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LuAnn Heinen:
That's Andrew Penn, a board-certified psychiatric nurse practitioner who has more than 20 years of experience and extensive training in psychedelic assisted psychotherapy. He's a clinical professor at the University of California-San Francisco School of Nursing, where he teaches psychopharmacology and sees patients at the San Francisco Veterans Administration.

I'm LuAnn Heinen, and this is the Business Group on Health podcast, conversations with experts on the most relevant health and well-being issues facing employers. Today we tap into Andrew Penn's expertise in psychedelic assisted therapy to discuss clinical trials that may before long lead to FDA approval of therapies like MDMA and psilocybin for specific mental health conditions.

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Welcome, Andrew. I'm so glad that you're able to join us today.

Andrew Penn:
Thanks for having me.

LuAnn Heinen:
You have some 20 years of experience as an advanced practice nurse with special training in psychedelic assisted therapy. Would you give us just a quick recap of your career leading to the research and teaching position that you hold now at the University of California-San Francisco?

Andrew Penn:
Sure. I teach psychopharmacology in a classroom-type setting and I do clinical work at the San Francisco VA. We have a nurse practitioner residency program in which I'm attending there and I also see patients at the San Francisco VA. I spend a little bit of my time doing research in the translational psychedelic research project, program rather, which is headed by Dr. Josh Woolley, and we are a lab in the Department of Psychiatry that focuses on novel therapeutic techniques. So primarily we've been focusing on psychedelic therapies, largely psilocybin. We did some work in the early phases of the Phase 3 MDMA assisted therapy for PTSD study, which recently resulted in a new drug application to the FDA, which is actually just submitted. Since that time, that part of the study ended around 2020 and in the time since then we've been working on several different psilocybin studies, including recently published in *JAMA*, results of the Phase 2 Usona-sponsored single dose of psilocybin for major depression. That was a placebo-controlled trial that we were one of the eight sites around the country that we worked on that and we're doing other projects with psilocybin too. Sorry, that's a mouthful.

LuAnn Heinen:
Let me back you up though, to the new drug application just submitted. Is that the only psychedelic drug application pending at FDA right now?

Andrew Penn:
I don't know if it's the only one, but it's probably the most well-known one at this point. I don't think anybody else has put in an NDA application yet for a psychedelic that I'm aware of.

LuAnn Heinen:
So that's an NDA for MDMA for PTSD, is that right?

Andrew Penn:
Yeah, can you repeat that three times fast. It's a lot of alphabet soup. NDA, for those who are unfamiliar, is a new drug application. This is essentially the end of Phase 3 results that a sponsor, in this case the MAPS Public Benefit Corporation. MAP stands for the Multidisciplinary Association for Psychedelic Studies. They have a public benefit corporation. They're the ones that have been heading up the Phase 3 studies of which the second one was published earlier this year, and both of which were positive. That then goes to the FDA who will then have typically 6 to 10 months to come back with a response, which could be an approval of the drug.

LuAnn Heinen:
They'll have how many months did you say?

Andrew Penn:
I believe it's typically 6 to 10 months.

LuAnn Heinen:
Okay. Back 20 years ago when you started working as a psychiatric nurse and got advanced training, were you doing psychedelics back then? And I want to know how you got into that, because this looks now, from today's vantage point, to be an exciting, really fortuitous path, but what led you to pursue that course back when psychedelics were not so promising?

Andrew Penn:
Yeah, it's interesting. If you'd asked me that question 20 years ago, I would not have any idea that I'd be doing the things that I'm doing now. It just goes to show a career is sometimes a series of happy accidents. I've had an interest, an academic interest in psychedelics, a curiosity really since I was in high school. I read Aldous Huxley's, *The Doors of Perception*, when I was maybe 16. This was in the mid-80s when the 60s seemed like a million years ago. I was certainly not raised in an environment where psychedelics were a thing. They were sort of a historical relic as far as I was aware. And developed this sort of curiosity about them, but it was never really something I imagined being brought forward as a therapeutic modality. I think it was around 2010 that I became aware of the work that MAPS was doing. At that time, very early Phase 2 studies looking at MDMA assisted therapy for PTSD, started to follow the research there and did some teaching around it and continuing medical education conferences when it was still kind of a radical idea. This whole space has moved so quickly that even 8, 10 years ago, we didn't have the proliferation of say, ketamine clinics that we have now, and psychedelics seemed like this very far away thing. There were some really pivotal studies that were published around 2016 that came out of NYU and Hopkins looking at people who had life-threatening illnesses that were treated for existential distress with a psilocybin-assisted therapy protocol, which showed some really promising results and also showed a strong antidepressant signal. It was from that secondary data in those two studies that I believe launched the two entities, Usona Institute and Compass Pathways, that are really leading the charge in bringing psilocybin for depression. In the case of Usona, in treatment resistant depression. In the case of Compass, through Phase 2 and Phase 3 clinical trials. Both organizations have finished Phase 2 results and are beginning Phase 3 at this point. It was still a number of years away from a potential application to the FDA for approval, but definitely well underway. I didn't see this coming at all is the short answer to the question.

LuAnn Heinen:
So today you're providing psychedelic assisted therapy in clinical trials at UCSF. Can you walk us through what the combined drug and therapy process looks like end-to-end? A quick walkthrough.

Andrew Penn:
Yeah, that's a great question. I think a lot of people imagine that you're going to go down to your local Walgreens and get psilocybin, which would not be how this would be administered. In a clinical setting, the way this happens is that there's preparatory psychotherapy that is done without any drug and depending on the study, we might have one or two therapists be part of that psychotherapy. In that session we're getting to know the patient or the subject as they're called in research, they're getting to know us, we're establishing a relationship, creating a sense of trust, answering all of their questions and concerns about the experience and really preparing them to have this experience. And then on the day of dosing, those same therapists are with the subject all day long. Subject usually comes in first thing in the morning. We have our dosing room set up like a comfortable living room like environment. We have a couch that we make into a bed that people can lie down in and we have a couple of chairs for therapists to sit in. We have music on usually throughout the entirety of the session. The person ingests the study drug and then we settle in.

LuAnn Heinen:
Hang on one second. Let me just stop you. So it's not intravenous?

Andrew Penn:
No, no. It's oral. It's an oral or sublingual administration depending on the study, and we settle in for the day and the drug effects of psilocybin are fairly predictable in terms of their onset and duration. Usually effects are felt within an hour or so and will last for about five or six hours. By about three or four o'clock we're wrapping up for the day. That whole time, to be clear, we're keeping the person safe. If they want to talk, we certainly don't require people to talk in that session. In fact, we encourage people to direct their attention inward. We provide them with an eye shade and we have this music that they can have on headphones if they want or through a speaker, and we're monitoring vital signs through the entire process.

LuAnn Heinen:
Then when they're done at the end of the so many hours, six hours, seven hours, they get up and drive home?

Andrew Penn:
We have somebody bring them home. We do arrange for transportation home. Occasionally, depending on the study, we have people stay overnight in the lab. That's less frequent now, but we've done that in the past with some of our studies and we still do it with some of our studies that involve people that have more medical complexities. For example, we're doing a study of people with Parkinson's disease and major depression, and those folks would stay overnight to make sure that we can monitor them safely overnight and then the next day we begin a non-drug integration therapy. Those same therapists will talk with the subject about their experience and we will make sense out of it, unpack it a little bit, and then really look for opportunities to start to implement maybe some of those insights or learnings from the dosing session into their day-to-day life in a way that might help them to feel better. So that's really the goal of integration therapy. It's these three parts that really comprise the psychedelic assisted therapy process, and it's not a take home drug in these protocols. It may be taken as infrequently as once. Sometimes we will repeat this process a second or third time over the course of several months, but it's a limited use of the drug over a period of time and certainly not the conventional sort of way we think about pharmacology now, which is that you have to take something every day to get an effect.

LuAnn Heinen:
How many hours is the integration therapy on average, would you say?

Andrew Penn:
It depends on the protocol, but typically sort of four to six hours of integration. There may be several sessions. Again, depends on the study protocol, but usually at least a couple hours of integration between the sessions and then we sort of pick up integration/preparation for the next session, if it's one of these multi-dose sessions, a few weeks later.

LuAnn Heien:
I know that you have really emphasized the therapy piece of this. The therapy is not just a footnote, I mean the therapy is the thing.

Andrew Penn:
I would say this is a psychotherapy protocol that is enhanced with a drug.

LuAnn Heinen:
What's it like to be in the moment with someone experiencing psychedelic therapy, when they're actually feeling the effects and they're on the bed with eye shades on and with music on, what can you see? What can you discern about their experience?

Andrew Penn:
It's funny, I get asked this question a lot. Honestly, sometimes it's sort of like watching paint dry, and I say that not disparagingly, but really just because psilocybin for many people is such an internal personal experience. They may be having an incredibly rich experience internally, but there's not a lot to observe on the outside when somebody's sort of lying there and reflective. They really might not be talking that much. Now there are times when people do experience some anxiety or discomfort, and that's one of the reasons why the therapists are there, is to reassure people and keep them safe, help them get to the bathroom and back and make sure they drink water, things like that. That part is important from a safety standpoint. I would say most of the real psychotherapy happens before and after. That's what looks more like what you think of conventional psychotherapy where somebody is reflecting on their lived experience and talking about it with a professional.

LuAnn Heinen:
Is psilocybin a gentler form of psychedelic or would MDMA or other forms be the same?

Andrew Penn:
They have subjectively different signatures, I would say. MDMA is sort of known to be more interpersonal and relational and have a softer experience for many people and it tends to engender trust between people, which is one of the reasons why it has such a sort of a social history when people use it outside of clinical settings. Psilocybin is a little more, I don't want to say unpredictable, but definitely see people go more into a personal narrative, a spiritual experience, perhaps. It definitely seems to engender more of a kind of reflection that sometimes can be kind of intense. It really depends on the person and what they're coming in with. We often talk about psychedelics as being nonspecific amplifiers, which is a term Stan Grof used to use, meaning whatever really the person is coming in with tends to get louder during that time, and that's okay because part of what we're doing here is we're helping people to fully feel their feelings.

One of the downsides of conventional psychopharmacology, and I'm not interested in disparaging conventional psychopharmacology, I treat people with that all the time and I think it has some utility, but one of the downsides is particularly with things like selective serotonin reuptake inhibitors, antidepressants like Prozac and such, is that people will often report that their emotions feel kind of flattened, that they don't feel depressed, but they also don't feel as much of anything. That can be thought of as way of contributing to a phenomenon we call experiential avoidance. Experiential avoidance are all the different ways that we use to not feel our feelings, and that could be compulsively looking at our phones or drinking or the myriad of ways that we distract ourselves from our inner worlds. Antidepressants, while certainly useful and lifesaving for some people, can encourage this sort of feeling of not really feeling much of anything. Psychedelics, I would say, tend to have the opposite effect. In this setting, which is obviously very different than a recreational or ceremonial kind of setting, people tend to go into the stuff that brought them into the study. If they're here to talk about their trauma or their depression, they end up having experiences that are related to that. Those experiences sometimes help them gain insight into those feelings and we're able to work with that material in the integration portion of the therapy protocol.

LuAnn Heinen:
I've heard you say, I think it was on the Aspen Institute stage, you may not always get the trip you want, but may get the trip you need.

Andrew Penn:
Yeah, that's a bit of a chestnut in our work.

LuAnn Heinen:
Can you tell if someone's in obvious emotional anguish and what can you do in the moment?

Andrew Penn:
Yes, we can. When I said earlier, that's sort of like watching paint dry, a lot of people are having this sort of quiet internal experience, but definitely when big emotions come up, you see people cry in there, you see people feel sad, and a lot of what we're talking about in the preparatory work is how can we be most supportive to you through those experiences. One of the things that we talk about before the person ever ingests the drug is, would it be helpful if somebody held your hand during this session. We talk about what they would feel comfortable with in terms of appropriate therapeutic non-sexual touch, would you want me to rest my hand on your forearm or hold your hand, and how do you signal that you'd like to break that contact when you're ready. We try and remain very attuned to how people are feeling in the moment and let them know that we are there for them if they sort of need to come up for air.

LuAnn Heinen:
Let's talk about who is this kind of therapy not good for. Obviously in a clinical trial setting you can be highly selective, but in general, who is this not good for?

Andrew Penn:
Yes, that's an important question, which I think we are a little further behind in identifying for whom this may not be a good idea. There are certain groups that historically have been excluded from this kind of treatment, and the most obvious one is people with psychotic illnesses such as schizophrenia or bipolar 1, people that are prone to having psychotic symptoms when they're having a severe mood episode in bipolar disorder, for example. Typically, those folks have been excluded from studies to date. There are also some cardiovascular exclusionary criteria, so people that have untreated hypertension or heart valve issues or arrhythmias would likely be excluded from some of these studies to date. We also generally have people come off of most of their medications, their psychiatric medications, and for some people that's sort of a non-starter. The reasons for that are both for the fidelity of the data, but also because some of these compounds don't work as well when people are on some conventional psychiatric medications. So in order to prevent that sort of dampening of effect, we generally take people off of those medications and some people aren't willing to do that, which is understandable. We generally exclude people that are actively suicidal. As studies have gone on though, the typical pattern of clinical trials is that you begin with the highest levels of exclusion, and what that results in is a group of people that often is not really representative of what you see in clinical practice. As you go on with these studies, you can begin to very cautiously work at the edges of those exclusionary criteria. For example, we're doing a study right now in our lab that is looking at people with bipolar 2 disorder, which is a form of bipolar disorder, which doesn't involve psychosis and doesn't involve what we call full-blown mania. These are people with more of a chronic cyclical depression picture, and we're looking to see if we can have the same efficacy with psilocybin that we have in unipolar major depression, but more importantly, can we do it safely? Can we do this without causing a worsening of somebody's condition if they have bipolar 2? That's an example of an area where you start to wear away at the edges. The other one would be our Parkinson's study, because usually people with active neurological diseases are also excluded from these studies, and so that's unfortunate because many of those folks also have depression. We want to see if we can give psilocybin safely to people with mild to moderate Parkinson's disease and if that can be done safely without worsening their Parkinson's, and also can it be done effectively and help their depression.

LuAnn Heinen:
What about people who struggle with SUD or addiction? Because I understand there's some small possibility that psychedelics could be addictive, but also they could be indicated as a potential treatment for addiction. How does that all sort out?

Andrew Penn:
Yes, right. It seems kind of counterintuitive to a lot of people that you would use a drug that some people have historically thought of as a drug of abuse to treat a drug of abuse. I would call into question the addictive properties of at least classical psychedelics. When I say classical psychedelics, I'm talking about LSD, psilocybin, DMT (dimethyltryptamine), typically are not reinforcing in both lab animal models, so a rat will not press a bar to repeatedly dose itself with psilocybin in the same way that it will, say, for cocaine. We generally don't see compulsive use of classical psychedelics in human populations either. Typically, these things tend to be somewhat self-limiting. Somebody might use a psychedelic a few times a year, but this is not something you're seeing somebody using every day. I mean, of course there's exceptions, but they're infrequent. With MDMA and ketamine, there probably is a little more of a potential for reinforcement there, and so you can see more kind of addiction-type behavior there, but again, nowhere near as common as say something such as cocaine or opiates, which have a clear tendency towards compulsive use. There's a couple areas that have been studied with psilocybin-assisted therapy as an intervention for substance use disorders. The biggest one to date has been alcohol use. Michael Bogenschutz at NYU did an interesting study looking at psilocybin intervention and then measuring a number of heavy drinking days and number of days drinking. Their outcome goal was a reduction in alcohol use and found positive results there. There's been small studies done to date looking at nicotine dependency. There's a larger study that's underway that's been recently funded for the first time by the federal government. It's worth noting that most research in this country is funded by the federal government, but that is not the case with psychedelics. Most of these have not been NIH funded studies. They've been privately funded and psilocybin intervention, so there's potentially a lot of promise in those areas as well.

LuAnn Heinen:
A lot of public health benefit.

I'm speaking with Andrew Penn, an advanced practice nurse who has served as principal investigator and study therapist in a number of clinical trials for psychedelic-assisted treatment. Most recently, he served as a therapist in a Phase 3 trial looking at MDMA to treat PTSD as well as co-PI in a Phase 2 study looking at psilocybin facilitated therapy for major depression. We'll be right back.

LuAnn Heinen:
I should have asked you earlier when we were talking about integration therapy, that there is a study that you mentioned at Johns Hopkins fairly recent suggesting that a learning window may open during psychedelic-assisted therapy. Can you just quickly share what that's about?

Andrew Penn:
Yes, so this is a mouse model, to be clear, and this is Gul Dolen's work out of Johns Hopkins. The idea of a learning window is that in mice there's something called a social learning window, which is that mice a certain

number of days after birth have this opportunity to sort of learn certain behaviors through play and through interacting with other mice. After a certain number of days, I don't remember exactly how many, that window sort of closes, and it's difficult for the mouse to learn some of those same behaviors that it learned when the window was open. And what Dr. Dolen's lab found was that psychedelics reopened that window for a period of time in the days following the administration of the psychedelic to the mouse. What was interesting was that the duration of effects of the psychedelic, so a short acting psychedelic like ketamine opened the window for a couple of days, a longer acting drug like LSD opened up for several more days and something like ibogaine opened it for a long period of time. Ibogaine has a long duration of action, sometimes up to like 36 hours, the drug effects itself. If this is replicable in humans, it has some really interesting implications for integration. It implies that there is a period of time in which people can really possibly utilize some of those learnings and experiences from the psychedelic where they're maybe most able to integrate those changes into their lives. I do think that integration in general is a long-term process. People talk about integrating psychedelic experiences that they had years ago that they keep returning to it and thinking about it and not dissimilar in the way that you might reflect on a really powerful dream that you had that maybe you still remember years later that just has this sort of a noetic sense of importance, like I don't know why this matters, but it really feels important and I think I need to think about this. So integration really can go on for a long period of time, but there may be a window of time that is most optimum for integration and that would be something we'd want to build into our systems of care. If this becomes something that we can offer people in the future, how do we best optimize that period of time. In much the same way that a surgeon thinks about getting their patient into physical therapy at a certain window of time, you don't want to wait too long because the person loses mobility and strength, but you don't want to do it too soon because they'll reinjure themselves. So there's probably this sort of sweet spot where you're going to get the most out of that aftercare.

LuAnn Heinen:
So interesting. Tell me a little bit about your practice at the VA. Are you seeing veterans who may have received psychedelic-assisted therapy in the past or what are you seeing?

Andrew Penn:
Not exclusively. We do offer ketamine treatment for veterans at the VAs, so we do have some veterans in our clinics who have undergone ketamine therapy in the past. That is a treatment that we use largely for depression. I think the VA in future obviously has a lot of interest in some of these treatments and there is increasing work that's being done within the VA.

LuAnn Heinen:
And veterans have been among the most powerful advocates.

Andrew Penn:
Yes, they really have been, and rightly so. A lot of this need is coming from the shortfall of treatments that we have to date. It's really a confluence of frustration with the shortcomings of the treatments that we have available right now, such as SSRIs and also unfortunately increasing prevalence of psychiatric conditions in our population at large, some of which may be related to the pandemic. We're certainly seeing a lot more demand for mental health services than we have in the past.

LuAnn Heinen:
It does bring me to want to talk a little bit about the unique skills that nurses bring with the kind of psychiatric training that you have, which is different from when you think of a therapist, you don't think of someone who's trained as a nurse. You think of a therapist. I'm going to read a quote from an article that you co-authored in the *American Journal of Nursing*, and it says, “nurses are skilled in holding space as patients endure challenging events in real time and for prolonged periods, whether that be during childbirth, a sudden illness, an anxiety attack, or the time surrounding death. And this skill translates well to being able to sit with the patient undergoing a therapeutic psychedelic experience, allowing space for whatever arises at physical, emotional, mental, or spiritual levels.”

Andrew Penn:
Hey, that's pretty well written.

LuAnn Heinen:
We like it.

Andrew Penn:
Nurses are likely present at the very first day of our lives and the last day of our lives. One of the things that's interesting about nursing is that nurses are really good at presence and when we have the space and time to do it, at delivering care. Irrespective of if we get to cure anything, we can always care even if we can't cure. A lot of what you need when you're under a psychedelic isn't necessarily somebody doing something to you. When we talked earlier about what does the therapy part look like, it's often not what people imagine when they think of psychotherapy, which is much more conversational and interventional. This is really about holding that space and allowing the person to heal. This term gets used a lot in the psychedelic space of an inner healing intelligence, the idea that your body knows how to heal if it's given the right conditions to do so and what we're trying to do is make the conditions optimum for healing. I think nurses are particularly good at that.

The other advantage to nurses, and this is one of the reasons why I was a co-founder of an organization called the Organization of Psychedelic and Entheogenic Nurses or OPENurses, https://www.openurses.org/ is our website, is because we have a lot of nurses in this country. There's almost 4 million nurses in the American workforce. We're the largest health care employee type. I think that we are optimally suited to learn how to be psychedelic therapists and it would do wonders for helping what is likely to be a significant bottleneck with regards to workforce, because as people who work in mental health know, we don't have enough regular clinicians as it is right now, let alone psychedelic-trained clinicians. If we're going to add an additional modality, which requires a fair amount of time and some training to deliver, we're going to have to think about how we're going to fill that gap. My proposal is we take 1% of the American nursing workforce, and by the way, depending on who you ask, between 25% and 75% of nurses currently say that they're burned out and a portion of those are considering leaving the professional altogether, so this might be an opportunity for people who want to remain in nursing but maybe don't want to work in a hospital anymore, to be able to translate those skills into a different kind of care that would help solve the workforce issue. Some really interesting data that came out of a survey that the Berkeley Center for Psychedelics did this year where they asked what kind of clinician would you feel comfortable with you on a psychedelic experience, close to the top of the list, if not the top of the list, was nurses. That's an idea that resonates with the public as well as with the profession.

LuAnn Heinen:
We love nurses. It's true. High trust.

Andrew Penn:
High trust and the most trusted profession year after year in the Gallup Poll. Also, there's an approachability to nurses. Nurses are excellent translators of technical information to people that don't have the same technical training. There's a lot of skills that we bring to this that would line up nicely with psychedelic training. Also, we care for the physical body as well and we're comfortable with that, because things can happen during these sessions. People can throw up. Occasionally, somebody could become incontinent. You got to help people get to and from the bathroom. Things that nurses don't bat an eye at. We do that all the time. And also, it's a long session too. It's not a therapy session that lasts for 50 minutes. It's a therapy session that can last for five, even ten hours, to which an ICU nurse says, well, I do 12-hour shifts with people in non-ordinary states of consciousness all the time. We call it delirium in the ICU, but an 8-hour therapy session is really quite within their wheelhouse.

LuAnn Heinen:
You mentioned a staffing bottleneck. When or if FDA approves MDMA and psilocybin, what other practical considerations or things need to happen to scale up psychedelic-assisted therapy? I'm thinking we do know

there's a new CPT code for a six- to eight-hour therapy session that begins January 1, 2024, and you've told me about professional practice guidelines, a new or first version of those that have been developed by consensus to offer some guidance. We know they'll need lots of updating. It's unclear how far FDA will go in labeling, regulating, or prescribing the delivery of psychedelic-assisted therapy. I think you said not their usual wheelhouse.

Andrew Penn:
It's not, because their wheelhouse is regulating drugs, the sale and safety of drugs and the efficacy of drugs. They're not involved in the regulation of psychotherapy, and so this is a really kind of out of their familiar territory. No, that's a nice summary that you've laid out there. There will also be likely a REMS program, a risk evaluation mitigation strategy that the FDA puts in with drugs that have greater complexity to their use and which will regulate things like the physical custody of the drug and possibly who is qualified to deliver it. That's really the big unanswered question right now from the regulatory standpoint is will there be regulatory standards that say who can and cannot deliver this treatment. There are organizations such as the Board of Psychedelic Medicine and Therapies that is looking at creating a credentialing exam for future practitioners. There's the American Psychedelic Practitioners Association, which is a professional group which wrote those guidelines that you mentioned, so there's a lot of things that are going to need to be worked out.

Then there's the issue of formulary coverage. One of the things that's going to be really important for access to this is that it's covered by insurance including Medicare, because if it's not, these are very expensive treatments. Just looking at the time alone in our MAP study, even if you are paying the therapists, which would be below market in some areas, say $200 an hour, you're looking at a possible cost of $20,000 for a single patient going through a set of three treatments, and then there's the cost of the drug on top of that. Now you can make the argument that the long-term cost savings of that will be considerable, because if we can treat somebody for PTSD, say early on and then not incur all the costs of chronic ongoing treatment over the course of their lives, then that could definitely incur some serious cost savings.

There's other ways to think about reducing cost in this too, such as the delivery of this treatment in groups. Chris Stauffer as I mentioned before, and Elliot Marseille who is at Berkeley, just wrote a fantastic paper doing some Elliot as a health care economist looking at potential cost savings with delivering this in group therapy settings and not just cost savings, but there's really something that's very powerful about these being given in a group setting. As a footnote, that is often how these were used traditionally in a lot of indigenous cultures that used psychedelic plants or entheogenic plants and fungi. These things are given not to the individual but in a group. There's this common experience, but also an ability to connect to other people and a larger sense of the world at large, which is a very common experience under psychedelics where people realize, wow, I'm not just this lonely speck on this planet. In the infinite universe, we're connected by things as prosaic as love and family and friendship, and that matters, and those things are healing.

LuAnn Heinen:
Let's go back and talk a little bit about the money, because there is concern about this kind of gold rush or wild west mindset right now where we're not seeing anybody funding studies of generic LSD and there must be generic versions of these compounds that have been around for a long time. But it's not just that labor costs, it's the drug cost itself. The patents that are being sought are for adaptations, I guess, of the legacy drugs. Is that right?

Andrew Penn:
Well, there is some of that. So MDMA that has gone into the FDA on the new drug application, that's a drug that was patented in 1912, so its patent is long since expired. There are some entities that are looking at changing these molecules in ways that makes them patentable, but also sometimes makes them more useful to work with. For example, there's a company called Cybin that created a deuterated version of dimethyl tryptamine. Deuteration, for those who are unfamiliar, is a way of adjusting the chemical structure so that the pharmacokinetics of the drug, that the duration of the drug is increased, but without having to use higher doses. That might be a useful adaptation because DMT could be a very useful drug in the treatment of say,

depression, but it only lasts for about 15 or 20 minutes. It's a very short acting drug. By making the effects of that drug longer and smoother, it might give you more to work with. One could cynically say that these things are being patented so that they can be more monetized, and there's an element of truth to that, but there also might be some functional utility in changing the structure of some of these drugs as well. The question of intellectual property is a really interesting one because a lot of these things have been around for a long time and are not patentable. Sandoz made LSD starting in the 1940s, but its patent ran out I think in 1965. It raises these questions of where does the intellectual property lie, which is outside of my area of expertise, but some companies have tried to have patented the manufacturing process and made that proprietary. Bear in mind with all these psilocybin studies that we're doing, to be clear, we're not using ground up mushrooms in a capsule. This is synthetic psilocybin, so those manufacturing synthesis pathways can be patented. Sometimes they're attempting to patent sort of the context in which this is delivered. There are people that understand intellectual property better than me that could speak to that.

LuAnn Heinen:
Can you share with us your greatest concern once these products are on the open market? I mean, I know they will be FDA regulated, but no longer in the clinical trial setting that you're used to. So your biggest concern and then maybe what you're most excited about.

Andrew Penn:
I'll start with what I'm excited about, which is that I would love to have treatments for my patients that work as decisively as say an antibiotic does when you have a simple infection. I think back to last time I had to take an antibiotic for something and a day and a half after starting it, I felt like a human being again. I felt normal again, and I would love to have treatments that I don't have to ask patients, well, this might work and we'll know in about six weeks or so. Now, that's a big ask when you're suffering, and so I really look forward to the idea of more rapidly acting treatments, but more importantly, I also look forward to the idea of treatments which help people to engender meaning in their lives and maybe forge a different relationship with whatever suffering they're experiencing that don't necessarily just mute symptoms but help people really heal. That's something that's very encouraging to me and that's what keeps me going in this.

There's a number of things that I have concerns about, one of which is that I fear that we're sort of overpromising and possibly we'll under deliver in these treatments, and the history of psychiatry is kind of littered with the next greatest cure. If you look back to the 1980s, we were going to cure depression with SSRIs. If you read *Listening to Prozac* by Peter Kramer, there's this amazing belief that these new drugs on the market are really going to absolutely change depression. I don't want to disparage SSRIs. It's very fashionable in the psychedelic space to sort of knock conventional treatments, and I don't believe that. I think we're going to need both new treatments and our existing treatments, because those existing treatments have helped a lot of people, but they certainly haven't necessarily been curative for most. I would love to see treatments that maybe offer something beyond just palliation, but I do worry that the way that the media has sort of taken this story is that these are sort one and done cures. You hear these things like 10 years of therapy in one afternoon, and I think that's asking a lot. I think that's really making some really overstated claims.

Then the other issue, which we haven't really touched on, which is the wild card in all of this, unlike a patented medicine which you need to be an organic chemist to know how to make, some of these compounds such as psilocybin are naturally occurring. One can grow psilocybin in your garage. There are a number of states that have initiated pathways to decriminalization or supervised adult use, such as Oregon, will likely create kind of a parallel system. There may be the FDA approval system and you go see your psychiatrist for this, and there may be this sort of parallel system in which people can go to, say a retreat center, and have a psilocybin experience in a different type of setting. Or in a state that has decriminalization, you might be able to obtain this through some channel and do this on your own. That I worry about. These can be very big experiences for people and you need to have some idea of what you're getting into, and I think it's helpful to have people that have familiarity with these experiences to be with you through that process, not only to keep you physically safe, which is obviously important, but also to help make sense of the experience and to deal with distress if it were to come up. I think those are all really critical experiences too, and that in a less controlled setting is

going to be a little less predictable, but I think we can do a better job of educating the public about this. We've spent 50 years essentially pedaling a lot of exaggerations and sometimes outright lies about these drugs. There's a lot to be undone within the public education space that we need to do if this is going to become part of American culture, which it may well become.

LuAnn Heinen:
Andrew, thank you so much for being here today. Your work is fascinating. Your patients are lucky to have you.

Andrew Penn:
Thank you, LuAnn. It's really been a pleasure to talk with you today.

LuAnn Heinen:
I've been speaking with Andrew Penn, a leading voice for nurses in psychedelic therapy and co-founder of OPENurses, a professional organization for nurses interested in psychedelic research and practice. He's been invited to speak at South by Southwest, the Aspen Ideas Festival, TEDxMarin, and the Singapore Ministry of Health. He's written for the *Los Angeles Times* and been interviewed in *Forbes* and by the *BBC World Service*. You can find him on the web at https://www.andrewpennnp.com/.

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