Corporate Presentation

February 2026

GENFIT
TOWARDS BETTER MEDICINE

Disclaimer

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Strategic Highlights and Value Drivers

1

Iqirvo®: Strong commercial sales[1] trajectory in PBC

- Key contributing factor to GENFIT 's robust financial position
- Next update by IPSEN: February 12, 2026

2

G1090N in ACLF: Safety profile and anti-inflammatory activity

- A promising investigational candidate for patients with ACLF and acute decompensation
- Solid foundation to progress into Phase 2 POC studies across the ACLF continuum

3

GNS561 in CCA: Safety profile and early antitumor activity

- Recommended Phase 2 doses expected for 1H26, Phase 2 initiation targeted for 2H26
- A potential to expand beyond CCA & to combine with other anticancer agents

4

Other R&D programs

- Continuum ACLF: SRT-015, CLM-022, VS-02-HE, *EViv*[2]
- UCD/OA: VS-01-HAC

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PBC: Primary Biliary Cholangitis | ACLF: Acute-on-Chronic Liver Failure | HE: Hepatic Encephalopathy | CCA: Cholangiocarcinoma | UCD/OA: Urea Cycle Disorders/Organic Acidemias
1, Commercialized by IPSEN - . 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. PR EVerZom

1. Who we are

2. R&D focus

3. Iqirvo® in PBC

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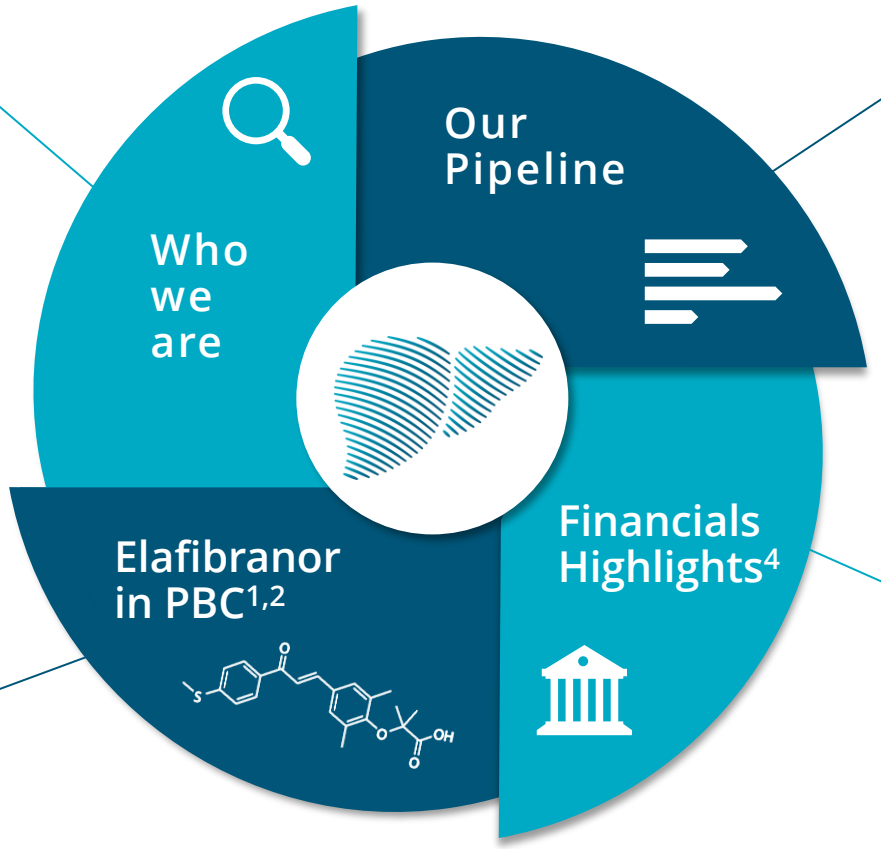
Corporate Highlights

French biopharmaceutical company
Listed on EURONEXT "GNFT"

25+ years in liver diseases, taking early assets to commercial stage[1]

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



ACLF Continuum[3]
- Lead asset: G1090N
- Other assets: SRT-015 | CLM-022 | VS-02-HE
- *EViv (Research collaboration)*

CCA
- GNS561

Other
- VS-01-HAC in UCD/OA

Licensed to IPSEN
~ €90M milestones received
Total potential milestones: €360M
Mid-teen royalties

Launched in 2024
Approved in major markets including the US, Europe, and UK

Royalty deal with HCRx (capped)
€130M received (eligible to additional €55M)
Ipsen milestones excluded from the deal

Cash position: €119M (3Q25)
Cash runway: beyond 2028
No debt overhang

1. In-house from discovery to interim Phase 3 data readout, today commercialized by IPSEN - , 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
PR - GENFIT to receive a €26.5 million milestone payment following the approval of pricing and reimbursement of Ipsen's Iqirvo® in Italy
3. The ACLF pipeline covers a broad spectrum of conditions that patients with ACLF (Acute-on-Chronic Liver Failure) may experience, including Acute Decompensation (AD) or Hepatic Encephalopathy (HE). - PR - Research Collaboration with EVerZom to Advance Exosome-based Regenerative Technology in ACLF
4. PR - GENFIT Reports Third Quarter 2025 Financial Information and Provides a 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

▶ RESEARCH & DEVELOPMENT[1]		Preclinical	Phase 1	Phase 2	Next expected/targeted steps[2]
ACLF Continuum*	G1090N[3]				Potential initiation of Phase 2 POC[F]
	SRT-015[4]				Potential initiation of FIH[G] targeted **2H26**
	CLM-022[5]				Potential initiation of FIH[G] targeted **1H27**
	VS-02-HE				Potential initiation of FIH[G] targeted **2H27**
	EViv[6]	*Exploratory efficacy studies*	*Research Collaboration with EVerZom[1]*		*Decision point **~1H27***
CCA	GNS561[A]	Phase 1b			Potential initiation of Phase 2 targeted **2H26**
HAC	VS-01-HAC (UCD[B]/OA)				Potential initiation of FIH[G] targeted **2H26**

▶ COMMERCIAL

PBC	IPSEN Innovation for patient care / IQIRVO elafibranor 80 mg tablets	Commercialized by Ipsen since 2024[7] – Launched in several markets incl. US, EU, UK, Canada

▶ DIAGNOSTICS

MASH	NIS2+®	EASL/EASD/EASO Guidelines – Qualified NIMBLE – several publications	IVD[H]

[A] Orphan Drug Designation (ODD) FDA
[B] Rare Pediatric Disease Designation FDA ; ODD FDA
[C] HV = Healthy Volunteers
[D] HI = Hepatic Impairment Studies
[E] RI = Renal Impairment Studies
[F] POC = Proof of Concept
[G] FIH = First-in-Human Study
[H] 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 2024 Financial Results and Provides Corporate Update
3. 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

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Targeting Untapped Markets with High Potential

ACLF

Prevalence of ACLF
294,000 in 2021, US, EU4, UK
~300,000 by 2036

Growing at Epidemic Rates
+26% between 2006 and 2014[1]

16 days
Average length of **hospital stay**
(vs 7 days for cirrhotic patients)

$52,000
Average cost per hospitalization **per patient** in US

$6.4Bn
Estimated **annual cost burden** in US in 2021

~$4Bn
Potential **Market Opportunity** for grade 1-2 ACLF in US, EU4, UK by 2030

Oncology

Prevalence of CCA
20,000 to 30,000 for US, EU4, UK

~$3.1Bn
Market estimates for CCA
for US, EU4, UK

Prevalence of iCCA 2L KRAS Mut.
~4,500-6,000 for US, EU4, UK, CN, JP

~€160-200M
Peak annual sales opportunity in iCCA 2L KRAS Mut. for US, EU4, UK, CN, JP

Prevalence of hepatobiliary cancer
~85,000 for US, EU4, UK, CN, JP

Prevalence of liver/GI cancers
~450,000 for US, EU4, UK, CN, JP

UCD/OA

Prevalence
2,000 to 3,000
for US, EU4, UK

~$1.1Bn
Market estimates
for US, EU4, UK

Data from IQVIA market research (2022 & 2025) | EU4 = France, Germany, Italy, Spain

1. due to an aging population and a higher prevalence of steatotic liver disease, diabetes, obesity, as well as alcohol consumption - Axley P, Ahmed Z, Arora S, Haas A, Kuo YF, Kamath PS, Singal AK. NASH Is the Most Rapidly Growing Etiology for Acute-on-Chronic Liver Failure-Related Hospitalization and Disease Burden in the United States: A Population-Based Study. Liver Transpl. 2019 May;25(5):695-705. doi: 10.1002/lt.25443. PMID: 30861321

1. *Who we are*

2. R&D focus

3. *Iqirvo® in PBC*

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 | SRT-015 | CLM-022 | VS-02-HE | *EViv*[1]

Cholangiocarcinoma (CCA)

GNS561

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

VS-01-HAC

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1. Research Collaboration wih EVerZom - PR

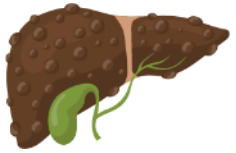
ACLF: A High Unmet Need

CHRONIC PHASE | **ACUTE PHASE**

Chronic Liver Disease → Cirrhosis → Acute Decompensation → ACLF → 23-74% mortality at 28 days

= UNDERLYING CONDITION

- Alcohol Consumption
- Viruses
- Medications
- Metabolic Dysfunction
- Autoimmune Diseases
- Hereditary Diseases



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

= PRECIPITANT

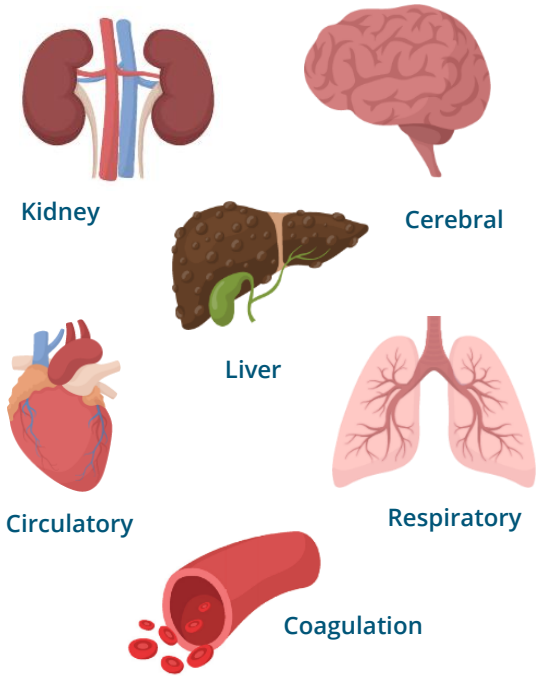
- Bacterial Infection
- Alcohol Consumption
- ... Other

Liver function deteriorates and **serious complications** develop

- Ascites
- Hepatic encephalopathy
- Gastrointestinal bleeding

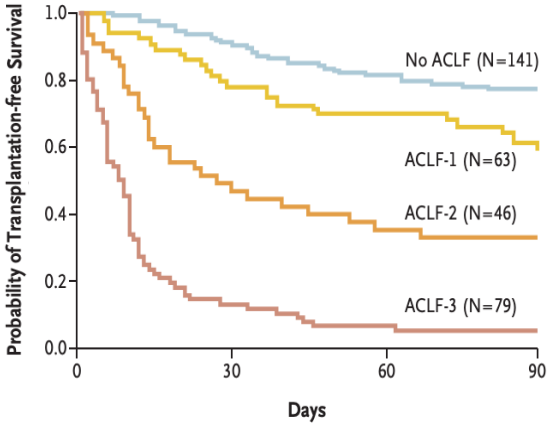
Urgent Hospitalisation

≥ 1 ORGAN DYSFUNCTIONS/FAILURES



Hospitalisation / Intensive Care Unit

► NO APPROVED DRUGS



Death

Sources: Wong F, *et al*. Liver Transpl 2022 | Arroyo V, *et al*. J Hepatol 2015 | Arroyo et al. NEJM 2020 | Jalan et al. J Hepatol 2015 | Moreau et al J Hepatol 2021 | Bernal W, et al. J Hepatol 2021 | PREDICT-study Trebicka, Fernandez, et al. J Hepatol 2021 | Trebicka J et al. Visceral Medicine 2018 | EASL- Clinical Practice Guideline on Decompensated Cirrhosis J Hepatol 2018 | Gustot T, et al. Hepatol 2015 | Arroyo V et al., Nat. Rev. Dis. Primers 2 2016 | Huang DQ, et al. Nat Rev Gastroenterol Hepatol 2023 | Gaspar R, et al. Dig Liver Dis 2019

ACLF: 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
Oral

Anti-inflammatory and anti-bacterial

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

Potential initiation of Phase 2 Proof-of-Concept

SRT-015
Injectable

ASK1 inhibitor

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

Potential initiation of First-in-human targeted 2H26

CLM-022

NLRP3 inflammasome inhibitor

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

Potential initiation of First-in-human targeted 1H27

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[1]

EViv
Injectable

Exosome Technology

Novel approach to **regenerative therapies**

Decision point ~1H27

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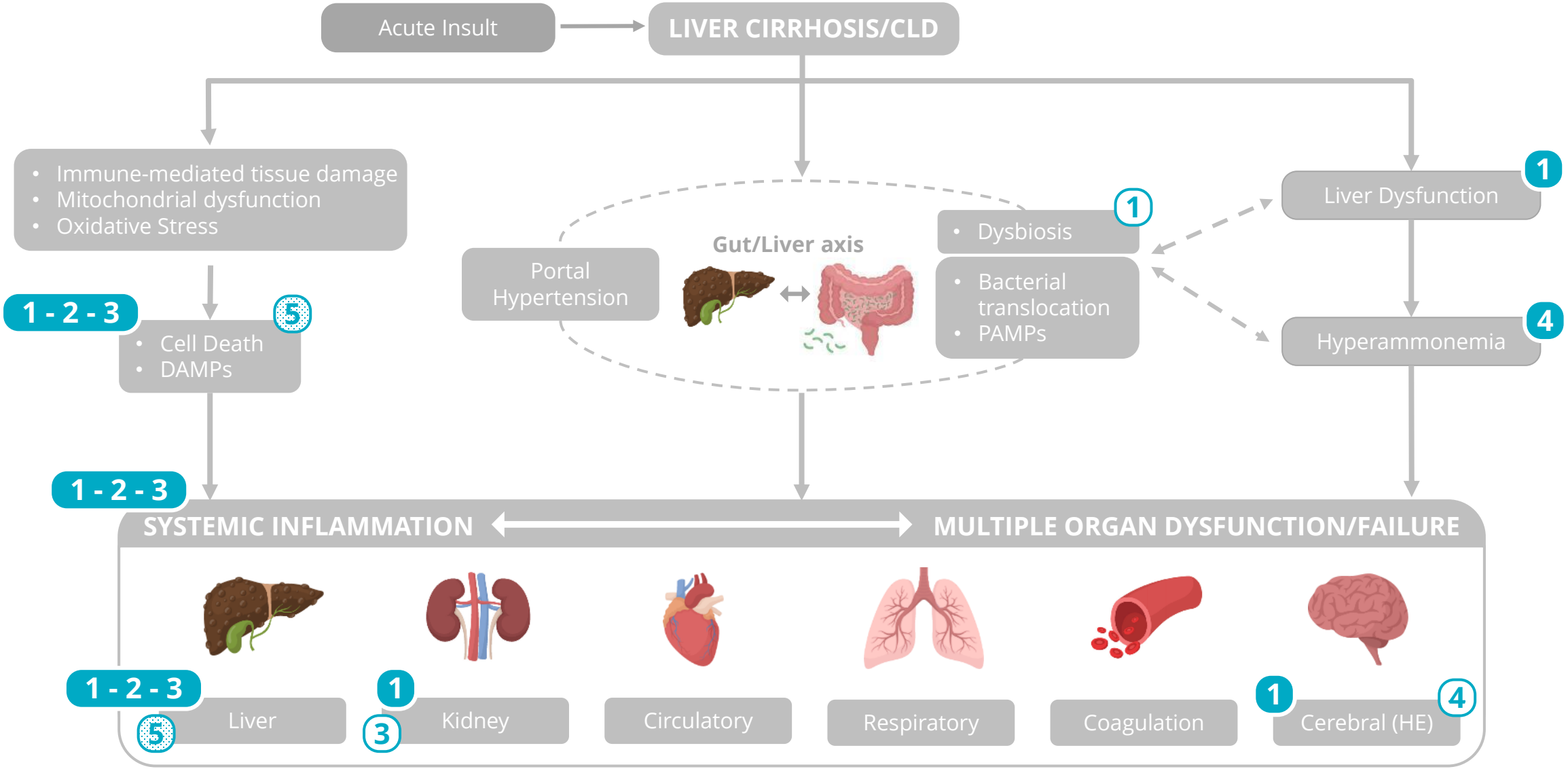
Reflects management's anticipated times, which are subject to change

1. PR EVerZom

Target Multiple Pathways



Demonstrated effect | Expected effect

1 1 G1090N | 2 2 SRT-015 | 3 3 CLM-022 | 4 4 VS-02-HE | 5 *EViv (Research Collaboration with EVerZom)*

A Strong Scientific Rationale for investigational drug G1090N, Our Lead Asset in ACLF

G1090N

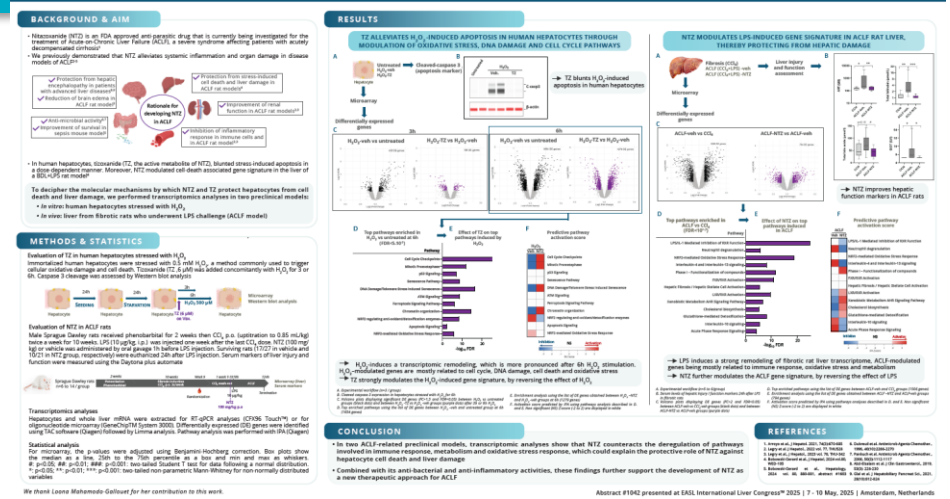
Anti-inflammatory

Oral

Findings to date:

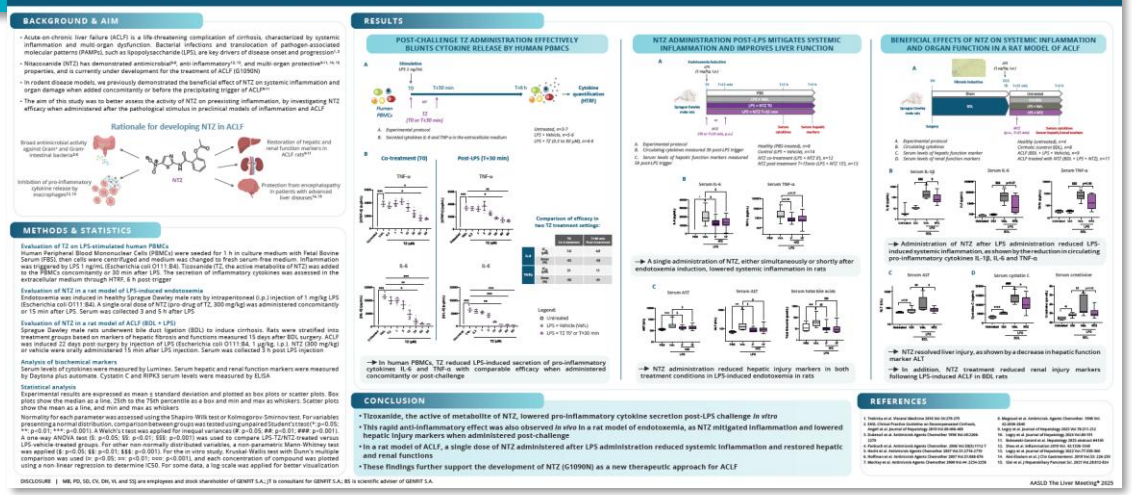
- ✓ Decreases systemic inflammation in animal models, including in ACLF models
- ✓ Protects liver, kidney & brain in rat models of ACLF by decreasing tissue damage
- ✓ Protects mice from mortality in a model of sepsis induced by gut leakage (AASLD 2024 poster)
- ✓ Prevents cell death via anti-apoptotic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

EASL 2025



- ► 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



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

G1090N: Phase 1 Study Design

CT.gov #: NCT07110441

G1090N

Anti-inflammatory

Oral

Key inclusion criteria

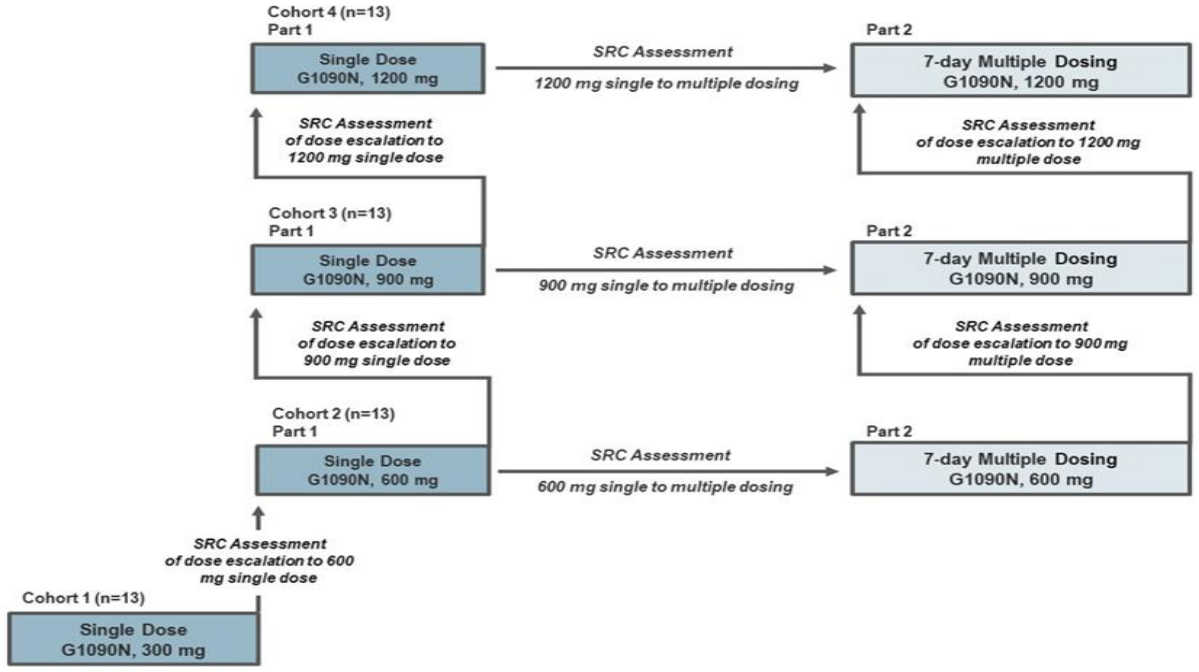
- **Healthy** Volunteers
- Normal liver and renal function

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's Potential Recently Confirmed in the Clinic

G1090N

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**

SRT-015

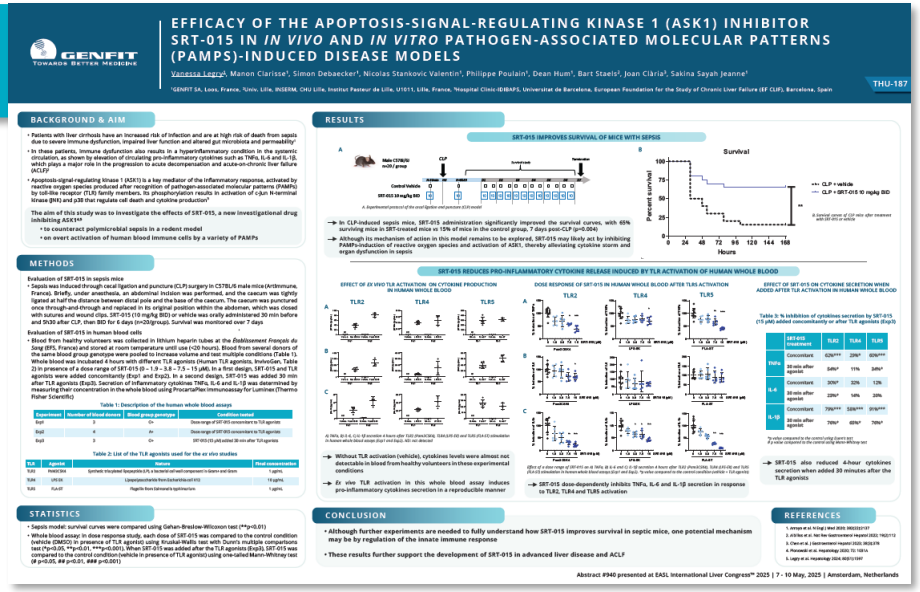
SRT-015
ASK1 inhibitor

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[1], Manon Clarisse[1], Simon Debaeckere[1], Nicolas Stankovic Valentin[1], Philippe Poulain[1], Dean Hum[1], Bart Staels[1], Joan Clària[2], Sakina Sayah Jeanne[1]

THU-187

BACKGROUND & AIM

METHODS

RESULTS

STATISTICS

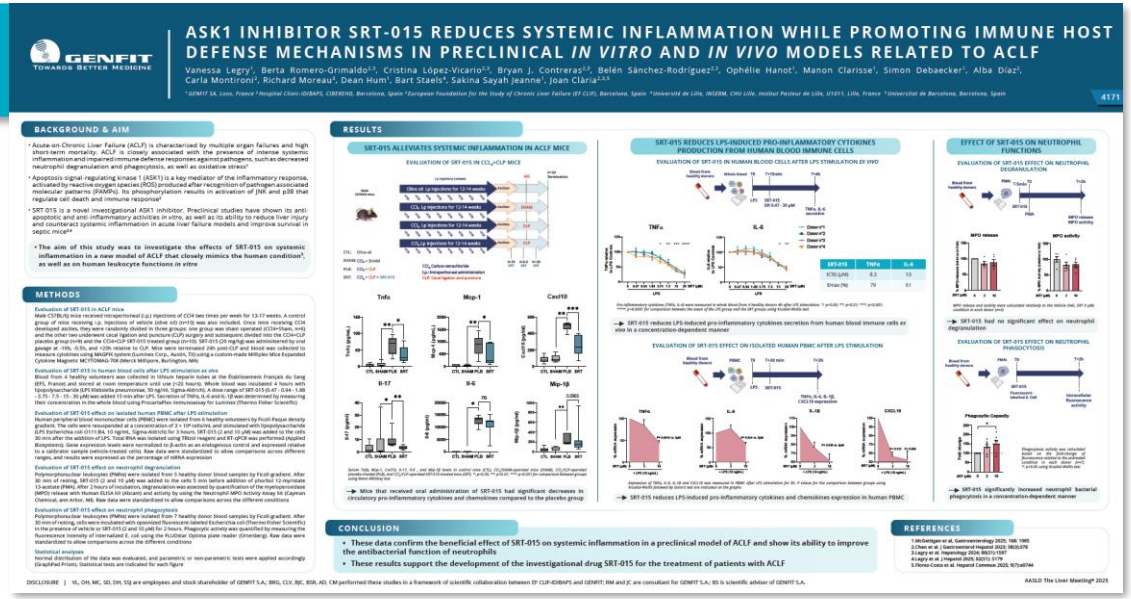
CONCLUSION

REFERENCES

Abstract #940 presented at EASL International Liver Congress™ 2025 | 7 - 10 May, 2025 | Amsterdam, Netherlands

- ► SRT-015 dose-dependently inhibits TNF-α, IL-6 and IL-1β 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

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[1], Berta Romero-Grimaldo[2,3], Cristina López-Vicario[2,3], Bryan J. Contreras[1,3], Belén Sánchez-Rodríguez[2,3], Ophélie Hanot[1], Manon Clarisse[1], Simon Debaeckere[1], Alba Díaz[1], Carla Montironi[2], Richard Moreau[1], Dean Hum[1], Bart Staels[4], Sakina Sayah Jeanne[1], Joan Clària[2,4,5]

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BACKGROUND & AIM

METHODS

RESULTS

CONCLUSION

REFERENCES

- ► 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

Next Step: Potential **First-in-human** trial could be initiated as early as **2H26**

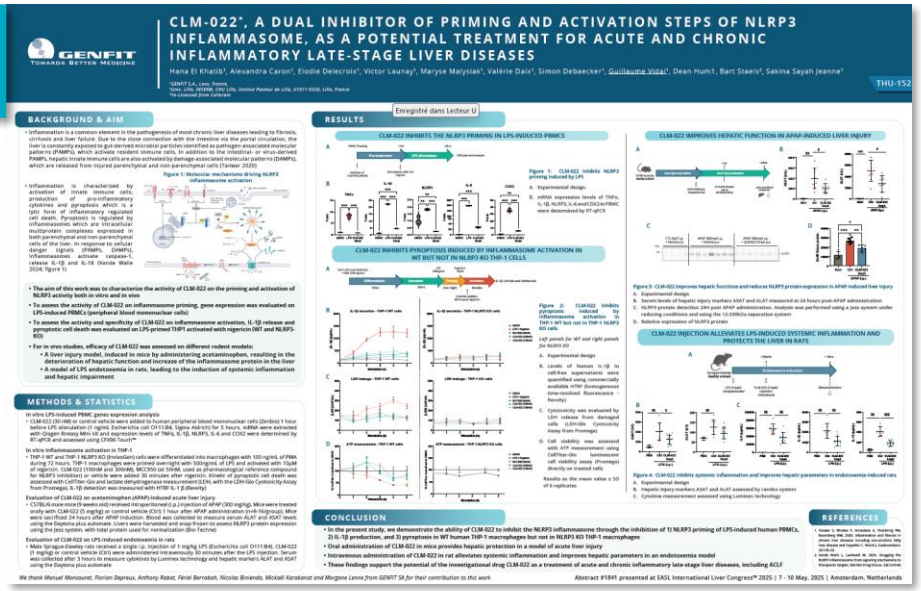
CLM-022

CLM-022
NLRP3 inflammasome inhibitor

Findings to date:

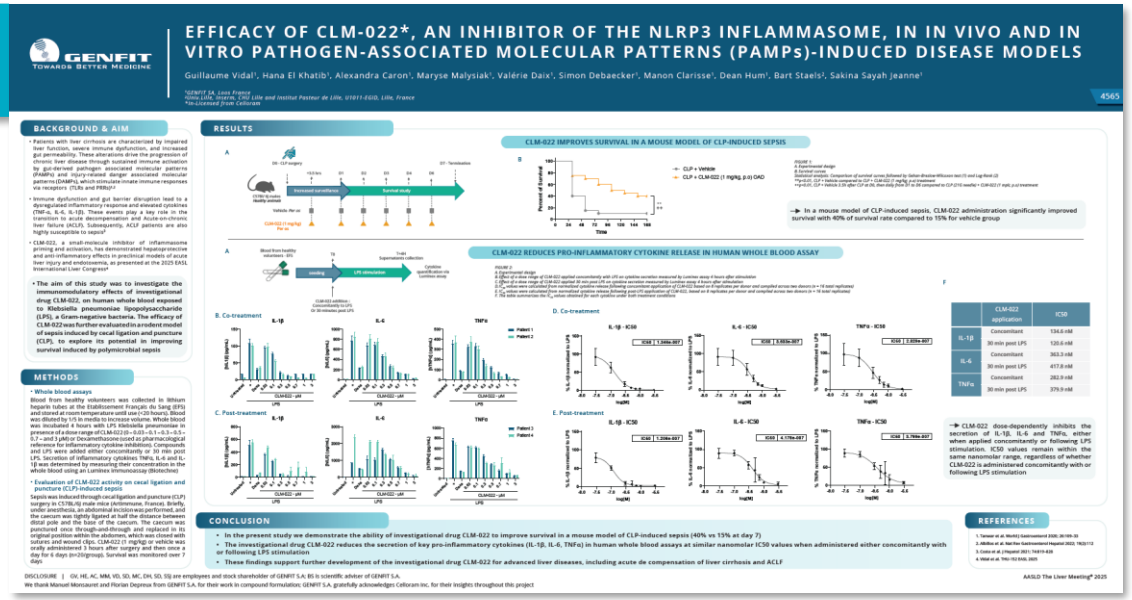
- ✓ Protects the liver in pre-clinical ALF models
- ✓ Protects mice from mortality induced by gut leakage-induced sepsis
- ✓ Dose-dependently inhibits IL-1β secretion (AASLD 2024 poster)
- ✓ Shows potent inhibition of priming and activation steps of NLRP3 inflammasome

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

- ► CLM-022 inhibits NLRP3 inflammasome priming of LPS-induced human PBMCs
- ► Inhibition of IL-1β 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

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

- ► 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: Pending further positive developments, potential **First-in-human** trial could be initiated in **1H27**

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VS-02-HE

VS-02-HE
Urease inhibitor

Hepatic Encephalopathy

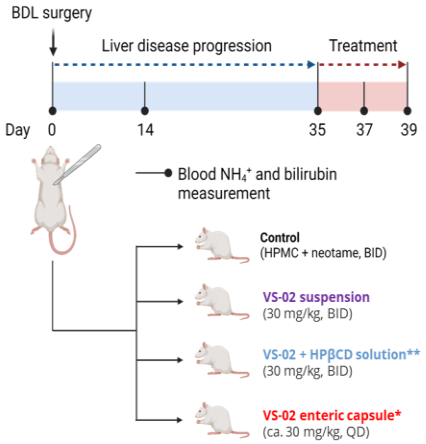
Oral

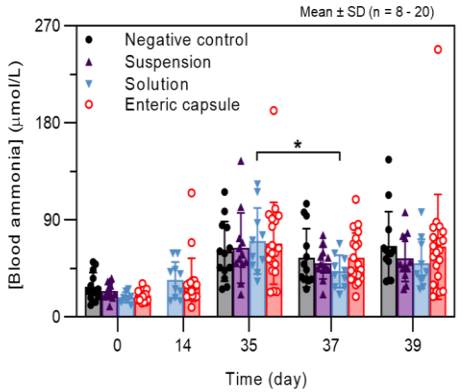
About Hepatic Encephalopathy (HE)

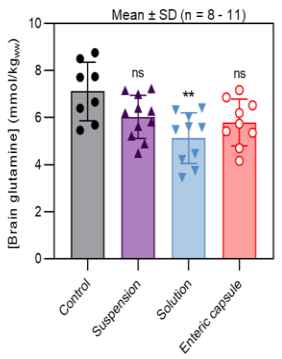
- One of the **most common complications of liver cirrhosis and ACLF**
- A **central nervous system disorder** representing a diverse spectrum of neurologic symptoms
- **Excess ammonia** induces alteration of cell metabolism and can result in brain edema
- **> 45% of patients with cirrhosis** will experience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

Findings to date:

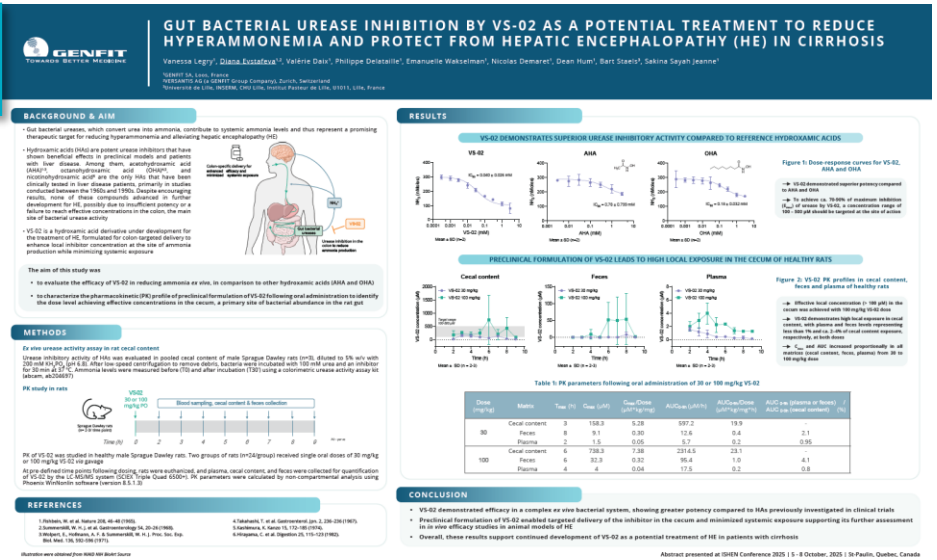
- ✓ VS-02 lowers ammonia levels in an acute liver injury model
- ✓ VS-02 lowers ammonia & brain glutamine levels in a chronic liver disease model
- ✓ VS-02 demonstrates gut bacterial urease inhibitory activity







ISHEN 2025


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

BACKGROUND & AIM

METHODS

RESULTS

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

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

CONCLUSION

REFERENCES

- ▶ 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: Nonclinical studies and formulation development
Potential **First-in-human** trial could be initiated in **2H27**

HAs: Hydroxamic Acids

Eviv: A Research Collaboration with EVerZom

EViv
Exosome Technology
Injectable

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**

Press release

1. *Who we are*
2. **R&D focus**
3. *Iqirvo® in PBC*

Acute-On-Chronic Liver Failure (ACLF)

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

Cholangiocarcinoma (CCA)

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

GNS561

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

VS-01-HAC

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[1] Lamarca et al. 2021

CCA with KRAS mutation: A High Unmet Need

Rare and aggressive liver malignancy that develops in the bile ducts

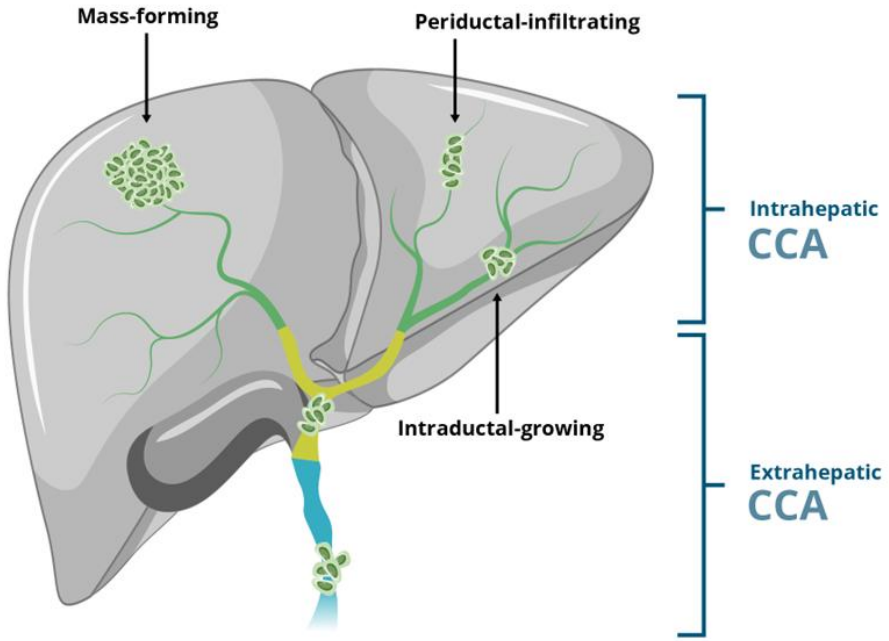
- As the cancer grows, it can **block the bile ducts** and lead to damage to the liver and other organs
- Without treatment **<20% of patients survive 5 years** from diagnosis[1]

Unmet needs

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

~30% of patients with CCA harbor **KRAS mutations**[4]

- **one of the most common genes that might be mutated** or amplified resulting in the overactivation of some of these pathways[5]
- associate with **shorter survival**[6]
- 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, pages557–588 (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)

Beneficial anti-cancer effects

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

Autophagy: tumor cell survival mechanism

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

#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

Blocks cancer cell survival

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

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GNS561: Phase 1b/2a Study Design

CT.gov #: NCT05874414

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

Ongoing recruitment

N_{TOTAL} = 74 PTS

PHASE 1b
Dose finding

- Cohort 4a: GNS561 200mg qd 5/7 d + T 1.0mg qd
- Cohort 4: GNS561 200mg qd + T 2.0mg qd
- Cohort 3a: GNS561 150mg qd 5/7 d + T 1.0mg qd
- Cohort 3: GNS561 150mg qd + T 2.0mg qd
- Cohort 2a: GNS561 100mg qd 5/7 d + T 1.0mg qd
- Cohort 2: GNS561 100mg qd + T 2.0mg qd
- Cohort 1 (start): GNS561 50mg qd + T 2.0mg qd
- Cohort -1: GNS561 50mg qd + T 1.5mg qd
- Cohort -2: GNS561 50mg qd + T 1.0mg qd

STOP

RP2DC

PHASE 2a POC
Single arm
N=50

Simon 2-stage

Stage 1
N= 20§

Interim Analysis

Stage 2
N= 30

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

Primary endpoint:
Efficacy – objective response rate

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

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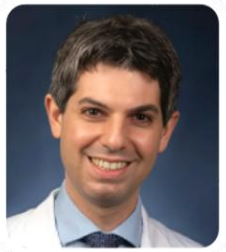
Phase 1b: Highly Encouraging Early Data

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**

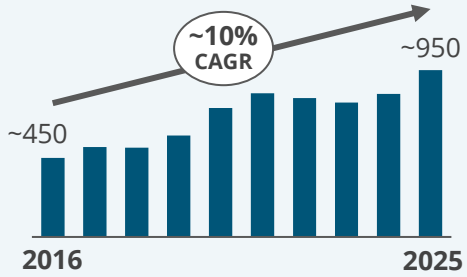
Press release

Moving Forward

- **Phase 1b dose escalation** will continue as planned to confirm activity signal
- **1Q2026** - New data from next patient cohorts expected
- **1H2026** - Completion expected results will be used to establish recommended Phase 2 combination doses
- **2H2026** – 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[1,2]



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)[1]

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

Anti-PD-1 | RAFi

Ex: Evidence already exists in HCC for GNS561 in combination with anti-PD-1 in a mouse model[3]

1. Data from IQVIA market research (2022) | 2. PubMed (accessed 05/12/2025) | EU4 = France, Germany, Italy, Spain | 3. Bestion et al., Ezurpimtrostat, A Palmitoyl-Protein Thioesterase-1 Inhibitor, Combined with PD-1 Inhibition Provides CD8+ Lymphocyte Repopulation in Hepatocellular Carcinoma, Targ. Oncol., 2024

1. *Who we are*
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Acute-On-Chronic Liver Failure (ACLF)

G1090N | SRT-015 | CLM-022 | VS-02-HE

Cholangiocarcinoma (CCA)

GNS561

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

Ultra-rare disease: 1,900 HAC[2,3,4] per year in children in US+EU4+UK. High mortality (75% at 5 years[2]). 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

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[2.] Maillot et al. (2007) | [3.] Batshaw et al. (2015) | [4.] Nettesheim (2017)

VS-01-HAC in UCD/OA

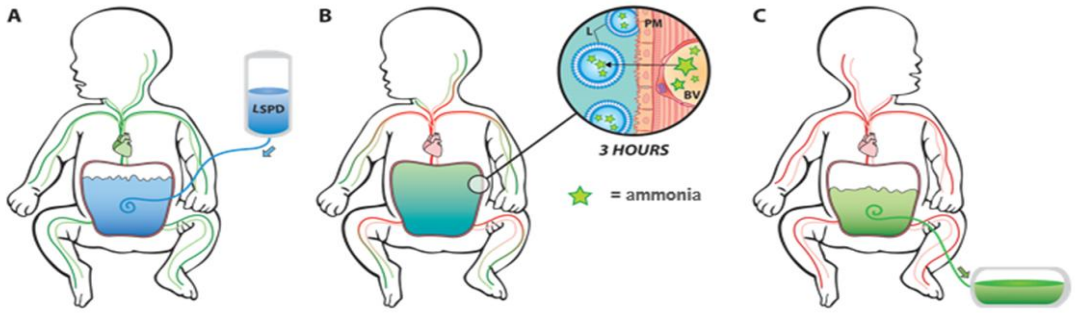
VS-01-HAC
Potential bridging therapy or first-line treatment

Peritoneal

Findings to date:

✓ **Preclinical proof of concept:**
- VS-01 achieved robust ammonia clearance, ranging from 6.0 ± 2.8 mL/min on Day 1 to 9.5 ± 3.8 mL/min on Day 10[1,2,3,4] 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[5]



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[6]

Next Step: Juvenile toxicology study ongoing with data expected early 1H26, pharmacological validation in HA models expected in 1H26
Potential launch of First-in-human targeted 2H26

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[1.] Forster V. et al. Sci Transl Med 2014 | [2.] Agostoni V. et al., Adv Funct Mater 2016 | [3.] Giacalone G. et al., J Cont Release 2018 | [4.] Matoori S. et al., J Cont Release 2020 | [5.] VS-01 Phase 1b Uschner et al., Lancet Gastroenterol Hepatol, in press | [6.] Subject to FDA prolonging validity of the voucher program

1. *Who we are*
2. *R&D focus*

3.Iqirvo® in PBC

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Solid Commercial Performance from Ipsen in PBC

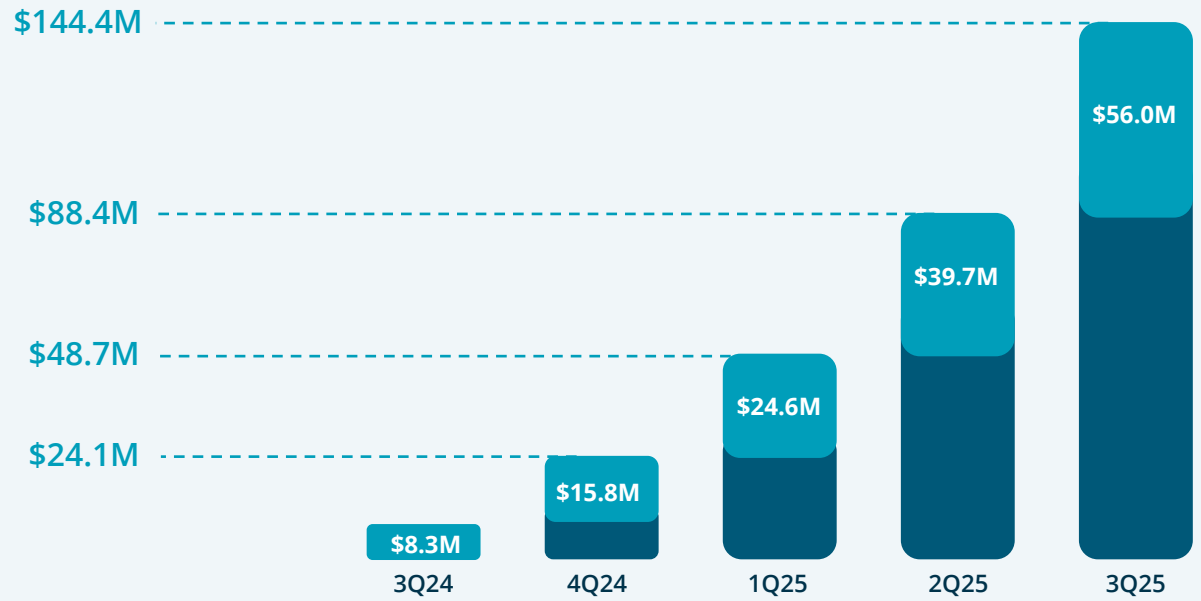
1. Rapid regulatory approvals[1]

IQIRVO® elafibranor 80 mg tablets

2024	2025
FDA	3 major EU countries **Reimbursement**
EMA	
MHRA	

2. Successful commercial launch

Iqirvo® sales (global, quarterly) since commercial launch[2]



Feb12 2026

IPSEN 2025 results

Cumul. milestones payments received[3]
€88.5M

Cumul. royalties received[4]
€15.3M

Sep'25: Intercept Announces Voluntary Withdrawal of OCALIVA® for Primary Biliary Cholangitis (PBC) from the US Market[5]

1. Ipsen's Iqirvo® receives U.S. FDA accelerated approval
   Ipsen's Iqirvo® (elafibranor) approved in the European Union
2. Ipsen delivers strong sales in the first quarter 2025
   Ipsen publishes its URD2024
   Ipsen sales 3Q25
3. 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
4. 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 OCEANEs holders
5. Intercept Announces Voluntary Withdrawal of OCALIVA® for Primary Biliary Cholangitis (PBC) from the US Market