Unlocking Therapeutic Potential in Fibrosis

NXP002 Pathway and translation update, September 2025

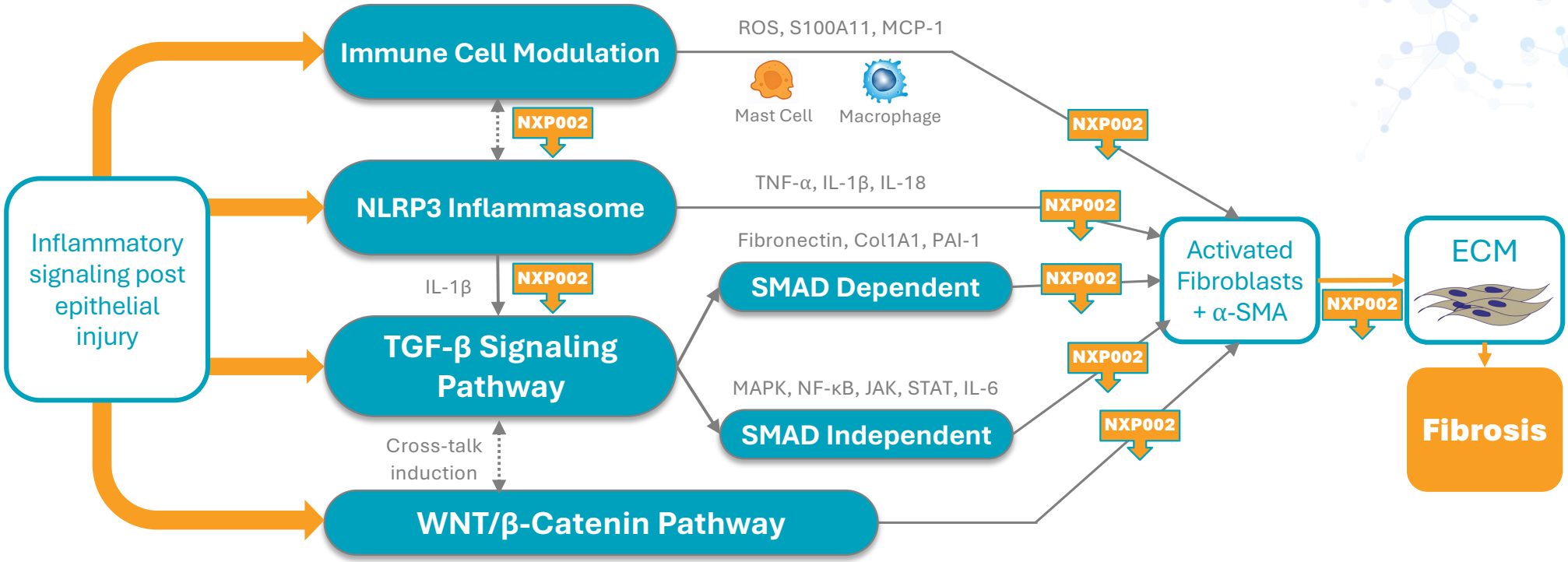
Lessons learnt from 10 years of intense R&D in IPF:

Future therapies should be…

- ✓ **Inhaled:** *IPF = fibrosing alveolitis (∴ treat disease from where it originated and propagates)*
  - Developability, avoidance of DDIs, avoidance of systemic AE's, allow healthy tissue repair, increased efficacy…
  - Maximise patient access (e.g. early-stage patients who currently decline SoCs) and minimise discontinuation
  - Growing clinical evidence of patient preference and efficacy
- ✓ **Pleiotropic/poly-pharmacology:**
  - IPF is not a single target disease (multiple co-activated pathways)
  - Must modulate multiple master disease mechanisms (fibrosis and inflammation)
- ✓ **Additive/synergistic with Standards of Care:**
  - 50% of patients cannot tolerate SoC – genericization unlikely to change this
  - Leverage benefits of SoC's where tolerated, bringing additivity and synergy
- ✓ **Potential to reverse disease/restore tissue function**
- ✓ **Clinical proof of concept established in fibrotic indications across multiple organs**

Poly-pharmacology: Compelling evidence for NXP002's utility

Modulation of immune cells, WNT/β-Catenin and NLRP3 pathways in parallel to core TGF- β signal suppression



Collectively NXP002 provides multi-nodal regulation of fibrosis via core and emerging pathways

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Clinical Translation: Antifibrotic efficacy across multiple organs

	Skin*	Heart	Lung*	Kidney	Liver
Cell & Tissue Models	**Scar Fibroblasts** ✓ ↓ Collagen I, Collagen III, α-SMA, Fibronectin & CTGF **Scleroderma F'blasts** ↓ Collagen, TGF-β	**Cardiac Fibroblasts** ✓ ↓ Collagen I, Collagen III, α-SMA, Fibronectin & CTGF **Pluripotent Stem Cells** ↓ WNT signaling	**Fibroblasts** ✓ ↓ proliferation & myofibroblast transition **A549** ↓ TGF-β ECM markers	**Rat Mesangial Cells** ✓ ↓ H-proline **Cortical Fibroblasts** ↓ CTGF mRNA & pSMAD2	✓ **Human PCLS** ↓ Col1A1 and MCP-1 following LPS & TGF-β1+ PDGF-ββ stimulation
Animal Models	**Rosacea-like Mice** ✓ ↓ TNF-α, IL-6, IL-1β, IL-18 β1 ↓ TGF-β1/Smad2/3 **Burn Injury (Rat)** ↓ Collagen, TGF-β1/Smad2	**Hypertensive Rat** ✓ ↓ WNT/β-Catenin and TGF-β signaling **AMI Mouse** ↓ IL-1β, M1→M2 phenotype	**Bleomycin (old rat)** ✓ ↓ fibrosis, ECM proteins, ROS, lung TGF-β p-SMAD2 **Smoke injury, LPS, OVA...**	**Nephrectomised Rat** ✓ ↓ fibrosis, p-SMAD2 and macrophage accumulation **UUO Fibrosis (Rat)** ↓ TGF-β, p-SMAD2 & EMT	**Dietary NASH (Rat)** ✓ ↓ TGF-β, procollagen, PAI-1 **Parasitic Fibrosis (Rat)** ↓ Collagen, plasma TGF-β1 ↑ Liver function
Clinical Studies	**Scleroderma** ✓ ↓ Deep dermal fibrosis & refractory lesions **Acne/Surgical Scarring** ↑ Scar appearance	✓ **Heart Failure** ↓ Worsening of cardiac functioning in muscular dystrophy patients	**Lung Fibrosis** ✓ ↓ Fibrotic tissue (CT) ↑ Restored FVC **ARDS/COVID-19** ↓ Mortality by 75%	**Kidney Fibrosis** ✓ ↓ Collagen IV ↓ Advanced nephropathy progression ↓ Tubulointerstitial fibrosis	
Pathways	TGF-β/SMAD NLRP3 Inflammasome	WNT/β-Catenin TGF-β/SMAD NLRP3 Inflammasome	TGF-β/SMAD NLRP3 Inflammasome Immune Cell Modulation	TGF-β/SMAD NLRP3 Inflammasome	TGF-β/SMAD NLRP3 Inflammasome

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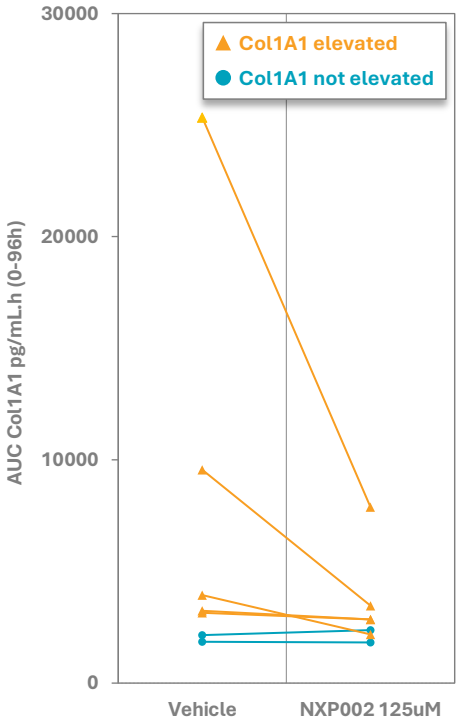
*approved for use in diseases affecting these organs

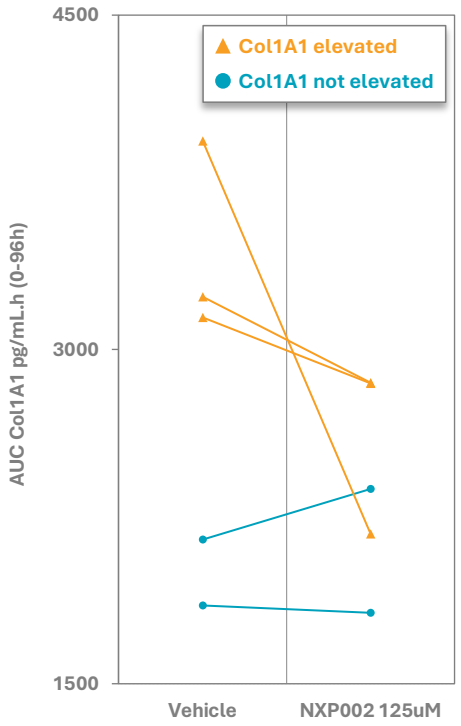
NXP002: Fibrosis regulation in 7 IPF patient lung tissue donors

Col 1A1: All 7 donors:



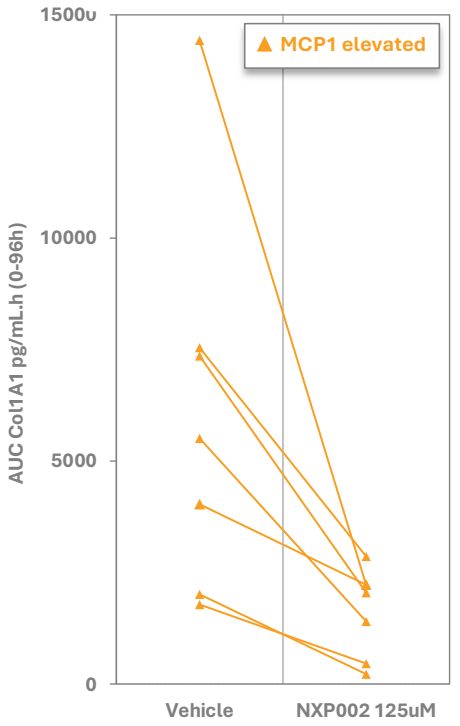
- NXP002 significantly attenuates Col1A1 where elevated.
- Col1A1 elevation in 5 donors – tissue turnover on-going & inhibited by NXP002.

Zoom: Low Col1a1 donors:



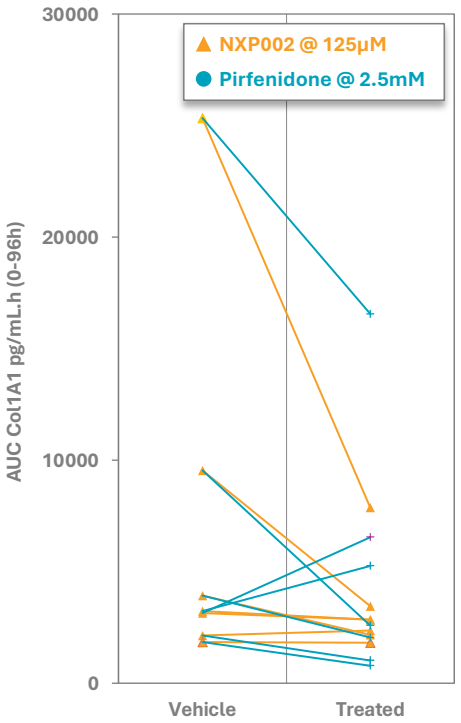
- Col1A1 is not elevated in 2 patients ∴ cannot be attenuated by NXP002.
- NXP002 may regulate fibrotic disease; limits progression yet allows healthy healing.

MCP-1: All 7 donors:



- MCP-1 linked with pro-fibrotic tissue environment – expected for late stage IPF
- MCP-1 is elevated in all donors & significantly attenuated by NXP002 (↓ ECM)

Col1A1: Vs. Pirfenidone



- Pirfenidone shows less significant & consistent Col1A1 attenuation vs NXP002.
- Pirfenidone attenuates Col1A1 when not over-expressed (impact on healthy healing).

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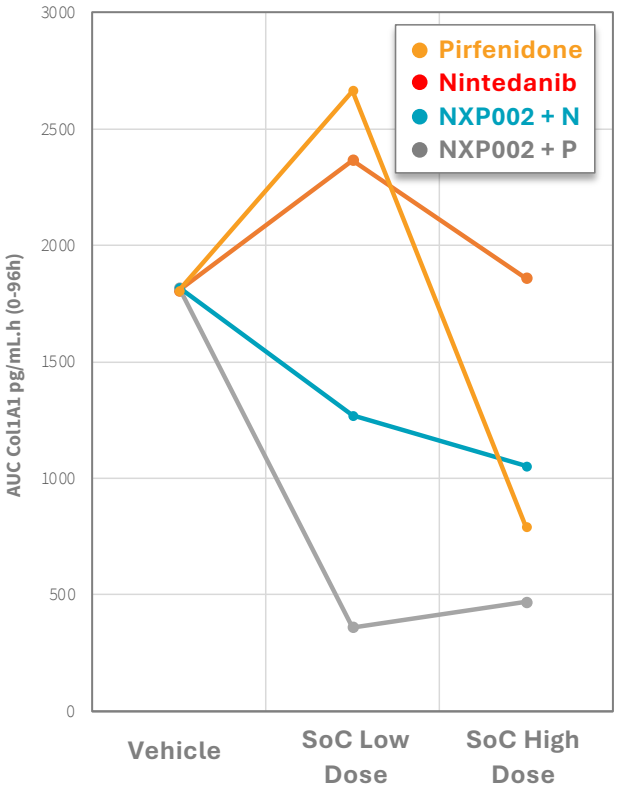
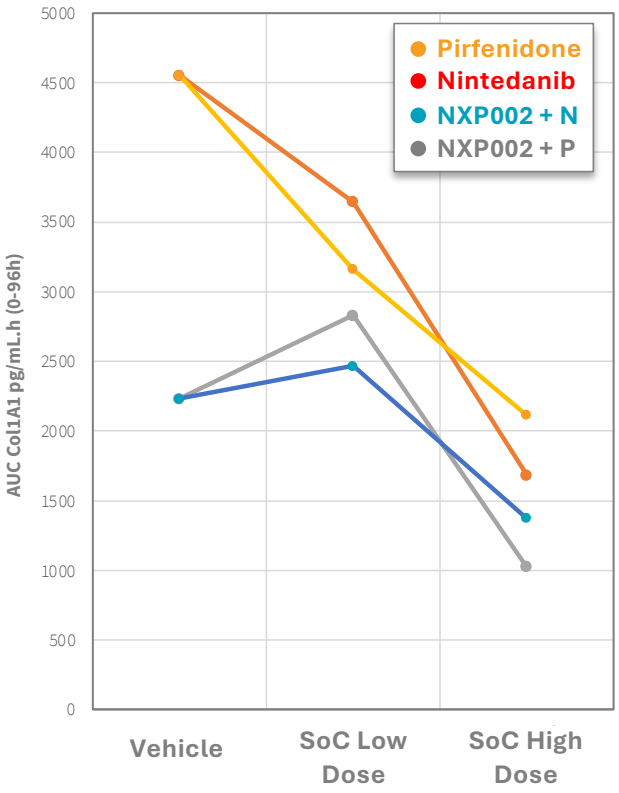
NXP002: Synergy/additivity in combination with SoC's

SoC Combination IPF Donor 1:



SoC Combination IPF Donor 2:



Result:

- NXP002 125µM SoC combinations always achieve superior attenuation of Col1a1 versus NXP002 or SoCs alone.
- Similar result achieved for other fibrosis biomarkers (e.g. fibronectin) and biomarkers related to inflammation and a pro-fibrotic tissue environment (e.g. MCP-1).
- Further data demonstrates NXP002 acting via additional pathways to SoCs.
- These results may support dose-sparring of oral SoCs for patients managing their AEs.

Conclusions and next steps

NXP002 satisfies multiple key criteria for further development in fibrotic ILDs:

- ✓ **Inhaled:** *Now a validated and attractive treatment option for IPF and PPF*
- ✓ **Poly-pharmacology:** *Clear evidence for regulation of multiple validated and emerging pathways in fibrosis*
- ✓ **Compelling translational evidence base:**
  - *Multiple tissue/disease studies demonstrate consistent results across multiple institutions*
  - *Complimentary to and consistent with Nuformix proprietary data*
  - *Clinical proof of concept established in multiple fibrotic conditions, including lung, providing confidence in a challenging therapeutic area*
  - *Includes clinically proven potential to reverse disease/restore tissue function*
- ✓ **Additive to SoCs:** *Synergistic pathway suppression, increasing efficacy*
- ✓ **Orphan and long-term IP position in place:** *EMA ODD in place – FDA decision Nov' 25. IP granted.*

Objectives: Establish a long-term development partner now to access specialist clinical development expertise with flexibility on partnering terms.