

FT Magazine Drugs research

Anorexia is the deadliest psychiatric disorder. Could psychedelics help?

A Nasdaq-listed biotech is trialling the active ingredient in magic mushrooms as a possible new treatment

Hannah Kuchler 18 MINUTES AGO

Aly began to cry as she took a sip of water. For years, she was afraid of anything — food or liquid — passing her lips. The 34-year-old Californian had spent more than a decade in and out of hospital since developing anorexia as a teenager. Now she felt something new. As she drank, she discovered that the usual sensation of fear was completely absent. Instead, she felt a curious affinity. “It was just this beautiful moment where I was like, ‘Oh, I’m water,’” she says. “It was so strange, but really healing.”

Quietly spoken, with large dark eyes, Aly is talking to me on a video call. (She asked me not to use her last name.) The hood of her jumper is up and, as she recalls the decades during which she suffered seizures and damage to her heart and kidneys, her tone becomes flat with exhaustion. She became anorexic at the age of 14 in the wake of a traumatic event. “I found restriction was my way to just try to be invisible and try to control my thoughts,” she says. When she refused treatment in her twenties, courts ordered her to be force fed.

Anorexia nervosa is the deadliest psychiatric disorder. Patients are at risk from the physical impacts of starving themselves, as well as from a high rate of suicide. Medical knowledge of the condition dates back to the 19th century, but no drug has been approved to treat it. Psychiatrists tend to offer a combination of therapy, antidepressants and nutritional programmes aimed at helping the patient regain weight. But these frequently fail, with some experts estimating that only about one-third of people make a full recovery.

So, two years ago, when Aly heard about a small medical trial in San Diego investigating the effects on anorexia of psilocybin, the active ingredient in magic mushrooms, she felt a flicker of hope. “Something in me knew that if I didn’t do it,” she says, “I was going to be dead by the end of last year.”

Ekaterina Malievskaia stands in her small office in London's Soho, gazing at a self-portrait by Lene Marie Fossen, a Norwegian photographer. The picture shows Fossen hunched over, her bones protruding, in an abandoned hospital. She died from anorexia in 2019 at the age of 33. It was while watching a documentary about the photographer that Malievskaia, a 56-year-old doctor and co-founder of the biotech firm Compass Pathways, says she began to understand some hard truths about the disorder. "She was talking about her experience, and kind of . . . how slowly she was dying, and no one could understand that . . . it's not a disease of vanity," she says. She also noticed how Fossen, who agreed to be filmed, was frustrated with medical professionals' relentless focus on weight gain, while feeling that the root causes of her illness were not being addressed. "They were treating her symptoms, but they were not looking at her as a whole person."

Born in Ekaterinburg, Russia, Malievskaia trained as a doctor in St Petersburg before moving to the US in 1991, where she received an MSc in public health at New York University. She met her husband, the US software entrepreneur George Goldsmith, in 2008. The couple were drawn into the world of psychedelics in 2013, when Malievskaia was searching for new treatments for her son's obsessive compulsive disorder. Reading medical journals in the middle of the night, she found an early study using psilocybin to treat the condition. She was surprised that there was "such a strong signal" that it could work. "I've never used any drugs. As a doctor, that never interested me. So, I woke up George and said, 'You grew up in the '60s and '70s, you know something about that!'" she says. (Goldsmith is 11 years older than her.)



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She was right. As a teen in the late 1960s, Goldsmith had taken [LSD](#) recreationally, experiencing what he calls a “really interesting” trip. (Malievskaia attributes the drug-taking to “peer pressure”, but Goldsmith says it was “peer exposure”.) He became fascinated by the work of psychiatrists who had explored the therapeutic potential of psychedelics in the 1950s and early 1960s, until the experiments ground to a halt amid a political backlash against drug abuse and Richard Nixon’s 1971 announcement of a “[war on drugs](#)”.

By the mid-2010s, medical interest in hallucinogenic drugs had returned, with clinical trials taking place at universities in the US and Europe. Goldsmith and Malievskaia began to privately fund small studies. In 2015, they created the “Center of Mental Health Pathways And Support for Self-directed care”, Compass, as a non-profit and began meeting with academics in the field. But they quickly decided that there was, in Goldsmith’s words, “no way in God’s green earth” that a non-profit could drive the expensive and laborious development of a psychedelic drug towards regulatory approval. So, in 2016, they founded [Compass Pathways](#). “From the beginning, it was not a psychedelic company. And the difference is that we are not inspired by the particular psychedelic drug,” says Malievskaia. “We are inspired by significant unmet need and patient suffering.”

The company's first study investigated the impact of psilocybin on patients suffering "treatment-resistant depression", a severe clinical condition that is unresponsive to medication or therapy. After promising results, they started the first phase 3 trial for psilocybin last year. They have also launched trials for post-traumatic stress disorder and anorexia. Malievskaia tears up when describing how eating disorders have some similarities with OCD. Both can be "ego-dystonic", behaviours that persist against a person's will and beliefs. "They understand that this is not the right way. And there's nothing they can do. So these people, they kill themselves, not because they want to die, but because they cannot go on like this," she says.

Compass's psilocybin was used in the San Diego trial that Aly took part in. She was one of four out of 10 patients who showed clinically significant reductions in eating disorder symptoms after three months. The study was far too small to be conclusive, and similar studies from Imperial College London and Johns Hopkins have not yet reported results. But the results gave Compass enough hope to start a phase 2 trial of 60 participants late last year.

When Aly decided to participate in the trial, part of her feared that she was "failing" her eating disorder. "I really looked at my eating disorder as this thing that has always been there for me throughout all of these hard times in my life, so I almost felt I was betraying the anorexia and, like, abandoning it."

In a small therapy room at King's College Hospital in London, eating disorder specialist Hubertus Himmerich explains that people suffering from anorexia struggle to separate themselves from the condition. "This is the challenge . . . that you have patients who might superficially say to you, 'I know that I'm suffering from anorexia', but in front of the food they wouldn't eat," he says. "Whereas a patient with depression would do anything to get rid of the depression, take medications, go to group therapies, individual therapies and so on. This leads to a revolving-door situation."

Himmerich estimates that about one-third of his patients will reach full recovery with treatment. Another third will have some symptoms for the rest of their life. And about 30 per cent will remain severely unwell, usually dying far younger than they should due to the toll of prolonged starvation.

At the Bethlem Royal Hospital in south-east London where Himmerich treats patients, he said about 300 or 400 people were on a waiting list for their first assessment when I met him in October, a dramatic increase from an average of 50 before the pandemic. During the Covid-19 pandemic, many patients' conditions worsened without in-person check-ups and others, isolated and anxious, developed eating disorders for the first time. In the UK, hospital admissions for eating disorders have soared 84 per cent in the past five years.



So-called pro-Ana messaging is not hard to find on social media, with posts like “What I eat in a day” and “thinspo” (short for “thin inspiration”) trending and hashtags sending users from healthy eating posts into pro-anorexia content © Jules Julien

Treatment for anorexia typically includes cognitive behavioural therapy, which is aimed at addressing rigidity of thinking, learning new ways of managing emotions and enabling patients to become comfortable returning to a healthy weight. For patients so unwell that they have to be hospitalised, the last resort is feeding by tube, either with the patient's permission or after they have been sectioned. Himmerich is also working on a trial for an antipsychotic called Olanzapine but patients can be reluctant to take it because, unlike psilocybin, it directly helps them gain weight.

Anorexia is defined by low body weight, fear of weight gain and body-image disturbance. The body has three systems that make us eat: the homeostatic system that releases hormones to ensure we get the energy we need for growth and movement, the hedonic system, which gets pleasure from eating, and the self-regulatory system in the prefrontal cortex, integrating personal values and social expectations. The latter could make us eat when we're not hungry — because we're at a wedding, for example — or not eat because we're afraid of being overweight. In people with anorexia, the prefrontal cortex is thought to have too much power.

Rebecca Lester is a medical and psychological anthropologist who almost died from anorexia when she was a teenager. Now recovered, she is a professor at Washington University in St Louis and works as a licensed social worker with people with eating disorders. She notes that the disease is often bound up with issues of morality and signalling to one's self and others that you are a "good and worthy person". While anorexia is probably underdiagnosed in men — an estimated 2.2 per cent of women and 0.3 per cent of men are diagnosed with the condition — she says it is not surprising that more women are affected by the disease. "Still, we are predominantly judged by our bodies," she says.

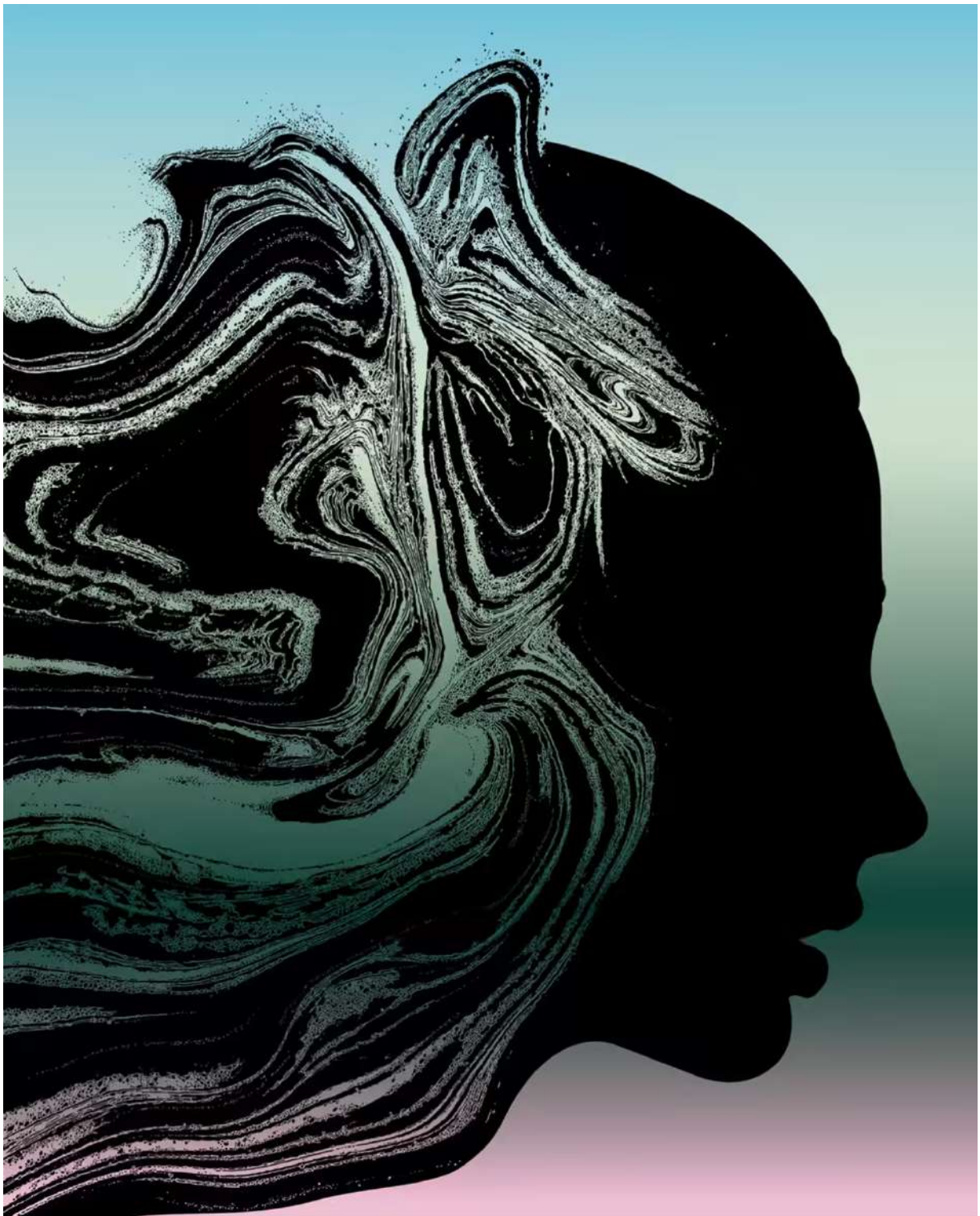
Vulnerable people today face a uniquely image-obsessed online culture, with Instagram, TikTok and photoshopped images leading to unprecedented pressure around appearance and weight. So-called pro-Ana messaging is not hard to find on social media, with posts like "What I eat in a day" and "thinspo" (short for "thin inspiration") trending and hashtags sending users from healthy eating posts into pro-anorexia content. The Social Media Victims Law Center in Seattle and San Francisco has filed 19 cases against social media companies in the past year, claiming they have caused eating disorders. On niche online message boards, some people even advertise their services as "coaches" to push people deeper into anorexia, promising "meanspo", bullying to keep people from eating.

Lester hopes that if psychedelics work, they could help change the conversation around anorexia to show that it is much more about “deeper existential issues” than “about somebody who stayed on a diet too long”. But she warns it could also feed into a wider movement to “biologise” all mental illness, which can ignore the cultural dynamics that are producing the problem in the first place.

When Malievskaia and Goldsmith first met with regulators in Europe in October 2016, they found the door surprisingly open. Legally, psychedelics are still scheduled as dangerous drugs, but medical regulators could see their promise. In fact, the European Medicines Agency brought to their attention a study that had been published by Imperial College London that year on the positive effects of psilocybin on severe depression. Instead of Malievskaia and Goldsmith’s initial plan to treat cancer patients with depression or existential distress, the EMA suggested Compass target a larger group: patients with treatment-resistant depression.

The next hurdle was creating a synthetic version of psilocybin, which could deliver a precise and pure dose and could be trademarked, unlike the substance found in magic mushrooms. Psilocybin was first clinically manufactured in 1959 by Sandoz, now part of Novartis, but the company had never commercialised it. If Compass could make psilocybin to meet today’s more exacting standards, it could own the manufacturing patents that would justify spending on expensive clinical trials, gaining about 20 years’ monopoly to sell the substance from when it filed patents. “The first organisation crossing the finish line with this becomes a new chemical entity and that makes it difficult for others to do,” says Goldsmith.

A number of Compass’s rivals, who are further behind, are already focusing on alternative versions, for example, modifying the substance to cut the time of a trip. The value of the market for drugs for treatment-resistant depression alone is expected to hit \$2.8bn by 2029, according to Fortune Business Insights.



'Psychedelic medicine is not medicine like we currently understand it,' says Maya Albert, a participant in the San Diego study. 'It's not a pill that you take one day, and you're better the next. You can't extract the dosing from the work that needs to be done before and after' © Jules Julien

In February 2017, the couple bumped into someone at a breakfast who introduced them to the billionaire [Mike Novogratz](#), a former Goldman Sachs partner and hedge fund manager turned cryptocurrency investor. "It was almost like everybody we met along the way, we were meeting at exactly the right time," Goldsmith says. "There was no deck..." he adds, before his wife interrupts. "We had a deck. We had a drug. We had scientific advice. We were prepared," she says.

Novogratz introduced the company to Christian Angermayer, a German fintech investor who went on to found Atai Life Sciences, another company focused on psychedelics. Through him, they met venture capitalist Peter Thiel. With funding from these three billionaires, Compass then also attracted money from family offices and hedge fund investors, particularly those whose families had experienced mental illness, gaining some \$115mn in seed funding. The day after its oversubscribed IPO hit the Nasdaq in 2020, the company reached a market capitalisation of \$1bn.

While Goldsmith was raising money, Malievskaia was running a small team recruiting clinical trial sites one by one. She says she still has “scar tissue” from the experience. While hospitals were keen, there were significant delays as many had to apply for licences to handle psychedelics for the first time. Then, Compass had to train therapists in how to guide patients on a hallucinogenic trip.

Maya Albert was not at death’s door when she signed up for the same psilocybin trial as Aly in San Diego. Years of therapy had helped stabilise her anorexia, but it still lived in her head, making her obsess about food and the way her body looked. “I had resigned to being that way forever and didn’t have any hope of getting better,” she recalls.

Albert was already working in psychedelics as a conference organiser when she heard about the trial. So she knew that preparation was key to being receptive to the experience. Early pioneers of psychedelics emphasised the importance of “set and setting” – mindset and environment. This was underlined in the 1960s and 1970s when psychedelics were administered in uncontrolled environments, sometimes even without people’s permission. Trial protocols now include therapy sessions before the dosing day to prepare for the experience and after to “integrate” it.

“Psychedelic medicine is not medicine like we currently understand it,” says Albert. “It’s not a pill that you take one day, and you’re better the next. You can’t extract the dosing from the work that needs to be done before and after.” Her first intention was to find “any sort” of hope. “There was no light at the end of the tunnel for me and my recovery . . . But I thought, at minimum, I could get hope that there might be a way to change in the future,” she says.

As well as blood tests, vital measurements and surveys, Albert was able to visit the room where her trip would take place in advance. The trial organisers do their best to transform clinical rooms into places of comfort, with soft lighting, flowers and a gentle soundtrack designed to accompany the experience. Participants can lie under a weighted blanket and wear an eye mask. Albert brought along an aromatherapy diffuser and a photo of her with a loved one.

Just after 8am, she took the capsule of psilocybin. Therapists are trained to ask participants to take a mindful breath and think about what brought them there. About 15 minutes later, Albert felt herself slipping under the covers into a lucid dream. “The most surprising thing at the beginning is that I didn’t feel like I fully lost control. I felt like I had agency over what I was experiencing,” she says. Two therapists were in the room in case she needed them but they rarely interact with patients, only sometimes offering reminders to let go or, if agreed in advance, holding the participant’s hand.

Her early hallucinations were dark, discomfoting, shadowy figures. “I was so committed to whatever it was going to offer me that I just opened my arms to whatever it was. When I saw something I didn’t like, I made sure to look even longer. And it would just disappear. It felt like a skill I was practising over and over again,” she says.

At one point, she saw herself in a coffin, surrounded by nature and seeming to experience her own birth and her own death. Soon, it all became one and dissolved into the world. “I sat with that moment for however long it lasted and was as present as I could be and just experiencing the wonder and awe of it,” she recalls. While still on the trip, she realised this was a form of “ego death”, a term describing a transcendent loss of subjective self-identity.

After this turning point, she spent several hours floating in the “most profound bliss and euphoria” she has ever experienced. The whole session can last six to eight hours. She says she laughed with herself, accepted herself, loved herself. “When I finally woke up and looked next to my bed at that photo of myself and someone who I loved, I thought ‘Oh that’s a nice photo, who’s that girl?’. I really did not recognise myself,” she says.

The days after were incredible. “I would live there forever if I could,” she says. The therapy sessions to “integrate” the experience were essential. “Nothing about my journey had anything to do with body or food. It was way beyond that.” She felt like she was handed a “tabula rasa, this blank slate of possibility”, cut off from her eating disorder. “OK, now, you have a fresh start . . . Do you want to go back and live that way? Do you want to let that control you?”

Stephanie Knatz Peck is the clinical psychologist at the University of California San Diego who ran the trial, a small independent study using Compass’s synthetic psilocybin. She believes integration therapy is vital. “If there is, in fact, this window of neuroplasticity that opens up, we really want people to leverage that for behaviour change,” she says.

Scientists don’t yet know exactly why this window appears to open, but Knatz Peck says there is significant evidence that anorexia is linked to serotonin disturbances in the brain and that psilocybin activates a serotonin receptor. MRI scans of people taking psilocybin show activity is spread far further around the brain, with more connections between networks and less activity on the well-trodden neural pathways, leading to a broader experience of consciousness.



The week after Aly’s treatment in 2021, she tried to stop herself eating — and failed. ‘I remember trying to restrict just to see: is this for real? And after just like day one, I was like, “This is so dumb. Why, why would I ever do this again?”’ © Jules Julien

One of the big challenges is trying to understand who responds to the treatment and who does not. Knatz Peck says those who were treated successfully in her trial either had trauma memories emerge during the session or, like Albert, experienced a loss of self. Separating from your eating disorder also appears significant. On her trip, Aly saw her anorexia as a skeleton, with red eyes. All the organs where she was suffering glowed red inside. “I think it was like the first time I’ve seen that like outside of myself or that I was able to be like, ‘Oh, this is not my identity. This is a totally separate thing,’” she says.

Even though not everyone improved as considerably as Aly did after the dose, the majority described it as among the most meaningful experiences of their life. In the three months the study ran, it did not show an impact on weight itself, although participants did have to be of a minimum weight — significantly above that of an inpatient with anorexia — in order to take part. (Doctors in charge of the trial believe that over time they will be able to treat people who weigh less.) Some participants suffered headaches or fatigue but no serious side effects.

In November 2021, Compass published its initial results from the study on people with treatment-resistant depression. A single dose of psilocybin, combined with therapy, was shown to have a significant effect in the short term, improving depression scores for 37 per cent of patients three weeks after the trial, with 29 per cent in remission.

James Rucker, a consultant psychiatrist and the principal investigator on the trial at King’s College Hospital, felt the results were “amazing”. The fact that the study didn’t show a runaway success with a population that other drugs had failed to treat was reassuring to him because it was credible. “There’s so much magic ascribed to psychedelics,” he says, “and it’s rubbish. And it’s dangerous, because it creates huge hype and expectation and then huge disappointment.” Desperate patients fill his email inbox asking about psychedelics every day. “How would you feel if you were given the ‘miracle cure’ for your depression, and it didn’t work?” he says. “That’s the danger.”

Others were clearly disappointed. Compass's stock price fell 28 per cent in a week. Some investors may have had too-high expectations. Others were spooked by safety concerns because some participants experienced suicidal behaviours or suicidal ideation after the treatment. About 14 per cent in the highest dose group saw a worsening of suicidal state, as did 17 per cent in the dose below and 9 per cent at the lowest dose. Andrew McIntosh, a professor of psychiatry at the University of Edinburgh who has no relationship with Compass, said the results were "concerning", even with small numbers, because you don't want to make a condition worse with psychiatric treatment.

The results also showed that for many participants the effect of the drug waned over time. By 12 weeks the remission figure had fallen from 29 to just 20 per cent. McIntosh said it was early to draw conclusions but that even if future trials showed only one-fifth of people benefited, the treatment would still be worth having. "Treatment-resistant depression is a pretty awful disease, it shortens lifespans, there's a great deal of suffering and suicide," he said. He believes the study was probably "the most convincing evidence so far" that psilocybin has promise for people with the condition.

Compass says it is looking at the effects of a second dose as part of its phase 3 trial, though the idea of repeated treatments raises other questions. Ravi Das, an associate professor in psychology at University College London who is also independent from Compass, said repeated dosing may be less practical. "Clinical psychologists are already up to their eyeballs in workload."

If the phase 3 results show similar promise, the company hopes it could bag the first approval of a hallucinogenic psychedelic, either from the EMA or the FDA. Recently, the US regulator has shown it is open to considering versions of drugs better-known for their recreational properties, approving Johnson & Johnson's drug based on ketamine for treatment-resistant depression in 2020. The Multidisciplinary Association for Psychedelic Studies, a US-based public benefit corporation, started its clinical research programme for [MDMA](#) in 2004. Now armed with positive results trialling the drug with therapy for PTSD, it expects to apply for approval soon.

"What the regulator has demonstrated is that there are no ideological, political, spiritual or religious barriers to this," Malievskaia says.

Debra Safer, co-director of the Stanford Adult eating and weight disorders programme, who was not involved in the trial, said that the long list of people it excludes — including people with a history of psychosis or psychosis in an immediate family member — shows Compass is being careful. If it works, she says, psilocybin therapy would be “amazing”. But she has a list of challenges: keeping anorexic patients from dropping out of the study, showing a sustained impact over a longer period of time and, importantly, proving a direct impact on weight. “Ultimately, I think we are interested in weight and does weight go up? We believe food is medicine,” she says.

How Compass will fare until then is an open question. Since the IPO in 2020, its share price has fallen 51 per cent, underperforming the broader biotech sector, as investors have turned on riskier companies without revenue. The stock battering was not the first bout of controversy in the company’s short history. Its switch from being a non-profit disappointed some of the researchers that the founders had initially partnered with and some in the psychedelic community, especially after Compass successfully applied for patents on its synthetic version of a substance that had been used so freely for decades. When I put this criticism to the company, a spokesperson responded that it believes the therapy should be widely accessible to patients if approved, and that this is only possible through the well-established drug development model.

To navigate the pharmaceutical and regulatory landscape, Compass has recruited Kabir Nath, a new chief executive with a background at a large drugmaker, the Japanese company Otsuka. Nath, who took the reins of the 160-person start-up last year, first encountered Compass just before his former employer invested in its series B round in April 2020.

In a meeting room over a darkening Soho street, Nath says the company is beginning to attract investors who had been wary about psychedelics: long-term healthcare specialists. “Some of those people who have perhaps stood back until now are starting to come in and understand that the opportunity and the promise is here,” he says. He is already talking to the healthcare providers and insurers that will eventually pay for an approved treatment about how to deliver it.

Charles Duncan, an analyst at Cantor Fitzgerald, says institutional investors are interested, but so far only “very casually”. The big change, he believes, is that a couple of years ago the market was dominated by short-term investors. Now, the field has narrowed from about 30 companies to a few with solid prospects such as Compass. Duncan says anorexia could be even more important for Compass than treatment-resistant depression, where there is more competition. “Anorexia could be a really interesting programme going forward, in part because I haven’t heard of any other company talking about it,” he says.

But there are still unanswered questions: can Compass train enough therapists to supervise such long sessions? Will patients only need a single dose or a series of sessions? And how will doctors distinguish who will benefit and who will not?

Malievskaia and Goldsmith know the road to improving mental health is never smooth. Their son is now grown up and mostly recovered. “It’s not the story of a boy who was failed by traditional psychopharmacology, took mushrooms, got better the next day and then the parents set up a mushroom company,” Malievskaia says. “It’s a journey. It’s a path. There are ups and downs. We’re talking about serious mental illness and there are no magic solutions.”

The week after Aly’s treatment in 2021, she tried to stop herself eating — and failed. “I remember trying to restrict just to see: is this for real? And after just like day one, I was like, ‘This is so dumb. Why, why would I ever do this again?’ And I remember being like, ‘Oh my god, it’s really gone,’” she says.

Previously a vegan, she’s enjoyed trying new foods, especially smoked barbecue meats. But mostly she’s relieved that she doesn’t even think about food or her body anymore. She has moved in with her girlfriend, who she describes as the first partner she’s had who doesn’t encourage her eating disorder. Having left school at 18, she was scared her anorexia had damaged her brain’s ability to learn. But she recently completed a course to become an emergency medical technician.

Psilocybin provided Aly with hope. Psychedelics could eventually do that for millions. To do so, scientists need to further investigate the mechanism behind how a break with reality can transform people’s relationship with the real world. Regulators must resist the hype and only approve drugs with robust trial results. And healthcare systems will have to invest in the therapists crucial to making the drugs effective and safe.

Aly is now fighting forest fires in Northern California. “I want to do something that gives me purpose and that I can work outside and do a really physical job, because it is so opposite to the years I spent just not being able to get out of bed,” she says. “I don’t think anyone in my life thought it was possible because everyone was just waiting for me to die.”

Hannah Kuchler is the FT’s global pharmaceuticals correspondent

If you or someone you know is struggling with an eating disorder, information and support is available from BEAT in the UK: beateatingdisorders.org.uk and the National Eating Disorders Association in the US: nationaleatingdisorders.org

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