world use case for roluperidone, I can imagine physicians would be incentivized to take patients off of antipsychotics, which come with a lot of safety liabilities. Then I can also imagine there's hesitancy to take patients that are well-controlled on their positive symptoms as well. As we think about discontinuing an antipsychotic and then cross-titrating or even using adjunctively, where do you think the ultimate real-world use case will kind of skew towards?

Remy Luthringer

Executive Chairman and CEO

Maybe we can start with Brian. Brian? You're on mute.

Brian Kirkpatrick

Professor of Psychiatric Research

My apologies. I suspect that both will happen. Some people will start monotherapy, some people will continue an antipsychotic. I think the company would then have the option of providing some education for those people. If a lot of people continue an antipsychotic, might be able to present them with a way, an educational effort that perhaps includes talking about tapering off the antipsychotic slowly. I think Christoph had some thoughts about that yesterday he might want to add.

Remy Luthringer

Executive Chairman and CEO

Yeah, Christoph, please.

Christoph Correll

Professor of Psychiatry and Molecular Medicine

Yeah, I do believe that clinicians will be wary of the worsening positive symptoms, so there will be first an adjunctive treatment. Then since patients always ask us to lower the dose or stop their treatment over months, I think then very slowly go down so that we could catch them should these patients not be guarded or protected against relapse and wouldn't have a bad outcome. I also, and many patients, I think, will continue this and finish the cross-titration. I think that there are two other groups that we haven't really focused on where this will be used the most and fastest. About 50% of patients are non-adherent themselves, and there are those that are not on an antipsychotic anymore, but they still have negative symptoms.

That's where families might bring them in, where patients are still in contact, and they could be started safely, and maybe the relapse prevention with roluperidone's effect could then be stronger. I think also first episode patients. First episode patients that get schizophrenia treatments, the clinicians are often very unclear, will they have a second relapse or not? Negative symptoms are very common, and patients' families want us to try at least once without. That's the perfect population where we, at the moment, have nothing to offer. We say, "I think 80% chance that you will have a relapse, so we need to continue." But what if I'm in the 20%? So those patients that are often even based on guidelines given at least one chance, that's the perfect treatment for roluperidone.

Remy Luthringer

Executive Chairman and CEO

Yeah, and Frank.

Frank Sasinowski

Director

Let me say this, and by the way, I'm Frank Sasinowski, the guy Remy kept referring to as Frank.

Remy Luthringer

Executive Chairman and CEO

Oh, sorry.

Frank Sasinowski

Director

No, no. I left the FDA 39 years ago as Deputy Director of Health Policy, Commissioner's Office. 39 years, I was with one law firm helping people get new drugs through the FDA pre-approval call. I have helped over 200 new chemical entities get approved, including REXULTI, COBENFY, and CAPLYTA in the world of schizophrenia. Let me say this, that FDA, I am all about FDA. You have been hearing about science, now a little bit about marketing. I have a myopia. I only think about FDA. That is all I think about. With respect to FDA and getting to market, the FDA cares about making sure that it has the right evidence for which it can label so that doctors have adequate directions for use.

Beyond that, so that they will approve it, the FDA, if the Phase A results come in next year and they are positive, the drug will get approved. It will be approved because it is effective. The questions about relapse are a safety question. Safety questions are, the FDA has a lot of tools in its toolkit to deal with safety issues, including labeling. The relapse issue, it is not a big issue. In fact, at our September meeting with the FDA, the FDA said, "Yeah, we agree with you, Remy. We agree with Minerva. Your relapse rate is likely lower than it is in general because of the patients that you are going after." What I want to get to is your question about label. The FDA only cares about labeling it on the evidence that it is provided with.

It would be provided just for the patients that were studied in C03, C07, C19. The rest of it, which you are talking about, like Christoph is talking about, first episode and these other things, and what you were talking about. That, the FDA says, is not on our shoulders. It is not in our task. We are not responsible for the practice of medicine. What people do off-label is up to the medical community. We only are empiricists. We just deal with data. I just want to make sure that you understand there is a difference-

between what the FDA will approve you for, which I think will happen if the Phase III results, 12-week results, are positive. In fact, in our discussions with the FDA, what is fascinating to me is that in this discussion today, as a regulator, there was no discussion about whether or not this drug works. There was no discussion of that in September with the FDA. The CRL, the complete response letter, which we got in February 2024, which says, "We are not approving you on the basis of C03 and C07," the first issue was substantial evidence of effectiveness. The most important issue to the FDA was, does it really work? Does it provide benefit? Yet, where are we today? Nobody is even talking about it, not even the FDA much, when we met with them in September.

Which means that, to me, as a guy who knows nothing but FDA, this drug is getting approved. Those Phase III results at 12 week come in, and FDA almost has no doubt that they are going to come in positive.

Remy Luthringer

Executive Chairman and CEO

Thank you, Frank. Yes, but I think it is very important to make these distinctions. Really, thank you, Frank. By the way, the FDA does not call me Remy. I am not yet at this stage. But a small thing I would like to add. We already have a lot of data because obviously we are very well aware that, I mean, this drug might be administered on top of something else, antipsychotic, but it can be also on top of another treatment, as you have heard. I mean, this will be also maybe prescribed beyond the schizophrenia. So, we have already a study we have performed, which is called the C18 study, where we have co-administered olanzapine with our drug, just to demonstrate that, I mean, it is possible. I am not speaking about the efficacy, just that it is safe.

I think it is a small study we have done, but definitely it is safe. We have a lot of preclinical data showing that the risk of DDI is extremely limited with our drug. But again, this will be taken care of during the labeling. What I wanted also to mention, because, I mean, this was often a comment I received from a lot of people, "Why are you not doing like everybody, put this on top of an antipsychotic?" So we decided, and I was stubborn, and I got a lot of criticism. I said, "No, let us first focus on this patient population we have discussed today to demonstrate that we are improving the primary negative symptoms, and afterwards we move to something else." But think one second about developing it on top of an antipsychotic. Which dose should we use of the antipsychotic.

What is the level of binding of dopamine in the brain we should have in order to co-administer the drug? I think this is something which is a little bit more sophisticated than just to say, "Put it on top of an antipsychotic and hope for the best." Just to mention that we are thinking about it, we are conscious about it, and we're working on it.

Frank Sasinowski

Director

Let me say this about that. Slide 11 that you saw in this slide deck quoted Stephen Marder at UCLA for saying that a monotherapy is the best design to look at a treatment for primary negative symptoms. Okay? Stephen Marder at UCLA was the person for whom Mike Davis, who is currently the head of the Center for Drugs at the FDA, Mike Davis worked under Stephen Marder at UCLA. Mike Davis then is a psychiatrist who's keenly interested in schizophrenia, studied under Stephen Marder. When Mike Davis left the FDA temporarily, he was at the FDA, he left for a little while to go to a nonprofit called Usona to help work on psychedelics for treating PTSD. When he left, he called me, he said, "Frank, the best work I saw at FDA when I was at FDA was from you.

I'm now the CMO at Usona. Would you represent me?" I said, "Sure, Mike. I'll do that." Mike now is back at the FDA, a psychiatrist, head of the Center for Drugs, whose profession was built on looking at schizophrenia, and with people like Stephen Marder who focus on negative symptoms. Guess what happens when you have somebody like me who knows people like that, who are interested in this issue? It means that we have an ability to invoke, escalate these kind of reviews, so that if we have any hiccup in our review when these Phase A results come in, we have many ways in to talk to people who can help with the decisions to be made.

Remy Luthringer

Executive Chairman and CEO

Thank you, Frank. Next question, because I think if we take as long for each question, I think we will be here until 4:00.

Frank Sasinowski

Director

I can go on.

Remy Luthringer

Executive Chairman and CEO

No, no, it's not because of the criticism. Next question, please. Mikhail.

Frank Sasinowski

Director

Do we have any from the audience?

Remy Luthringer

Executive Chairman and CEO

Let's go through the room and after.

Mikhail Keyserman

Managing Director

Sure. Mikhail Keyserman, LifeSci Capital. Maybe two questions. One is, when you look at this patient population and think about quality of life, obviously PSP is measuring a lot of that function on a daily basis, but how are you guys thinking of capturing the quality of life benefit that roluperidone really offers for these patients? That will be obviously very important for the pharmacoeconomic argument as you guys are going to go to payers and really think through that. I would love to get some more thoughts around that. Thank you.

Remy Luthringer

Executive Chairman and CEO

Who would like to take this question?

Christoph Correll

Professor of Psychiatry and Molecular Medicine

I can. Basically, there is no dedicated quality of life scale in this study at the moment because the more rarefied the assessments, the more likely you will beat placebo. But we have clear data that functioning improvement really translates into quality of life. So there could be triangulation studies looking at other studies where when PSP improves and it did have a quality of life measure, that that also improved. So I think that is less in question, and functionality is measurable and observable. So I think that has more traction even with payers than quality of life, which is a very subjective and neither here nor there kind of an outcome. But maybe Greg, what is your opinion?

Gregory Strauss

Professor of Psychology and Neuroscience

Yeah, I definitely agree. I can also add there are some of the items on some of the scales that are being administered that get at the subjective experience of the patient. So how much, in addition to what they are doing, how much do they want things to change? How important is that? How connected do they feel with other people, not just how much are they actually engaging in those interactions? That subjective portion is very important for quality of life.

Remy Luthringer

Executive Chairman and CEO

Brian, do you want to add something?

Brian Kirkpatrick

Professor of Psychiatric Research

Well, you may not like what I want to add. My thought was, how difficult would it be to ask the patients at the end of the study if their quality of life has improved and look at it for placebo versus drug?

Remy Luthringer

Executive Chairman and CEO

You are spot on because we have this kind of question at the end of in our new study. Definitely we have it and we will document it. Hopefully the two things will match together.

Frank Sasinowski

Director

For some reason that I do not quite understand, FDA is fascinated with what we call exit interviews in all studies across all disciplines. I say I am perplexed by it because the FDA really does dig into those exit interviews, the very thing that Brian was asking.

The very thing that is being done in Study 19. The FDA, the Associate Director of the Office of Neuroscience, Dr. Michelle Campbell, is a pharmacometrician, and she likes to look to see the correlation between what those exit interviews say about how people are changing their activities of daily life and look at their scores on instruments like PSP or the PANSS, or the NSFS. There is a great regulatory interest in looking at that. It is a very good question. I do not know if you knew how relevant your question was, but it was a great question.

Remy Luthringer

Executive Chairman and CEO

Michael is an open book, so probably knew it. Any other question, please? If not, is there a question from Doug.

Unknown Speaker 1

Wait for the mic. It is coming.

Unknown Speaker 3

Dexal from H.C. Wainwright. I am just curious how, given the introduction of new mechanisms of late, as well as over the years there have been some drugs that have tried to make claims around treating negative symptoms, although have never been able to get labeling. I am just curious from your perspective, like a product like VRAYLAR, how effective they are, and even some of the newer agents that have been approved, how has that affected the pervasiveness of negative symptoms or their severity, if you will, and the need for both primary as well as secondary negative symptoms?

Gregory Strauss

Professor of Psychology and Neuroscience

Do you want to go first?

Remy Luthringer

Executive Chairman and CEO

Go first.

Gregory Strauss

Professor of Psychology and Neuroscience

I was going to say, I think it’s becoming clear that drugs that have shown an improvement on negative symptoms measured very broadly, they also concurrently are having improvements in these other domains, positive, depression, anxiety, disorganization, et cetera. The real question is there a temporal effect? Are those improvements lagged in producing the improvements in negative symptoms? I am not aware of companies doing

those specific analyses. That is one way to test it. The assumption is, because they are occurring concurrently, that there are secondary effects occurring, and I think it is a very logical assumption. So to date, no drug has really been thought to cross that threshold. That has been an actual change in primary negative symptoms. The other issue is the enrollment criteria. Most studies have had a very broad enrollment criteria. They have not enriched for the primary phenotype as Minerva has.

That over-inclusion results in a high amount of these secondary phenotype patients who are driving the improvement in negative symptoms due to the secondary source improvements in positives of depression, anxiety.

Remy Luthringer

Executive Chairman and CEO

No, I think you're, and Greg, you're addressing a very important point because if you take the example of VRAYLAR, when you're comparing VRAYLAR to risperidone, obviously you will win because risperidone is known to be very sedative, to have a lot of side effects. I think the study design and the patient population is important. Just speaking about depression, so we have capped in our study the level of depression. This is very important because I always remember first time Brian came, he said, "I don't believe your data because you have probably not controlled for mood." Indeed, we controlled for mood. Here we have Brian still supporting us. I think all these kind of things are very important.

They are not seen when you're looking to a study design, but this is exactly what we are implementing in our study in order to really being able to claim that there is an effect on primary negative symptoms. We have even taken a patent on mood. I think the drug is doing something on mood, but, I mean, to really demonstrate what we wanted to demonstrate, you have to come up with this kind of criteria. I agree, often it is much too large, and to claim that, I mean, you have an improvement is a little bit a conclusion which is taken too rapidly, basically. But yeah, good question. Yeah.

Christoph Correll

Professor of Psychiatry and Molecular Medicine

You also mentioned how the landscape might change with some of the agents that are coming. Most likely, implicitly, you talked about the muscarinic modulators. The muscarinic agents have, especially M1 and four, some reason to believe that they may help cognition, but there are not good data at the moment at all that independent of improvement of positive symptoms, they can improve negative symptoms.

The partial agonists you mentioned, that's aripiprazole, but also aripiprazole, brexpiprazole, they lack some of the secondary negative symptoms due to over-sedation and D2 blockade, but we don't have a solution for these residual true primary negative symptoms, so they are still out in the open. I don't think that any agent at the moment in the making really has a very strong prospect, except maybe for LB-102, but there is no study ongoing at the moment, which is an N- methylated amisulpride.

That will be a small subgroup of patients, whereas the muscarinics, I don't think they are used mostly in combination, and with the combination, it's hard to break through any of the D2 blockade. I think roluperidone at the moment would be the sole potential option that I see that's viable.

Remy Luthringer

Executive Chairman and CEO

Thank you. Frank?

Frank Sasinowski

Director

What I was going to say is that if you went back to that February 2024 complete response letter, the FDA said no when we first tried to get marketing approval, you will see that one of their comments, I think it was the third comment down, it talked about how difficult it is if you had a drug on top of an antipsychotic. Because the antipsychotic, as Greg explained, the antipsychotic can either induce secondary negative symptoms or can treat secondary negative symptoms. If you are just looking broadly at negative symptoms, like I helped in the approval of COBENFY, and I know when they came out with their analysis, they said, "We treat secondary, and we treat negative symptoms," because if you looked at the PANSS, you looked at the negative symptom domains, you would see they had an improvement.

As Greg was explaining, and as FDA said in our complete response letter, you cannot tell where that is coming from. I think that you need, it is just like Stephen Marder on Slide 11 said, and that is why ISCTM has endorsed this idea that if you are going to look at primary negative symptoms, you have to look at a monotherapy study design.

Remy Luthringer

Executive Chairman and CEO

Any other question before maybe questions coming from people who are connected to?

Operator

We have several questions that have come in through the webcast in written form, a lot of which are a good continuation of what we've just been discussing here. This one's directed to Dr. Kirkpatrick. If a treatment for negative symptoms, like roluperidone, has more of an effect on function than the treatments for the positive symptoms, wouldn't you expect it to have a stronger effect size on the PSP scale than, say, the antipsychotics in the populations that they've studied?

Brian Kirkpatrick

Professor of Psychiatric Research

Well, just not necessarily. Keep in mind the comments I was making about the history of these patients. They have a long history of not being successful in a number of areas as a group, and overcoming that, partly through encouragement and better experience and treatment, it would be really important. Antipsychotics work relatively quickly. Recovering from a lifetime of habits would, I think, reasonably take longer. What's interesting is that in 12 weeks, you could see a significant effect on PSP at all.

Christoph Correll

Professor of Psychiatry and Molecular Medicine

Just one more point. The effect size for PSP with the antipsychotics used in the acute studies are again suffering from the pseudo-specificity, because your functioning goes up when you're not withdrawn and anxious that people might hurt you. You can't compare that effect size versus the residual negative symptoms that you're describing.

Operator

We have another question that's directed specifically to Dr. Correll. Your comments about the possible effect in early prodromal symptoms was interesting, and were you trying to imply that it could alter the future disease progression? Secondarily, it asks, among the nine indications that you showed on Slide 50, you said MDD would be your number one choice, but would you envision this being used as monotherapy, adjunctive therapy, or in the treatment-resistant depression setting? How best to show the effect in a clinical trial setting in MDD?

Christoph Correll

Professor of Psychiatry and Molecular Medicine

Yeah. I mentioned with the clinical high-risk syndrome that this is really something to try to figure out. These patients are not so easy to identify while they're on the path to maybe psychosis or other disorders. It is a testable hypothesis whether intervening with the mechanisms that underlie negative symptoms, one could stop the progression into other illnesses. I think we do not know enough about it, but that could be a Phase IV question. It would not be my first question, but it is certainly something very intriguing. Now, for the antidepressant side, there we do not have dopamine blockade that could counter some of the roluperidone effects.

I think here, one could try the combination treatment in patients who have needed antidepressants in the past and have residual symptoms, but there are others that might have residual symptoms even though they are coming off the antidepressant and have still some cognition, insomnia, and negative anhedonia type of symptoms. That would be a separate group that one could try as monotherapy.

Gregory Strauss

Professor of Psychology and Neuroscience

I can add a comment too about the clinical high-risk group. One of the really important things to know is that population, it is very prevalent for them to have negative symptoms, over three-quarters. I think the published numbers are 82% will have negative symptoms in the clinical range. Importantly, these are not attenuated. They are not attenuated like their positive symptoms are. Their negative symptoms are as severe as people with schizophrenia. That is point number one. Point number two is when they occur, even if they do not convert, meaning even if these at-risk youth never develop full psychotic disorder, they continue to have poor functioning. Whether their positive symptoms improve, whether they develop depression, anxiety, et cetera, they continue to have poor functioning. This drug could be very helpful for many people in this clinical high-risk syndrome group. Treating their negative symptoms is going to improve functioning.

These kids need clinical attention and help regardless of whether they convert. They are a clinical target that should be tackled.

Brian Kirkpatrick

Professor of Psychiatric Research

If you are a teenager, it is better if you are having some social success and learning how to maneuver in the adult world than not. So if you give them some success by helping them with the negative symptoms, that can only help them in later life.

Operator

I agree. We probably have time for one more question that came in, unless there is any more in the room, or ask this one. This is directed for all three of the speakers, and it is asking, in everyday clinical practice, how good are clinicians in their initial diagnosis and workup in identifying the same kind of symptoms that are specific in this clinical trial for roluperidone? Or is it going to involve a lot more education so that they can diagnose the patients that are most likely to benefit from this? Whichever one of the three of you.

Brian Kirkpatrick

Professor of Psychiatric Research

They routinely assess positive symptoms and negative symptoms. The finer points of negative symptoms, I think, are usually not well taught, and they are going to be a little fuzzier on that. But I think it is one of these things where they say, “Well, I cannot define it, but I know it when I see it.” It would be helpful to help them. It would be helpful if we could teach more people to some of the finer points in the assessment of negative symptoms. On the other hand, I think that actually the drug itself will end up teaching them a great deal.

Operator

Greg? Christoph?

Gregory Strauss

Professor of Psychology and Neuroscience

Yeah, I definitely agree with that. I think clinicians are almost always very adept at assessing depression, anxiety, disorganization, understanding when there are antipsychotic-induced effects. They’re implicitly aware of these factors that are common secondary sources. Whether they label them that or not may not matter that much. I think that they’ll be very good at knowing when they’re present, and by default, knowing when they’re absent as well, which will define the treatment group. I think in routine clinical practice, they are very adept at making this determination. It’s just really formalizing.

Christoph Correll

Professor of Psychiatry and Molecular Medicine

Yeah, I agree that clinicians know about positive and negative symptoms, so that’s the basic teaching. But it’s more like a qualitative, dimensional way. It will be very helpful for Minerva to develop some tools that accompany that in order to make people much more focused on it, because you watch for what you know, and you recognize what you can measure. It has to be very simple, just absent, mild, or more than that. But that’s doable, and we’ve had also examples for that, like quetiapine going into many billions of dollars for bipolar depression when there was a tear-off sheet and patients filled out something, how they felt and what symptoms they had. Having tools available sharpens the eye and brings out that there is a new treatment for a condition that we currently couldn’t treat. Education will be crucial for that.

Frank Sasinowski

Director

Yeah. Well, one thing I want to say on that from a regulatory perspective, and that’s all I can bring, what strikes me is that if the question was saying, can people trained in the field identify these patients that are the patient population, an indicator to me, as a kind of a regulatory maven, an indicator to me is that the speed with which C03, C07, and C19 enrolled, if you needed to go out and have a whole campaign to teach physicians how to identify these patients, then it would have taken longer than a normal antipsychotic study in schizophrenia to enroll. The pace at which these studies enrolled was the same. It’s as though physicians understood.

It's like Brian said, it's like Justice, as the lawyer in the room, Justice Potter Stewart said about pornography, "I know it when I see it." Brian didn't quote the good justice, but that's what he said, "You know it when you see it.

Remy Luthringer

Executive Chairman and CEO

Yeah. No, it is definitely a paradigm shift, and it needs definitely some help to educate a patient, caregiver, and also to help the prescriber. It is completely right. I think, Christoph, we have to think about these kind of tools, because they are simple. The beauty here is that we are not speaking about a fancy biomarker. We are not speaking about I spend my complete life on biomarkers, but definitely, this is very simple to identify these patients and to make sure that it means they are the right patients for our drugs, which is not always the case, to be very honest, in medicine.

Operator

All right.

Remy Luthringer

Executive Chairman and CEO

Any other questions?

Operator

I think we have exhausted the questions. If you want to turn it back to Remy to close things up.

Remy Luthringer

Executive Chairman and CEO

Yeah. I hope it was helpful. I hope you enjoyed it. I enjoyed it much, because it shows what we are doing is important for patients, and this is exactly what is motivating us. We will continue. We promise that we will continue to do all what we can in order to get to successful C19 study. Things are ongoing, are going well. We are really recruiting. We are still on time for the readout of second half of next year. Obviously, when we are coming closer, we will be more precise. Today, I keep this as generic as possible, because we need to work, focus, and come up with good data for the best of patients in need. Thank you again, and I think we have some snacks or something to eat.

You are more than welcome to stay, to speak with everybody, Minerva colleagues, our KOLs. Thank you again, Christoph, Greg, and Brian, and my friend Frank. Really, thank you for this.

Christoph Correll

Professor of Psychiatry and Molecular Medicine

Thanks for coming.

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Exhibit 99.2

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From Unmet Need to Reality

Roluperidone is potentially the first treatment for negative symptoms of schizophrenia

Corporate deck I November 2026

Updated: 2026.11.16

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 the clinical development of roluperidone; the potential therapeutic benefits and market opportunities of roluperidone; Minerva's expectations regarding the confirmatory clinical trial of roluperidone and related regulatory developments; Minerva's belief that it has reached alignment with the U.S. Food and Drug Administration ("FDA") on the Phase 3 confirmatory trial of roluperidone for the treatment of negative symptoms of schizophrenia; the timeline and results of the Phase 3 confirmatory trial; regulatory review and approval of roluperidone to be marketed in the United States and elsewhere; and management's ability to successfully achieve its goals. 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 (the "SEC"), including our Annual Report on Form 10-K for the year ended December 31, 2025, filed with the SEC on March 11, 2026, as may be updated by subsequent 10-Qs. 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.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. Neither we nor any other person makes any representation as to the accuracy or completeness of such data or undertakes any obligation to update such data after the date of this presentation. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

De-risked path to first approved therapy for negative symptoms of schizophrenia

Unmet Need	Negative symptoms drive profound, lifelong disability and remain untreated, with no FDA-approved therapies and clinical practice focused primarily on positive symptoms.
Only Therapy of its Kind	Roluperidone is only late-stage drug in development targeting primary negative symptoms of schizophrenia.
Clinical Evidence	Roluperidone monotherapy had a meaningful improvement in negative symptoms while supporting stable positive symptoms with a low relapse rate in two registrational trials (C03 & C07 studies).
De-risked Execution	Confirmatory Phase 3 trial design (C19 study) established following extensive FDA engagement; topline 12-week efficacy data expected in 2H 2027.
Financial Strength & Large Opportunity	$200 million financing in October 2025 provides funding through C19 Study data, NDA resubmission and preparation for negative symptoms of schizophrenia commercialization.* Roluperidone MOA provides label expansion opportunities for negative symptoms beyond schizophrenia.

*Led by Vivo Capital LLC, with participation from new and existing investors including Janus Henderson, Federated Hermes Kaufmann Funds, Farallon Capital, Coastlands Capital, Balyasny Asset Mgmt, Logos Capital, BSQUARED Capital, Trails Edge Capital Partners, Ally Bridge Group, Foresite Capital and Spruce Street Capital as well as several healthcare-focused funds, with Jefferies LLC acting as sole placement agent; $200 million consists of (i) $80 million up front, (ii) up to an additional $80 million subject to the full exercise of Tranche A warrants and (iii) a further $40 million that may be received in connection with cash exercise of Tranche B warrants contingent upon achievement of milestone event.

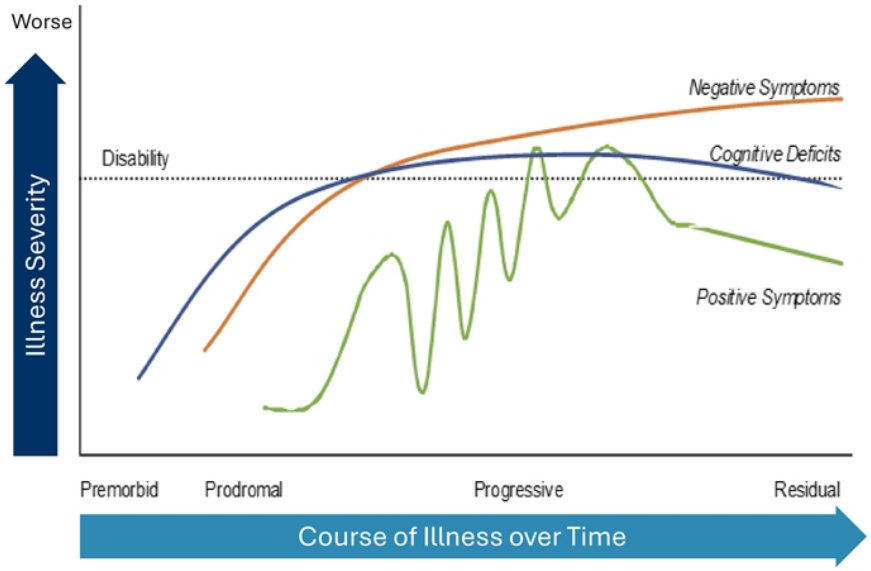
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Negative symptoms of schizophrenia drive lifelong disability and remain untreated

Current treatment options improve positive symptoms, but negative symptoms remain untreated and drive long-term disability

Schizophrenia has three symptom domains

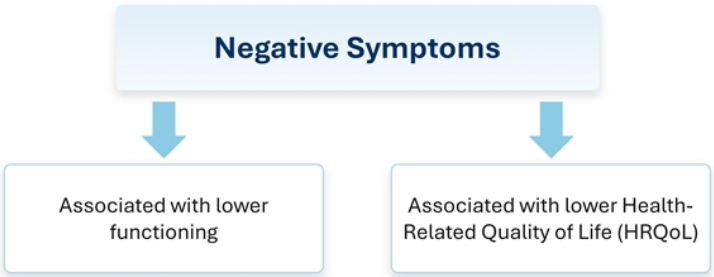
1) **Positive Symptoms** - delusions, hallucinations, disorganized behavior
2) **Negative Symptoms** - diminution or absence of normal behaviors related to motivation and interest
3) **Cognitive Deficits**



Source: Correll and Schooler, 2020

Negative symptoms, not positive symptoms, are the primary drivers of disability in schizophrenia

> *"While positive symptoms are often the most recognized features of schizophrenia due to their external observation of distorted normal function,* ***negative symptoms*** *are the lack of normal functions that* ***differentially affect schizophrenia treatment and prognosis.***" [1]



Improved functioning associated with improved HRQoL[1]

80%–90% of people with schizophrenia are **unemployed**[2,3,4,5]

vs. ~4–5% in the general population

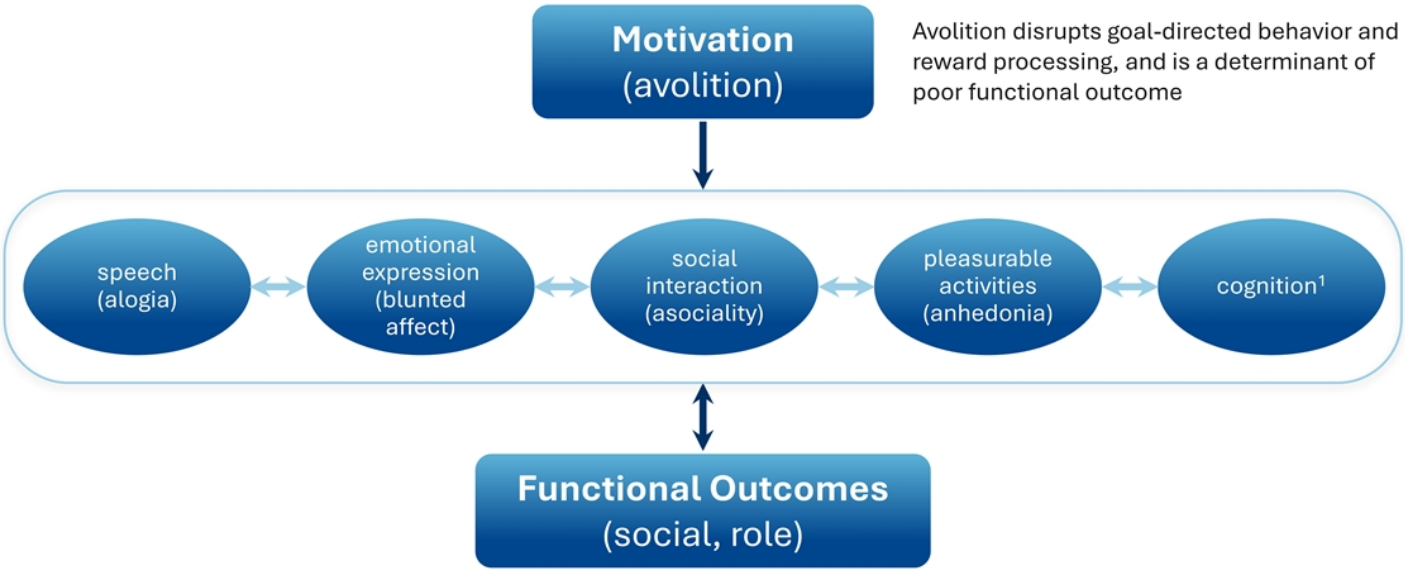
Negative symptoms; not positive symptoms drive disability in schizophrenia[6]

Consistent finding across >25 studies; yet no approved treatment targets negative symptoms

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[1] Chan A et al., Assoc between negative symptoms and HRQoL and functional outcomes in persons with schizophrenia. *Schizophrenia Research* (2026); [2] Evensen S et al. Prevalence, Employment Rate, and Cost of Schizophrenia in a High-Income Welfare Society. *Schizophr Bull.* 2016;42(2):476–483; [3] Holm M et al. Employment among people with schizophrenia or bipolar disorder. *Acta Psychiatr Scand.* (2021); [4] Rosenheck R et al. Barriers to Employment for People With Schizophrenia. *Am J Psychiatry.* (2006); [5] Davidson M et al. Nation-Wide Study on Percentage of Schizophrenia and Bipolar Disorder Patients Who Earn Minimum Wage or Above. *Schizophr Bull.* (2015); [6] Rabinowitz, J et al. Negative symptoms have greater impact on functioning than positive symptoms in schizophrenia: Analysis of CATIE data. *Schizophrenia Research* (2012).

Targeting avolition improves entire constellation of negative symptoms & functional outcomes



Avolition disrupts goal-directed behavior and reward processing, and is a determinant of poor functional outcome

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[1] Keefe, R et al. Cognitive Effects of MIN-101 in Patients with Schizophrenia and Negative Symptoms. *J.Clin.Psychiatry* (2018).

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Roluperidone for negative symptoms of schizophrenia

Clinical data that matters

C03 & C07 Studies: similar designs and similar results – guiding C19 confirmatory trial

	C03 Study 244 patients	C07 Study 515 patients
Negative symptoms (NSFS)*	**p ≤ 0.001** Statistically significant (64 mg)	**p ≤ 0.043** Nominally significant (64 mg)**†
Function (PSP total score)	**p ≤ 0.002** Statistically significant (64 mg)	**p ≤ 0.016** Statistically significant (64 mg)†
Avoids side effects of antipsychotics, like	❑ Metabolic syndrome ❑ Sedation ❑ Motor symptoms (extra pyramidal symptoms (EPS))	❑ Prolactin elevation ❑ Nausea

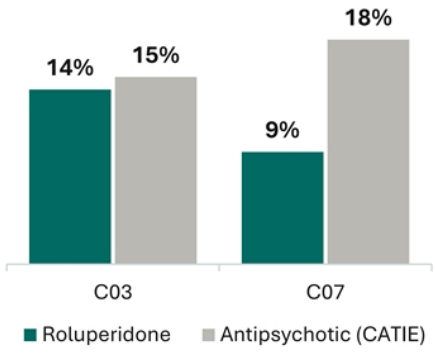
C03 & C07 Studies: 12-week DB efficacy, then OL extension (24 weeks in C03, 40 weeks in C07)

Relapse rate, psychotic symptoms

C03: after 12-week DB + 24-week OL

C07: after 12-week DB + 40-week OL

Roluperidone Studies vs. CATIE[1,2] ††



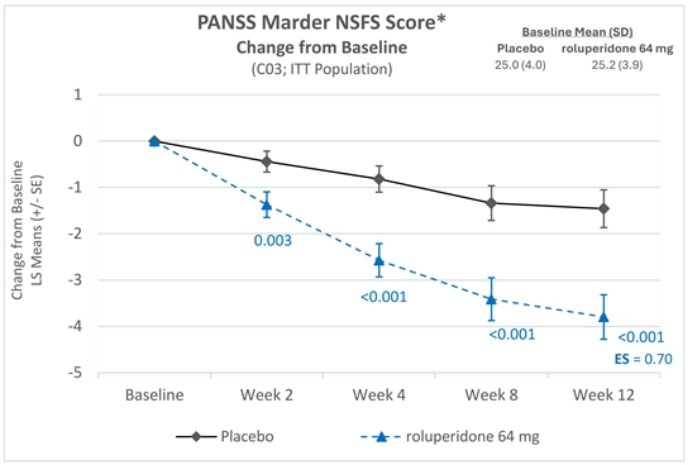
*NSFS was not primary endpoint of C03 Study but is shown because it is primary endpoint agreed with FDA for ongoing C19 Study (primary endpoint of C03 Study was PANSS Pentagonal-NFS, which also showed statistically significant improvement (0.004 for 64 mg); **C07 Study's primary endpoint met only on nominal basis (p ≤ 0.043) due to statistical plan's use of Hochberg Type 1 error correction; †mITT population (excludes 1 site for reasons of implausible data). ††Historical comparison data from CATIE study in patients meeting inclusion-exclusion criteria of Minerva's C03 and C07 studies. [1]Lieberman JA et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *NEJM* (2005); [2]Speyer H, et al. Moderate to severe negative symptoms predict low risk of symptoms worsening in schizophrenia patients in CATIE. *Schizophr Res.* (2026). Other source: Minerva Neurosciences.

DB: double-blind. **OL:** open-label extension. **NSFS:** PANSS Marder Negative Symptoms Factor Score. **PSP:** Personal and Social Performance scale.

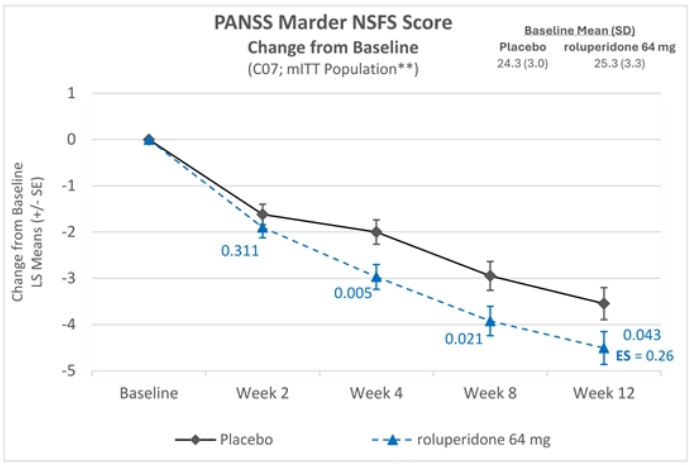
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C03 & C07 Studies: Negative Symptom Factor Score

C03 Study



C07 Study



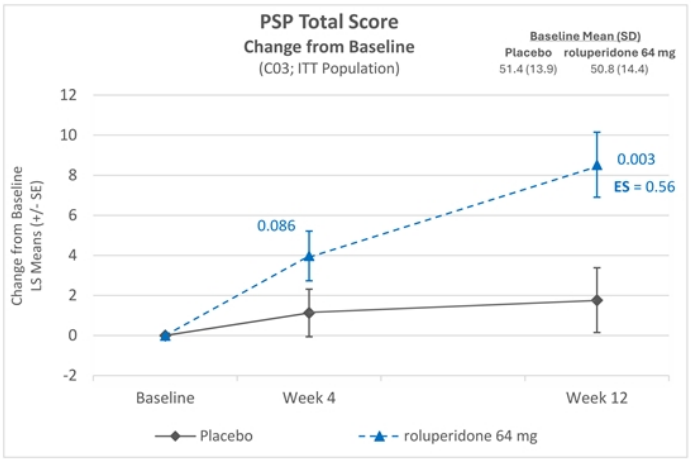
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* NSFS: Negative Symptom Factor Score calculated from PANSS scale (Marder et al., 1997)

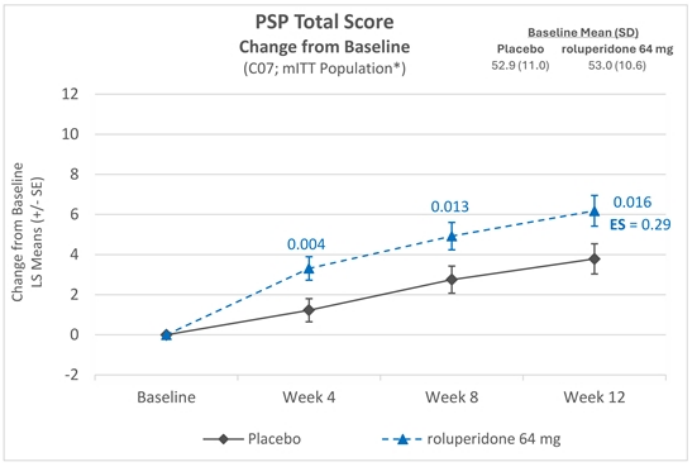
** mITT population (excludes 1 site for reasons of implausible data)

C03 & C07 Studies: Personal and Social Performance (PSP) Score

C03 Study



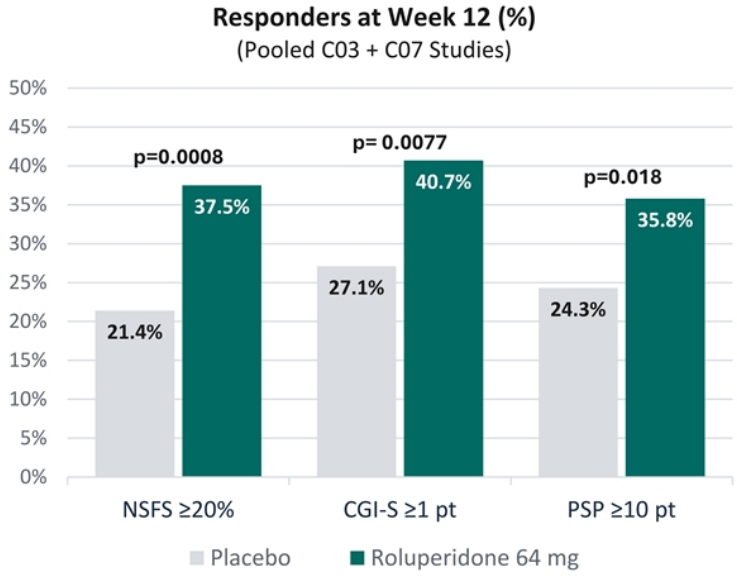
C07 Study



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

Responder Analysis: meaningful across three independent anchors



NUMBER NEEDED TO TREAT

7	8	9
NSFS ≥20%	CGI-S ≥1 pt	PSP ≥10 pt

Higher responder rates than placebo on symptoms (**NSFS**), clinician global (**CGI-S**), and functioning (**PSP**) (RR 1.47–1.75).

NNTs of 7–9 fall within the range of approved antipsychotics (NNT 5) and antidepressants (NNT 8); comparisons are indirect.

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Pooled analysis of C03 + C07 studies, roluperidone 64 mg vs placebo,12-week completers. **NSFS:** Marder Negative Symptoms Factor Score; **CGI-S**: Clinical Global Impression - Severity of illness; **PSP:** Personal and Social Performance scale. Source: Minerva Neurosciences. Source: Minerva Neurosciences.

Conclusions from C03 and C07 Studies

Roluperidone demonstrated clear statistical significance on multiple efficacy endpoints:

- ✓ Improves primary negative symptoms (i.e., NSFS)
- ✓ Improves functioning (i.e., PSP)
- ✓ Improves avolition
- ✓ Stable positive symptoms, with a low relapse rate

Roluperidone avoids well-known troubling sides effects seen with atypical antipsychotics:

- ✓ Metabolic syndrome
- ✓ Sedation
- ✓ Motor symptoms (extra pyramidal symptoms (EPS))
- ✓ Prolactin elevation
- ✓ Nausea (for muscarinic antipsychotics)

Unique pharmacological profile that drives the differentiated clinical benefits in previous clinical trials

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De-risked, execution-focused confirmatory C19 trial design

FDA Alignment on C19, confirmatory trial design: ***actively enrolling NCT07565428***

Alignment reached on 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]

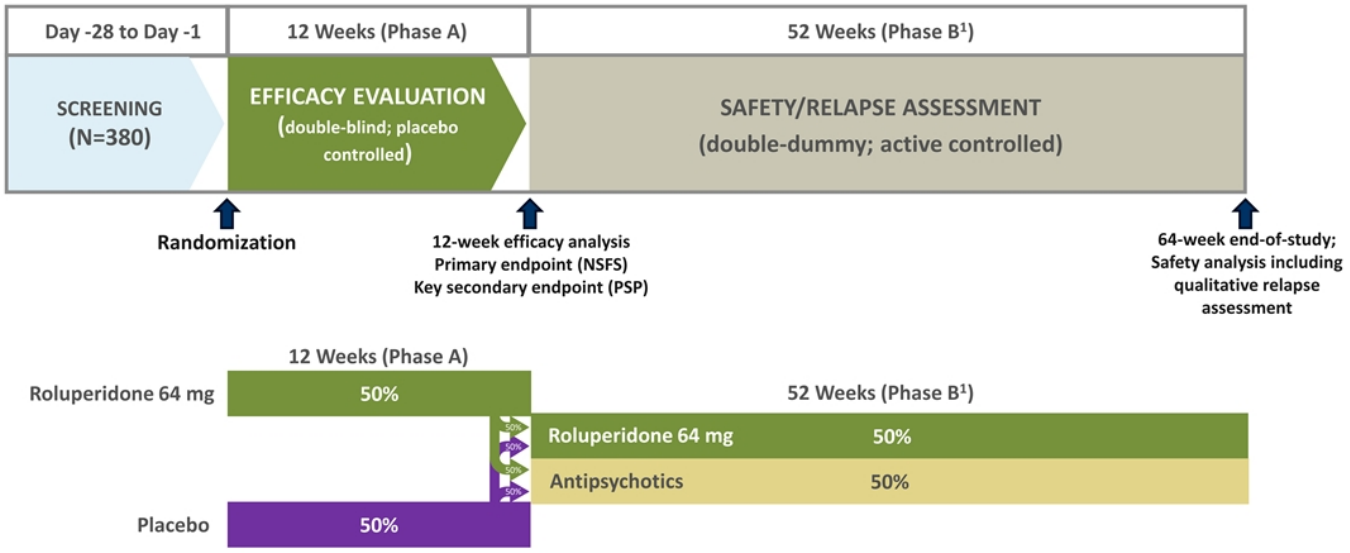
Excerpts from FDA Meeting Minutes

- ***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 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.*
- *[The approach]* ***would represent a new treatment paradigm.***

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[1]- FDA Meeting August 16, 2024

C19 Study: ***actively enrolling***



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

Execution-focused trial maximizes probability of a clean, interpretable C19 Study outcome

Trial Design Improvements

- **64 mg of roluperidone** in treatment arm, the dose which showed greater symptom improve in C03 and C07 trials
- Single active dose (64 mg) versus placebo **eliminates need for Type I error correction** applied in C03 and C07 trials
- Single active dose (64 mg) versus placebo **reduces treatment expectation bias**, which inflates placebo response
- Fewer patient assessment visits to **limit the "nursing effect,"** which inflates placebo response in CNS trials
- Rigorous, systematized **inclusion and exclusion criteria** to ensure enrollment of appropriate patients

Scale, Monitoring and Data Quality Controls

- ~380 patients across ~40 sites in the U.S. (25–30%) and four European countries
- **Focused site footprint** reduces variability and supports statistical integrity; and selection accounts for **prior site performance** in C03 and C07 trials
- **Standardized training** in PANSS ratings; and **oversight to support patient selection consensus** between investigators and sponsor
- Independent expert **oversight of rating quality** with real-time monitoring
- **Centralized data collection** using electronic tablets with built-in prompts to reduce rater error

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Market opportunity in negative symptoms of schizophrenia & beyond

~900,000 US adults fit the roluperidone target profile amid massive need for negative symptoms treatments

~3.4M
Adults with schizophrenia, U.S.
1.17% age-adjusted prevalence[1]

→

~2.2M
Diagnosed schizophrenia prevalence, U.S.[2]
Estimated to increase to ~2.5M by 2035[2]

→

~1.3M
Clinically relevant, impairing negative symptoms
~60% of treated patients[3]

→

~900k
Stable patients: target patients for roluperidone
~68.9% of diagnosed patients have stable positive symptoms[4]

~$7.1B
US schizophrenia drugs market, 2025
Growing at ~4.5% CAGR[2]

$0
Approved treatments for negative symptoms in the US

>$2B
Roluperidone peak annual US net sales potential as the first approved negative-symptoms therapy[5]

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[1]Krasa et al., National and State Societal Costs of Schizophrenia in US in 2024. *JAMA Psychiatry* (2026); [2]Clarivate Schizophrenia Disease Landscape & Forecast (Major Markets) (2026); [3]Correll CU, Schooler NR. Negative Symptoms in Schizophrenia: A Review and Clinical Guide for Recognition, Assessment, and Treatment. *Neuropsychiatr Dis Treat.* (2020); [4] Starzer M et al., 20-year trajectories of positive and negative symptoms after the first psychotic episode in patients with schizophrenia spectrum disorder: results from the OPUS study. World Psychiatry (2023); [5]Based on estimates including Minerva Neurosciences estimates of TAM, market share, pricing and adoption including input from 2024 Payer survey conducted by Lumanity Inc.

Pipeline of label expansion opportunities with roluperidone

Negative symptoms occur in 19 DSM-5 disorders[1]

Adjacent Psychiatry & Mood Disorders

Schizoaffective & Related Schizophrenia-Spectrum Disorders
Mechanistically aligned

Major Depressive Disorder (MDD) residual symptoms
Anhedonia and low motivation; possible adjunct to antidepressants

Apathy in Neurodegenerative Disorders

Alzheimer's Disease apathy
No approved therapy; established apathy endpoints

Parkinson's Disease apathy
Under-treated; distinct from motor symptoms

Apathy in Other Neurologic Disorders

Traumatic Brain Injury (TBI) · Multiple sclerosis
Apathy and reduced initiative after injury or in MS

Autism Spectrum Disorder · Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) · Long COVID
Areas of high unmet need involving social withdrawal or reduced ability to engage in goal directed behavior

Cognitive Impairment

Cognitive Impairment in Schizophrenia (CIAS)[2]

Cognitive Impairment in Alzheimer's Disease

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[1]Strauss, GP & Cohen, AS. A transdiagnostic review of negative symptom phenomenology and etiology. *Schizophrenia bulletin* (2017); [2]Keefe, R et al. Cognitive Effects of MIN-101 in Patients with Schizophrenia and Negative Symptoms. *J.Clin.Psychiatry* (2018).

Summary: The Minerva Confluence

Right pharmacology and MOA

- **Only drug to date** to show a significant, clinically relevant improvement
- Specific to **primary negative symptoms** of schizophrenia
- **Label expansion** opportunity for multiple indications beyond schizophrenia

Right patient profile

- Clinically relevant population with predominant and **impairing negative symptoms**
- Moderate to severe negative symptom patients, as shown in C03, C07, and several other studies, have a relatively **low risk of relapse**

Right phase 3 trial design

- **Previous experience** with two statistically significant (one nominally) trials
- **FDA alignment** on ongoing Phase 3 trial
- **Ongoing 'high touch'** confirmatory Phase 3 trial increases probability of success

Right moment

- **Growing awareness** of unmet need in psychiatry community
- Backed by **world-class investors**
- Near-term opportunity to be the first treatment for negative symptoms of schizophrenia

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From Unmet Need to Reality

Roluperidone is potentially the first treatment for negative symptoms of schizophrenia

Corporate deck I November 2026