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**Voice-Over:** The *BioWorld Insider Podcast*.

**Lynn Yoffee:** This is the *BioWorld Insider Podcast*. I'm Lynn Yoffee, BioWorld's publisher. An analyst recently said that mental health treatments remain stuck where cancer was 50 years ago, but there's new hope on the horizon with major advancements and the development of psychedelic medicines. Today, BioWorld staff writer Lee Landenberger is talking with James Lanthier, the CEO of Mindset Pharma, a company that's developing what it calls next-generation psychedelic medicines to treat neurological and psychiatric disorders.

Companies developing psychedelic therapies face challenges that are unique and traditional pharmaceutical development. James is with us to discuss those challenges and how Mindset plans to overcome them because the one-size-fits-all, trial-and-error approach to mental health treatment doesn't seem to be working. Lee, over to you.

**Lee Landenberger:** Thanks, Lynn. James, it's a pleasure to have you with us today.

**James Lanthier:** Oh, thank you so much, Lee. I really appreciate it.

**Lee:** Happy to have you. I think you can probably explain a lot of things and questions that we have when we talk about these kinds of treatments and the development process that goes through it. In looking at Mindset, we noticed that you recently expanded your portfolio with three additional non-tryptamine families of next-generation psychedelic compounds. Can you tell us what is a next-generation psychedelic compound and what is a non-tryptamine? It sounds like they're probably the same thing.

**James:** [laughs] Sure, I will do my best. We use this distinction of first-generation versus next-generation really to try to convey novelty. In the medical psychedelic world, there are a few drugs that have attracted a lot of attention, most notably, psilocybin, which is the psychoactive component of what people have referred to as magic mushrooms, and MDMA. Then to somewhat of a lesser degree, LSD and then DMT and 5-MeO-DMT, and so on.

What Mindset was really founded with around a straightforward insight that first-known psychedelic drugs like the ones I just mentioned were, by now, thanks to the level of clinical study and academic study around them, it's pretty well-established that they have a potential role to play as therapeutics. In our view, they're really a great kind of proof of concept for what psychedelic medicine is capable of.

There are some shortcomings associated with those drugs that could potentially be addressed through applying real medicinal chemistry and behavioural pharmacology to try to design and pick out some optimized drug candidates that can work better as really predictable therapeutics for bigger patient groups. That's what we mean by first-generation and next-generation. Next-generation really refers to drugs that leverage, or at least the first set of families that Mindset designed really refer to families that leverage the chemical structure and the backbones of known psychedelic drugs.

We've made some range of different modifications to the backbone and then tested the results of those compounds in some predictive models to try to understand what the differentiation would be in humans. That was really kind of the first set of discovery work that Mindset was focused on. Since then, the innovation engine never stops running here. We've tried to expand our discovery work into some even more novel areas.

Rather than starting with the tryptamine structure, and tryptamine, generally speaking, describes a common chemical structure that's shared between a number of different psychedelic drugs like psilocybin and DMT, we've tried to expand beyond tryptamines really to try to understand with even more novel drug structures, what the potential benefits of that could be. One of the things that we're looking for in our new families is whether there could be greater receptor selectivity.

Psychedelic drugs tend to act on a range of different serotonin receptors. One of those receptors, in particular, the 5-HT2B receptor, is implicated in cardiotoxicity, valvulopathy. One of the things we're trying to understand is, could we create new drugs that could deliver the same psychedelic experience or therapeutic benefit as known psychedelic drugs, but could they do so with a lower level of 2B activity? In doing so, could we create, potentially, an even safer drug?

Those are sort of some of the things that we're looking for and some of that discovery work, generally speaking, from the scientists and chemists who really pioneered this field like Alexander Shulgin. There are hundreds of psychedelic drugs that he was able to discover. We think that those really could act as kind of building blocks for yet another set of drugs. We're only going to figure this out if we do the science and follow a good screening program. That's kind of what we're trying to do there.

**Lee:** This sort of research goes back decades, and then it'll come to a halt, and then it'll start again. We're going through a period where it's starting. I'm curious. With the approval or just even the discovery of new treatments along these lines, how much of a game-changer could they end up being?

**James:** I think it's fair to say. They really could be quite a game-changer. There's been really not a lot of innovation in psychiatry in the last few decades if you look at the level of investment by pharma in neuropsychiatric drugs. I think it's trended down quite dramatically over the last few decades. There was just sort of this general consensus that it was really hard to develop a new psychiatric drug. That just happened at the same time as there's this increasing awareness and prevalence of mental health afflictions.

At least, on the research that we have today and I think that we can legitimately say this without hype that it does look like psychedelic therapeutics could offer some hope for patients, who have suffered from some of these really hard-to-treat mental health disorders like post-traumatic stress and treatment-resistant depression. To the extent that psychedelic medication could put a dent in some of those numbers, that legitimately would be a real game-changer.

**Lee:** Can you tell me how this works, how a treatment would work that you're developing, and what a treatment session might be like for a participant?

**James:** Sure, so I think it's important to understand, or I should caveat this with the statement that Mindset's focus really is on the upfront discovery and development work. We're not a company that specialized in the downstream clinical end of things. I think I can generally speak to this and it is really fascinating. The model for psychedelic-assisted therapy is very different than the treatment model for something like depression today.

Essentially, what it involves is rather than taking a drug every day, waiting six to eight weeks for you to start benefiting from the effects of that drug, psychedelic-assisted psychotherapy is much more immediate. Instead of a daily dose, it involves, typically, a couple of very large dosing sessions. The current kind of paradigm is to do some treatment beforehand, some psychotherapy beforehand to prepare you for what's to come, and then typically doing anywhere from two to three sessions in a specialized clinic.

Most of the protocols involve having two people, both a man and a woman, oversee your trip experience. Then, typically, it's bracketed on the other end with some additional therapy to help you integrate, in process, your experience, but that's it. It's two to three sessions. Then a lot of the data so far suggests that those two to three sessions could get you some meaningful relief for at least a period of time from your depressive symptoms. That's the model. We kind of refer to it as the macro-dosing model. Contrary to what some people might have assumed, it's not micro-dosing, which is a practice that you hear a lot about these days. It involves undergoing a full psychedelic experience.

**Lee:** James, can you tell me a little bit about the difference between synthetic and natural psychedelics like what the strengths and weaknesses of each of them are?

**James:** Sure. Now, this is a topic where within, I'd say, the psychedelic community, there's often a passionate level of debate around this. Obviously, the origin of psilocybin is before we had the synthetic version. It was a natural product derived from a certain type of mushroom. There's very much a point of view amongst some folks. You'll find this certainly across the medical and health and wellness communities that there are benefits to the natural product that are not obtainable through the synthetic version.

A very strong point of view that the natural product deserves a far greater level of support than a synthetic version. This is an argument that tends to get wrapped up with, I think, a number of other issues and points of view. From Mindset Pharma's point of view, the work that we're doing is to advance drugs along a regulated pathway in regulated jurisdictions that meet the relevant requirements. That can be prescribed by physicians on a wide scale. The goal is to try to get drugs that work to as many patients as possible.

That's much harder to do with a natural product, particularly with a natural product where the psilocybin content and a psilocybin mushroom can really vary wildly. I think it's about by a factor of 10 between different mushrooms within an individual mushroom. It's very, very hard to work with a regulator to get a drug like that approved, especially when psilocybin has such profound effects on people. Our focus is exclusively on the synthetic pathway. We believe, at the end of the day, this is all about chemistry.

We don't believe that there's anything lost with a synthetic version. All of the clinical trials that have been conducted to date have been really with a synthetic version. I think as you're seeing greater openness and acceptance, I think it could very well be that there could be-- In some jurisdictions, we are already seeing a certain level of decriminalization and acceptance of the natural product.

From our point of view, there's just a much, much larger patient groups that are accessible via the regulated pathway patient groups for whom the natural product wouldn't be appropriate, or who wouldn't feel comfortable with it and will want something where their physician has signed off and is aware of the dosing and uniformity of the product. Lots of debate around this. As far as we're concerned, if the goal was to get advanced drugs along a regulated pathway, it's a pretty simple answer.

**Lee:** You just met with the UK's MRHA. Can you talk to me about what kind of direction they gave you for planning a phase I study?

**James:** Sure, we went to the UK regulator with some pretty specific questions as we're planning our clinical trial process for MSP-1014, which is really our first lead candidate. MSP-1014 is a drug that's similar to psilocybin and offers, we think, some pretty pronounced improvements around safety and manufacturing. The guidance that we got from the UK regulator was what we had hoped for and was quite positive.

Essentially, what they've indicated, at least on a preliminary basis, is that due to MSP-1014's structural similarity to psilocybin, we won't have to undertake the expensive and time-consuming IND-safety studies. We can simply move straight to clinical trials. Additionally, we can move straight to dosing patients rather than healthy volunteers. I think it certainly shortens the runway for us to get 1014 into clinical trials and reduces the cost. I think it means that we should start to have some more compelling data around this earlier than we would with a different drug.

**Lee:** I'm curious about the jurisdictions that you mentioned. Do you think the MRHA guidelines are similar or will be similar to what the FDA may give you?

**James:** Pretty similar, although we can't say that yet definitively, but I think pretty similar. I think both those regulators have shown quite a bit of interest in advancing psychedelic therapeutics as fast as they responsibly can. Yes, we're fairly optimistic on that point.

**Lee:** When can we expect you to get into the clinic? Can you give me an idea of what the size of a patient trial might be?

**James:** I can't give you an idea on the size just yet, but we're certainly expecting 1014 or hoping 1014 should be into clinical trials by around the middle point of next year and hoping to get a second candidate as well into clinical trials by the end of next year. The hope is that we have at least two candidates in clinical trials by the end of next year.

**Lee:** Looking at next year, and money is always part of the equation, I'm curious, does Mindset face any barriers in fundraising that traditional pharmas don't face?

**James:** I would say no. Mindset has been fortunate to be the first real biotech company in the space working with psychedelic drug structures to form a big pharma partnership. In January of this year, we announced a partnership, a collaboration with the US development arm of Otsuka Pharmaceutical. That's really the first of its kind in the space partnership between a biotech and a big pharma. Otsuka would be a top 10 global psychiatric drug company. That was a huge win for Mindset. Also, it has been a great source of non-dilutive funding as we've been developing two of our novel drug families with Otsuka.

It's been a challenging time for the biotech sector as well as the psychedelic sub-sector generally in the public markets. We're certainly seeing, I'd say, that start to come around and seeing a more elevated level of interest from a whole range of different investors. I think that for psychedelic companies working with first-generation drugs, it's probably a dip where they will struggle to get real composition of matter IP rights. That could be a different story, but I think Mindset was fortunate to pick the path that it picked early on.

**Lee:** The benefit for investors of getting into next-generation psychedelics, can you expand on that a little bit? It's just a better product and treatment. Is that your feeling?

**James:** Well, really, I think there's two reasons why next-generation drugs are ultimately going to be the place where the value is really created in the sector and flows. I think one is that we do think there's an opportunity to improve on some of the shortcomings in first-generation drugs. I think we've been able, at least preclinically, to prove that or demonstrate that with significantly shortened duration times with some improved safety data.

This is just a class of drugs that, frankly, pharma had to screen out for decades because they had really no incentive to work with these drugs. It's a class of drugs that really haven't been optimized. The other reason why I think that you're going to see the value accrue to next-generation drugs is simply because known psychedelic drugs have been in the public domain for decades.

It's really difficult to get strong IP rights on first-generation drugs. You'll see that companies today really fighting over pretty bearing grounds and filing a lot of patents that may not really stand up to challenges. With next-generation drugs, there's an opportunity to actually get composition of matter IP rights on an active pharmaceutical ingredient, the actual active molecule.

That's a much, much stronger place to be. That's naturally where pharma wants to go to. I think it's in next-generation drugs that you'll see real pharma investment being made to actually advance new drugs to market. I don't think we haven't seen, so far, real pharma really get behind first-generation drugs. I think it's just much more likely that there'll be a much higher level investment with new drugs.

**Lee:** Last question for you. I guess this plays into the background of almost everything we've talked about, which is the ethics of this kind of drug development. Does that play into what you do every day? Who should profit from all this and what should they control?

**James:** It's an excellent question. I think it's a very relevant question when it comes to first-generation drugs. First-generation drugs are drugs that really, many of them at least, exist here and are being studied today. Thanks to their use in Indigenous cultures for thousands of years. Obviously, it's pretty obnoxious when companies try to patent things that already exist in nature, that kind of thing. I think there are some real issues when it comes to who should own and who should profit from first-generation drugs.

On the other hand, creating a whole new therapeutic area does require real investment. It's very difficult to get that investment unless there's an opportunity to achieve a return on it. In particular, with next-generation drugs, this requires real biotech work, real medicinal chemistry. These are truly novel drugs that Mindset's working with that haven't existed in nature before and are truly new. I certainly think that with next-generation drugs, their novelty and the investment that's required to actually advance them certainly merits real return on investment.

**Lee:** This is fascinating. Well, the best of luck to you, James. We look forward to you getting into the clinic and we can check back in with you then.

**James:** Awesome. Thank you so much, Lee, really enjoyed, and thanks for your time.

**Lee:** Ah, my pleasure. Lynn?

**Lynn:** Truly fascinating, and we'll definitely track this. Maybe we can have you back, James, for a follow-up when we have some clinical data. It's very promising in the field of psychiatric and neurological disorders. We look forward to updates.

**James:** Thank you so much.

**Lynn:** As always, BioWorld will continue to keep you informed of all the most important scientific, clinical, and business updates. That's our show for today. If you need to track the development of drugs, turn to bioworld.com. Follow us on Twitter or email us at newsdesk@bioworld.com. Also, if you're enjoying the podcast, don't forget to subscribe. Thanks for joining us.

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