

Envisioning a psychedelic future for psychiatric treatment

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Jason Wallach has a vision. He sees Philadelphia becoming a center for

psychedelic studies. From his laboratory at the University of the Sciences, Wallach is leading a network of national researchers delving into the mind-altering substances.

In August, Wallach paired with Compass Pathways, the mental health company backed by entrepreneur Peter Thiel, a founder of Paypal and Palantir Technologies.

Compass gave the researcher \$500,000 to launch a Drug Discovery Center in West Philadelphia to investigate "new serotonergic compounds." These substances work on a specific neuroreceptor in the brain, 5-HT_{2A}, and include the active ingredients in psilocybin, DMT, mescaline, ibogaine and LSD.

Last week, Compass (NASDAQ: CMPS) announced it is building on its Wallach-led project to include researchers at the University of California, San Diego (UCSD) and the Medical College of Wisconsin (MCW).

"We're looking for new molecules with useful properties," said Wallach, 34, an assistant professor of pharmaceutical sciences. "We're expanding and hope to do exciting work. It would be great to put USciences on the map for determining the direction of the pharmaceutical industry."

Last summer USciences announced three new online certificate programs on marijuana that train students looking to join the rapidly growing industry.

Also last week, USciences announced it was considering a merger with St. Joseph's University to foster growth. The two institutions could become the latest case of consolidation in a sector that is contending with fewer students and high tuition.

Psychedelics—once identified with the counterculture of the 1960s and CIA mind control experiments—are undergoing a renaissance.

About two dozen companies and several nonprofits are leading active investigations. Compass Pathways is running a Phase 2b clinical trial with COMP360, a synthetic version of psilocybin for treatment-resistant depression. Results are due at the end of the year. Psilocybin has been granted a "breakthrough therapy" designation from the FDA, indicating that the agency believes the substance may offer a significant improvement over existing treatments.

"There's a leading hypothesis that these drugs cause changes in synaptic plasticity and strengthen the networks of the brain," Wallach said. "In truth, though that happens, whether that underlies the clinical effects is still not established."

Compass went public last year with a market cap now around \$1.6 billion. About a dozen companies pursuing investigations of psychedelics are listed on Canadian stock exchanges.

"There's so much hype," said Wallach, who studied cell biology at Indiana University of Pennsylvania before earning his PhD in Pharmacology and Toxicology at USciences.

His early research focused on cannabinoids, the psychoactive compounds in marijuana. "I think many of them have promise. But the lines are much clearer here with our project."

For now Wallach is investigating non-psilocybin substances that work on the 5-HT_{2A} receptor that exists throughout the human central nervous system.

Those receptors bind to drugs such as psilocybin and LSD and trigger

psychedelic experiences. Those receptors also play a crucial role in higher level functioning of the brain, Wallach said.

"So ketamine and PCP-like substances, those are what we're exploring. We are very focused on the similarities to psilocybin. "

The \$500,000 in funds from Compass will let Wallach add staff to his Philadelphia-based team "to use the tools of drug discovery to tailor the molecules for specific therapeutic indications," he said.

When Wallach started as an instructor at USciences in 2017, research was not on his job description, "but the university was kind enough to give me some lab space."

"At that time it was me, Hamilton (Morris, host of Vice TV's docuseries "Hamilton's Pharmacopeia") and several hard working undergraduate students. The responsibilities quickly changed," he said. "I currently have two lab technicians, a PhD candidate student, as well as two undergraduate students and one volunteer, Hamilton. We are also looking to hire a lab technician and post-doctoral researcher immediately. We have collaborators all over the world and so are working with many well-renowned teams."

Wallach, who often appears on Hamilton's Pharmacopeia, keeps his staff busy. He has around 10 projects ongoing at various stages that will lead to publication in scientific journals.

A handful of major universities and research centers are pursuing similar research. Last summer, the University of North Carolina received nearly \$27 million from DARPA, the research arm of the Department of Defense, to develop new psychiatric medicines from psychedelics. In September, Johns Hopkins University in Baltimore launched the first-of-its-kind Center for Psychedelic and Consciousness Research to

investigate the substances. The same month, UC Berkeley opened the Center for the Science of Psychedelics. Hopkins, along with New York University, recently completed Phase 3 clinical trials with the nonprofit Multidisciplinary Association for Psychedelic Studies for MDMA-assisted therapy for PTSD.

Lars Christian Wilde, co-founder of Compass Pathways, said he chose Wallach to lead research after a worldwide search.

"Wallach is one of the most knowledgeable people in the psychedelic research world," said Wilde from his home in Dusseldorf, Germany. "But Wallach also has a broad understanding of neuroscience. He had read every paper under the sun. So I asked him if he'd be interested in collaborating. We were fortunate that he said 'yes'."

USciences has a "rich history" with Big Pharma, Wallach said. The school, founded in 1821 as the Philadelphia College of Pharmacy, counts many industry titans among its alumni. Eli Lilly (1907), whose doctoral thesis was on "The Comparative Physiological Effects of Several Varieties of Cannabis Sativa," founded Eli Lilly and Company ; Gerard Rorer (1931) started Rorer Pharmaceuticals, now Sanofi; William Warner (1856) founded Warner-Lambert, now part of Pfizer; And Robert L. McNeil (1938) began McNeil Laboratories which became part of Janssen.

"I don't think every company is jumping at the bit to enter the psychedelic space, but they're taking notice," Wallach said.

Janssen, a division of Johnson & Johnson (NYSE JNJ) is the only Big Pharma company known to currently market a drug with psychedelic roots. Its FDA-approved esketamine drug, a powerful version of ketamine sold under the brand name Spravato, is used for people with severe treatment-resistant depression.

"Janssen laid the foundation," said Wallach.

Wallach has remained busy during the pandemic. He is working with Bexson Biomedical to develop a subcutaneous pump for ketamine to manage pain. Additionally, Wallach serves on the advisory board of MindCure Health Inc.(OTC: MCURF) , a Vancouver, Canada-based psychedelic therapeutics company. In addition to his assistant professor position at USciences, he serves as an adjunct instructor at Cooper Medical School of Rowan University in Camden.

Wallach's virtual partners in the Drug Discovery Center include Adam Halberstadt of UCSD, an expert on the behavioral neuropharmacology of psychedelics and John McCorvy at Milwaukee's MCW, a pharmacologist who has investigated psychedelic, anti-psychotic, and antidepressant drugs.

His West Philadelphia lab has already produced 100 novel compounds, Wallach said.

"I see medicinal chemistry in many ways as an art," he said. "Often there is logic to a proposed modification but sometimes the molecule just looks beautiful or you have a gut feeling. The process is exciting, as a minor change in the structure can lead to profound changes in the activity. And you can learn a lot from studying these changes in activity.

"It's fun to create things which may not exist anywhere else in the universe."

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