

# Corporate Presentation

April 2026

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# Strategic Highlights and Value Drivers

1

## Ipsen's Iqirvo® in PBC: Strong commercial sales<sup>1</sup> trajectory

Major contributor to GENFIT's financial strength (>US\$200M first full year)

2

## MASH Diagnostics: Upcoming momentum from therapeutics

Therapeutics market ~\$1bn first full year, driving demand for LDT and IVD development

3

## GNS561 in CCA: Safety profile and early antitumor activity

Novel combination positioned as a potential new therapeutic approach for difficult-to-treat cancers

4

## G1090N/NTZ in ACLF: Safety profile and anti-inflammatory activity

Solid foundation to progress into proof-of-concept studies across the ACLF Continuum

5

## Ipsen's Iqirvo® in PSC: Phase 3 launched early 2026

Market potential estimates comparable in size to PBC 2L

6

## Other Research and preclinical programs

ACLF Continuum (SRT-015, CLM-022, VS-02-HE, *EViv*<sup>2</sup>) / UCD (VS-01-HAC)

### NEXT STEPS

**Ipsen 1Q26 results**  
(April 23, 2026)

**NASHnext®  
reimbursement**

**Ph1b data** (Mid-2026)  
**Ph2 initiation** (2H26)

**Ph2 initiation** (2H26)  
**Estimated completion** (4Q27)

**Estimated completion** (2031)<sup>3</sup>  
*Long term clinical outcomes*

**Pipeline update** (3Q26)

# 1. Who we are

2. *Iqirvo<sup>®</sup> in PBC & PSC*

3. *MASH Diagnostics*

4. *Our lead clinical-stage assets in ACLF & CCA*

5. *Other research programs in ACLF & UCD/OA*

# Corporate Highlights

French biopharmaceutical company  
Listed on Euronext "GNFT"

25+ years in liver diseases, taking  
early assets to commercial stage<sup>1</sup>

Focused on rare, severe liver diseases  
with high unmet medical need

## IPSEN

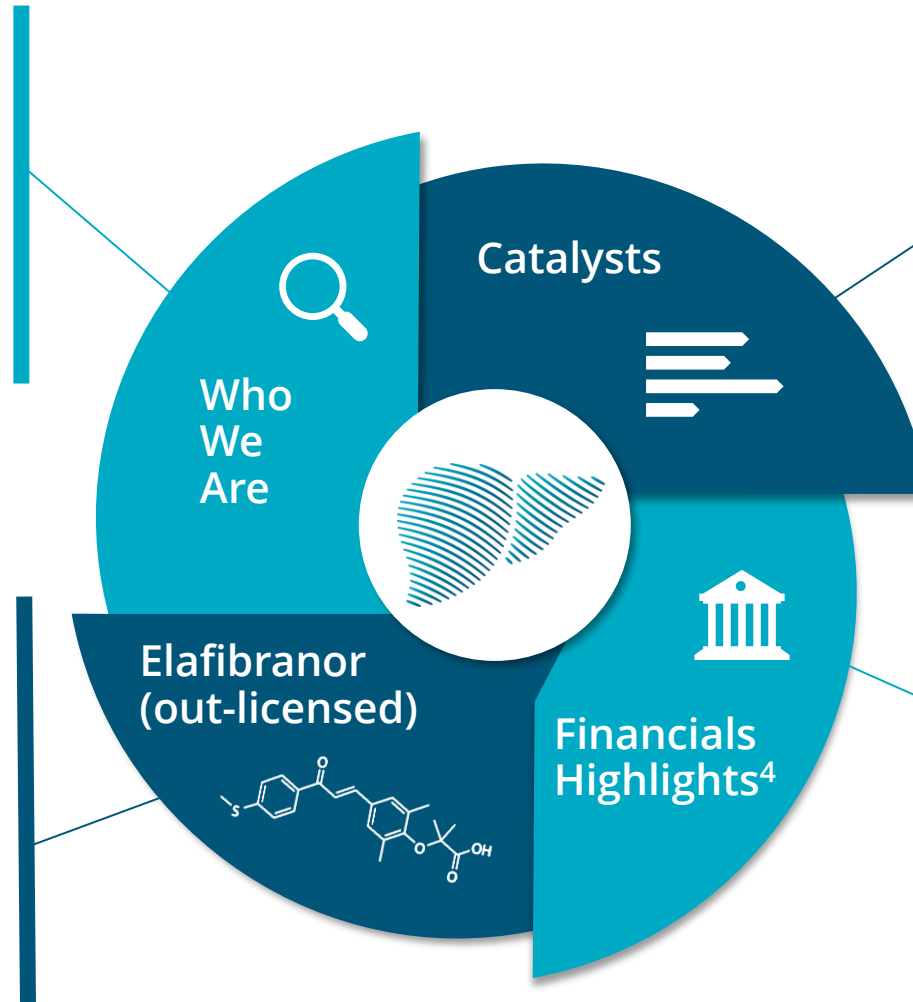
**PBC:** Iqirvo® launched in 2024<sup>1,2</sup>

- €105.5M milestones received<sup>3</sup>
- €254.5M remaining potential milestones
- Mid-teen royalties

**PSC:** Phase 3 launched with elafibranor

## Royalty deal with HCRx

- Capped
- €160M received<sup>3</sup>
- Ipsen milestones excluded from the deal



4 growth drivers in addition to PBC

- + MASH Non-invasive diagnostic technology
- + CCA Phase 2 (GNS561 combination)
- + ACLF Phase 2 (G1090N/NTZ)
- + PSC Phase 3 (by IPSEN)

Cash position of €101.1M (4Q25), excluding:

- €30M (from HCRx)
- €17M (from Ipsen)

Cash runway beyond 2028

No debt overhang

1. In-house from discovery to interim Phase 3 data readout, today commercialized by IPSEN - Approved in major markets including the US, Europe, and UK - [PR - Ipsen and GENFIT enter into exclusive licensing agreement for elafibranor, a Phase III asset evaluated in Primary Biliary Cholangitis, as part of a long-term global partnership](#)  
2. Closing subject to approval by the 2025 OCEANE bondholders at upcoming bondholders meeting - [PR - January 2025, 30 - GENFIT Announces Non-Dilutive Royalty Financing Agreement and Debt Overhang Resolution Plan](#) | [PR - GENFIT Reports First Quarter 2025 Financial Information](#)  
3. PR - GENFIT to receive a €26.5 million milestone payment following the approval of pricing and reimbursement of Ipsen's Iqirvo® in Italy  
4. PR - GENFIT to receive US\$20M milestone after Ipsen's Iqirvo® exceeds the US\$200M threshold in its first full year of net sales  
4. GENFIT Reports Full-Year 2025 Financial Results and Provides Corporate Update - This estimation is based on current assumptions and programs and does not include exceptional events. This estimation assumes (i) our expectation to receive significant future commercial milestone revenue pursuant to the license agreement with Ipsen and Ipsen meeting its sales-based thresholds and (ii) drawing down all additional installments under the Royalty Financing agreement with HCRx.

# Pipeline

Preclinical

Phase 1

Phase 2

Phase 3

Next expected/targeted steps<sup>2</sup>

## CLINICAL Programs<sup>1</sup>

ACLF Continuum\*

G1090N/NTZ<sup>A,3</sup>

Phase 1 completed

Potential initiation of Phase 2 POC<sup>C</sup> targeted **2H26**

CCA

GNS561<sup>A</sup>

Phase 1b on going (dose escalation)

Potential initiation of Phase 2 targeted **2H26**

## RESEARCH Programs<sup>1</sup>

ACLF Continuum\*

SRT-015<sup>4</sup>

FIH<sup>D</sup> Go/No-Go Decision **1H26**

CLM-022<sup>5</sup>

Further explorations of NLRP3 inhibition

VS-02-HE

Potential initiation of FIH<sup>D</sup> targeted **2H27**

EViv<sup>6</sup>

Exploratory efficacy studies

Research Collaboration with EverZom<sup>6</sup>

Decision point **mid 2027**

HAC

VS-01-HAC (UCD<sup>B</sup>/OA)

Further explorations of developability

## COMMERCIAL and/or PARTNERSHIP Programs

PBC<sup>8,9</sup>



Commercialized by Ipsen since 2024 in several major markets

PSC<sup>9</sup>



elafibranor

ELASCOPE, first and only global Phase 3 launched in Feb 26 by IPSEN

MASH

NIS

Non-invasive diagnostic technology

NASHnext<sup>®</sup> Reimbursement - **Labcorp**  
Explore IVD<sup>E</sup> partnerships (NIS2+<sup>®</sup>)

The diagnostic franchise also includes the TS-01 prototype, which targets blood ammonia levels

<sup>A</sup> Orphan Drug Designation (ODD) FDA

<sup>B</sup> Rare Pediatric Disease Designation FDA; ODD FDA

<sup>C</sup> POC = Proof of Concept <sup>D</sup> FIH = First-in-Human Study <sup>E</sup> IVD = In Vitro Diagnostic

\* The ACLF pipeline covers a broad spectrum of conditions across a disease continuum including acute decompensation (AD) of liver cirrhosis, hepatic encephalopathy (HE), etc.

1. All drugs under development are investigational compounds that have not been reviewed nor been approved by a regulatory authority in targeted indications

2. Reflects management's anticipated timelines, which are subject to change | based on industry benchmark/average - PR: GENFIT Reports Full-Year 2025 Financial Results and Provides Corporate Update

3. G1090N: Reformulation of Nitazoxanide (NTZ)

4. In-licensed from Seal Rock Therapeutics

5. In-licensed from Celloram

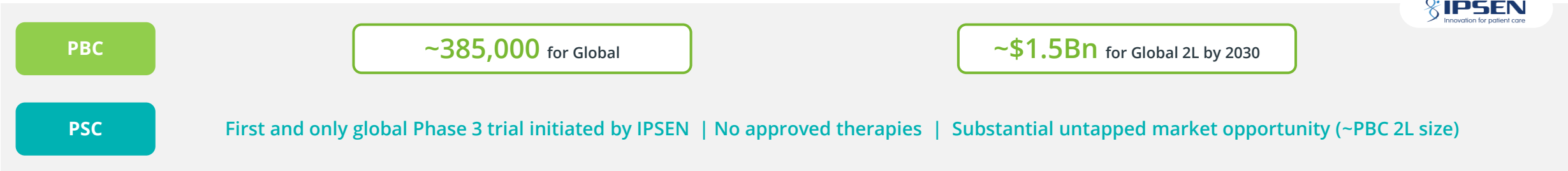
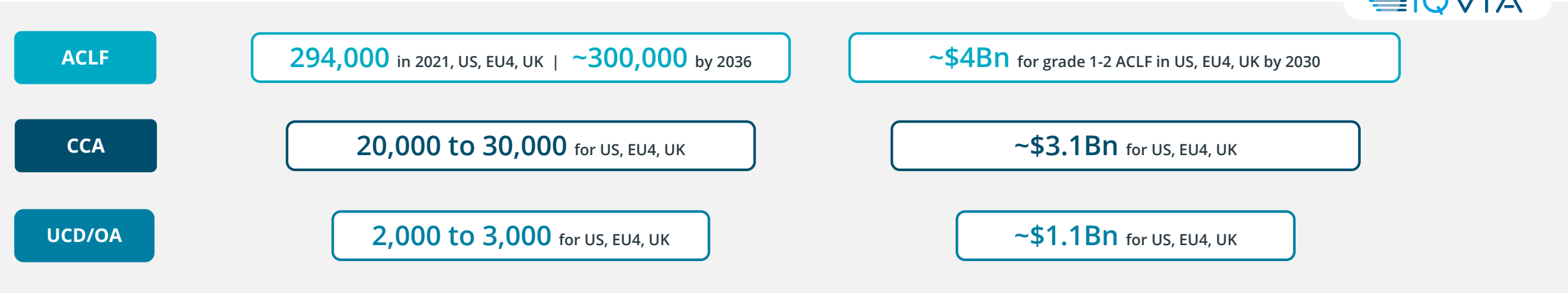
6. PR - Research Collaboration with EverZom to Advance Exosome-based Regenerative Technology in ACLF

7. Out-licensed to Ipsen | US-FDA-accelerated-approval n | UE-EMA-approval | UK-MKRA-approval | Canada-approval; Potentially eligible for priority review voucher upon approval by the FDA

8. Global 2L PBC market estimated at -€1.5bn (2030) - IPSEN - Investor presentation - June 2024

9. IPSEN 2025 Full-Year Financial Results - PR: GENFIT Reports Fourth Quarter 2025 Financial Information and Provides a Corporate Update

# Targeting Untapped Markets with High Potential



*1. Who we are*

## **2. Iqirvo<sup>®</sup> in PBC & PSC**

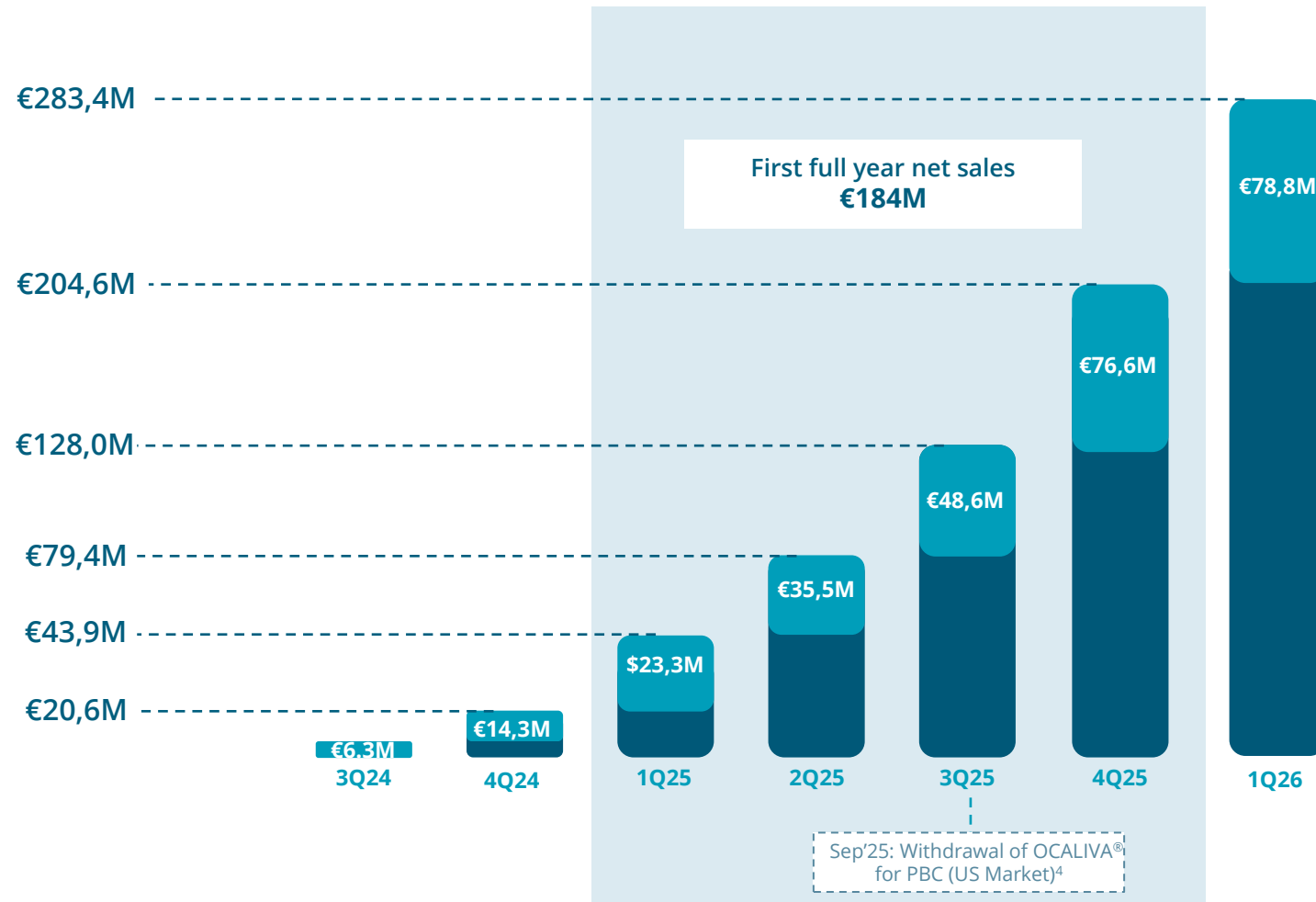
*3. MASH Diagnostics*

*4. Our lead clinical-stage assets in ACLF & CCA*

*5. Other research programs in ACLF & UCD/OA*

# Solid Commercial Performance from Ipsen

Iqirvo® sales (global, quarterly) since commercial launch<sup>1</sup>



Cumulative milestone payments received<sup>2</sup>

**€105.5M**

Cumulative royalties received<sup>3</sup>

**€24.5M**

July 30, 2026  
IPSEN 1H26 results

Sales are reported in U.S. dollars (USD), while payments are made in euros (EUR). Currency conversion is performed in accordance with the contractually agreed exchange rate

<sup>1</sup> Ipsen sales 1Q2025 | Ipsen 1H2025 | Ipsen sales 3Q25 | Ipsen FY2025 | Ipsen 1Q26

<sup>2</sup> €88.5M received + €17M expected in 1H26. FDA New Drug Application and EMA Marketing Authorization Application accepted | First commercial sale of Iqirvo® in the US | Reimbursement in a 3rd European country - Italy | \$200M threshold in its first full year of net sales

<sup>3</sup> GENFIT Announces Non-Dilutive Royalty Financing Agreement and Debt Overhang Resolution Plan | GENFIT Announces Completion of Non-dilutive Royalty Financing Agreement with HCRx and Results of Repurchase Offer to 2025 OCEANs holders PR: GENFIT Reports Fourth Quarter 2025 Financial Information and Provides a Corporate Update

<sup>4</sup> Intercept Announces Voluntary Withdrawal of OCALIVA® for Primary Biliary Cholangitis (PBC) from the US Market

# PSC: Ongoing Phase 3 Launched by Ipsen

[Click here for details on this trial](#)  
(Ipsen's 2025 Full-Year Results)



In February 2026, Ipsen confirmed the initiation of the first and only global Phase 3 clinical trial, addressing a significant unmet medical need, as no approved therapies currently exist for this severe and progressive disease.

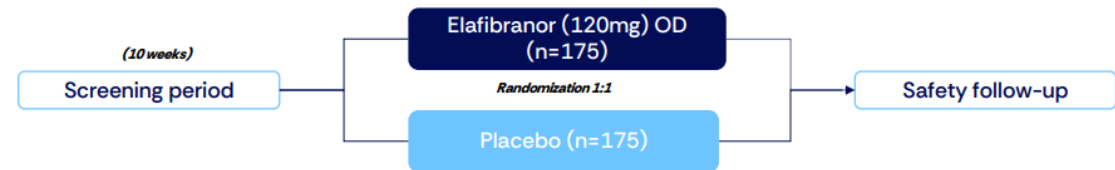
PSC represents a substantial untapped market opportunity, comparable in size to second line PBC.

Should Iqirvo® ultimately receive regulatory approval for this indication, GENFIT would be eligible for additional milestone payments as well as additional double-digit royalties.

## Evaluating elafibranor in PSC

ELASCOPE: Phase III program initiated following positive Phase II data

- **Primary endpoint:** efficacy & safety of elafibranor (120mg) vs placebo based on time to first occurrence of clinical outcomes events
- **Secondary endpoints:** change from baseline in ALP, pruritus (WI-NRS) and fatigue (FACIT), alongside other exploratory endpoints



**No approved treatments  
~40k patients in the U.S.  
Transplant rates – 50% at 10 years**

Trial	Indication	Patients	Design	Primary Endpoint(s)	Status
Iqirvo ELASCOPE Phase III NCT07387549	PSC	350	Placebo or Iqirvo	Event-Free Survival	Not yet recruiting <sup>1</sup>

1. *Who we are*

2. *Iqirvo<sup>®</sup> in PBC & PSC*

### **3. MASH Diagnostics**

4. *Our lead clinical-stage assets in ACLF & CCA*

5. *Other research programs in ACLF & UCD/OA*

# MASH: Non-invasive diagnostic technology



## GENFIT Reports Full-Year 2025 Financial Results and Provides Corporate Update

April 2, 2026

In metabolic dysfunction-associated steatohepatitis (MASH), GENFIT's diagnostic technology targets a very large and rapidly expanding market, supported by accelerating therapeutic development and deepening engagement from major industry players. In this context, our non-invasive technology is recognized as a critical component of this evolving ecosystem. We believe that the potential royalties deriving from our technology could be very significant. Key catalysts will be reimbursement status and industry partnerships, with multiple initiatives currently underway to drive broader deployment.

### 2025 Highlights

The MASH therapeutics market accelerated in 2025, with near-blockbuster performance (~US\$1 billion in sales) achieved by the first approved therapy in its first year of commercialization, increasing the need for large-scale, non-invasive diagnostic, further reinforced by the entry of an additional major therapeutic player in August. Against this backdrop, pricing for NASHnext®—developed by Labcorp as a Laboratory Development Test (LDT) under license from GENFIT and based on GENFIT's proprietary non-invasive diagnostic technology for identifying at-risk patients in MASH (formerly NASH)—, was established by U.S. Medicare and Medicaid at the end of 2025. This represents an important step toward reimbursement.

### 2026 Outlook

Building on the therapeutic market momentum observed in 2025, and the expected evolution of the competitive landscape with the entry of additional large pharmaceutical players, the MASH diagnostics market is expected to further develop in 2026. Addressing this opportunity at scale will require reliable and scalable solutions to support patient identification, treatment decision-making and longitudinal monitoring across care pathways. In this context, GENFIT's technology is already referenced in international clinical guidance as the only fully blood-based approach for identifying at-risk MASH patients, recognized by the LITMUS and NIMBLE consortia and supported by a robust body of scientific literature. Looking ahead, further progress in 2026 will depend on a combination of factors, including reimbursement and payer adoption, demand generated through broad pharmaceutical programs, and advances toward an IVD-labeled version to support wider clinical use.

## Acute-on-Chronic Liver Failure (ACLF)

Life-threatening worsening of pre-existing advanced chronic liver disease covering a broad spectrum of conditions across a disease continuum including acute decompensation (AD) of liver cirrhosis and hepatic encephalopathy (HE)

**G1090N/NTZ** | SRT-015 | CLM-022 | VS-02-HE | *EViv*<sup>1</sup>

## Cholangiocarcinoma (CCA)

GNS561

1. *Who we are*
2. *Iqirvo<sup>®</sup> in PBC & PSC*
3. *MASH Diagnostics*
4. **Our lead clinical-stage assets in ACLF & CCA**
5. *Other research programs in ACLF & UCD/OA*

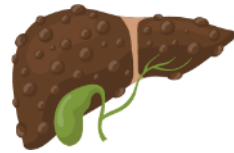
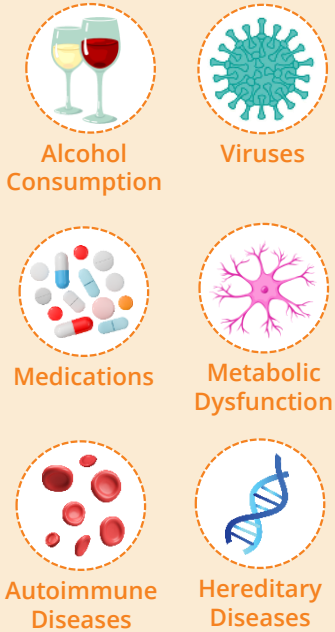
# ACLF: A High Unmet Medical Need

## CHRONIC PHASE

Chronic Liver Disease

Cirrhosis

= UNDERLYING CONDITION

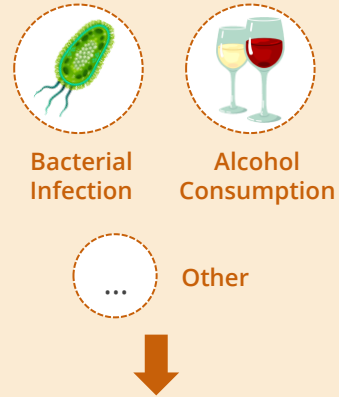


The liver is scarred but **still functioning** and people can live for **years** in this state **without noticeable symptoms**

## ACUTE PHASE

Acute  
Decompensation

= PRECIPITANT



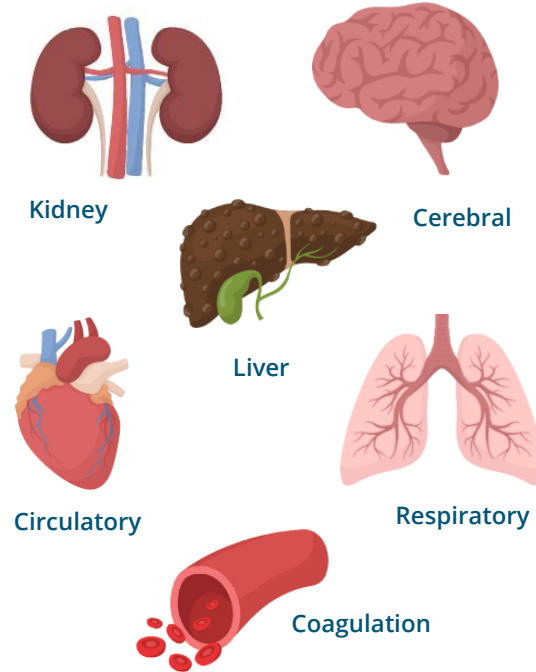
Liver function deteriorates and **serious complications** develop

- Ascites
- Hepatic encephalopathy
- Gastrointestinal bleeding

Urgent Hospitalisation

ACLF

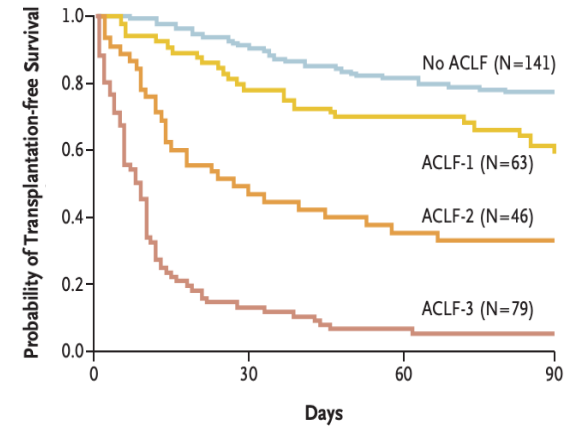
≥ 1 ORGAN DYSFUNCTIONS/FAILURES



Hospitalisation / Intensive Care Unit

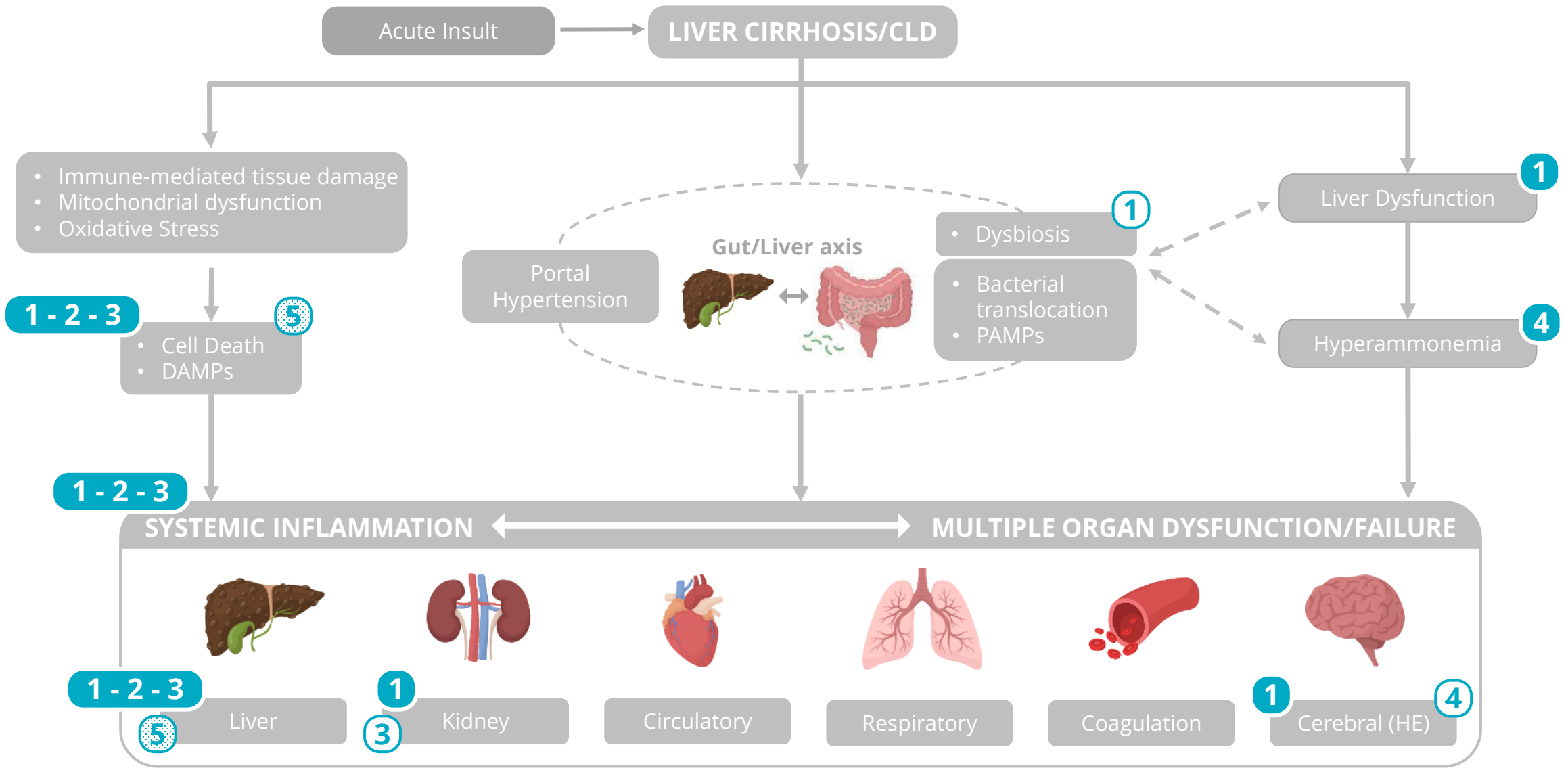
23-74% mortality at 28 days

▶ NO APPROVED DRUGS



Death

# Our approach in ACLF Continuum: Targeting Multiple Pathways



# ACLF Continuum: R&D Programs

We are developing a **diversified pipeline based on pathophysiology** to better address the **complexities** of the condition and improve **treatment outcomes**




**G1090N/NTZ**  
*Oral*

**Anti-inflammatory and anti-bacterial**

To reduce **cell death**, (systemic) **inflammation**, and **bacterial translocation**

Potential initiation of Phase 2 Proof-of-Concept targeted 2H26



**SRT-015**  
*Injectable*

**ASK1 inhibitor**

To inhibit **apoptosis**, **inflammation** (liver-centric), and **fibrosis**

First-in-human Go/No-Go Decision 1H26




**CLM-022**

**NLRP3 inflammasome inhibitor**

To inhibit **inflammation** (systemic), and **cell death** (pyroptosis)

Further explorations of NLRP3 inhibition




**VS-02-HE**  
*Oral*

**Urease inhibitor**

To reduce **hyperammonemia**, stabilize blood ammonia and **prevent HE**

Potential initiation of First-in-human targeted 2H27

*Research Collaboration with EVerZom<sup>1</sup>*



**EViv**  
*Injectable*

**Exosome Technology**

Novel approach to **regenerative therapies**

Decision point mid 2027

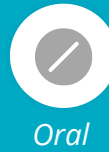
Find details on these preclinical programs in section 4 – Other programs - slide 24

# Our Lead Asset in ACLF: G1090N/NTZ A Strong Scientific Rationale

## Findings to date:

- ✓ Decreases systemic inflammation in animal models, including in ACLF models
- ✓ Protects liver, kidney & brain in rat models of ACLF by decreasing tissue damage
- ✓ Protects mice from mortality in a model of sepsis induced by gut leakage (AASLD 2024 poster)
- ✓ Prevents cell death via anti-apoptotic and anti-necroptotic effects (EASL 2024 poster)
- ✓ Reduces PAMPs-induced inflammation (AASLD 2024 poster)

**G1090N/NTZ**  
Anti-inflammatory



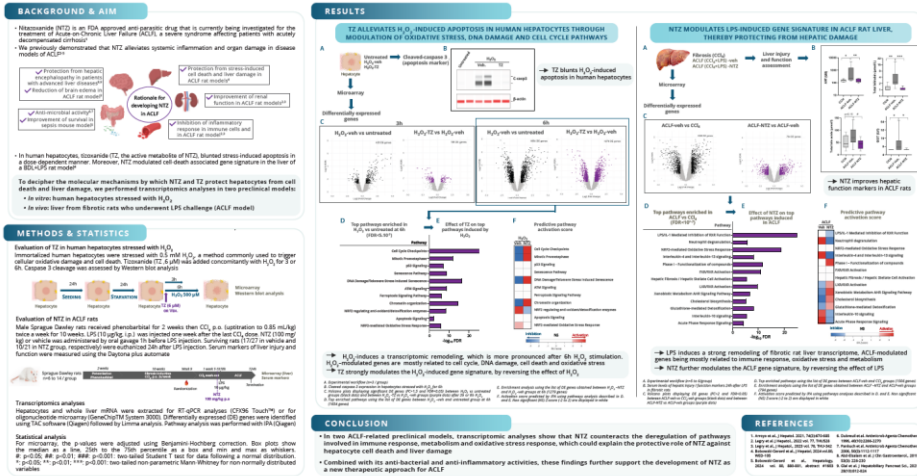
**EASL 2025**

**NTZ ALLEVIATES STRESS-INDUCED HEPATOCYTE CELL DEATH THROUGH MODULATION OF OXIDATIVE STRESS AND DNA DAMAGE SIGNALING PATHWAYS IN ACLF MODELS**

Marie Bobowski-Gerard<sup>1</sup>, Nicolas Stramkovic Valentin<sup>1</sup>, Sylvie Delacourte<sup>1</sup>, Simon Debaecker<sup>1</sup>, Nina S'Ervenste<sup>1</sup>, Philippe Delattelle<sup>1</sup>, Saïna Sayah Jeanne<sup>1</sup>, Dean Hum<sup>1</sup>, Vanessa Legry<sup>1</sup>, Jérôme Eeckhout<sup>1</sup>, Joan Clariá<sup>1</sup>, Bart Staels<sup>1</sup>

<sup>1</sup>GENFIT SA, Louvain-la-Neuve, Belgium; <sup>2</sup>CHU Lille and Institut Pasteur de Lille, U1011 EDD, Lille, France; <sup>3</sup>Hospital Clinic IDIBAPS, Universitat de Barcelona, European Foundation for the Study of Chronic Liver Failure (EFCLF), Spain

THU-166



- ▶ TZ blunts the apoptotic response in hepatocytes
- ▶ NTZ counteracts the dysregulation of pathways involved in immune response, metabolism and oxidative stress in the liver of ACLF rats, in relation with its in vitro protective activity in hepatocytes

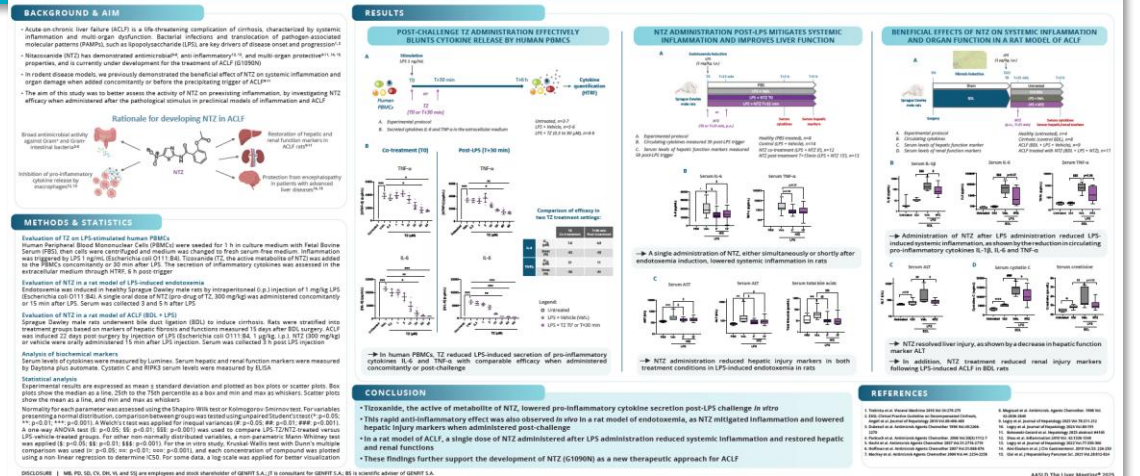
**AASLD 2025**

**EFFICACY OF NITAZOXANIDE (NTZ) ON SYSTEMIC INFLAMMATION AND ORGAN FUNCTION IN DISEASE MODELS OF ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) WHEN ADMINISTERED POST-ACLF TRIGGER**

Marie Bobowski-Gerard<sup>1</sup>, Philippe Delattelle<sup>1</sup>, Simon Debaecker<sup>1</sup>, Camille Vanbèsien<sup>1</sup>, Dean Hum<sup>1</sup>, Vanessa Legry<sup>1</sup>, Bart Staels<sup>1</sup>, Joël Trebicka<sup>1</sup>, Saïna Sayah Jeanne<sup>1</sup>

<sup>1</sup>GENFIT SA, Louvain-la-Neuve, Belgium; <sup>2</sup>CHU Lille and Institut Pasteur de Lille, U1011 EDD, Lille, France; <sup>3</sup>Hospital of the Geneva University, University Hospital, Geneva, Switzerland

4165



- ▶ TZ lowers pro-inflammatory cytokine secretion post-LPS challenge in PBMCs
- ▶ In a rat model of ACLF, a single dose of NTZ administered after LPS administration reduces systemic inflammation and restores hepatic and renal functions

▶ ▶ Combined with its anti-bacterial properties, all these findings further support the development of NTZ as a new therapeutic approach for ACLF ◀ ◀

## G1090N: an investigational drug

G1090N: Reformulation of Nitazoxanide (NTZ); Tizoxanide (TZ): Active metabolite of NTZ | PAMPs = Pathogen-Associated Molecular Patterns

**G1090N/NTZ**

Anti-inflammatory



Oral

### Key inclusion criteria

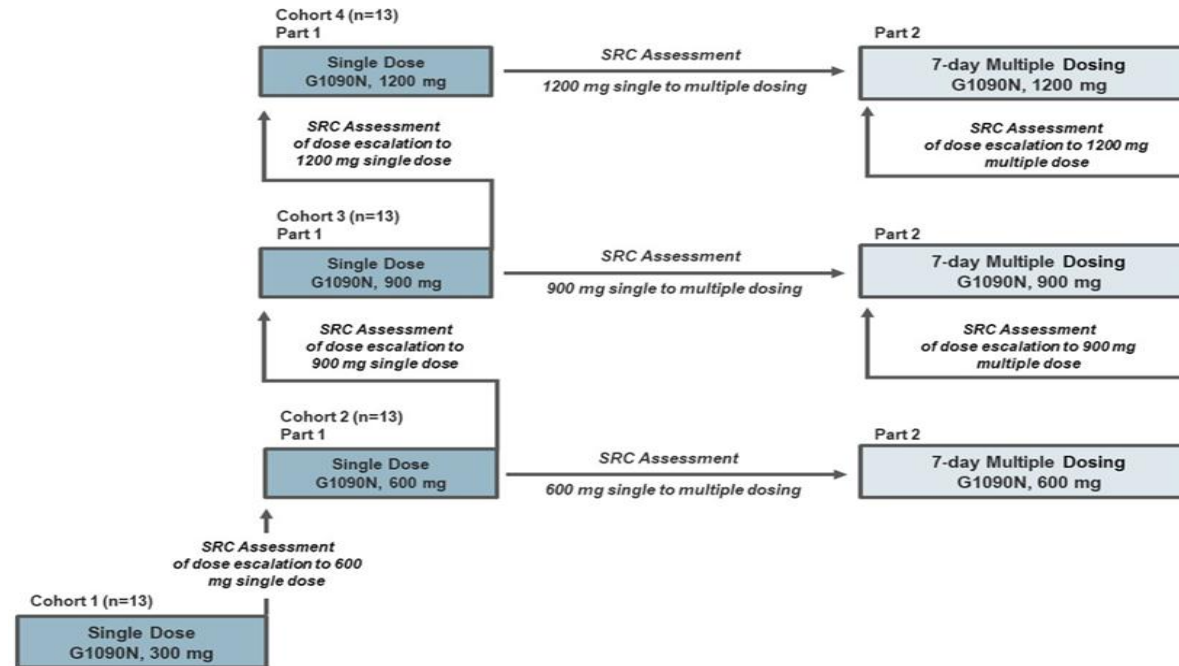
- **Healthy** Volunteers
- Normal liver and renal function

### Key exclusion criteria

- **Significant medical history** or recent illness

$N_{TOTAL}$   
=  
**52**  
**PTS**

A Phase 1 open-label study to assess pharmacokinetics, safety, and tolerability of G1090N in healthy subjects



n = number of subjects; PK = pharmacokinetic(s); SRC = Safety Review Committee.

Investigational drug G1090N is a promising therapy in ACLF due to:

- **major metabolite tizaxozanide targets major pathophysiological pathways** relevant in decompensated liver cirrhosis and ACLF
- shows **impact on systemic and tissue inflammation, cell death, apoptosis**

♦ **Primary endpoint:**  
Pharmacokinetic parameters following single and multiple ascending dose administration

**Secondary endpoints:**  
Safety and tolerability following single and multiple ascending dose administration

# G1090N/NTZ's Potential Recently Confirmed in the Clinic

G1090N/NTZ

Anti-inflammatory



Oral



*The safety profile observed in Phase 1 and the consistent biological activity evidenced in ex vivo assays represent a meaningful step in development. These findings position G1090N as a promising candidate for patients with AD and for patients with ACLF, a life-threatening condition with no approved therapies and significant unmet medical need. We are eager to see more patient data as the program moves forward, to confirm G1090N's safety and strengthen the case for its activity in patients with organ failure*

**Dr. Jacqueline O'Leary**

MD at the UT Southwestern Medical Center, Dallas, TX (USA)



January 6, 2026

## GENFIT: Favorable Phase 1 Safety Profile and Strong Anti-inflammatory Activity for ACLF Lead Asset G1090N

- Phase 1 results confirm investigational drug-candidate G1090N has a favorable safety and tolerability profile, supporting further clinical evaluation
- Compelling anti-inflammatory activity of G1090N was evidenced through functional ex vivo assays on blood samples from study participants and cirrhotic donors, showing inhibition of pro-inflammatory pathway
- Findings provide a solid foundation for advancing G1090N into Phase 2 proof-of-concept studies across the ACLF continuum

March 9, 2026

## GENFIT Receives FDA Orphan Drug Designation for NTZ for the treatment of ACLF

- NTZ is being advanced in ACLF through its G1090N reformulation, designed to unlock its clinical potential for patients facing this life-threatening condition

## Acute-On-Chronic Liver Failure (ACLF)

G1090N/NTZ | SRT-015 | CLM-022 | VS-02-HE | *EViv*

## Cholangiocarcinoma (CCA)

Malignancy of bile ducts. Without treatment <20% of patients survive 5 years from diagnosis<sup>1</sup>. KRAS mutation is not addressed by current treatments.

**GNS561**

1. *Who we are*
2. *Iqirvo<sup>®</sup> in PBC & PSC*
3. *MASH Diagnostics*
4. **Our lead clinical-stage assets in ACLF & CCA**
5. *Other research programs in ACLF & UCD/OA*

# CCA with KRAS Mutation: A High Unmet Medical Need

## Rare and aggressive liver malignancy that develops in the bile ducts

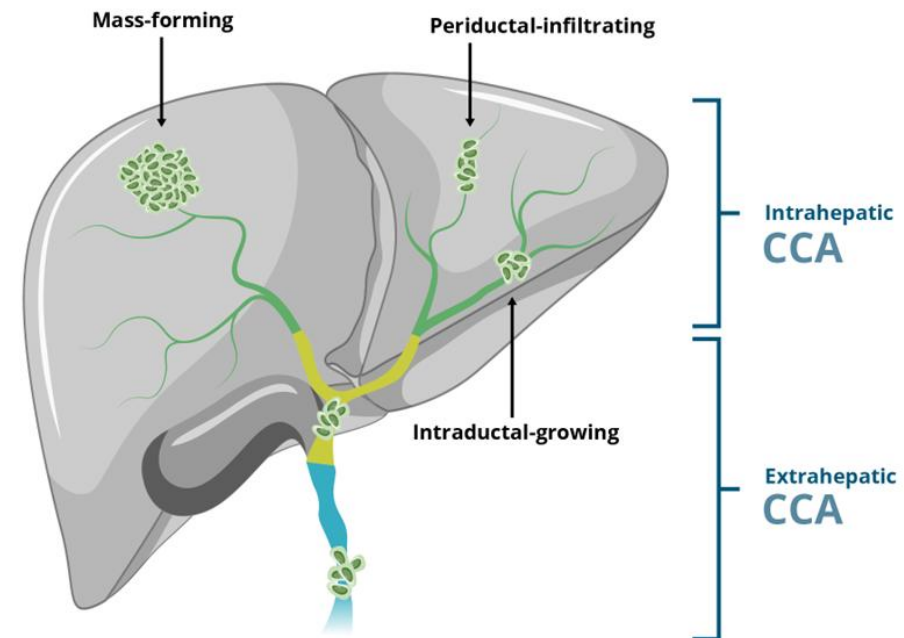
- As the cancer grows, it can **block the bile ducts** and lead to damage to the liver and other organs
- Without treatment **<20% of patients survive 5 years** from diagnosis<sup>1</sup>

## Unmet needs

- **Surgery** = primary treatment of CCA but **only 30%** of patients present with resectable tumors<sup>2</sup>
- First line and second line therapy = **survival is limited**<sup>2</sup>
- Rapid progression of the tumor until the **patient's death = 10–12 months** on current SoC<sup>3</sup>

## ~30% of patients with CCA harbor **KRAS mutations**<sup>4</sup>

- **one of the most common genes that might be mutated** or amplified resulting in the overactivation of some of these pathways<sup>5</sup>
- associate with **shorter survival**<sup>6</sup>
- KRAS mutation is **not addressed by current treatments** = **unmet needs** remain **very high** for these patients



Drawing: Adapted from Nature Reviews Gastroenterology & Hepatology volume 17, p. 557–588;

1. Lamarca et al. 2021 | 2. Jesus M. Banales et al. 2020, Cholangiocarcinoma 2020: the next horizon in mechanisms and management. Nature Reviews Gastroenterology & Hepatology volume 17, p. 557–588;

3. Banales et al., Cholangiocarcinoma 2026: status quo, unmet needs and priorities, Nat. Rev. Gastroenterol. Hepatol., 2025 | 4. Banales et al., Cholangiocarcinoma 2020: the next horizon in mechanisms and management, Nat Rev Gastroenterol Hepatol, 2020 | 5.

Fitzwalter BE, Thorburn A. Recent insights into cell death and autophagy. FEBS J. 2015;282:4279–88. | 6. Signaling pathways involved in cholangiocarcinoma development and progression. Nature Reviews Gastroenterology & Hepatology volume 17, pages 557–588 (2020)

# Rationale for Combining Anticancer Therapies and investigational drug GNS561, an Autophagy Inhibitor

**GNS561**  
PPT1 inhibitor in  
combination with  
a MEK inhibitor



Oral

## #1 Anticancer Therapies

Chemotherapeutic agents

MAP Kinase pathway targeted therapies

Immune checkpoint inhibitors  
(anti-PD-1/PD-L1)

## #2 GNS561

(Autophagy inhibitor)

By **entering the lysosomes and inhibiting PPT1**, GNS561 acts to block late-stage autophagy, which can lead to tumor cell death

### ✓ Beneficial anti-cancer effects

- ▼ Cancer **cell survival**
- ▼ Tumor **growth**

### ✗ Autophagy: tumor cell survival mechanism

- ▲ Cancer **cell survival**
- ▲ Tumor **growth**
- ▲ **Resistance** to treatment

### ✓ Blocks cancer cell survival



Enabling simultaneous targeting of tumor growth and adaptive mechanisms of cancer cells

**GNS561**  
PPT1 inhibitor in  
combination with  
a MEK inhibitor



Oral

A Phase 1b/2a open-label, multicenter study to evaluate safety, pharmacokinetics (PK), pharmacodynamics (PD) and efficacy of GNS561 in combination with trametinib in advanced KRAS mutated CCA after failure of standard-of-care first line therapy

## ✓ Key inclusion criteria

- Patients with **KRAS mutated CCA** who have **failed 1st line** treatment therapy

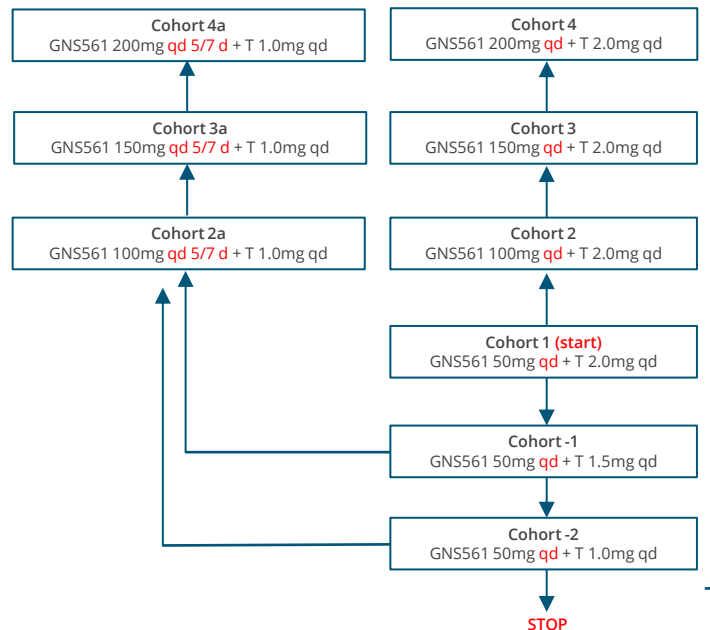
## ⊘ Key exclusion criteria

- **Prior** MEK or autophagy inhibitor **treatment**
- Uncontrolled **significant illness**
- Active **HBV/HCV**
- Hypersensitivity to **quinoline** derivatives / study drugs

Ongoing recruitment

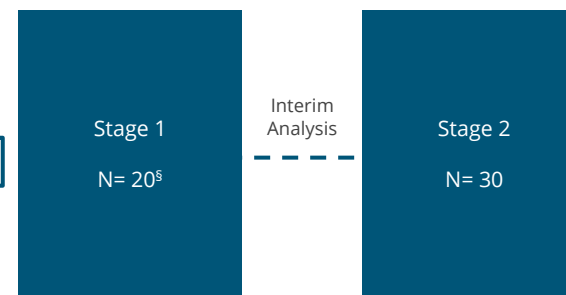
$N_{TOTAL}$   
=  
**74**  
**PTS**

### PHASE 1b Dose finding



### PHASE 2a POC Single arm N=50

#### Simon 2-stage



♦ **Primary endpoint:**  
Efficacy – objective response rate

**Secondary endpoints:**  
Efficacy - progression free survival ; Pharmacokinetics ; Pharmacodynamics ; Safety and tolerability

# Phase 1b: Highly Encouraging Early Data

## GNS561

PPT1 inhibitor in combination with a MEK inhibitor



Oral



*Advanced KRAS-mutated cholangiocarcinoma remains a formidable clinical challenge, and the emerging activity seen in this initial study is encouraging. Because MEK inhibition alone has historically shown limited efficacy in this setting, the early signs of benefit with dual targeting of autophagy and MAPK signaling provide meaningful rationale for continued evaluation of this combination strategy*

### **Dr. Mark Yarchoan**

Associate Professor of Oncology at John Hopkins Medicine (Baltimore, MD, USA)  
Principal investigator of the program



December 10, 2025

## **GENFIT: GNS561 Shows Promising Antitumor Activity in Combination Therapy**

- **Highly encouraging early data from the ongoing Phase 1b study evaluating investigational drug GNS561 with a MEK inhibitor (MEKi) in KRAS mutated cholangiocarcinoma (CCA), positioning this novel combination as a potential new therapeutic approach for difficult-to-treat cancers:**
  - **No dose limiting toxicity reached to date, enabling recruitment of a third patient cohort**
  - **GNS561 and MEKi combination demonstrated disease stabilization in all evaluable patients with evidence of tumor shrinkage in a subset of patients, warranting further investigation**
  - **Recommended Phase 2 doses expected for 1H26**

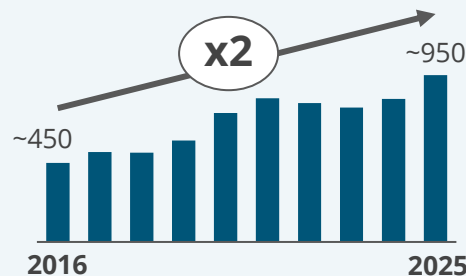
# Moving Forward



- **Phase 1b dose escalation** will continue as planned to confirm activity signal
- **1H26** - Completion expected results will be used to establish recommended Phase 2 combination doses
- **2H26** - targeted Phase 2 initiation

## Beyond CCA: a potential to explore the benefit of autophagy inhibition in other cancers

The number of **publications** implicating **autophagy** in **cancer treatment resistance** has **increased by ~10% each year** over the past 10 years<sup>1,2</sup>




### Rationale to expand GNS561 program into GI/liver tumors where:

- ✓ Autophagy plays a key role in resistance
- ✓ GNS561 has shown to accumulate the most
- ✓ There is a high incidence of MAPK alternations
- ✓ There is potential to combine with SoC (ICI, small molecules)

 Hepatocellular carcinoma (HCC)

 MSS colorectal cancer (CRC)

 Pancreatic ductal adenocarcinoma (PDAC)

 Gastro-pancreatic NET (GEP-NET)

**~450,000 patients** (in US, EU4+UK, and JP/CN)<sup>1</sup>

## Beyond MEKi: a potential to explore combinations with other anticancer agents

**Anti-PD-1** | **RAFi** | **Other**

*Ex: Evidence already exists in HCC for GNS561 in combination with anti-PD-1 in a mouse model<sup>3</sup>*

## Acute-on-Chronic Liver Failure (ACLF)

Life-threatening worsening of pre-existing advanced chronic liver disease covering a broad spectrum of conditions across a disease continuum including acute decompensation (AD) of liver cirrhosis and hepatic encephalopathy (HE)

G1090N/NTZ | **SRT-015** | **CLM-022** | **VS-02-HE** | **EViv<sup>1</sup>**

Urea Cycle Disorders (UCD) & Organic Acidemias (OA)  
VS-01-HAC

1. *Who we are*
2. *Iqirvo<sup>®</sup> in PBC & PSC*
3. *MASH Diagnostics*
4. *Our lead clinical-stage assets in ACLF & CCA*
5. **Other research programs in ACLF & UCD/OA**

# SRT-015

## SRT-015 ASK1 inhibitor




Injectable

### Findings to date:

- ✓ Decreases systemic inflammation in animal models, including in an ACLF model
- ✓ Protects mice from mortality in a model of sepsis induced by gut leakage
- ✓ Demonstrates efficacy when injected in mice with acute liver failure (AASLD24 poster)
- ✓ Shows anti-inflammatory and immuno-modulatory activities on human immune cells

### EASL 2025



#### EFFICACY OF THE APOPTOSIS-SIGNAL-REGULATING KINASE 1 (ASK1) INHIBITOR SRT-015 IN *IN VIVO* AND *IN VITRO* PATHOGEN-ASSOCIATED MOLECULAR PATTERNS (PAMPs)-INDUCED DISEASE MODELS

Vanessa Legry<sup>1</sup>, Berta Romero-Gimaldos<sup>1</sup>, Cristina López-Vicario<sup>1</sup>, Bryan J. Contreras<sup>1,2</sup>, Belén Sánchez-Rodríguez<sup>1,2</sup>, Ophélie Hanot<sup>1</sup>, Manon Clarisse<sup>1</sup>, Simon Debacquer<sup>1</sup>, Alba Díaz<sup>1</sup>, Carla Montironi<sup>1</sup>, Richard Moreau<sup>1</sup>, Dean Hum<sup>1</sup>, Bart Staels<sup>1</sup>, Sakina Sayah Jeanne<sup>1</sup>, Joan Clariá<sup>1,2,3,4</sup>

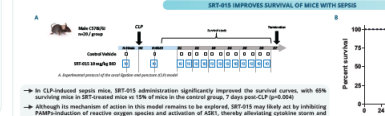
<sup>1</sup>GENFIT SA, Spain; <sup>2</sup>INSERM U1163, Institut Pasteur de Lille, U1163, Lille, France; <sup>3</sup>Hospital Clinic, IDIBAPS, Universitat de Barcelona, European Association for the Study of Chronic Liver Failure (EASL), Barcelona, Spain; <sup>4</sup>INSERM U1163, Institut Pasteur de Lille, U1163, Lille, France

**BACKGROUND & AIM**

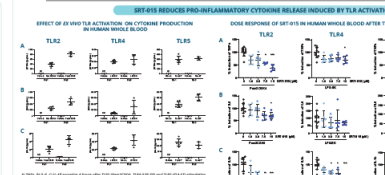
- Patients with liver cirrhosis have an increased risk of infection and are at high risk of death from sepsis. To reverse immune dysfunction, impaired liver function and altered gut microbiota and permeability.
- In these patients, immune dysfunction also results in a hyperinflammatory condition in the sepsis model, as shown by elevation of circulating pro-inflammatory cytokines such as TNF $\alpha$ , IL-6, IL-1 $\beta$ , IL-8, IL-10, IL-17, IL-22, IL-27, IL-33, IL-36, IL-37, IL-38, IL-39, IL-40, IL-41, IL-42, IL-43, IL-44, IL-45, IL-46, IL-47, IL-48, IL-49, IL-50, IL-51, IL-52, IL-53, IL-54, IL-55, IL-56, IL-57, IL-58, IL-59, IL-60, IL-61, IL-62, IL-63, IL-64, IL-65, IL-66, IL-67, IL-68, IL-69, IL-70, IL-71, IL-72, IL-73, IL-74, IL-75, IL-76, IL-77, IL-78, IL-79, IL-80, IL-81, IL-82, IL-83, IL-84, IL-85, IL-86, IL-87, IL-88, IL-89, IL-90, IL-91, IL-92, IL-93, IL-94, IL-95, IL-96, IL-97, IL-98, IL-99, IL-100, IL-101, IL-102, IL-103, IL-104, IL-105, IL-106, IL-107, IL-108, IL-109, IL-110, IL-111, IL-112, IL-113, IL-114, IL-115, IL-116, IL-117, IL-118, IL-119, IL-120, IL-121, IL-122, IL-123, IL-124, IL-125, IL-126, IL-127, IL-128, IL-129, IL-130, IL-131, IL-132, IL-133, IL-134, IL-135, IL-136, 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**RESULTS**

**SRT-015 IMPROVES SURVIVAL OF MICE WITH SEPSIS**




**SRT-015 REDUCES PRO-INFLAMMATORY CYTOKINE RELEASE INDUCED BY TLR ACTIVATION OF HUMAN WHOLE BLOOD**



**CONCLUSION**

- Although further experiments are needed to fully understand how SRT-015 improves survival in septic mice, one potential mechanism may be by regulation of the innate immune response.
- These results further support the development of SRT-015 in advanced liver disease and ACLF.

### AASLD 2025



#### ASK1 INHIBITOR SRT-015 REDUCES SYSTEMIC INFLAMMATION WHILE PROMOTING IMMUNE HOST DEFENSE MECHANISMS IN PRECLINICAL *IN VITRO* AND *IN VIVO* MODELS RELATED TO ACLF

Vanessa Legry<sup>1</sup>, Berta Romero-Gimaldos<sup>1</sup>, Cristina López-Vicario<sup>1</sup>, Bryan J. Contreras<sup>1,2</sup>, Belén Sánchez-Rodríguez<sup>1,2</sup>, Ophélie Hanot<sup>1</sup>, Manon Clarisse<sup>1</sup>, Simon Debacquer<sup>1</sup>, Alba Díaz<sup>1</sup>, Carla Montironi<sup>1</sup>, Richard Moreau<sup>1</sup>, Dean Hum<sup>1</sup>, Bart Staels<sup>1</sup>, Sakina Sayah Jeanne<sup>1</sup>, Joan Clariá<sup>1,2,3,4</sup>

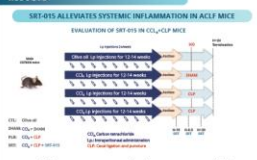
<sup>1</sup>GENFIT SA, Spain; <sup>2</sup>INSERM U1163, Institut Pasteur de Lille, U1163, Lille, France; <sup>3</sup>Hospital Clinic, IDIBAPS, Universitat de Barcelona, European Association for the Study of Chronic Liver Failure (EASL), Barcelona, Spain; <sup>4</sup>INSERM U1163, Institut Pasteur de Lille, U1163, Lille, France

**BACKGROUND & AIM**

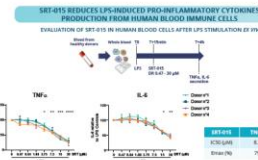
- Acute on Chronic Liver Failure (ACLF) is characterized by multiple organ failures and high systemic immune mortality. ACLF is closely associated with the presence of systemic inflammation and impaired immune defense responses against pathogens, such as decreased neutrophil degradation and phagocytosis, as well as oxidative stress.
- Apoptosis signal-regulating kinase 1 (ASK1) is a key mediator of the inflammatory response, activated by reactive oxygen species (ROS) and other recognition of pathogen-associated molecular patterns (PAMPs). Its phosphorylation results in activation of p38 and p53 that regulate cell death and immune response.
- SRT-015 is a novel investigational ASK1 inhibitor. Preclinical studies have shown its anti-apoptotic and anti-inflammatory activities *in vitro*, as well as its ability to reduce liver injury and counteract systemic inflammation in acute liver failure models and improve survival in sepsis mice.
- The aim of this study was to investigate the effects of SRT-015 on systemic inflammation in a new model of ACLF that closely mimics the human condition, as well as on human leukocyte functions *in vitro*.

**RESULTS**

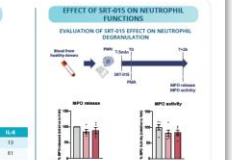
**SRT-015 ALLEVIATES SYSTEMIC INFLAMMATION IN ACLF MICE**



**SRT-015 REDUCES LPS-INDUCED PRO-INFLAMMATORY CYTOKINE PRODUCTION FROM HUMAN BLOOD IMMUNE CELLS**



**EFFECT OF SRT-015 ON NEUTROPHIL FUNCTIONS**



**CONCLUSION**

- These data confirm the beneficial effect of SRT-015 on systemic inflammation in a preclinical model of ACLF and show its ability to improve the antibacterial function of neutrophils.
- These results support the development of the investigational drug SRT-015 for the treatment of patients with ACLF.

- ▶ SRT-015 dose-dependently inhibits TNF- $\alpha$ , IL-6 and IL-1 $\beta$  secretion in response to TLR2, TLR4 and TLR5 activation in human whole blood assay
- ▶ Improves survival in septic mice, one potential mechanism being through the regulation of innate immune response

- ▶ Improves the antibacterial function of neutrophils
- ▶ Decreases systemic inflammation in a preclinical model of ACLF

▶ ▶ These data support the development of investigational drug SRT-015 for the treatment of advanced liver disease and ACLF ◀ ◀

## CLM-022 NLRP3 inflammasome inhibitor



### Findings to date:

- ✓ Protects the liver in pre-clinical ALF models
- ✓ Protects mice from mortality induced by gut leakage-induced sepsis
- ✓ Dose-dependently inhibits IL-1 $\beta$  secretion (AASLD 2024 poster)
- ✓ Shows potent inhibition of priming and activation steps of NLRP3 inflammasome

EASL  
2025

**CLM-022\*, A DUAL INHIBITOR OF PRIMING AND ACTIVATION STEPS OF NLRP3 INFLAMMASOME, AS A POTENTIAL TREATMENT FOR ACUTE AND CHRONIC INFLAMMATORY LATE-STAGE LIVER DISEASES**  
Hana El Khatib\*, Alexandra Caron\*, Eudine Delecré\*, Victor Lanay\*, Maryse Malysiak\*, Valérie Daix\*, Simon Debaecker\*, Guillaume Vidal\*, Dean Huml\*, Bart Staels\*, Sakina Sayah Jeanne\*

**BACKGROUND & AIM**

- Inflammation is a common element in the pathogenesis of most chronic liver diseases leading to fibrosis, cirrhosis and liver failure. Due to the close connection with the intestine, the liver is particularly susceptible to gut leakage-induced sepsis. Gut leakage-induced sepsis is characterized by the presence of pathogen-associated molecular patterns (PAMPs), which activate resident immune cells. In addition to the traditional or endogenous PAMPs, hepatic tissue immune cells are also activated by exogenous PAMPs (e.g. LPS), which are released from injured parietal and non-parietal cells (Farnier 2012).
- Inflammation is characterized by activation of innate immune cells, production of pro-inflammatory cytokines, and generation of reactive oxygen and nitrogen species. Liver damage is regulated by inflammatory cells, which release pro-inflammatory cytokines (IL-1, IL-6, TNF- $\alpha$ ) and chemokines, leading to recruitment of leukocytes. In addition, hepatocellular damage is induced by oxidative stress and mitochondrial dysfunction. Inflammation is also associated with liver injury and fibrosis (Lieberman 2019).

**RESULTS**

**CLM-022 INHIBITS THE NLRP3 PRIMING IN LPS-INDUCED PBMCs**

**CLM-022 IMPROVES HEPATIC FUNCTION IN APAP-INDUCED LIVER INJURY**

**CLM-022 INHIBITS PYROPTOSIS INDUCED BY INFLAMMASOME ACTIVATION IN WT BUT NOT IN NLRP3-KO T84-182 CELLS**

**CLM-022 IMPROVES HEPATIC FUNCTION AND REDUCES NLRP3 PROTEIN EXPRESSION IN APAP-INDUCED LIVER INJURY**

**CLM-022 INHIBITS SYSTEMIC INFLAMMATION AND PROTECTS THE LIVER IN RATS**

**CONCLUSION**

**REFERENCES**

**METHODS & STATISTICS**

**CONCLUSION**

**REFERENCES**

AASLD  
2025

**EFFICACY OF CLM-022\*, AN INHIBITOR OF THE NLRP3 INFLAMMASOME, IN IN VIVO AND IN VITRO PATHOGEN-ASSOCIATED MOLECULAR PATTERNS (PAMPs)-INDUCED DISEASE MODELS**  
Guillaume Vidal\*, Hana El Khatib\*, Alexandra Caron\*, Maryse Malysiak\*, Valérie Daix\*, Simon Debaecker\*, Manon Clarisse\*, Dean Huml\*, Bart Staels\*, Sakina Sayah Jeanne\*

**BACKGROUND & AIM**

- Patients with liver cirrhosis are characterized by impaired liver function, severe immune dysregulation, and increased gut permeability. These alterations drive the progression of gut leakage-induced sepsis. Gut leakage-induced sepsis is characterized by the presence of pathogen-associated molecular patterns (PAMPs), which activate resident immune responses via receptors (TLRs and NLRs).
- Immune dysregulation and gut barrier dysfunction lead to a dysregulated inflammatory response and elevated cytokines (TNF- $\alpha$ , IL-6, IL-1 $\beta$ ). These events play a key role in the transition to acute decompensation and liver failure in cirrhotic patients. Importantly, cirrhotic patients are also highly susceptible to sepsis.
- CLM-022, an oral, small-molecule inhibitor of inflammasome priming and activation, has demonstrated hepatoprotective and immunomodulatory effects in pre-clinical models of liver injury and endotoxemia, and prevented the 2025 EASL International Liver Congress.

**RESULTS**

**CLM-022 IMPROVES SURVIVAL IN A MOUSE MODEL OF CLP-INDUCED SEPSIS**

**CLM-022 REDUCES PRO-INFLAMMATORY CYTOKINE RELEASE IN HUMAN WHOLE BLOOD ASSAY**

**CONCLUSION**

**REFERENCES**

**METHODS**

**CONCLUSION**

**REFERENCES**

- ▶ CLM-022 inhibits NLRP3 inflammasome priming of LPS-induced human PBMCs
- ▶ Inhibition of IL-1 $\beta$  production and pyroptosis by CLM-022 is lost in NLRP3-KO macrophages
- ▶ Oral CLM-022 provides hepatic protection in a model of acute liver injury in mice
- ▶ IV CLM-022 decreases cytokines levels and improves hepatic parameters in a rat endotoxemia model

- ▶ Improves survival in a mouse model of CLP-induced sepsis (40% vs 15% at day 7)
- ▶ Reduces the secretion of key pro-inflammatory cytokines in human whole blood assays at similar nanomolar IC50 values when administered either concomitantly with or following LPS stimulation

▶ ▶ These data support investigational drug CLM-022 as a potential treatment for inflammatory acute late-stage liver diseases ◀ ◀

Next Step: Further explorations of NLRP3 inhibition

# VS-02-HE

**VS-02-HE**  
Urease inhibitor

**Hepatic Encephalopathy**



Oral

**About Hepatic Encephalopathy (HE)**

- One of the **most common complications of liver cirrhosis and ACLF**
- A **central nervous system disorder** representing a diverse spectrum of neurologic symptoms
- **Excess ammonia** induces alteration of cell metabolism and can result in brain edema
- **> 45% of patients with cirrhosis** will experience **at least one episode of HE<sup>1</sup>**
- HE is **largely underdiagnosed and undertreated** and is associated with poor quality of life

**Findings to date:**

- ✓ VS-02 lowers ammonia levels in an acute liver injury model
- ✓ VS-02 lowers ammonia & brain glutamine levels in a chronic liver disease model
- ✓ VS-02 demonstrates gut bacterial urease inhibitory activity

ISHEN 2025

## GUT BACTERIAL UREASE INHIBITION BY VS-02 AS A POTENTIAL TREATMENT TO REDUCE HYPERAMMONEMIA AND PROTECT FROM HEPATIC ENCEPHALOPATHY (HE) IN CIRRHOSIS

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**BACKGROUND & AIM**

- Gut bacterial ureases, which convert urea into ammonia, contribute to systemic ammonia levels and thus represent a promising therapeutic target for reducing hyperammonemia and alleviating hepatic encephalopathy (HE).
- Hydroxamic acids (HAs) are potent urease inhibitors that have shown beneficial effects in preclinical models and patients with liver disease. Among them, *α*-hydroxycarboxylic acid (AHA), *α*-ketoisobutyric acid (AKIA), *α*-ketoglutaric acid (AKG), and *α*-ketoglutaric acid (AKG) are the only ones that have been clinically tested in liver disease patients. However, in studies conducted between 1970 and 1975, these encouraging results of these compounds, advanced in further development for HE, possibly due to insufficient potency or a failure to reach effective concentrations in the colon, the main site of bacterial urease activity.
- VS-02 is a hydroxamic acid derivative under development for the treatment of HE, formulated for colon targeted delivery to enhance local inhibitor concentration at the site of urease production while minimizing systemic exposure.

**The aim of this study was:**

- to evaluate the efficacy of VS-02 in reducing ammonia *in vivo*, in comparison to other hydroxamic acids (AHA and AKIA)
- to characterize the pharmacokinetic (PK) profile of preclinical formulation of VS-02 following oral administration to identify the dose level achieving effective concentrations in the cecum, a primary site of bacterial urease activity in the rat gut.

**METHODS**

**In vivo urease activity assay in rat cecal content**

Urease inhibitory activity of HAs was evaluated in pooled cecal content of male Sprague Dawley rats (n=3), diluted to 1% w/v, with 200 mM Na<sub>2</sub>CO<sub>3</sub> pH 8.5. After low speed centrifugation to remove debris, bacteria were incubated with 100 mM urea and an inhibitor for 30 min at 37°C. Ammonia levels were measured before (T0) and after incubation (T30) using a colorimetric urease activity assay kit (Sigma-Aldrich®).

**PK study in rats**

PK of VS-02 was studied in healthy male Sprague Dawley rats. Two groups of rats (n=2/group) received single oral doses of 30 mg/kg or 100 mg/kg VS-02 in gavage.

At pre-defined time points following dosing, rats were euthanized, and plasma, cecal contents, and feces were collected for quantification of VS-02 by the LC-MS/MS system (Sciex Triple Quad 6500+). PK parameters were calculated by non-compartmental analysis using Phoenix WinNonlin software (version 8.5.1).

**REFERENCES**

1. Hoshino, M. et al. *Nature* 285, 46-49 (1982).
2. Hoshino, M. et al. *Gastroenterology* 83, 213-219 (1982).
3. Lagry, V., Wekerman, E. & Demarez, N. *J. Hepatol.* 76, 113-120 (2017).
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5. Lagry, V. et al. *Aliment. Pharmacol. Ther.* 32, 209-218 (2010).

**RESULTS**

**VS-02 DEMONSTRATES SUPERIOR UREASE INHIBITORY ACTIVITY COMPARED TO REFERENCE HYDROXAMIC ACIDS**

Figure 1: Dose response curves for VS-02, AHA, and AKIA. VS-02 demonstrated superior potency compared to AHA and AKIA. VS-02 achieved ~70-80% of maximum inhibition of urease activity at 100 μM, a concentration range of 100-1000 μM should be targeted at the site of action.

**PRECLINICAL FORMULATION OF VS-02 LEADS TO HIGH LOCAL EXPOSURE IN THE CECUM OF HEALTHY RATS**

Figure 2: VS-02 PK profiles in cecal content, feces and plasma of healthy rats. VS-02 demonstrated high local exposure in the cecum, with plasma and feces levels representing less than 1% of the total amount of VS-02 in the rat body.

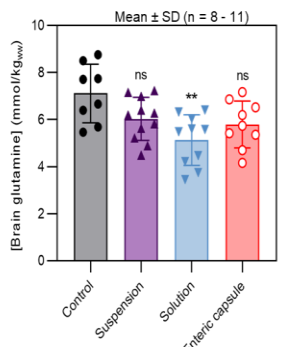
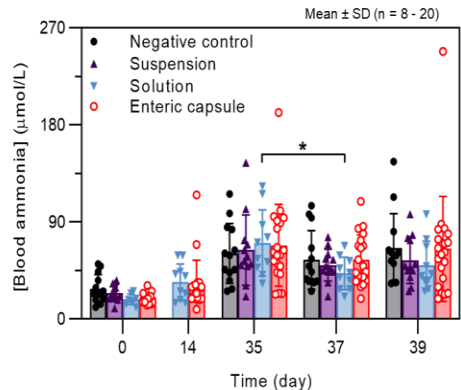
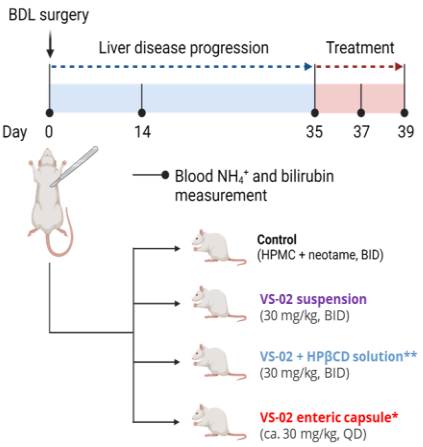
Table 1: PK parameters following oral administration of 30 or 100 mg/kg VS-02

Dose (mg/kg)	Matrix	Time (h)	C <sub>max</sub> (μg/g)	C <sub>min</sub> (μg/g)	AUC <sub>0-24h</sub> (μg·h/g)	AUC <sub>0-24h</sub> (Systemic or Feces) / AUC <sub>0-24h</sub> (Cecal content)
30	Cecal content	3	153.3	5.28	597.2	19.9
	Feces	8	9.1	0.30	12.6	0.4
100	Cecal content	2	1.5	0.05	5.7	0.2
	Feces	6	32.3	0.82	196.4	1.0

**CONCLUSION**

- VS-02 demonstrated efficacy in a complex *in vivo* bacterial system, showing greater potency compared to HAs previously investigated in clinical trials.
- Preclinical formulation of VS-02 enabled targeted delivery of the inhibitor in the cecum and minimized systemic exposure supporting its further assessment in an efficacy studies in animal models of HE.
- Overall, these results support continued development of VS-02 as a potential treatment of HE in patients with cirrhosis.

Abstract presented at ISHEN Conference 2025 | 5 - 8 October, 2025 | St Paulin, Quebec, Canada



- ▶ VS-02 shows greater potency in the inhibition of gut bacterial urease activity as compared to other HAs
- ▶ Preclinical formulation of VS-02 enables targeted delivery in the cecum and minimized systemic exposure

▶ ▶ These results support the development of VS-02 as a potential treatment of HE in patients with cirrhosis ◀ ◀

**Next Step: Potential First-in-human trial could be initiated in 2H27**



## GENFIT Enters Research Collaboration with EVerZom to Advance Exosome-based Regenerative Technology in ACLF

- EVerZom's investigational drug candidate EViv, developed to treat ACLF, using its proprietary exosome platform, represents a novel approach to regenerative therapies
- Pending successful *in vivo* proof-of-concept results, GENFIT has an exclusive option to take a license to drive EViv into clinical development
- Under this research collaboration, EVerZom will contribute exosome expertise with associated bioproduction platform, while GENFIT will spearhead preclinical evaluation of EViv

Acute-On-Chronic Liver Failure (ACLF)

G1090N/NTZ | SRT-015 | CLM-022 | VS-02-HE | EViv

## Urea Cycle Disorders (UCD) & Organic Acidemias (OA)

Ultra-rare disease: 1,900 HAC<sup>2,3,4</sup> per year in children in US+EU4+UK. High mortality (75% at 5 years<sup>2</sup>). Survivors often have severe brain injuries. Neonatal RRT necessitates trained personnel, not available in non-specialized hospital, highly invasive. Delays timely critical medical care.

**VS-01-HAC**

1. *Who we are*

2. *Iqirvo<sup>®</sup> in PBC & PSC*

3. *MASH Diagnostics*

4. *Our lead clinical-stage assets in ACLF & CCA*

**5. Other research programs in ACLF & UCD/OA**

# VS-01-HAC in UCD/OA

## VS-01-HAC

Potential bridging therapy or first-line treatment



Peritoneal

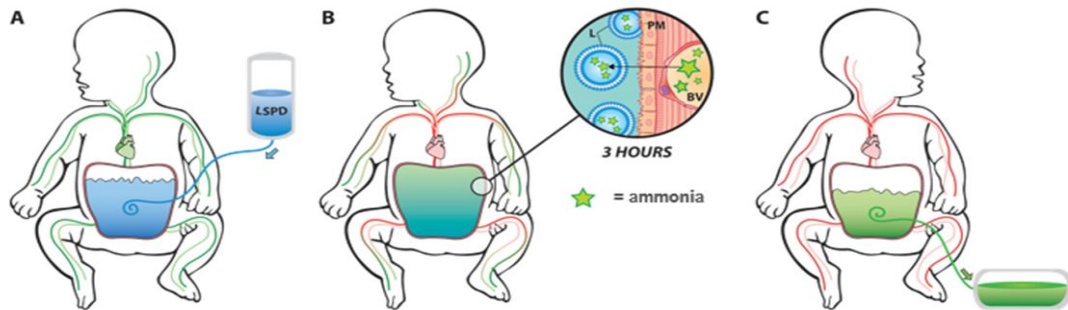
### Findings to date:

#### ✓ Preclinical proof of concept:

- VS-01 achieved robust ammonia clearance, ranging from  $6.0 \pm 2.8$  mL/min on Day 1 to  $9.5 \pm 3.8$  mL/min on Day 10<sup>1,2,3,4</sup> in minipigs

#### ✓ Clinical proof of concept:

- Ammonia clearance in adult patients with decompensated cirrhosis was markedly higher than that reported for conventional renal replacement therapy (RRT) modalities<sup>5</sup>



### Optimal treatment setup

- Allows treatment onset without delay even outside of specialized centers
- Complementary to other therapeutical approaches

### Promising data generated via ACLF program

- Efficient ammonia removal

### Regulatory

- Orphan drug & rare pediatric disease designated (FDA)
- Potentially eligible for FDA priority review voucher upon approval

Next Step: Further explorations of developability