Institutional Equity Research: LIFE SCIENCES

Synthetically-Derived Cannabinoids: The Next Generation of Cannabinoid Production

The Future is Now: Moving Towards a Fundamental Addition to the Supply Chain Dynamics of the Cannabis and Cannabinoid-Derived Pharmaceutical Sectors

February 20, 2019

Highlights:

- **Synthetic and Biosynthetic cannabinoid production presents potential to disrupt the cannabis industry supply chain:** With the expected shift in consumer preferences for derivative cannabis product formats, and the applications for cannabinoids in the pharmaceutical space, the demand for cannabinoid extracts and isolates is expected to grow exponentially in the coming years. We see the immense potential for chemical synthetic and biosynthetic production methods to be a disruptive force the supply chain for cannabinoids.
- **Key differences between the processes:** The process of chemical synthesis involves the use of two or more chemical inputs, including catalysts, in a controlled chemical reaction to produce a more complex molecule, which is the desired output. Biosynthesis is a similar process, however, the "engine" for the chemical reaction is a genetically modified biological (living) organism, which is designed to produce the necessary enzymes to create the desired output, in this case, cannabinoids.
- **Both processes offer some unique advantages:** The repeatability of the chemical and biosynthetic processes ensures that each batch is consistent in terms of its content and purity. Both approaches also offer the potential to create larger quantities of rare cannabinoids that occur only in small quantities within the cannabis plant. Biosynthetic production, in particular, offers potentially significant cost advantages when commercially scaled, with estimates typically under $1,000 per kg of pure cannabinoids
- **We do not see plant-derived extraction being replaced by synthetic methods:** We highlight that we do not see these synthetic processes as a replacement for plant-derived cannabinoid extraction, due to different benefits offered by each methodology. In addition, most estimates forecast at least an 18-24 month lead time before the commercialization of biosynthetic cannabinoid production.
- **Numerous cannabis and biotech companies have begun pursuing the commercialization of these methods:** We highlight the numerous biotech companies pursuing chemical synthetic and biosynthetic production of cannabinoids, as well as some of the cannabis companies which have chosen to partner with them.

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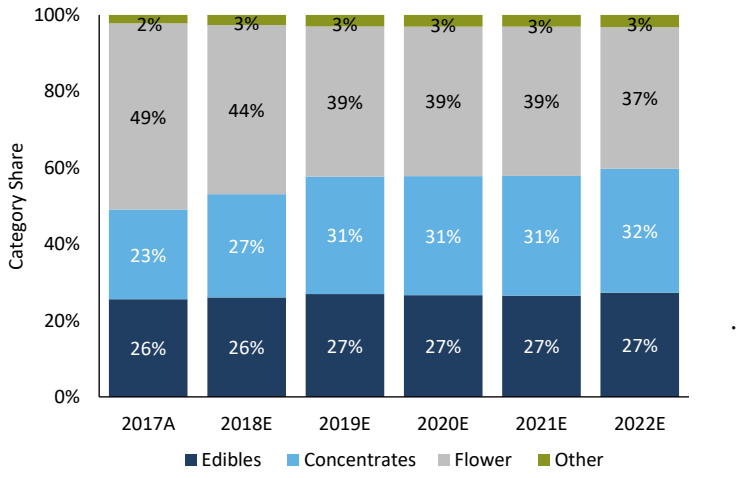
What Are the Options for Producing Cannabinoids?

From Plant to Active Pharmaceutical Ingredients ("API"): Why Cannabinoids as an API Represent a key Component to the Future of the Cannabis Market

The cannabis plant is an incredibly complex organism. It contains over 400 phytochemicals, including terpenes and flavonoids, and more than 100 cannabinoids, most of which have not yet been studied sufficiently to fully understand their potential impacts and benefits for both recreational and medicinal use. The most commonly known cannabinoids are tetrahydrocannabinol ("THC") and cannabidiol ("CBD"), though these two are just the tip of the proverbial iceberg in terms of the different compounds the cannabis plant contains. They are also the cannabinoids that are generally found in the highest concentrations in the plant. As scientific innovation in the sector continues to advance, we are very likely to discover many new applications for these compounds, and combinations thereof, in humans, and animals.

With the continued advancements in the market for cannabis products across all three segments – recreational, medical and cannabinoid-derived pharmaceuticals – the progress and innovation with respect to product development, in our view, is certain to result in a significant increase in demand for cannabinoid extracts and isolates. The market will not only demand more quantity, but will require increasing standards of quality, production and specificity. The consensus outlook for markets across Canada and the US forecast derivative products - where cannabinoids are used as simply an input, or active ingredient in the product - will make up an increasing share of total sales relative to dried flower, in the coming years.

Category Share Forecast – Colorado and California (2017 – 2022)



Estimates of market share by category see dried flower accounting for just 37% of total spending in Colorado and California by 2022, having previously made up half of the total market. Derivative-based categories are forecasted to account for the remaining share of spending, which would indicate a sharp increase in the overall quantity, quality and variety of cannabinoid extracts and isolates for use in the manufacturing of these various products.

Figure 1. Total Share of Spending by Product Segment in US Markets
Source: Brightfield Group, AltaCorp Capital Inc.

With respect to the recreational and medical markets, the growth in demand for products such as edibles, concentrates, topicals and beverages require isolated cannabinoids with consistency in supply and specifications in order to manufacture at scale. Currently, the Canadian market, as well as some US markets, have significant shortfalls in the supply chain for cannabis flower, as well as cannabis extracts.

With respect to cannabinoid-derived pharmaceuticals, even greater standards of quality, purity and consistency of the cannabinoids is necessary to meet the high rigours required for pharmaceutical products. As clinical trials advance, and new drugs come to market in the years to follow, the demand for high quality cannabinoid isolates that meet these requirements, will, in our view, increase.

Differences in Cannabinoid Production Methods

With the supply chain for cannabis products, including whole-plant cannabinoid extracts and isolated cannabinoids still in its infancy, companies are searching for ways to secure a cost-effective, consistent and

purified supply of cannabinoids for use in the production of derivative products for the medical and recreational markets, as well as cannabinoid-derived pharmaceuticals.

Comparison of Recreational, Medical and Cannabinoid-Derived Pharmaceuticals by Level of Rigour

	Clinical Trials	Eligible for insurance reimbursements	Manufactured to GMP Standards	Product Consistency	Time Horizon to Market	Margin	Operates to Pharma Standard
Recreational	No	No	Not Required	Medium	Short	Moderate	No
Medical	Not Required	Some	Not Required	Medium	Short to Medium	Moderate	Not Required
Cannabinoid-derived Pharmaceutical	Yes	Yes	Yes	High	Long	High	Yes

Figure 2. Regulatory and Timeline Comparison Matrix (Cannabinoid-Derived Pharmaceuticals vs Others)
Source: AltaCorp Capital Inc.

Currently, there are three primary methods of producing cannabinoid extracts, each in varying stages of development, commercialization and viability as long-term sources of supply:

- **Plant-based extraction:** Involves extraction of the cannabinoids and other phytochemicals directly from the plant. Today, this is the most commonly used method of cannabinoid production;
- **Synthetic production which includes:**
  - **Chemical synthesis:** Use of two or more compounds in controlled chemical reaction to create (synthesize) desired cannabinoids;
  - **Biosynthesis:** Use of biological (living) organisms, such as bacteria, fungus or algae, as agents in a controlled chemical reaction which yields the desired cannabinoids.

Methods for Production of Cannabinoids

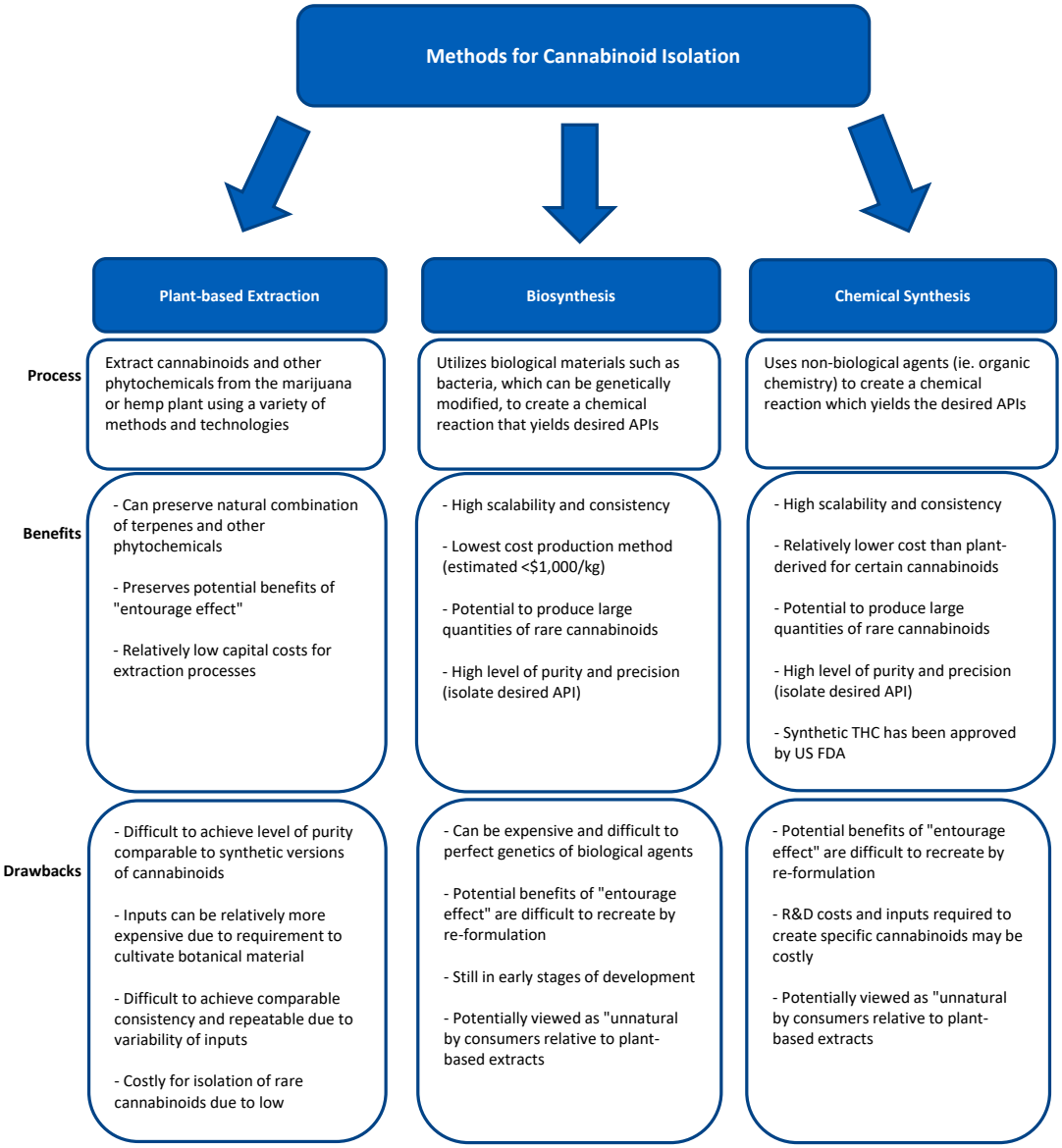


Figure 1. Overview of Methodologies for Cannabinoid Production
Source: AltaCorp Capital Inc.

Synthetic Cannabinoids Will Not Replace Plant-Based Extraction

There is no doubt that there are certain benefits to traditional plant-based extraction methodologies, which, in our view, means that this methodology will continue to have an important and meaningful place in the industry's supply chain. We do not view chemical synthetic and biosynthetic production of cannabinoids as a replacement for plant-based extraction, but rather, as an addition to the available methodologies for cannabinoid production. Amongst the advantages of plant-based extraction are:

- **The preservation of terpenes and flavonoids:** The cannabis plant contains more than 400 phytochemicals, including terpenes and flavonoids that vary based on the particular strain, and provide each with their characteristic scent and taste profile. These compounds, while possible to synthesize, can be difficult to replicate in the unique combinations and concentrations which occur in the plant, and require post-production processes to achieve a similar output to a plant-derived cannabinoid from a specific strain.

- **The preservation of other phytochemicals that contribute to the "entourage effect":** As noted, the numerous cannabinoids and phytochemicals that accompany the primary cannabinoids found in the plant are theorized to have a synergistic effect, which may be at least partially responsible for some the positive impacts experienced by users. This phenomenon is known as the *entourage effect*, and without the combination of these phytochemicals found in the plant itself, some of the beneficial effects of the plant may not be preserved. More R&D is required on this to better understand the phenomenon.

- **Capital investment for an extraction operation is relatively low:** The capital investment required to set up an extraction operation is relatively low, with fairly minimal floor space and capital equipment being the bulk of the investment. Industrial scale extraction machines may cost anywhere from $1.5 to $2mm each. The expertise required to operate these machines effectively is another necessity, but in terms of capital investment, the requirements are low compared to the R&D costs required to achieve commercial scale production using chemical synthesis and biosynthesis at this time.

As mentioned, virtually all of the cannabinoid extracts and isolates produced today are done so using plant-based extraction. Synthetically-derived cannabinoid usage is reserved to a select few pharmaceutical companies using synthetic versions of CBD and THC in pharmaceutical products. We have yet to see any recreational or medical cannabis products in Canada or the United States using synthetic or biosynthetically-derived cannabinoids for sale as a CPG product.

Due to these important benefits, we do not see synthetic production as a replacement for plant-based extraction, but rather, a process that can be used to augment the production of cannabinoids for certain types of products which are suited for the methodology. With the expected explosion in demand for cannabis extracts and isolated cannabinoids, we see both methodologies occupying an important place in the industry's supply chain.

Understanding the Chemical Synthesis and Biosynthesis Processes

Chemical synthesis and biosynthesis are processes by which controlled chemical reactions using two or more reagents are used to produce the desired compounds. In the context of cannabinoids, this differs from the traditional plant-based or botanically-derived production methodology, where the APIs are extracted from the harvested plant. Chemical synthesis and biosynthesis are processes where no plant material is required, which is a significant departure from traditional methodologies. Utilizing these synthetic processes, cannabinoids are essentially created in a laboratory.

These processes are already very common in the pharmaceutical industry for the production of many drugs. Some well-known examples of this include Eli Lilly (LLY-NYSE, NR) using yeast fermentation to biosynthesize insulin, which was previously harvested from livestock pancreases, as well as the production of Aspirin (acetylsalicylic acid) being produced synthetically, after initially being derived from chemicals found in the bark of a willow tree. The primary benefits of synthetic manufacturing are its **commercial scalability**, **precision** and **repeatability**, which ensures consistency of product.

Understanding Chemical Synthesis

Chemical synthesis is a process where two or more non-biological (non-living) compounds are used in a controlled chemical reaction in order to combine (synthesize) to create a desired output. In its most simplistic form, it is best thought of as a combination of two or more starting materials to create a more complex output as a result of the reaction. In most cases, a catalyst is used in combination with these raw materials to help accelerate the chemical reaction between the input substances.

Illustration of Chemical Synthesis

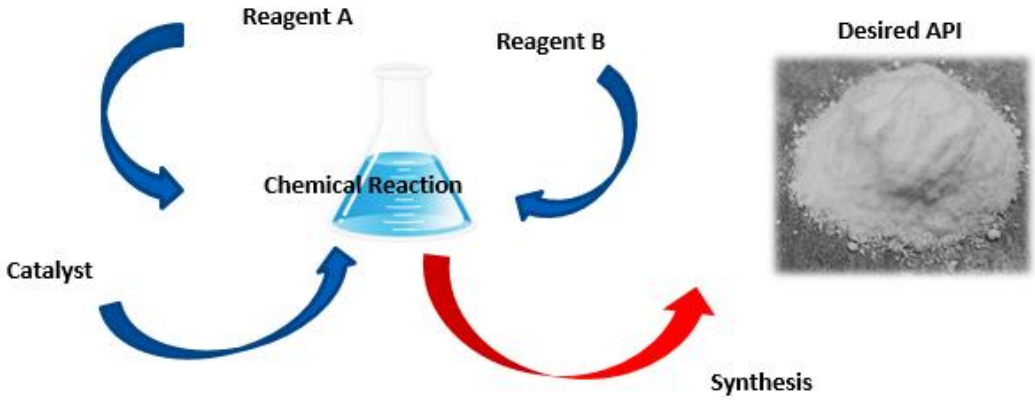


Figure 2. Illustration of Chemical Synthesis Process
Source: Noramco Marketing Materials (photo of API only), AltaCorp Capital Inc.

This process is used to generate various outputs, which may or may not be naturally occurring. Depending on the complexity of the molecule being produced, the process can be perfected in order to create desired end products in large quantities, and in a short period of time. Whether a cannabinoid is derived via plant-based extraction or synthetic processes, the compounds can be designed to have the identical chemical structure to the naturally occurring one.

Then What is the Difference Between Chemical Synthesis and Biosynthesis?

Biosynthesis differs from chemical synthesis in that one of the inputs used in the chemical reaction is a **biological (ie. living) organism**. This is traditionally a simple organism, such as a **bacteria, fungus** (eg. yeast) or **algae**.

Very simply, these simple organisms act as the "engine" for the chemical reaction, as they produce enzymes (proteins used by the cells as a catalyst) to metabolize a type of "fuel", such as a sugar, and in-turn, produce a desired by-product. A very simple analogy for this process is alcohol production:

- A **fuel**, such as maltose (sugar from malted grains) is combined with **water** and **yeast**;
- The yeast **metabolizes** (processes for energy) the sugar in the fermentation process;
- The by-product of the metabolism is **carbon dioxide** and **alcohol**.

The Brewing Process: A Simple Analogy for Biosynthesis

Figure 3. Illustration of Brewing Process: A Simple Analogy for Biosynthesis
Source: AltaCorp Capital Inc.

Using Synthetic Biology to Engineer Biosynthetic Processes

The example in Figure 3 is a relatively simple and natural process that can be performed with inputs found in nature. In many cases, however, the desired output may be far more complex than simple ethanol (alcohol), and furthermore, may not be something that is naturally produced by any of the inputs being used – such as cannabinoids.

In these cases, the biological organisms are **genetically engineered** - which involves making changes to the DNA of the organism - so that the cells produce the necessary enzymes to create the desired by-product. The process leverages the organism's natural chemical processes to create the desired output, which if not for the genetic modification, they otherwise would not produce. This DNA modification may be difficult to achieve, and could require years of research and development to perfect so that the desired API can be produced at scale.

Illustration of the Biosynthesis Process

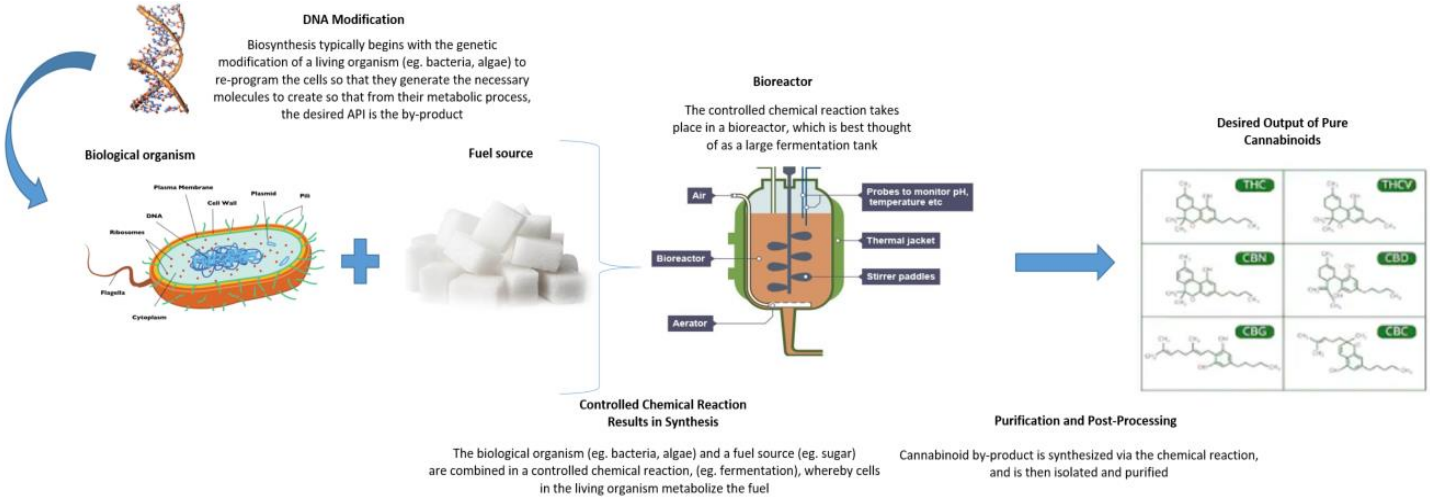


Figure 4. Illustration of the Biosynthesis Process
Source: AltaCorp Capital Inc.

The field of research which involves the engineering and modification of biological organisms, systems and processes, such as biosynthesis, is called **synthetic biology**. This field of study is rapidly evolving to change the way we produce many compounds used in a wide range of goods from pharmaceuticals, consumables, industrial items and wellness products.

Why Use Chemical Synthesis or Biosynthesis for Cannabinoid Production?

The processes of chemical synthesis and biosynthesis in the manufacturing of compounds used in pharmaceuticals, have significant potential benefits in the manufacturing of cannabinoids. When comparing these methods, chemical synthesis and biosynthesis may offer several advantages over traditional plant-based extraction:

- **The process for cultivation of the inputs is land and capital intensive:** While the capex requirements for extraction are relatively low, the land, energy and capital required to produce the inputs for plant-based extraction are very high. Greenhouses and indoor cultivation facilities of commercial scale can costs tens of millions, to several hundred million dollars to construct, and the mass of the plant is simply a waste product in this process, as most flower used in extraction would not exceed 15% cannabinoid content, and many times, is significantly lower, due to the use of trim – a less valued part of the plant which is a by-product from the trimming process with lower cannabinoid concentrations than the actual flower. Therefore, much of the biomass produced in cultivation of flower used in extraction is not useable as a final product.

- **Biosynthetic production in particular, is significantly cheaper on a per kilogram basis:** Even with the expected commoditization of dried flower, the cost of using plant material as an input is likely to remain more expensive than the inputs required for biosynthetic production (eg, using yeast

and sugar will be significantly cheaper than even the lowest cost cannabis flower and trim used as inputs), and to a lesser extent, chemical synthetic production as well. Estimates for the cost to produce a gram of cannabinoid concentrate using biosynthesis, once commercially scaled, have ranged from $0.50 to $1.00, which is below the cost of plant material alone required to produce a gram of plant-derived cannabinoid extract.

- **Chemically synthesized and biosynthetically-derived cannabinoids can achieve higher levels of purity:** For those looking to isolate specific cannabinoid compounds, in particular, pharmaceutical companies that seek to isolate the effects of a specific compound, synthetic methods can achieve levels of purity that would require significant difficulty to achieve using plant-based extraction methods. Synthetic and biosynthetic methods have been shown to achieve levels of purity in excess of 99.5% (as an example, Noramco's (private) synthetically-derived CBD).

- **It is very expensive and difficult to isolate rare cannabinoids with plant-based methods:** Many of the cannabinoids with potential medical benefits aside from THC and CBD are found in the cannabis plant in very low concentrations. A number of these cannabinoids occurring in low concentrations have been identified as compounds of interest for use in recreational and medical cannabis products for their different effects, such as THCA, THCV, CBG, CBDV, CBCV and CBC, just to name a few. Even strains bred specifically to achieve higher concentrations of these compounds yield relatively lower quantities as compared to the relatively higher concentrations of THC and CBD found in certain strains of the cannabis plant. Therefore, the amount of plant material needed to isolate these compounds in meaningful qualities makes the process of extraction inefficient and expensive. By producing these compounds synthetically, they will potentially be able to be produced in much larger quantities, and at a much lower cost.

- **Processes are highly repeatable and outputs less variable with synthetic production:** Synthetically-derived processes, once scaled commercially, will be highly repeatable, and expected yields should not differ from batch to batch. With plant-derived methods, the content and quality of inputs can differ from batch to batch, potentially requiring fine-tuning in the extraction process to achieve the same end product, making it less ideal for production of a commoditized, pure isolate.

We see this aspect of synthetically-derived cannabinoids as being an attractive feature for CPG companies who may eventually look to enter the cannabis space with infused products, such as The Coca Cola Company (KO-NYSE, NR), Diageo (DGE-LON, NR) and Pepsi Co (PEP-NASD, NR), who, in our view, are likely to value a lack of variability in cannabinoid production to ensure the highest levels of consistency in all products sold, as well as superior scalability in the manufacturing processes.

For applications which require a highly repeatable, commoditized isolate of a pure cannabinoid, the synthetic processes may prove to be superior due to their repeatability, consistency and low cost.

We also note an added potential benefit of chemical synthetically-derived and biosynthetically-derived cannabinoids with respect to their use in pharmaceutical and medical cannabis products is the fact that they are produced in laboratory conditions, which generally meet the high standards required of controlled substances and pharmaceutical manufacturers. We note laboratories, such as Noramco, a major manufacturer of controlled substances who also produces Nabilone, Dronabinol and synthetic CBD, which operate out of facilities that meet pharmaceutical manufacturing standards under the FDA, DEA and Health Canada, with cGMP certification. This would meet or exceed any requirements for export to international medical cannabis markets, which normally require production in EU-GMP certified facilities for plant-derived cannabis products.

As noted, while we expect each method to have a place in the supply chain for the cannabinoid market, different producers will find each process useful based on different types of products being made.

Who is Pursuing this Chemical Synthetic and Biosynthetic Technology for Cannabinoid Production?

There are a number of players in the market today pursuing research and development and commercialization of chemical synthetic and biosynthetic cannabinoid production methods. With the highly disruptive potential of this technology, the rewards from pursuing its commercialization for both the manufacturers, as well as their potential customers, are very attractive. With more attention being shone on the possibilities of this technology as a result of several high-profile agreements in the past six months between biotechnology firms and cannabis companies to pursue its development, we have seen significant

investment by a number of players seeking to commercialize these methods. While not an exhaustive list, we highlight these companies as a general overview.

Overview of Companies Pursuing Synthetic and Biosynthetic Cannabinoid Production

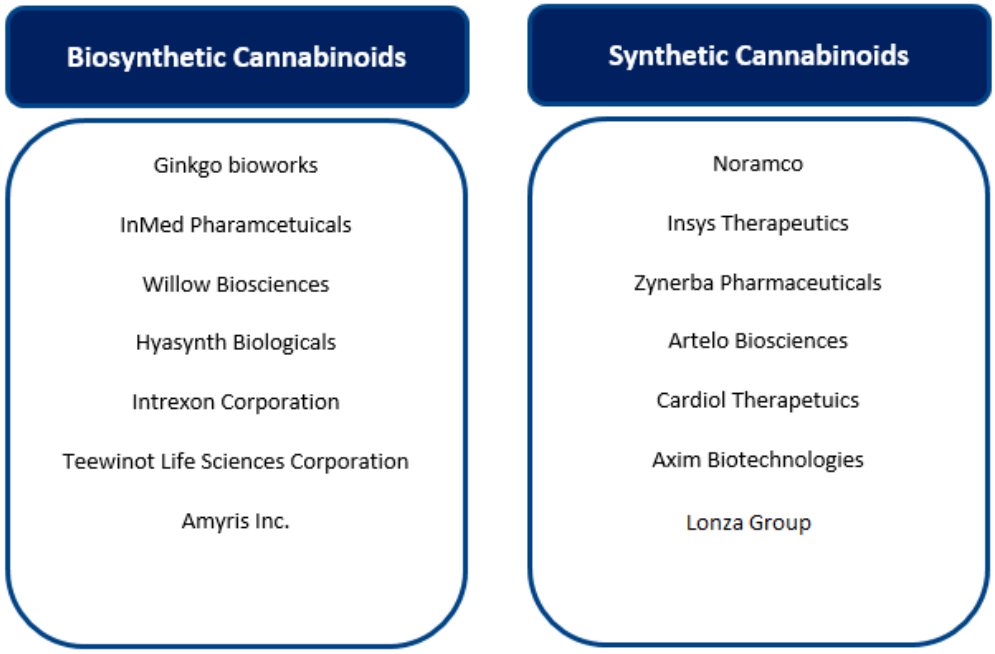


Figure 5. List of Companies Pursuing Chemical Synthetic and Biosynthetic Production of Cannabinoids
Source: AltaCorp Capital Inc.

Biosynthetic Cannabinoid Production

Ginkgo Bioworks (private)

Ginkgo Bioworks is a Boston, MA-based genetic engineering R&D firm, who engages in the modification and development of biological organisms used in manufacturing and industrial applications such as fragrances, flavours, agriculture and pharmaceuticals. The Company applies custom software and robotics to automate the DNA sequencing process which allows them to experiment with different iterations at many times the speed of the traditional manual process. The Company was founded by PhDs from MIT, including Tom Knight, a pioneer in the field of synthetic biology. Ginkgo has raised US$429mm in capital to date, and has received investments from, amongst others, Bayer (BAYN-ETR, NR), Bill Gates and Y Combinator, having raised US$429mm in funding to date. Of particular note, Cronos (CRON-TSX, NR) announced in September of 2018 that it entered into a partnership with Ginkgo Bioworks to develop cannabinoids cultured using yeast fermentation. The project is estimated to take approximately two years to commercialize, and has set milestones to be able to produce a number of different cannabinoids, at scale, at a cost of under USD$1,000 per kilogram.

InMed Pharmaceuticals (IN-TSX, NR)

Vancouver, BC-based InMed Pharmaceuticals is a drug development company specializing in cannabinoid-derived pharmaceuticals for indications with unmet needs, including glaucoma, epidermolysis bullosa and orofacial pain. The Company is in the process of developing their microbial-based biosynthetic manufacturing process using fermentation with the genetically modified E. coli bacteria, for the production of cannabinoids at pharmaceutical grade for use in their therapeutic drugs.

Cellibre (private)

Cellibre, based in San Diego, CA, is a synthetic biology company that specializes in genetic modification of organisms used in manufacturing of consumer, medical and industrial products – a process which they refer to as *cellular agriculture*. Cellibre is currently pursuing commercialization of biosynthetically produced cannabinoids. They intend to be a disruptor in the supply chain for cannabinoids to the recreational, pharmaceutical and animal health markets.

Willow Biosciences (private)

Calgary-based Willow Biosciences is a start-up biotechnology firm that is engaged in the development of biosynthetic production processes for a variety of cannabinoids, with an initial focus on CBD. The research team brings extensive experience in plant biochemistry and genomics from their previous work. The research team at Willow Biosciences was previously engaged to scale a yeast-based biosynthetic production program for thebaine, an opiate API, in which they successfully helped to increase yields by more than 10,000x. The team will look to bring this expertise to the cannabis space, where they plan to produce cannabinoids as APIs for wholesale to manufacturers of cannabinoid-derived pharmaceuticals and other products.

Hyasynth Biologicals (private)

Montreal, QC-based Hyasynth is a biotechnology company that specializes in biosynthesis, and have already demonstrated small-scale production of phytocannabinoids. They have also received a Dealer's License from Health Canada. Notably, they received a $10mm investment from Organigram (OGI-TSX, NR) in 2018, which is subject to the achievement of certain milestones. Organigram also entered a non-binding LOI for an off-take agreement with Hyasynth to purchase biosynthetically produced cannabinoids once they are commercially scalable.

Intrexon Corporation (XON-NASD, NR)

Maryland-based Intrexon is a biotechnology firm focused on synthetic biology and its applications for health care, food and agriculture, energy and industrial chemicals. The Company applies over 20 years of experience in genetic engineering to biological organisms across four categories, including microbes, plants, animals and human cells, in order to produce the desired functions and outputs. In September 2018, the Company announced that they have engineered a strain of yeast capable of producing consistent and low-cost output through fermentation, with a goal of eventually achieving a cost of less than US$1,000 per kg of pure cannabinoids. While not a play with their biosynthetic production technology, of note, Intrexon also announced a deal to license their plant tissue propagation technology to Next Green Wave Holdings (NGW-CNQ, NR), a Vancouver-based cannabis company focused on the recreational and medical cannabis markets in California. As mentioned, the Company also has an extensive plant cell engineering platform, which makes them well positioned to transition into the cannabis space.

Teewinot Life Sciences Corporation (private)

Tampa, FL-based Teewinot Life Sciences is a biopharmaceutical firm focused on the biosynthesis of pharmaceutical grade cannabinoids using their patented processes. They are also developing formulations and delivery technologies for cannabinoids for applications in pharmaceuticals, nutraceuticals, foods and cosmetics, including liposomal (fat-based molecule) and micellular (water-based) delivery technologies.

Amyris Inc. (AMRS-NASD, NR)

The California-based bioscience firms describes itself as an "integrated renewable products company", which applies its technology to the production of a wide range of products, including pharmaceuticals, fragrances, cosmetics, fuels, chemicals and others. The Company uses genetic modification of microorganisms, mainly yeast, and plant sugars in their fermentation processes to create biosynthetically-derived outputs. Just recently, in early February 2019, the Company announced an agreement with an unnamed partner for a US$255mm cannabinoid development program, in which the company will look to have products ready to commercialize in the next 18 to 24 months.

Chemical Synthetic Cannabinoid Production

Noramco (private)

Wilmington, DE-based Noramco is one of the largest manufacturers of controlled substances in the world, supplying major global pharmaceutical companies with compounds produced at their FDA, DEA and Health Canada-approved facilities. Noramco is a wholesale manufacturer and supplier of controlled substances, and does not conduct their own clinical trials for the purposes of investigating the efficacy of, and marketing newly developed drugs.

Noramco is a manufacturer of synthetically-derived CBD, which is pharmaceutical-grade, with assurance of >99.5% purity, which meets Health Canada's threshold for "**THC-free**" products. They have an agreement to supply their pure CBD to Cardiol Therapeutics (CRDL-TSX, NR) for use within Canada and Mexico. They also produce nabilone, a synthetic compound used in pharmaceuticals which mimics the effects of THC, as well as Dronabinol.

Insys Therapeutics (INSY-NASD, NR)

Insys markets Dronabinol under the tradename Syndros, which is a synthetic drug that is an isomer of THC. The drug is FDA approved, and is used to treat HIV/AIDS induced anorexia and chemotherapy induced nausea and vomiting. The Company is also developing new treatments using Dronabionol via inhalation for cancer-induced anorexia as well as agitation from Alzheimer's disease. In addition, Insys is in Phase II and Phase III trials for various indications using synthetic CBD administered orally.

Zynerba Pharmaceuticals (ZYNE-NASD, NR)

Zynerba is currently investigating the efficacy of ZYN002, the company's synthetically produced CBD gel with patented technology to enhance transdermal delivery (through the skin). The formulation is being investigated for the treatment of a number of different conditions including Autism Spectrum Disorder, Fragile X Syndrome, Development and Epileptic Encephalopathies, and others. The clinical trials for the various indications are at different stages of progress, ranging from pre-clinical stage to Phase III.

Artelo Biosciences (ARTL-OTC, NR)

Based in La Jolla, CA, Artelo is a biotech company that is pursuing therapies for treatment of a wide range of indications through stimulating the endocannabinoid system (the body's internal system of cannabinoid receptors). Some of the indications being pursued include anorexia, cancer, PTSD, inflammation and pain. The company is using a combination of naturally occurring and synthetic cannabinoids as the basis of these therapies.

Cardiol Therapeutics (CRDL-TSX, NR)

Cardiol Therapeutics is a Canadian biotechnology company pursuing the development and commercialization of cannabinoid-derived pharmaceutical treatments for heart failure and glioblastoma, as well as a line of medical cannabis products. All of Cardiol's pharmaceutical and medical cannabis products will use synthetically produced, pharmaceutical-grade CBD produced by Noramco, through their exclusive supply agreement, under which Cardiol has the sole rights to purchase the product wholesale for use in manufacturing in Canada and Mexico.

Axim Biotechnologies (AXIM-OTC, NR)

New York-based Axim Biotechnologies is a biotechnology company focused on the development of cannabinoid-derived pharmaceuticals, as well as cannabinoid-based products in the nutraceutical and cosmetic product markets. They are applying their patented trans-mucosal, controlled release chewing gum delivery system for various new drugs under development, including a Dronabinol-based (synthetic THC) treatment for nausea and appetite loss. They also market a hemp-derived CBD chewing gum using their delivery technology.

Lonza Group AG (LONN-SWX, NR)

Lonza group is a Swiss-based global biotechnology and manufacturing company, and a supplier and solutions provider to the pharmaceutical, nutritional supplement and healthcare industries. Recently, they signed an agreement to perform large-scale manufacturing of a new API which is a synthetic derivative of CBD (referred to as VCE-004.8) for use in oral drugs to treat conditions such as multiple sclerosis and system sclerosis. The agreement was signed with Emerald Health Pharmaceuticals (private), a San Diego, CA-based biotechnology company that specializes in the development and commercialization of cannabinoid-derived pharmaceuticals to address a variety of indications with unmet needs.

Concluding Thoughts

Although synthetically-derived processes have been around for numerous years, including their use by the pharmaceutical industry for well-known products such as Aspirin (acetylsalicylic acid) and insulin, we highlight this innovative field for its almost-certainly disruptive impact on the production of cannabinoids, to encourage investors to start familiarizing themselves with this technology and the relevant players. We view synthetically-derived cannabinoid businesses as key component to the overall supply chain within the cannabis industry. While much of the space is still somewhat early-stage, we believe that cannabis LP's will begin to pay much closer attention to these companies' technology and its application to their industry, as it offers the potential for significant advantages on an operational and cost basis, as well as product quality and purity. We believe the possible synergies between the cannabis and synthetic biology/synthetic pharmaceutical spaces being unparalleled to either sector on its own.

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