

# Corporate Overview

October 2025

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This presentation contains certain forward-looking statements, including those within the meaning of the Private Securities Litigation Reform Act of 1995 with respect to GENFIT, including, but not limited to statements about GENFIT's corporate strategy and objectives, our achievement of key milestones enabling us to receive payments under our license agreements, the potential of Iqirvo® (elafibrator) to receive marketing authorization and successful launch and commercialization in countries other than those in which it is currently approved and commercialized and/or in indications other than PBC, our achievement of the necessary objectives to obtain the future €55 million in additional payments under the royalty financing agreement signed with HCRx (Royalty Financing), anticipated timing for study enrollment and data readouts, in particular regarding our development programs for G1090N in the prevention and/or treatment of ACLF and for GNS561 in CCA, and development plans for our other pipeline programs, in particular those related to SRT-015, CLM-022 and VS-02 HE in ACLF, and VS-01 in UCD, the expected timing for potential regulatory approvals and the impact of the development of our programs and our internal organization, our ability to qualify for and obtain specific regulatory pathways, as well as our financial outlook including cash flow and cash burn projections as updated following the termination of our VS-01 in ACLF research program and business and R&D activity projections for 2025 and beyond. The use of certain words, such as "believe", "potential", "expect", "target", "may", "will", "should", "could", "if" and similar expressions, is intended to identify forward-looking statements. Although the Company believes its expectations are based on the current expectations and reasonable assumptions of the Company's management, these forward-looking statements are subject to numerous known and unknown risks and uncertainties, which could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking statements. These risks and uncertainties include, among others, the uncertainties inherent in research and development, including in relation to safety of drug candidates, cost of, progression of, and results from, our ongoing and planned clinical trials, patient recruitment, review and approvals by regulatory authorities in the United States, Europe and worldwide, of our drug and diagnostic candidates, pricing, approval and commercial success of elafibrator in the relevant jurisdictions, exchange rate fluctuations, and our continued ability to raise capital to fund our development, as well as those risks and uncertainties discussed or identified in the Company's public filings with the AMF, including those listed in Chapter 2 "Risk Factors and Internal Control" of the Company's 2024 Universal Registration Document filed on April 29, 2025 (no. 25-0331) with the Autorité des marchés financiers ("AMF"), which is available on GENFIT's website ([www.genfit.fr](http://www.genfit.fr)) and the AMF's website ([www.amf.org](http://www.amf.org)), and those discussed in the public documents and reports filed with the U.S. Securities and Exchange Commission ("SEC"), including the Company's 2024 Annual Report on Form 20-F filed with the SEC on April 29, 2025 and subsequent filings and reports filed with the AMF or SEC, including the Half-Year Business and Financial Report at June 30, 2025 or otherwise made public, by the Company. In addition, even if the results, performance, financial position and liquidity of the Company and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. These forward-looking statements speak only as of the date of publication of this press release. Other than as required by applicable law, the Company does not undertake any obligation to update or revise any forward-looking information or statements, whether as a result of new information, future events or otherwise.

# 1. Who we are

2. *R&D focus*

3. *Iqirvo<sup>®</sup> in PBC*

4. *Takeaways*

# Highlights

 Lille (HQs) & Paris  Zurich  Cambridge, MA

French **biopharmaceutical** company  
Dual-listed on Euronext & NASDAQ (GNFT)

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

Now focused on rare, severe liver diseases with high unmet medical need

Licensed to IPSEN ✓  
€120M in upfront payment  
€90M in milestone (to date, out of €360M)  
Mid-teen royalties

Approved ✓  
US FDA (June 2024)  
EMA (September 2024)  
UK (October 2024)

Royalty deal with HCRx ✓  
Secured €130M  
2 additional tranches (€55M)  
Ipsen milestones excluded from the deal  
Capped



4 assets in in ACLF<sup>3</sup>

- G1090N ACLF (HV, POC)
- SRT-015 ACLF (preclinical)
- CLM-022 ACLF (preclinical)
- VS-02-HE (preclinical)

2 additional programs

- GNS561 in CCA (Phase 1b/2a)
- VS-01-HAC in UCD/OA (preclinical)

Cash position: €107.5M (2Q25) excl. €26.5M milestone received from IPSEN in July 2025

Cash runway: beyond 2028<sup>5</sup>

No debt overhang<sup>4</sup>



1. In-house from discovery to interim Phase 3 data readout, today commercialised 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 OCEANES 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. 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).  
4. PR - GENFIT Reports First Half 2025 Financial Results and Provides Corporate Update  
5. 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, ii) drawing down all additional installments under the Royalty Financing, and iii) the reimbursement at maturity in October 2025 of any OCEANES not converted or repurchased and cancelled 7 and iv) the discontinuation of the VS-01 program in ACLF as outlined above

# 25 Years of Liver Disease Innovation: Expertise from Discovery to Launch



## Inception & early years



## Clinical development in **chronic** liver diseases



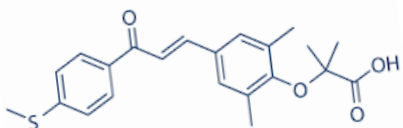
## Pivot to acute, rare and life-threatening liver diseases with high unmet needs

1999

2022

Development of R&D know-how via collaborations with Big Pharma

Shift to in-house discovery: elafibranor (GFT505)



Development of elafibranor in MASH up to Phase 3 included

Positive 52-week ELATIVE® Phase 3 trial evaluating elafibranor in PBC

Know-how and experience in liver diseases

- **Research** (collaborations with academia, liver disease models, spheroids, etc.)
- **Clinical** (large international trials, KOL networks, patient engagement, etc.)
- **Regulatory** (FDA/EMA interactions, etc.)

- 6 programs
- 2 data readouts expected **end of 2025**

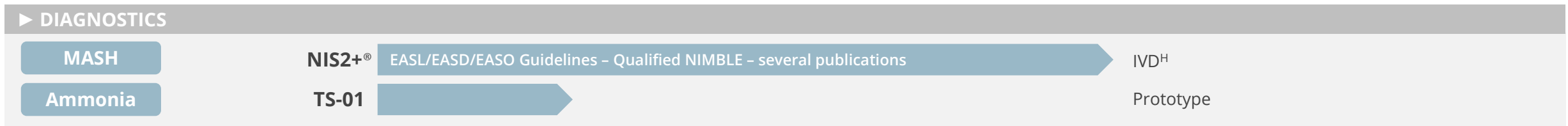
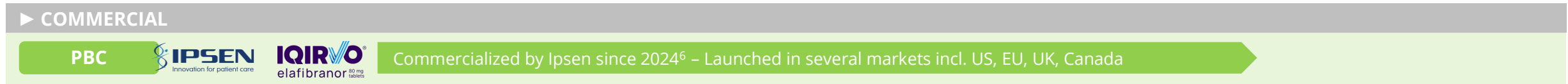
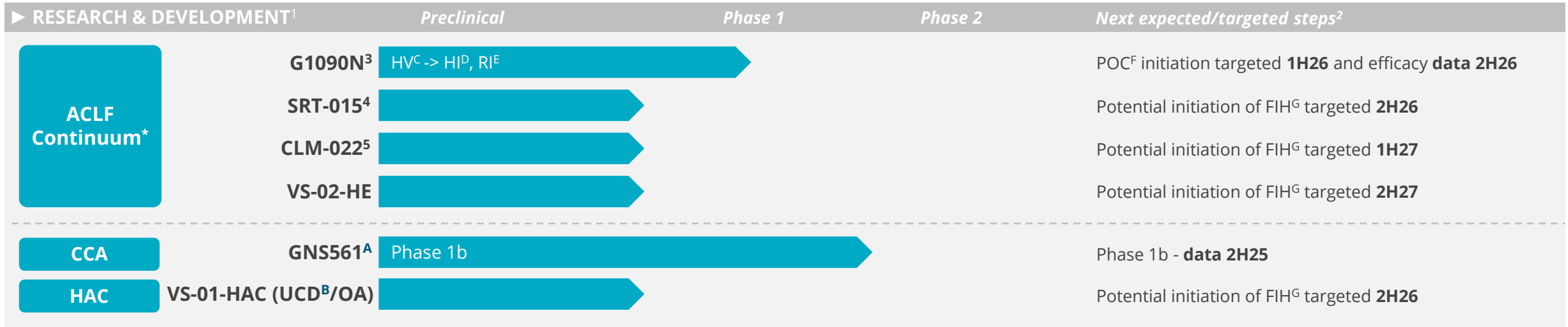
### Acute-on-Chronic Liver Failure (ACLF) Pipeline

- A diversified pipeline with a strategic focus on ACLF, including AD of liver cirrhosis and HE
- 4 assets: G1090N, SRT-015, CLM-022, VS-02-HE
- Safety data (healthy volunteers) and markers of early efficacy expected **by end 2025** with G1090N

### Other life-threatening liver diseases

- 2 assets: GNS561 in CCA, VS-01-HAC in UCD/OA
- Phase 1b data **end of 2025** with GNS561

# Pipeline



<sup>A</sup> Orphan Drug Designation (ODD) FDA  
<sup>B</sup> Rare Pediatric Disease Designation FDA ; ODD FDA  
<sup>C</sup> HV = Healthy Volunteers    <sup>D</sup> HI = Hepatic Impairment Studies  
<sup>E</sup> RI = Renal Impairment Studies    <sup>F</sup> POC = Proof of Concept  
<sup>G</sup> FIH = First-in-Human Study    <sup>H</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 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. Out-licensed to Ipsen. | [US-FDA-accelerated-approval](#) | [UE-EMA-approval](#) | [UK-MKRA-approval](#) | [Canada-approval](#); Potentially eligible for priority review voucher upon approval by the FDA

# Targeted Markets

High unmet medical needs

## ACLF

### Prevalence of ACLF

**294,000** in 2021, US, EU4 & UK  
**~300,000** patients by 2036

**\$52,000**

**Average cost** per hospitalization  
**per patient** in US

### Growing at Epidemic Rates

**+26%** between 2006 and 2014<sup>1</sup>

*due to an aging population and a higher prevalence of steatotic liver disease, diabetes, obesity, as well as alcohol consumption*

**\$6.4Bn**

Estimated **annual cost burden**  
in US in 2021  
(a nearly 4-fold increase since 2011)

**16 days**

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

**~\$4Bn**

Potential **Market Opportunity**  
for grade 1-2 ACLF in the  
US, EU4 & UK by 2030

## CCA

### Prevalence

**20,000 to 30,000**  
for US, EU4 & UK

**~\$3.1Bn**

**Market estimates**  
for US, EU4 & UK

## UCD/OA

### Prevalence

**2,000 to 3,000**  
for US, EU4 & UK

**~\$1.1Bn**

**Market estimates**  
for US, EU4 & UK

1. *Who we are*
- 2. R&D focus**
3. *Iqirvo<sup>®</sup> in PBC*
4. *Takeaways*

## 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**

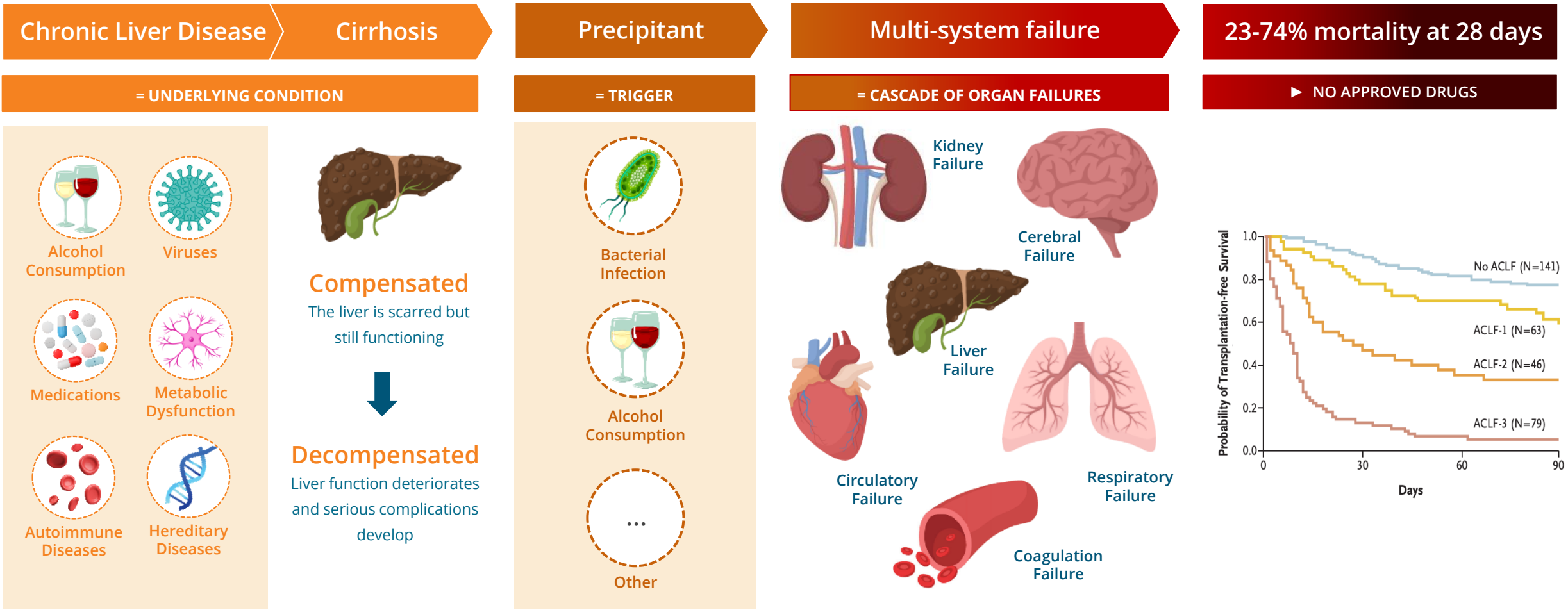
## Cholangiocarcinoma (CCA)

GNS561

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

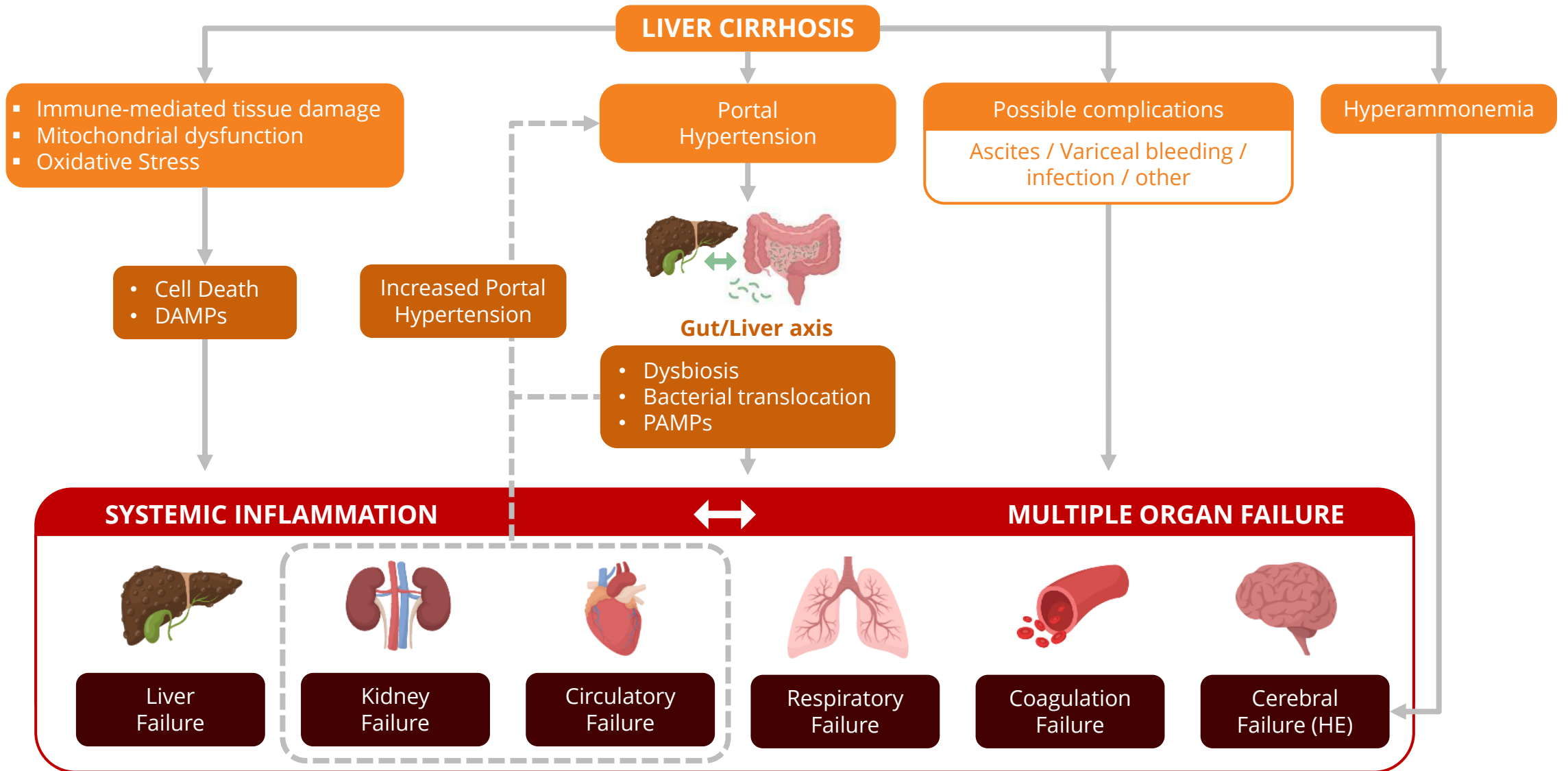
VS-01-HAC

# What is ACLF?



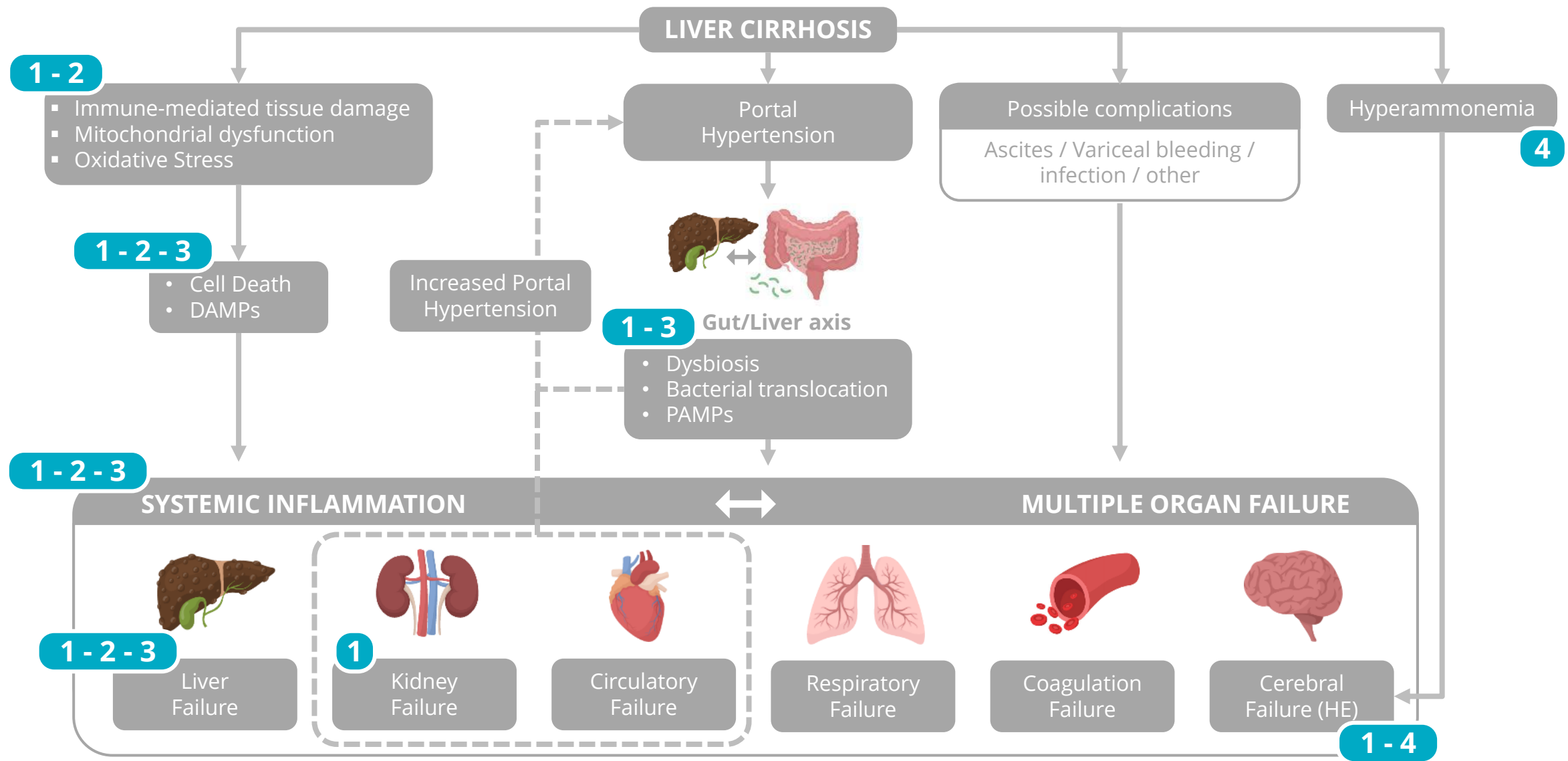
Sources: Wong F. *et al.* Liver Transpl 2022 | Arroyo V. *et al.* J Hepatol 2015 | Arroyo *et al.* NEJM 2020 | Jalan *et al.* J Hepatol 2015 | Moreau *et al.* J Hepatol 2021 | Bernal W. *et al.* J Hepatol 2021 | PREDICT-study Trebicka, Fernandez, *et al.* J Hepatol 2021 | Trebicka J *et al.* Visceral 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

# Pathophysiology of ACLF



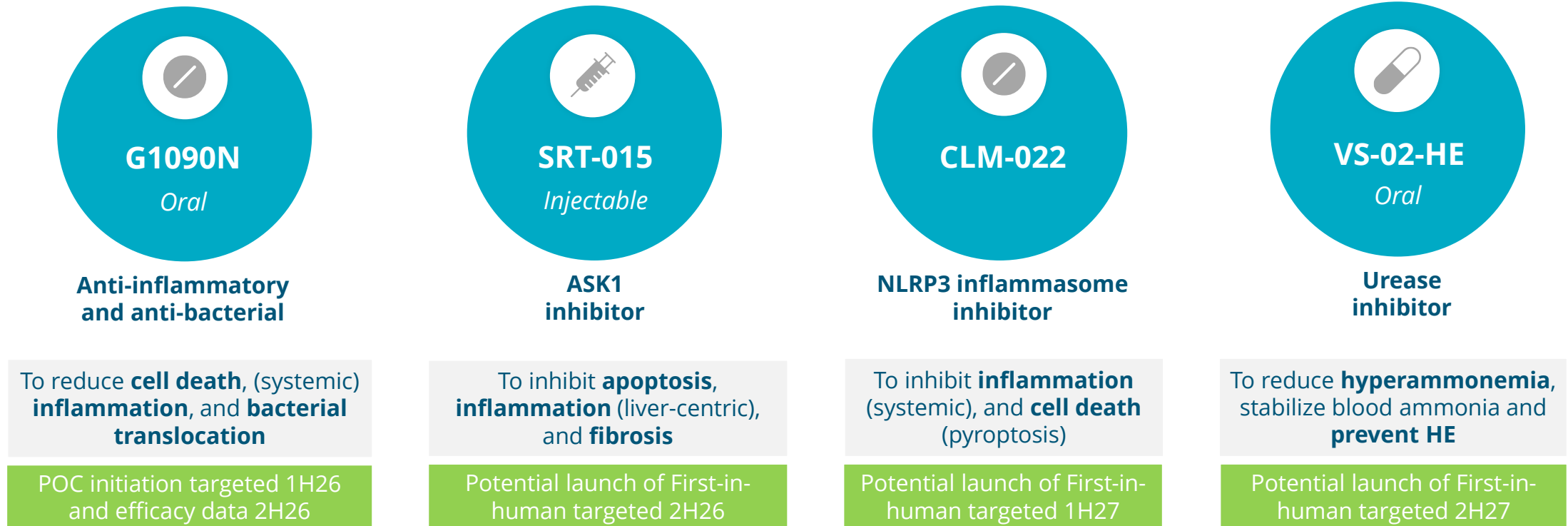
PAMPs = Pathogen-Associated Molecular Patterns | DAMPs = Damage-Associated Molecular Patterns

# Our Approach to ACLF: 4 Assets Targeting Multiple Pathways



# Our ACLF Pipeline: Complementary Mechanisms of Action

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



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

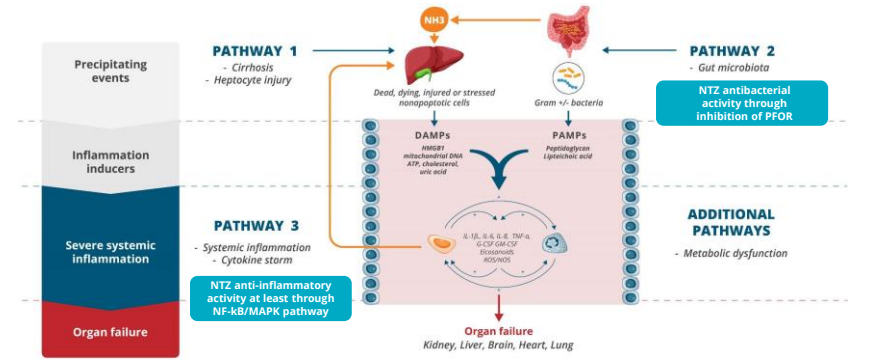
# G1090N

**G1090N**  
Anti-inflammatory and anti-bacterial

Oral

## Findings to date:

- ✓ Protects liver, kidney & brain in rat model of ACLF
- ✓ Prevents cell death via anti-apoptotic and anti-necroptotic effects
- ✓ Reduces PAMPs-induced inflammation
- ✓ Counters LPS-induced liver damage



**AASLD 2024**

GENFIT  
TOWARDS BETTER MEDICINE

### EFFICACY OF NITAZOXANIDE (NTZ) IN PATHOGEN-ASSOCIATED MOLECULAR PATTERNS (PAMPs)-INDUCED DISEASE MODELS

Main: Bobowski-Gerard, Simon Debecker\*, Philippe Delatour\*, Philippe Poulain\*, Yacine Hajj\*, Sakina Sayah Jeanne\*, Dean Hum\*, David Dombrowski\*, Vanessa Legry\*, Bart Staels\*

**BACKGROUND & AIM**

- Miscellaneous in FDA approved anti-infective drug that is currently under development for the treatment of Acute on Chronic Liver Failure (ACLF). It was used while waiting patients with finally demonstrated efficacy.
- We previously demonstrated that NTZ alleviates systemic inflammation and organ damage in disease models of ACLF.

**RESULTS**

**NTZ DOSE-DEPENDENTLY ALLEVIATES LPS-INDUCED SYSTEMIC INFLAMMATION AND IMPROVES HEPATIC FUNCTION IN RATS**

**NTZ IMPROVES SURVIVAL OF MICE WITH SEPSIS**

**TZ REDUCES PRO-INFLAMMATORY CYTOKINES RELEASE INDUCED BY A LARGE RANGE OF TLR AGONISTS IN MACROPHAGES**

**CONCLUSION**

Oral NTZ treatment alleviates systemic inflammation and improves survival in endotoxemia and sepsis models, respectively.

**REFERENCES**

**DISCUSSION**

**EASL 2025**

GENFIT  
TOWARDS BETTER MEDICINE

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

Main: Bobowski-Gerard\*, Nicolas Stankovic Valentin\*, Sylvie Detelique\*, Simon Debecker\*, Nina S'Ersteven\*, Philippe Delatour\*, Sakina Sayah Jeanne\*, Dean Hum\*, Vanessa Legry\*, Jérôme Eeckhout\*, Joakim Clarin\*, Bart Staels\*

**BACKGROUND & AIM**

- Nitazoxanide (NTZ) is an FDA approved and generic drug that is currently being investigated for the treatment of Acute on Chronic Liver Failure (ACLF). It was used while waiting patients with finally demonstrated efficacy.
- We previously demonstrated that NTZ alleviates systemic inflammation and organ damage in disease models of ACLF.

**RESULTS**

**TZ ALLEVIATES H<sub>2</sub>O<sub>2</sub>-INDUCED APOPTOSIS IN HUMAN HEPATOCYTES THROUGH MODULATION OF OXIDATIVE STRESS, DNA DAMAGE AND CELL CYCLE PATHWAYS**

**NTZ MODULATES LPS-INDUCED GENE SIGNATURE IN ACLF RAT LIVER, THEREBY PROTECTING FROM HEPATIC DAMAGE**

**CONCLUSION**

In two ACLF-related preclinical models, transcriptomic analyses show that NTZ counteracts the deregulation of pathways involved in immune response, metabolism and oxidative stress responses, which could explain the protective role of NTZ against hepatocyte cell death and liver damage.

- ▶ NTZ dose-dependently alleviates LPS-induced systemic inflammation and improves hepatic function in rats
- ▶ Improves survival of mice with sepsis
- ▶ TZ reduces pro-inflammatory cytokines release induced by a large range of toll-like receptor (TLR) agonists in macrophages

- ▶ TZ alleviates H<sub>2</sub>O<sub>2</sub>-induced apoptosis in human hepatocytes through modulation of oxidative stress, DNA damage and cell cycle pathways
- ▶ NTZ modulates LPS-induced gene signature in ACLF rat liver, thereby protecting from hepatic damage



**G1090N**  
Anti-inflammatory and anti-bacterial



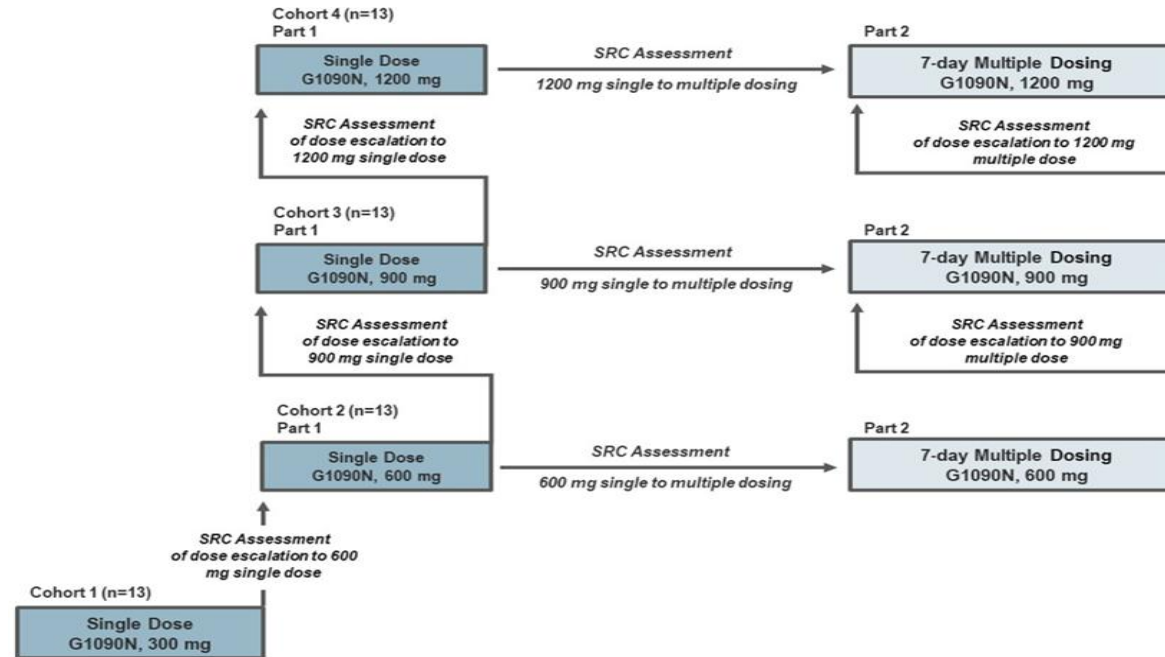
Oral

- ✓ Key inclusion criteria**
- **Healthy** Volunteers
  - Normal liver and renal function

- ⊘ Key exclusion criteria**
- **Significant medical history** or recent illness

N<sub>TOTAL</sub>  
=  
**52**  
PTS

Ongoing 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.

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

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

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**
- has **antibacterial** properties

**Next Steps: Safety data (healthy volunteers) and markers of early efficacy expected by end 2025  
POC targeted to start 1H26 to generate efficacy data by the end of 2026**



# CLM-022

## CLM-022 NLRP3 inflammasome inhibitor



### Findings to date:

- ✓ Investigational drug CLM-022 dose-dependently inhibits IL-1 $\beta$  secretion
- ✓ In vivo efficacy demonstrated in ALF models
- > a potent inhibitor of NLRP3 inflammasome-mediated pyroptosis
- > a potential treatment for acute and chronic inflammatory liver diseases

AASLD  
2024

**INVESTIGATIONAL DRUG CLM-022, A POTENT INHIBITOR OF NLRP3 INFLAMMASOME-MEDIATED PYROPTOSIS, AS A POTENTIAL TREATMENT FOR ACUTE AND CHRONIC INFLAMMATORY LIVER DISEASES**

Hani El Khattabi<sup>1</sup>, Alexandra Caron<sup>1</sup>, Etienne Delbecq<sup>1</sup>, Marjolein Muijsers<sup>1</sup>, Nicolas Stankovic<sup>1</sup>, Valentin<sup>1</sup>, Vanessa Lagry<sup>1</sup>, Guillaume Vidal<sup>1</sup>, Dean W. Hum<sup>1</sup>, Bart Staerck<sup>1</sup>, Sasina Sayah Jeanne<sup>1</sup>

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**BACKGROUND & AIM**

Inflammation is a common feature in the pathogenesis of liver diseases leading to fibrosis, cirrhosis and liver failure. One of the main contributors to the liver damage is the activation of the inflammasome, a multi-protein complex that is involved in the activation of caspase-1, which in turn leads to the activation of pro-inflammatory cytokines and gasdermin D (GSDMD), which are released from injured hepatocytes and contribute to liver damage. Inflammation is characterized by activation of innate immunity cells, production of pro-inflammatory cytokines and gasdermin D, which is a key factor in inflammasome-mediated cell death. Pyroptosis is required for inflammation which is a key factor in liver damage. Inflammation is also required for liver damage. Inflammation is a key factor in liver damage. Inflammation is a key factor in liver damage.

**RESULTS**

**CLM-022 ACTIVITY ON NLRP3 BLOCKS COMPLEX ASSEMBLY, REFLECTED BY LOSS OF ASC OLIGOMERS**

CLM-022 inhibits NLRP3 activity and blocks the assembly of the inflammasome complex, leading to a reduction in ASC oligomer levels. This is reflected by a decrease in the levels of ASC oligomers in the culture supernatant of LPS-stimulated PBMCs.

**CLM-022 INHIBITS PYROPTOSIS INDUCED BY INFLAMMASOME ACTIVATION**

CLM-022 inhibits the activation of caspase-1 and the release of IL-1 $\beta$  and IL-18, which are key markers of pyroptosis. This is demonstrated by a reduction in the levels of IL-1 $\beta$  and IL-18 in the culture supernatant of LPS-stimulated PBMCs.

**CLM-022 INHIBITS IL-1 $\beta$  PRODUCTION INDUCED BY INFLAMMASOME ACTIVATION**

CLM-022 significantly reduces the production of IL-1 $\beta$  in LPS-stimulated PBMCs, as measured by ELISA. This is consistent with the inhibition of caspase-1 activity.

**ORAL ADMINISTRATION OF CLM-022 ALLEVIATES GALN/LPS-INDUCED LIVER INJURY**

Oral administration of CLM-022 to mice with GalN/LPS-induced liver injury significantly reduces liver damage, as measured by ALT and AST levels. This is associated with a reduction in inflammatory markers and improved liver function.

**CONCLUSION**

CLM-022 is a potent inhibitor of NLRP3 inflammasome-mediated pyroptosis and inflammation. It shows promise as a potential treatment for acute and chronic inflammatory liver diseases.

**REFERENCES**

1. El Khattabi H, Caron A, Delbecq E, Muijsers M, Stankovic N, Valentin V, Lagry V, Vidal G, Hum DW, Staerck B, Sayah Jeanne S. CLM-022, a potent inhibitor of NLRP3 inflammasome-mediated pyroptosis, as a potential treatment for acute and chronic inflammatory liver diseases. *Journal of Hepatology*. 2024;81(1):123-134.

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**

Hani El Khattabi<sup>1</sup>, Alexandra Caron<sup>1</sup>, Etienne Delbecq<sup>1</sup>, Victor Lamy<sup>1</sup>, Marjolein Muijsers<sup>1</sup>, Valérie Daux<sup>1</sup>, Simon Debaecker<sup>1</sup>, Guillaume Vidal<sup>1</sup>, Dean W. Hum<sup>1</sup>, Bart Staerck<sup>1</sup>, Sasina Sayah Jeanne<sup>1</sup>

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**BACKGROUND & AIM**

Inflammation is a common feature in the pathogenesis of liver diseases leading to fibrosis, cirrhosis and liver failure. One of the main contributors to the liver damage is the activation of the inflammasome, a multi-protein complex that is involved in the activation of caspase-1, which in turn leads to the activation of pro-inflammatory cytokines and gasdermin D (GSDMD), which are released from injured hepatocytes and contribute to liver damage. Inflammation is characterized by activation of innate immunity cells, production of pro-inflammatory cytokines and gasdermin D, which is a key factor in inflammasome-mediated cell death. Pyroptosis is required for inflammation which is a key factor in liver damage. Inflammation is also required for liver damage. Inflammation is a key factor in liver damage.

**RESULTS**

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

CLM-022 inhibits the priming of NLRP3 in LPS-stimulated PBMCs, leading to a reduction in the levels of IL-1 $\beta$  and IL-18. This is demonstrated by a reduction in the levels of IL-1 $\beta$  and IL-18 in the culture supernatant of LPS-stimulated PBMCs.

**CLM-022 INHIBITS PYROPTOSIS INDUCED BY INFLAMMASOME ACTIVATION IN WT BUT NOT IN NLRP3 KO THP-1 CELLS**

CLM-022 inhibits the activation of caspase-1 and the release of IL-1 $\beta$  and IL-18 in WT THP-1 cells, but not in NLRP3 KO THP-1 cells. This is demonstrated by a reduction in the levels of IL-1 $\beta$  and IL-18 in the culture supernatant of LPS-stimulated THP-1 cells.

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

Oral administration of CLM-022 to mice with APAP-induced liver injury significantly improves liver function, as measured by ALT and AST levels. This is associated with a reduction in inflammatory markers and improved liver function.

**CONCLUSION**

CLM-022 is a potent inhibitor of NLRP3 inflammasome-mediated pyroptosis and inflammation. It shows promise as a potential treatment for acute and chronic inflammatory liver diseases.

**REFERENCES**

1. El Khattabi H, Caron A, Delbecq E, Lamy V, Muijsers M, Daux V, Debaecker S, Vidal G, Hum DW, Staerck B, Sayah Jeanne S. 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. *Journal of Hepatology*. 2025;82(1):123-134.

- ▶ Activity on NLRP3 blocks complex assembly, reflected by loss of ASC oligomers
- ▶ Inhibits of IL-1 $\beta$  production induced by inflammasome activation
- ▶ Inhibits of pyroptosis induced by inflammasome activation
- ▶ Oral administration alleviates GalN/LPS-induced liver injury

- ▶ Inhibits of the NLRP3 priming in LPS-induced Peripheral Blood Mononuclear Cells (PBMC)
- ▶ Inhibits of pyroptosis induced by inflammasome activation in WT but not in NLRP3 KO THP-1 cells
- ▶ Improves hepatic function in APAP-induced liver injury
- ▶ Injection alleviates LPS-induced systemic inflammation and protects the liver in rats

Next Step: Pending further positive developments (efficacy in AD and ACLF, formulation, and toxicological studies in 2025), potential First-in-human trial could be initiated in 1H27

# VS-02-HE

**VS-02-HE**  
Urease inhibitor  
Hepatic  
Encephalopathy



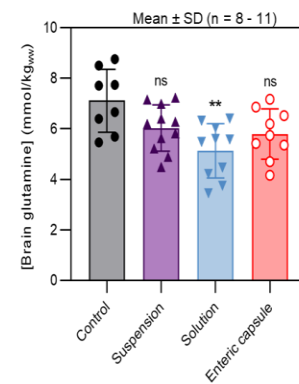
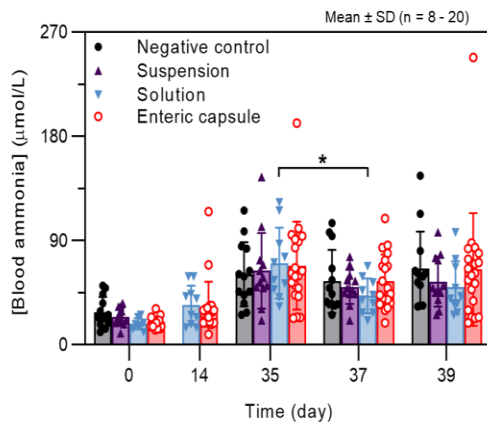
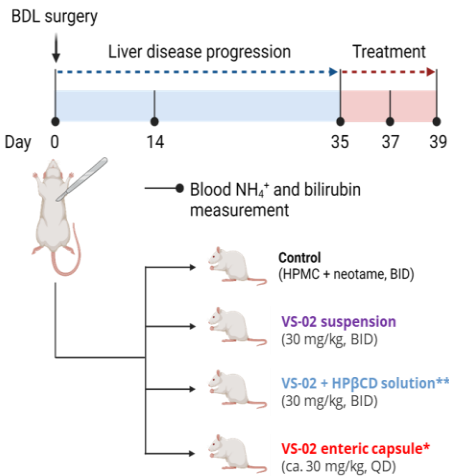
**About  
Hepatic  
Encephalopathy  
(HE)**

- 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:

- ✓ In vivo efficacy in acute liver injury model: lower ammonia levels vs control group
- ✓ In vivo efficacy in chronic liver disease model: lower ammonia & brain glutamine levels vs control group

Animals receiving VS-02 exhibited lower ammonia and brain glutamine levels vs. control group



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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<sup>1</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>2</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>3</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>4</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>5</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>6</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>7</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>8</sup>Genfit, 11 rue de la République, 92000 Nanterre, France; <sup>9</sup>Genfit, 11 rue de la République, 92000 Nanterre, France

**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, hydroxamic acid (HAs) and hydroxamic acid (HAs) are the only HAs that have been clinically tested in liver disease patients. Currently, studies conducted between the 1950s and 1970s, despite encouraging results, none of these compounds, especially in further development for HE, possibly due to insufficient potency or a failure to reach effective concentrations in the cecum, 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 ammonia 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 (HAs) and HAs
- to characterize the pharmacokinetics (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 abundance in the rat gut

**METHODS**

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

Urease inhibitory activity of VS-02 was evaluated in pooled cecal content of male Sprague-Dawley rats (SD), diluted to 5% w/v with 200 mM Tris-HCl pH 7.4. 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 (150) and after incubation (150) using a colorimetric urease activity assay kit (Sigma).

**PK study in rats**

PK of VS-02 was studied in healthy male Sprague-Dawley rats. Two groups of rats (n=3/group) received single oral doses of 30 mg/kg or 100 mg/kg VS-02 via gavage.

Urea, ammonia levels, and feces were collected for quantification of VS-02 by the LC-MS/MS system (Sciex). Type Quad 6500+ PK parameters were calculated by non-compartmental analysis using Phoenix WinNonlin software (version 8.3.1.1).

**RESULTS**

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

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

Figure 1: Dose response curves for VS-02, HAs, and OHA. VS-02 demonstrated 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**

Figure 2: VS-02 PK profile in cecal content, feces and plasma of healthy rats. VS-02 demonstrated high local exposure in the cecum, with plasma and feces concentrations being significantly lower.

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

Dose (mg/kg)	Matrix	n	C <sub>max</sub> (ng/g)	C <sub>min</sub> (ng/g)	AUC <sub>0-24h</sub> (ng·h/g)	AUC <sub>0-24h</sub> (ng·h/g)	AUC <sub>0-24h</sub> (ng·h/g)	AUC <sub>0-24h</sub> (ng·h/g)	%
30	Cecal content	3	158.2	0.18	597.2	93.9			
	Feces	8	9.1	0.30	12.6	0.4			2.1
100	Cecal content	2	118.3	7.38	2314.5	23.1			0.95
	Feces	6	32.3	0.32	95.8	1.0			4.1
	Plasma	4	4	0.04	17.5	0.2			0.8

**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 to the cecum and minimized systemic exposure supporting its further assessment in *in vivo* 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

- ▶ VS-02 demonstrates superior urease inhibitory activity compared to reference hydroxamic acids
- ▶ Formulation of VS-02 leads to high local exposure in the cecum of healthy rats

**Next Step: Nonclinical studies and formulation development are expected by the end of 2025**  
Potential launch of First-in-human trial could be initiated in 2H27

# GENFIT Establishing Leadership as ACLF Rises on the Scientific Agenda



Leveraging  
**Real-world Data**  
**>270,000 U.S patients**  
corresponding to our  
target population



**EF CLIF partnership:**  
Access to unique data  
and cutting-edge  
academic expertise



**Strategic dialogue  
with experts:**  
ACLF KOL Advisory  
Board



**Building knowledge,  
onboarding the  
ecosystem:**  
Learned societies,  
KOLs, patients, caregivers,  
patient associations,  
regulators



## Number of abstracts mentioning "ACLF"



2023

29

2024

76



2023

59

2024

87

2025

97

1. *Who we are*
2. **R&D focus**
3. *Iqirvo<sup>®</sup> in PBC*
4. *Takeaways*

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

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

## 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**

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

VS-01-HAC

<sup>1</sup> Lamarca et al. 2021

# GNS561 in CCA

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



Oral

Findings to date:

- ✓ Autophagy allows cancer cells to become resistant to the cellular stress induced by chemotherapy and targeted therapy
- ✓ Phase 1: Safety profile, exposure, and preliminary signal of activity support the investigation of GNS561 in combination

## #1 Anti-cancer Therapies

↓  
Chemotherapeutic agents

MAP Kinase pathway targeted therapies

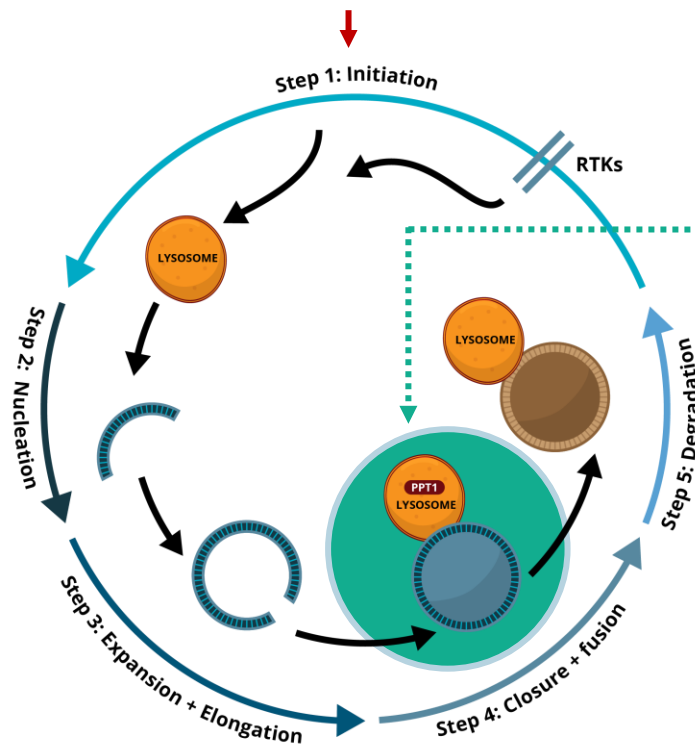
Immune checkpoint inhibitors (anti-PD-1/PD-L1)



**Beneficial anti-cancer effects**

- ▼ Cancer cell survival
- ▼ Cancer growth

..... Induces cancer cell survival mechanisms



## #2 GNS561 (PPT1 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**

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



Oral

A Phase 1b/a 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

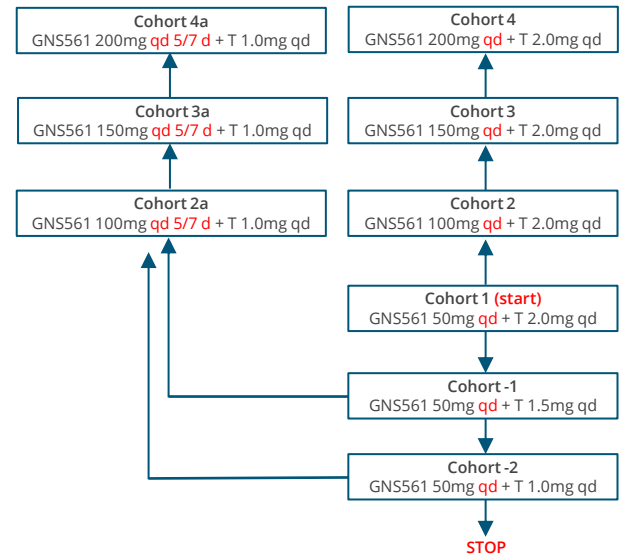
## ⊘ Key exclusion criteria

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

Ongoing recruitment

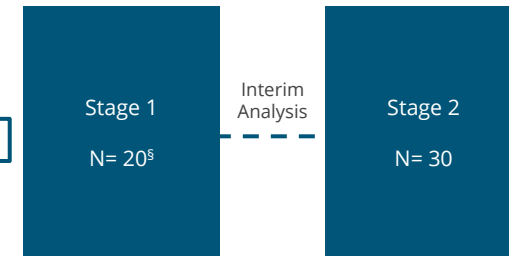
$N_{TOTAL}$   
=  
**74**  
**PTS**

### 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

Next Step: Phase 1b data are expected by the end of 2025

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3. *Iqirvo<sup>®</sup> in PBC*
4. *Takeaways*

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<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**

<sup>2</sup>- Maillot et al. (2007) |

<sup>3</sup>Batshaw et al. (2015) |

<sup>4</sup> Nettlesheim (2017)

# VS-01-HAC in UCD/OA

## VS-01-HAC

Potential first-line treatment or bridging therapy *Peritoneal*



### Findings to date:

- ✓ Preclinical proof of concept:
  - Investigational drug VS-01 demonstrated superior ammonia clearance than commercial peritoneal dialysis in-vivo<sup>1,2,3,4</sup>
  - Ammonia clearance in adult patients with decompensated cirrhosis was at least comparable with renal replacement therapy (RRT)<sup>5</sup>

### Optimal treatment setup

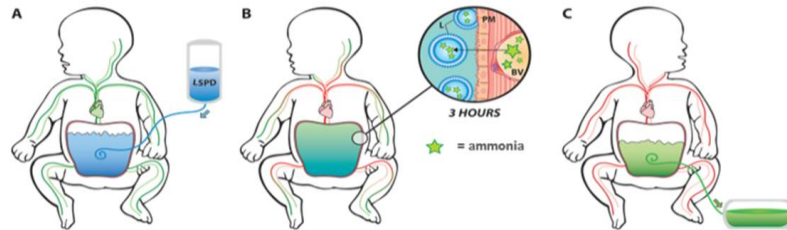
- Peritoneal route is well adapted to pediatric patients
- Rapid treatment onset in all hospitals
- Complementary to other therapeutical approaches

### 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<sup>6</sup>



### VS-01 ammonia clearance vs. current dialysis modalities

TYPE OF DIALYSIS	BLOOD FLOW (ML/MIN)	DIALYSATE FLOW (ML/MIN)	AMMONIA CL (ML/MIN)	DIALYSIS DURATION (H)	REFERENCES
CPD	NA	NA	1.4 ± 1.1	59 ± 87.2	Arbeiter et al., 2010
CAVHD	16	8.3	2.86	33	Picca et al., 2001
HD	10	500	9.5	9	Picca et al., 2001
HD	15	500	14.4	7.5	Picca et al., 2001
CVVHD	40	33.3	21.5	5.5	Picca et al., 2001
CVVHD	-	-	18.9 ± 7.7	42 ± 30.4	Arbeiter et al., 2010
VS-01 ~ 300 mL (Minipigs 30 mL/kg)	NA	NA	6.0 ± 2.8 – 8.0 ± 3.9	3	Matoori et al., 2020
VS-01 ~ 1 L (Patients 15 mL/kg)	NA	NA	31.5 ± 16.7	2	2021 AASLD abstract
VS-01 ~ 2 L (Patients 30 mL/kg)	NA	NA	74.4 ± 25.0	2	2021 AASLD abstract
VS-01 ~ 3 L (Patients 45 mL/kg)	NA	NA	96.8 ± 64.3	2	2021 AASLD abstract

CAVHD: Continuous Arteriovenous Hemodialysis | HD: Hemodialysis | CVVHD: Continuous Venovenous Hemofiltration | CPD: Continuous Peritoneal Dialysis  
 Based on CVVHD (Picca et al.), ~3 sessions of VS-01 15 mL/kg would be required to decrease ammonemia from 1334 to 139 µg/dL  
 Sources: Picca et al., *Pediatr Nephrol* 2001 | Arbeiter et al., *Nephrol Dial Transplant* 2010 | Matoori S et al., *Journal of Controlled Release* 2020

**Next Step: Juvenile toxicology study started and data are expected before the end of 2025**  
**Potential of First-in-human trial could be initiated as early as 2H26**

1. *Who we are*

2. *R&D focus*

3. **Iqirvo<sup>®</sup> in PBC**

4. *Takeaways*

# Solid Commercial Performance from Ipsen in PBC

## 1. Rapid regulatory approvals<sup>1</sup>

**IQIRVO®**  
elafibranor 80 mg tablets

June  
2024  
FDA



September  
2024  
EMA



October  
2024  
MHRA



May 2025  
3 major EU countries  
**Reimbursement**



Milestone payments

Dec'23: €13.3M<sup>3</sup> | June'24: €48.7M<sup>4</sup> | May'25: €26.5M<sup>5</sup>

Sep'25: Intercept Announces Voluntary Withdrawal of OCALIVA® for Primary Biliary Cholangitis (PBC) from the US Market<sup>7</sup>

## 2. Successful commercial launch

Iqirvo® sales (global, quarterly) since commercial launch<sup>2</sup>



€8M

3Q24

€14M

4Q24

€23M

1Q25

€36M

2Q25

Royalty payments<sup>6</sup>

2H24: €2.7M | 1Q25: €2.8M | 2Q25: €4.1M

<sup>1</sup> Ipsen's Iqirvo® receives U.S. FDA accelerated approval  
Ipsen's Iqirvo® (elafibranor) approved in the European Union  
<sup>2</sup> Ipsen delivers strong sales in the first quarter 2025 Ipsen-S1-2025-Announce-des-resultats  
Ipsen publishes its Universal Registration Document 2024  
<sup>3</sup> FDA New Drug Application and EMA Marketing Authorization Application accepted

<sup>4</sup> First commercial sale of Iqirvo® in the US  
<sup>5</sup> Reimbursement in a 3rd European country - Italy  
<sup>6</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 OCEANes holders  
<sup>7</sup> Intercept Announces Voluntary Withdrawal of OCALIVA® for Primary Biliary Cholangitis (PBC) from the US Market

1. *Who we are*
2. *R&D focus*
3. *Iqirvo<sup>®</sup> in PBC*
4. **Takeaways**

# Takeaways

1

## Strong financial position

- 3+ years of cash (all programs financed)
- Encouraging Iqirvo<sup>®</sup> commercial sales trajectory

2

## Diversified pipeline, multiple shots on goals

- 6 programs
- 2 data readouts end of 2025

3

## Established leadership in ACLF

- Strategic engagements with the ecosystem
- Multiple RWD publications