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Investment Case for PSY,
Defiance's Psychedelic ETF

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PSY (Defiance Next Gen Altered Experience ETF) invests in the companies positioned to bring paradigm-changing disruption to the treatment of mental health. Recent breakthrough studies in the medical repurposing of psychedelics and ketamine, have signaled a new direction. Scientists, psychiatrists, and governments are revisiting their assumptions and regulations as they realize the power of these substances to bring relief and meet a major unmet need in those with poor mental health.

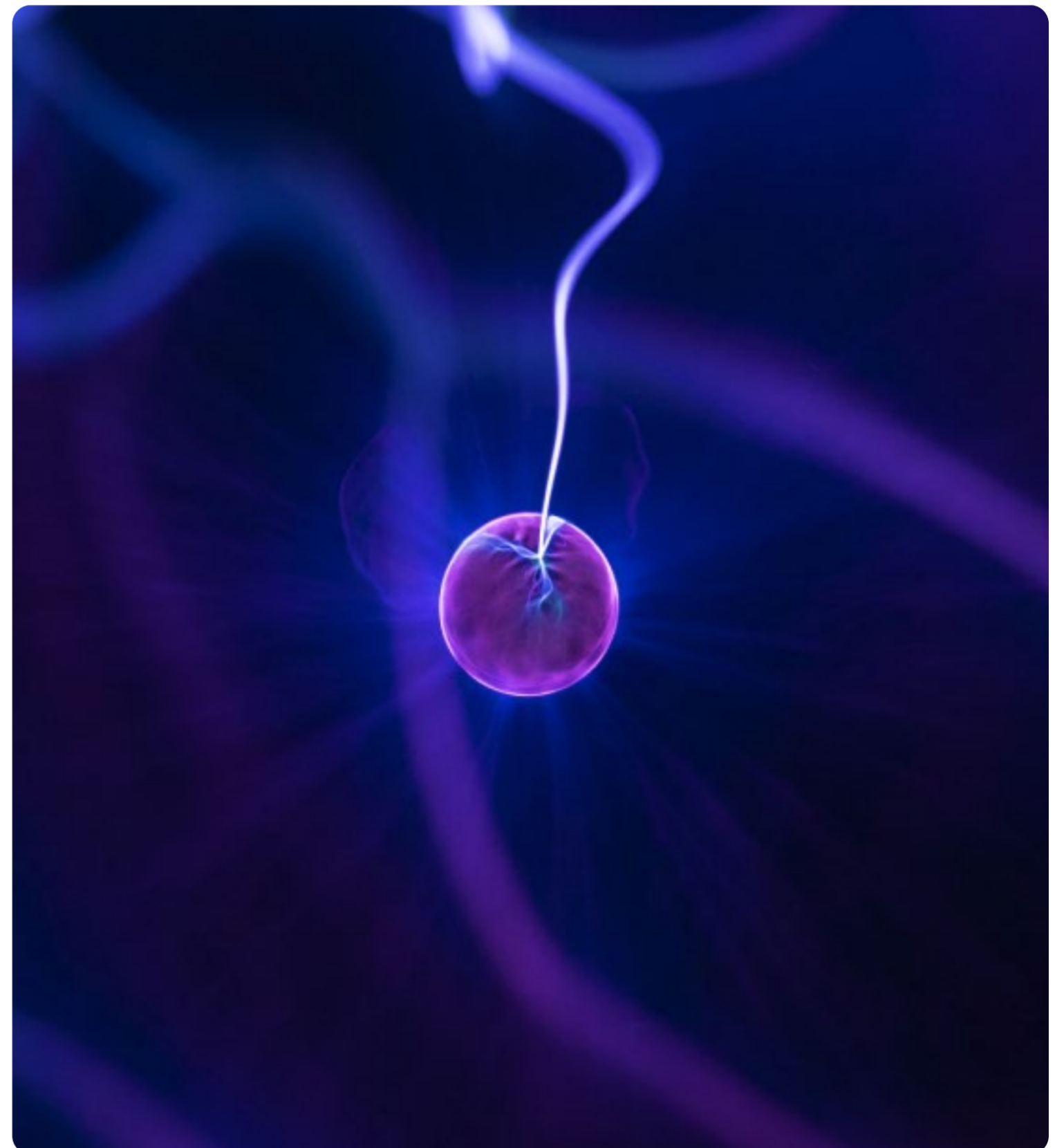
PSY seeks to track the BITA Medical Psychedelics, Cannabis, and Ketamine Index, a rules-based index that tracks the performance of a portfolio of companies listed on North American Exchanges conducting legal activities under the national laws of the applicable country related to medical psychedelics, medical cannabis, cannabis pharmaceuticals and cannabidiol ("CBD") derivatives, and ketamine.



Mental health is worsening on a global scale, and existing paradigms of modern medicine are not meeting the challenge. One in four people will be affected by mental or neurological disorders at some point in their lives.¹ One in ten people currently suffer from a psychopathology and over 700 million people are affected globally with some sort of mental illness, addiction or eating disorder.² According to the National Institute of Mental Health, more than 17 million people in the U.S. and 300 million people worldwide have experienced major depression.³ Apart from the anguish and torment these conditions cause sufferers and their families, the estimated economic cost of mental disorders in the USA is \$467 billion; \$2.5 trillion globally.⁴

The isolation, anxiety and loss experienced by many during the Covid pandemic can only exacerbate these trends. And current treatment options and paradigms have been found wanting. A staggering 30% of depression patients do not respond to any currently available treatment⁵ so while diagnoses continue to rise – the rate of adults with major depression increased from 6.1% in 1996 to 10.4% in 2015⁶ – and prescriptions skyrocket,⁷ many are not finding the help they need.

Even more concerning, big pharma seem to have given up. Research budgets for psychiatric medicine in large companies have fallen by 70% in 10 years, as generic alternatives provide steep competition and confidence is waning that more investment in the same direction will produce improved results.⁸ What's needed is a radical re-think of mental illness and the tools available to heal; a re-conception of depression and other conditions as illnesses of the mind, not diseases of brain.⁹



1 "The World Health Report 2001: Mental Disorders affect one in four people," WHO, September 2001. <https://www.who.int/news/item/28-09-2001-the-world-health-report-2001-mental-disorders-affect-one-in-four-people#:~:text=One%20in%20four%20people%20in%20the%20world%20will,the%20leading%20causes%20of%20ill-health%20and%20disability%20worldwide>

2 "Compass Pathways (NASDAQ:CMPS) IPO Proves Psychedelic Medicine Investment Thesis, WPSS Investments Newswire," October 1, 2020. <https://www.globenewswire.com/news-release/2020/10/02/2102708/0/en/COMPASS-PATHWAYS-NASDAQ-CMPS-IPO-PROVES-PSYCHE%20ACDELIC-MEDICINE-INVESTMENT-THESIS.html>

3 "Psychedelic Treatment with Psilocybin Relieves Major Depression, Study Shows, Hopkins Medicine," November 4, 2020. <https://www.hopkinsmedicine.org/news/newsroom/news-releases/psychedelic-treat-ment-with-psilocybin-relieves-major-depression-study-shows>

4 "Compass Pathways (NASDAQ:CMPS) IPO Proves Psychedelic Medicine Investment Thesis, WPSS Investments Newswire," October 1, 2020. <https://www.globenewswire.com/news-release/2020/10/02/2102708/0/en/COMPASS-PATHWAYS-NASDAQ-CMPS-IPO-PROVES-PSYCHE%20ACDELIC-MEDICINE-INVESTMENT-THESIS.html>

5 "Compass Pathways (NASDAQ:CMPS) IPO Proves Psychedelic Medicine Investment Thesis, WPSS Investments Newswire," October 1, 2020. <https://www.globenewswire.com/news-release/2020/10/02/2102708/0/en/COMPASS-PATHWAYS-NASDAQ-CMPS-IPO-PROVES-PSYCHE%20ACDELIC-MEDICINE-INVESTMENT-THESIS.html>

6 "National Prescription Patterns of Antidepressants in the Treatment of Adults With Major Depression in the US Between 1996 and 2015: A Population Representative Survey Based Analysis," Yan Luo et al., Psychiatry, 14 February 2020 | <https://doi.org/10.3389/fpsy.2020.00035>

7 "Antidepressants: Doctors are increasingly prescribing SSRIs to treat more than just depression," Julia Calderone, November 1, 2014. <https://www.scientificamerican.com/article/the-rise-of-all-purpose-antidepressants/>

8 "Why 'big pharma' stopped searching for the next Prozac," Mary O'Hara and Pamela Duncan, January 27, 2016. <https://www.theguardian.com/society/2016/jan/27/prozac-next-psychiatric-wonder-drug-research-medicine-mental-illness>

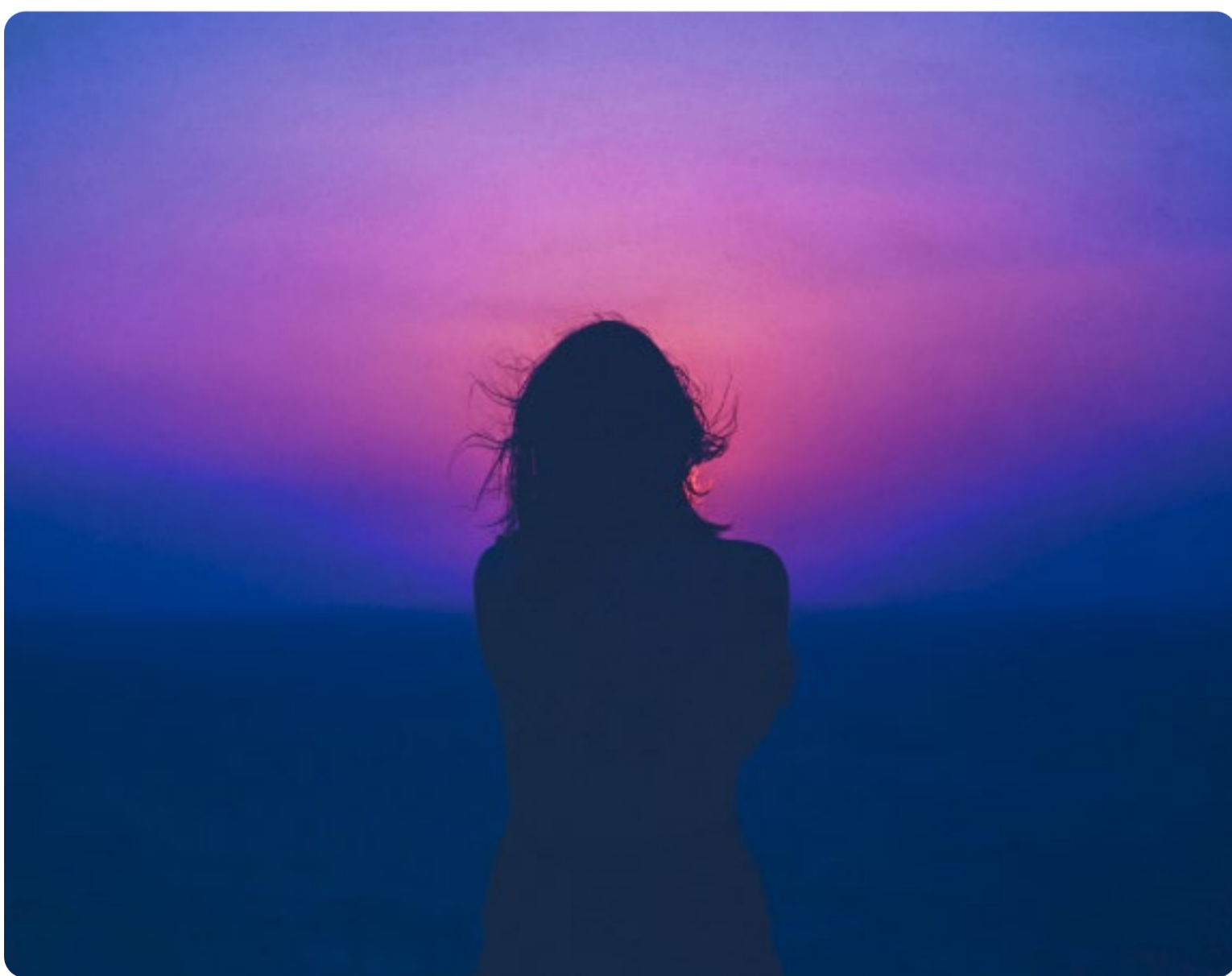
9 "Why 'big pharma' stopped searching for the next Prozac," Mary O'Hara and Pamela Duncan, January 27, 2016. <https://www.theguardian.com/society/2016/jan/27/prozac-next-psychiatric-wonder-drug-research-medicine-mental-illness>

Psychedelics to heal the mind, not just the brain

Psychedelics (serotonergic hallucinogens) are powerful psychoactive substances that can alter perception and mood and affect numerous cognitive processes. They are sometimes pejoratively referred to as hallucinogens, to imply that they principally produce hallucinations. Though in normal doses for ordinary users this is not usually the case, and hallucinogens is also used to describe other psychoactive molecules such as cannabinoids, “ecstasy,” dissociative agents, and others.¹⁰ The term “psychedelic” was coined by Humphrey Osmond in 1957, from the Greek words psychē (ψυχή, ‘soul’) and dēloun (δῆλον, ‘to make visible, to reveal’), connoting their mind-revealing capability.¹¹

Psychedelics are distinguished by their reliable capacity to create states of altered perception, thoughts and feelings; states that are not usually achievable other than in dreams or perhaps at moments of religious or spiritual exaltation. Plant-based psychedelics have had holistic healing roles in traditional societies for hundreds or perhaps thousands of years, and there exists a considerable culture of self-medication for mental health.¹²

Between 1950 and the mid-1960s there were more than a thousand clinical papers discussing 40,000 patients, several dozen books, and six international conferences on psychedelic drug therapy.¹³ In the 1960s and ‘70s psychedelics received a bad rap mainly due to their political associations. Their uptake among counterculture, anti-Vietnam war protestors convinced elites of the need to marginalize them. Their therapeutic message, which disputed the brain disorder paradigm that could be treated relatively cheaply (for the insurance companies) with medication, and instead reflected upon a patient’s entire social context – including their housing, income, and education– also did not suit the historical political agenda. In the last decade however, as current paradigms of malfunctioning brain chemistry as the cause of mental illness have been found wanting, some serious researchers have returned to psychedelics.



10 “Psychedelics,” David E. Nichols, *Pharmacol Rev.* 2016 Apr; 68(2): 264–355. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4813425/>
11 “A review of the clinical effects of psychotomimetic agents,” Osmond H. (1957) *Ann N Y Acad Sci* 66:418–434.
12 “LSD: My Problem Child,” Hofmann A (1980) McGraw-Hill: New York
13 “Psychedelics,” David E. Nichols, *Pharmacol Rev.* 2016 Apr; 68(2): 264–355. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4813425/>

Firstly to address the claim that these drugs are somehow more addictive, dangerous or detrimental than currently available medications, consider the 2013 study of data drawn from the National Survey on Drug Use and Health (NSDUH), which evaluated possible associations between lifetime use of psychedelics and current mental health in the U.S. adult population. In a sample of 152 respondents, 13.4% reported lifetime psychedelic use. No significant associations were found between lifetime use of any psychedelic or past-year use of LSD and increased rate of any mental health outcome. Surprisingly, in several cases, use of psychedelics was associated with a lower rate of mental health problems.¹⁴ The same researchers later analyzed a new much larger data set of 135,095 randomly selected U.S. adults that included 19,299 users of psychedelics, again using data from the NSDUH for 2008–2011. Again they found no significant associations between lifetime use of psychedelics and increased likelihood of past-year serious psychologic distress, mental health treatment, depression, anxiety, or suicidal thoughts, plans, or attempts. This study found that lifetime use of psychedelics was associated with *decreased* inpatient psychiatric treatment.¹⁵



These studies give force to the claim that psychedelics, even used recreationally, do not exacerbate and might even have a healing effect on mental ill health. But that would not be enough to convince the Canadian government to allow health professionals to use psilocybin mushrooms in end-of-life care.¹⁶ This leap was propelled by other studies performed by John Hopkins, University College London and others, which have demonstrated the potentially positive effects of psychedelics in treating a range of mental disorders. These are early phase clinical trials but they could be the start of a growing body of evidence attesting to the therapeutic potential of these substances.

In 2006, for example, a double-blind randomized controlled (DB-RC) study compared the acute and longer-term psychological effects of single high doses of psilocybin (30 mg) and methylphenidate (40 mg) in 36 healthy volunteers. Greater improvements in psychological well-being were observed after psilocybin than methylphenidate after 2-months. More than half considered their psilocybin experience to be among the most personally meaningful experiences of their lives.¹⁷ Since then, three DB-RC trials have assessed the impact of a single dose of psilocybin on depressive symptoms in patients with life-threatening cancer¹⁸ and an open-label trial of psilocybin for treatment-resistant depression (TRD) has been completed.¹⁹

14 "Psychedelics and mental health: a population study," Krebs TS, Johansen PO. (2013) PLoS One 8:e63972.

15 "Psychedelics not linked to mental health problems or suicidal behavior: a population study," Johansen PO, Krebs TS. (2015) J Psychopharmacol DOI: 10.1177/0269881114568039

16 "Canada Will Let Health Care Professionals Legally Use Psychedelic Mushrooms, Health Minister Says," Ben Adlin, December 8, 2020. <https://www.marijuanamoment.net/canada-will-let-health-care-professionals-legally-use-psychedelic-mushrooms-health-minister-says/>

17 "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance" Griffiths RR, Richards WA, McCann U, Jesse R (2006), Psychopharmacology 187: 268–283.

18 See "Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial," Griffiths et al. (2016) J Psychopharmacol 30: 1181–1197; "Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer," Grob et al (2011) Arch Gen Psychiatry 68: 71–78; "Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial," Ross et al (2016) J Psychopharmacol 30: 1165–1180.

19 "Psilocybin with psychological support for treatment-resistant depression: six-month follow-up," Carhart-Harris et al (2016a) The British Association for Psychopharmacology Summer Meeting. 17–20 July, Brighton, UK; "Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study," Carhart-Harris et al (2016b) Lancet Psychiatry 3: 619–627.

All four studies, and particularly the three most recent, found rapid, marked, and enduring anti-anxiety and depression effects post psilocybin. Significant improvements in obsessive compulsive disorder symptoms²⁰ and alcohol dependence with psilocybin,²¹ anxiety with LSD,²² and depression with ayahuasca²³ help supplement the case for psilocybin and inspire creative thinking regarding the potential generalized therapeutic action of psychedelics.

In 2018 and again in 2019, the FDA declared psilocybin a “breakthrough therapy,” which means that it sees its potential to be an enormous improvement over already available therapy.²⁴ These designations were based on research conducted by two U.S. medical research organizations, COMPASS Pathways and the Usona Institute, on the use of psilocybin for treatment-resistant depression and major depressive disorder, respectively. In 2019, Johns Hopkins and Imperial College London both launched centers devoted to psychedelics research.

*“The magnitude of the effect we saw was about four times larger than what clinical trials have shown for traditional antidepressants on the market,” Alan Davis, Ph.D., adjunct assistant professor of psychiatry and behavioral sciences at the Johns Hopkins University School of Medicine.”*²⁵



20 “Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder,” Moreno et al (2006) J Clin Psychiatry 67: 1735–1740.

21 “Psilocybin-assisted treatment for alcohol dependence: a proof-of-concept study,” Bogenschutz et al (2015). J Psychopharmacol 29: 289–299.

22 “Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases,” Gasser et al (2014) J Nerv Ment Dis 202: 513–520.

23 “Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a preliminary report,” Osorio et al (2015) Rev Bras Psiquiatr 37: 13–20; “Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: a SPECT study,” Sanchez et al (2016) J Clin Psychopharmacol 36: 77–81..

24 “FDA Calls Psychedelic Psilocybin a ‘Breakthrough Therapy’ for Severe Depression,” Yasemin Saplakoglu, November 25, 2019. <https://www.livescience.com/psilocybin-depression-breakthrough-therapy.html>

25 “Psychedelic Treatment with Psilocybin Relieves Major Depression, Study Shows, Hopkins Medicine,” November 4, 2020. <https://www.hopkinsmedicine.org/news/newsroom/news-releases/psychedelic-treat-ment-with-psilocybin-relieves-major-depression-study-shows>

In Griffith's work at John Hopkins, he showed that psilocybin could be administered safely in healthy volunteers and produce experiences that the volunteers described as among the most meaningful events in their lives. At a follow-up six months after the study, 80% of participants continued to show clinically significant improvements in depression and anxiety.²⁶

Exactly how psychedelics work is unclear, though it seems that they activate serotonin receptors. While serotonin is responsible for modulating many brain functions, the effects often associated with psychedelics are heightened empathy, sudden insight, and dream-like states. Psilocybins also include glutamate, a neurotransmitting amino acid, with myriad roles in the brain. Both serotonin and glutamate pathways are thought to play an important role in learning and memory, which might help explain how psychedelics can have anti-depressant and anti-anxiety inducing effects (i.e., by helping to "re-wire" the brain).²⁷



"In a single six-hour session, participants can have experiences that they interpret as being profoundly meaningful, with enduring positive changes years later... There's something profoundly important about these experiences." Roland Griffiths, PhD, founding director of the Johns Hopkins Center for Psychedelic and Consciousness Research.²⁹

All studies have emphasized the importance of set and setting to the therapeutic effect. Study participants were guided through their psychedelic experience by trained professionals, who ensure patient safety and also enhance outcomes by helping the patient process their experience. The combination of psilocybin with psychological support (PwPS) could also have a role in the early (and not just chronic) treatment of depression. While current antidepressants or cognitive behavioral therapies suppress or side-step difficult memories, even a limited exposure to PwPS could directly confront the feelings with the potential for rapid and enduring effect.²⁸

26 Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial," Griffiths et al. (2016) J Psychopharmacol 30: 1181-1197

27 "Altered reality? An update on psychedelics in Canada," Morgan T. McDonald & Becky Rock, Jun 30, 2020, <https://www.dlapiper.com/en/canada/insights/publications/2020/06/an-update-on-psychedelics-in-canada/>

28 "The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future," Carhart-Harris & Goodwin, 26 April 2017, Neuropsychopharmacology volume 42, p. 2105-2113. <https://www.nature.com/articles/npp201784>

29 "Trip of a lifetime, Kirsten Weir," American Psychological Association, March 1, 2020. <https://www.apa.org/monitor/2020/03/cover-trip>

A Mushrooming Market

The antidepressant drug market alone was valued at around \$13.7 billion in 2018 and was projected to grow as much as 24% by 2020.³⁰ But psychedelics could also bring relief to sufferers of post-traumatic stress disorder, addiction or chronic pain. One estimation is that 1 billion people suffer from disorders that studies have found could be treated using psychedelics. This could be why the sector was valued at approximately US\$2 billion in 2019, and forecasted to reach a market capitalization of US\$6.8 billion by 2027.³¹ Canaccord Genuity Corp. are estimating psychedelic medicines and psychedelic-assisted therapy could eventually become a \$100 billion market.³²

It's early days, but there are signs that governments and the investment community are recognizing and ready to back the innovation suggested by the latest scientific trials. Companies recognizing the potential of psychedelics are getting involved in the whole range of the potential treatment space – from clinics for guided psychedelic treatment sessions to drug chemical design to exploring the treatment design and effectiveness for different health conditions.



On September 18, 2020 Compass Pathways, which has patented a synthetic form of psilocybin for use in treatment-resistant depression, became the first psychedelic company to be listed on a U.S. exchange, following the FDA's designation of its research as "breakthrough therapy". CMPS' s price per share has risen more than 100% since its initial listing price of US \$17, making it the first and most valuable unicorn psychedelic medicine company in the world.³³ More recently in Canada, a few psychedelics companies have IPO-ed: Toronto-based MindMed, which is developing therapies based on psychedelics including Psilocybin, LSD, MDMA and DMT, announced a \$50 million IPO on December 14, 2020.³⁴ Its shares are now traded on the Canadian, US and German exchanges. Salvation Botanicals, a wholly-owned subsidiary of Numinus Wellness Inc. (Numinus), which IPO-ed in May 2020, recently received approval "to conduct research to standardize the extraction of psilocybin from mushrooms".³⁵ Salvation Botanicals also has a dealer's license to "import, export, possess, test and distribute" MDMA, psilocybin, psilocin, DMT, and mescaline.³⁶

30 "Thiel Backs Psychedelic-Drug Startup in Latest Funding Round," Tereza Elisabeth Pusca and Erin Roman, April 23, 2020.

<https://www.bloomberg.com/news/articles/2020-04-23/thiel-backs-psychedelic-drug-startup-in-latest-funding-round>

31 "Psychedelic Drugs Market Projected to Reach \$6,859.95 Million by 2027," June 3, 2020.

<https://www.prnewswire.com/news-releases/psychedelic-drugs-market-projected-to-reach-6-859-95-million-by-2027--301069861.html>

32 "Psychedelic Drug Company MindMed Applies For Nasdaq Up-Listing," Will Yakowicz, Sep 25, 2020

<https://www.forbes.com/sites/willyakowicz/2020/09/25/psychedelic-drug-company-mindmed-applies-for-nasdaq-up-listing/?sh=7eed92d16cf7>

33 "Compass Pathways (NASDAQ:CMPS) IPO Proves Psychedelic Medicine Investment Thesis, WPSS Investments Newswire," October 1, 2020. <https://www.globenewswire.com/news-release/2020/10/02/2102708/0/en/COMPASS-PATHWAYS-NASDAQ-CMPS-IPO-PROVES-PSYCHE%20ACDELIC-MEDICINE-INVESTMENT-THESIS.html>.

34 "MindMed Announces \$50 Million Bought Deal Public Offering," Mind Newswire, December 14, 2020.

<https://www.newswire.ca/news-releases/mindmed-announces-50-million-bought-deal-public-offering-847758161.html>

35 "Numinus receives Health Canada licence amendment to produce and extract psilocybin from mushrooms," Press Release, June 11, 2020

<https://numinus.ca/investors/news-release/numinus-receives-health-canada-licence-amendment-to-produce-and-extract-psilocybin-from-mushrooms/>

36 "Numinus Wellness: A rising star in the Psychedelic Investing space!" Kirsteen Mackay, 10 Dec 2020.

<https://www.valuethemarkets.com/2020/12/10/numinus-wellness-a-rising-star-in-the-psychedelic-investing-space/>

In the US, some states and cities are decriminalizing certain psychedelics – this does not legalize them, but it makes it easier to use them for research and treatment and makes their removal of the lowest priority for the police. Santa Cruz and Oakland have decriminalized a variety of psychoactive plants and fungi, and Denver has specifically decriminalized magic mushrooms containing psilocybin. In November 2020, Oregon became the first state to legalize magic mushrooms.³⁷

Large corporations are waking up to the potential future of psychedelic market. In 2019 the world's largest healthcare company, Johnson & Johnson, received FDA approval for a ketamine-based nasal spray, Spravato, to treat depression.³⁸ In May 2020, pharma giant AbbVie bought Allergan for US\$63 billion, thereby acquiring its ketamine-like treatment for depression.

As more and more corporations and universities enter the research ring, and regulatory bodies continue their willingness to reward sound science with pharmaceutical freedom, this may be the beginning of a radical new direction in mental health treatment.

Medical Cannabis

More than two thirds of U.S. states and the District of Columbia have legalized the use of marijuana for medical treatments and more are considering bills to do the same. The FDA is committed to expediting the distribution of research licenses. PSY is not the first cannabis ETF, but in its unique combination with psychedelics, it points to the next generation of medicine.

PSY includes companies involved in the cultivation, production, distribution, or services related to medical cannabis or CBD derivatives. While regulations differ between states, medicinal marijuana has been proven effective and is prescribed in the following cases: Alzheimer's disease, amyotrophic lateral sclerosis (ALS), HIV/AIDS, cancer, Crohn's disease, epilepsy and seizures, glaucoma, multiple sclerosis and muscle spasms, severe and chronic pain and severe nausea.



³⁷ "Oregon becomes first state to legalize magic mushrooms as more states ease drug laws in 'psychedelic renaissance,'" Will Feuer, November 4, 2020. <https://www.cnn.com/2020/11/04/oregon-becomes-first-state-to-legalize-magic-mushrooms-as-more-states-ease-drug-laws.html>

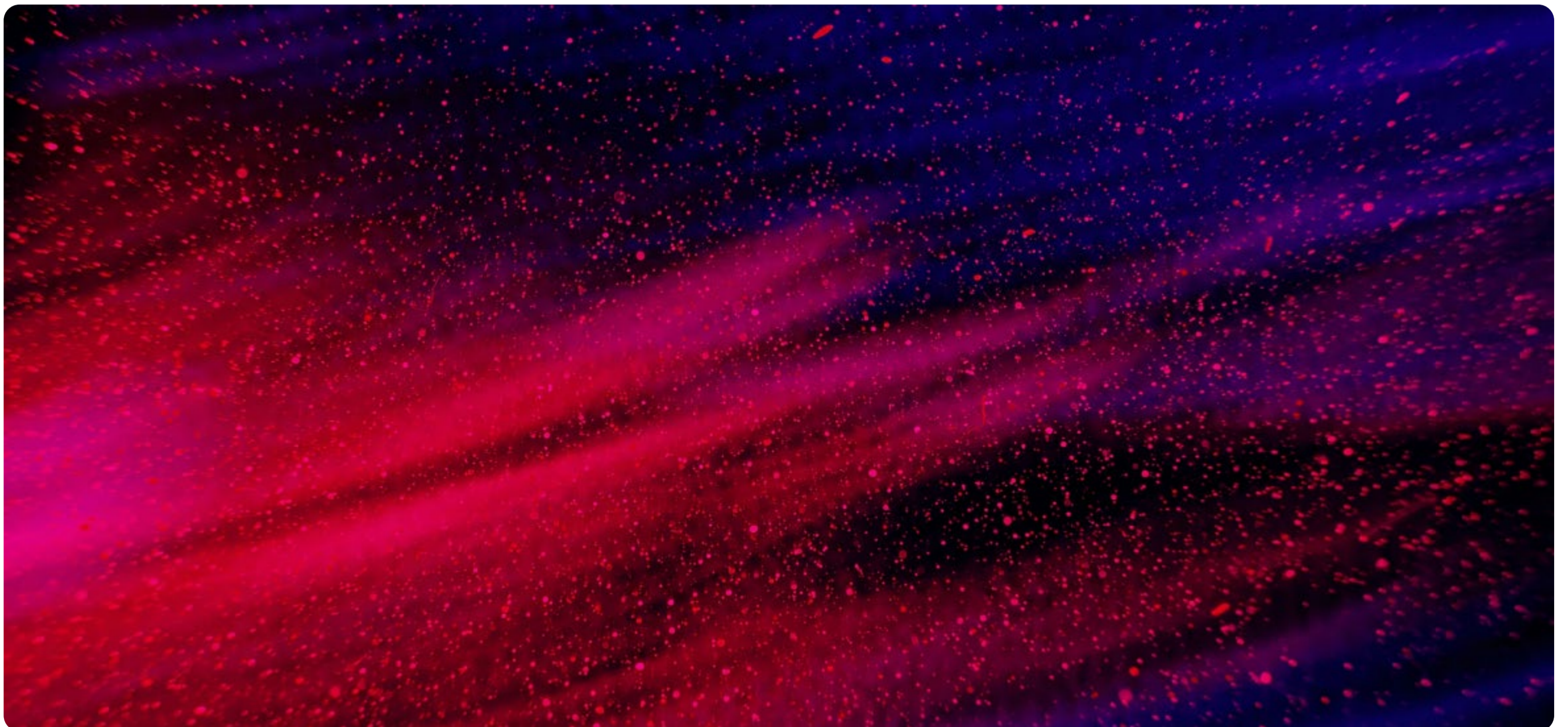
³⁸ "FDA approves new nasal spray medication for treatment-resistant depression; available only at a certified doctor's office or clinic," March 5, 2019. <https://www.fda.gov/news-events/press-announcements/fda-approves-new-nasal-spray-medication-treatment-resistant-depression-available-only-certified>

Why Defiance PSY?

Defiance's PSY is the first US-listed psychedelic ETF. Following the success of our first US-listed 5G, SPAC and hydrogen fuel ETFs, we once again believe we have identified a powerful sector with potential for significant disruption. We aim to bring investors diversified exposure to the themes that they believe in.

We know that it will take time for regulators, practitioners and patients to consider psychedelics as an alternative to opioids as treatment for depression, eating disorders, anxiety or other illnesses. And we know that not every company that enters this space will thrive. That's why we offer a weighted, rules-based index that mitigates risk of over-exposure to any single company. Companies included in the index must have a minimum market capitalization of \$75 million, and operate in the production, distribution, or services related to medical psychedelics, medical cannabis or ketamine and its derivatives.

Psychedelics is a fledgling industry with massive potential. PSY is a passively-managed ETF that can be traded intra-day or held for the long term while the space grows. It can provide exposure to the disruptive future of psychedelic medicine.



What types of psychedelics are there?



LSD (Lysergic acid diethylamide) is made from a substance found in ergot, which is a fungus that infects rye.

Psilocybin is a naturally occurring substance found in mushrooms and is found in many parts of the world.

Mescaline is derived from the Mexican peyote and San Pedro cactus and produces similar effects to LSD.

DMT (Dimethyltryptamine) is structurally similar to psilocin, an alkaloid found in psilocybin mushrooms. It can be synthesised in the laboratory but is also a naturally occurring component of several plants.

DOM is a member of the DOx family of compounds which are known for their high potency, long duration, and mixture of psychedelic and stimulant effects.

2C-B (4-Bromo-2,5-dimethoxyphenethylamine) is a psychedelic drug first synthesised in 1974. 2C-B is considered both a psychedelic and a mild entactogenic. 'Entactogen' means 'touching within' and is a term used by psychiatrists to classify MDMA and related drugs.

Peyote (*Lophophora williamsii*) is the most well-known and potent psychedelic cactus, although the smallest and slowest growing. Instead of growing upward to form a column, it grows as 'buttons' low to the ground. It has been used by Native Americans for over 5000 years.

25[-x]-NBOMe NBOMe (N-methoxybenzyl) is the name for a series of drugs that have psychedelics effects. Reports indicate that there are a number of different versions of NBOMe available – all with differing effects.³⁹

³⁹ Psychedelics, Australian Alcohol and Drug Foundation, October 7, 2020. <https://adf.org.au/drug-facts/psychedelics/>

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The Funds' investment objectives, risks, charges, and expenses must be considered carefully before investing. The prospectus contains this and other important information about the investment company. Please read it carefully before investing. A hard copy of the prospectus can be requested by calling 833.333.9383 or at defianceetfs.com.

Investing involves risk. Principal loss is possible. As an ETF, the fund may trade at a premium or discount to NAV. Shares of any ETF are bought and sold at market price (not NAV) and are not individually redeemed from the Fund. The Fund is not actively managed and would not sell a security due to current or projected under performance unless that security is removed from the Index or is required upon a reconstitution of the Index.

A portfolio concentrated in a single industry or country, may be subject to a higher degree of risk. Specifically, the Index (and as a result, the Fund) is expected to be concentrated in Psychedelics Healthcare and Medical Cannabis companies. Such companies may depend largely on the government regulation and their profitability can be significantly affected by restriction on government reimbursements for medical expenses, rising costs of products and services, pricing pressure, limited product lines, intellectual property rights, and long and costly government product approval processes. The investments rely on U.S. and Canadian regulation of psychedelic, healthcare and cannabis, and the fund could be adversely affected by changes in these regulations.

The Fund will not invest directly in or hold ownership in any companies that engage in cannabis- or psychedelics-related business unless permitted by national and local laws of the relevant jurisdiction, including U.S. federal and state laws. Accordingly, the Fund does not currently invest (directly or indirectly) in companies located in the United States if their cannabis- or psychedelics-related business activities are illegal under U.S. federal law, even if such activities are legal under state law. In the United States and Canada, the medical and recreational use of certain psychedelic drugs, including psilocybin, is currently illegal. There is no guarantee that psychedelic drugs or psychedelic inspired drugs will ever be approved as medicines in either jurisdiction.

The Fund is considered to be non-diversified, so it may invest more of its assets in the securities of a single issuer or a smaller number of issuers. Investments in foreign securities involve certain risks including risk of loss due to foreign currency fluctuations or to political or economic instability. Small and mid-cap companies are subject to greater and more unpredictable price changes than securities of large-cap companies.

The BITA Medical Psychedelics, Cannabis, and Ketamine Index is a rules-based index that tracks the performance of companies, listed in North American Exchanges, that operate business models focused on the usage of Psychedelics, Medical Cannabis, and Ketamine for medicinal and health treatment purposes. The index is owned, calculated, administered and disseminated by BITA GmbH.

PSY is new with a limited operating history.

Go to defianceetfs.com/PSY to read more about PSY including current performance and holdings information.

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