Gyre THERAPEUTICS

Developing **Anti-Fibrotic Therapeutics** for Chronic Organ Diseases

January 2026

Forward Looking Statements

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Gyre Therapeutics (Nasdaq: GYRE): At a glance

1ST

to receive **IPF[1] treatment approval** (pirfenidone) in **China** (2011):

Pioneering fibrosis treatment with a track record of success

#1

IPF market share in China for **10 consecutive years[2]**

(~50% IPF market share, 90% + share in pirfenidone in 2024)

~ 600

dedicated global employees:

~ 400 commercial team across **China** and the **U.S.**
~ 70 focused on **R&D**

150,000 +

IPF patients treated with **pirfenidone**

3,000+

hospitals and pharmacies covered in **China** across **870+ cities**

EBITDA positive

since 2017[3], while revenue grew at **~32%** compounded annual growth rate **(CAGR)[3]** during the same period

2023 Revenue	**$113.5M**
2024 Revenue	**$105.8M**

2 state-of-the-art, **GMP compliant manufacturing** facilities built for growth in China, currently running at **40%** and **18%** capacity

1. IPF = Idiopathic Pulmonary Fibrosis.
2. Per IQVIA CHPA.
3. Financial data inclusive of pro forma data prior to GNI Group and Catalyst Biosciences business combination for comparison purposes only.

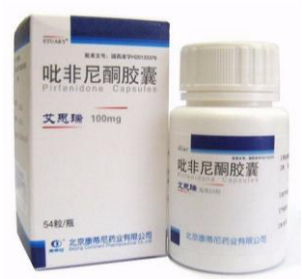
Innovative fibrosis focused development pipeline with sentinel indications in liver and lung

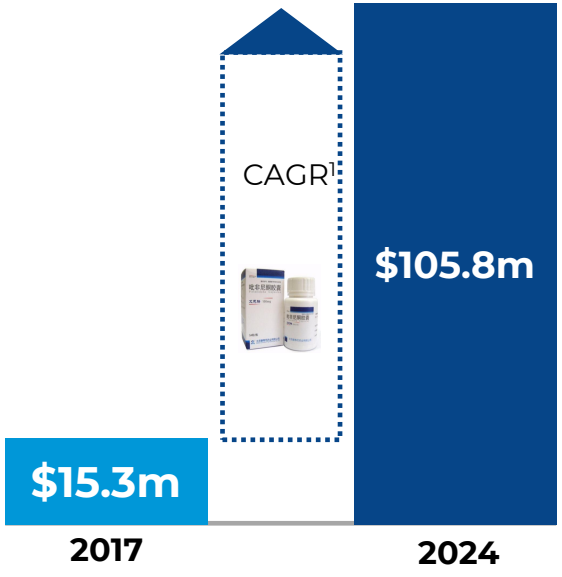
Gyre THERAPEUTICS

CANDIDATE	INDICATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	MARKETED	RIGHTS	TRIAL
F351 (hydronidone)	Advanced Liver Fibrosis	IND preparation in progress ★					Global	
	Chronic Hepatitis B (CHB) Liver Fibrosis							First
F573	Acute Liver Failure / Acute-on-Chronic Liver Failure							
F230	Pulmonary Arterial Hypertension (PAH)							
F528	Chronic Obstructive Pulmonary Disease (COPD)							
ETUARY (pirfenidone)	Idiopathic Pulmonary Fibrosis (IPF)						China	First
	Radiation-induced lung injury (RILI) with or without immune-related pneumonitis (CIP)	4Q 2025: Start Phase 2/3 Trial		(Adaptive Approach)				
	Pneumoconiosis (PD)	4Q 2025: Complete enrollment						
	Diabetic Kidney Disease (DKD)							

Strategic moves to strengthen our pirfenidone franchise and prepare for potential future Hydronidone launch

ETUARY® (pirfenidone)[1]





Etorel - Launched in 2025

Contiva – Launched in 2025

Expanding Our IPF Market:

Gyre's **ETUARY** has **dominated China's IPF market.** Through the strategic acquisition of a generic Etorel (nintedanib), we further strengthen our leadership by offering physicians a full spectrum of IPF treatments.

Securing a Foothold in Liver Disease

We acquired rights to a generic **Contiva (avatrombopag)** as a strategic entry point into the liver physician network—paving the way for the future **launch of Hydronidone.**

ETUARY was approved in 2011 before the Reference Listed Drug (RLD) requirement. Without RLD, generic competitors can not conduct the required bioequivalence (BE) studies. This creates a market exclusivity beyond patent protection.

Financial data inclusive of proforma data prior to GNI Group and Catalyst Science merger for comparison purposes only.

Note: 2017 sales number is audited (China) and 2024 is audited (U.S. GAAP). See Note 2 above for further clarification.

Phase 3 CHB-associated liver fibrosis - recently announced positive topline results

1

Primary Endpoint Met with High Statistical Significance

≥1-stage fibrosis regression at **Week 52**: Hydronidone: **52.85%** vs. Placebo: **29.84% (P = 0.0002;** ITT[1] analysis with central blinded pathology review)

2

Key Secondary Endpoint Achieved

≥1-grade inflammation improvement without fibrosis progression at Week 52: Hydronidone: **49.57%** vs. Placebo: **34.82%** (P = 0.0246)

3

Favorable Safety & Tolerability Profile

- Serious Adverse Events: **4.88%** (6/123, Hydronidone) vs**. 6.45%** (8/124, Placebo)
- **No discontinuations** due to adverse events

4

Clinical and Regulatory Pathways

- Breakthrough Therapy Designation (China NMPA[2] , 2021), potentially **first-in-class approval**
- **New Drug Application** (NDA) to **NMPA** expected in **Q3 2025,** with accelerated approval to be sought
- **U.S. IND** filing for **advanced fibrosis** expected in **2025**; trial initiation planned pending regulatory review

ITT = Intent-To-Treat. 2. NMPA = National Medical Products Administration of China

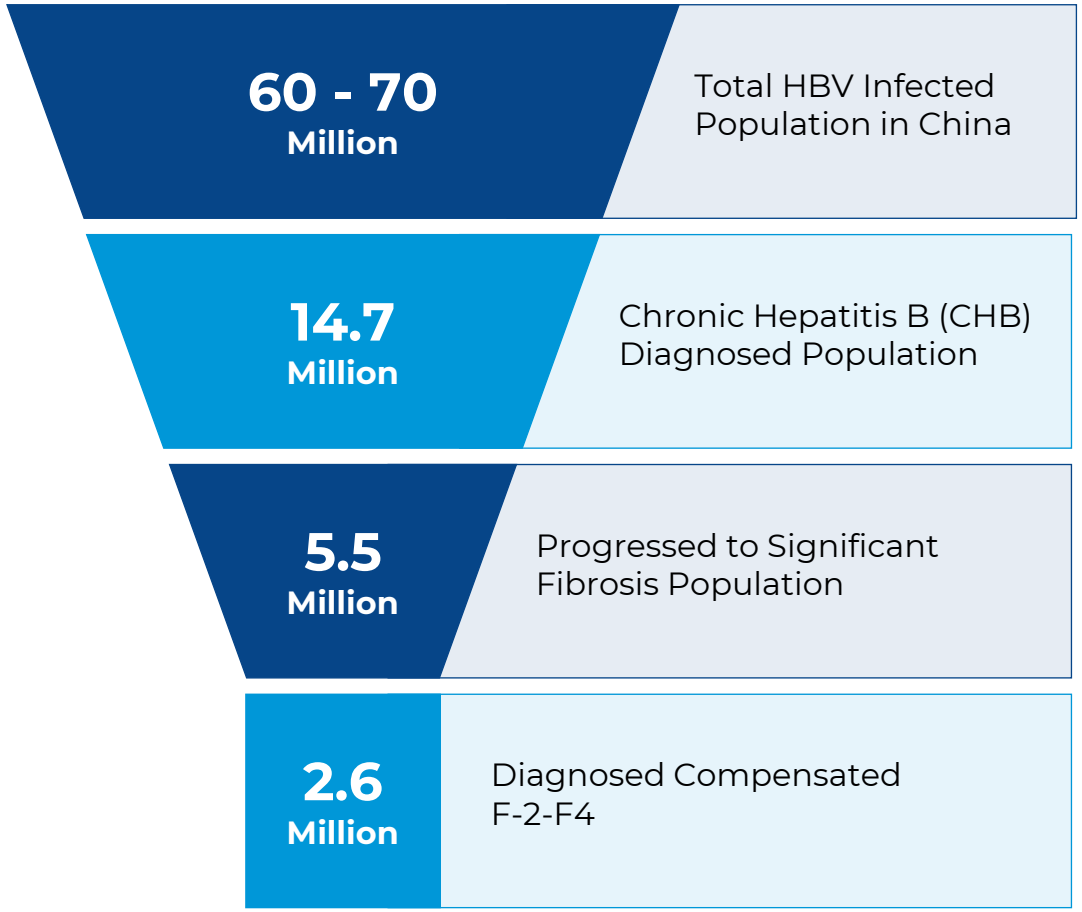
Phase 3 Safety Profile

Safety Event	Hydronidone (N=123)	Placebo (N=124)
Any TEAE	98 (79.67%)	103 (83.06%)
Grade 1 AES	27.64%	33.06%
Grade 2 AES	43.90%	43.55%
Grade ≥3 AES	8.13%	6.45%
Drug-related AEs (ADRs)	32.52%	33.87%
Grade ≥3 ADRs	1.63%	1.61%
Discontinuation due to AE	0	0
Temporary interruption due to AE	0	0.81%
Dose reduction due to AE	0	0
Any SAE	6 (4.88%)	8 (6.45%)
Due to Investigational Drug:		
Possibly unrelated	2	3
Unrelated	4	5
Death	0	0

All SAEs were assessed to be **unrelated to Hydronidone**

No discontinuations due to SAEs across either treatment arm.

Hydronidone targets CHB fibrosis -- a high-need and untapped market in China



Initial Target

The market for **CHB-associated liver fibrosis** is significantly **unmet.**

Current standard of treatment, e.g. entecavir, tenofovir, focuses on only **reducing liver inflamation**.

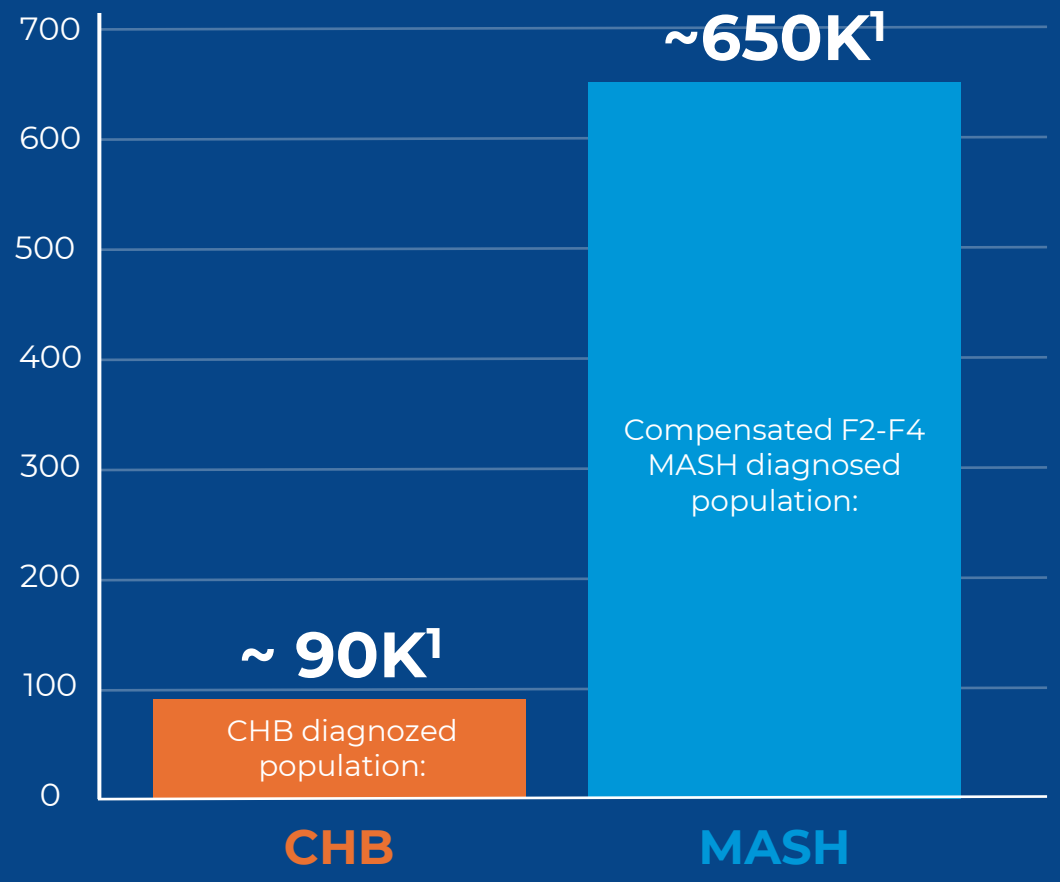
Patients with **F2 - F4** fibrosis are at a **high risk of progression** to **cirrhosis** and **HCC**, major causes of liver-related mortality.

Hydronidone, a structural analog of pirfenidone, reverses fibrosis by modulating **TGF-β / p38γ / Smad7** signaling pathway — a key driver of fibrosis progression. It received **Breakthrough Therapy designation** from PRC's NMPA in 2021, enabling expedited review.

Note: The Fourth National Serological Survey on HBV in China (2020) provided baseline HBV prevalence data. The 60-70M total HBV cases and F2-F4 fibrosis estimates are derived using internal modeling based on this survey's fibrosis prevalence rates and awareness levels.

Expanding Hydronidone's potential: from CHB fibrosis in China to MASH in the U.S.

CHB vs. **MASH** Liver Fibrosis Population in the U.S.(000s)



Market Opportunity

In the U.S., the MASH fibrosis market is approximately **7.2 times larger** than the CHB fibrosis market.

Clinical Rationale

Hydronidone modulates **TGF-β / p38γ / Smad7** signaling pathway — directly targeting fibrosis progression and **offering a differentiated approach from metabolic agents**.

Regulatory Pathway

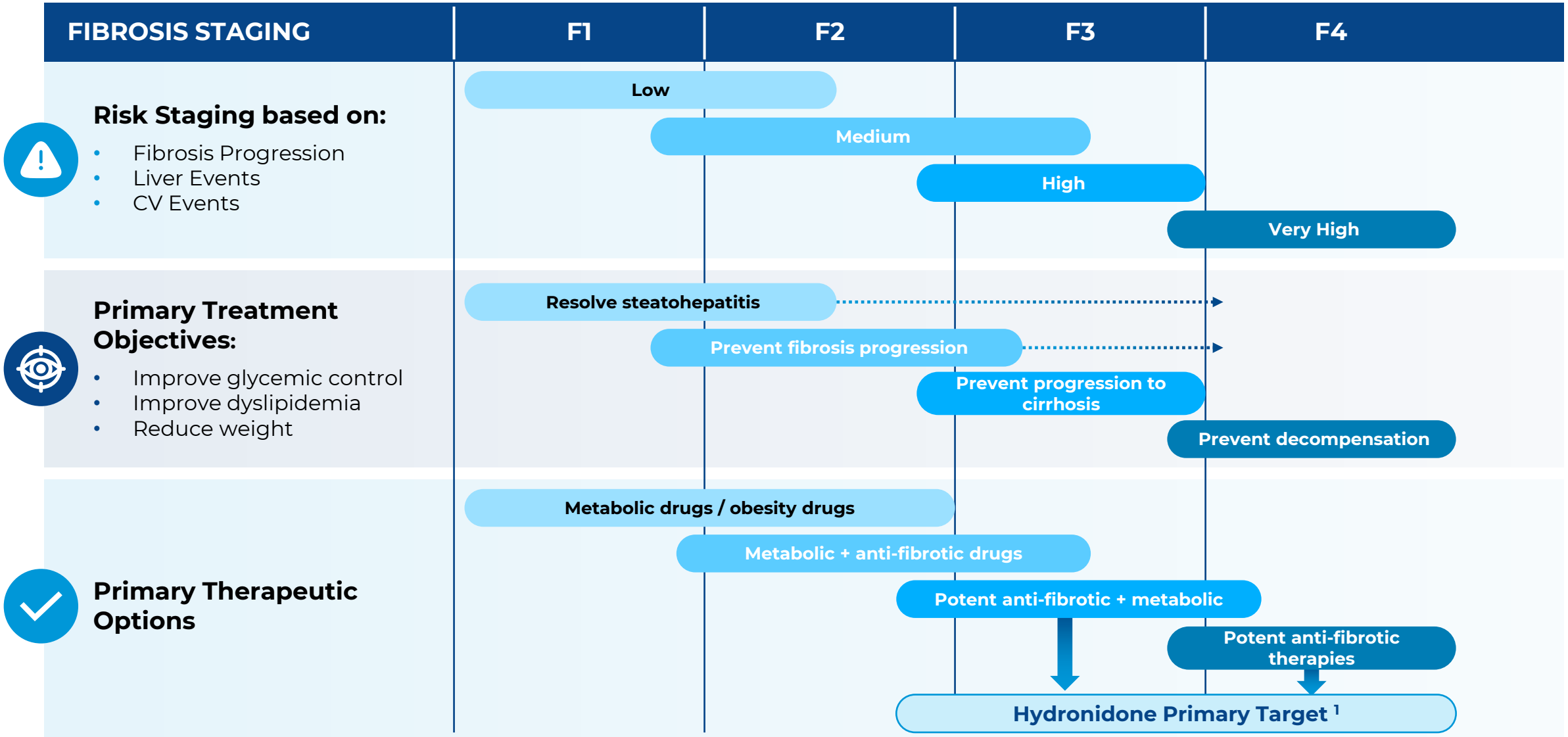
Hydronidone's CHB data **helps to reduce risks in MASH development** and potentially supports *accelerated regulatory review and fast track*.

Competitive Differentiation

Hydronidone's unique anti-fibrotic approach positions it as a **complementary therapy** — not a competitor — to metabolic agents like THR-β, GLP-1s, and FGF21.

1. Based on analysis of third-party epidemiological research, published academic studies, and internal modeling.

Hydronidone Targets Fibrosis Specifically for Advanced MASH



1. We estimate ~650K compensated F2–F4 MASH patients in the U.S., based on market data and internal modeling.

What makes Gyre different ?

Strong Pipeline

Our lead asset, F351 (Hydronidone), has the potential to become a **first-in-class therapy** for CHB-related liver fibrosis, addressing a significant unmet medical need in China.

Robust pipeline spanning various clinical stages focused on treating organ diseases.

Efficient R&D Strategy

China-first validation strategy leveraging faster patient enrollment and cost efficiency, followed by expansion into the U.S. helps mitigate clinical and regulatory risks.

Hydronidone U.S. IND filing for advanced fibrosis expected in 2025, trial initiation planned pending regulatory review.

Proven Commercial Execution

Maintaining market leadership since the commercialization of first-in-class pirfenidone in 2014, with extensive and effective nationwide commercial coverage in China across more than 3,000 hospitals and pharmacies.

Fully Integrated Platform

Comprehensive in-house capabilities covering discovery, clinical development, regulatory affairs, manufacturing, and commercialization.

Two GMP-compliant manufacturing facilities are strategically located to support robust expansion.

1. IPF = Idiopathic Pulmonary Fibrosis. 2. Per IQVIA CHPA. 3. Financial data inclusive of pro forma data prior to GNI Group and Catalyst Biosciences business combination for comparison purposes only.

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Thank you

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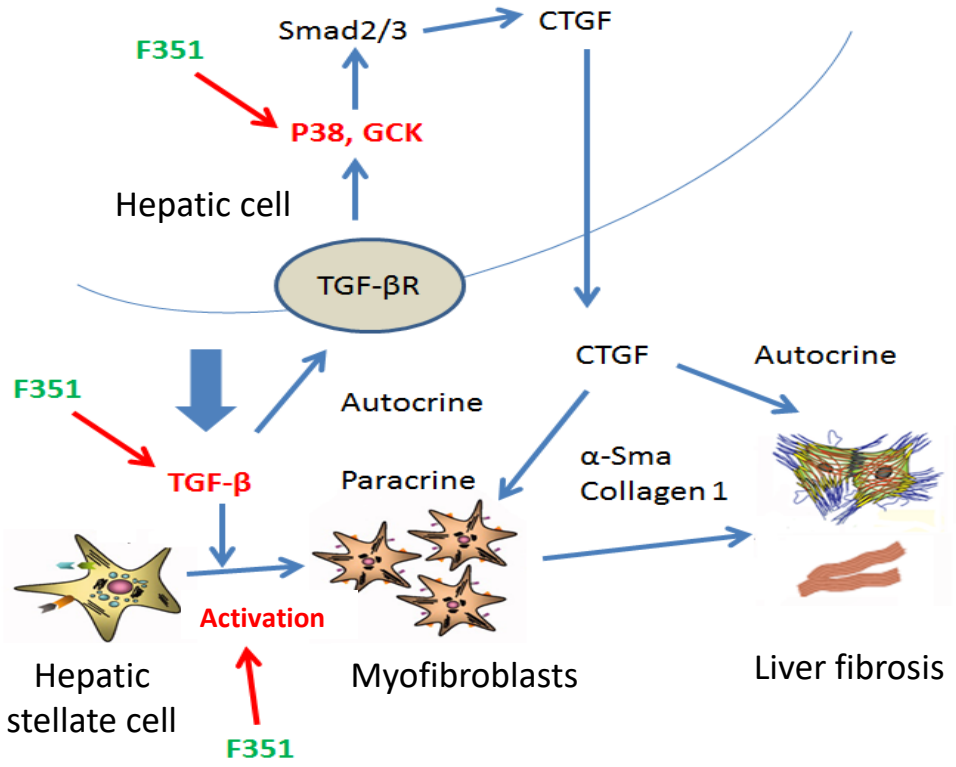
Comparison of Hydronidone and Pirfenidone metabolism

Liver Injury → TGF-β ↑ triggers multiple fibrosis pathways:
1. → p38γ → HSC Activation → α-SMA ↑ → ECM Accumulation → Fibrosis
2. → Smad2/3 (phosphorylation) → Fibrosis
3. ⊣ Smad7 (inhibitory) → Upregulation of TGF-beta signaling → Activation of both p38gamma and SMAD2/3 cascades



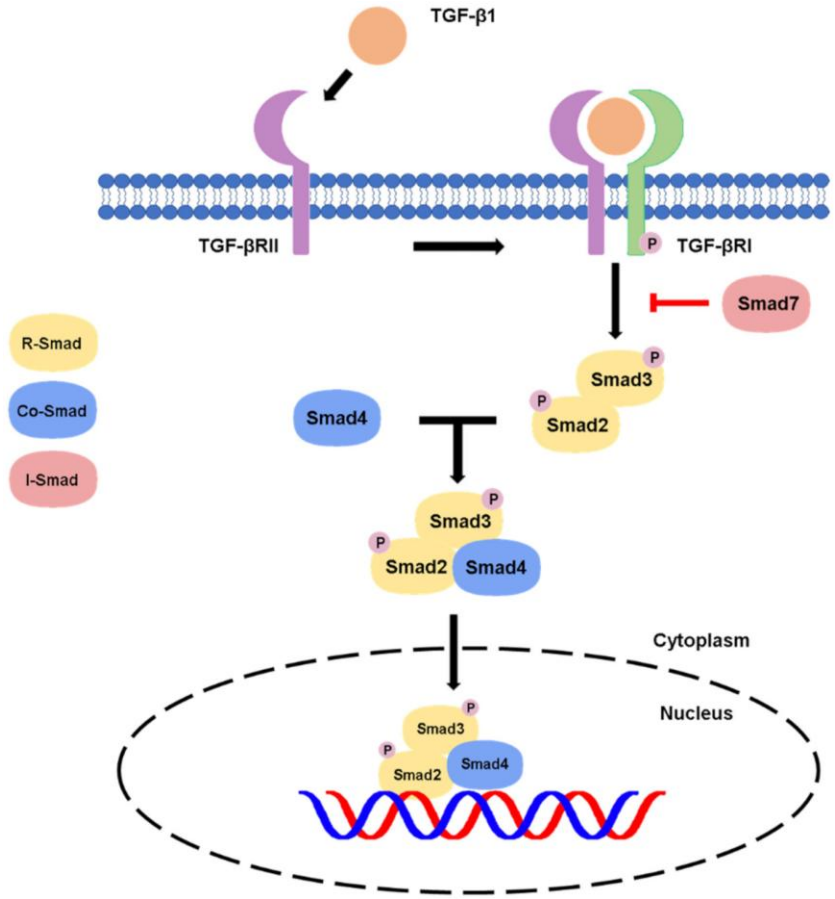
As a key profibrotic cytokine, TGF-β drives hepatic stellate cell (HSC) activation, promotes extracellular matrix (ECM) deposition, and triggers fibrogenesis.

The p38γ isoform plays a pivotal role in TGF-β-stimulated collagen production. Hydronidone attenuates fibrosis, at least in part, by targeting the p38 MAPK transduction pathway.

During hepatic injury, TGF-β upregulation triggers hepatic stellate cell (HSC) activation and differentiation into myofibroblasts. This phenotypic transformation is characterized by cytoskeletal remodeling, including α-smooth muscle actin (α-SMA) expression, which serves as a specific marker for myofibroblasts and the onset of fibrogenesis.

Extensive preclinical and clinical studies indicate that activated myofibroblasts with elevated α-smooth muscle actin (α-SMA) expression serve as the dominant producers of fibrillar collagen and key ECM proteins, thereby driving hepatic fibrogenesis.

TGF-β plays important role in liver fibrosis by activating HSCs

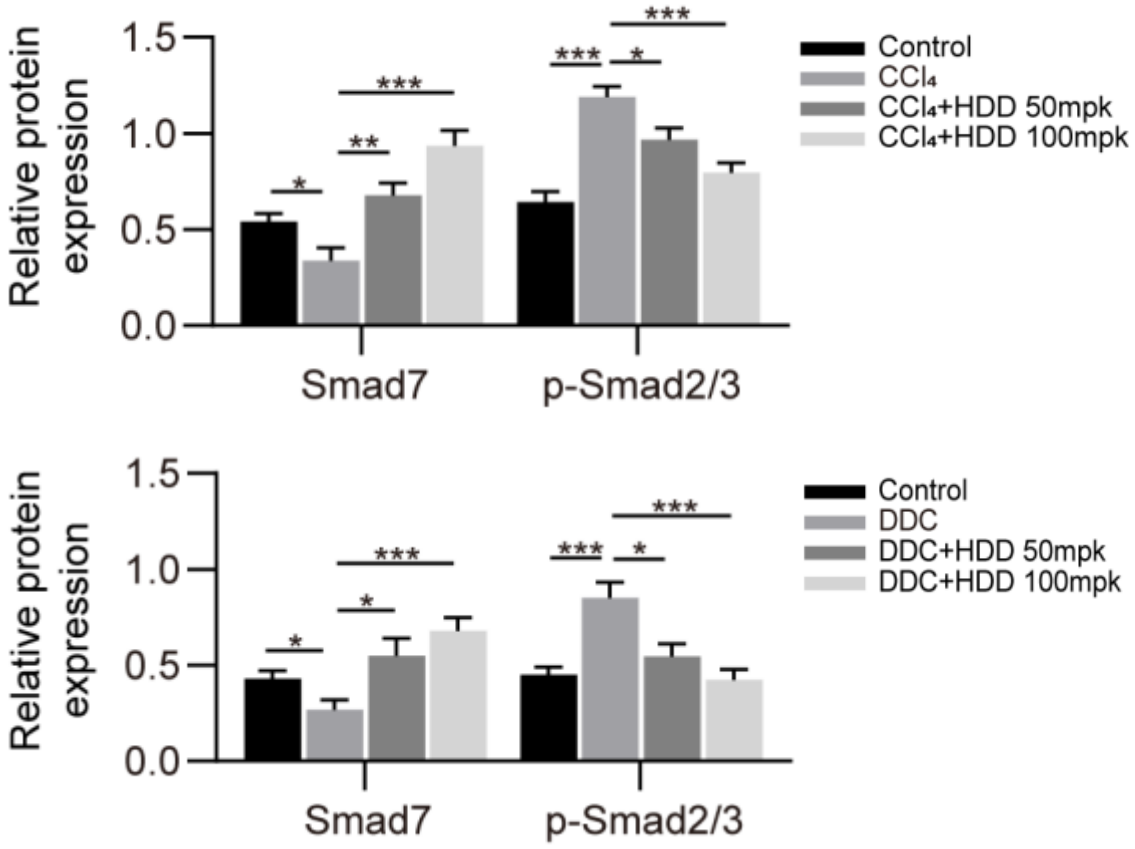


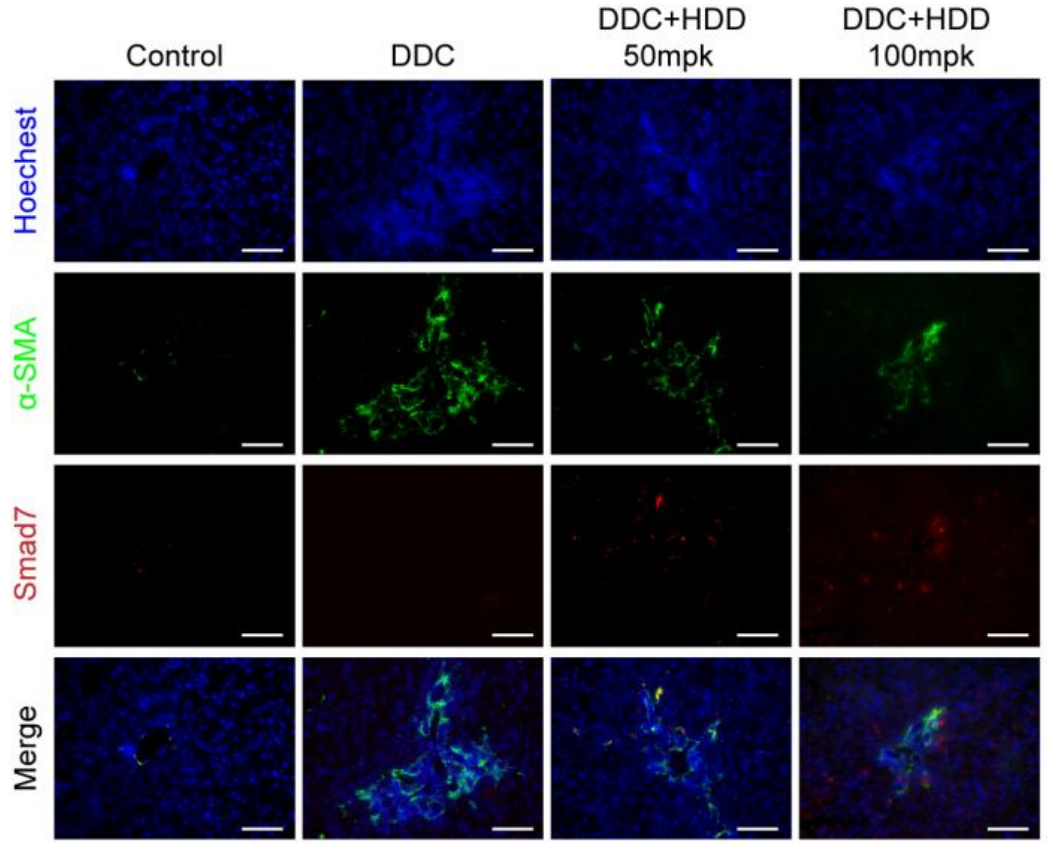
- Smad7 is a negative regulator of TGF-β signaling.
- Smad7 knockdown can promote HSC activation and liver fibrosis.
- Smad7 overexpression can prevent liver fibrosis.
- **Hydronidone is believed to effectively target this pathway.**

Inhibiting HSC activation is believed to be one of the most effective therapeutic strategies to fight liver fibrosis

1. Xu, Xianjun et al. “Hydronidone ameliorates liver fibrosis by inhibiting activation of hepatic stellate cells via Smad7-mediated degradation of TGFβRI.” *Liver international : official journal of the International Association for the Study of the Liver* vol. 43,11 (2023): 2523-2537. doi:10.1111/liv.15715

Animal studies demonstrated Hydronidone upregulated the expression of Smad7 and inhibited phosphorylation of Smad2/3



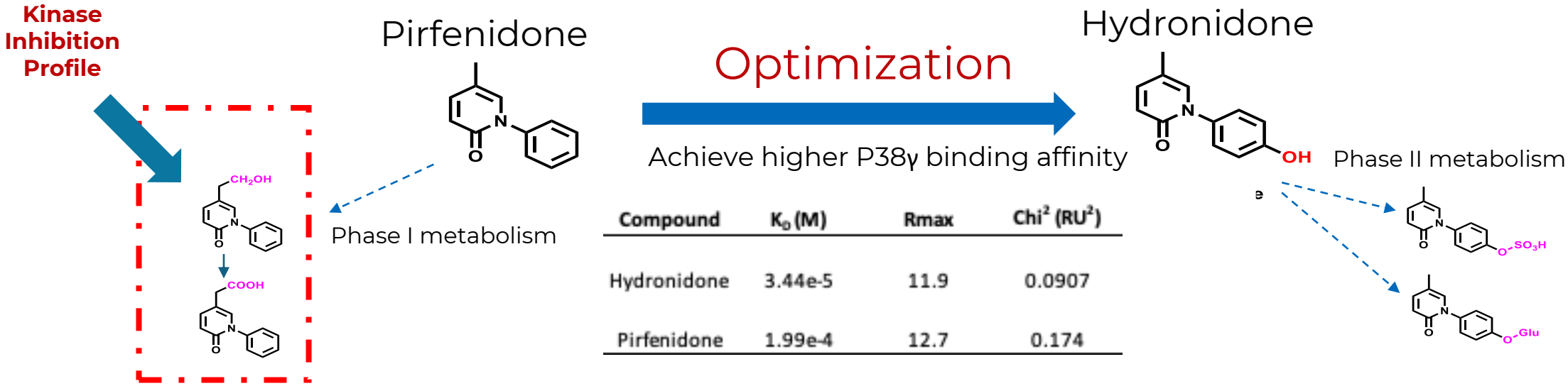


Smad7 is a known negative regulator of liver fibrosis, suggesting clinical potential in a recognized cascade

Note: Statistical significance: *p < .05, **p < .01, *p < .001 (one-way ANOVA with post hoc tests). Data from Xu et al., Liver International (2023), 43(11): 2523–2537. doi:10.1111/liv.15715.

Hydronidone vs. Pirfenidone: Mechanistic and safety advantages

- The introduction of a hydroxyl group shifts its metabolic profile from Pirfenidone's dominant Phase I oxidation to preferential Phase II conjugation (M3/M4 metabolites). Phase II metabolism, known as "detoxification metabolism," can prevent the formation of active metabolites and covalent binding to proteins, suggesting a mechanistic basis for hydronidone's improved hepatic safety profile compared with Pirfenidone.



Compound	K_D (M)	Rmax	Chi^2 (RU^2)
Hydronidone	3.44e-5	11.9	0.0907
Pirfenidone	1.99e-4	12.7	0.174

- In vitro kinase assay shows that both hydronidone and Pirfenidone effectively inhibit p38γ activity, with hydronidone exhibiting a higher inhibition potency than Pirfenidone.
- These findings indicate that hydronidone exhibits stronger inhibition of the p38γ pathway, potentially contributing to its enhanced antifibrotic activity.

Hydronidone shaping up to be Pirfenidone 2.0

Feature	Hydronidone	Pirfenidone
Mechanism of Action	Tri-pathway mechanism: inhibits p38γ, upregulates Smad7, and suppresses TGF-β/Smad2/3 signaling	Broadly downregulates TGF-β levels, with less defined pathway specificity
Metabolism	Undergoes Phase II metabolism, known for safer detoxification and fewer reactive byproducts	Primarily metabolized through Phase I oxidation (CYP1A2), which can generate reactive metabolites
Liver Safety	Designed to reduce hepatotoxicity; favorable liver safety profile in trials	Observed increases in liver enzymes in some patients; rare hepatic events documented
Fibrosis Efficacy (in humans)	Shown to reverse fibrosis in 55% of patients with CHB (270 mg group)[1]	Exploratory clinical data in liver fibrosis; not approved for fibrotic liver disease

1. Cai et al. Clin Gastroenterol Hepatol. 2023;21(7):1893–1901. doi:10.1016/j.cgh.2022.05.056

Hydronidone is Purpose-Built on Pirfenidone's Foundation - with Enhanced Potency and Safety

Pirfenidone → [Structural Analog + Hydroxyl Group] → Hydronidone

↓ ↓

Modest Liver Activity ↑ Hepatotoxicity

Enhanced Smad7 Upregulation + Phase II Metabolism[1] → ↓ *Hepatotoxicity* + ↑ Anti-fibrotic Potency

Attribute	Pirfenidone	Hydronidone	Benefit
Structure	Parent compound	Analog with –OH group	↑ Smad7
MoA	TGF-β	TGF-β + p38γ + Smad7	↑ Potency
Metabolism	Phase I (oxidation)	Phase II (conjugation)	↓ Toxicity
Hepatic Safety	Known liver risk	Improved	↑ Tolerability
MASH Evidence	Some benefit (PROMETEO, model)[2]	Strong effect in a validated preclinical model	↑ Rationale

Hydronidone enhances pirfenidone's anti-fibrotic effect by also inhibiting p38γ and upregulating Smad7, improving hepatic safety and supporting its expansion into metabolic liver diseases like MASH.

1. Phase II metabolism is associated with improved hepatic safety due to faster detoxification. 2. González-Huezo M, et al. Real-life proof-of-concept trial of prolonged-release pirfenidone in advanced liver fibrosis (PROMETEO study). Hepatol Int. 2021;15(2):377–388.