180 LIFE SCIENCES

NASDAQ: ATNF

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

Corporate Presentation

March 2024

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180 Life Sciences Overview

Robust IP-Protected Product Pipeline with Large Market Potential

- **Three families of drugs** address significant market opportunities in inflammation, fibrosis and pain with multiple programs in synchronized stages of development
  - **Fibrosis & Anti-TNF**
  - **Synthetic CBD Analogs (SCAs)**
  - **a7nAChR**
- **Strong IP Portfolio:** 24 granted patents, 33 filed patent applications

Numerous Near-Term Inflection Points

- **Anti-TNF programs:** expecting to initiate a Phase 2 trial in 2024 in POCD
- **SCA programs:** validation ongoing, with a planned PK study

Scientific Pioneers Backed by Experienced Operators and Board

- **Founders:** pioneers with 100+ cumulative years of discovery and clinical experience; successes include Remicade and Tysabri
- **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 sciences companies

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

Three Therapeutic Families Targeting Multiple Indications

	Indication	Early-Stage Development		Late-Stage Development		Milestones
		Discovery/Validation	Phase 1	Phase 2	Phase 3	
Fibrosis & Anti-TNF*	Dupuytren's Contracture	adalimumab				Planning Phase 3
	Frozen Shoulder	adalimumab				UK feasibility study closed, new clinical trial site and country to be determined
	POCD	infliximab				Initiate Phase 2 2024
	NASH					Ongoing Validation
Synthetic CBD Analogs (SCAs)	Chronic Pain					Ongoing Validation
	Weight Loss / Early Arthritis					Ongoing Validation
Nicotine Acetylcholine Receptor (a7nAChR)	Smoking Cessation Induced Ulcerative Colitis					Ongoing Validation

*Repurposed drugs in new indications may not need to follow standard regulatory approval pathways. 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 marketing applications or requests for marketing approval have been submitted to the FDA for any products at this time.

Experienced Leadership Team

Management Team

James Woody, MD, PhD
Director, CEO

Jonathan Rothbard, PhD
Chief Scientific Officer

Ozan Pamir
Chief Financial Officer

Founders

Prof. Sir Marc Feldmann
Co-Founder
University of Oxford

Prof. Lawrence Steinman
Executive Chairman
Co-Founder
Stanford University

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

Board of Directors

Prof. Lawrence Steinman
Chairman

James Woody, MD, PhD
Chief Executive Officer

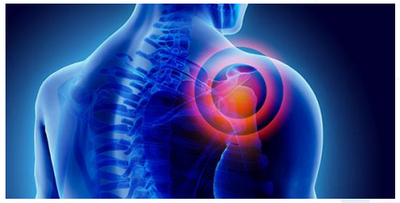
Blair Jordan
Lead Director

Omar Jimenez
Director

Ryan Smith
Director

Fibrosis & Anti-TNF Therapeutics: Lead Clinical Indications

Dupuytren's Contracture



Frozen Shoulder

POCD

Novel Treatments for TNF-Driven Conditions

- All three conditions are primarily driven by a pro-inflammatory protein called tumor necrosis factor (TNF)
- Proof-of-Concept in Dupuytren's Contracture has broader applications in Frozen Shoulder and POCD
  - No treatment options currently available that target and prevent early-stage fibrosis of the hand
  - Treating early-stage fibrosis can halt disease progression
  - Clinically significant Phase 2b data in Dupuytren's Contracture, published in The Lancet Rheumatology
  - Phase 2b clinical data in Dupuytren's Contracture provides a strong rationale to investigate anti-TNF treatment in Frozen Shoulder and POCD
- Shorter development timeline for repurposing drugs
  - Can leverage previous studies and clinical data of anti-TNF approved drugs
  - Studies typically commence at Phase 2 and are potentially pivotal

Initial Indication Targeting Dupuytren's Contracture

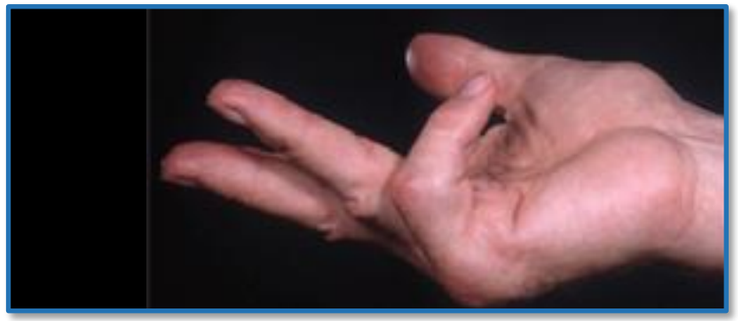
Characteristics

- 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
Large unmet need
Phase 2b trial treated early disease

Late Disease – Results in Impaired Hand Function



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

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

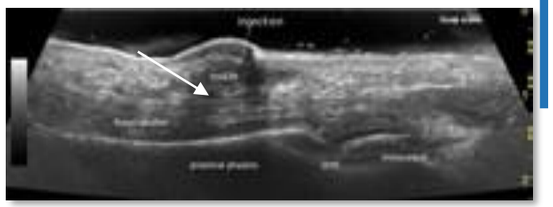
Phase 2a Completed: 40mg (in 0.4ml) Adalimumab is Effective

The First Trial of Any Targeted Therapy in Early Dupuytren's Contracture

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(1)

Trial Overview

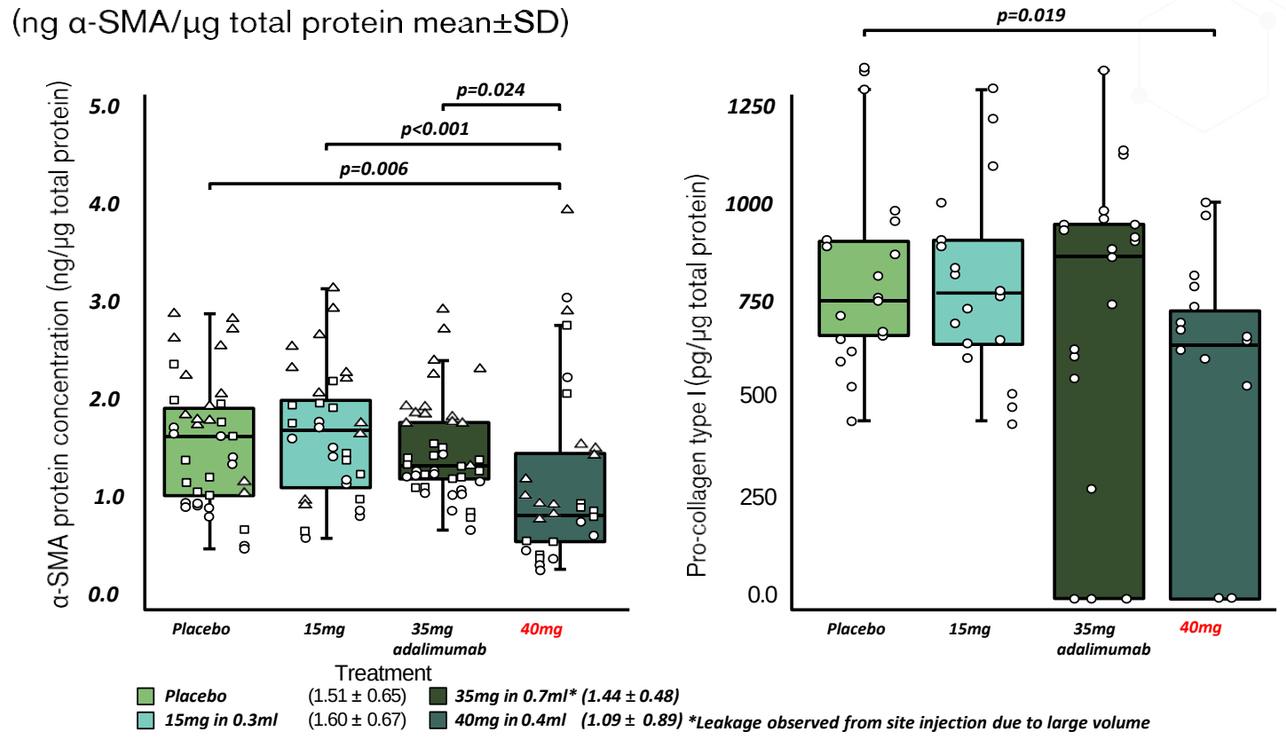


Adalimumab injected directly into the nodule

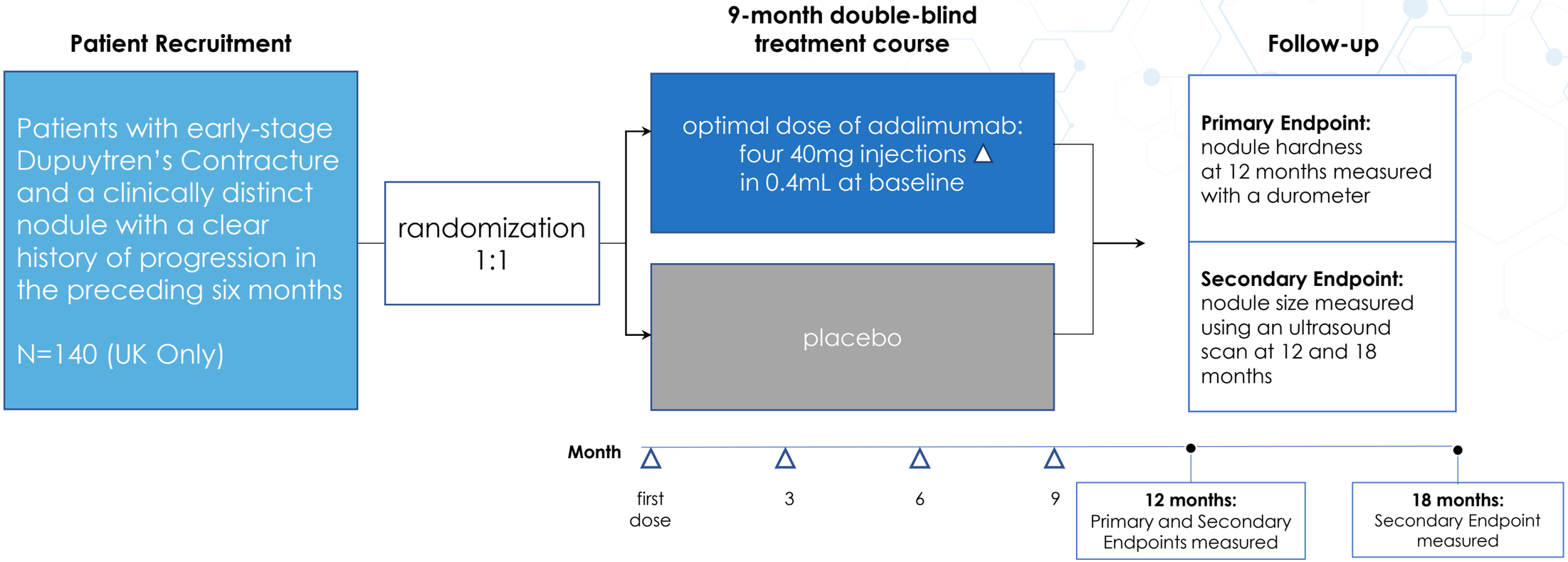
- Dose ranging with 28 patients
- **40 mg in 0.4ml – effective dose**
- Funded by HICF (Wellcome Trust + Dept of Health) and 180 Life Sciences

(1) EBioMedicine 33 (2018) 282-288

Demonstrated Efficacy at High Concentration & Dose



Phase 2b Study in Patients with Dupuytren's Contracture

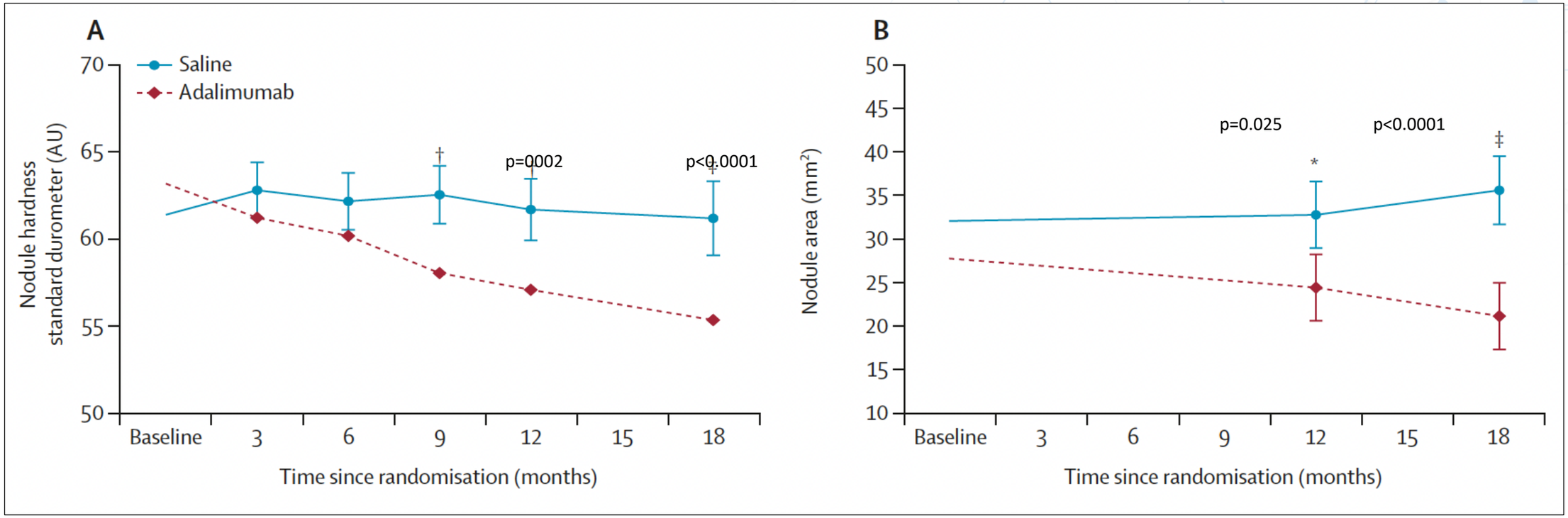


Description

- Randomized, placebo-controlled clinical trial in patients with early-stage Dupuytren's 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 the UK (Oxford, Edinburgh) and Netherlands (Groningen)

Phase 2b: Primary and Key Secondary Endpoint Met

Endpoints selected as reductions potentially indicate disease no longer progressing



Nodule hardness -4.6 AU at 12 months
Nodule hardness -5.8 AU at 18 months

Nodule size -8.4mm^2 at 12 months
Nodule size -14.4mm^2 at 18 months

Results were clinically significant vs. placebo

Early-Stage Dupuytren's Contracture Prevalence

~32.5M

Patients with Early-Stage Dupuytren's Contracture

(U.S., U.K., EU)

~12M	~2.5M	~18M
U.S. Prevalence	U.K. Prevalence	EU Prevalence

Approximately 20-35% of patients with a palmar nodule progress to finger contractures

Additional Near-Term Anti-TNF Indications

Post Operative Delirium/Cognitive Deficit (POCD)

- Over 300,000 hip fractures each year in the US alone[1]
- Grants for Phase 2 trial received based on 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 in 2024; 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
- Trial protocol completed and NIHR grant received for feasibility study. Feasibility study closed for enrollment
- **Phase 2** clinical trial site and country to be determined

(1) https://www.cdc.gov/homeandrecreationalsafety/falls/adulthipfx.html
(2) Walker-Bone K et al (2004) Arthritis Rheum 51(4):642-651

SCA Family: Synthetic CBD Analogs for Pain & Inflammation

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	180 Life Sciences Solution
Variable composition, potency, and may contain **undesirable contaminants**	Use **SYNTHETIC** >99.5% **pure** SCAs
Side effects can be triggered by THC (e.g., psychosis)	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**

a7nAChR Family: Novel Platform for Ulcerative Colitis

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

Advancing Multiple Programs into the Clinic

	Indication	2024
 **Fibrosis & Anti-TNF***	**Dupuytren's Contracture**	Out licensing partner
	Frozen Shoulder	Determine clinical trial site and country for Phase 2
	POCD	Initiate Phase 2
 **Synthetic CBD Analogs** (SCAs)	**Chronic Pain**	**PK study planned**

Advancing lead program towards commercialization and initiating new programs for additional Proof-of-Concept

180 Life Sciences Highlights

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Numerous Near-Term Inflection Points

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Thank you

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