

treatments

# Depression Treatments Inspired By Club Drug Move Ahead In Tests

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Experimental medicines related to ketamine, an anesthetic and club drug, are making progress in clinical tests.

Antidepressant drugs that work in hours instead of weeks could be on the market within three years, researchers say.

"We're getting closer and closer to having really, truly next-generation treatments that are better and quicker than existing ones," says Dr. Carlos Zarate, a researcher at the National Institute of Mental Health.

The new drugs are based on the anesthetic ketamine, which is also a popular club drug known as Special K. Unlike current antidepressants, which can take weeks to work, ketamine-like drugs have an immediate effect. They also have helped people with depression who didn't respond to other medications.

The drug that is furthest along is esketamine, a chemical variant of ketamine that has been designated a potential breakthrough by the Food and Drug Administration. Esketamine is poised to begin Phase 3 trials, and the drug's maker, Johnson & Johnson, plans to seek FDA approval in 2018.



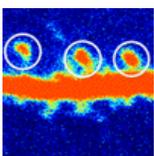
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Another ketamine-like drug on the horizon is rapastinel. It has completed Phase 2 studies, which showed "rapid, substantial, and sustained reductions in depressive symptoms," according to the drug's maker, Naurex.

"I think it's highly probable that we'll see some version of one of these treatments being approved in the relatively near future," says Dr. Gerard Sanacora, director of the Yale Depression Research Program. "In my mind it is the most exciting development in mood disorder treatment in the last 50 years."

Sanacora has done consulting work for both Naurex and Johnson & Johnson. He is also an investigator for a study in which esketamine will be given to suicidal patients.



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The new drugs come nearly a decade after Zarate and other researchers from the National Institutes of Health published a study showing that ketamine helped most people with major depression in less than two hours. "When we saw the first initial responses you say, wow, this will

definitely revolutionize our treatments for mental illness," Zarate says.

Since then, many other studies have confirmed that ketamine usually works even when other drugs have failed. "At this point I think it's incontrovertible that the drug has clear, robust rapid antidepressant effect," Sanacora says. Studies suggest that effect usually lasts for a week or so.

But ketamine itself has shortcomings. It can cause hallucinations, and it's a drug that is frequently abused.

Also, from the perspective of drug companies, ketamine is problematic because it is already available as an inexpensive generic drug. So companies including Naurex and Johnson & Johnson began searching for compounds they could patent that would have a similar effect in the brain.

If esketamine and repastinel reach the market, they could be blockbuster sellers. Johnson & Johnson included esketamine on a list of drugs with potential annual sales of more than \$1 billion.

In the meantime, many psychiatrists are already prescribing ketamine to severely depressed patients who haven't been helped by other drugs, even though ketamine hasn't been approved by the FDA for that purpose. This sort of "off-label" prescribing is common in psychiatry, Zarate says.

"I don't think it's necessarily irresponsible," says Sanacora, who has prescribed off-label ketamine to some of his own patients. But it's important that patients who get the drug understand that it's still experimental and are warned of potential risks. He also recommends that patients who want to try ketamine enter a clinical trial.

One looming question about all the ketamine-like drugs is whether they will be safe and effective after months or years of use. "Maintaining is going to be key," Zarate says.

ketamine   depression   antidepressants   mental health