Mark Noble:
Hi there. It's Mark Noble, Executive Vice-President of ETF strategy at Horizons ETFs, and welcome to the latest episode of Generation ETFs Podcast. It's always exciting when a new sector is created and that's exactly what we are witnessing with the emergence of the global psychedelic sector. These are companies that are in the early stage research and development in the therapeutic use of psychedelics, largely for the treatment of mental illnesses. A number of companies have offered initial public offerings the last 18 months, primarily on Canadian exchanges. And these companies are solely focused on this research and development of psychedelics. In fact, the market has gotten large enough that in late January Horizons ETFs, we garnered a lot of attention by launching the world's first psychedelics-focused equity ETF, which trades on the NEO Stock Exchange under the ticker P-S-Y-K, or PSYK. And so PSYK would be the Horizons Psychedelic Stock Index ETF, and again, under the ticker PSYK or P-S-Y-K.

Mark Noble:
Now some market commentators have tapped the psychedelics sector as the next cannabis industry, but there are some really crucial differences both between the research being conducted on psychedelics and of course the eventual size and utilization of that market. So with us today is Tania Gonsalves, Vice-President of Institutional Equity Research for Healthcare for Canaccord Genuity Corporation. And she is here to provide some insight into what is going on with the psychedelics market and where it fits into the larger healthcare equity space. Now, I should note that she has no opinion or affiliation with our PSYK ETF and this podcast is really one focused on education and understanding the risks and the market opportunity around the psychedelic sector. So, Tania, thank you so much for being with us here today.

Tania Gonsalves:
Yeah, thanks for having me Mark. It's a pleasure.

Mark Noble:
I think it would really be helpful for our listeners if we can get a good sense of your background and how you got into being an equity research analyst on this particular aspect of the healthcare sector because as we just mentioned, it's a new sector and I think there's very few people, you being one of them, that have in-depth expertise on understanding the investment case for these companies.

Tania Gonsalves:
Yeah. So I guess I should give most of the credit to my firm being Canaccord Genuity as most of you know, we were one of the first early movers in the cannabis market too. And I think we like to stay ahead of the curves and always be looking at new themes. And it was the firm that identified this opportunity in psychedelics. Now, myself, I joined about a year and a half ago covering healthcare. And, in the Canadian space at least, you ended up being a bit of a jack of all trades in healthcare so covering everything from biotechnology stocks to medical devices, I even cover some plant-based protein stocks. So very broad coverage universe and psychedelics fit really nicely within that niche because they are akin to biotech stocks.

Mark Noble:
And how do we define the psychedelic industry? We're getting this question a lot. What is the psychedelic industry and how does it stand apart from other life sciences and pharmaceutical companies? If you could give us a little bit of a summary of what it is we're looking at when we're looking at psychedelic companies and what it is they're doing, I think that'd be really helpful.

Tania Gonsalves:
Yeah. So, the psychedelic companies developing drugs in the clinic and in accordance with the FDA or EMA or whatever regulatory body, I think in my opinion are very much so similar to other early stage biotech companies. So I don't know if you do necessarily group them apart from other life sciences companies. With that said, if I had to name a difference between the psychedelic drug developers and your average small molecule biotech company, let's say, I say they differ in three big ways. So, one is how these compounds are manufactured and handled in the clinics. Specifically, since most classical psychedelics are schedule one drugs in the US. Everyone from that CMO manufacturing the drug, to the clinic where trials will be conducted to the investigator overseeing that trial, will potentially require a license from the DEA to work with these compounds.

Tania Gonsalves:
And those licenses can be somewhat challenging and expensive to attain. So a little bit different than typical small molecules. The number two is the clinical risk in the trial design. Psychedelic drugs, unlike most new drugs under development, have been used by humans for decades. So we have some understanding, at least, of their safety and efficacy in treating mental illness, and this reduces the risk associated with clinical development. You're not starting from scratch with a brand new molecule, but on the flip side then too, they produce these very real and apparent physiological effects. So I'm referring to that trip, if you will.

Tania Gonsalves:
Typically, the FDA likes to see double-blind, placebo-controlled studies proving the drug under investigation is better than standard care or no treatment, whatever is typically used in a real-world setting. But I guess the question is how do you blind a hallucinogenic experience? Subjects are going to know whether they're in the treatment arm or the placebo arm. So you'll need some really creative thinkers design these trials as development moves forward.

Mark Noble:
Yeah, I hadn't even thought about that.

Tania Gonsalves:
I don't think a lot of investors are thinking about it because we're still pretty early stage right now. But as we move into late phase two, where you're actually designing controlled experiments, it's going to be interesting. And then the most common question I get by far is on IP. I think there's a lot of uncertainty on how to patent molecules that have been in existence and used by many cultures for decades. Perhaps you can get manufacturing patents or formulation patents, or method of use patents, but the strongest patent, your composition of matter patent, I think it's going to be difficult to get on classical, well-known psychedelics. And seeing as IP is the bread and butter of the traditional pharmaceutical company, it'll be interesting to see how they work around this challenge.

Mark Noble:
Yeah. I mean, if it's a widely used, cultivated product, how do they create IP around that unless they're doing something synthetic from it? Just with a follow-up to that question. So when we're looking at the different types of psychedelic compounds that they're looking at, I think this is important as well, because we're talking about cannabis, people were referring really to the THC-based compound of cannabis and its usage or non-THC in the form of some of the non-THC compounds like hemp or CBD oils. But when we're looking at psychedelics, are we primarily looking at two or three psychedelics? I mean the big one being psilocybin, which would be normally affiliated with what we call magic mushrooms and ketamine, would that be accurate? Would those be where most of the research is on these?

Tania Gonsalves:
Yeah, I think you're accurate. Most of the research is being focused on psilocybin today, but the classical psychedelics there's a handful of them. So it includes things like LSD, like DMT, some people group ketamine, MDMA into that group, LSD, of course. So there is a handful of them.

Mark Noble:
Now, one of the big differences here between cannabis and this business is that cannabis was a schedule one narcotic in United States, but clearly in Canada, we moved to the access for cannabis for medical purposes legislation early last decade, which really opened up the usage and cultivation of cannabis to be studied for the medical purposes, distributed for medical purposes and then that obviously lead the way for the retail business, but I'm not quite sure what's prompted the explosive growth in these psychedelic companies over the last two years, because for the most part, these drugs still remain highly regulated, illegal narcotics outside of places like Oregon. So I'm curious if you could provide a little bit more context of what has really pushed this sector into warp speed growth over the last couple of years. What has allowed for these companies to pop up and what's driving them?

Tania Gonsalves:
Yeah, it's a really good question. This isn't the first time, actually, that this has happened. So taking it back a step, the first wave of psychedelic research actually took place between 1950 and '65. And during this span of 15 years, there were over a thousand scientific papers published. And these are not written by Joe Blow in his basement taking acid, you had really accredited, academic and scientific institutions like Harvard, like NYU running studies and big pharma companies like Sandoz, which is now Novartis, supplying drug to, really, any therapist willing to use it. So you have this historic body of evidence and literature supporting psychedelics efficacy in treating everything from depression to PTSD to addiction. The problem is back then there were no double blind placebo controlled trials, which are pretty much standard today. In fact, it wasn't until, I think, 1962 after the whole thalidomide disaster that the FDA was granted explicit authority by Congress to regulate new drugs using these well-controlled studies to prove safety and substantial evidence of efficacy.

Tania Gonsalves:
So basically the quality of historic psychedelic data is just not up to modern standards, making it unusable. And there was this big taboo for decades, even any scientist referencing the word psychedelic, I think it was a bit of a stigma, but I feel like enough time has passed that we're over that, it's not as taboo anymore. So scientists are more and more coming back to the field and it's very well accepted that there is evidence for these molecules, efficacy and safety, which is why I think there's so much interest in it again. And certainly helps that... Or I shouldn't say helps, but mental health, it's a very topical subject right now, especially given COVID-19. We don't have enough good treatments on the market. So having these molecules that have been studied in the past, that proved to be efficacious, there's a lot more eyes on it.

Tania Gonsalves:
And really, I would say, this industry started taking off, you're right, probably a couple of years ago, so late 2018. And that's when COMPASS Pathways was granted breakthrough therapy designation by the FDA for its psilocybin program. And this designation really marks some work by the FDA saying we want to support you in this program, we are on your side and we want you to succeed. Having an institution like the FDA back you, I think has made other scientists realize that this is not taboo anymore. We can move forward with this kind of research.

Mark Noble:
Most of this is focused on the mental illness part. My understanding is drug resistant depression. So we have X hundreds of millions of people that have suffered from some sort of depression but the research is suggesting that people with acute depression, drug resistant depression, this is where there may be some therapeutic benefit using some of these compounds. Is that an accurate understanding of where most of this research is focused?

Tania Gonsalves:
Sometimes, but not always. So COMPASS Pathways, which I think is one of the well-known players in this space is going after treatment resistant depression, because yes, there's a substantial portion of the population that fails on first line, second line antidepressant therapy, but there are companies going after and not-for-profits going after that first line group as well, just because there is evidence that they are more efficacious than today's antidepressants. The side effects may not be quite as bad if you have a medication that perhaps you only need to take once a year instead of every day, there are advantages to that.

Mark Noble:
As someone who covers the pharmaceutical industry, there really hasn't been any breakthrough drugs on the antidepressant side, probably since the heyday of late 90s when you had Zoloft and the SSRI drugs, that'd be accurate as well?

Tania Gonsalves:
Yep. That's accurate.

Mark Noble:
So, I guess that would jump into my next question. So the opportunity set for disruption for this business would be then in the pharmaceutical aspects these companies will be looking to create a sector that is entering into a disruption of an established business, which would be the treatment of mental illness with pharmaceuticals?

Tania Gonsalves:
That's correct. Yep. There are certainly companies going after, I'll call it, the recreational space where it's not for sick individuals necessarily, but for healthy individuals. So maybe you take a trip to Jamaica [inaudible] retreats, that's not the market we're focused on though.

Mark Noble:
And that segues nicely into my next question. I mean, people say this is the next cannabis space, but I think we need to be a little bit careful on that. The big opportunity with cannabis was the adult use or recreational market. And I don't know if that exists with this market. So I'm hoping to get, from you, a little bit of sense of, ultimately, what is the big market opportunity with the psychedelics? Where do you see that business evolving over the next two to three years in terms of disruption and potential revenue growth?

Tania Gonsalves:
Yeah, that's a really good question. Personally, I don't like to make the comparison between psychedelics and cannabis because you're right, cannabis was primarily valued for the recreational opportunity. In my opinion, psychedelics will never be broadly legalized and recreationally permitted. There's too much risk that comes with that hallucinogenic experience. You're not quite comparing apples to apples but I still think the market is very, very sizable. We recently published an analysis of the total addressable market for psychedelic drugs since they are, for the most part, being developed as prescription pharmaceuticals. I think it's fair to say they would steal share from current prescription pharmaceuticals for mental illness, think of your antidepressants, benzodiazepine, stimulants, et cetera. And if you add up the global sales in 2020 of all drugs used to treat mental illness, substance use disorders, eating disorders, and certain neurological disorders as well, that psychedelics are going after like, let's say, narcolepsy and Alzheimer's you come up with a $50 billion global TAM, which is massive.

Mark Noble:
Wow. Yeah, huge.

Tania Gonsalves:
Yeah, so the opportunity is sizable and I want to note another thing there is it's sizable on its own, but one caveat here is that a lot of these indications included in that TAM that psychedelics are going after aren't really treated with pharmacotherapy today. So take addiction for instance, be it alcohol, nicotine, prescription opioids, cocaine, heroin, whatever, pick your poison, perhaps there are handful of drugs that can reduce withdrawal symptoms, but for the most part, these patients are best treated by attending rehab and therapy. And in the US alone, the addiction rehab industry is estimated to be worth upwards of $40 billion. So if psychedelics are successful at creating this new class of drugs for some of these indications that perhaps reduce the labor and facility cost burden, I think your TAM could be over a hundred billion globally, potentially.

Mark Noble:
Now, at Horizons we are equity agnostic. We don't have an opinion on the stocks. Our goal is to provide broad exposure to the sector. But as an equity analyst, I was hoping I'd get a little bit of sense of in terms of treatments and companies that are leading the way in this particular space. Is there some particular examples you could share with us where the therapeutic or the research seems fairly interesting or, at least, positive in terms of some of the work that's being done? Maybe just one or two examples that might be helpful for listeners to understand the real life applications of some of these drugs.

Tania Gonsalves:
Maybe, first to focus on the class of drugs...

Mark Noble:
Sure.

Tania Gonsalves:
One of the interesting things about the classical psychedelics is these similar, long lasting and almost transformational effects they have on both sick patients and healthy individuals. There are shortcomings though, associated with certain psychedelics. So ibogaine, for instance, comes with cardiac risk. DMT is metabolized much too quickly for practical use. You have LSD and MDMA, although applicatious, being chemicals that are more readily associated with party use, may be viewed less favorably, I'd say, by regulators. So, that leaves us with psilocybin. It comes from nature. There's this aura of wellness around it. It's not something you think of when you think of a rave or a party drug, it's been used by many ancient cultures for centuries, for the specific purpose of healing and then most importantly, there's a lot of promising data for its use in treating a very broad range of illnesses like depression, anxiety, eating disorders, cluster headaches, the list is quite extensive.

Tania Gonsalves:
So I do think that psilocybin particularly has a lot going for it, which is why it's much more saturated. There's a lot of players going after that specific drug. And then I guess if you want to turn to which programs we're watching closely, I want to go back to what I mentioned on the difficulty in patenting these molecules. I think the ones that have the opportunity to disrupt and transform are going to be the ones that get to market first. I'm going to explain a bit of an intricacy here, sorry if I bore you but it sings to something called new chemical entity exclusivities. And while patents are granted by the US Patent and Trademark Office, new chemical entity status is granted by the FDA and it's a completely separate path of protection for drugs approved in the US. Basically it can only be granted to active chemicals that have never before been approved by the FDA.

Tania Gonsalves:
And this provides that new drug with at least five years of market exclusivity. And this basically means no generic copycats can launch within this timeframe. Considering most psychedelics had never been approved by the FDA, I think it's reasonable to assume they'd be eligible for this sort of protection but remember, this can only be granted to the candidate that's approved first. So that's why I'd be looking at the players furthest along in their trials, like the COMPASS Pathways of the world, because they have the best chance of getting to market first. One of the most advanced players, so MAPS, which is a not-for-profit, has one of the most advanced programs today, it's in phase three. If they're successful at winning the FDA approval to use MDMA to treat PTSD, I think they have a real chance of shaking up the PTSD market, but this means anyone developing MDMA that comes later on, likely won't qualify for that exclusivity. I mean, you have to ask yourself, does it make financial sense to develop and launch a drug with no patent and no exclusivity protection, leaving the door wide open for generic competition?

Mark Noble:
Right.

Tania Gonsalves:
So look at the trial, what phase of development they're in and I think you can gauge what the potential there is.

Mark Noble:
Okay. And then just brings us to our final question. I mean, let's take over the next two years, what sort of things are you looking at from an investment perspective on these companies? Because they're all early stage, they're all trading at fairly high evaluations because we're not really seeing earnings right now. There's a lot of R and D happening. What do you need to see further from an investment case perspective where things would be attractive to enter in at this point forward? And what sort of milestones would you be looking for to highlight that that thesis is the right one when looking at buying these companies?

Tania Gonsalves:
Yeah, that's a really good question. These valuations are not atypical biotechnology stocks. A lot of these companies don't turn revenue positive for years and years, but you're really valuing them off that ultimate TAM that I referenced, that hundred billion dollar potential. So over the next couple of years, I'm going to be tracking data readouts and clinical trial progress really closely. I want to see continued safety, continued efficacy data and see some of these preclinical assets move into the clinic. I think it's very difficult to value preclinical companies just because there's so little data, there's no human data for us to look at. So it's very, very risky at these early stages, but I think a lot of these programs are going to be advancing into human trials over the next couple of years. So we're keeping a close eye on that.

Mark Noble:
Phenomenal and we can't wait to have you back, Tania, this is going to be something I think we're going to want to revisit it in six months or so. I found this really fascinating and actually makes me a lot more excited that we launched an ETF on this particular sector. But thank you so much for that again. And, again, just want to make it clear for investors that Tania works with Canaccord Genuity. Her research is from there. She's completely independent from Horizons ETFs and no opinion on our ETF PSYK, but hopefully this did give you a good sense of really the sector opportunity and the excitement that people have about this space. So as you go forward and look at some of these offerings that we have at Horizons and particularly the PSYK offering, it gives you a little more educational context of what the opportunity is and what some of the risks are. So thanks again everybody. And thank you, Tania, for joining us today on our Generation ETFs Podcast.

HORIZONS ETFs
by Mirae Asset

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