180 LIFE SCIENCES

NASDAQ: ATNF

Leading Research into Solving One of the World's Largest Drivers of Disease: **INFLAMMATION**

Corporate Presentation

January 2022

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180 Life Sciences Highlights

Scientific Pioneers Backed by Experienced Operators and Board

Founders: pioneers with proven track record from Oxford, Hebrew and Stanford University

- Successes include Remicade and Tysabri
- 100+ cumulative years of discovery and clinical experience

Board: seasoned and diverse executives with broad skillsets that complement the Company's needs

Senior Management: operators with decades of experience at large & small life science companies

Numerous Near-Term Inflection Points

Anti-TNF programs: Phase 2b/3 trial met primary and secondary endpoints; two additional Phase 2 trials projected to start Q1/Q2 2022 and Q3/Q4 2022

- **Funding:** initial anti-TNF clinical trials funded by grants (UK)
- **Regulatory approvals obtained:** 1) UK Medicines and Healthcare Products Regulatory Agency (MHRA), 2) Dutch Centrale Commissie Mensgebonden Onderzoek (CCMO) and 3) relevant accredited ethics committees to perform clinical trials in the UK and The Netherlands for anti-TNF products*

Robust Product Pipeline with Large Market Potential

Three families of novel drugs: address significant market opportunities in inflammation, fibrosis and pain

- Fibrosis & Anti-TNF
- Synthetic CBD Analogs (SCAs)
- a7nAChR

Multiple programs: in synchronized stages of development

Strong IP Portfolio

Filed: 28

- Fibrosis & Anti-TNF: 23
- Synthetic CBD Analogs (SCAs): 2
- a7nAChR: 3

Granted: 18

- Fibrosis & Anti-TNF: 9
- Synthetic CBD Analogs (SCAs): 6
- a7nAChR: 3

*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.

Pioneering Founders

Prof. Sir Marc Feldmann
University of Oxford
Executive Co-Chairman

- Pioneer of anti-TNF therapy, world's biggest drug class ($40B/yr)
- Anti-TNF discovery of Remicade eventually led to Centocor's acquisition by J&J for $4.9B
- International awards for biomedical innovations: Crafoord, Lasker, Canada Gairdner, Janssen, EU Inventor of the Year, Tang
- UK and Australian knighthood
- Fellow of Royal Society and Australian Academy of Science; member of National Academy of Sciences

Prof. Lawrence Steinman
Stanford University
Executive Co-Chairman

- Discovered role of integrins, which led to natalizumab (Tysabri, sold to Biogen for $3.25B), a highly effective treatment for MS and IBD
- Founder of Neurocrine Biosciences
- Board member of Centocor, sold to J&J for $4.9B
- International awards for biomedical innovations: Sasse, Dystel, Charcot, Cerami, Javits (twice)
- Member of National Academy of Medicine and National Academy of Sciences

Prof. Raphael Mechoulam
Hebrew University
Co-Founder

- Father of cannabis research; isolated numerous cannabinoids, including delta9-THC
- Discovered endogenous cannabinoids 2AG and anandamide
- Published over 400 papers in esteemed scientific journals
- International awards for biomedical innovations: Israeli Prize in Exact Sciences, NIDA Discovery, Rothschild, Lifetime Achievement at CannaMed
- Member of Israel Academy of Sciences and Humanities

Prof. Jagdeep Nanchahal
University of Oxford
Co-Founder; Chair, Clinical Advisory Board

- Pioneered the treatment of fibrosis of the hand (Dupuytren's disease) by identifying TNFα as a target
- Surgeon-scientist, leading Phase 2b/3 trial for Dupuytren's disease funded by Wellcome Trust and UK Dept. of Health
- Fellow of the Royal College of Plastic Surgeons

Experienced Senior Management Team

James Woody, MD, PhD
Director, CEO

- General Partner of Latterell Venture Partners
- Founded Avidia & Proteolix, both sold to Amgen
- Board member of ForteBio & ProteinSimple, both successfully acquired
- Past President & GM of Roche Bioscience (Syntex)
- Developed Remicade at Centocor while serving as CSO and SVP of R&D
- Prior Commanding Officer and Director of US Naval Medical Research and Development Command
- US Navy Legion of Merit recipient

Ozan Pamir
Chief Financial Officer

- Oversaw the merger of 180 Therapeutics, Katexco and Cannbiorex to form 180 Life Sciences and led the go-public process of the company
- Former CFO of Enosi Life Sciences and CFO and board member of Unify Pharmaceuticals, both pre-clinical companies focused on autoimmune diseases
- Previously, a venture capitalist and investment banker, leading more than 30 financings and raising ~$400M
- Economics and Finance degree from McGill University; CFA Charterholder

Jonathan Rothbard, PhD
Chief Scientific Officer

- Broad experience spanning three different departments at Stanford: neurology, chemistry and rheumatology
- Former head of the Molecular Immunology Laboratory at the Imperial Cancer Research Fund in London
- Founder/co-founder of 5 biotech companies, including Amylin, CellGate and ImmunLogic; Amylin sold to BMS for $5.4B
- BA from Hamilton College; PhD from Columbia University; fellowship at The Rockefeller University

Quan Vu
Chief Operating Officer/Chief Business Officer

- CBO/CFO Consultant at LS Associates, a division of LifeSci Partners
- Former CEO of Baleena Bioscience, a consolidator of healthspan assets
- Past MD/Co-Head of Healthcare IT at Solganick & Co.
- Other corporate leadership roles: VP at Opiant Pharmaceuticals; Staff VP at Anthem; Director at Impax Labs; Senior Manager at Amgen
- Prior consultant and healthcare investment banker at LECG, Morgan Stanley, Goldman Sachs
- BA, Economics, Summa Cum Laude, UCLA; Certified Treasury Professional (inactive)

Diverse Board of Directors

Frank Knuettel II, MBA
Independent Director

- CEO and Director of Terra Tech
- Director of two private companies (anti-viral platform and smart intubation devices)
- Former Director at Viridian Capital Advisors
- Served as CFO of One Cannabis Group, sold to Item 9 Labs
- Served as CFO of MJardin and later CSO post merger with GrowForce
- Prior, held numerous CFO and CEO positions at early-stage companies

Pamela Marrone, PhD
Independent Director

- Former CEO and Director, Marrone Bio Innovations
- Started and led AgraQuest, acquired by Bayer for ~$500M
- Formed BPIA.org, a trade group with more than 150 members, to streamline the US EPA registration process
- Industry though leader & high-demand public speaker
- Received numerous awards: Growing Green, Sustie, California Governor's Economic & Environmental Leadership, American Chemical Society Innovation, Sacramental Business Journal Most Admired CEO

Prof. Larry Gold, PhD
University of Colorado, Boulder
Independent Director

- Board of CompleGen, Lab79, CNS Biosciences
- Founder, Chairman Emeritus, former CEO of SomaLogic
- Founded and was Chairman, EVP of R&D and CSO of NeXagen/NeXstar, which later merged with Gilead
- Co-Founder and Co-Director of Research at Synergen, later acquired by Amgen
- Received numerous awards: NIH Merit, Lifetime Achievement, Chiron, Hoogendijk
- Member of American Academy of Arts &Sciences, Nat'l Academy of Sciences, Nat'l Academy of Inventors

Donald McGovern, Jr.
Independent Director

- Former Vice Chairman, Global Assurance, PwC
- Director, Chair of the Audit Committee and member of the Compensation Committee at Cars.com
- Former Board member with CRH, serving as Senior Independent Director, Chair of the Renumeration Committee, member of the Nomination Committee and of the Audit Committee

Russell Ray, MBA
Independent Director

- Chairman, Audit & Finance Committee, Merrimack Pharmaceuticals; former Board member of Allergan
- Former Partner/Senior Advisor to HLM Venture Partners
- Served as Managing Director and Vice Chairman of Healthcare Investment Banking at Stifel, Nicolaus & Co.
- Founded Chesapeake Strategic Advisors and served as Managing Director and President
- Prior MD/Co-head of Global Healthcare IB at CSFB
- Former MD/Global Co-Head of Healthcare IB at Deutsche Bank

Teresa DeLuca, MD, MBA
Independent Director

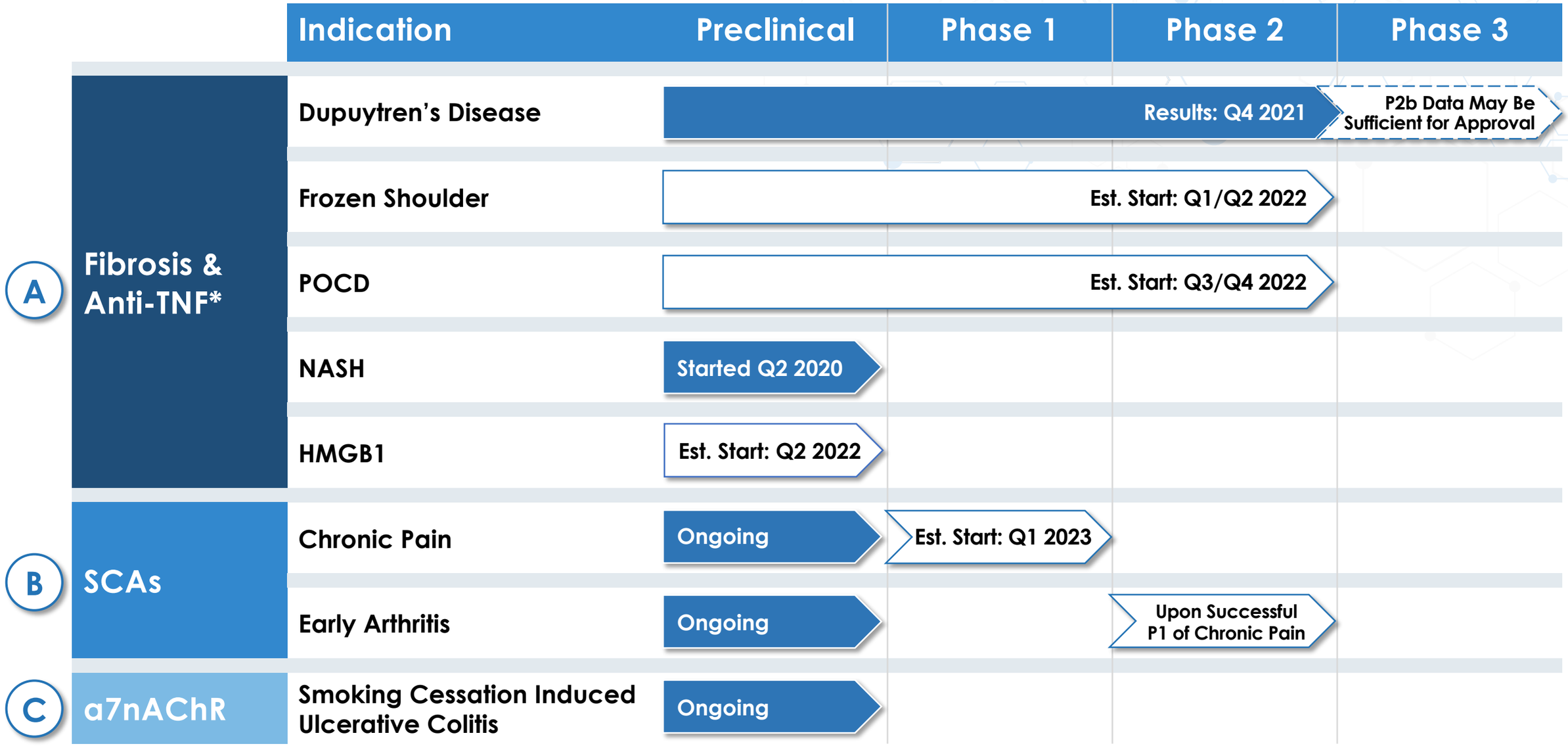
- Member of Audit Committee and Chair of Compliance & Ethics Committee, Surgery Partners
- Former Managing Director at Columbia University's NY Life Science Venture Fund
- Prior Assistant Clinical Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai in NY
- Past CMO of Magellan Pharmacy Solutions
- Former SVP at Humana, VP at Walgreen, VP at Medco, Senior Medical Scientist at GSK
- Was a Director at North Bud Farms

Development Programs Summary Overview

	FIBROSIS & ANTI-TNF (CLINICAL STAGE)*	SYNTHETIC CBD ANALOGS (SCAs)	a7nAChR
TECHNOLOGIES	**Repurposing of anti-TNF for major unmet needs, other patented drugs**	**Novel non-psychoactive synthetic cannabidiol (CBD) analogs**	**Novel a7nAChR 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:** If effective, first treatment for early disease • **Frozen Shoulder:** If effective, will be first treatment to provide long-term benefit • **POCD:** If approved, will be first effective treatment • **HMGB1:** No current liver regenerative treatment	• 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:** Positive Phase 2b results in early DD* • **Frozen Shoulder:** Phase 2 first patient dosing in Q1/Q2 2022 • **POCD:** Initiate Phase 2 trials Q3/Q4 2022 • **NASH:** Preclinical studies started Q2 2020 • **HMGB1:** Preclinical studies to start in Q2 2022	• **Preclinical:** Lead SCAs and formulations already identified • Initiate Phase 1 trial in chronic pain Q1 2023 • Upon successful Phase 1, initiate Phase 2 for chronic pain and early arthritis	• **Preclinical:** Optimizing new compounds based on safe a7nAChR 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 • Patents have a lifespan that expires between 2031 or later	• **Patent issued for Cyclohexenyl compounds**, compositions and uses thereof • Patents pending & to be filed • Patents' lifespan expires 2036 or later	• **Three patents issued, three patents pending** • Patents' lifespan expires 2031 or later

*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



*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.

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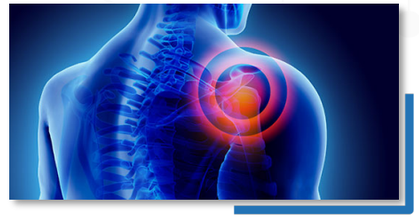
Fibrosis & Anti-TNF Platform: Clinical Stage Lead Program

Led by Profs. Jagdeep Nanchahal and Sir Marc Feldmann, Oxford

Targeting common diseases → facilitates trials and potential sales

Dupuytren's Disease



Frozen Shoulder

Nash

POCD

Developing targeted therapies for:

- Early-stage Dupuytren's Disease (DD) – patent issued; positive Phase 2b results announced(1)
- Frozen Shoulder – patent issued; Phase 2 first patient dosing in Q1/Q2 2022
- Post Operative Cognitive Decline (POCD) – patent issued; Phase 2 clinical trials projected in Q3/Q4 2022
- Liver Fibrosis (NASH) – laboratory studies in collaboration with Celgene-BMS on human tissue; preclinical studies started Q2 2020
  - Licensed-in HMGB1 technology: a regenerative molecule for promoting liver repair and regeneration

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

Competitive Advantages

Developing the Only Treatment for Early-Stage Fibrosis

- **Currently no competition for targeting and preventing early-stage fibrosis**
- Non-surgical, easy to administer
- Short-term treatment, intended to halt disease progression

Novel Use of Human Disease Tissue to Identify New Targets in Fibrosis

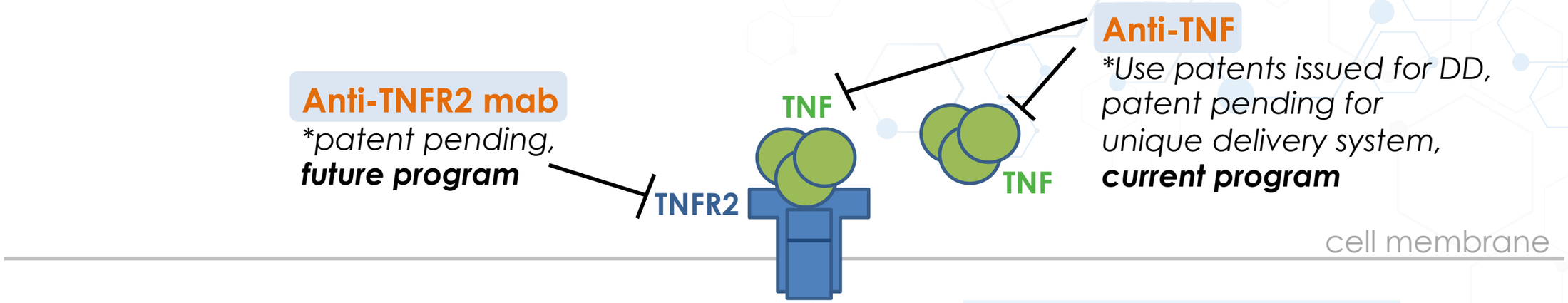
- Studies in DD lead the way for novel approach to develop clinical programs in other fibrotic diseases:
  - Tissues and cells from most fibrotic diseases not readily accessible as diagnosed late
  - Competitors use animals or late-stage cells in culture, neither reflect human disease
  - **Our use of human tissue makes preclinical discovery more relevant and accurate, mitigating risk for clinical stage**

Cost Effective, Time Efficient, Academic-Led Clinical Trials Performed in the UK

- **Expert Investigators**
  - Established reputation in conducting clinical trials across academic and clinical networks(1)
  - Well practiced in publishing trial results in peer reviewed clinical journals
- **Cost Effective**
  - No payment for trial patients required in the UK/EU
  - Staff costs can be largely covered by academic grants (Wellcome Trust, NIHR)
- **Shorter Timeline for Recruitment and Execution**
  - Access to large cohorts of patients/diseases
  - Expertise in writing protocols, seeking regulatory approvals, conducting trials

(1) https://www.ndorms.ox.ac.uk/octru

Rationale for TNF Blockade in Fibrosis



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

180 LS drugs block TNF induced activation of pro-fibrotic pathways to reduce fibrosis

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 Reconstructive Surgery, Erasmus Medical Centre, 3015, Rotterdam, The Netherlands*
[c] *Department of Plastic Surgery, St John's Hospital, Livingston EH54 6PP, United Kingdom*

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

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Initial Indication Targeting Dupuytren's Disease

Characteristics

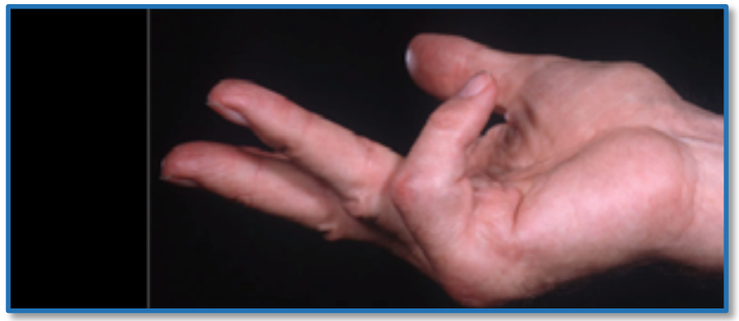
- Common localized fibrotic condition of the hand, develops over years
- Nodules form under skin – eventually creating a thick cord pulling one or more fingers
- Can limit hand functions
- Unlike liver and lung fibrosis, can be identified early

Early Disease

No approved treatment: unmet need

Our trial is in early disease[1]

Late Disease – Results in Impaired Hand Function



Current treatment options suboptimal:[2]

- 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

(1) Approval only from MHRA/CCMO and relevant accredited ethics committees.
(2) Layton T & Nanchahal J. F1000Research 2019, 8(F1000Faculty Rev): 231

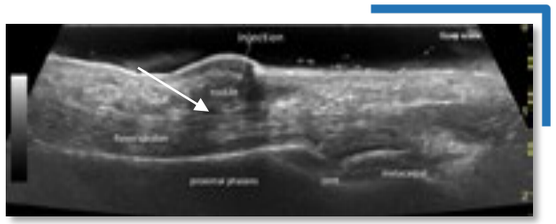
Phase 2a Completed: 40mg (in 0.4ml) Adalimumab is Effective

The First Trial Of Any Targeted Therapy In Early DD[1]

EBioMedicine
Published by THE LANCET

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

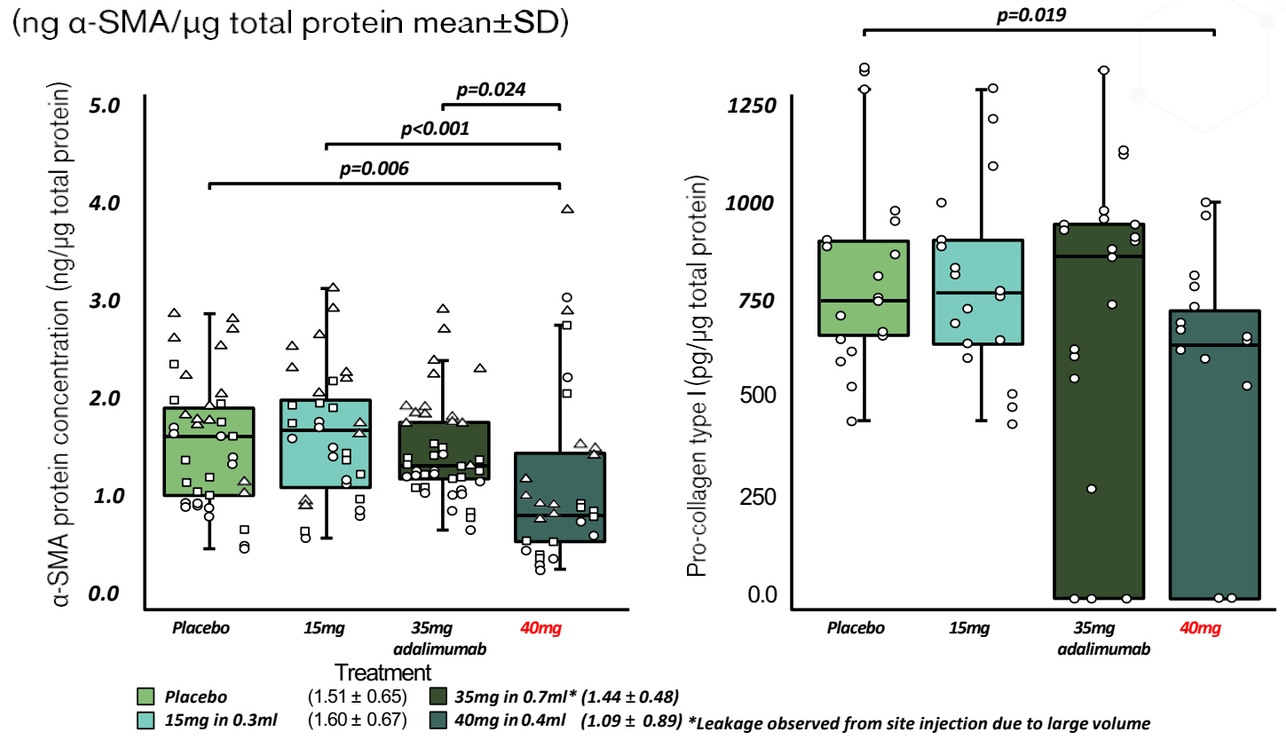
Trial Overview



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 180 Life Sciences

Demonstrated Efficacy at High concentration & Dose



(1) Approval only from MHRA/CCMO and relevant accredited ethics committees.
(2) EBioMedicine 33 (2018) 282-288

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Phase 2b Trial: Local Adalimumab in Early Dupuytren's Disease

Description

- Randomized blinded trial in patients with early DD injected with optimal dose adalimumab[1]
- 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 the UK (Oxford, Edinburgh) and Netherlands (Groningen)

Funding

- Fully paid for by grants

Status

- Met both primary and secondary endpoints
- Almost all of the patients returned for all injections
- No related serious adverse events
- Manuscript submitted to a prestigious journal

	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.

180 LIFE SCIENCES clinical trial 2b/3 – Nanchahal J et al, 2017 Wellcome Open Research, 2:37

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

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Relatively High Prevalence of Dupuytren's Disease

~16M

US Prevalence

(5% of population; range 1-7%)

~12M	~3M	~800-900K
Fingers Not Sufficiently Bent to Need Treatment	Fingers Sufficiently Bent to Need Treatment	Severe Dupuytren's Treatment In-Effective
(75%; range 70-90%)	(19%; range 8-33%)	(5%)

Dr. Charles Eaton, Director of the Dupuytren's Foundation, provides the best prevalence estimates based on his regular assessment of the literature. Red Sky Partners reviewed his data with him.

Many patients not seeking treatment and lack of a biological biomarker prevent accurate population estimates.

In a given year, the actual treated population is between 10% and 20% of the three million

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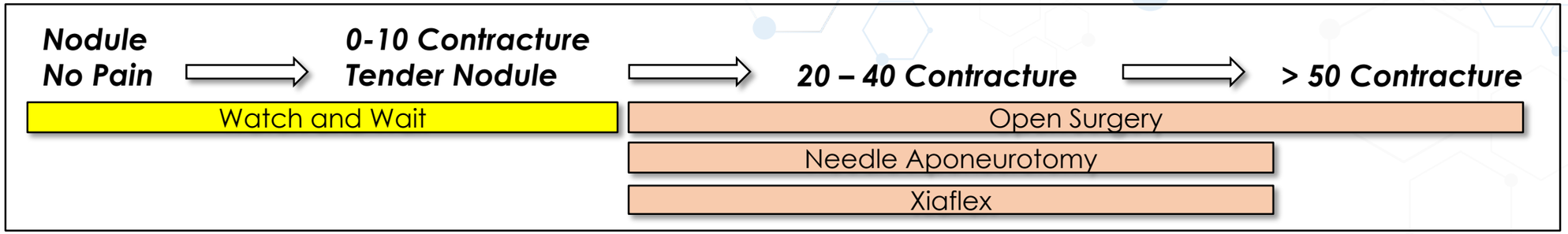
Large Market Opportunity for Early Dupuytren's Disease

Estimated future market: >$1B worldwide(1)
All current treatments (surgery, Xiaflex): for LATE-stage disease only

Current Treatment Paradigms



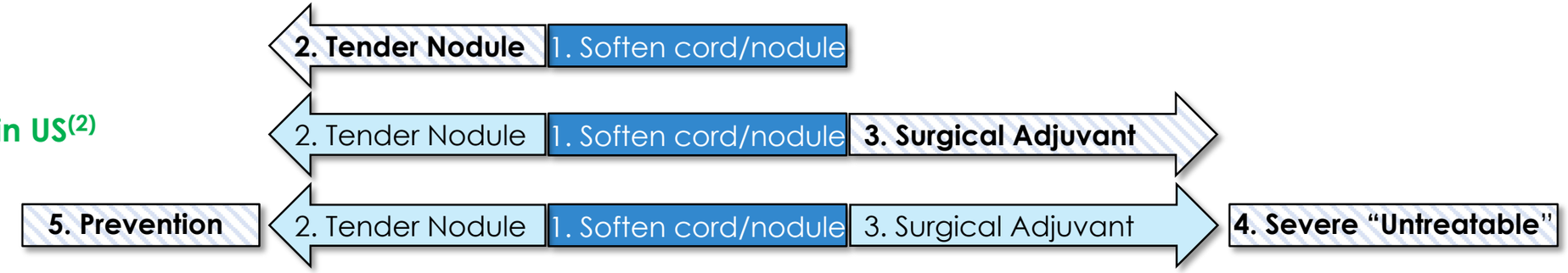
Initial Launch and Label

$300M-350M in US(2)

1. **Soften cord/nodule**

Market Expansion Opportunities

$500-800M in US(2)



(1) Hindocha S, McGrouther DA, Bayat A (2009) Hand (NY) 4(3):256-69.
(2) Estimate by Red Sky Partners, 2021

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Large Market Opportunity for Early Dupuytren's Disease *cont'd*

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Estimated future market: >$1B worldwide(1)
All current treatments (surgery, Xiaflex): for LATE-stage disease only

Initial Launch and Label: $300M to $350M (US only)(2)

Initial population target similar to Xiaflex but safer and non-invasive

- Proven effective at softening cord and nodule
- Does not preclude downstream options
- Aggressive social media patient outreach
- Physician education on mechanism
- Priced comparable to Xiaflex for treatment course
- Acceptable reimbursement plan to facilitate surgeon adoption

Market Expansion: $500M to $800M (US only)(2)

Further expand treated population and established efficacy drives share gains

- Safety and non-invasive profile drives earlier trial
- Patient outcomes and QOL improvements are positive
- Physicians have a new, safe option to offer patients seeking treatment and prevention of progression
- More, early patients seek and request treatment
- Improved cost benefit relative to Xiaflex and needle aponeurotomy
- Possibly expand to use by rheumatologists

(1) Hindocha S, McGrouther DA, Bayat A (2009) Hand (NY) 4(3):256-69.
(2) Estimate by Red Sky Partners, 2021

Additional Indications

Post Operative Delirium/Cognitive Deficit (POCD)

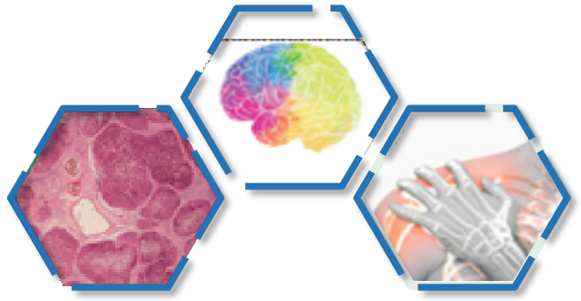
- Over 300,000 hip fractures each year in the US alone[1]
- Strong **clinical evidence** for anti-TNF as preventative therapy
- Patent claims granted, patent is licensed from Kennedy Trust, UK
- **Phase 2** multi-center trial of pre-operative anti-TNF in hip fracture surgery planned to initiate by Q3/Q4 2022; single dose administered just prior to surgery; to be completed in 2 years

Frozen Shoulder

- Affects 9% of the of the population aged 25-64yr, more common in diabetics[2]
- Only treatment for early stage is local steroid injection for short term relief
- **Phase 2** clinical trials planned for local injection of anti-TNF; first patient dosing planned for Q1/Q2 2022
- Trial protocol completed and £250,000 NIHR grant received

Fibrosis of the Liver (NASH)

- Most commonly caused by non-alcoholic fatty liver disease (NAFLD), which affects ~30% of the US population[3]
- ~2% of patients with non-alcoholic fatty liver disease and 15-20% with non-alcoholic steatohepatitis (NASH) progress to cirrhosis[4]
- No approved therapeutic for NASH
- Lab program in collaboration with Celgene-BMS for target discovery using human liver samples



(1) https://www.cdc.gov/homeandrecreationalsafety/falls/adulthipfx.html
(2) Walker-Bone K et al (2004) Arthritis Rheum 51(4):642-651
(3) Rinella ME & Sanyal AJ (2016) Nat Rev Gastroenterol Hepatol 13(4):196-205
(4) Ibid.

B

SCAs Platform: Synthetic CBD Analogs for Pain & Inflammation

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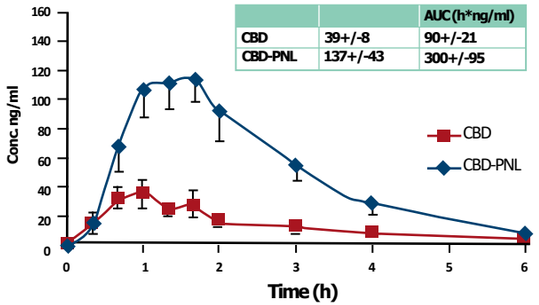
Led by Prof. Sir Marc Feldmann; key players include Mechoulam, Domb

Developing proprietary compounds which aim to be:

- Safe & non-psychoactive
- Formulated to offer improved oral bioavailability (>3x)
- 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 cannabis or OTC CBD (no clinical evidence, not FDA approved, unreliable composition, unpredictable dosing and safety)

Challenges with Medical Cannabis / 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 ProNanoLiposphereS (PNL) which **enhance bioavailability**

CBD-PNL Enhances Bioavailability >3x(1)



- 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 Hebrew U.

(1) Cherniakov I, et al. (2017) European J of Pharm. Sci 109:21-30

a7nAChR Platform: Novel Platform for Ulcerative Colitis

Led by Dr. Jonathan Rothbard and Prof. Larry Steinman

a7nAChR is a nicotine acetylcholine receptor and a central factor in evolutionarily ancient neural circuit to control of inflammation[1,2]

- Large pharma initially touted a7 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
- 180 Life Sciences aims to repurpose a7nAChR for inflammation
  - Nicotine binds a7 and is a known immune suppressive
  - A subgroup of patients who cease smoking subsequently acquire ulcerative colitis (a large, growing market: 2012 - $4.2B; 2022 - $6.6B)
  - Treatment has a high probability of therapeutic success (can be viewed as nicotine replacement therapy without issues of addiction)

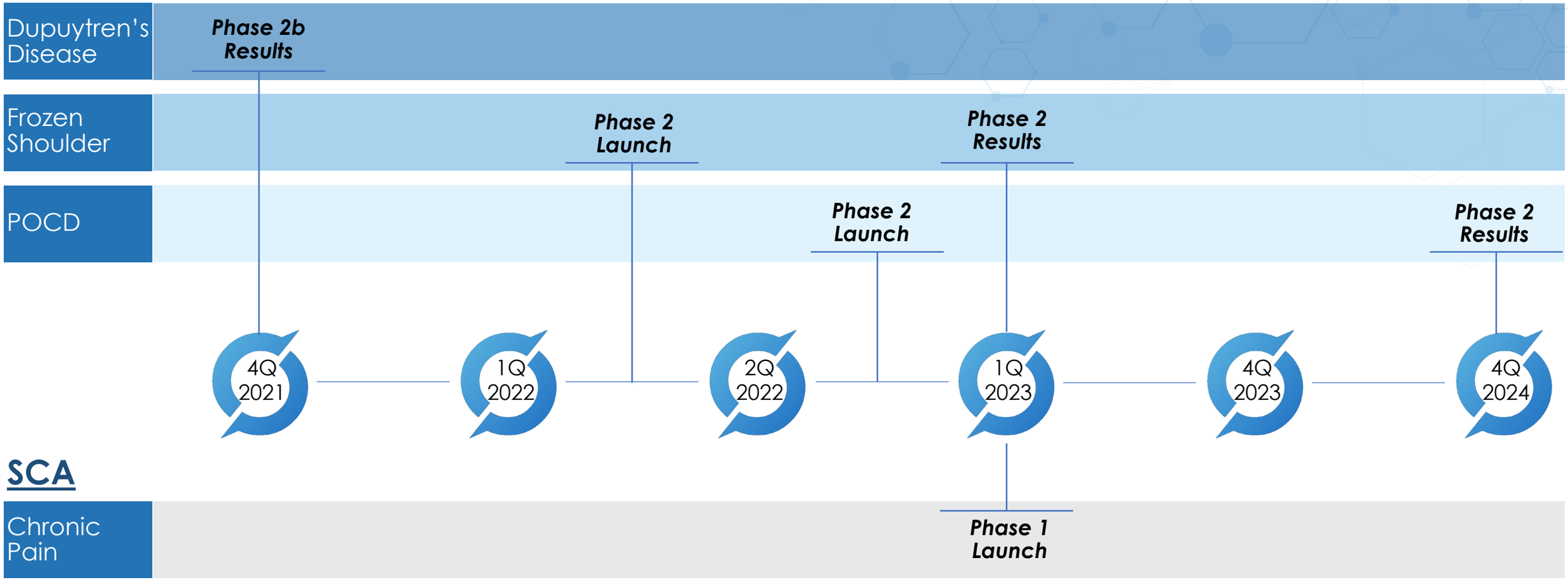
Existing Therapies Sub-Optimal	
Anti-inflammatory drugs (5-aminosalicylates, corticosteroids)	× Capability to induce remission is quite low × Known deleterious side effects of steroids
Immunosuppressants	× Long-term administration of thiopurine may correlate with increased risk of lymphoma × Cyclosporine 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

a7nAChR Competitive Advantages	
Better safety and efficacy	✓ Fewer opportunistic infections ✓ Reduced risk of kidney damage ✓ Higher anticipated success rate
Faster time to market Lower development costs	✓ Repurposing drugs previously proven safe (targeted Alzheimer's & Schizophrenia)
Novel therapeutic target	✓ Drugs stimulate vagal nerve, leading to localized anti-inflammatory response, similar to nicotine's MoA
Targeted clinical trial	✓ First clinical trial targeting patients who ceased smoking and developed ulcerative colitis

(1) Rothbard JB et al. 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

Upcoming Clinical Milestones

Anti-TNF



SCA

IP Portfolio Overview

Territory	Fibrosis Program	SCA Program	α7nAChR Program	TOTAL PATENTS(1)
Filed				
US	8	--	1	**9**
EU	5	2	--	**7**
Other	10	--	2	**12**
Granted				
US	3	2	2	**7**
EU	2	1	1	**4**
Other	4	3	--	**7**

(1) Please see Appendix for detailed list

Capitalization

NASDAQ:ATNF

Shares Issued and Outstanding (December 15, 2021)	34,035,664
Current Price (December 15, 2021)	$4.07
Basic Market Cap	**$138,525,152**
Shares Issuable Upon Exercise of Options	2,741,000
Shares Issuable Upon Exercise of Warrants [1]	11,153,908
Fully Diluted Shares Outstanding	47,930,572
Fully Diluted Market Cap	**$195,077,428**

Float: ~23m shares

(1) (i) 6,001,250 with a strike price of $11.50
(ii) 63,658 with a strike price of $5.28
(iii) 2,564,000 with a strike price of $5.00
(iv) 25,000 with a strike price of $7.07
(v) 2,500,000 with a strike price of $7.50

180 LIFE SCIENCES

Thank you

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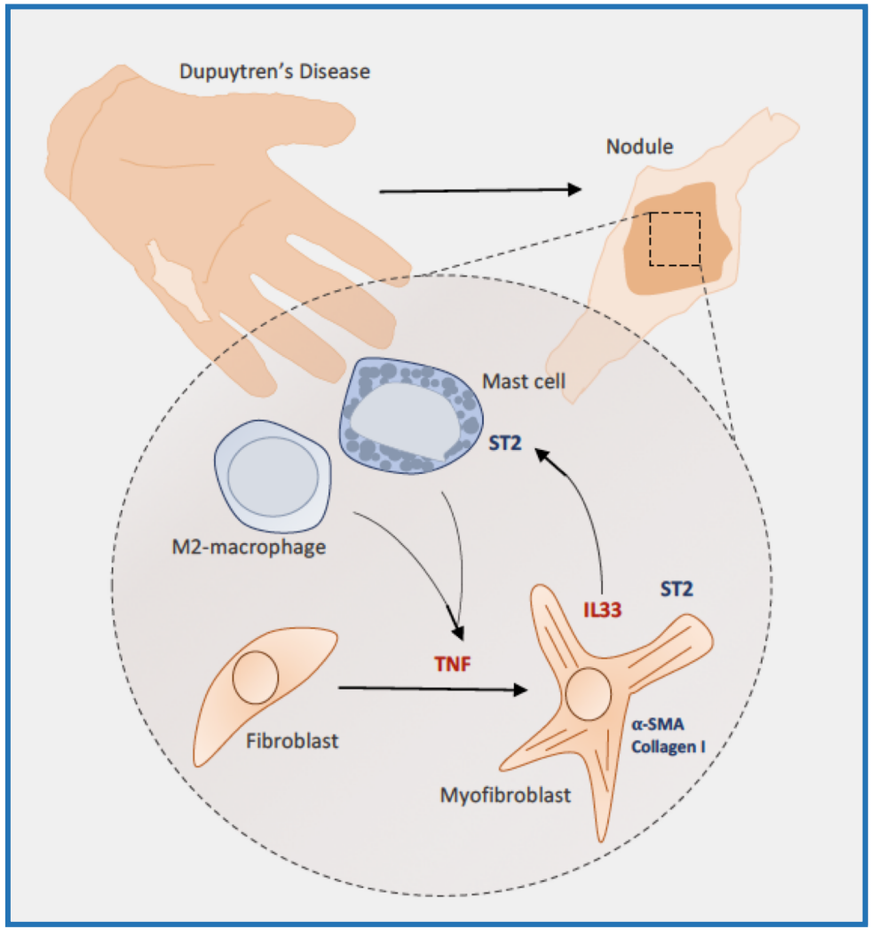
3000 El Camino Real, Bldg. 4, Suite 200, Palo Alto, CA

Appendix

180 LIFE SCIENCES

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*

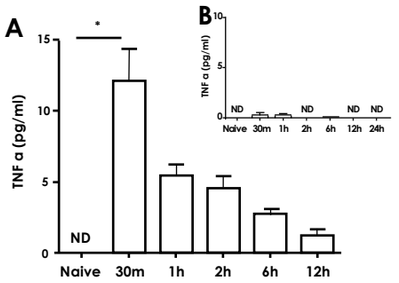
Patents filed for anti-TNFR2 and anti-IL-33
Claims in USA granted for IL-33, others pending

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

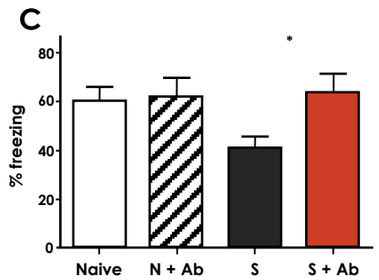
Evidence that TNF Plays a Role in POCD

Plasma TNF increases after surgery and correlates with post operative delirium

In mice

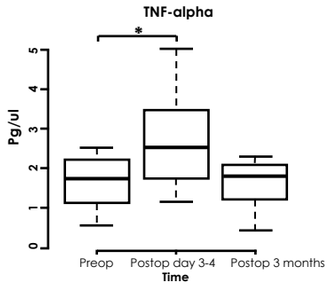


Plasma TNF increases after surgery



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

In humans



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

Post-op TNF-a (pg/ml)	
NON-DELIRIOUS (n=72)	**10.5 (7.65-12.65)**
DELIRIOUS (n=41)	**13.4 (10.5-16.7)***
OR (95% CI)	1.12 (1.036-1.210)
P value	0.001

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

PNAS

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

- 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]

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

SCAs 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, e.g. **CB2R, TRPV-1, 5HT1a, GPR55, GPR18** and others
- Anti-inflammatory, analgesic and anxiolytic properties

OUR PRODUCTS:

NON-PSYCHOACTIVE SCAs

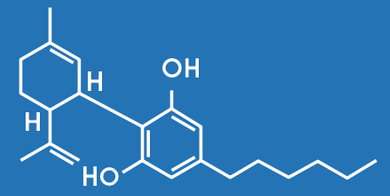
- Scientifically formulated analogs of CBD (SCAs) have been synthesized and patented, new formulations under analysis
- Analyzed in animal models of inflammation and pain

WHY MAN-MADE?

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

OUR DRUGS

1. HU-436[1]
2. Domb patent 1[2]
3. Mechoulam patent 2[3]
4. Mechoulam patent 3 & others[3]



(1) Patented drug we licensed from HU, but expect to discover superior drugs from ongoing research
(2) CBD derivative, patent being filed, agreement with Domb & HU completed
(3) Not yet filed

CBD – A Superior Treatment for Arthritis

Problem

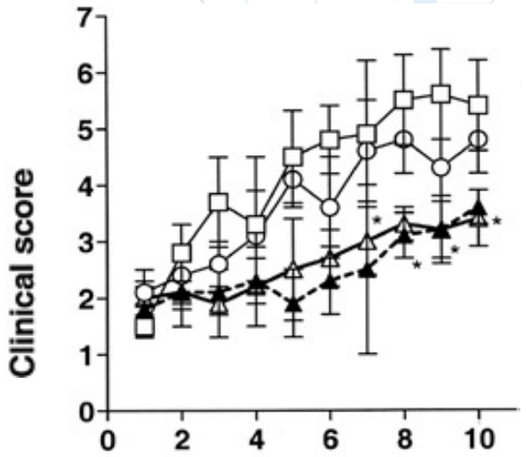
- Very early arthritis, pain & swelling is not effectively treated clinically
- Nonsteroidals do not help, can increase TNF(1)
- Existing therapies are suboptimal:
  - Methotrexate has side effects patients dislike
  - Anti-TNF is costly and use restricted / delayed by NICE (National Institute of Clinical Evidence, in UK)
  - Early rheumatoid arthritis (RA) or psoriatic arthritis (PsA) 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, Turner JJ, Brown AC, Timms EM, Inglis JJ, Brennan FM, Foxwell BM, Ray KP, Feldmann, M. Nonsteroidal anti-inflammatory drugs increase TNF production in rheumatoid synovial membrane cultures and whole blood. J Immunol. 2010;185(6):3694-701.

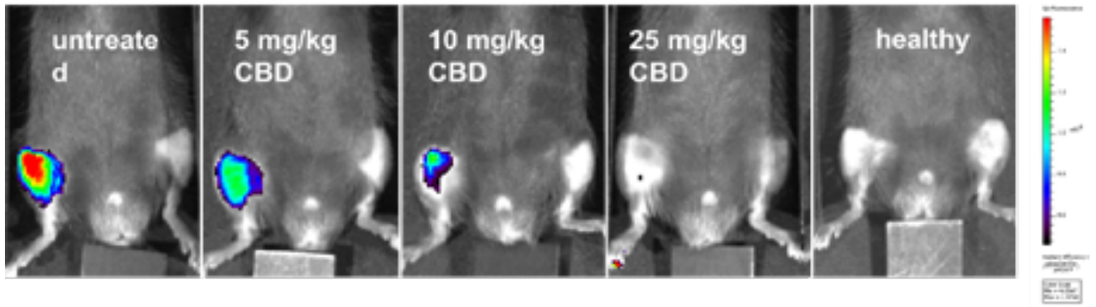
Oral CBD is effective in mouse model of RA



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).

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

CBD reduces inflammation in knee arthritis – unpublished new data



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

Fibrosis Program Patents

METHOD OF TREATING EARLY STAGE DUPUYTREN'S DISEASE			
Country	**Application No.**	**Date Filed**	**Status**
Australia	2017248273	16/10/2018	Filed
Canada	3020327	05/10/2018	Filed
Europe	17779836	05/11/2018	Filed
Hong Kong	19128046	12/08/2019	Filed
U.S.	62/320,151	08/04/2016	Filed
U.S.	16/089,234	27/09/2018	Filed

METHOD OF TREATING A LOCALIZED FIBROTIC DISORDER USING AN IL-33 ANTAGONIST			
Country	**Application No.**	**Date Filed**	**Status**
Australia	2016226414	15/09/2017	Filed
Canada	2,978,449	29/02/2016	Filed
Europe	16759325	25/09/2017	Filed
Hong Kong	18107063.7	30/05/2018	Filed
U.S.	15/555,027	15/12/2017	Granted 10/12/2019 (US10500273B2)

METHOD OF TREATING A LOCALIZED FIBROTIC DISORDER USING A TNF RECEPTOR 2 ANTAGONIST			
Country	**Application No.**	**Date Filed**	**Status**
Australia	2016226415	18/09/2017	Filed
Canada	2,978,431	29/02/2016	Filed
Europe	16759326.8	25/09/2017	Filed
Hong Kong	18107062.8	30/05/2018	Filed
U.S.	15/555,030	31/08/2017	Filed

Fibrosis Program Patents

METHOD OF TREATING OCULAR FIBROSIS USING AN IL-33/TNF BISPECIFIC ANTIBODY			
Country	**Application No.**	**Date Filed**	**Status**
U.S.	62/722,263	24/08/2018	Filed

METHOD OF TREATING LOCALIZED FIBROTIC DISORDERS USING AN IL-33/TNF BISPECIFIC ANTIBODY			
Country	**Application No.**	**Date Filed**	**Status**
U.S.	16/328,979	27/02/2019	Filed
Europe	17924768.9	01/04/2019	Filed

METHOD OF TREATING SYSTEMIC FIBROTIC DISORDERS USING AN IL-33/TNF BISPECIFIC ANTIBODY			
Country	**Application No.**	**Date Filed**	**Status**
U.S.	16/329,013	27/02/2019	Filed
Europe	17847574.5	01/04/2019	Filed
Hong Kong	62020001194	09/01/2020	Filed

METHOD OF TREATING FIBROPROLIFERATIVE DISORDERS INCLUDING DUPUYREN'S WITH ONE OR MORE SPECIFIC HUMAN MMP AND ATNF ANTAGONIST			
Country	**Application No.**	**Date Filed**	**Status**
U.S.	61/845,366	11/07/2013	Filed

USES OF IL-33 RECEPTORS ANTAGONIST			
Country	**Application No.**	**Date Filed**	**Status**
U.S.	62/127,157	02/03/2015	Filed

Fibrosis Program Patents (cont'd)

TREATMENT FOR DUPUYTREN'S DISEASE					
Country	**Application No.**	**Date Filed/Granted**	**Status**	**Patent Number**	**Note**
Australia	2011322482	06/07/2017	Granted	2,011,322,482	
Australia	2017204267	05/09/2019	Granted	2,017,204,267	
Canada	2,847,197	28/02/2014	Filed		
					The European patent valid or being validated in:
Europe	11779628.4	20/02/2019	Granted	E-1075071	Austria
Europe	11779628.4	12/02/2019	Granted	2,362,446	Belgium
Europe	11779628.4	14/02/2019	Granted	60 2011 054 785.2	Germany
Europe	11779628.4	07/03/2019	Granted	2,362,446	Finland
Europe	11779628.4	09/01/2019	Granted	2,362,446	France
Europe	11779628.4	07/03/2019	Granted	2,362,446	Iceland
Europe	11779628.4	02/01/2019	Granted	2362446-IE	Ireland
Europe	11779628.4	11/03/2019	Granted	502,019,000,019,925	Italy
Europe	11779628.4	12/02/2019	Granted	2,362,446	Netherlands
Europe	11779628.4	28/02/2019	Granted	2,362,446	Norway
Europe	11779628.4	11/03/2019	Filed		Spain
Europe	11779628.4	28/02/2019	Granted	2,362,446	Sweden
Europe	11779628.4	26/02/2019	Granted	2,362,446	Switzerland/Liechtenstein
Europe	11779628.4	21/12/2018	Granted	2,362,446	United Kingdom
Japan	2013-535462	16/09/2016	Granted	6004494	
U.S.	16/399,547	02/06/2020	Granted	10669334	

Fibrosis Program Patents (cont'd)

METHODS OF PREVENTION OR TREATMENT OF TRIGGERED INFLAMMATORY REACTIONS USING TNF ALPHA ANTAGONIST					
Country	**Application No.**	**Date Granted**	**Status**	**Patent Number**	**Note**
Europe	11710004	03/06/2020	Granted	2,547,363	Austria
Europe	11710004	03/06/2020	Granted	2547363	Belgium
Europe	11710004	03/06/2020	Granted	2547363	Switzerland
Europe	11710004	03/06/2020	Granted	602,011,067,119	Germany
Europe	11710004	03/06/2020	Granted	DK/EP 2547363	Denmark
Europe	11710004	03/06/2020	Granted	2547363	Spain
Europe	11710004	03/06/2020	Granted	2547363	Finland
Europe	11710004	03/06/2020	Granted	2547363	France
Europe	11710004	03/06/2020	Granted	2547363	Ireland
Europe	11710004	03/06/2020	Granted	2547363	Italy
Europe	11710004	03/06/2020	Granted	2547363	Netherland
Europe	11710004	03/06/2020	Granted	2547363	Norway
Europe	11710004	03/06/2020	Granted	2547363	Sweden
Europe	11710004	03/06/2020	Granted	2547363	United Kingdom

METHOD FOR TREATMENT OF POST OPERATIVE COGNITIVE DYSFUNCTION					
Country	**Application No.**	**Grant Date**	**Status**	**Patent Number**	**Note**
U.S.	13/579,555	12/04/2016	Granted	9,308,254	
Japan	2012-553396	24/06/2016	Granted	5,955,227	

SCA Program Patents

SCA: CYCLOHEXENYL COMPOUNDS, COMPOSITIONS COMPRISING THEM AND USES				
Country	**Application No.**	**Date Filed/Granted**	**Status**	**Note**
US2	10239848	26/03/2019	Granted	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 – issued
US3	11,149,014B2	19/10/2021	Granted	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	31/07/2018	Granted	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
Europe	EP3134393 B1	09/12/2020	Granted	Claims directed to a pharmaceutical composition for use in the treatment of chronic pain. Valid in: Austria, Belgium, Germany, Finland, France, Iceland, Ireland, Italy, Netherlands, Norway, Spain, Sweden, Switzerland/Liechtenstein and the United Kingdom
CN	ZL201580020978.7	14/01/2020	Granted	This invention relates to phenyl substituted cyclohexenyl compounds, compositions comprising them and uses thereof for the preparation of medicaments as defined in claim 1
CA	CA2944837A1	26/10/2021	Granted	Claims directed to use of HU-435 or a salt thereof, e.g. the molecule salt thereof (HU-436), for the preparation of a pharmaceutical composition for treatment of chronic pain

SCA: CANNABINOID DERIVATIVES AND THEIR USE IN THE TREATMENT OF INFLAMMATION AND/OR PAIN AND/OR OBESITY				
Country	**Application No.**	**Date Filed/Granted**	**Status**	**Note**
Europe	PCT/IL2021/051398	24/11/2021	Filed	PCT filed via EPO, priority date 24 Nov, 2020

SCA: BIOACTIVE PHENOLATE IONIC COMPLEXES				
Country	**Application No.**	**Date Filed/Granted**	**Status**	**Note**
Europe	PCT/IL2021/05045	21/04/2021	Filed	PCT filed via EPO, priority date 22 Apr, 2020

a7nAChR Program Patents

a7nAChR				
Country	Date Filed/Granted	Status	Patent/Application Number	Note
US Grant	16/09/2014	Granted	US8835391B2	Alpha B-crystallin as a therapy for multiple sclerosis
US Grant	25/01/2011	Granted	US7875589B2	Alpha B-crystallin as a therapy for rheumatoid arthritis
Europe	06/01/2021	Granted	EP 3377178B1	Peptide for use in the treatment of medical conditions with inflammatory or autoimmune components
US Application	16/09/2019	Filed	US20180333451A1	B-1a lymphocyte and/or macrophage targeting and activation to treat medical conditions with inflammatory or autoimmune components
Canada	18/11/2016	Filed	3004908	B-1a lymphocyte and/or macrophage targeting and activation to treat medical conditions with inflammatory or autoimmune components
Japan	18/11/2016	Filed	2018-526196	B-1a lymphocyte and/or macrophage targeting and activation to treat medical conditions with inflammatory or autoimmune components