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For Sufferers of Negative Symptoms of Schizophrenia, a New Medication Offers Hope

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In late 2008, Tanara went from a thriving college student with a restaurant server job to someone she didn't recognize.

"I didn't want to get dressed or even get out of bed. I didn't understand what was going on."¹

By July 2009, she was hospitalized.

"The doctors there thought I had a mood disorder—they thought maybe I was bipolar—and put me on a number of medications. But once I got out of the hospital, I stopped taking them. My symptoms were gone, so I assumed I'd be fine."

She didn't know it at the time, but Tanara had been experiencing the early symptoms of schizophrenia.

Schizophrenia is most known for hallucinations (hearing or seeing things that aren't there), persistent false beliefs, disorganized speech, and bizarre behavior. These symptoms are known collectively as the positive symptoms of schizophrenia. But among the earliest symptoms of the disease are negative symptoms. Patients seem depressed. They can't get out of bed; they don't get pleasure out of things they used to enjoy. They don't show emotion, they don't talk as much, and they withdraw from other people.

Schizophrenia	
Positive symptoms	Negative symptoms
- Delusions - Hallucinations - Disorganized speech - Disorganized behavior 	- Flat affect - Lack of motivation - Lack of enjoyment of fun activities - Lack of social interaction - Decreased speech 

Table 1. Positive and Negative Symptoms of Schizophrenia

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Dr. John Lauriello is the Chair of Psychiatry at the University of Missouri in Columbia, Missouri and a leading expert on schizophrenia.²

“What isn’t always appreciated, and what has the most impact on functioning, are the negative symptoms: the lack of normal affect, speech, pleasure, sociality – those negative symptoms, and the cognitive problems that people with schizophrenia have, that really affects how one does on their day-to-day activities.”

These symptoms also can be the most stubborn to treat.

“What makes matters even more complicated is that often our antipsychotics mimic some of the problems that people have with negative symptoms through their side effects.”

Dopamine, most known for being the “reward” neurotransmitter that is associated with motivation and involved in the process of addiction, is also hyperactive in certain parts of the brain in schizophrenia.³ So for years, treatments of schizophrenia have been focused on blocking the transmission of dopamine between neurons in the brain. The problem is, these medications block dopamine transmission throughout the entire brain, including parts where the transmission is already too low in schizophrenia. It’s as if you are trying to carve a precise, lifelike, human sculpture from a block of marble, but instead of a chisel, you have a jackhammer. This widespread blocking of dopamine transmission affects the mesocortical pathway, where dopamine is needed for emotional regulation, so it can directly worsen mood. It also affects the nigrostriatal pathway, where dopamine is critical for voluntary movement. So after years of high doses of these antipsychotics, patients can develop a form of Parkinsonism, resulting in slowed body movements. These drugs also tend to have antihistamine effects, similar to diphenhydramine (Benadryl), which causes drowsiness.

A team of researchers with Minerva Neurosciences led by Dr. Michael Davidson and Dr. Jay B. Saoud set out to solve this problem by testing an antipsychotic that worked in a new way. Instead of blocking dopamine transmission, this medication, known as roluperidone, would block other receptors implicated in negative symptoms of schizophrenia: the sigma-2 receptor, the Serotonin (5-HT_{2A}) receptor, and the alpha-1A receptor.⁴

To do this, they enlisted 513 patients with schizophrenia with moderate to severe negative symptoms, as determined by a widely validated and accepted psychometric instrument for measuring the severity of schizophrenia conditions (PANSS). These patients were randomly assigned to 12-week treatments with one of three medications: high-dose roluperidone, low-dose roluperidone, or an inactive placebo.

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The results were promising. At the end of the 12 weeks, negative symptom scores decreased (improved) significantly in the high-dose group. Compared with the placebo group, the high dose group was almost twice as likely to show a 20% decrease in their negative symptoms scores (39% vs. 23%) and their overall schizophrenia symptoms scores (20% vs. 9%).

The researchers found several different adverse effects emerged in 33-42% of patients during the experiment, but they indicated that most of these symptoms were mild to moderate, and there weren't significant differences between the roluperidone groups and the placebo group.

Minerva Neurosciences faces an uphill climb to get the drug to market. In February 2024, the Food and Drug Administration (FDA) rejected the company's New Drug Application (NDA), on the grounds that the study wasn't long enough in duration (less than 12 months), it didn't assess interactions with other antipsychotics, and the statistical evidence wasn't strong enough to prove clinical efficacy.⁵ Undeterred, in October 2025, the company announced financing of up to \$200 million to advance a new and improved, 52-week-long Phase 3 confirmatory trial and resubmission of its New Drug Application (NDA).⁶ In March 2026, the company announced it had screened its first patient for the Phase 3 confirmatory trial, and would be expecting top-line efficacy data in the second half of 2027.⁷

Tanara was started on a monthly injectable antipsychotic medication for schizophrenia (approved before the roluperidone studies). She was lucky that her schizophrenia symptoms, positive and negative, improved with treatment.

"My schizophrenia symptoms were under control, and I started feeling better. I regained interest in the things I used to enjoy, like calling my family and going for walks in the park."

For other sufferers of negative symptoms of schizophrenia the development of roluperidone offers a ray of hope.

It is the kind of hope that Tanara, now a peer support specialist at a rehabilitation facility, strives to cultivate.

"My goal is to help other patients get their confidence back. If you don't have that confidence, you won't ever feel that you deserve to be happy. I know because I lost my confidence for a while. I try to let them know it's possible to have the happy and beautiful life you had before the diagnosis."

References

1. Derrow P. Living with schizophrenia: one story of coping with the mental illness. *JNJ.com*. Published May 8, 2017. Accessed June 14, 2026. <https://www.jnj.com/health-and-wellness/i-have-schizophrenia-what-its-really-like-living-with-the-mental-illness>.
2. CME Outfitters. Novel strategies addressing negative symptoms of schizophrenia. *YouTube*. Published July 29, 2019. Accessed June 14, 2026. <https://www.youtube.com/watch?v=iZfja55OCVM>.
3. Brisch R, Saniotis A, Wolf R, et al. The role of dopamine in schizophrenia from a neurobiological and evolutionary perspective: old fashioned, but still in vogue. *Front Psychiatry*. 2014;5:47. doi:10.3389/fpsy.2014.00047.
4. Davidson M, Saoud J, Staner C, et al. Efficacy and safety of roluperidone for the treatment of negative symptoms of schizophrenia. *Schizophr Bull*. 2022;48(3):609-619. doi:10.1093/schbul/sbac013.
5. Minerva Neurosciences receives complete response letter from FDA for new drug application for roluperidone for the treatment of negative symptoms in patients with schizophrenia. *Minerva Neurosciences, Inc*. Published 2024. Accessed June 14, 2026. <https://ir.minervaneurosciences.com/news-releases/news-release-details/minerva-neurosciences-receives-complete-response-letter-fda-new>.
6. Minerva Neurosciences announces financing of up to \$200 million to advance roluperidone for the treatment of negative symptoms in patients with schizophrenia through a phase 3 confirmatory trial and resubmission of its new drug application and preparation for US commercial launch, if approved. *Minerva Neurosciences, Inc*. Published 2025. Accessed June 14, 2026. <https://ir.minervaneurosciences.com/news-releases/news-release-details/minerva-neurosciences-announces-financing-200-million-advance>.
7. Minerva Neurosciences announces first patient screened in global phase 3 confirmatory trial of roluperidone for the treatment of negative symptoms of schizophrenia. *Minerva Neurosciences, Inc*. Published 2026. Accessed June 14, 2026. <https://ir.minervaneurosciences.com/news-releases/news-release-details/minerva-neurosciences-announces-first-patient-screened-global>.