# Yale Startup BioHaven Pharmaceutical Developing New Treatments for Anxiety and Depression

*By Brita Belli*

Yale researchers were among the first to identify ketamine – a drug best known for its use by club goers for its hallucinogenic effects—as a promising therapy for patients with treatment-resistant depression and anxiety. The finding was a major discovery that revealed a new pathway for treating these neuropsychiatric disorders. Rather than acting on the brain's levels of serotonin, norepinephrine and dopamine as other mood and anxiety drugs do, ketamine worked on regulating levels of a neurotransmitter called glutamate. "It's a completely different approach," says Gerard Sanacora, professor of psychiatry and director of the Yale Depression Research Program. "It's an all-purpose approach that's physiologically-based across diagnostic categories."

Having witnessed successful results using ketamine on depressed patients, Sanacora, along with colleagues John Krystal, chair of the Department of Psychiatry at Yale and Chief of Psychiatry at Yale New Haven Hospital and Vlad Coric, associate clinical professor of psychiatry at Yale, turned to the Yale Office of Cooperative Research (OCR) to file the necessary patents and begin the process of translating their research into new therapies. What emerged last year was the startup BioHaven Pharmaceutical Holding Company, Ltd, a company dedicated to developing a new generation of drugs for treating anxiety and depression by regulating glutamate.

The company received an initial $3.5 million investment from Portage Biotech Inc. to advance product development in early January. This will enable BioHaven to raise the additional capital to fund the subsequent clinical efficacy trials.

Regulating glutamate is a delicate process – too much is toxic, too little results in behavior problems. Sanacora has developed a novel method of measuring glutamate using magnetic resonance spectrometry (MRS)—a scanning device that is similar to an MRI but is used to measure chemical concentrations. That makes it easier for the researchers to get an immediate understanding of the therapeutic dose range at which patients may best respond to treatment.

The scientists have seen compelling results in patients with treatment-resistant anxiety and depression. "When we give patients one dose of the NMDA antagonist ketamine, we see an antidepressant effect in one to three hours," Coric says. "Other treatments can take up to four weeks to work." BioHaven will leverage Yale's expertise in the glutamatergic space and take new formulations of glutamate modulating agents into Sanacora's MRS studies to find the optimal dosage with minimal side effects.

Pfizer veteran and Portage CEO Declan Doogan is serving as executive chairman of BioHaven. "We have access to top talent and compounds with known safety profiles to be reformulated for the clinic," Doogan says. "This will allow us to go into Phase II and Phase III trials. Our goal is to have these new drugs characterized in two to three years."

The startup's R&D efforts will be based in New Haven to be close to the scientific founders and a vibrant scientific community. "At OCR, we're constantly working to create a critical mass of biotech companies, to enable people committed to the biotech industry to remain in New Haven and close to the Yale community," says David Lewin, senior associate director of licensing for OCR.