



How Research, Regulations, and Innovation Will Drive and Disrupt the CBD Industry



Dave Neundorfer

CEO, Open Book Extracts

Tech and cannabis entrepreneur with deep channels to capital in Ohio, Silicon Valley, and Europe. Executed exclusive, royalty-based software licensing partnerships with leading semiconductor and industrial partners.

Dartmouth and Stanford GSB



Andrea Baillo, PhD

VP of Product Innovation & Research, Open Book Extracts

Experienced scientist with a demonstrated history of working in cannabis research, development, and manufacturing, cancer research, and food and beverage industries. Baillo most recently served as Senior Director, Research & Development, Quality at Green Thumb Industries (GTI), and she is known for her focus on product safety and stability of cannabinoid focused formulations in highly regulated markets.

Wayne State University and Wayne State Medical School



Nicole Brown

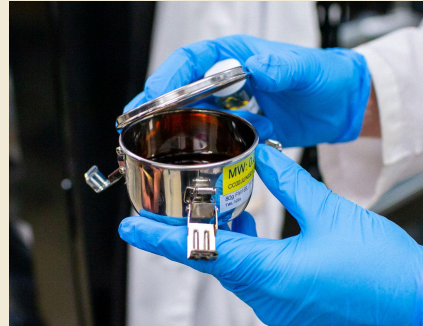
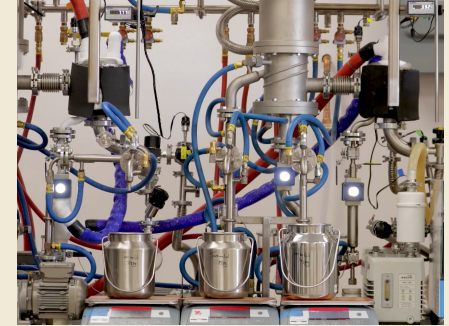
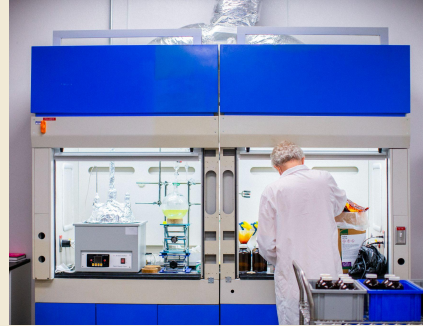
Chief Innovation Officer, Open Book Extracts

Seasoned marketing and innovation executive in the consumer and lifestyle space, including LVMH and Shiseido Cosmetics. Founded and sold a mapping technology company to TripAdvisor. Known for her keen sense of ever-changing consumer wants to drive huge growth.

Harvard University



cGMP certification for food processing (CFR 117) & nutraceuticals (CFR 111), with an audit rating of “Excellent”.



GMP-Certified Facility in Roxboro, NC



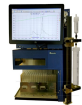
Particle Reduction



Ethanol Extractor



2-Stage Distillation



Flash Chroma



Gas Chroma



Liquid Chroma



Solvent Recovery



Nano Emulsion



Easysnap



Supply Chain Partner That Brands Rely On

Deliver our clients have access to a trusted, reliable supply chain, from ingredients, to formulations, to finished goods.

Trusted
Supply Chain
Partner

1 Product Selection

- Market sales data
- Consumer trends
- Product strategy

2 Cannabinoid Selection

- Specifications
- Volume
- Pricing

3 Formulation

- Desired effect
- Ingredient selection
- Testing

4 Product Engineering

- Infusion tech
- Delivery systems
- Flavoring

5 Manufacturing

- Lead times
- Fulfillment
- Pricing

6 Testing & Documentation

- Third-party COAs on all ingredients and finished goods

7 Packaging & Marketing

- Regulatory compliance
- Private label programs

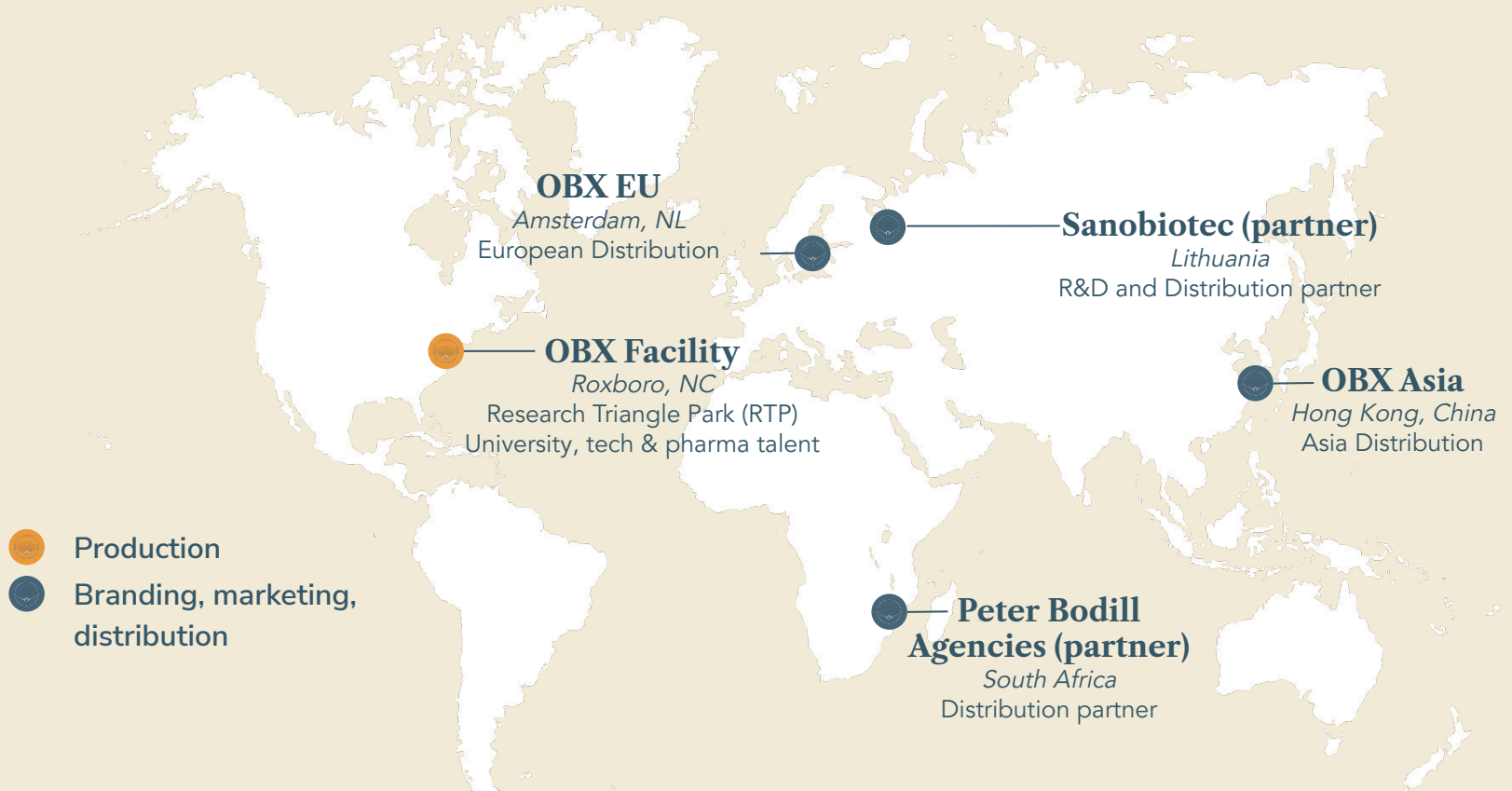
8 Product Distribution

- Introductions to distribution partners



Our footprint spans core global research and distribution centers, and enables us to capture global opportunities as regulatory pathways open worldwide for the safe manufacturing & distribution of cannabinoids.

Operating on
A Global Scale
to Stay Ahead
of the Curve



- Production
- Branding, marketing, distribution



Agenda

01 Regulatory Update

02 Research Base Camp

03 Innovation & Technology

04 Q & A

Regulatory Update





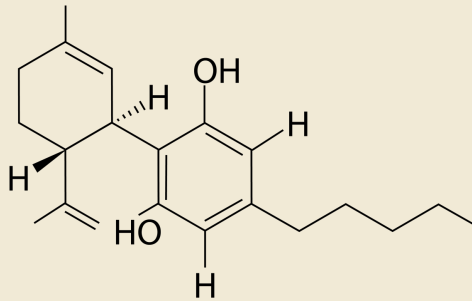
There are > 480 naturally occurring components found in the *Cannabis sativa* plant—66 of these are classified as cannabinoids.

Cannabinoid Group	Common Abbreviation	Number of Known Variants
Δ9-Tetrahydrocannabinol	Δ9-THC	9
Δ 8-Tetrahydrocannabinol	Δ 8-THC	2
Cannabichromene	CBC	5
Cannabicyclol	CBL	3
Cannabidiol	CBD	7
Cannabielsolin	CBE	5
Cannabigerol	CBG	6
Cannabinidiol	CBND	2
Cannabinol	CBN	7
Cannabitriol	CBT	9
Miscellaneous Types	--	11

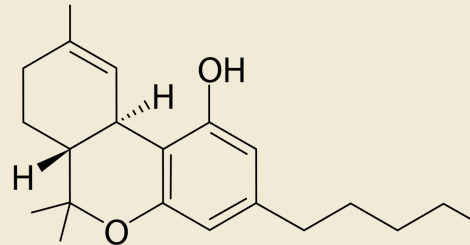


- THC concentration is the difference between hemp and marijuana

- Tetrahydrocannabinol (THC) - psychoactive
- Cannabidiol (CBD) - non-psychoactive



Cannabidiol
(CBD)



Delta-9-tetrahydrocannabinol
(THC)



Marijuana
(>0.3% THC)



Hemp
(<0.3% THC)

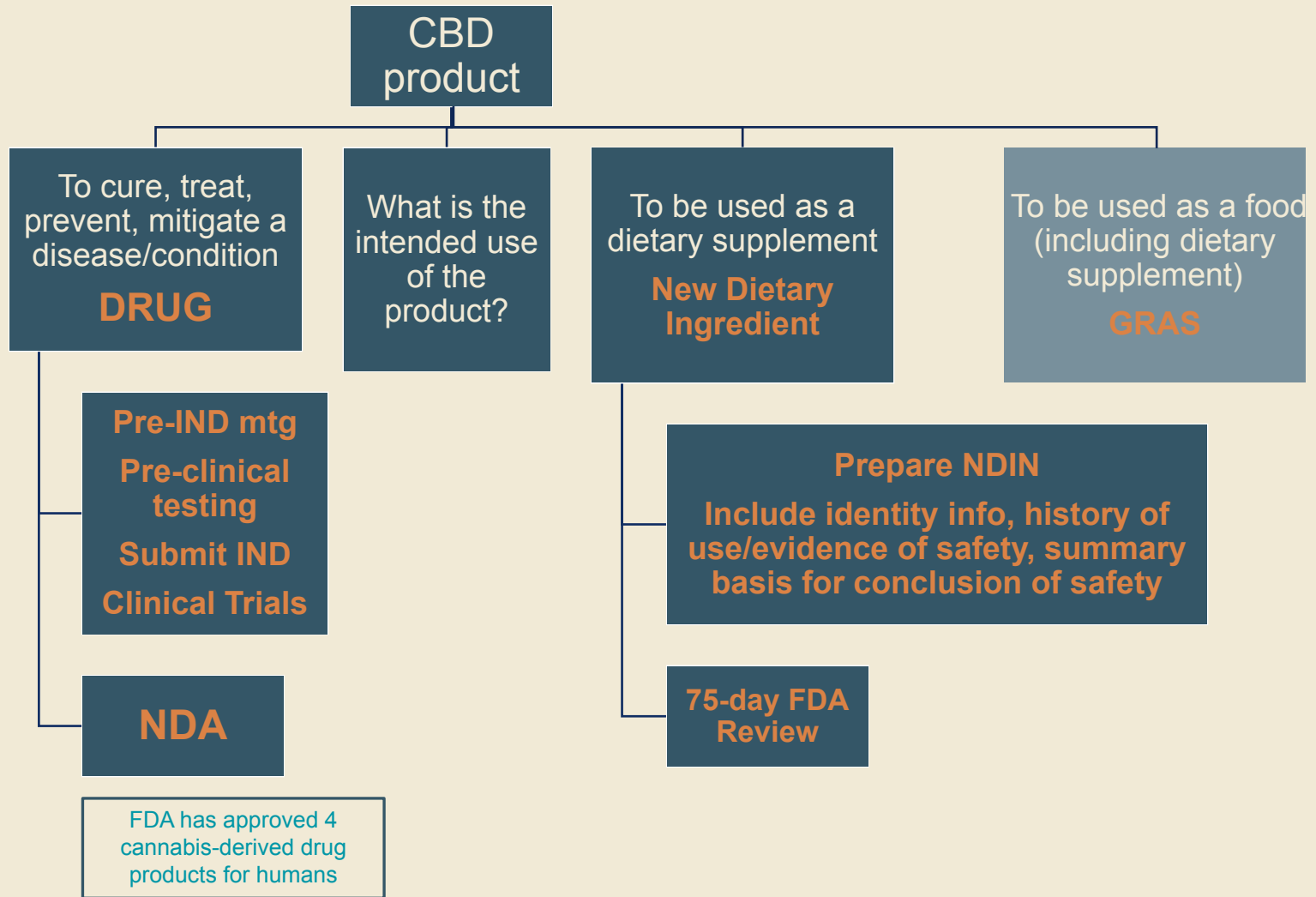


- Removed hemp from definition of marijuana
- Gave USDA authority over hemp production
- Preserved FDA's authorities under FDCA and §351 PHSA:
 - Support scientific research on potential therapeutic uses of CBD
 - Regulation of CBD products (e.g., as foods including dietary supplements, drugs, cosmetics)
 - Enforcement actions as necessary against violative CBD products that present serious human or animal health risks
- Marijuana still regulated by DEA (Drug Enforcement Agency) under Schedule 1 of CSA (Controlled Substances Act)





- Use of CBD in cosmetics is permitted
- According to the FDA, it is not currently lawful to add CBD to food or dietary supplements due to the *prescription drug preclusion*
 - If a substance is the active ingredient of an approved new drug, or the active ingredient of a new drug in clinical trials that have been made public, that ingredient cannot be used in a food or dietary supplement
 - THC and CBD are subject to the prescription drug preclusion
 - Minor cannabinoids are likely not subject to the prescription drug preclusion
- However, the FDA has been exercising *broad enforcement discretion*, and has not taken any action to stop the sale of ingestible CBD products, with the exception of brands making medical claims, to whom the FDA has sent warning letters
 - Under the FD&C Act, any product, including a cannabis product (hemp or otherwise), that is marketed with a claim of therapeutic benefit, or with any other disease claim, is considered to be a drug, which must be approved by the FDA for its intended use before it may be introduced into interstate commerce





- FDA recently rejected two NDIs submitted by Charlotte's Web and Irwin Naturals
- Both sought clearance to market full-spectrum hemp extract containing CBD
- Two main reasons for rejection:
 - Drug Exclusion Rule (see Epidiolex)
 - Insufficient Data
 - "Vagueness" of preclinical and clinical studies
 - Failure to sufficiently address certain tox endpoints

Can These
Cannabinoids
Be Marketed
Legally?



July 23, 2021

Mr. Tim Orr
Charlotte's Web, Inc.
1600 Pearl Street
Boulder, Colorado 80302

Dear Mr. Orr:

This letter is to inform you that the notification that you submitted pursuant to 21 United States Code (U.S.C.) § 350b(a)(2) (section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)), was received and filed by the Food and Drug Administration (FDA or we) on March 31, 2021. Additional information was received on May 7, May 12, and June 21, 2021. The amendment received on May 12, 2021, was deemed a substantive amendment, which reset the filing date to May 12, 2021, as per 21 CFR 190.6(d). Your notification concerns the new dietary ingredient (NDI) "Charlotte's Web Full Spectrum Hemp Extract" (CW FSHE) (hereinafter "NDI 1202") that you intend to market in a dietary supplement tincture.

According to your notification, the conditions of use are: "The proposed maximum daily intake of dietary supplement tincture is two (2) servings per day. Each 0.15 mL serving of the tincture provides 12.9 mg of the CW FSHE extract (9.75 mg CBD). Suggested daily intake is 0.30 mL of the tincture providing 25.8 [mg of the] CW FSHE [extract] (19.5 mg CBD). Duration of use is intermittent. Target population is adults (18+ years) with instructions to consult your physician before use if you are pregnant, nursing, have or suspect a medical condition or are taking any medications. Also includes instructions to keep out of the reach of children."

Under 21 U.S.C. § 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C. § 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the condition recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. § 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

U.S. Food and Drug Administration
5001 Campus Drive
College Park, MD 20740
www.fda.gov



- What does this tell us?
 - FDA is not making distinctions between full-spectrum products and CBD isolates
 - FDA wants additional data demonstrating product safety
 - FDA needs Congress to remove CBD from the Drug Exclusion Rule through legislation



- Congressional efforts are underway – through HR 841 and S 1698 – to allow CBD companies to have access to all of the same safety pathways provided to other food and dietary supplements (GRAS, NDI)



- State legislatures are making headway despite delays in Congress
- States collectively representing over 40% of US GDP, including California, New York, Texas, Florida, and Ohio, have passed legislation permitting CBD in supplements, food, and beverage
- The legislation imposes cGMP requirements on manufacturers, and imposes testing and labeling requirements on consumer-facing brands



01 Ensure your products are produced in compliance with well-established cGMP guidelines for food and nutraceuticals

02 Do not make medical claims

03 Consider using minor cannabinoids if pursuing NDI approval

04 Look to state-level legislation as a potential guide to future federal legislation

05 Adhere to state-level labeling and testing requirements

Research Base Camp





Summits on
the horizon

Nervous System Disorder

Skin Disorder

Metabolic Disorder

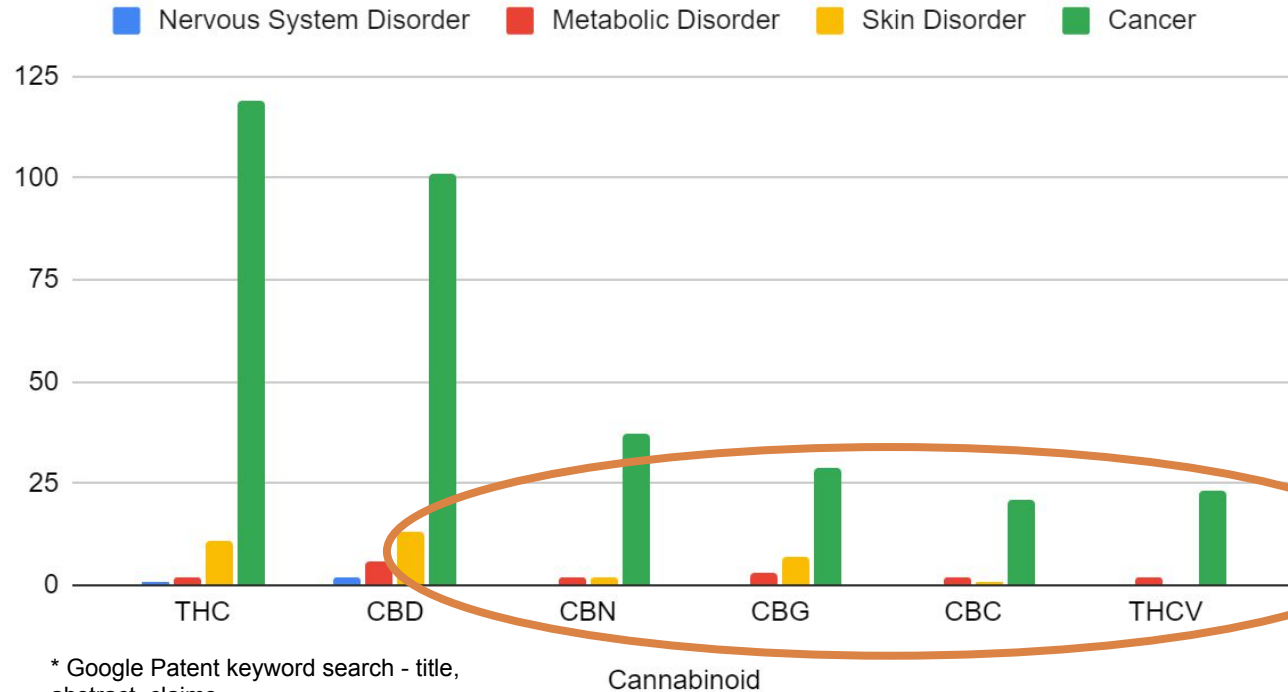
Cancer





Major opportunities for cannabinoid IP

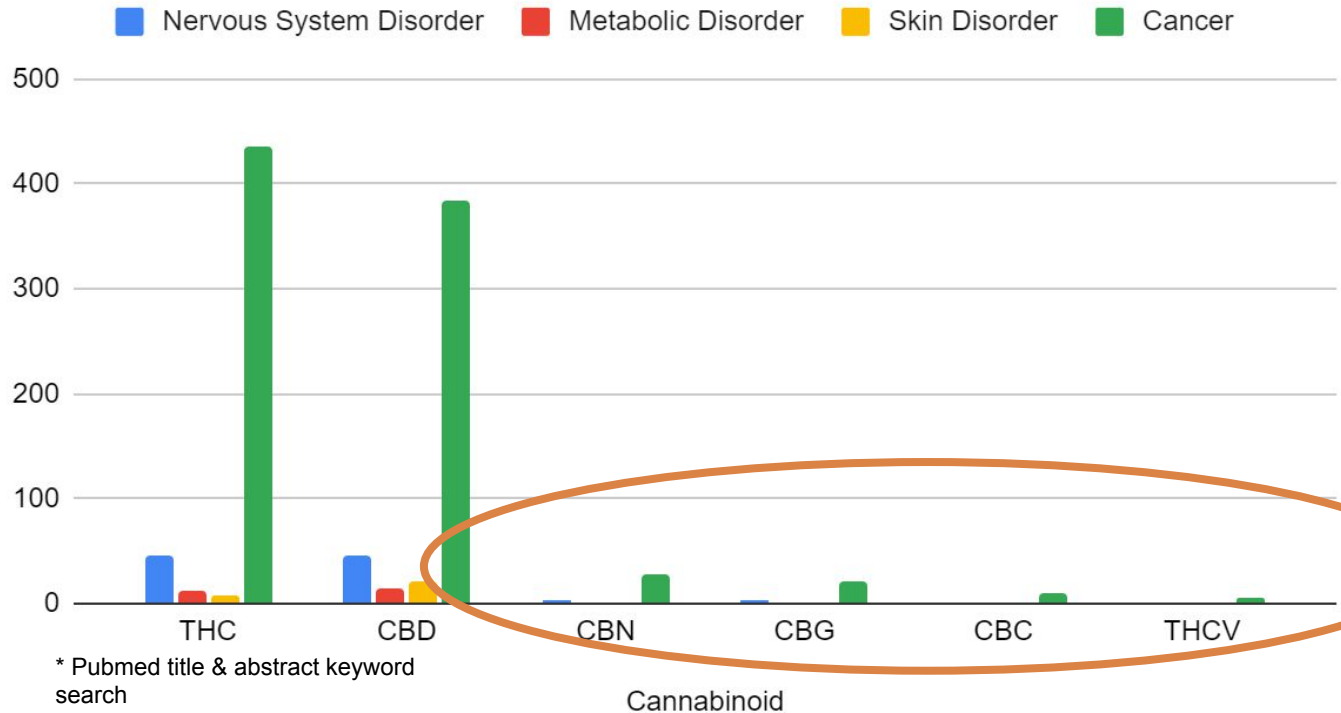
Patents*





Major opportunities for cannabinoid publications

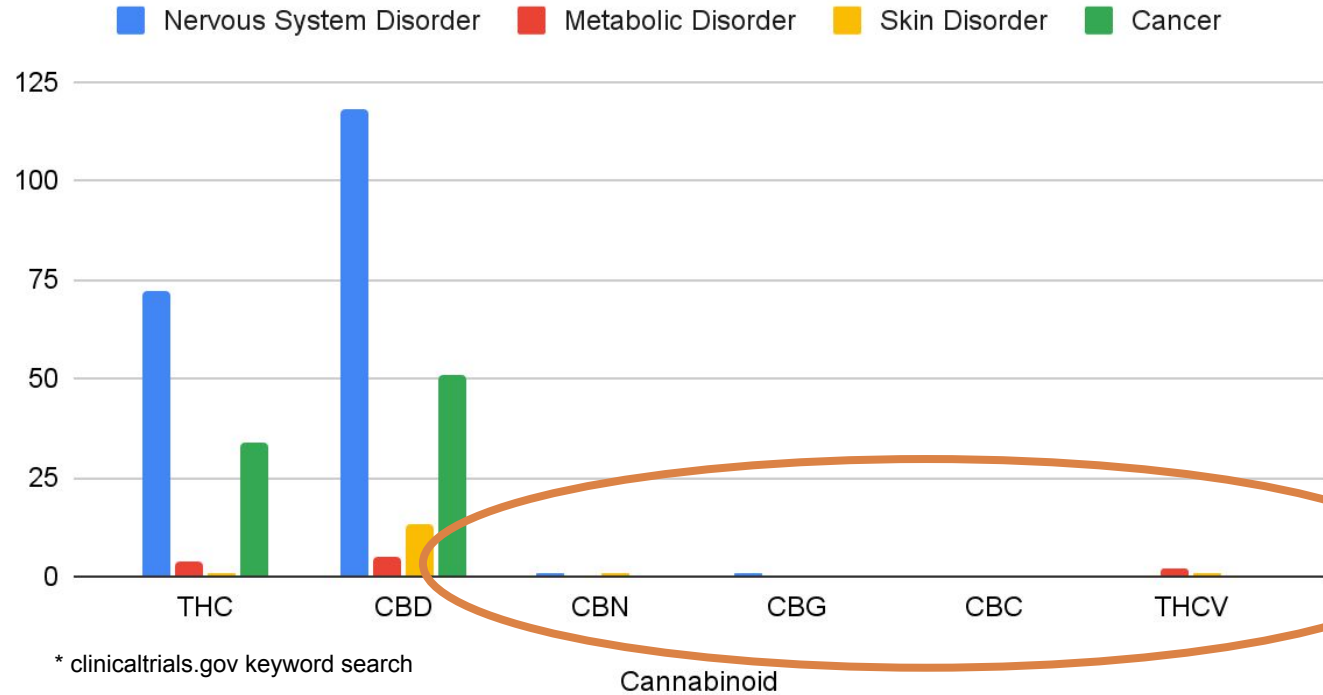
Research Articles*





Major opportunities for cannabinoid clinicals

Clinical Trials*





Enhancement

Formulation

Purification

Extraction

Chemistry

Intellectual Property

We are your
Sherpa





The Team

- 150 years of cumulative cannabinoid experience
- 2 drug development veterans, 7 PhDs & 3 Masters Degrees
- Production, purification, and formulation experts



Gang Tian, MS
Chief Technology Officer



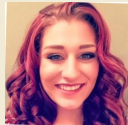
Andrea Baillo, PhD
VP of Product Innovation & Research



Nicole Brown
Chief Innovation Officer



David Temelkoff, MS
R&D and QC Manager



Alexandra DePalma
Director of Product Innovation



Garry Southan, PhD
Prodrug Advisor



Trevor Gentry, PhD
Director of Product Development and R&D



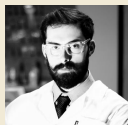
Gabriel Smith, MS
Production Manager



Prakash Jagtap, PhD
Prodrug Advisor



Edward Nikitin, PhD
Production Scientist



Zach Bell, PhD
Chief Innovation Officer, OBX Asia



John Weatherspoon, PhD, JD
IP Advisor

Deep cannabinoid, science, and drug dev experience



University Partnerships:

FLORIDA **A&M** UNIVERSITY



SCHOOL OF MEDICINE
CASE WESTERN RESERVE
UNIVERSITY



UNIVERSIDAD NACIONAL
AUTÓNOMA DE MÉXICO



NC STATE UNIVERSITY

Industry Related:





The Alliance

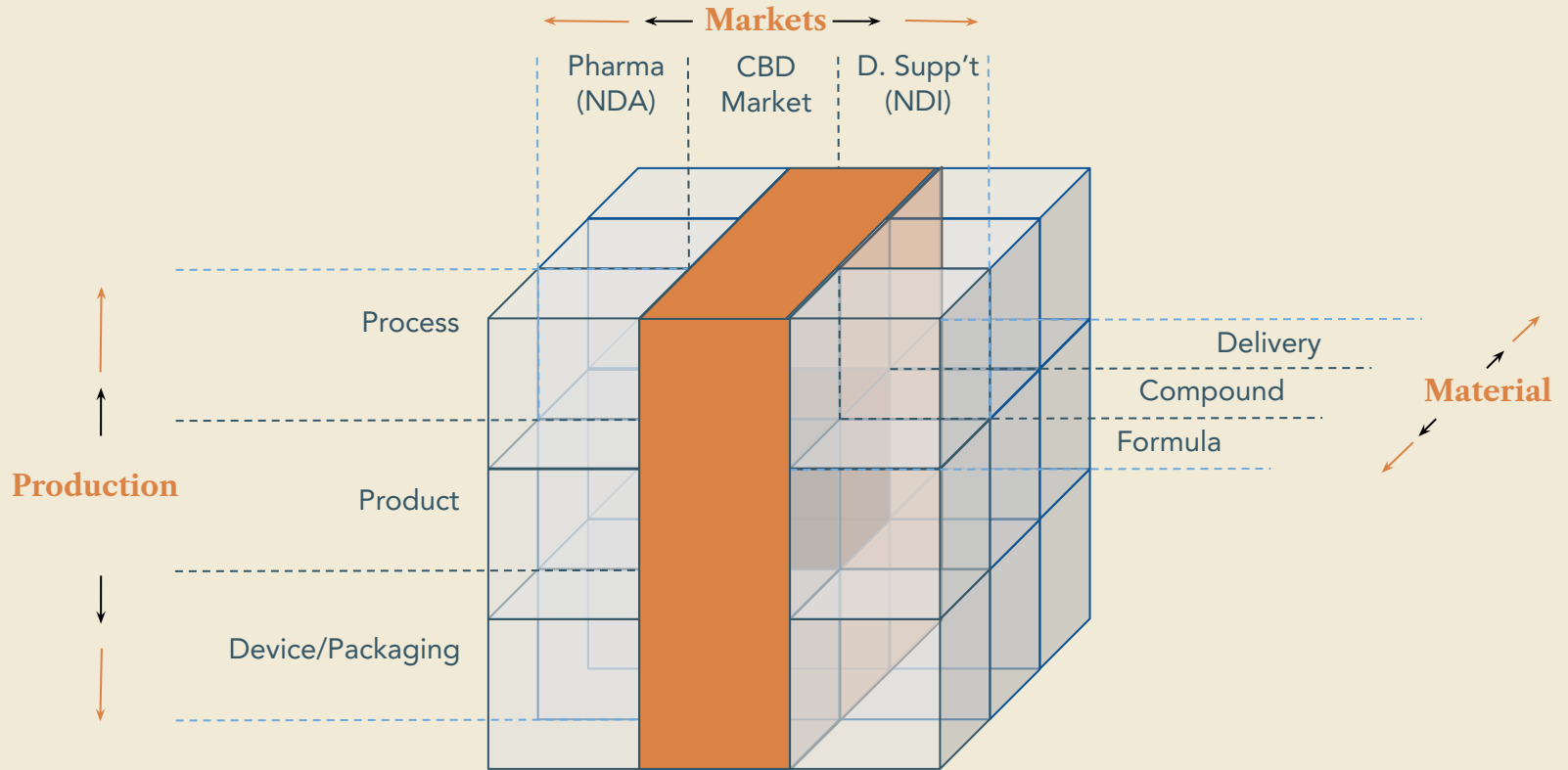


OBX brings scientific rigor to every ingredient we sell and formulate, from traditional medicine, to modern nutrition science, to clinical program design, and translate our data into messages you can use.

With this in mind, OBX partnered with **Radicle Science, a transformative health tech company validating natural products for the first time in history. Their proprietary approach, powered by a virtual, direct-to-consumer (D2C) model, delivers objective health outcome data for diverse populations and conditions at a fraction of the time and cost.**

Our Research Services include –

- **Virtual, direct-to-consumer, in-home, 4-week study of orally ingestible cannabinoid products**
- **Tests multiple products (including formulations, form factors, or dosages), randomized across participants**
- **Simultaneously assesses effects on well-being, pain, sleep, and anxiety**
- **Accelerates product development by defining the most effective product for given conditions for target participants**
- **Yields raw data + summary Radicle Discovery Insight Report**



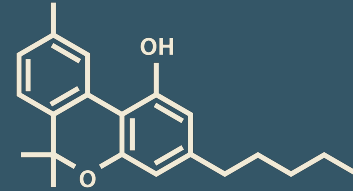
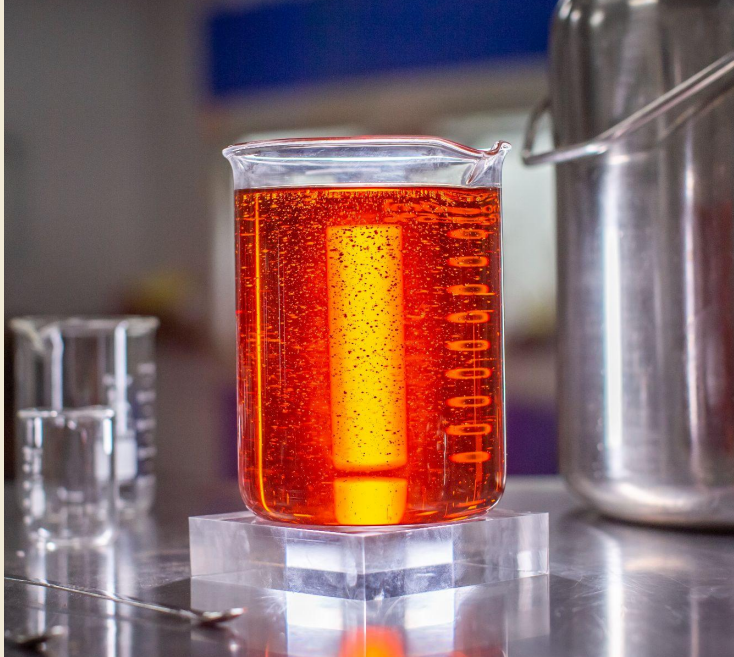
Foundation:
market
leadership,
open
innovation,
and research

Foundation



Cannabichromene

(CBC)



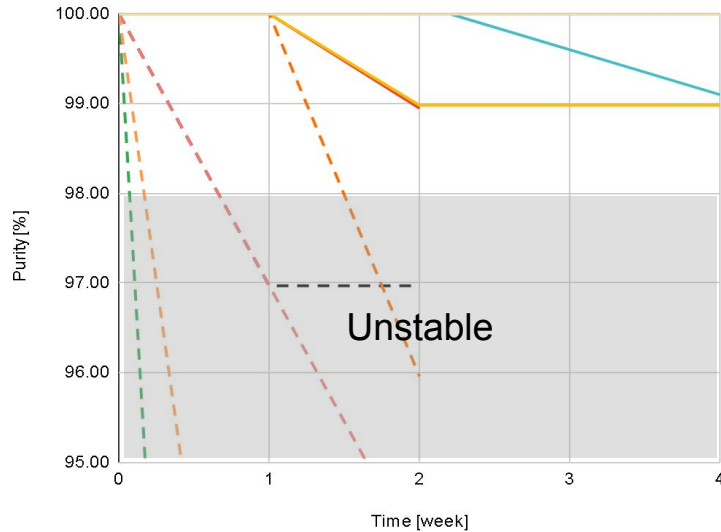
CBC

CBC is a non-psychoactive cannabinoid with a host of potential therapeutic applications. CBC may have powerful anti-inflammatory and analgesic properties. Multiple animal studies have found that CBC can reduce painful inflammation and swelling. Plus, CBC has also been shown to block pain perception in rodents. Together, these studies suggest that CBC can fight pain and inflammation by reducing pain-causing inflammation and swelling, and by reducing the perception of pain.

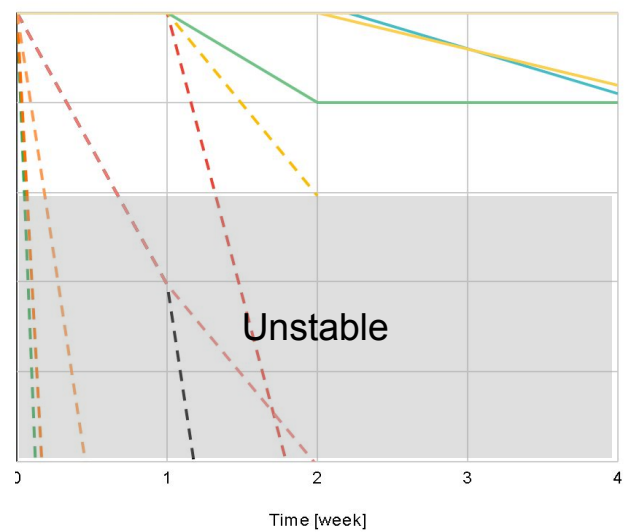


Proprietary
prodrugs
designed &
synthesized
are stable

Stability Test: Degradation in Room temperature



Test: Degradation in 40°C

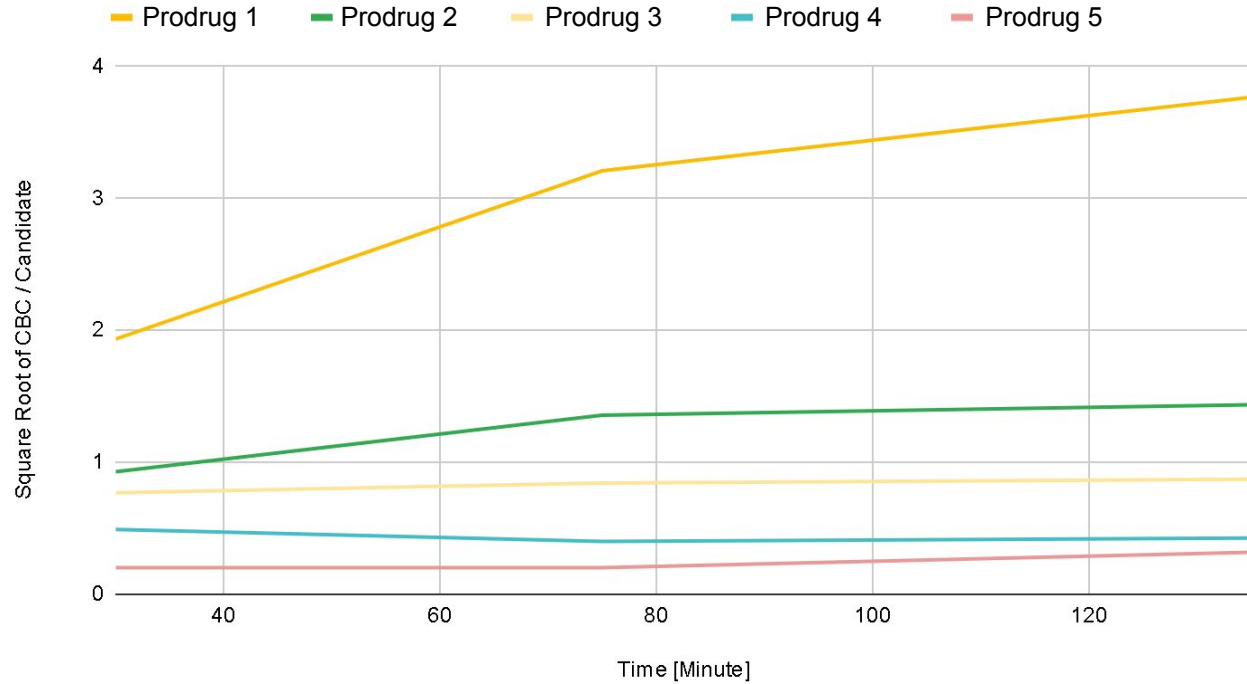


- CBC
- Prodrug 1
- Prodrug 2
- Prodrug 3
- Prodrug 4
- Prodrug 5
- Prodrug 6
- Prodrug 7
- Prodrug 8
- Prodrug 9
- Prodrug 10
- Prodrug 11
- Prodrug 12
- Prodrug 13
- Prodrug 14



Multiple prodrug candidates fully hydrolyze to CBC in 1st 30 minutes

Plasma Test: CBC Release Rate Over Time





Processing and production innovation

Methods

(Production & application methods)

Methods for producing, purifying, formulating, and applying cannabinoids, terpenoids, flavonoids, mercaptans, and thiols.

Status:

- Issued US Patent: [US 9,532,593 B2](#) "Herbal Smoking Blend" with priority date of December, 2013.
- PCT Application that expands "Herbal Smoking Blend" claim set to include flavonoids, mercaptans and thiols and extends coverage internationally, to be filed in March, 2021.
- Provisional patent: production methods for synthesizing, purifying, stabilizing, and formulating minor cannabinoids, to be filed in April, 2021.

Target market: Licensing & acquisition opportunities in cannabis markets (280E and non-280E), tobacco, pharmaceutical and nutraceutical.

Monetization: Proprietary method development and licensing (comp: Canopy)

Function-specific solutions

CoM

(Composition of Matter)

Compositions, formulations and dosage forms comprising combinations of one or more cannabinoids and other co-active agents, in addition to clinical and non-clinical applications and uses thereof to address the long-felt and unmet need for significantly improved formulations of cannabinoids for both clinical and non-clinical applications and uses.

>**500 function-specific compositions** (anxiety, pain, irritation, etc.) across species (human & pet) and routes of administration (ingestible, buccal, topical, suppository), conjugating cannabinoids with known prescription (eg Adderall), OTC (eg Ibuprofen) & non-OTC (eg turmeric) co-actives.

Status: Provisional application to be filed with priority date of March 2021

Target market: Dietary supplement, OTC, and pharmaceutical

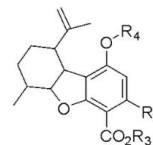
Monetization: Proprietary formulation development and licensing (comp: Proactiv)

Researched-backed ingredients

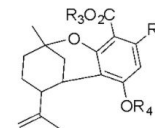
NCE

(New Chemical Entities)

Prodrugs of cannabinoids (CB1 or CB2 receptor ligands & stable esters) & **flavonoids** (cannflavins) & any enantiomers, diastereomers, racemate, or pharmaceutically acceptable salts, derivatives, compositions, formulations & dosage forms.



cannabielsoins (CBE)



iso-tetrahydrocannabinols (iso-THC)

>**115 novel prodrug structures** and extensions designed to enhance stability & bioavailability

Status: Prodrug research underway, provisional application filed with priority date of March 2021

Target market: pharmaceutical

Monetization: Collaborative research, IP licensing, portfolio sale (comp: Jazz acquires GW)

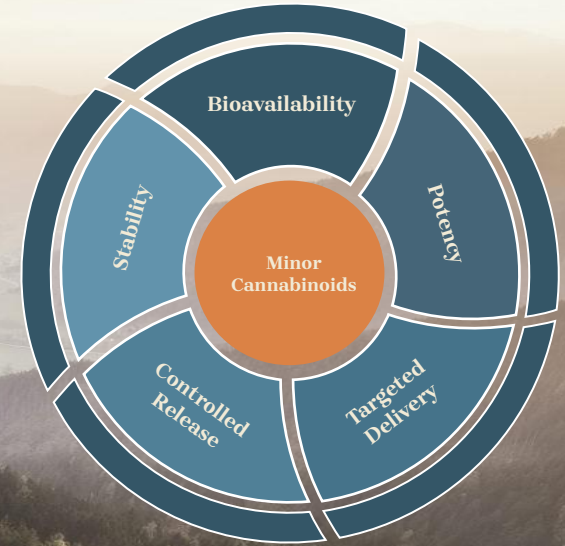


Call To
Action

IP Licensing

Research collaboration

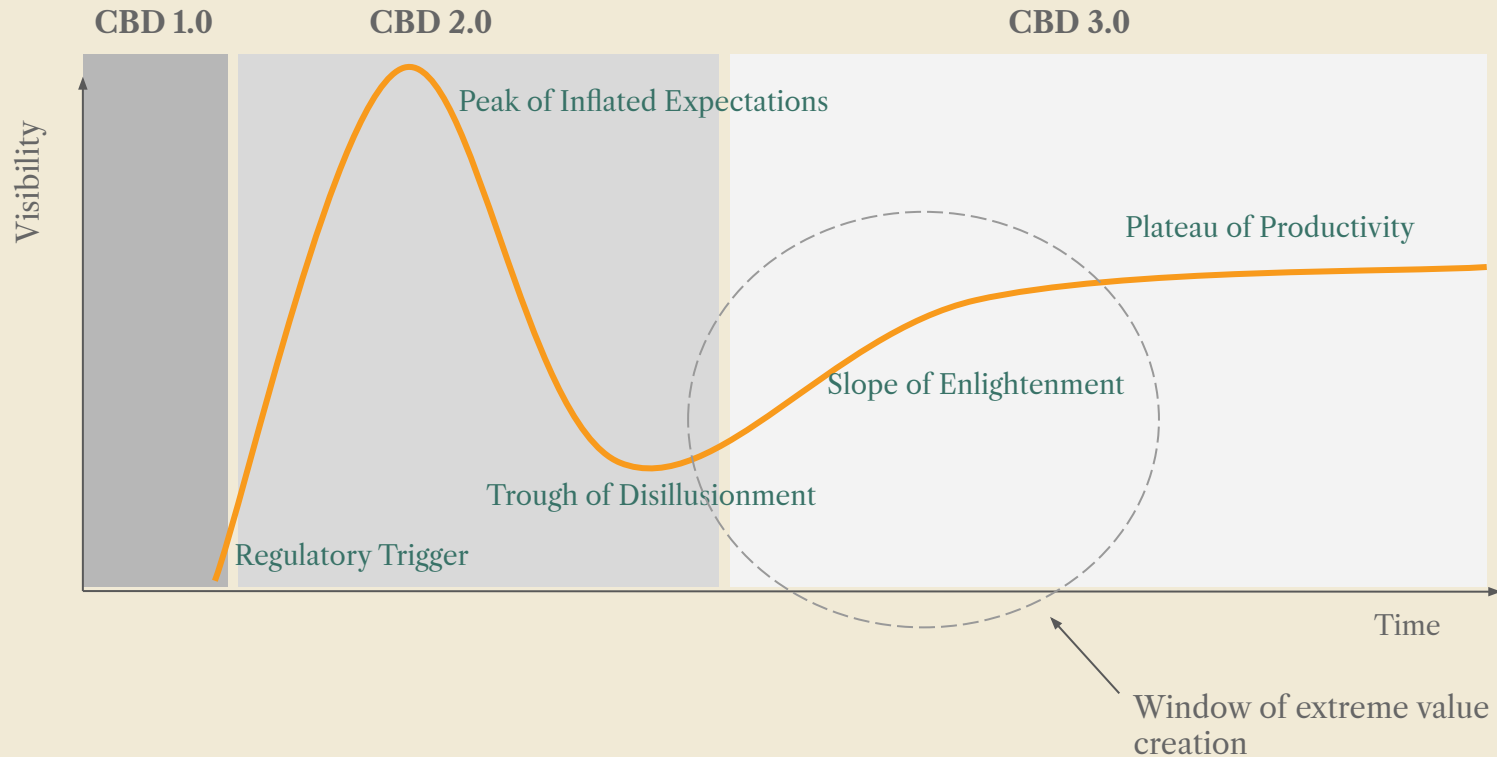
Cannabinoid inputs (MTA)



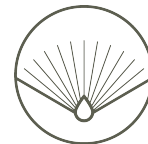
Innovation and Technology



Evolution of the CBD Industry



Our Portfolio



CBD Ingredient & Blends



Full
Spectrum
Distillate



Broad
Spectrum
Distillate



CBD
Isolate



10N & 5G
Specialty
Blends

Rare Cannabinoids



CBG
Isolate



CBN
Isolate



THCV
Isolate



CBC
Isolate



CBDV
Isolate

Finished Goods



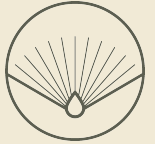
Water Soluble Cannabinoids



- CBD Liquid & Powder
- CBN, CBG, CBC, THCV

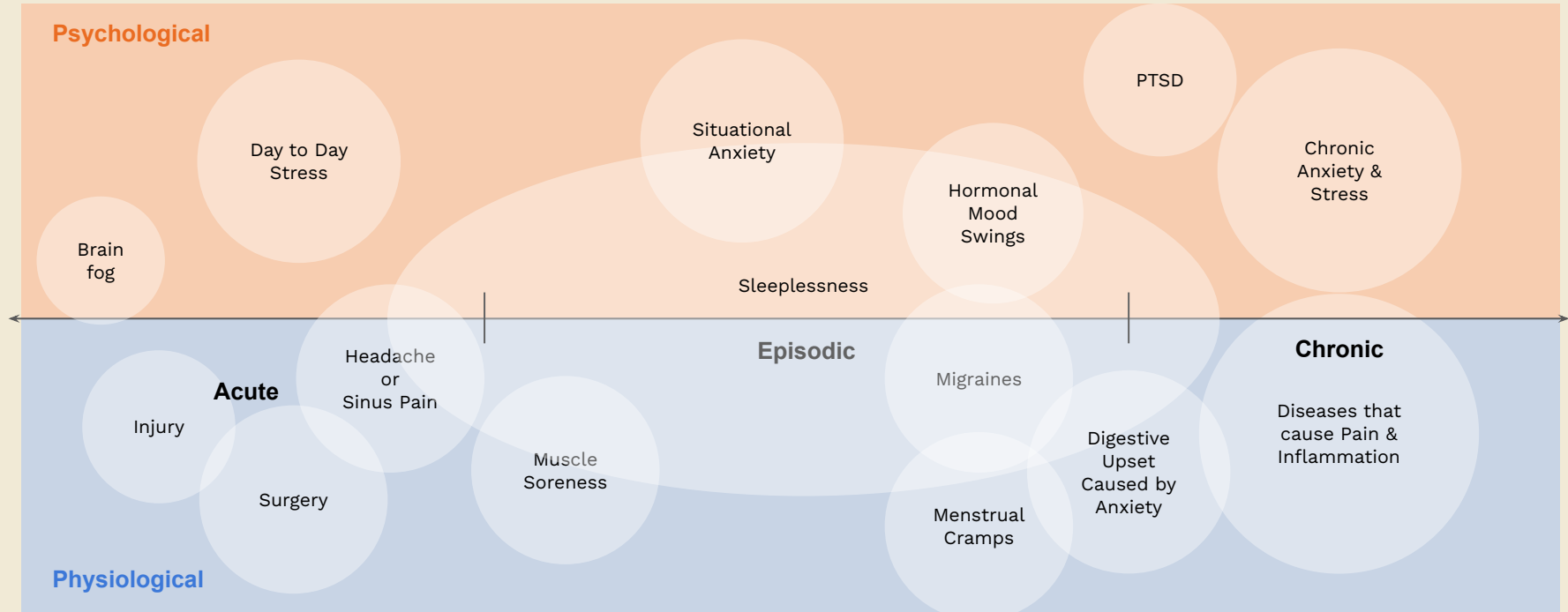


What is Innovation?



“Product Innovation” is defined as
**“the development and market introduction of a new,
redesigned, or substantially improved good or service.”**

Insights Driven Product Innovation





- **Water Soluble**
 - Quick Onset/Offset
 - More Precise
 - Controlled Dosage
- **Timed Release**
 - Quick Release
 - Extended Release
- **Targeted Delivery**

Delivery Mechanisms



- **Minor Cannabinoids**
 - THCV / CBDV / CBC / CBN / CBG / ETC...
- **NEW Cannabinoid Discovery and Isolation**
 - CBDp & THCp
 - CBT
 - CBL
- **Functional Ingredients**
 - Elderberry, Echinacea, Melatonin, Theanine, Valerian, Medicinal Mushrooms, Ashwagandha, Maca, etc...
- **Bitter Blocker / Masking**



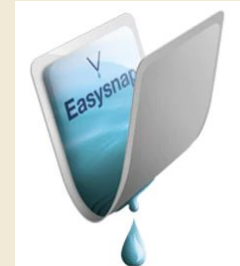
• Beverages – Easy to Administer / Convenient

- EasySnaps
- Effervescent Tablets
- Drops
- Cans/Bottles
- K-Cups



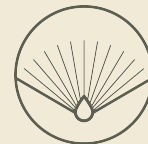
• Aerosols

- Inhalable
- Oral sprays
- Sublingual



Use Case

Trend #1: Focus On Need States, Such As Stress, Anxiety, Immune Support:

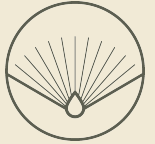


Exploding anxiety rates and associated mental health issues will provide hemp and cannabinoid brands with new opportunities to promote the efficacy of cannabinoids. We already are seeing increased focus on this niche, need-state market, and catch-all CBD product development and messaging (“CBD is good for everything and everyone”) will be replaced with more targeted product innovation and marketing campaigns.

- More than 25% of new market entrants purchased cannabinoids to cope with pandemic-related stress and anxiety, according to High Yield Insights.
- With more than 83% of U.S. employees reporting [mental health issues](#), and a whopping 67% of U.S. employers projecting a [mental-health crisis](#) within the next two years, we project heightened partnership and growth opportunities in cannabinoid products focused on stress, anxiety and sleep.



Core Need State: Sleep



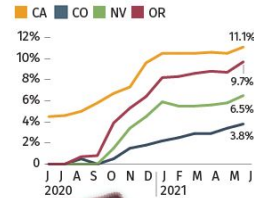
[Sleeper Hit: How CBN Sales Became A Surprise Hit In Marijuana Retail](#)

- CBN has officially earned its position as the sleeping giant of the cannabinoid industry -- and demand is climbing. "Sales of products containing CBN – almost entirely edibles, at this point – totaled more than \$65 million in the past four quarters for adult-use retailers in California, Colorado, Nevada and Oregon. There were only seven CBN products in those combined states a year ago, but that number grew to 55 in the second quarter of 2021, up 20% from the first three months of the year."

MJ Retailers See Sleeper Hit with CBN Products

Market share and revenue for products containing CBN continue to grow for adult-use marijuana retailers in four Western states.

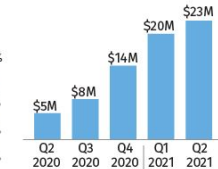
CBN edibles market share
CBN products have quickly taken a larger share of the edibles market in each state.



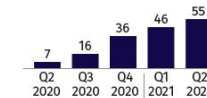
Source: Kiva Brands, Headset, FloraWorks

Revenue

Total revenue for products containing CBN in CA, CO, NV and OR ...



... is being driven, in part, by the number of new CBN products introduced.

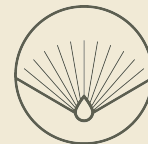


California's No. 1 edible
Introduced in January 2020, Kiva's Midnight Blueberry Camino, which contains 1 part CBN to 5 parts THC, was the top-selling edible the past two quarters.



© 2021 MJBizDaily, a division of Anne Holland Ventures Inc.

Core Need State: Energy



[Report: Energy Support - A Cross-Category Look](#)

- More than a year into the pandemic, our bodies and minds are starting to feel the long-term effects of the stress, anxiety and trauma that we've collectively experienced. And with many people experiencing poor quality sleep, fatigue increases.
- According to FONA International's latest report, "Consumers are in the midst of an energy crisis: 26% of U.S. adults feel constantly tired/exhausted, rising to 32% among 16-44 year olds. There has been a 300% increase in people searching 'how to get your brain to focus', an 110% increase in 'how to focus better', and 60% rise in 'how to increase focus.'"

TOP CATEGORIES WITH FUNCTIONAL - ENERGY CLAIM

Global New Product Introductions - Past 3 Years



Snacks

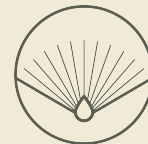


Sports & Energy Drinks



Nutritional Drinks & Other Beverages

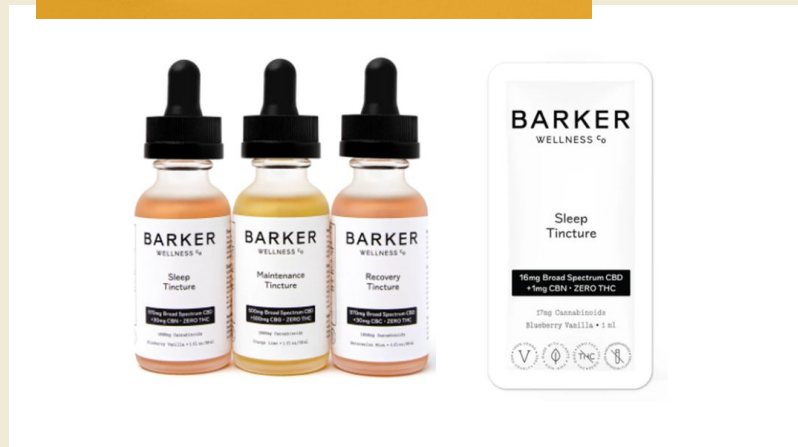
Core Need State: Mental Health



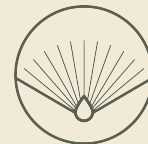
The number of people diagnosed with a mental health disorder was 1 in ten people globally – and anxiety outpaced those suffering from depression, making it the most prevalent mental health disorder. Now, many people are turning to CBD to treat their mental health disorders, rather than commonly prescribed treatments.

In 2019, the consumer research firm Hartman Group identified the prevalence of [anxiety](#), [depression](#), [fatigue](#), and [stress](#) as motivating factors for individuals to prioritize their mental and emotional health. (13) With the many routine disruptions and additional stressors resulting from the pandemic, including social [isolation](#), supporting mental health has now become even more essential. (14)

More than four in 10 adults (43%) report the pandemic has had a serious impact on their mental health, up from 37% in 2020. “Gen Z adults (46%) were the most likely generation to say that their mental health has worsened compared with before the pandemic, followed by Xers (33%), Millennials (31%), Boomers (28%) and older adults (9%).”



Trend #2: Organic, Natural, and Clean Products

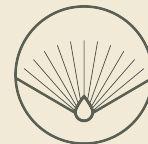


Generally, we've seen a shift in consumer trends this past year towards natural, clean, and organic products. A [Bloomberg report](#) released earlier in 2020 revealed that COVID-19 had accelerated organic food sales in the US due to increased demand for health-conscious foods and drinks. For example, organic food and beverage sales surged 25 percent during the 17-week period ending June 27.

Looking forward to 2022, we believe the demand for plant-based ingredients will be high this year across the natural products industry. In terms of [ingredient trends](#), "botanical ingredients including hemp CBD, sea buckthorn, shea, bakuchiol, and radish extract are on the rise in the natural personal care space."

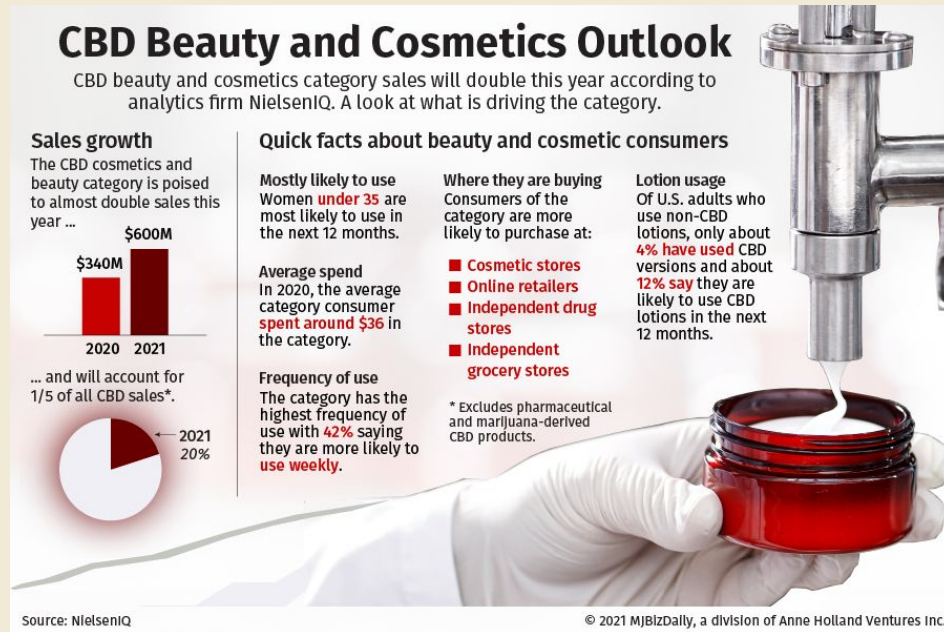


Trend #3: Beauty & Cosmetics

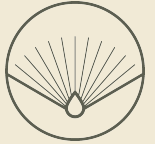


CBD Beauty and Cosmetics Sales Expected to Double in 2021

- According to analytics firm NielsenIQ, beauty and cosmetics products, including face lotions, serums, and skin nourishment/replenishment products accounted for about 18% of all hemp-CBD product sales in 2020, bringing in roughly \$340 million in sales.
- Nielsen predicts the category, which does not include pharmaceutical and marijuana-derived CBD products, will continue growing market share in the coming years and will eventually account for 20% of total CBD sales for 2021. The boost will be driven by more products coming to market this year in major retail chains as more stores follow Sephora, Ulta and others in the CBD-infused beauty categories.



Trend #4: Beverages



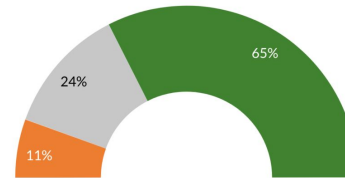
Growth Trends In CBD Beverages Driven By Demanding, "Conscious" Consumers

- More CBD consumers are turning to CBD drinks. An earlier study conducted by [High Yield Insights](#), a [cannabis consumer insights](#) firm, found in Spring 2019 that 17% of CBD users drink beverages infused with CBD. The data shows 29% of CBD consumers now drink CBD beverages with some frequency in the latest study.
- Among other results, the latest report found CBD drinks users are younger (62% being Gen Z or Millennials), affluent (33% having household income over \$100,000), with most (60%) having just adopted CBD since the outbreak of the coronavirus pandemic in the United States.

CBD Beverage Consumers Attuned to Latest Product Trends in Formulation, Functionality

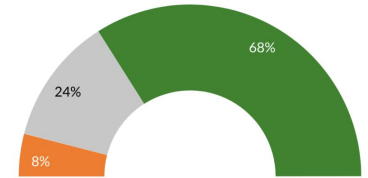


Look for Specific Terpenes



Disagree (11%) Neutral (24%) Agree (65%)

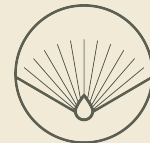
Prefer CBD Products with "Minor" Cannabinoids



Disagree (8%) Neutral (24%) Agree (68%)

Source: 2021 CBD NA Beverages Consumer Insights © High Yield Insights, Inc. 2021
Base: 1,193 current CBD consumers of hemp-derived CBD-infused beverages

Trend #5: Women's Wellness

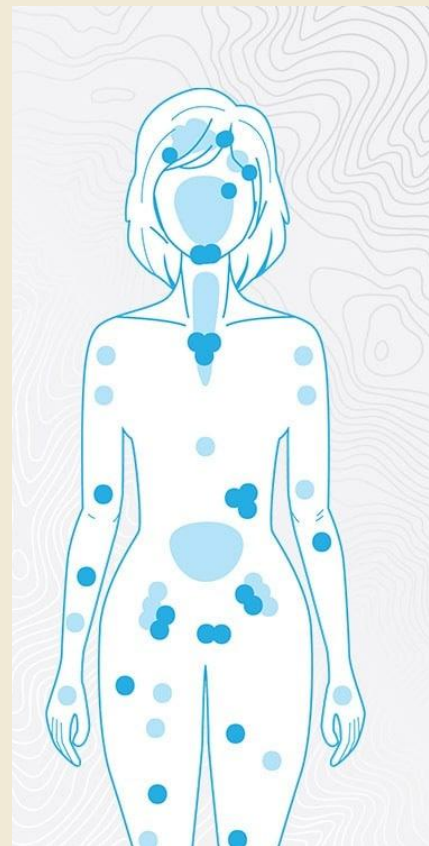


Women's Wellness

The legal cannabis industry is growing rapidly in the field of wellness, and women's health is a huge focus. Given that women's health is an unmet need, there has been a rush to develop products. Women, who have often been underserved by the medical and pharmaceutical industries, have much to gain from the acceptance of cannabidiol as treatment.

In female reproductive organs, CB1 receptors proliferate externally around the ovaries and the central nervous system. CB2 receptors are found in the ovarian cortex, medulla, and follicles. Both CB1 and CB2 have been identified to influence the operation of female reproductive organs.

- The endocannabinoid system is abundant in female reproductive organs.
- When activated by cannabinoids, it can induce pain relief and reduce inflammation.



Questions?





Thank you!