Experimental drug shows promise for schizophrenia
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An experimental drug may ease a range of symptoms that strike people with schizophrenia, without the side effects of existing medications, an early clinical trial suggests.

Researchers found that, over one month, the drug helped manage the different ways in which schizophrenia manifests—from delusions and hallucinations, to flattened emotions and social withdrawal.

Among 120 patients who took the drug, 65% were responding by week four. That compared with 44% of patients given a placebo.

The drug—dubbed SEP-363856—also appeared to avoid the side effects common with standard antipsychotic medications.

Experts were hopeful that the findings, published April 16 in the New England Journal of Medicine, will lead to a new treatment option.

While there is a laundry list of antipsychotic medications for schizophrenia, they are decades old. And for the millions of people worldwide with the mental illness, there is still a critical "unmet medical need," said study author Kenneth Koblan.

He is chief scientific officer at Sunovion Pharmaceuticals in Marlborough, Mass., the company developing SEP-363856.

One issue with existing medications is that side effects can make adherence difficult, Koblan said.

Older, "first-generation" drugs can cause movement impairments similar to those seen in Parkinson's disease—tremors, joint stiffness and coordination problems. Relatively newer, second-generation antipsychotics are less likely to cause those side effects, but they can spur weight gain and high blood sugar and cholesterol levels.

Beyond that, existing medications only address one group of schizophrenia symptoms—the hallucinations, delusions and confused thoughts that doctors call "positive" symptoms. (In this case, "positive" means present.)

The drugs work well against positive symptoms in about 70% of patients, said Dr. Donald Goff, a professor of psychiatry at New York University School of Medicine, in New York City.

But, Goff said, they do not ease the "negative" symptoms that plague people with schizophrenia. "Negative" refers to what's lost, and the symptoms include flattened emotions, difficulty feeling pleasure and withdrawal from others.

In this short-term trial, SEP-363856 eased both positive and negative symptoms.

"What's striking, to me," Koblan said, "is the efficacy against negative symptoms."

Goff, who wrote an editorial published with the study, agreed the initial results are "very
encouraging."

"This might help with symptoms that are not improved by current medications," he said, "and it might not have the same side effects."

It's not fully clear how the drug works, according to Koblan, but it does act through a different mechanism than current antipsychotics.

While those drugs are numerous, Goff said, they all work in a similar manner—by blocking a receptor on brain cells called D2, which interacts with the chemical dopamine. Blocking D2 can lessen psychosis symptoms, but is also responsible for the drugs' most troublesome side effects.

The experimental drug, in contrast, leaves D2 alone. Instead it stimulates a different brain receptor, called TAAR1. That receptor helps modulate dopamine transmission.

Dr. Ken Duckworth is medical director of the National Alliance on Mental Illness. He said, "I'm glad to see they're investing in a drug with a new mechanism of action. And I'm cautiously optimistic about it."

Cautious, he said, because this was a short-term trial. Significant side effects did not show up, but those issues can take time to manifest, Duckworth noted.

The trial involved 245 schizophrenia patients aged 18 to 40, all in the earlier course of the disease. About half were randomly assigned to take SEP-363856 capsules once a day, while the rest received placebo capsules.

After a month, almost two-thirds of patients on the drug were showing a response—meaning their scores on a standard measure of symptoms had improved by at least 20%.

After that point, all patients had the option to enter a six-month extension study where the drug was given to everyone. Overall, the effectiveness was maintained, Koblan said.

A larger trial of the drug is underway. If it proves