UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): **December 12, 2019**

KBL MERGER CORP. IV
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-38105**	**81-3832378**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

527 Stanton Christian Road Newark, DE 19713	**19713**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(302) 502-2727**

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☒ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e 4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	KBLM	The NASDAQ Stock Market LLC
Warrants, each warrant exercisable for one-half of one share of Common Stock at an exercise price of $5.75 per half share	KBLMW	The NASDAQ Stock Market LLC
Rights, exchangeable into one-tenth of one share of Common Stock	KBLMR	The NASDAQ Stock Market LLC
Units, each consisting of one share of Common Stock, one Warrant and one Right	KBLMU	The NASDAQ Stock Market LLC

Item 7.01 Regulation FD Disclosure.

Attached as Exhibit 99.l to this Current Report on Form 8-K and incorporated into this Item 7.01 by reference is the investor presentation dated December 12, 2019 that will be used by KBL Merger Corp. IV ("**KBL**") in making presentations to certain of its stockholders and other persons with respect to the transactions contemplated by that certain Business Combination Agreement, dated as of July 25, 2019 (as it may be further amended from time to time, the "**Business Combination Agreement**"), entered into among KBL, CannBioRx Life Sciences Corp., a Delaware corporation (the "**Company**"), Katexco Pharmaceuticals Corp., a British Columbia corporation ('**Katexco**"), CannBioRex Pharmaceuticals Corp., a British Columbia corporation ("**CBR Pharma**"), 180 Therapeutics L.P., a Delaware limited partnership ("**180**" and together with Katexco and CBR Pharma, the "**Company Subsidiaries**"), KBL Merger Sub, Inc., a Delaware corporation, and Lawrence Pemble, in his capacity as representative of the stockholders of the Company and the Company Subsidiaries.

The information in this Current Report on Form 8-K and Exhibit 99.1 attached hereto is being furnished pursuant to Item 7.01 and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), or otherwise be subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended (the "**Securities Act**"), or the Exchange Act, regardless of any general incorporation language in such filings. This Current Report on Form 8-K will not be deemed an admission as to the materiality of any of the information in this Item 7.01, including Exhibit 99.1.

Forward-Looking Statements

Certain statements made herein are "forward-looking statements" within the meaning of U.S. federal securities laws. Words such as "expect," "estimate," "project," "budget," "forecast," "anticipate," "intend," "plan," "may," "will," "could," "should," "believes," "predicts," "potential," "continue" and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant risks and uncertainties that could cause the actual results to differ materially from the expected results and, consequently, you should not rely on these forward-looking statements as predictions of future events. These forward-looking statements and factors that may cause such differences include, without limitation, statements relating to the timing and completion of the proposed business combination; KBL's continued listing on the Nasdaq Stock Market until closing of the proposed business combination; expectations regarding the capitalization, resources and ownership structure of the combined company; the inability to recognize the anticipated benefits of the proposed business combination, which may be affected by, among other things, the amount of cash available following redemptions by KBL stockholders; the ability to meet the Nasdaq Stock Market's listing standards following the consummation of the transactions contemplated by the proposed business combination; costs related to the proposed business combination; expectations with respect to future performance, growth and anticipated acquisitions; ability to recognize the anticipated benefits of the proposed business combination; the Company's ability to execute its plans to develop and market new drug products and the timing and costs of these development programs; the Company's estimates of the size of the markets for its potential drug products; potential litigation involving KBL or the Company or the validity or enforceability of the Company's intellectual property; global economic conditions; geopolitical events and regulatory changes; access to additional financing; and other risks and uncertainties indicated from time to time in filings with the Securities and Exchange Commission (the "**SEC**"). Other factors include the possibility that the proposed business combination does not close, including due to the failure to receive required security holder approvals, or the failure of other closing conditions. The foregoing list of factors is not exclusive. Additional information concerning these and other risk factors is contained in KBL's most recent filings with the SEC and will be contained in the proxy statement/prospectus to be filed as result of the transactions described above. All subsequent written and oral forward-looking statements concerning KBL or the Company, the transactions described herein or other matters and attributable to KBL or the Company or any person acting on their behalf are expressly qualified in their entirety by the cautionary statements above. Readers are cautioned not to place undue reliance upon any forward-looking statements, which speak only as of the date made. None of KBL or the Company undertake or accept any obligation or undertaking to release publicly any updates or revisions to any forward-looking statement to reflect any change in their expectations or any change in events, conditions or circumstances on which any such statement is based.

Additional Information and Where to Find It

KBL has filed a registration statement on Form S-4, which includes a preliminary proxy statement/prospectus for KBL's stockholders, with the SEC. KBL's definitive proxy statement/prospectus will be mailed to KBL's stockholders that do not opt to receive the document electronically. KBL and the Company urge investors, stockholders and other interested persons to read the preliminary proxy statement/prospectus, as well as other documents that will be filed with the SEC, because these documents will contain important information about the proposed business combination transaction. Such persons can also read KBL's Annual Report on Form 10-K for the fiscal year ended December 31, 2018, for a description of the security holdings of its officers and directors and their respective interests as security holders in the consummation of the proposed business combination transaction. KBL's definitive proxy statement/prospectus, which is included in the registration statement, will be mailed to stockholders of KBL as of a record date to be established. KBL's stockholders will also be able to obtain a copy of such documents, without charge, by directing a request to: KBL Merger Corp. IV, 150 West 56th Street, Suite 5901, New York, NY 10019; e-mail: admin@kblvc.com. These documents can also be obtained, without charge, at the SEC's web site (http://www.sec.gov).

Participants in the Solicitation

KBL and its directors and executive officers, may be deemed to be participants in the solicitation of proxies for the special meeting of KBL's stockholders to be held to approve the proposed transactions in connection with the business combination. Information regarding the persons who may, under the rules of the SEC, be deemed participants in the solicitation of KBL's stockholders in connection with the proposed transactions are set forth in the preliminary proxy statement/prospectus included in the registration statement that was filed with the SEC on November 12, 2019. You can find information about KBL's executive officers and directors in its Annual Report on Form 10-K for the fiscal year ended December 31, 2018, which was filed with the SEC on April 1, 2019. You can obtain free copies of these documents from KBL using the contact information above.

Disclaimer

This communication is not a proxy statement or solicitation of a proxy, consent or authorization with respect to any securities or in respect of the proposed transaction and shall not constitute an offer to sell or a solicitation of an offer to buy the securities of KBL and the Company, nor shall there be any sale of any such securities in any state or jurisdiction in which such offer, solicitation, or sale would be unlawful prior to registration or qualification under the securities laws of such state or jurisdiction. No offer of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the Securities Act.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Investor Presentation dated December 12, 2019.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: December 12, 2019

KBL MERGER CORP. IV

By: /s/ Marlene Krauss, M.D.
Name: Marlene Krauss, M.D.
Title: Chief Executive Officer

Exhibit 99.1

CANNBIORX LIFE SCIENCES

CORPORATE PRESENTATION
DECEMBER 2019

DISCLAIMER

This Presentation is for informational purposes only and does not constitute an offer to sell, a solicitation of an offer to buy, or a recommendation to purchase any equity, debt or other financial instruments of CannBioRx Life Sciences Corp. ("CannBioRx") or KBL Merger Corp. IV ("KBL") or any of CannBioRx's or KBL's affiliates' securities. This Presentation has been prepared to assist interested parties in making their own evaluation with respect to the proposed business combination of CannBioRx and KBL and for no other purpose. The information contained herein does not purport to be all-inclusive. The data contained herein is derived from various internal and external sources. No representation is made as to the reasonableness of the assumptions made within or the accuracy or completeness of any projections or any other information contained herein. Any data on past performance or projections contained herein is no indication as to future performance. CannBioRx and KBL assume no obligation to update the information in this Presentation.

Forward-Looking Statements

This Presentation includes "forward-looking statements" within the meaning of U.S. federal securities laws. Words such as "expect," "estimate," "project," "budget," "forecast," "anticipate," "intend," "plan," "may," "will," "could," "should," "believes," "predicts," "potential," "continue" and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant risks and uncertainties that could cause the actual results to differ materially from the expected results and, consequently, you should not rely on these forward-looking statements as predictions of future events. These forward-looking statements and factors that may cause such differences include, without limitation, statements relating to the timing and completion of the proposed business combination; KBL's continued listing on the Nasdaq Stock Market until closing of the proposed business combination; expectations regarding the capitalization, resources and ownership structure of the combined company; the inability to recognize the anticipated benefits of the proposed business combination, which may be affected by, among other things, the amount of cash available following redemptions by KBL stockholders; the ability to meet the Nasdaq Stock Market's listing standards following the consummation of the transactions contemplated by the proposed business combination; costs related to the proposed business combination; expectations with respect to future performance, growth and anticipated acquisitions; ability to recognize the anticipated benefits of the proposed business combination; CannBioRx's ability to execute its plans to develop and market new drug products and the timing and costs of these development programs; CannBioRx's estimates of the size of the markets for its potential drug products; potential litigation involving KBL or CannBioRx or the validity or enforceability of CannBioRx's intellectual property; global economic conditions; geopolitical events and regulatory changes; access to additional financing; and other risks and uncertainties indicated from time to time in filings with the Securities and Exchange Commission (the "SEC"). Other factors include the possibility that the proposed business combination does not close, including due to the failure to receive required security holder approvals, or the failure of other closing conditions. The foregoing list of factors is not exclusive. Additional information concerning these and other risk factors is contained in KBL's most recent filings with the SEC and will be contained in the proxy statement/prospectus to be filed as result of the transactions described above. All subsequent written and oral forward-looking statements concerning KBL or CannBioRx, the transactions described herein or other matters and attributable to KBL or CannBioRx or any person acting on their behalf are expressly qualified in their entirety by the cautionary statements above. Readers are cautioned not to place undue reliance upon any forward-looking statements, which speak only as of the date made. None of KBL or CannBioRx undertake or accept any obligation or undertaking to release publicly any updates or revisions to any forward-looking statement to reflect any change in their expectations or any change in events, conditions or circumstances on which any such statement is based.

Additional Information and Where to Find It

KBL has filed a registration statement on Form S-4, which includes a preliminary proxy statement/prospectus for KBL's stockholders, with the SEC. KBL's definitive proxy statement/prospectus will be mailed to KBL's stockholders that do not opt to receive the document electronically. KBL and CannBioRx urge investors, stockholders and other interested persons to read the preliminary proxy statement/prospectus, as well as other documents that will be filed with the SEC, because these documents will contain important information about the proposed business combination transaction. Such persons can also read KBL's Annual Report on Form 10-K for the fiscal year ended December 31, 2018, for a description of the security holdings of its officers and directors and their respective interests as security holders in the consummation of the proposed business combination transaction. KBL's definitive proxy statement/prospectus, which is included in the registration statement, will be mailed to stockholders of KBL as of a record date to be established. KBL's stockholders will also be able to obtain a copy of such documents, without charge, by directing a request to: KBL Merger Corp. IV, 150 West 56th Street, Suite 5901, New York, NY 10019; e-mail: admin@kblvc.com. These documents can also be obtained, without charge, at the SEC's website (http://www.sec.gov).

Participants in the Solicitation

KBL and its directors and executive officers, may be deemed to be participants in the solicitation of proxies for the special meeting of KBL's stockholders to be held to approve the proposed transactions in connection with the business combination. Information regarding the persons who may, under the rules of the SEC, be deemed participants in the solicitation of KBL's stockholders in connection with the proposed transactions are set forth in the preliminary proxy statement/prospectus included in the registration statement that was filed with the SEC on November 12, 2019. You can find information about KBL's executive officers and directors in its Annual Report on Form 10-K for the fiscal year ended December 31, 2018, which was filed with the SEC on April 1, 2019. You can obtain free copies of these documents from KBL using the contact information above.

Disclaimer

This Presentation is not a proxy statement or solicitation of a proxy, consent or authorization with respect to any securities or in respect of the proposed transaction and shall not constitute an offer to sell or a solicitation of an offer to buy the securities of KBL and CannBioRx, nor shall there be any sale of any such securities in any state or jurisdiction in which such offer, solicitation, or sale would be unlawful prior to registration or qualification under the securities laws of such state or jurisdiction. No offer of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the Securities Act of 1933, as amended.

INFLAMMATION DRIVES THE WORLD'S BIGGEST DISEASES

The experienced and world-renowned scientific team are proven leaders in this field.

- ***Sir Marc Feldmann:*** *Centocor sold to J&J for $4.9 B USD*
- ***Lawrence Steinman:*** *Tysabri sold to Royalty Pharma for $2.85 B USD*
- ***Jonathan Rothbard:*** *Amylin sold to AstraZeneca and Bristol-Myers Squibb for $7 B USD*
- ***Raphael Mechoulam:*** *Identified major phytocannabinoids (tetrahydrocannabinol (THC), cannabidiol (CBD) etc.) and discovered the endocannabinoid system*

Prof Raphael Mechoulam receiving Honorary Doctorate in Madrid.

Prof Sir Marc Feldmann in his office with Gairdner Award, European Inventor of Year, and Lasker Award.

Dr Lawrence Steinman signing National Academy of Science register.

CANNBIORX HIGHLIGHTS

- **Scientific team and founders are pioneers with proven track record in drug discovery from the University of Oxford, Hebrew University and Stanford University**

- **Developing three families of novel drugs addressing significant market opportunities in inflammation, fibrosis and pain:**
  - **-Fibrosis & Anti-TNF**
  - **-Synthetic CBD Analogs (SCAs)**
  - **-α7nAChR**

- **Multiple programs in synchronized stages of development combined with IP portfolio reduces risk**

- **Numerous near-term inflection points for anti-TNF programs: one program late stage 2b/3 trial, two additional clinical programs projected to start Q4 2020**

  - **Initial clinical anti-TNF clinical trials funded by investments and grants (UK and Dutch).**
  - ***Regulatory approvals obtained from the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and the Dutch Centrale Commissie Mensgebonden Onderzoek (CCMO) and the relevant accredited ethics committees to perform clinical trials in the UK and The Netherlands for anti-TNF products.**

- **Three anti-inflammatory therapeutic programs potentially used in combination**

**No meetings have been held with, and no applications or requests for approval have been submitted to the FDA for any products at this time.*

CO-FOUNDERS AND MANAGEMENT

Incredible discoveries in scientific fields; successful business leaders

Prof Sir Marc Feldmann *Co-Chairman*

- Pioneer of anti-TNF therapy, world's biggest drug class ($40B USD pa)
- Numerous accolades including Crafoord and Lasker Awards, fellow of the Royal Society

Prof Raphael Mechoulam *Founder, CBRx*

- Godfather of cannabinoid chemistry; discovered the body's endocannabinoid system
- Recipient of Israel Exact Sciences Prize, member of Israel Academy of Science and Humanities

Prof Lawrence Steinman *Co-Chairman*

- Discovered role of integrins, led to Natalizumab, highly effective treatment for MS and IBD
- Member of National Academy of Sciences, many accolades including Charcot Prize; founder of Centocor (sold to J&J for $4.9B USD)

Dr Marlene Krauss *CEO*

- Harvard Business School, Harvard Medical School, Cornell University
- CEO of 4 SPACs and 3 VC funds; invested more than $1B USD in early to mid-stage companies

Mr George Hornig *COO & Acting CFO*

- Harvard College, Harvard Business School, Harvard Law School
- Considerable banking experience, in high-level positions for Deutsche Bank and Credit Suisse

Prof Jagdeep Nanchahal *CMO*

- Surgeon-scientist, leading 2b/3 trial funded by Wellcome Trust and UK Dept. of Health
- Member of the Royal College of Surgeons; discovered new treatments for fibrosis

Dr Jonathan Rothbard *CSO*

- Stanford University, broad experience in small molecule development
- Founder of 5 biotech companies; Amylin sold to AstraZeneca and BMS for $5.3B USD

OVERVIEW:CANNBIORX DEVELOPMENT PROGRAMS

	FIBROSIS & ANTI-TNF (CLINICAL STAGE)*	SYNTHETIC CBD ANALOGS (SCAs)	α7nAChR
TECHNOLOGIES	**Repurposing of anti-TNF for major unmet needs, other patented drugs**	**Novel non-psychoactive synthetic CBD analogs**	**Novel α7nAChR agonists**
TARGETED DISEASES	**NEAR TERM** • **Early stage Dupuytren's disease (DD)** • **Frozen Shoulder** • **Post Operative Delirium/Cognitive Deficit (POCD)** **FURTHER OUT** • **Non-Alcoholic Steatohepatitis (NASH)**	• **Arthritis** • **Pain/Inflammation**	• **Smoking cessation induced Ulcerative Colitis (UC) initially** • **Other inflammatory indications will be targeted after results in UC**
COMPETITIVE ADVANTAGE	• **DD**: no treatment for early disease • **Frozen Shoulder:** local steroid only for short term pain relief, does not modulate long-term disease activity • **POCD**: No treatment available	• Novel, >99.5% pure, • Robust batch to batch consistency (non-botanical) • Developing advanced formulation for increased bioavailability	• Orally available • Potentially as effective as biologics (like anti-TNF) • Proven lack of toxicity
STAGE	• **DD**: Phase 2b/3 in early DD, results Q1/2 2021 • **Frozen Shoulder**: Initiate Phase 2 trials Q4 2020 • **POCD**: Initiate Phase 3 trials Q4 2020 • **NASH**: Preclinical studies to begin Q2 2020	• **Preclinical** – lead SCAs and formulations being identified • Trials planned in arthritis and pain	• **Preclinical** – optimizing new compounds based on safe α7nAChR agonists
INTELLECTUAL PROPERTY	• **Patents issued for treatment of DD & POCD with anti-TNF** • Additional patents issued (anti-IL-33) or pending in localized and systemic fibrosis and delivery systems	• **Patent issued for Cyclohexenyl compounds**, compositions and uses thereof • Patents pending & to be filed	• **Three patents issued, one patent pending**

**Regulatory approvals obtained from the MHRA and CCMO and the relevant accredited ethics committees to perform clinical trials in the UK and The Netherlands. No meetings have been held with, and no applications or requests for approval have been submitted to the FDA for any products at this time.*

THREE PLATFORM TECHNOLOGIES TARGETING MULTIPLE INDICATIONS

PLATFORM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Fibrosis & Anti-TNF*	• Dupuytren's contracture			ongoing	
	• Frozen shoulder			Est. start Q4 2020	
	• POCD				Est. start Q4 2020
	• NASH	Est. start Q2 2020			
SCAs	• Chronic pain	ongoing	Est. start Q3 2021	Est. start Q3 2022	
	• Early arthritis	ongoing		Est. start Q1 2023	
α7nAChR	• Smoking cessation induced ulcerative colitis	ongoing			

**Regulatory approvals obtained from the MHRA and CCMO and the relevant accredited ethics committees to perform clinical trials in the UK and The Netherlands. No meetings have been held with, and no applications or requests for approval have been submitted to the FDA for any products at this time.*

Led by
Profs Jagdeep Nanchahal & Sir Marc Feldmann, Oxford
Dr Glenn Larsen, USA
Clinical trials supported by ***Prof Sallie Lamb, UK***

CLINICAL STAGE LEAD PROGRAM

Targeting common diseases
- facilitates trials and potential sales

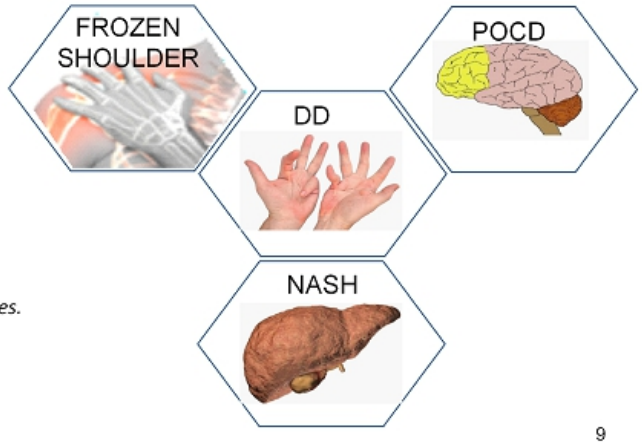
FIBROSIS & ANTI-TNF PROGRAM

Oxford

FIBROSIS & ANTI-TNF PLATFORM

Developing targeted therapies for:

- Early Stage Dupuytren's disease (DD) - patent issued; Phase 2b/3 results expected Q1/2 2021*
- Frozen shoulder - patent issued; clinical trials projected in Q4 2020
- Post operative cognitive decline (POCD) - patent issued, clinical trials projected in Q4 2020
- Liver fibrosis (NASH) - initial laboratory studies done with Celgene-BMS on human tissue; preclinical studies to begin in Q2 2020



Approval only from MHRA/CCMO and relevant accredited ethics committees.

UNIQUE COMPETITIVE ADVANTAGE #1

COST EFFECTIVE, TIME EFFICIENT, ACADEMIC LED CLINICAL TRIALS PERFORMED IN UK

- Working with disease experts and key opinion leaders, who are highly motivated to improve patient standard of care
- No payment for trial patients required in the UK/EU
- Easier recruitment. Access to large registries of patients/diseases
- Staff costs can be covered by academic grants (Wellcome Trust, NIHR)
- Established reputation and prestige in conducting clinical trials across academic and clinical networks[1]
- Skilled at writing protocols compliant with regulatory authorities, seeking approvals, accessing patient registries, establishing good working relations with trial centers and coordination of patient recruitment and data collection across multiple sites, industry standard statistical analysis of blinded data, report submission….
- Well practiced in publishing trials in peer reviewed clinical journals

OCTRU
Oxford Clinical Trials Research Unit


Prof Sallie Lamb


Prof Jagdeep Nanchahal

[1] https://www.ndorms.ox.ac.uk/octru

UNIQUE COMPETITIVE ADVANTAGE #2

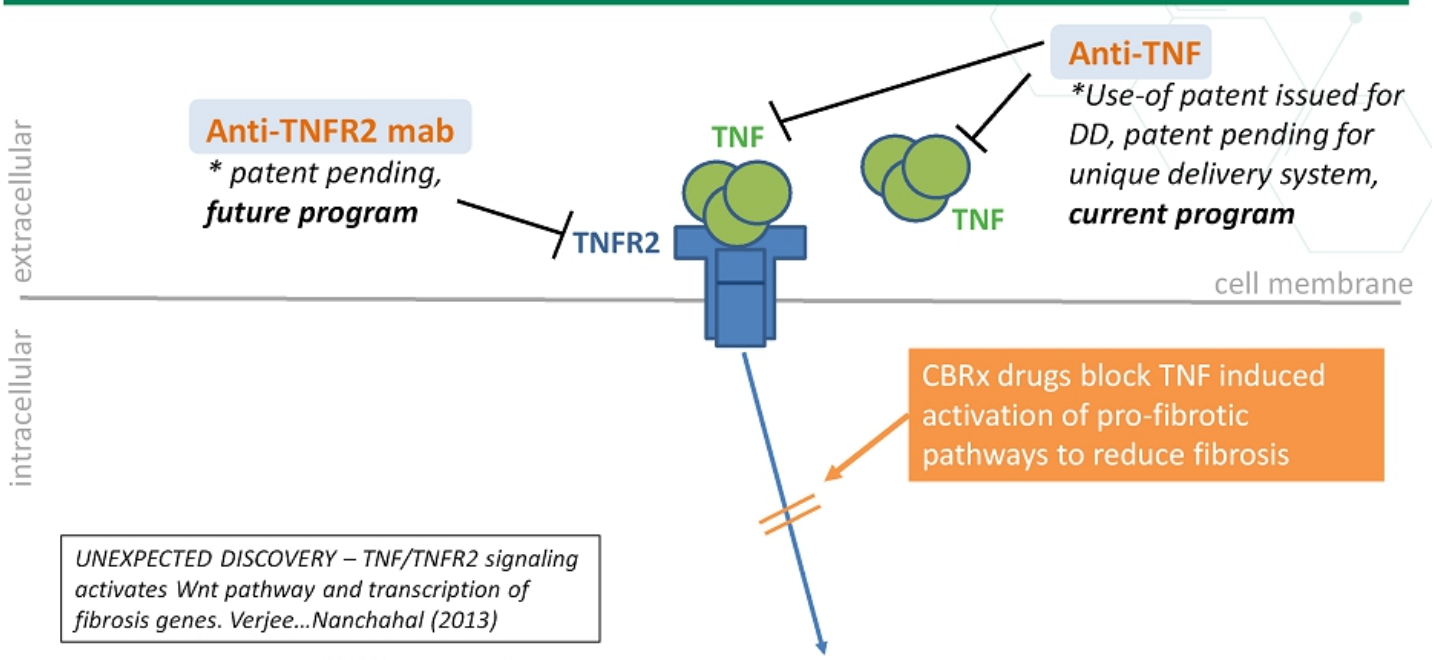
NOVEL USE OF HUMAN DISEASE TISSUE TO IDENTIFY NEW TARGETS IN FIBROSIS

Studies in DD lead the way for novel approach to develop clinical programs in other fibrotic diseases:

- **All fibrosis preceded by inflammation, involves myofibroblasts**
- **Our targets identified in patient myofibroblasts and associated immune cells**
- **Using human tissue from DD nodules**

- ***Tissue and cells from most fibrotic diseases not readily accessible as diagnosed late***
- ***Competitors use animals or late stage cells in culture, neither reflect human disease***
- ***Novel therapeutics testable, assessed by molecular changes***
- ***Same approach will be applied to target discovery in NASH***

RATIONALE FOR TNF BLOCKADE IN FIBROSIS



UNEXPECTED DISCOVERY – TNF/TNFR2 signaling activates Wnt pathway and transcription of fibrosis genes. Verjee…Nanchahal (2013)

Wnt activation leading to FIBROSIS
(↑ expression of α-SMA, Col1A1 genes etc)

PNAS

Unraveling the signaling pathways promoting fibrosis in Dupuytren's disease reveals TNF as a therapeutic target

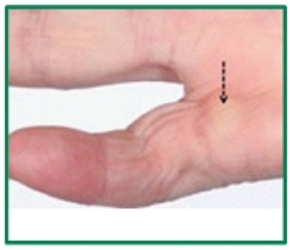
Liaquat S. Verjee [a], Jennifer S.N. Verhoekx [a,b], James K. K. Chan[a], Thomas Krausgruber [a], Vicky Nicolaidou[a], David Izadi [a], Dominique Davidson [c], Marc Feldmann [a,1], Kim S. Midwood [a], and Jagdeep Nanchahal [a,1]

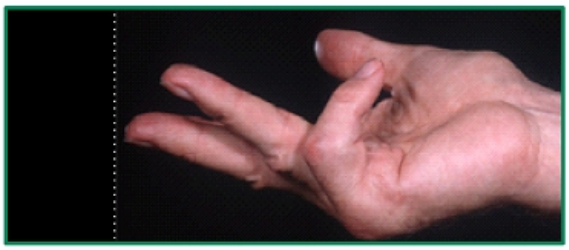
[a] Kennedy Institute of Rheumatology, University of Oxford, London W6 8LH, United Kingdom
[b] Department of Plastic and Rescontructive Surgery, Erasmus Medical Centre, 3015, Rotterdam, The Netherlands
[c] Department of Plastic Surgery, St John's Hospital, Livingston EH54 6PP, United Kingdom

INITIAL INDICATION TARGETING DUPUYTREN'S DISEASE

- **Common localized fibrotic condition of the hand**, develops over years
- Nodules form under skin – eventually creating a thick cord pulling one or more fingers
- **Can limit hand functions**
- Unlike liver and lung fibrosis <u>can be identified early</u>

Early disease → **Late disease – results in impaired hand function**





- **No approved treatment: unmet need**
- Our trial is in early disease*

Current treatment options suboptimal:(1)

- Surgery – long (3 month) recovery, 6% recurrence at 5yr
- Needle perforation – less invasive, 30% recurrence at 5yr
- Collagenase injections – office procedure, 47% recurrence at 5yr

**Approval only from MHRA/CCMO and relevant accredited ethics committees.*

Sources:
(1) Layton T & Nanchahal J. F1000Research 2019, 8(F1000Faculty Rev): 231

PHASE 2A COMPLETED: 40MG (in 0.4ML) ADALIMUMAB IS EFFECTIVE

*- The first trial of any targeted therapy in early DD**

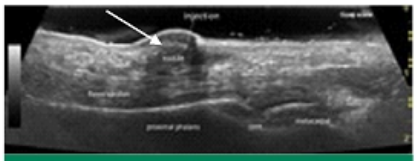
Anti-Tumour Necrosis Factor Therapy for Dupuytren's Disease: A Randomised Dose Response Proof of Concept Phase 2a Clinical Trial

EBioMedicine
Published by THE LANCET

Jagdeep Nanchahal [23,*], Catherine Ball [23], Dominique Davidson [24], Lynn Williams [23], William Sones [25], Fiona E McCann [23], Marisa Cabrita [23], Jennifer Swettenham [23], Neil J. Cahoon [24], Bethan Copsey [25], E. Anne Francis [23], Peter C. Taylor [23], Joanna Black [25], Vicki S. Barber [25], Susan Dutton [25], Marc Feldmann [23], Sarah E. Lamb [25]

EBioMedicine 33 (2018) 282-288

TRIAL OVERVIEW

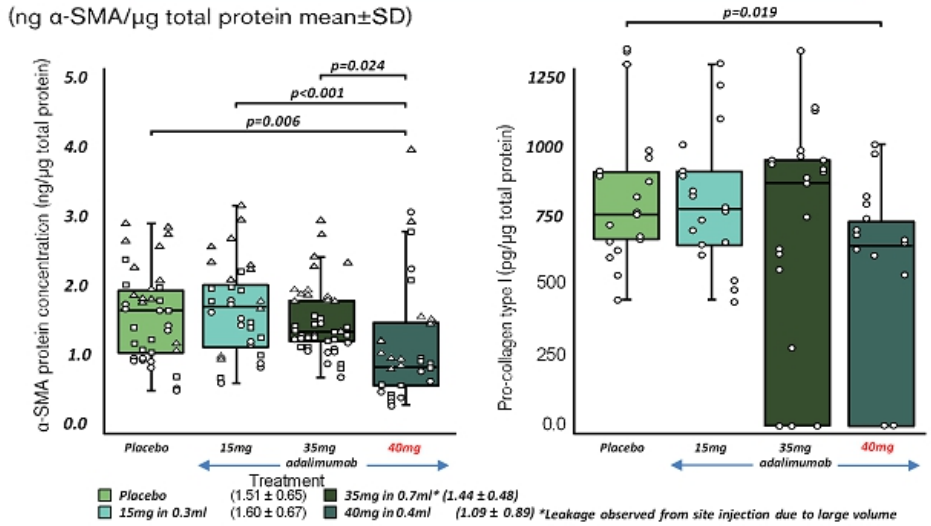


Adalimumab injected directly into the nodule

- Dose ranging with 28 patients.
- **40 mg in 0.4ml - effective dose.**
- Funded by HICF (Wellcome Trust + Dept of Health) and CannBioRx

**Approval only from MHRA/CCMO and relevant accredited ethics committees.*

Demonstrated efficacy at high concentration & dose



PHASE 2b/3 TRIAL FULLY ENROLLED – LOCAL ADALIMUMAB IN EARLY DD

- Randomized blinded trial in patients with **early DD** injected with **optimal dose** adalimumab*
- Every 3 months for 1 year (4 injections), following for a total of 18 months
- Outcome measures include nodule hardness, size and disease progression
- Randomized 181 patients across 3 sites in UK and the Netherlands
- **FULLY ENROLLED, FULLY PAID FOR**
- All UK patients have received final injection
- **Results expected Q1/2 2021**

	Objectives	Outcome measures
Primary Objective	To determine if injection with adalimumab is superior to placebo injection of normal saline in controlling disease progression.	Hardness of selected nodule.
Secondary Objectives	1. To compare the development of Dupuytren's nodules and associated cord, flexion deformities of the fingers and impairment of hand function for participants on each treatment.	1.1. Ultrasound imaging of nodule size. 1.2. Range of motion of the affected digit. 1.3. Grip strength. 1.4. Participant Reported Outcomes: Michigan Hand Outcomes Questionnaire (MHQ) Participant identified activity most restricted by DD scored on a scale of 1–10. 1.5. Clinical assessment of the hand.
	2. Monitor for adverse events.	2.1. Adverse event assessment comparing active and placebo groups using visual inspection of injection site and laboratory reports. 2.2. Progression to surgery of the digit being assessed.
Tertiary Objectives	3. To assess if early DD injection therapy represents good value for money compared to current clinical care. 4. Monitor circulating levels of adalimumab and antibodies to adalimumab in the blood	3. Analysis of health care resource utilisation data and EQ-5D-5L data to estimate cost and utilities from participants on each treatment. 4. Analysis of blood sample.

CannBioRx clinical trial 2b/3 - Nanchahal J et al, 2017 Wellcome Open Research, 2:37

Trial sites - Oxford, Edinburgh, Groningen

**Approval only from MHRA/CCMO and relevant accredited ethics committees.*

LARGE MARKET OPPORTUNITY FOR EARLY DUPUYTREN'S DISEASE

Estimated future worldwide market for Dupuytren's >$1B per year [1]
All current treatments for Dupuytren's are for LATE stage disease

- 4% of the EU & US population suffer from Dupuytren's disease [1,2]
- Assume ~25% of these (1% total) are symptomatic & require treatment [3]
  Potential patients in the U.S. (1% of 315M) = 3M patients

- Conservatively assume 25% of symptomatic patients get treatment [4]
  US 3M x 25% ~ 0.8M pa
  EU (Assume 50% of US) ~ 0.4M patients

1. Hindocha S, McGrouther DA, Bayat A (2009) Hand (NY) 4(3):256-69.
2. Lanting et al. (2014) PRS 133: 593-603
3. Nanchahal J, et al. (2017) Wellcome Open Res 2:37.,
4. Nanchahal J, personal communication

ADDITIONAL INDICATIONS:

Post Operative Delirium/Cognitive Deficit (POCD)

- **Over 300,000 hip fractures each year in the U.S. alone**[1]
- **Strong pre-clinical and clinical evidence for anti-TNF as preventative therapy**
- **Patent claims granted,** patent is licensed from Kennedy Trust, UK
- **Phase 3 multi-centre trial of pre-operative anti-TNF in hip fracture surgery planned to initiate by Q4 2020, single dose administered just prior to surgery, to be complete in 4 years**
- **Grant application submitted to EME (Efficacy and Mechanism Evaluation) board of National Institute of Health Research (NIHR)**
- **Trial to be executed in the UK, and therefore protocol will be approved by MHRA and Research Ethics Committee. Will seek advice from the FDA when appropriate**
- **Working with Prof Matt Costa, trauma surgeon** - *previously recruited 20,000 patients to hip fracture trials*

- ***Direct entry to phase 3 permissible:***
  - ***Anti-TNF has a well defined safety profile, dosing understood***
  - ***Have access to patients for large scale trial required for sufficient powering***

[1]https://www.cdc.gov/homeandrecreationalsafety/falls/adulthipfx.html

EVIDENCE THAT TNF PLAYS A ROLE IN POCD

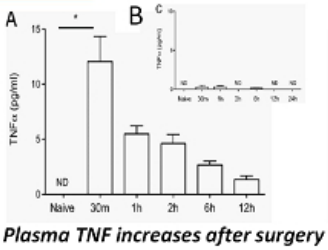
Tumor necrosis factor-α triggers a cytokine cascade yielding postoperative cognitive decline

Niccolò Terrando[a,b], Claudia Monaco[c], Daqing Ma[b], Brian M. J. Foxwell[c,1], Marc Feldmann[c,2], and Mervyn Maze[a,b,2]

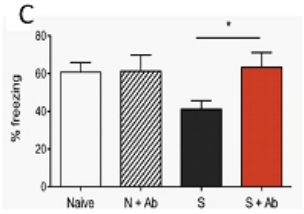
[a]Department of Anesthesia and Perioperative Care, University of California, San Francisco, CA 94143-0648; [b]Department of Anesthetics, Pain Medicine and Intensive Care, Imperial College London, Chelsea and Westminster Hospital, London SW10 9NH, United Kingdom; and [c]Kennedy Institute of Rheumatology, Faculty of Medicine, Imperial College London, London W6 8LH, United Kingdom

Generated patent, licensed from Kennedy Inst. for treatment of POCD with anti-TNF

In mice



Plasma TNF increases after surgery

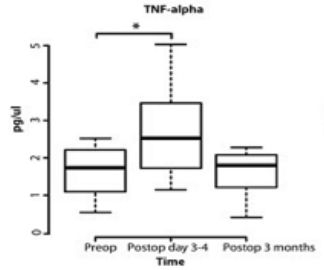


Surgery impaired fear memory is restored with pre-op anti-TNF

- Mice subjected to surgery (open tibial fracture) experience a rapid increase in plasma TNF levels (A) - not caused by anesthesia alone (B)
- Administration of pre-operative anti-TNF reduces freezing behavior, indicative of contextual fear memory, characteristic of cognitive decline (C)
- **Surgery in humans triggers TNF release, and is associated with reduced brain activity cognitive decline [1-2]**

In man

Plasma TNF increases after surgery and correlates with post operative delirium



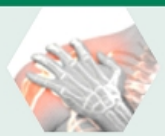
Forsberg A et al, Annals of Neurology (2017) 81:4, 572-582

Kazmierski J et al, International Psychogeriatrics (2014), 26:5, 845–855

1 Clark IA, Vissel B. *Front Neurosci* (2018) 12:257.
2 Alam A et al, EBioMedicine (2018) 37:547-556

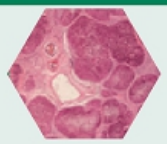
ADDITIONAL FIBROTIC INDICATIONS CONTINUED:

Frozen Shoulder



- Painful inflammatory condition that progresses to scarring, limiting movement
- Affects 9% of the of the population aged 25-64yr, more common in diabetics[1]
- Only treatment for early stage is local steroid injection for short term relief
- Phase 2 clinical trials planned for local injection of anti-TNF, initiates Q4 2020
- Trial protocol completed and grant application submitted to NIHR (National Institute of Health Research) in collaboration with leading experts who pioneered delivery of large trials in frozen shoulder
- Will obtain MHRA and Research Ethics Committee approval (clinical trial to be conducted in the UK) and will seek FDA advice when appropriate

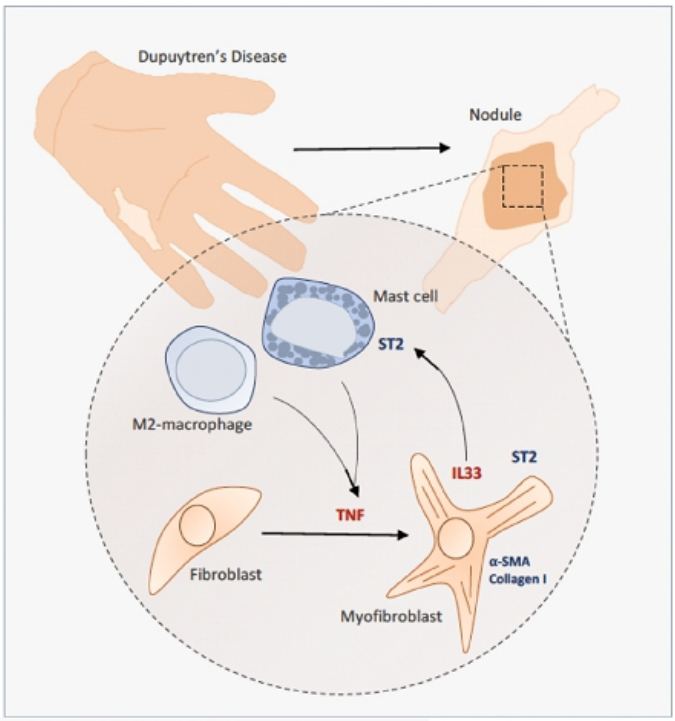
Fibrosis of the liver



- Long-term damage characterized by the replacement of normal liver tissue by scar tissue
- Most commonly caused by non-alcoholic fatty liver disease (NAFLD), which affects ~30% of the US population[2]
- ~2% of patients with non-alcoholic fatty liver disease and 15-20% with non-alcoholic steatohepatitis (NASH) progress to cirrhosis[3]
- No approved therapeutic for NASH
- Lab program in collaboration with Celgene-BMS for target discovery using human liver samples
- Optimised process for acquiring fresh human liver tissue from clinical network

[1]Walker-Bone K et al (2004) Arthritis Rheum 51(4):642-651
[2]Rinella ME & Sanyal AJ (2016) Nat Rev Gastroenterol Hepatol 13(4):196-205
[3] Ibid.

NEXT GENERATION THERAPEUTICS: ANTI-TNFR2 & ANTI-IL-33 INHIBITORS



SCIENCE ADVANCES | RESEARCH ARTICLE

HEALTH AND MEDICINE

Identification of TNFR2 and IL-33 as therapeutic targets in localized fibrosis

David Izadi[1]*, Thomas B. Layton[1]*, Lynn Williams[1], Fiona McCann[1], Marisa Cabrita[1], Ana I. Espirito Santo, Weilin Xie[2], Marco Fritzsche[1], Huw Colin-York[1], Marc Feldmann[1], Kim S. Midwood[1], Jagdeep Nanchahal[1†]

Dupuytren's disease fibrotic nodules comprise myofibroblasts and immune cells (macrophages and mast cells mostly)

Proposed mechanism:

1. Myofibroblasts secrete IL-33
2. IL-33 signals through ST2 receptor on mast cells and macrophages
3. Triggers production of TNF
4. TNF drives differentiation and activation of myofibroblasts

PUTATIVE THERAPEUTIC INTERVENTIONS

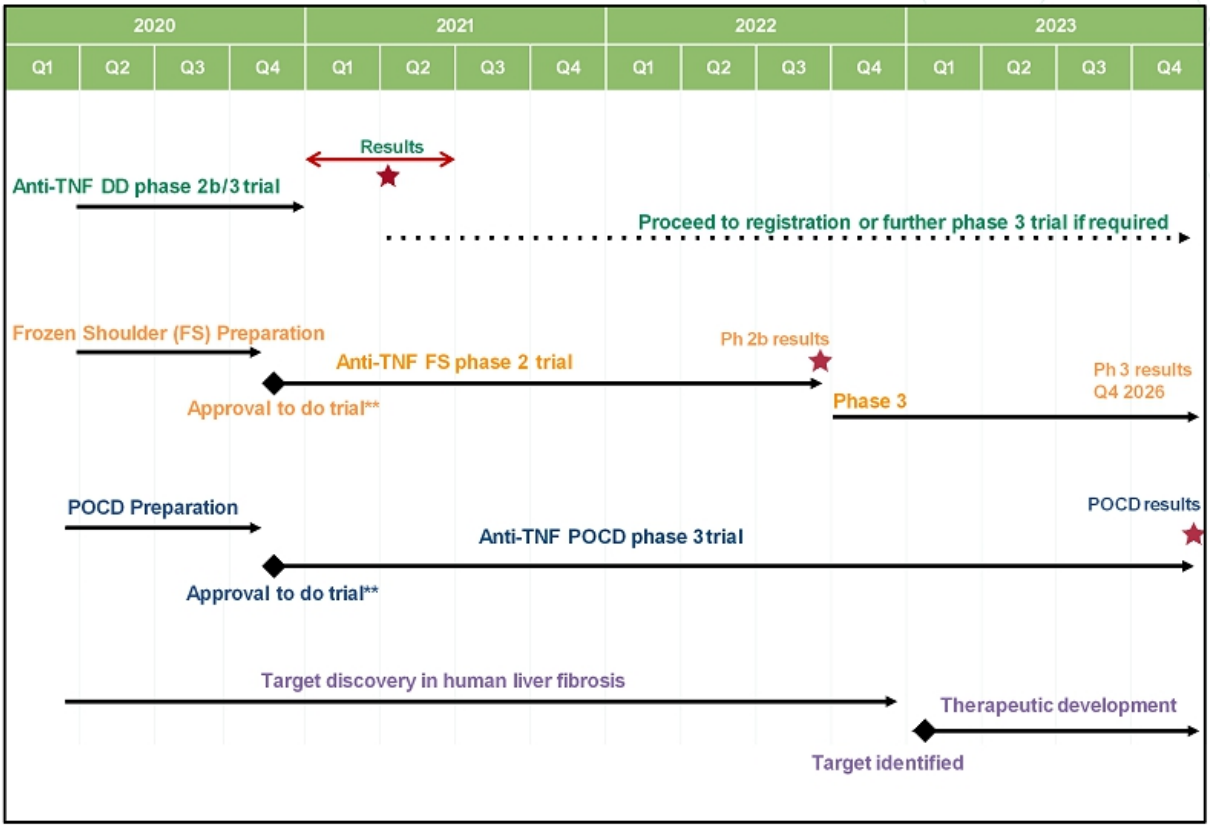
1. Anti-TNF (in Phase 2b/3 trial with approval only from MHRA/CCMO and relevant accredited ethics committees)
2. Anti-IL-33 and/or anti-TNFR2 (next generation)

➢ *Double pronged approach, blocking production of TNF and downstream signaling*

Patents filed for anti-TNFR2 and anti-IL-33
Claims in USA granted for IL-33, others pending

Soucre for Diagram Above:
Izadi D et al. Sci. Adv. 2019; 5 : eaay0370 4 December 2019 – *supp data*

FIBROSIS & ANTI-TNF CLINICAL DEVELOPMENT PLAN*



*Based on current proposals.
**Regulatory approvals obtained from the MHRA and CCMO and the relevant accredited ethics committees to perform clinical trials in the UK and The Netherlands. No meetings have been held with, and no applications or requests for approval have been submitted to the FDA for any products at this time.

Led by

Profs R Mechoulam, R Gallily, A Domb, A Hoffman – HU, Jerusalem

Prof Sir Marc Feldmann, Prof R Williams, Dr L Topping – Oxford

Clinical trials supported by ***Prof Sallie Lamb, UK***

Synthetic CBD analogs (SCAs) for unmet needs in pain and inflammation

Developing proprietary compounds which aim to be:

- **Safe** & non-psychoactive
- Formulated to offer improved oral bioavailability (> three-fold)
- **Rigorously tested in clinical trials** for inflammatory pain (efficacy and dosing)
- Granted market approval by FDA, EMA and others
- **A real alternative to unregulated consumption of medical marijuana or OTC CBD** *(no clinical evidence, not FDA approved, unreliable composition, unpredictable dosing and safety ….)*

Regulatory landscape

Only two drugs approved, both from GW Pharma, both cannabis derived:

1. **Epidiolex** - oral CBD for treatment of rare childhood epilepsies – Lennox Gastaut and Dravet Syndrome, FDA and EMA approved, - ***recently recommended by National Institute for Health and Care Excellence) NICE in UK for National Health Service (NHS) reimbursement***
2. **Sativex** (nabiximols) – THC:CBD (1:1) oromucosal spray for multiple sclerosis (MS) related spasticity, approved by EMA but not by FDA.

- **Points to opportunities across Europe and UK for uptake of medical cannabinoids [1]**
- **FDA warns about unregulated consumption of CBD [2,3]**
- **More trials needed to establish safety**

CBRx SCAs are pure, not derived from cannabis, offer more efficient & controlled oral dosing, easy to administer, positioned for treatment of residual pain in inflammatory arthritis and other *– not competing with GW products which are plant derived!*

[1] **"GW Pharma Shares Rise"** https://www.marketwatch.com/story/gw-pharma-shares-rise-after-uk-recommends-nhs-reimburse-its-cbd-based-epilepsy-drug-2019-11-11
[2] **"CBD has the potential to harm you"** https://www.marketwatch.com/story/cbd-has-the-potential-to-harm-you-fda-warns-consumers-2019-11-25
[3] **"FDA warns 15 companies"** https://www.fda.gov/news-events/press-announcements/fda-warns-15-companies-illegally-selling-various-products-containing-cannabidiol-agency-details

PLATFORM DESCRIPTION

- Non-psychoactive CBD analogs (SCAs) are anti-inflammatory, and elicit analgesic effects
- Studied by Mechoulam, Gallily, Feldmann since 1998 (Malfait et al, PNAS 2000)

HOW DOES IT WORK?

- CBD signals through multiple GPCR receptors, eg CB2R, TRPV-1, 5HT1α, GPR55, GPR18 and others
- Anti-inflammatory, analgesic and anxiolytic properties

OUR PRODUCTS:

NON-PSYCHOACTIVE SCAs

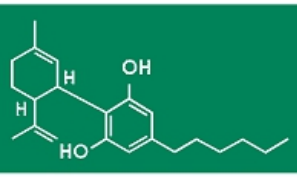
- Scientifically formulated analogs of CBD (SCAs) have been synthesized and patented, new formulations under analysis
- Analysed in animal models of inflammation and pain

WHY MAN-MADE?

- High purity (>99.5%)
- CBD from plants are typically ≤ 98% pure, contain THC, minor cannabinoids, terpenes, flavonoids etc.
- Consistent across batches, more favourable for obtaining regulatory approval

OUR DRUGS

1. HU-436*
2. Domb patent 1**
3. Mechoulam patent 2†
4. Mechoulam patent 3 & others†



* Patented drug we licensed from HU, but expect to discover superior drugs from ongoing research
** CBD derivative, patent being filed, agreement with Domb & HU completed
† not filed yet

PROBLEMS OF MEDICAL MARIJUANA (MM) & OTC CBD THAT CANNBIORX SOLVES

FDA position – Nov 25, 2019[1]

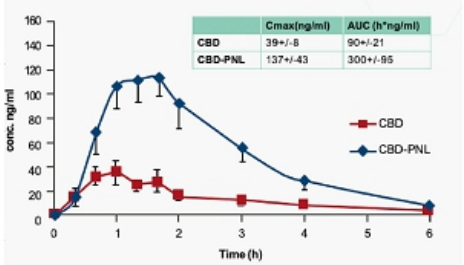
"There are many unanswered questions about the science, safety, and quality of products containing CBD. Some products are being marketed with unproven medical claims and could be produced with unsafe manufacturing practices".
"The agency is committed to supporting the development of new drugs, including cannabis and cannabis-derived drugs, through the investigational new drug and drug approval process…".

- **With the only cannabinoid FDA approved drug, GW Pharma shares have gained 15% in 2019, outperforming the broader cannabis sector [2].**
- **FDA warnings have been issued to 15 companies in US illegally selling CBD products with unproven medical claims.**
- **CBRx will develop SCAs for treatment of well-defined clinical indications, adhering fully to regulatory approved procedures for obtaining marketing authorisation.**

Problems with MM / OTC CBD	Our Solution
× **Variable composition, potency,** and may contain **undesirable contaminants**	✓ We will use **SYNTHETIC** >99.5% **pure** SCAs
× **Side effects** can be triggered by THC (e.g. psychosis)	✓ We will use synthetic CBD Analogs (SCAs) – **no THC**
× **Little clinical data** from approved drugs exist (outside of epilepsy) to determine dosing	✓ Planning blinded clinical trials initially in musculoskeletal pain and arthritis
× **Variable uptake and low absorption** (~4 - 9%) due to lipophilic properties of CBD / CBD-like	✓ Developing novel, patented ProNanoLiposphere (PNL) which **enhance bioavailability**

(opposite graph shows improvements offered by CBD-PNL vs CBD IN PEG)

CBD-PNL Enhances Bioavailability > 3 fold [3]



- CBD and CBD-PNL administered orally to rats & plasma levels assessed over time
- CBD-PNL >3x absorption compared to CBD alone
- CBD-PNL safe and well tolerated
- Additional methods to improve absorption are being patented under a recently completed agreement with HU

[1] **"What you need to know"** https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis
[2] **"GW Pharma shares rise"** https://www.marketwatch.com/story/gw-pharma-shares-rise-after-uk-recommends-nhs-reimburse-its-cbd-based-epilepsy-drug-2019-11-11
[3] Cherniakov I, et al. (2017) European J of Pharm. Sci 109:21-30

CBD - A SUPERIOR TREATMENT FOR ARTHRITIS

PROBLEM

- Very early arthritis, pain & swelling is not effectively treated clinically
- Nonsteroidals do not help, can increase TNF [1]
- Existing therapies are suboptimal:
  - Methotrexate has side effects patients dislike
  - Anti-TNF is costly and use restricted / delayed by NICE (National Institute of Clinical Evidence, in UK)
  - Early rheumatoid or psoriatic arthritis is badly treated: delays mean the "window of opportunity" for best results is missed

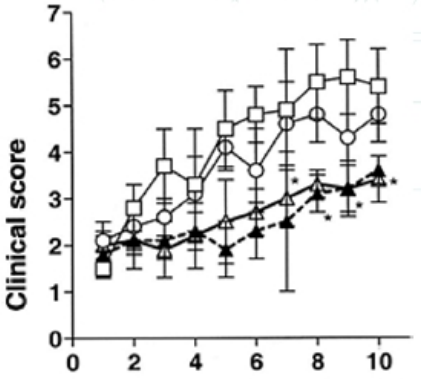
SOLUTION

- For very early arthritis: novel SCAs being developed
- Effective anti-inflammatory (better than NSAIDs)
- Effective analgesic
- For early established RA, PsA: SCA will be tried in combination (offers additional patentability)
- Trials will be performed by Oxford rheumatologists and trial experts

[1] *Page TH ..... & Feldmann M (2010), J Immunol.15;185(6):3694-701*

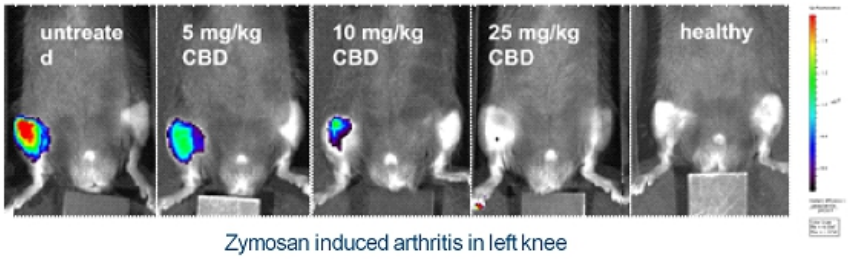
Oral CBD is effective in mouse model of RA

A. M. Malfait, R. Mechoulam, M. Feldmann, R. Gallily PNAS 2000;97:17:9561-9566



From the first clinical signs of arthritis, mice were given CBD **orally**, at the following doses: 50 mg/kg (△), 25mg/kg (▲), or 10 mg/kg (o).

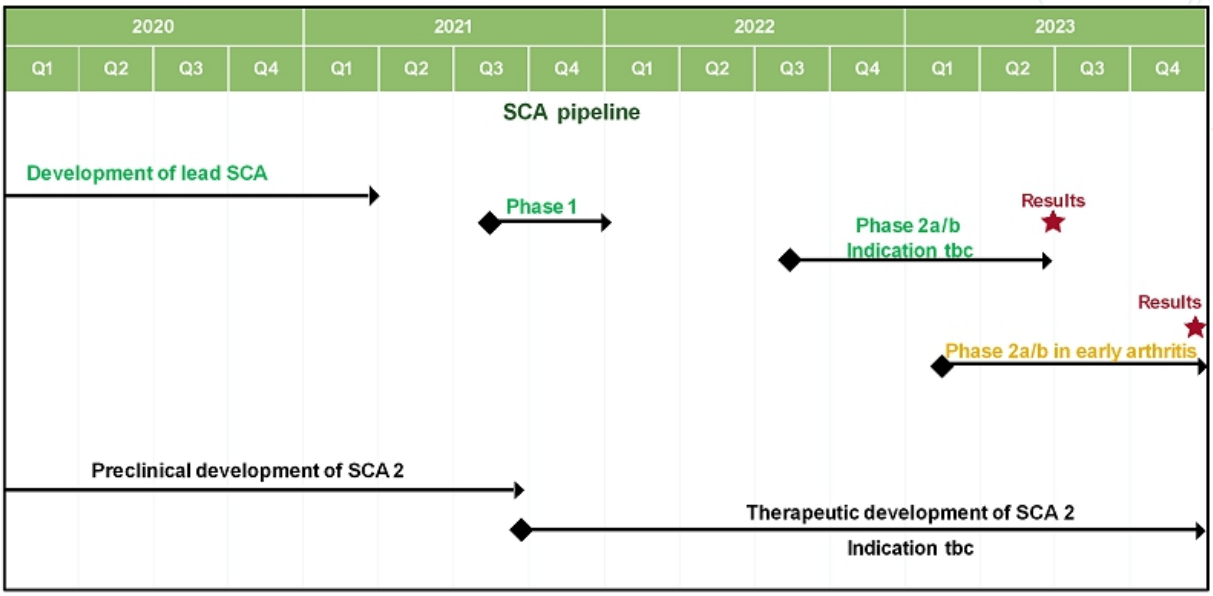
CBD reduces inflammation in knee arthritis – *unpublished new data*



Zymosan induced arthritis in left knee

CBD was administered intraperitoneally to mice with zymosan induced arthritis in the left knee. Inflammation intensity is marked by colour scale shown on right, using a fluorescent reporter of cathepsin. CBD (5-25 mg/kg) attenuates local inflammation in a dose dependent manner.

SCA PIPELINE*



Based on current proposals. No regulatory approvals sought from appropriate authorities at this time.


Prof L Steinman & Dr J Rothbard
Supported by Evotec, US
α7 n ACh R
PROGRAM
California, USA
28

WHY DEVELOP α7 AGONISTS FOR INFLAMMATION?

- Decade of research on immune suppression in multiple sclerosis led to realization of the importance of the α7 subunit of nicotinic Acetylcholine Receptor (nAChR)
- α7 nAChR also a central factor in evolutionarily ancient neural circuit to control of inflammation[1&2]
- Large pharma identified α7 as a pharmaceutical target for Alzheimer's disease and schizophrenia
  - multiple specific agonists developed
  - all shown to be safe, but did not meet milestones in human clinical trials
  - strategic goal of CannBioRx to repurpose drugs for inflammation

[1] Rothbard JB, Rothbard JJ, Soares L, Fathman CG, and Steinman L. Identification of a common immune regulatory pathway induced by small heat shock proteins, amyloid fibrils, and nicotine. Proc Natl Acad Sci U S A. 2018 115:7081-7086.

[2] Tracey KJ. Reflex control of immunity. Nat Rev Immunol. (2009) 9:418–28

α7 AGONIST DEVELOPMENT STRATEGY

CHEMISTRY

- Synthesize patentable, orally bioavailable α7 agonist
- Chemically modify known agonist to retain/improve anti-inflammatory activity
- Retain CNS penetration

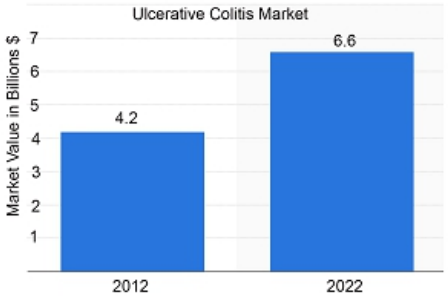
Bioassays

- Inhibition of TNFα & IL6 secretion after stimulation with LPS in cell lines and primary cells
- Stimulation of Ca+2 flux in α7 transfected HEK293 cells
- qPCR measurement of inhibition of a set of proinflammatory cytokines and transcriptional activators
- Inhibition of inflammation and secretion of proinflammatory cytokines *in vivo* in murine models of inflammation

SELECTION OF CLINICAL INDICATION

- Nicotine binds α7 and is a known immune suppressive
- a subgroup of patients who cease smoking subsequently acquire ulcerative colitis
- Treatment of these patients with α7 agonist has a high probability of therapeutic success (can be viewed as nicotine replacement therapy without issues of addiction)

Significant Unmet Need

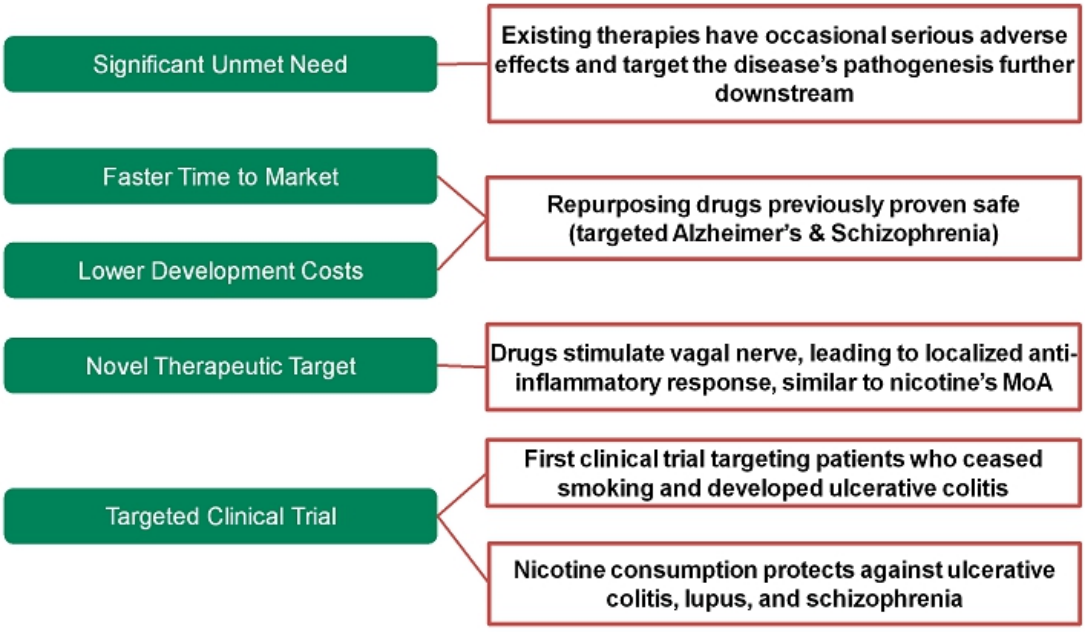


Existing Therapies Are Sub-Optimal

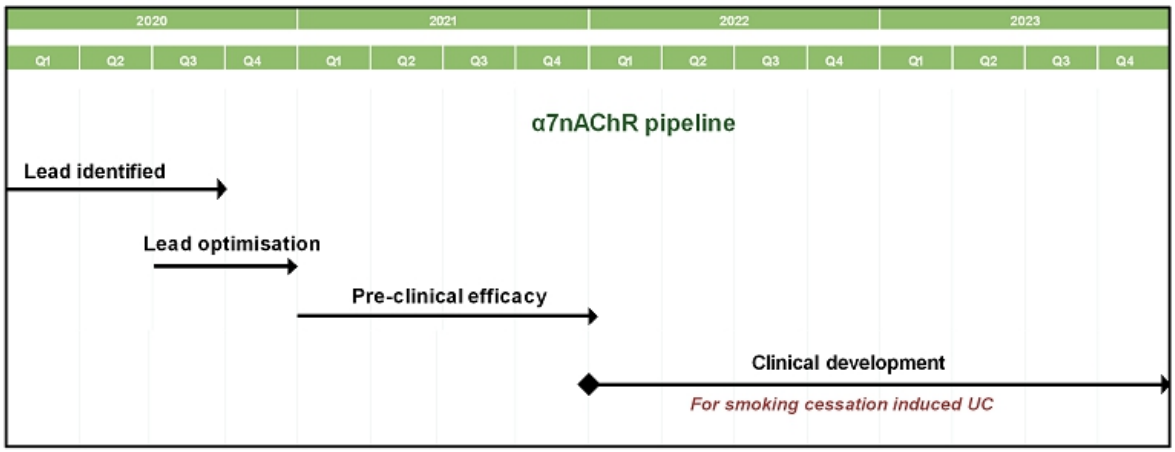
Existing Therapy	Issues
Anti-inflammatory drugs (5-aminosalicylates, corticosteroids)	× capability to induce remission is quite low × known deleterious side effects of steroids
Immunosuppressants	× long-term administration of thiopurine may correlate with an increased risk of developing lymphoma × cyclosporine leads to kidney damage
Infliximab (anti-TNF)	× serious adverse events, such as opportunistic infections, including tuberculosis, as well as congestive heart failure in cardiopathic patients

α7 nAChR PLATFORM, A NOVEL THERAPEUTIC PLATFORM FOR UC

- essential receptor in the neural circuit controlled by the vagus nerve



α7nAChR PIPELINE*



Based on current proposals. No regulatory approvals obtained from appropriate authorities at this time.

CONCLUSION

- Scientific team and founders are pioneers with proven track record in drug discovery from the University of Oxford, Hebrew University and Stanford University
- Developing three families of novel drugs addressing significant market opportunities in inflammation, fibrosis and pain:
  - -Fibrosis & Anti-TNF
  - -Synthetic CBD Analogs (SCAs)
  - -α7nAChR
- Multiple programs in synchronized stages of development combined with IP portfolio reduces risk
- Numerous near-term inflection points for anti-TNF programs: one program late stage 2b/3 trial, two additional clinical programs projected to start Q4 2020
  - Initial clinical anti-TNF clinical trials funded by investments and grants (UK and Dutch).
  - *Regulatory approvals obtained from the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and the Dutch Centrale Commissie Mensgebonden Onderzoek (CCMO) and the relevant accredited ethics committees to perform clinical trials in the UK and The Netherlands for anti-TNF products.
- Three anti-inflammatory therapeutic programs potentially used in combination

**No meetings have been held with, and no applications or requests for approval have been submitted to the FDA for any products at this time.*

CANNBIORX
LIFE SCIENCES

CANNBIORX LIFE SCIENCES CORP

Registered Address

1201 Orange Street

Suite 600

Wilmington, DE 19801 USA

APPENDIX

FIBROSIS PROGRAM PATENTS (Pg 1of 3)

METHOD OF TREATING EARLY STAGE DUPUYTREN'S DISEASE			
Country	**Application No.**	**C&D Docket No.**	**Status**
Australia	2017248273	8554-A-PCT-AU	Application pending in Australian Patent Office
Canada	3,020,327	8554-A-PCT-CA	Application pending in Canadian Patent Office
Europe	17779836.0	8554-A-PCT-EPO	Application pending in European Patent Office
U.S.	16/089,234	8554-A-PCT-US	Application pending in U.S. Patent Office
METHOD OF TREATING A LOCALIZED FIBROTIC DISORDER USING AN IL-33 ANTAGONIST			
Country	**Application No.**	**C&D Docket No.**	**Status**
Australia	2016226414	87158-A-PCT-AU	Application pending in Australian Patent Office
Canada	2,978,449	87158-A-PCT-CA	Application pending in Canadian Patent Office
Europe	16759325.0	87158-A-PCT-EPO	Application pending in European Patent Office
Hong Kong	18107063.7	87158-A-PCT-EPO-Hong Kong	Application pending in Hong Kong Patent Office
U.S.	15/555,027	87158-A-PCT-US	Notice of Allowance issued August 1, 2019.
METHOD OF TREATING A LOCALIZED FIBROTIC DISORDER USING A TNF RECEPTOR 2 ANTAGONIST			
Country	**Application No.**	**C&D Docket No.**	**Status**
Australia	2016226415	87158-B-PCT-AU	Application pending in Australian Patent Office
Canada	2,978,431	87158-B-PCT-CA	Application pending in Canadian Patent Office
Europe	16759326.8	87158-B-PCT-EPO	Application pending in European Patent Office
Hong Kong	18107062.8	87158-B-PCT-EPO-Hong Kong	Application pending in Hong Kong Patent Office
U.S.	15/555,030	87158-B-PCT-US	Application pending in U.S. Patent Office, filed August 31, 2017

FIBROSIS PROGRAM PATENTS (Pg 2 of 3)

TREATMENT FOR DUPUYTREN'S DISEASE			
Country	**Application No.**	**C&D Docket No.**	**Status**
Australia	2011322482	90330-A-PCT-AU	Australian Patent No. 2011322482, granted July 20, 2017
Australia	2017204267	90330-AZ-PCT-AU	Australian Patent No. 2017204267, granted September 19, 2019
Canada	2,847,197	90330-A-PCT-CA	Application pending in Canadian Patent Office
Europe	11779628.4	90330-A-PCT-EPO	The European patent is valid or being validated in: Austria (Patent No. E-1075071) Belgium (Patent No. 2362446) Denmark Finland (Patent No. 2362446) France (Patent No. 2362446) Germany (Patent No. 2362446) Iceland (Patent No. 2362446) Ireland (Patent No. 2362446-IE) Italy (Appl. No. 502019000019925) Netherlands (Patent No. 2362446) Norway (Patent No. 2362446) Spain (Appl. No. 300310256) Sweden (Patent No. 2362446) Switzerland/Liechtenstein (Patent No. 2362446) and United Kingdom (Patent No. 2362446)
Japan	2013-535462	90330-A-PCT-JP	Japanese Patent No. 6004494, granted September 16, 2016
U.S.	13/882,262	90330-A-PCT-US	U.S. Patent No. 9,138,458, granted September 22, 2015
U.S.	14/852,442	90330-AA-PCT-US	U.S. Patent No. 10273296, granted April 30, 2019

FIBROSIS PROGRAM PATENTS (Table 3 of 3)

METHOD OF TREATING LOCALIZED FIBROTIC DISORDERS USING AN IL-33/TNF BISPECIFIC ANTIBODY			
Country	**Application No.**	**C&D Docket No.**	**Status**
U.S.	16/328,979	87158-F-PCT-US	Filed February 27, 2019.
Europe	17924768.9	87158-F-PCT-EPO	Filed April 1, 2019.
METHOD OF TREATING SYSTEMIC FIBROTIC DISORDERS USING AN IL-33/TNF BISPECIFIC ANTIBODY			
Country	**Application No.**	**C&D Docket No.**	**Status**
U.S.	16/329,013	87158-G-PCT-US	Filed February 27, 2019.
Europe	17847574.5	87158-G-PCT-EPO	Filed April 1, 2019.

POCD PATENT

METHOD FOR TREATMENT OF POST OPERATIVE COGNITIVE DYSFUNCTION			
Country	**Application No.**	**C&D Docket No.**	**Status**
U.S.	15/063,775		Granted April 12, 2016.
Europe			
Japan			

SCA PROGRAM PATENTS

Cyclohexenyl compounds, compositions comprising them and uses thereof				
Country	**Application No.**	**Status**	**Activity expected**	**Comments**
US2	10239848	Granted	Maintenance due by September 21, 2022	Claims directed to a method for treating obesity or a disease/disorder associated therewith by administration of a compound of the formula as defined in claim 1
US3	16/274,107	Pending		Claims directed to a method for treating pain or associated condition or symptom by administration of a compound of the formula as defined in claim 1
IL	248256	Granted	Renewal due by April 21, 2021	Claims directed to a pharmaceutical composition for treatment of (i) obesity or a disease/disorder associated therewith; or (ii) abnormal food consumption or body weight, or a condition or symptom associated therewith, comprising a compound of the formula 1 as defined in claim 1
EP	15726740.2	Pending	OA/Allowance may be expected	
CN	2015820978	Pending	OA/Allowance may be expected	Decision on grant expected shortly (as of 25 Aug, 2019)
CA	2944837	Pending		Filed Jul 10, 2019

STATUS OF PATENT APPLICATIONS UPDATED Oct 09, 2019

CANN-001 – *Cyclohexenyl compounds, compositions comprising them and uses thereof* (HU436 & HU435)

Applicant: Yissum research development company of the Hebrew University of Jerusalem Ltd.

Inventors: Ruth Gallily, Raphael Mechoulam, Aviva Breuer

Priority: US Provisional Application No. 61/981,997, filed April 21, 2014 (expired)

International Filing Dates: April 21, 2015

OA = Office Action

α7nAChR PROGRAM PATENTS

Country	Application No.	Priority Date	Description
US Application Japan Canada	US20180333451A1 2018-526196 3004908	2015-11-18	B-1a lymphocyte and/or macrophage targeting and activation to treat medical conditions with inflammatory or autoimmune components
US Grant	US8835391B2	2006-12-11	Alpha B-crystallin as a therapy for multiple sclerosis
US Grant	US7875589B2	2006-12-11	Alpha B-crystallin as a therapy for rheumatoid arthritis
US Grant	US8771689B2	2006-12-11	Alpha B-crystallin as a therapy for ischemia or inflammation