R&D Showcase Webinars

Pharmaxis drug PXS-6302 targeting scarring

pharmaxis

developing breakthrough treatments for fibrosis and inflammation

Investor Presentation | 31 March 2022

Forward looking statement

This document contains forward-looking statements, including statements concerning Pharmaxis' future financial position, plans, and the potential of its products and product candidates, which are based on information and assumptions available to Pharmaxis as of the date of this document. Actual results, performance or achievements could be significantly different from those expressed in, or implied by, these forward-looking statements. All statements, other than statements of historical facts, are forward-looking statements.

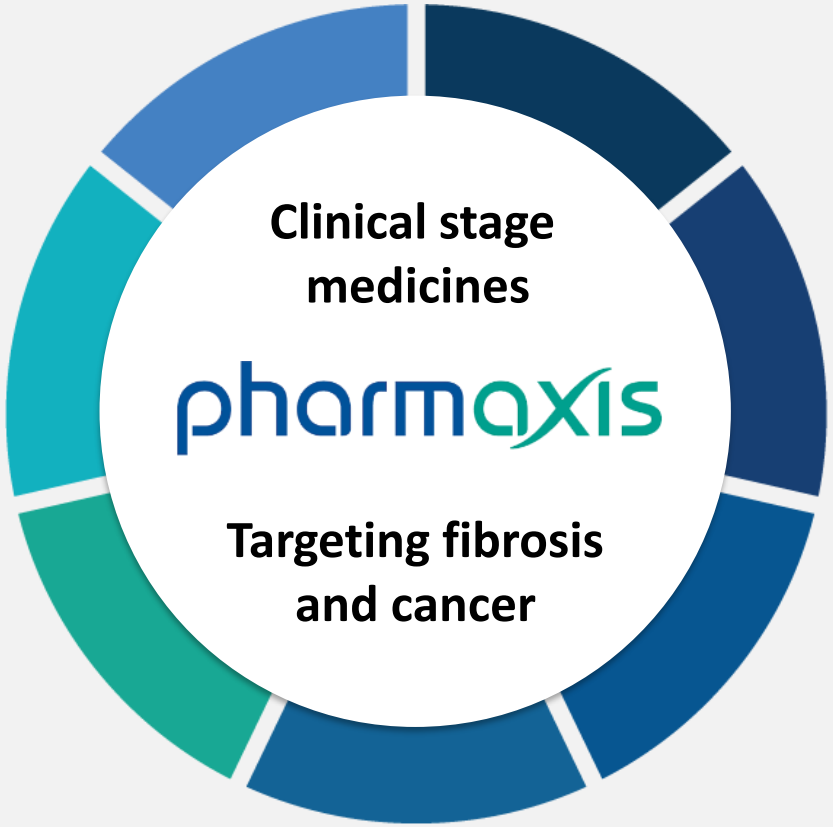
These forward-looking statements are not guarantees or predictions of future results, levels of performance, and involve known and unknown risks, uncertainties and other factors, many of which are beyond our control, and which may cause actual results to differ materially from those expressed in the statements contained in this document. For example, despite our efforts there is no certainty that we will be successful in developing or partnering any of the products in our pipeline on commercially acceptable terms, in a timely fashion or at all. Except as required by law we undertake no obligation to update these forward-looking statements as a result of new information, future events or otherwise.

Program

11.00	Welcome and introduction to program	Michael Woods
11:05	Pharmaxis – a global leader in lysyl oxidase chemistry and biology	Gary Phillips
11.15	The science of scarring and potential for LOX inhibition	Dr Mark Fear (UWA)
11.30	Clinical applications for LOX inhibition	Professor Fiona Wood (UWA)
11.45	Q&A with panel	
12.10	Pharmaxis Q&A	Gary Phillips
12.20	Close	

Executive Summary

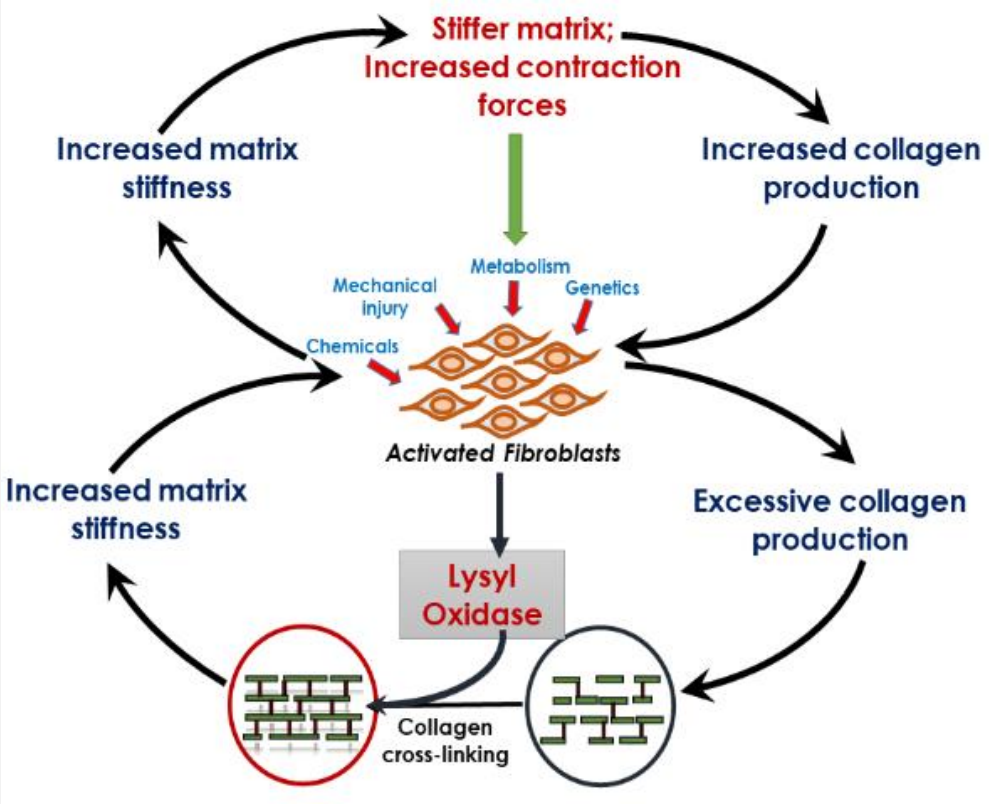
- Pharmaxis is a clinical stage drug development company targeting fibrosis and cancer indications with first in class or best in class small molecule drugs in markets of high value
- Pharmaxis is the global leader in fibrosis driven by lysyl oxidase enzymes having invested in a multi year research program leveraged with extensive external scientific collaborations
- Pharmaxis has 4 studies planned for 2022 that will lead to near term value opportunities
  - Lead asset PXS-5505 is in a multinational phase 2 trial – a breakthrough clinical program with disease modifying potential in Myelofibrosis
  - IND approval to commence US investigator led phase 2 trial in liver cancer with PXS-5505 as first line treatment added to existing chemotherapy.
  - Topical drug PXS-6302 is in a phase 1c trial in patients with potential to improve function and appearance of established scars with a study in burns patients to follow later this year.
- Specific corporate strategy to deliver non-dilutive cash and cost savings from commercial stage mannitol business
- Pharmaxis is well positioned to fund its focused clinical program



Pharmaxis is the global leader in lysyl oxidase chemistry and biology

Multi year research program leveraged with extensive scientific collaborations worldwide has delivered 2 drugs in the clinic

Lysyl oxidases are the final stage in fibrosis



Tissue stiffening due to increases in collagen and number of cross-links is preventable through lysyl oxidase inhibition and at the heart of a true anti-fibrotic therapy

- **PXS-5505**
  - Oral dosage form – twice a day dosing
  - Patent 2018
  - Strong pre clinical evidence in models of fibrosis and cancer
  - INDs approved for myelofibrosis and hepatocellular carcinoma
  - Potential in multiple cancer indications
  - Phase 1 data demonstrates a safe, well tolerated drug that gives >90% inhibition of LOX enzymes
- **PXS-6302**
  - Topical dosage form – one application per day
  - Patent 2019
  - Strong pre clinical evidence in models of skin fibrosis and scarring
  - Potential in prevention of scar formation and modification of existing scars
  - Phase 1 data demonstrates a safe, well tolerated drug that gives full inhibition of LOX enzymes in the skin with minimal systemic exposure

Four trials to deliver near term value

Pipeline creates multiple opportunities in high value markets

	Indication	Addressable market (US$)	Trial design	# patients	Status	Data
PXS-5505	Myelofibrosis (MF)	$1 billion	Phase 2 open label 6 month study in JAK intolerant / ineligible myelofibrosis patients	24	Recruiting	Year end 2022
	Hepatocellular Carcinoma (HCC)	$7 billion	Phase 1c open label dose escalation study in newly diagnosed patients with unresectable HCC on top of standard of care (PD-L1 inhibitor + anti VEGF)	18	First Patient Q2 2022	2H 2023
PXS-6302	Modification of established scars	$3.5 billion	Phase 1c 3 month placebo controlled study in patients with established scars (>1 year old)	50	Recruiting	Q4 2022
	Scar prevention post surgery	$3.5 billion	Phase 1c 3 month placebo controlled study in patients with scarring subsequent to a burns injury	50	First patient mid 2022	1H 2023

The science of scarring and potential for LOX inhibition

Dr Mark Fear(UWA)

PXS-6302 treatment in the amelioration of scar

Mark Fear

Burn Injury Research Unit
School of Biomedical Sciences
University of Western Australia

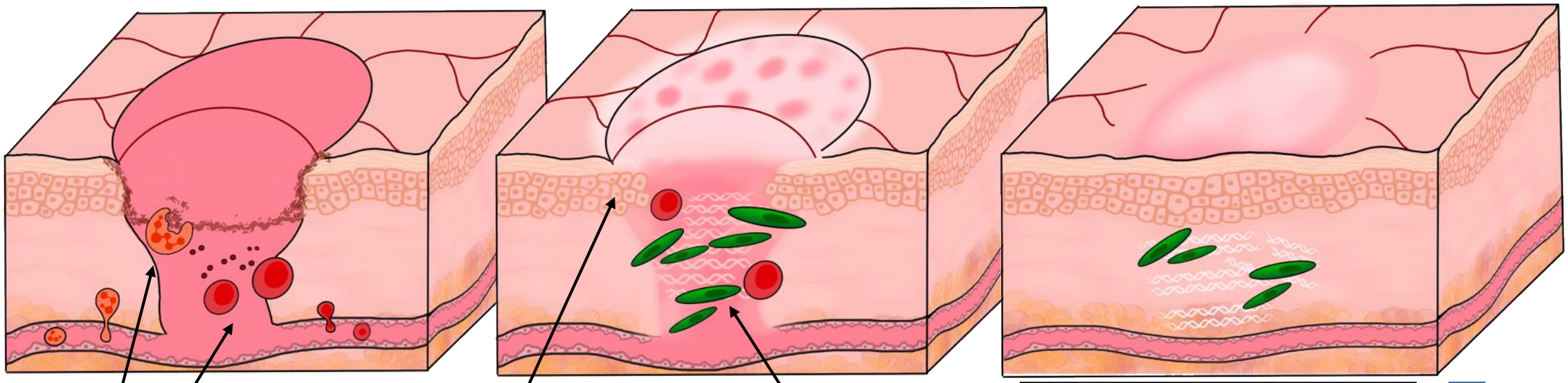
Scarring after injury

Mins Hours Days Weeks Months/Years

1. Hemostasis/Inflammation

2. Tissue formation/repair

3. Scar Remodelling



Inflammatory cells

- Removal of bacteria and necrotic tissue
- Cytokine and MMP production
- Stimulate tissue repair – growth factors

Keratinocytes

- Re-epithelialization
- Cover the surface

Fibroblasts

- Granulation tissue - collagen deposition

Collagen

Small parallel bundles

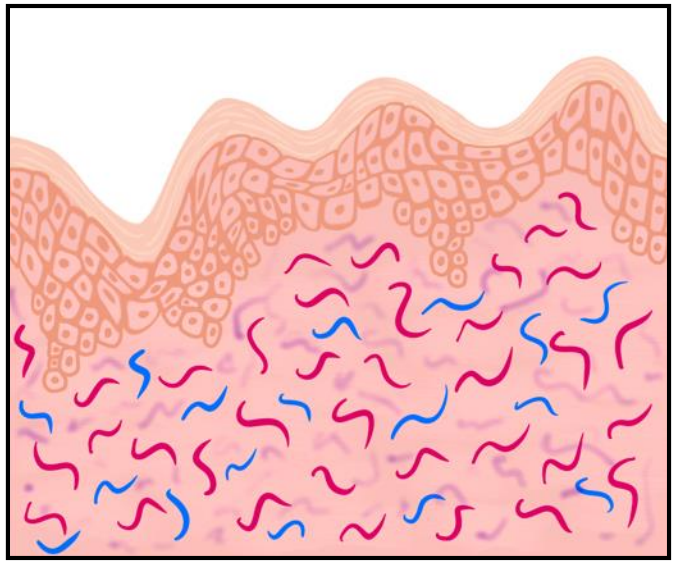
Parallel bundles with increased synthesis and crosslinks

Parallel bundles of thick fibres with increased production and crosslinks

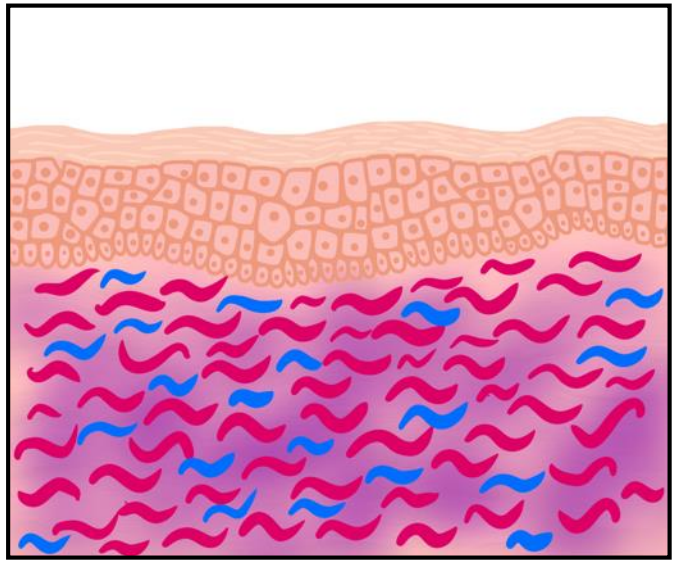
Worse Scar

Collagen is produced by fibroblasts in the dermis

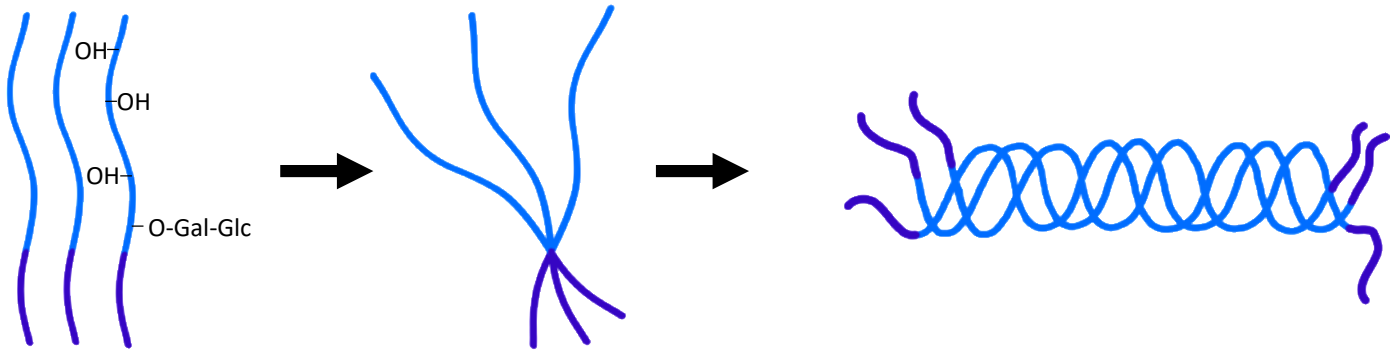
Normal skin



Scar skin



Endoplasmic reticulum

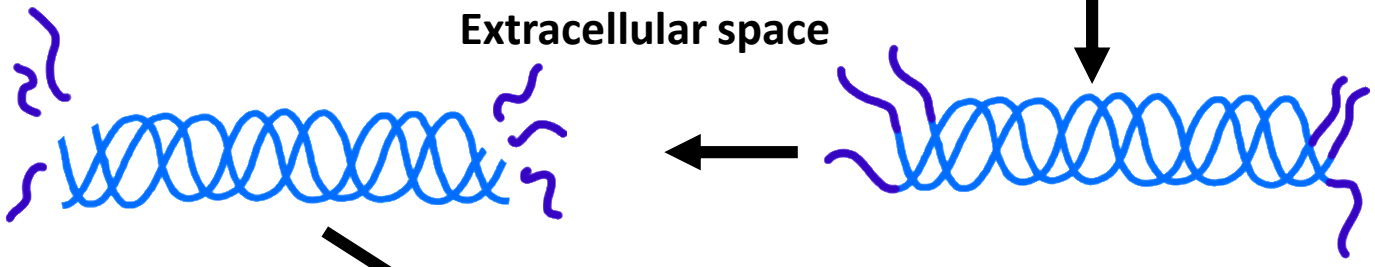


Procollagen

Assembly of 3 collagen chains

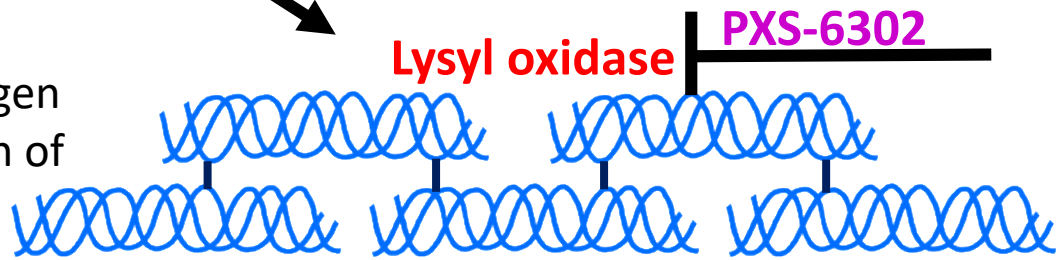
Assembly of triple helix and secretion

Extracellular space

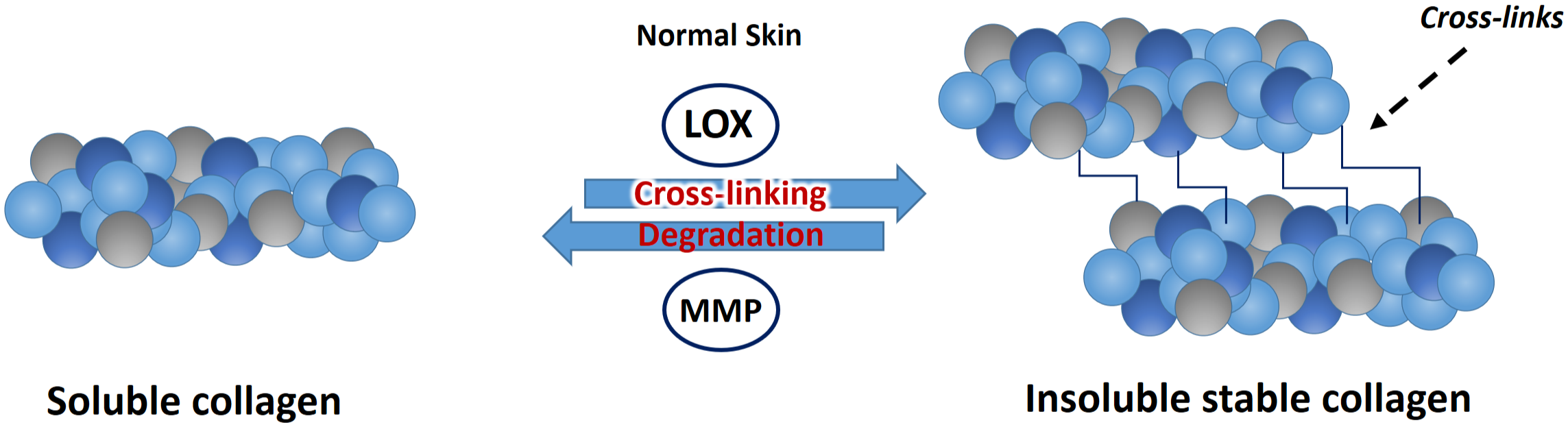


Cleavage of propeptides

Assembly into collagen fibrils and formation of covalent cross-links



PXS-6302 reduces collagen stability and increases remodelling



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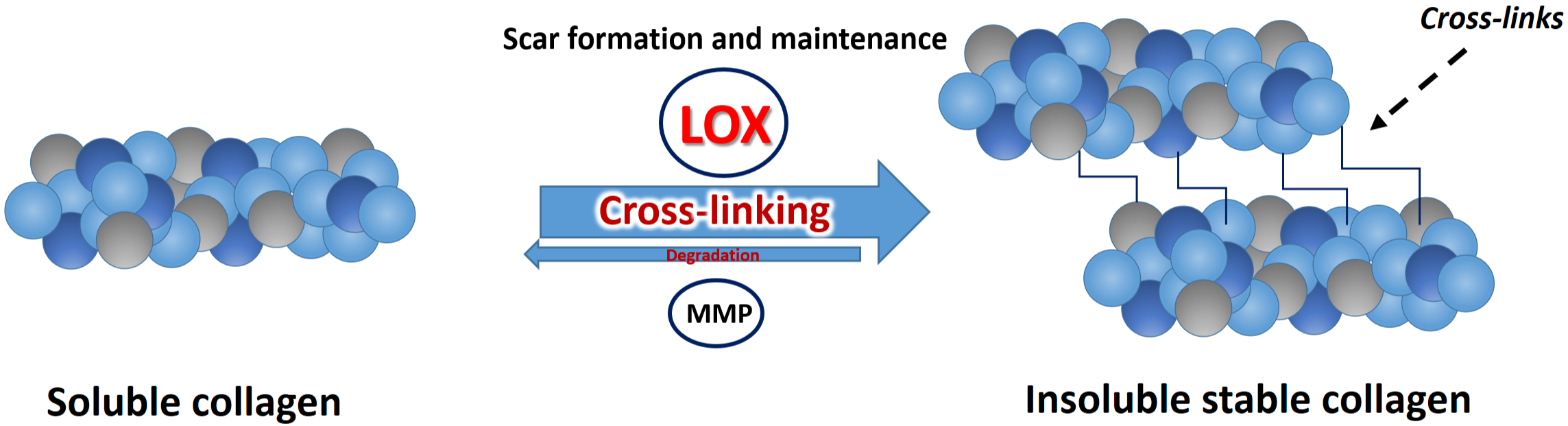
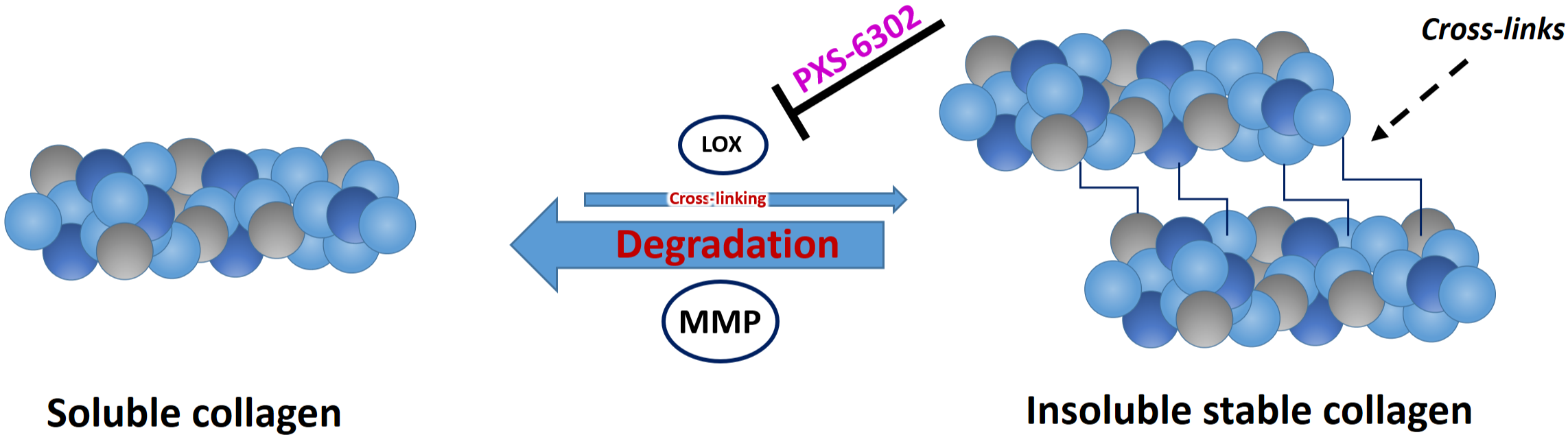
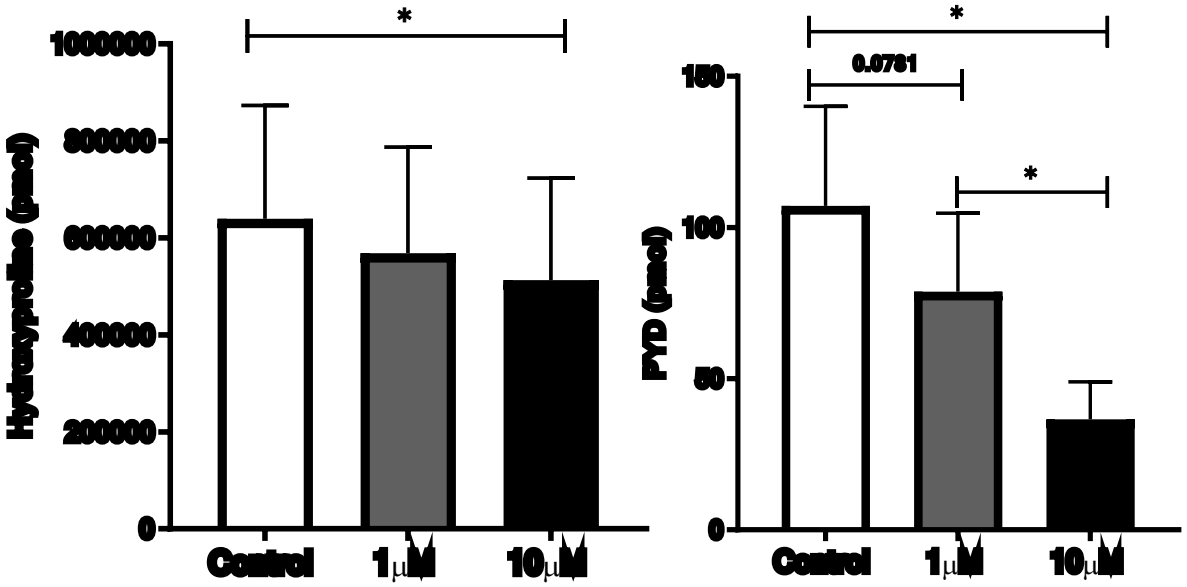


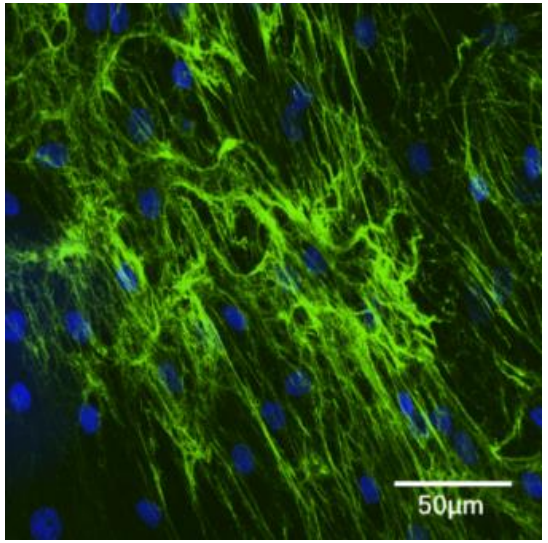
PXS-6302 reduces collagen stability and increases remodelling

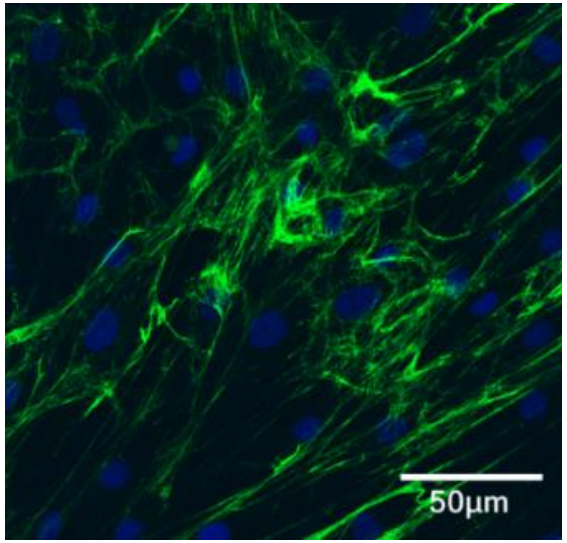


Inhibiting LOX reduces collagen cross-linking and production of fibroblasts

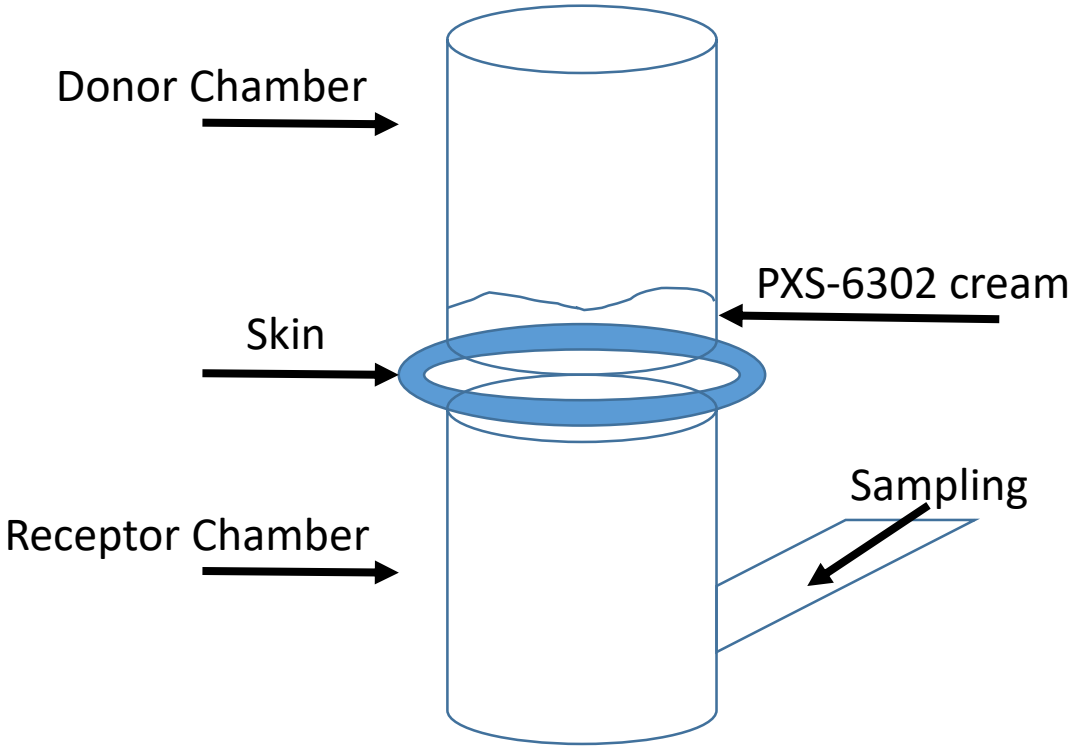
1. Treating fibroblasts with LOX inhibitor reduces;
    A. Collagen production
    B. Cross-linking of collagen

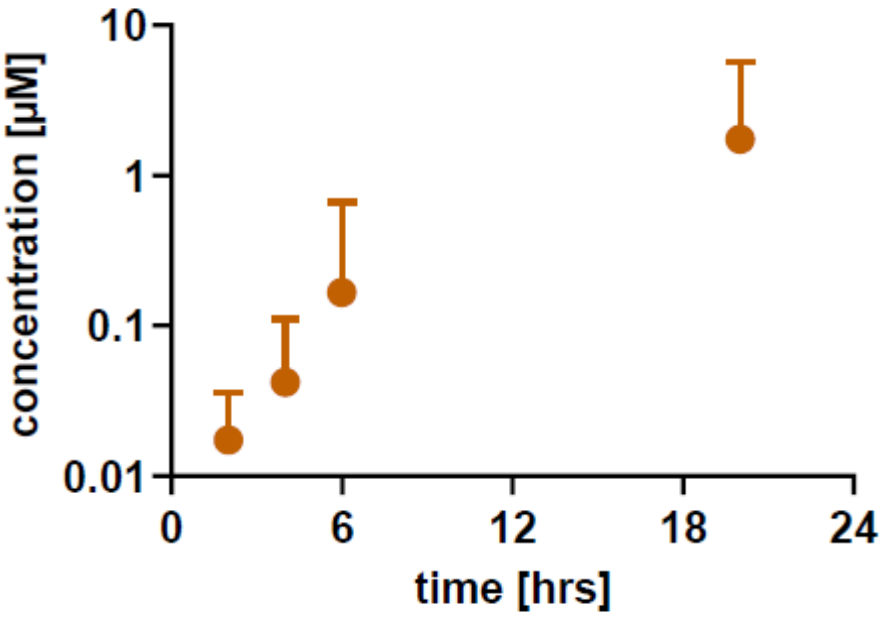






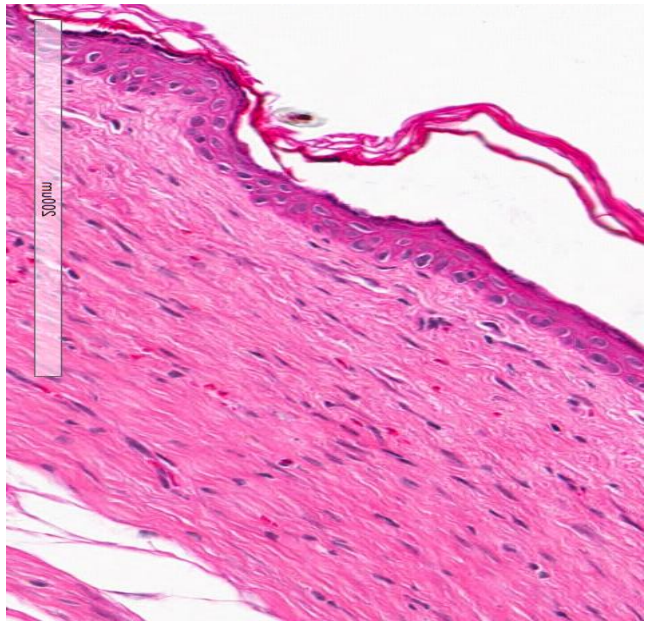
PXS-6302 penetrates skin when applied as topical cream



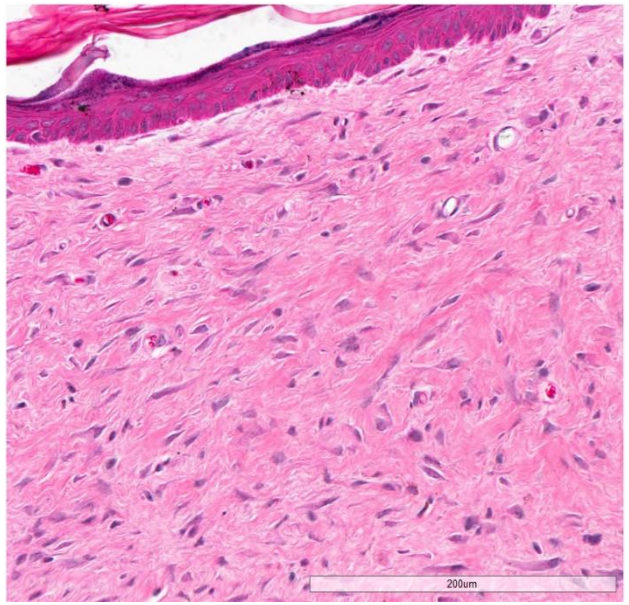


Pre-clinical models with PXS-6302

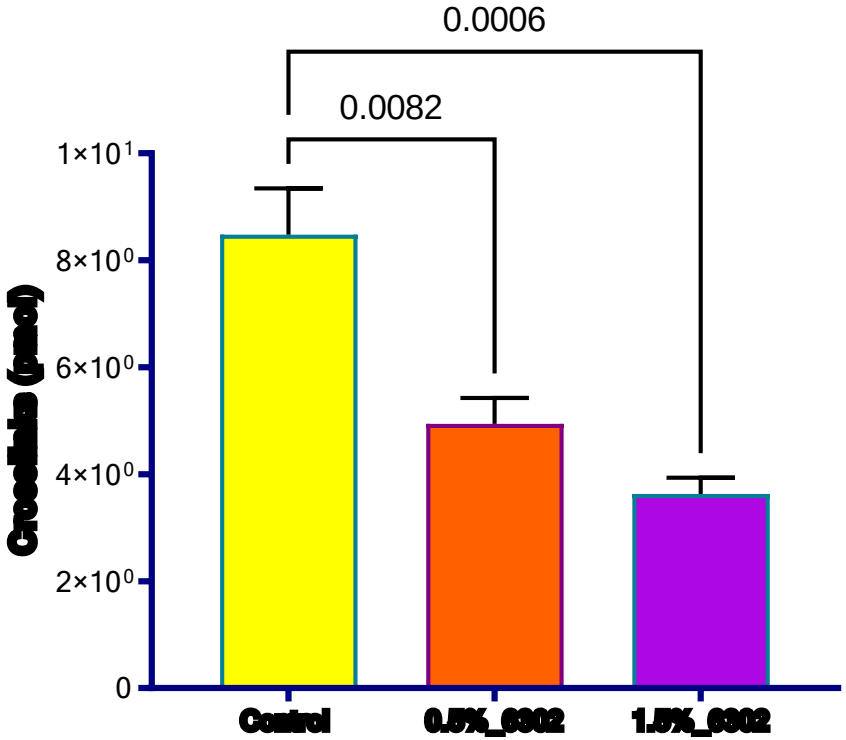
1. Small full-thickness excision injury
2. Topical treatment for 28 days (once per day)
3. Scar tissue analysed



Control



Treated

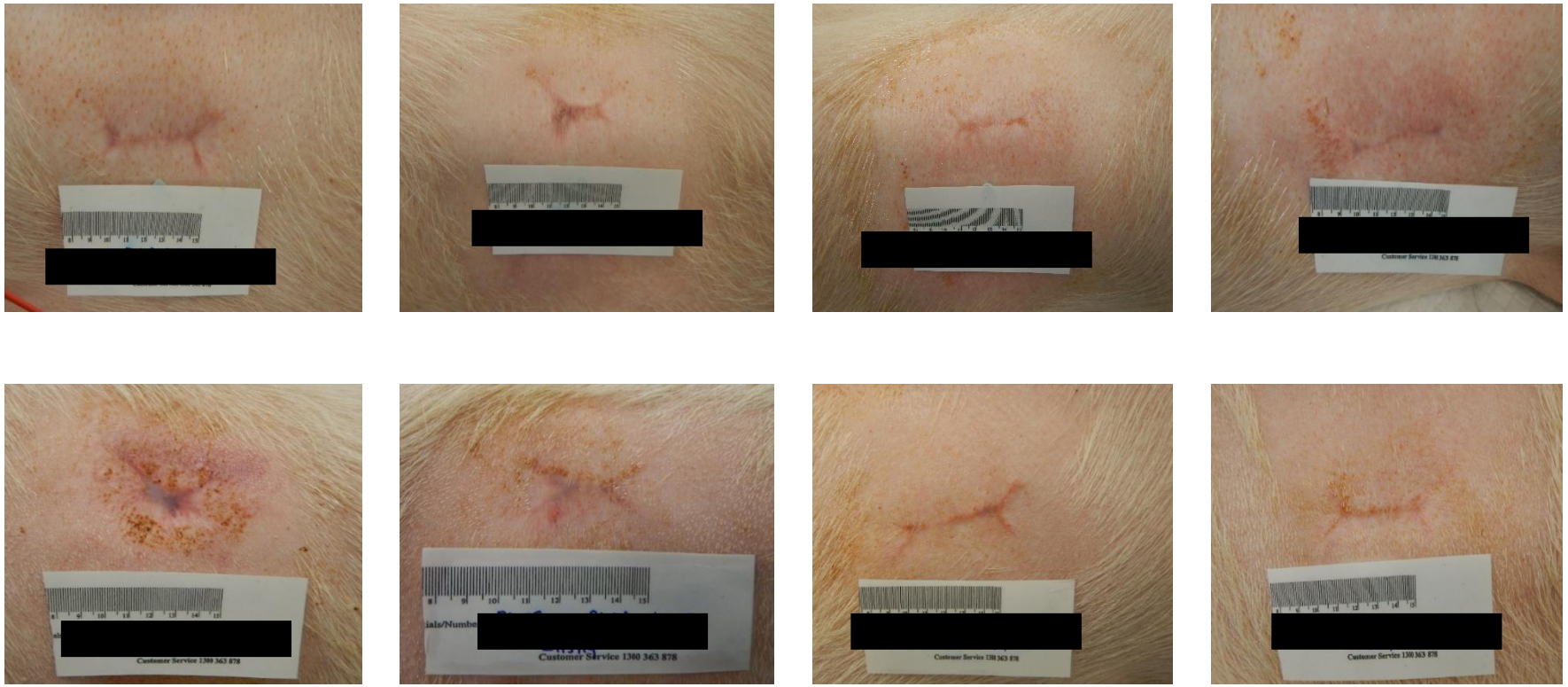


Improved scar appearance with PXS-6302 treatment

1. 10cm^2 large full-thickness excision injury

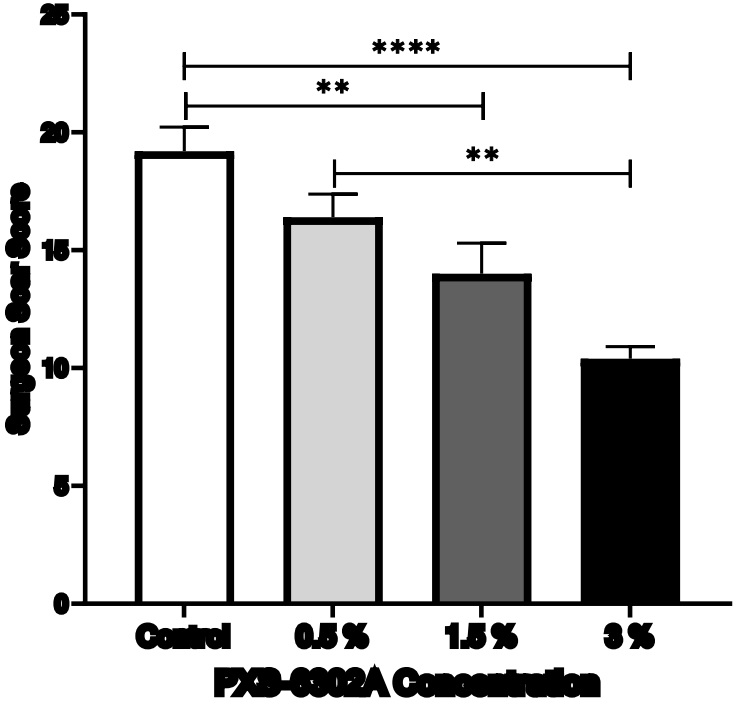
2. Topical treatment from time of healing for 10 weeks once per day

3. Scar tissue analysed



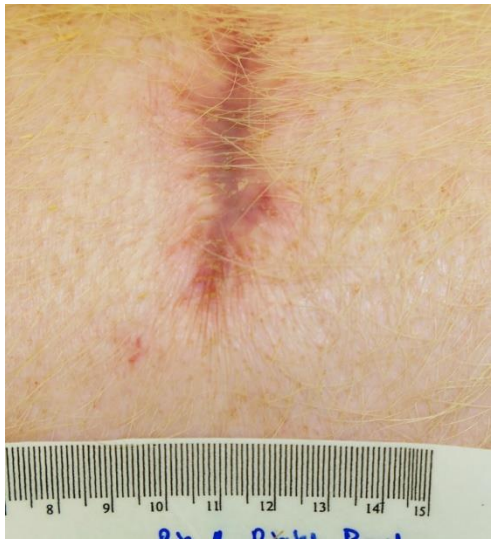
0% 0.5% 1.5% 3%

Increasing PXS-6302 concentration

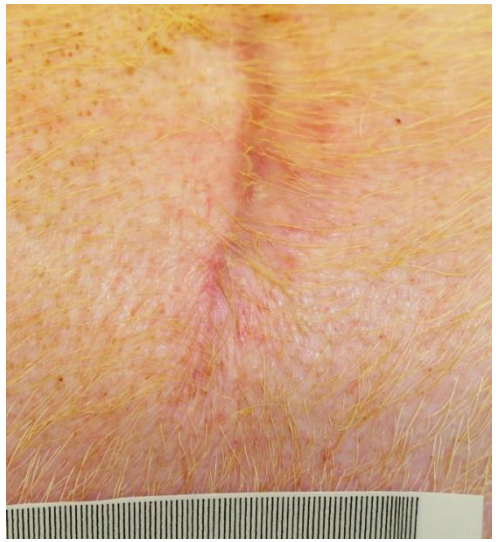


Improving appearance without losing tensile strength

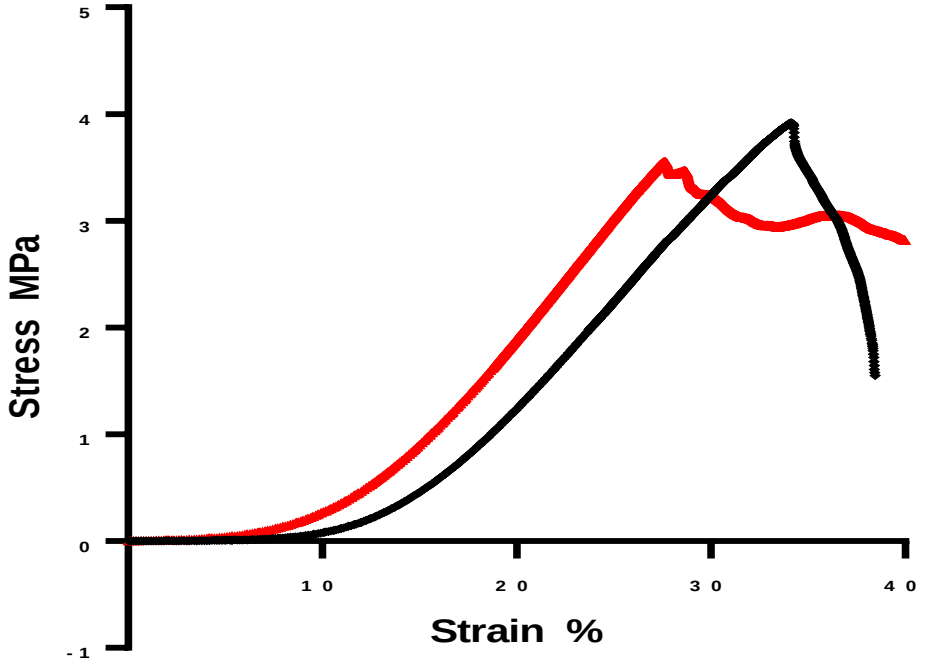
1. 10cm^2 large deep dermal burn injury
2. Topical treatment from time of healing for 10 weeks once per day
3. Scar tissue analysed



Placebo



3% PXS-6302



Red- placebo
Black – 3% PXS-6302

Summary

Once per day treatment with topical PXS-6302 cream;

1. Inhibited the target enzyme (LOX) in scar tissue

2. Improved scar appearance in small and large surgical injury models

3. Improved scar appearance in deep-dermal burn injury model

4. No loss of tissue strength and improvements in pliability

5. *Potential to treat both developing and established scars*

Clinical applications for LOX inhibition

Professor Fiona Wood (UWA)

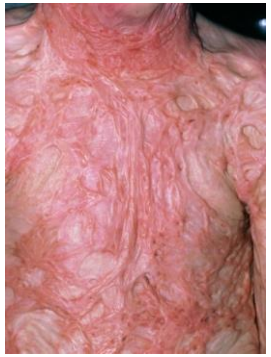
PXS-6302 treatment in the amelioration of scar

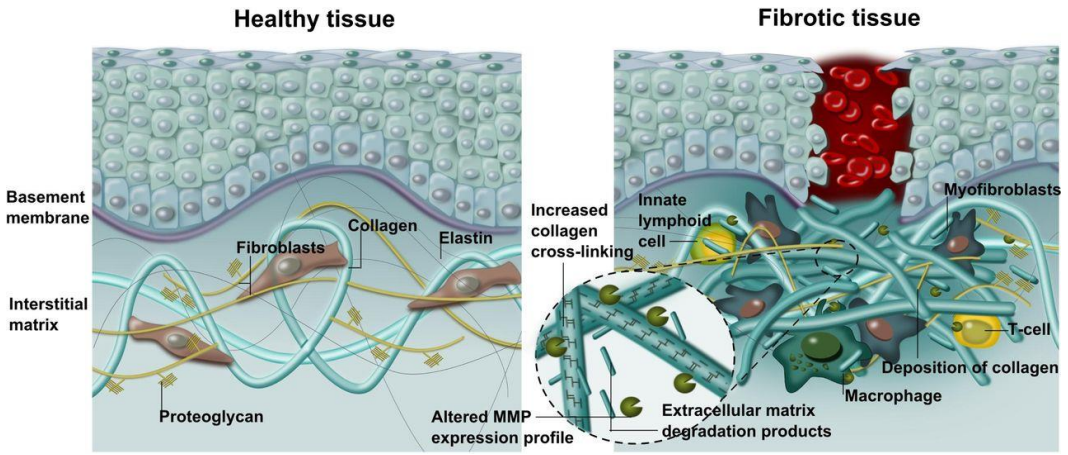
Fiona Wood
Burns Service of Western Australia
Burn Injury Research Unit
University of Western Australia

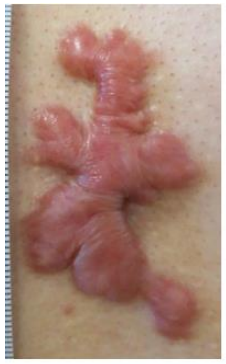
The impact of scars on patients

Fibrosis is the result of an imbalance in the deposition and degradation of Extracellular matrix (ECM).

Fibroblasts activated to a phenotype which drives excess matrix deposition

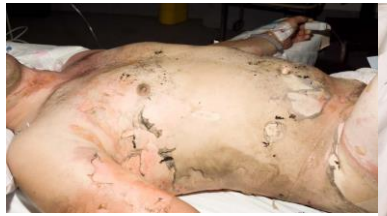


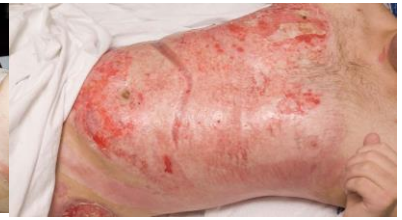


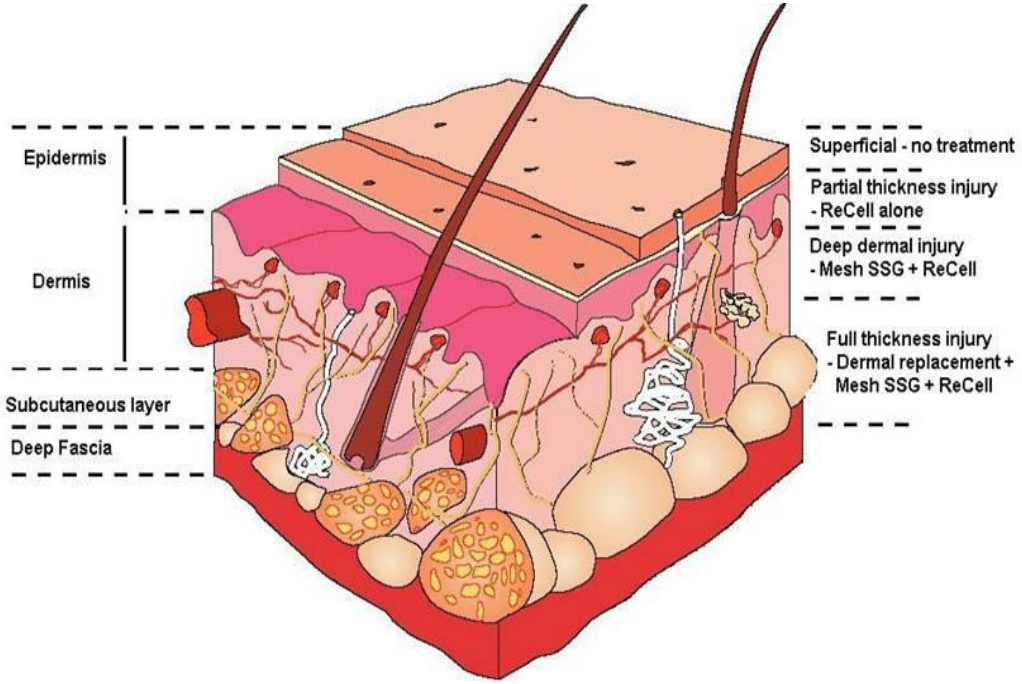


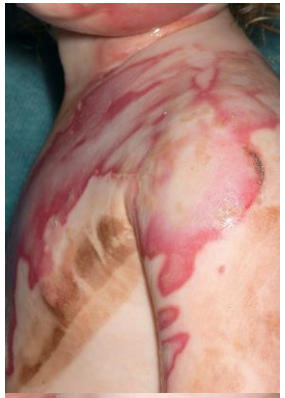
Morten A. Karsdal et al. Am J Physiol Gastrointest Liver Physiol 2015;308:G807-G830

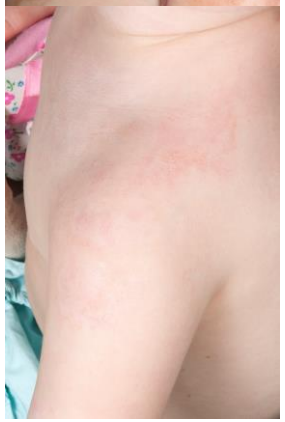
Treatment plan











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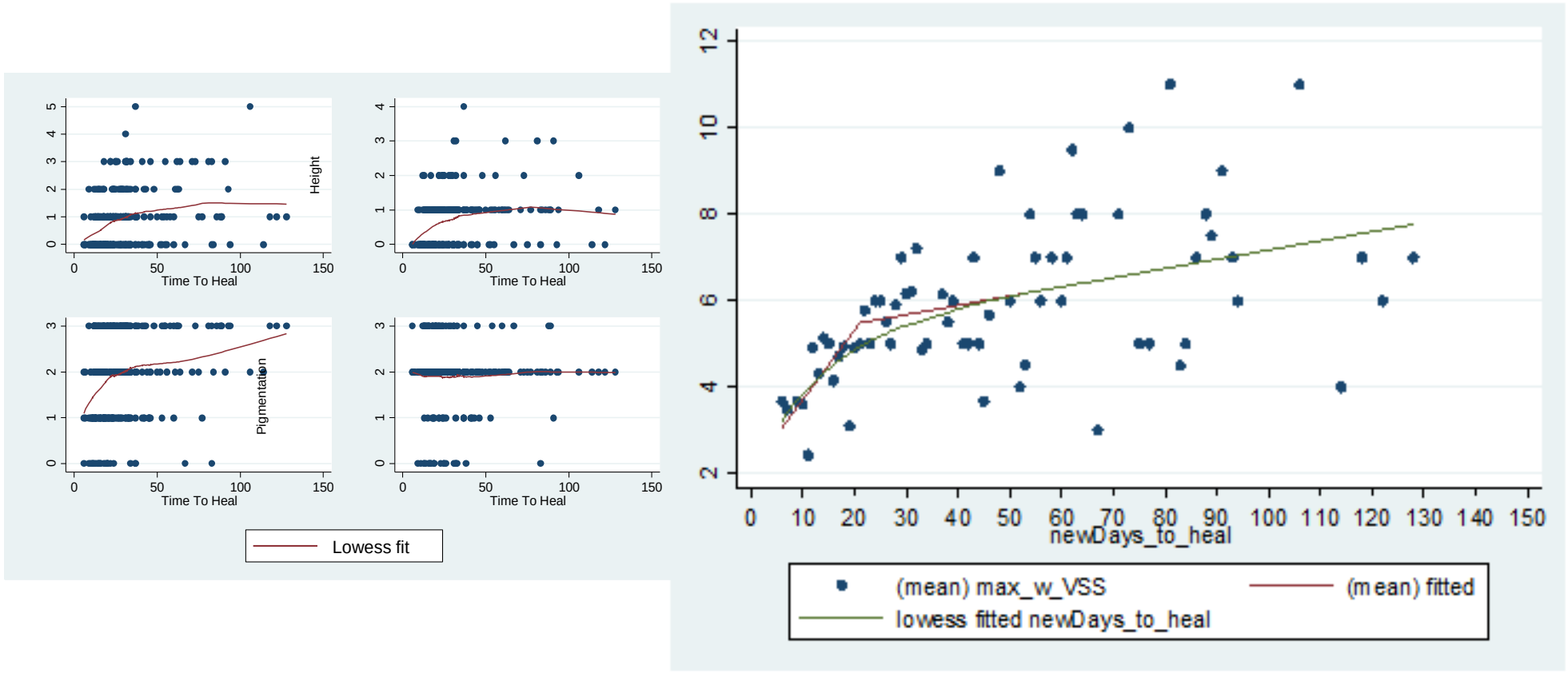
Time to Healing



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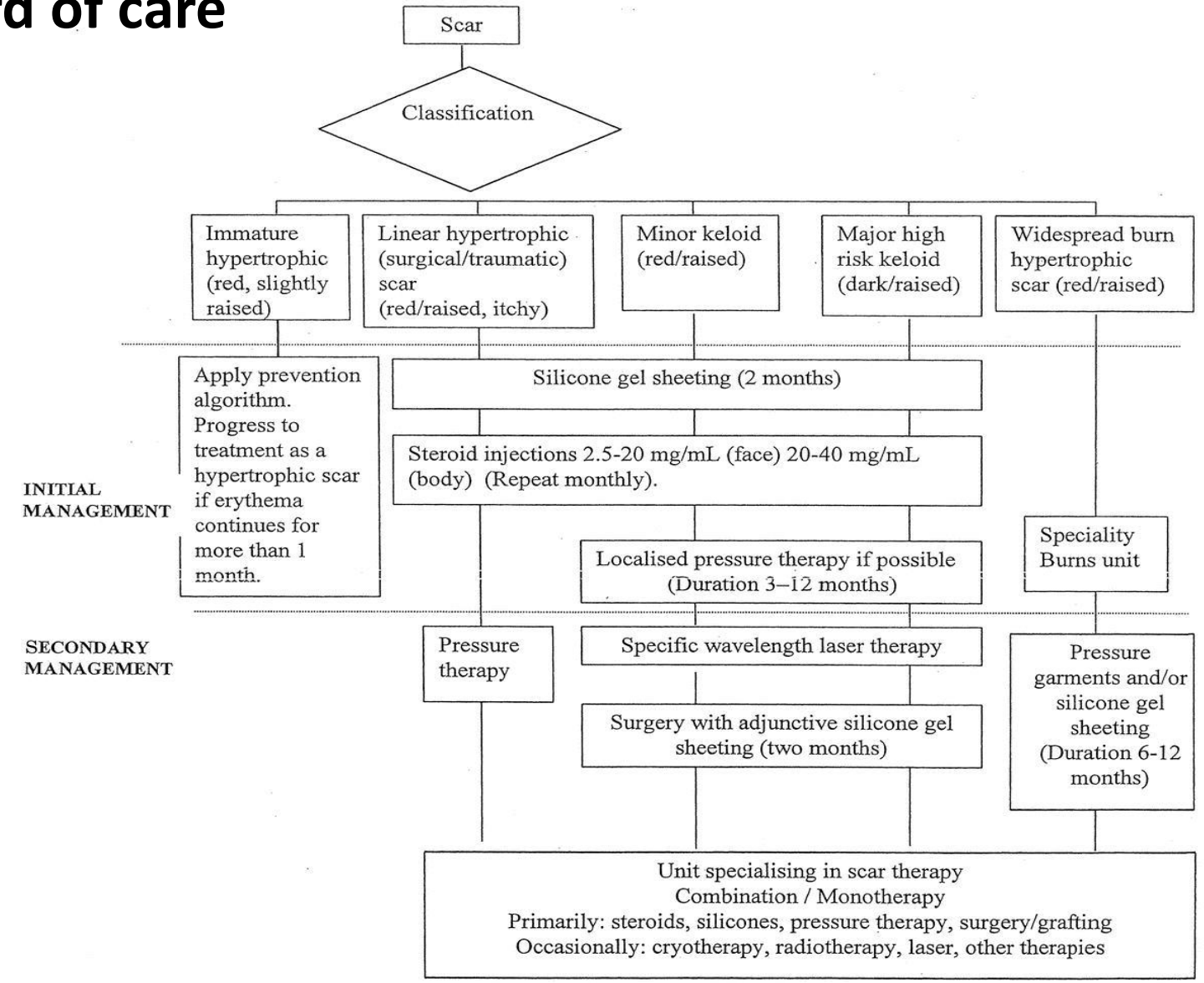
L Martin, M Byrnes, S McGarry, F Wood. Social challenges of visible scarring after severe burn injury: A qualitative analysis. Burns, Aug 2016.

Current standard of care



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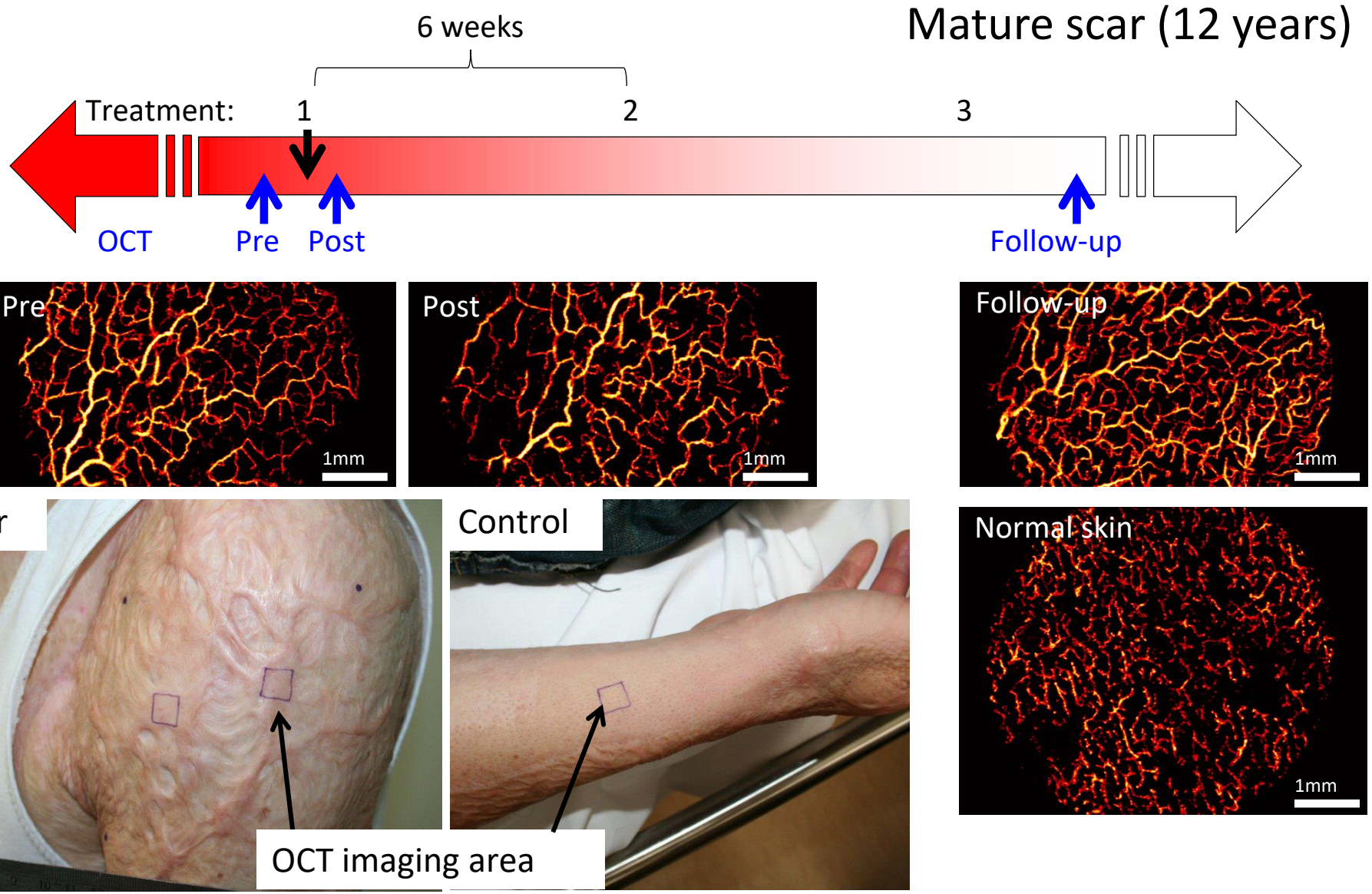
Assessing CO_2 fractional laser ablation



Gong P, McLaughlin, R.A., Liew, Y.M., Munro, P.R., Wood, F.M., Sampson, D.D Photonics

Unmet need and current clinical development pipeline

- Regeneration V repair cellular processes, control of the ECM to drive a regenerative phenotype and reduce scarring in the acute phase
- Scar control, enhance scar reduction over time
- Integration of new tissue into recipient area controlling the scar processes

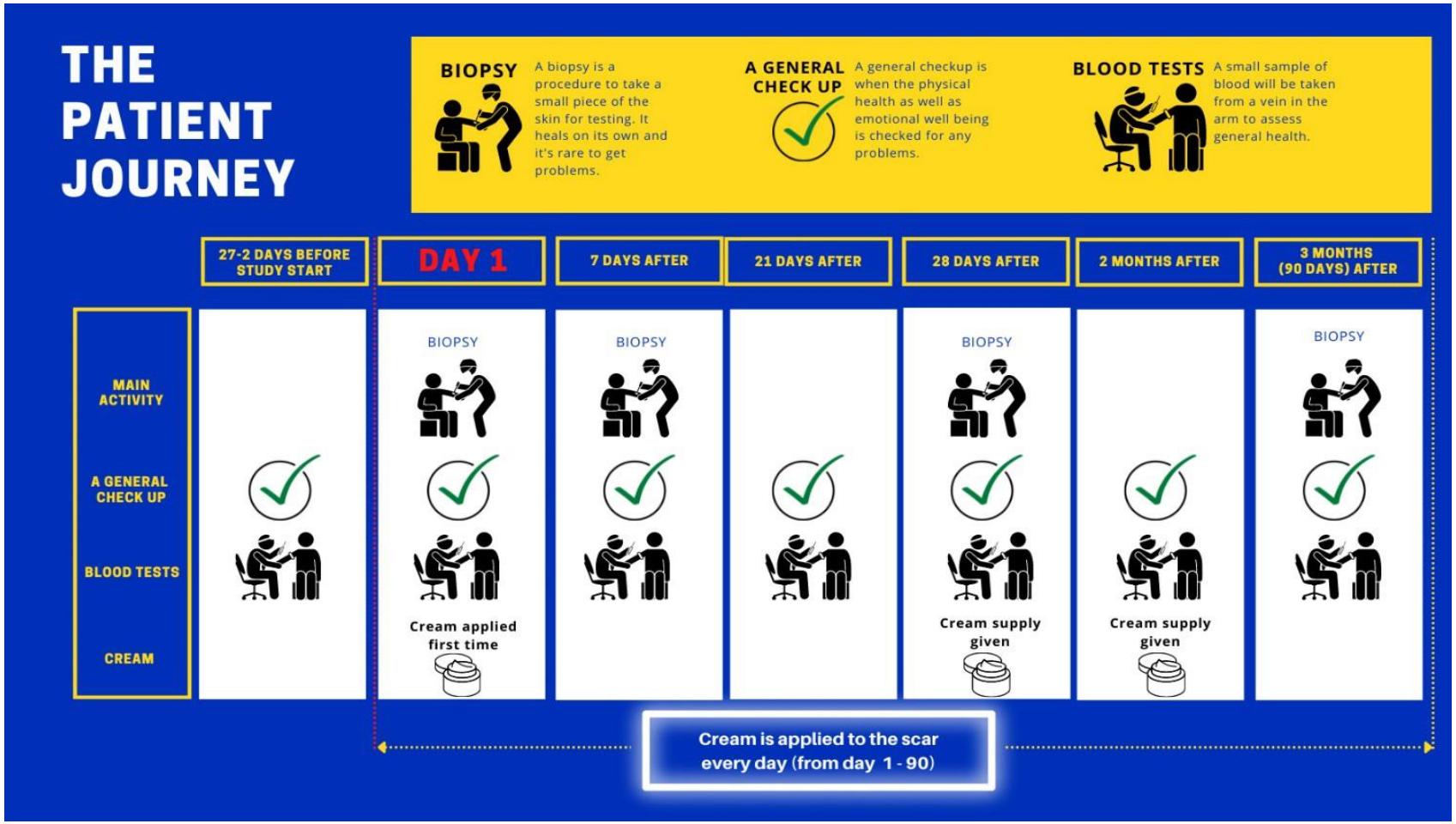
Solaria 2 Trial Outline –PART I

Population

Patients with established scar >10cm^2 area. 18-60 years old

Cohort 1

8 patients receive 2% PXS-6302 cream. Applied once daily to 10cm^2 area of scar (self-administered).



Solaria 2 Trial Outline – PART I

Cohort 2

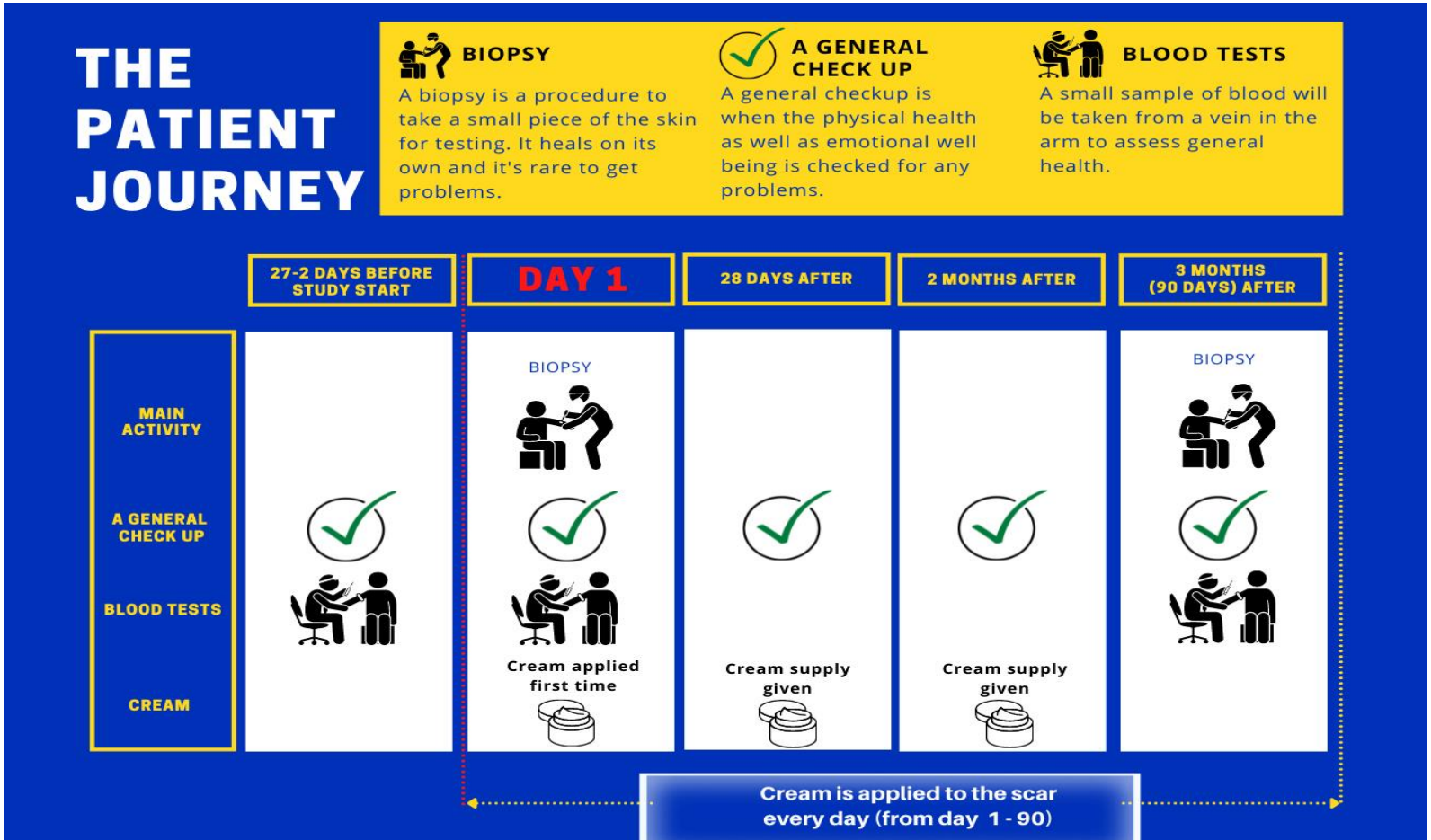
42 patients.

Patients randomized into two groups (placebo or PXS-6302 cream). Applied once daily to 10cm^2 area of scar (self-administered)

Samples collected at day 1 (commence treatment), 3 months only (final treatment)

Outcome measures: Primary - Safety – Adverse events

Secondary: Image assessment, POSAS, ultrasound, histology



Solaria 2 Trial Outline – PART II

Improving healing after a burn injury

Patient population

Adult with non-severe burn injury - Recruited at 2-3 weeks post-injury

Study design
RCT with placebo or treatment cream

3 months – once per day treatment

Outcome measures
Primary: Adverse events

Secondary: 3D scar scans, POSAS, ultrasound, histology, requirement for secondary intervention for scar (^{eg} laser therapy)


Q&A

pharmaxis

developing breakthrough treatments for fibrosis and inflammation

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