



ACLF Day

DECEMBER 12, 2023
Paris, FRANCE

Corporate
Presentation

Disclaimer

IMPORTANT NOTICE – YOU MUST READ THE FOLLOWING BEFORE CONTINUING. THIS PRESENTATION HAS BEEN PREPARED BY GENFIT AND IS FOR INFORMATION PURPOSES ONLY.

CERTAIN OF THE INFORMATION CONTAINED HEREIN CONCERNING ECONOMIC TRENDS AND PERFORMANCE IS BASED UPON OR DERIVED FROM INFORMATION PROVIDED BY THIRD-PARTY CONSULTANTS AND OTHER INDUSTRY SOURCES. WHILE GENFIT BELIEVES THAT SUCH INFORMATION IS ACCURATE AND THAT THE SOURCES FROM WHICH IT HAS BEEN OBTAINED ARE RELIABLE, GENFIT HAS NOT INDEPENDENTLY VERIFIED THE ASSUMPTIONS ON WHICH PROJECTIONS OF FUTURE TRENDS AND PERFORMANCE ARE BASED. IT MAKES NO GUARANTEE, EXPRESS OR IMPLIED, AS TO THE ACCURACY AND COMPLETENESS OF SUCH INFORMATION.

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, the potential of elafibranor to receive marketing authorization in the United States, Europe and United Kingdom for PBC, expected milestone and royalty payments for elafibranor in PBC, Ipsen's expectations regarding global peak sales for elafibranor in PBC, Ipsen's ability to effectively maximize commercialization of elafibranor, the potential scope and size of the market for ACLF, commercial certainty within that market, development plans for our pipeline programs and expected timing for potential regulatory approvals and clinical milestones for our drug candidates, as well as projections regarding our cash runway and sources of funding of our research and development. The use of certain words, including "believe," "potential," "expect" and "will" 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 other things, 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, review and approvals by regulatory authorities in the United States, Europe and worldwide, of our drug and diagnostic candidates, potential commercial success of elafibranor if approved, exchange rate fluctuations, 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 "Main Risks and Uncertainties" of the Company's 2022 Universal Registration Document filed with the AMF on April 18, 2023, which is available on the Company's website (www.genfit.com) and on the website of the AMF (www.amf-france.org) and public filings and reports filed with the U.S. Securities and Exchange Commission ("SEC") including the Company's 2022 Annual Report on Form 20-F filed with the SEC on April 18, 2023 and subsequent filings and reports filed with the AMF or SEC, including the Half-Year Business and Financial Report at June 30, 2023 or otherwise made public, by the Company.

In addition, even if the Company's results, performance, financial condition and liquidity, 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 document. 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.

Towards a new GENFIT

Pascal PRIGENT, CEO

ACLF disease state

Pr. Richard Moreau, MD, Senior Scientist (Outstanding Grade) at INSERM

Q&A

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Towards a new GENFIT

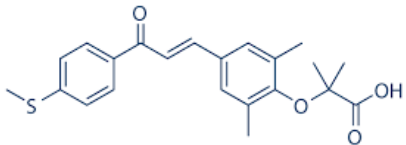


Inception & early years

1999

Development of **Research & Development know-how** via collaborations with Big Pharma

In-house **discovery of elafibranor** (GFT505)



Clinical development in chronic liver diseases

Development of **elafibranor in NASH/MASH¹** 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.)

Today



Pivoting to rare and life-threatening liver diseases with high unmet needs

2023

A **diversified pipeline in ACLF** (5 programs) and **other life-threatening diseases** (2 programs)

Acute on Chronic Liver Failure (ACLF)

- **VS-01** (Phase 2 initiated)
- **NTZ** (Phase 2 under preparation)
- **SRT-015** (preclinical)
- **CLM-O22** (preclinical)
- **VS-02-HE** (preclinical)

Other life-threatening liver diseases

- **GNS561** (Phase 2 initiated)
- **VS-01-HAC** (preclinical)

Potential future milestone payments and royalties from PBC² to partially fund pipeline development

- **Cash position:** \$94M as of Sept 30, 2023
- Eligible for up to **\$360 million** in milestone payments and tiered double-digit royalties under Ipsen agreement²

2024 Outlook Following Acceptance of Elafibranor Filings in PBC in U.S./EU

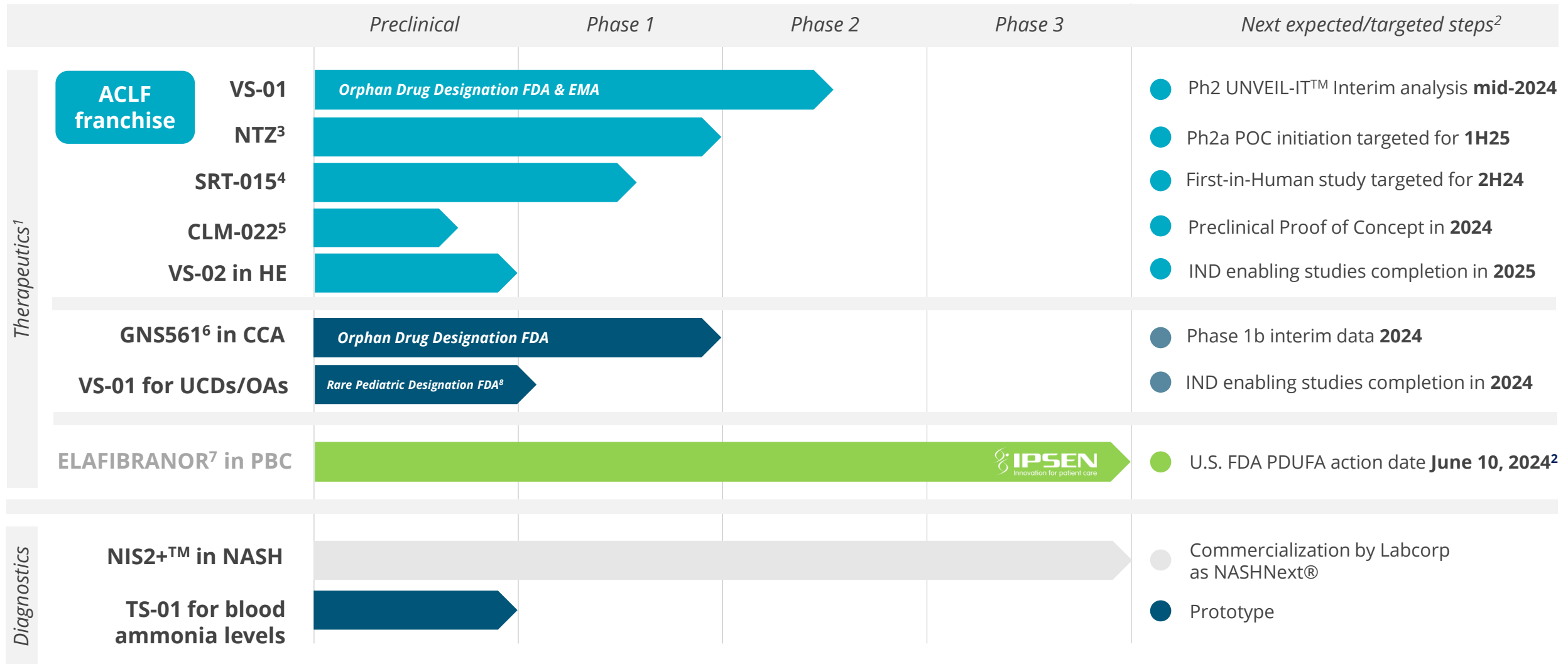


GENFIT Updates 2024 Outlook Following Acceptance of Elafibranor Filings in Primary Biliary Cholangitis (PBC)

- US Food and Drug Administration (FDA) has granted Priority Review for New Drug Application (NDA) for elafibranor in PBC, and European Medicine Agency (EMA) has also validated the Marketing Authorization Application (MAA) for elafibranor.
- Acceptance triggers a first milestone payment. Further milestones are expected upon US and European launches which could now happen in 2Q24 in the US (FDA PDUFA¹ action date: June 10, 2024) and 2H24 in Europe. These milestones total approximately 89M€.
- Launches in the US and Europe will also make GENFIT eligible for royalty payments.
- Revenues will fund the development of GENFIT's pipeline, now mainly focused on Acute On-Chronic Liver Failure (ACLF) with 5 differentiated assets.

- Regulatory filings U.S. and Europe
 - **<6 months** after topline data
- Expected launch of elafibranor in the U.S.
 - **Priority Review** granted by U.S. FDA
 - FDA PDUFA set to **June 10, 2024**
- Financial implications for GENFIT
 - Expected milestones of approx. **89M€ by the end of 2024**
- PBC market
 - **\$1.5bn by 2030** (source Ipsen Capital Market Day December 7, 2023)
- Global annual peak sales of elafibranor
 - **Expected to exceed >500M\$** (source Ipsen Capital Market Day December 7, 2023)

Pipeline



Towards a new GENFIT

Pascal Prigent, CEO

ACLF Disease state

Pr. R. Moreau, MD, Senior Scientist (Outstanding Grade), INSERM

Q&A

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Professeur Richard Moreau, Founding Member of EF-CLIF and Worldwide Leader in ACLF

RICHARD MOREAU

Senior Scientist, Directeur de Recherche de Classe Exceptionnelle (DRCE) à l'INSERM (French NIH)

FRANCE

City: Paris

Institution: UMR_S 1149, Centre de Recherche sur l'Inflammation CRI

Contact: richard.moreau@inserm.fr



BIOGRAPHY OF RICHARD MOREAU

Dr. Richard Moreau, Senior Scientist, Vice-Chairman of the Center for Research on Inflammation, INSERM, Paris Diderot University and Cnrs, Paris, France

Dr. Richard Moreau is: 1) Senior Scientist (Outstanding Grade) at the French NIH (INSERM); 2) Vice-Chairman of the Centre of Research on Inflammation (CRI, Paris, France), endorsed by the French NIH (INSERM), Paris Diderot University, and Cnrs; 3) Consultant in Hepatology at the Liver Unit at Beaujon Hospital, Assistance Publique Hôpitaux de Paris, Clichy, France; 4) Adjunct Professor at the Institute of Liver and Biliary Sciences (ILBS), New Delhi, India; 5) Advisor for Hepatology at the INSERM Institute "Pathophysiology, Metabolism, Nutrition"; 6) Deputy Director of the Grifols Chair for Translational Research at the European Foundation for the Study of Chronic Liver Failure (EF Clif), Barcelona, Spain.

His main research interest is pathophysiology and treatment of complications of cirrhosis, in particular acute-on-chronic liver failure (ACLF). He was responsible for the fact that France was the first country in the world to approve terlipressin as a first-line treatment for hepatorenal syndrome. Because of his interest for end-stage liver disease. In 2009, he was among founding members of the EASL-Chronic Liver Failure (CLIF) Consortium which includes now 90 European Centers and is dedicated to develop research on cirrhosis. He was PI of the first study (called CANONIC study) performed under the umbrella of the EASL-CLIF Consortium; this study was the first to provide an evidence-based definition for ACLF.

He is now Senior Editor of Journal of Hepatology (2015-19). He has been Associate Editor for Journal of Hepatology (2010-14) and Liver International (2007-9).

His scientific production consists of 318 Peer-Reviewed publications (PubMed, November 2017), of which 222 Original Articles, 96 Review Articles or Editorials; his h-index is of 63; his SIGAPS score (French score) is 4497.

He was Editor of 1 book and 34 book chapters

He gave 242 Invited lectures (70% outside France), 300 communications in International meetings.

ACLF Day
December 12, 2023

Acute-on-Chronic Liver Failure (ACLF)

Richard Moreau, MD, FAASLD,^{1,2,3}

**¹European Foundation for the Study of Chronic Liver Failure (EF CLIF),
Barcelona, Spain;**

**²Centre de Recherche sur l'Inflammation (CRI),
INSERM, Université Paris Cité, CNRS, Paris, France;**

³Service d'hépatologie, Hôpital Beaujon, APHP, Clichy, France.

Outline

- **Cirrhosis & ACLF**
- **Defining ACLF**
- **Pathophysiology**
- **Medical management**
- **Liver transplantation**
- **Unmet needs**

Cirrhosis

- **11th most common cause of death**
 - 2 million deaths worldwide/year (~4% of deaths worldwide)
- **2 billion consume alcohol**
 - At risk for alcohol-associated cirrhosis
- **2 billion overweight/obese**
 - At risk for metabolic-associated cirrhosis

Characteristics of Cirrhosis

- **Chronic liver disease**
- **Compensated for years**
- **Decompensated: ascites, gastrointestinal hemorrhage, hepatic encephalopathy**
 - Recent onset defines acute decompensation
- **Acute decompensation: often leads to nonelective hospital admission**
- **ACLF: cause of death in acute decompensation.**

Characteristics of ACLF

- **Men ~55 yr**
- **Seen among patients nonelectively admitted for acutely decompensated cirrhosis**
- **Defined by impaired function of major organ systems & intense systemic inflammation**
- **Associated with high short-term mortality (by 28 & 90 days)**
- **Engages health-care system resources (ICU, liver transplantation)**

ACLF Burden in Europe

- **Under evaluation (commissioned by Journal of Hepatology)**
- **Currently estimated to ~150,000 cases/yr (projection from German data).**

Evidence-Based Knowledge Produced by EF CLIF

- **Studies in patients nonelectively admitted for acute decompensation:**
 - CANONIC: 1343 European patients
 - PREDICT: 1273 European patients
 - ACLARA: 1274 LATAM patients

Moreau et al. *Gastroenterology* 2013;144:1426-37. Trebicka et al. *J Hepatol* 2020;73:842-54.
Farias, Curto Vilalta, et al. *Gastroenterology* 2023;165:696-16.

Outline

- Cirrhosis & ACLF
- **Defining ACLF**
- Pathophysiology
- Medical management
- Liver transplantation
- Unmet needs

Diagnostic Criteria & Prevalence of Organ System Failures (CANONIC Study)

Organ system	Diagnostic criteria*	Prevalence (%)
Liver	Bilirubin ≥ 12 mg/dL	15.4
Kidney	Creatinine ≥ 2 mg/dL or RRT	12.6
Coagulation	INR ≥ 2.5	7.8
Brain	Grade 3 or 4 HE	7.4
Circulation	Use of vasopressor	4.8
Respiration	SpO₂/FiO₂ ≤ 214	2.4

*According to CLIF-C OF score. Moreau et al. Gastroenterology 2013;144:1426-37.

The CANONIC Study Defined ACLF

**1343 patients nonelectively admitted for acutely decompensated cirrhosis
(*new ascites, encephalopathy, infection, GI hemorrhage*)**

70%

30%

Absence of ACLF

- **Low-grade systemic inflammation**
 - **No organ failure**
 - **Low 28-day mortality**

Presence of ACLF

- **High-grade systemic inflammation**
 - **Organ failures
(ACLF-1, ACLF-2, ACLF-3)**
 - **High 28-day mortality
(ACLF-3>ACLF-2>ACLF-1)**

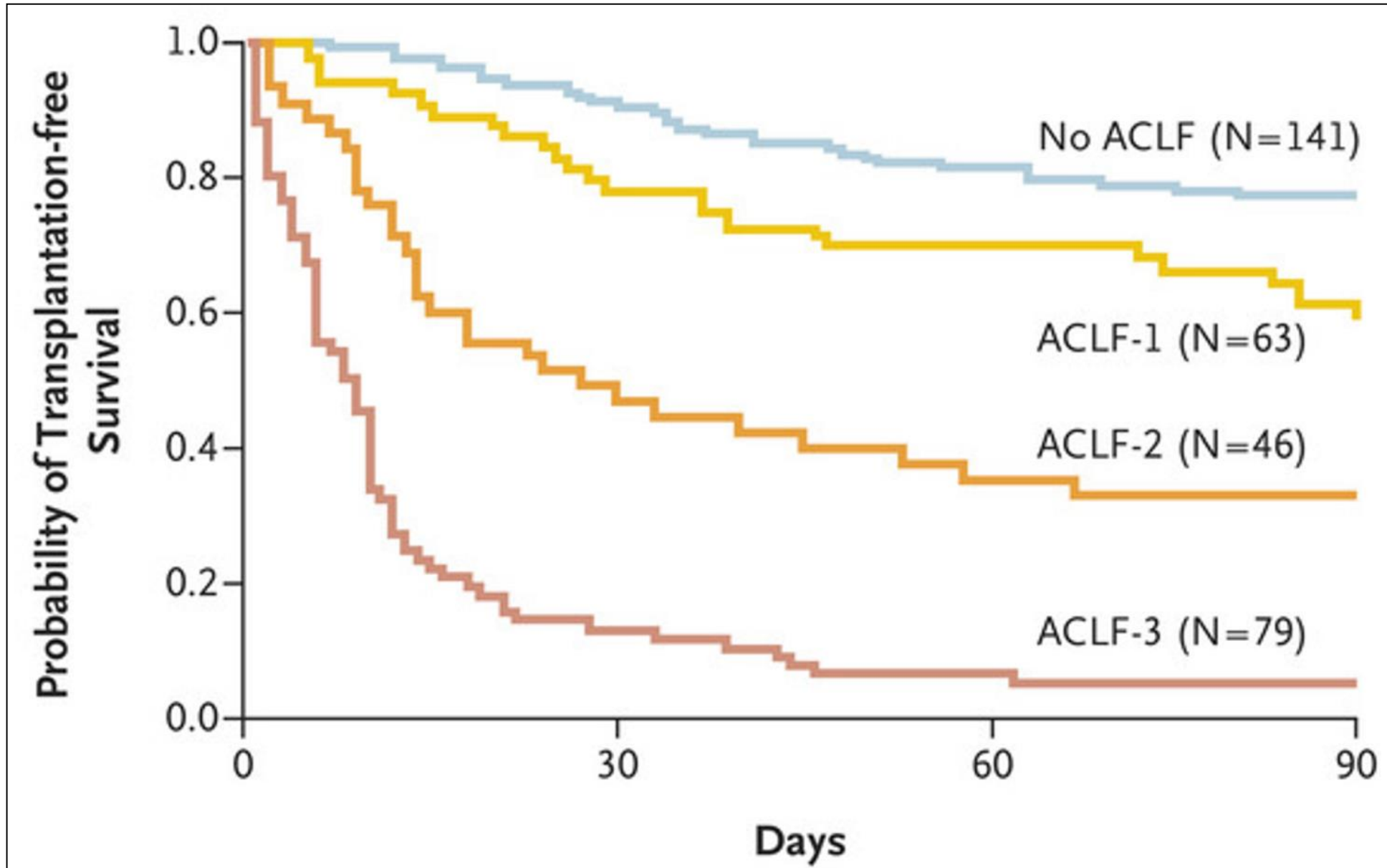
Triggers of Inflammation & ACLF (PREDICT Study)

Trigger	Prevalence
Type:	
Bacterial infection	44%
Alcohol-related hepatitis	44%
GI hemorrhage with shock	6%
Toxic encephalopathy	6%
Number:	
1	46%
≥ 2	25%
0	29%

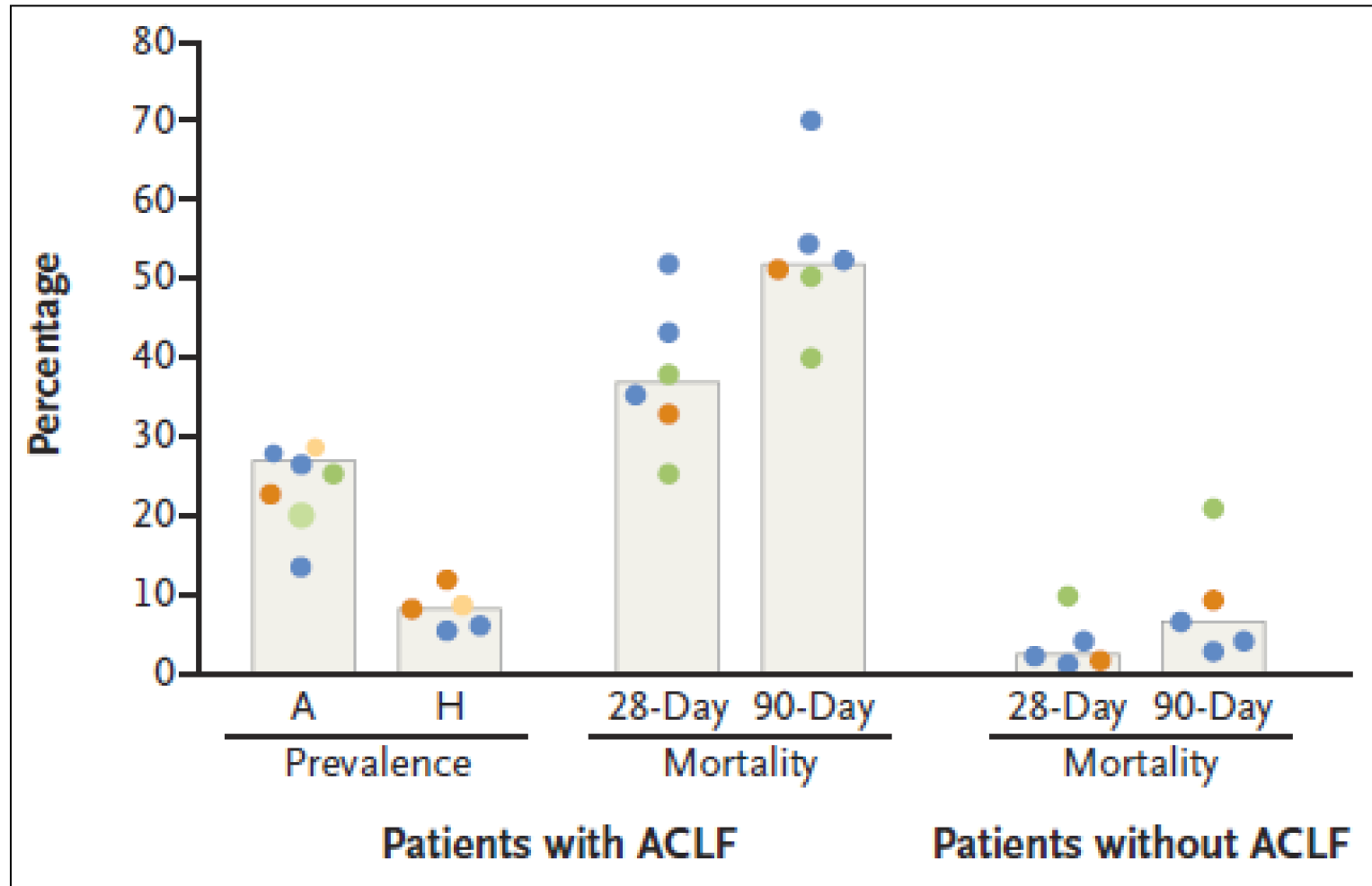
Clinical Course of ACLF Within the 1st Week

Initial Grade	ACLF Grade at Day 7			
	0	1	2	3
↓	<i>% patients</i>			
ACLF-1	55	24	8	12
ACLF-2	35	15	25	25
ACLF-3	16	4	12	68

90-Day Transplantation-Free Survival According to Status at Day 7 Among 329 Patients Had ACLF on Admission



ACLF is a Global Disorder



● Europe

● USA

● Asia

● Latin America

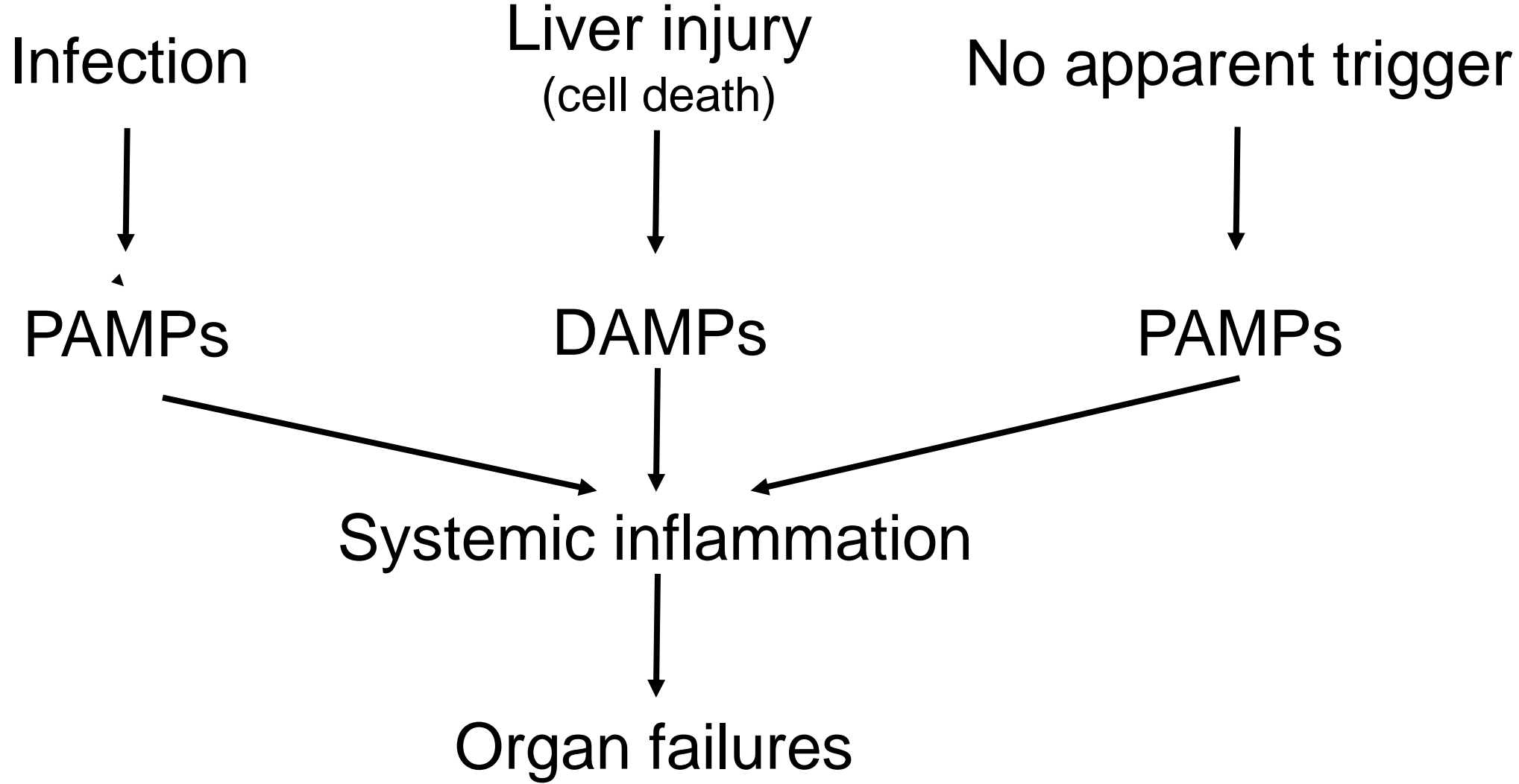
Outline

- Cirrhosis & ACLF
- Defining ACLF
- **Pathophysiology**
- Medical management
- Liver transplantation
- Unmet needs

Inducers of Inflammation

- **Pathogen-associated molecular patterns (PAMPs) = bacterial byproducts immediately recognized by immune system; induce inflammation**
- **Damage-associated molecular patterns (DAMPs) = intracellular molecules released by dying cells; immediately recognized by immune system; induce inflammation**

Inducers of Inflammation According to Triggers



Impaired Gut Barrier in Decompensated Cirrhosis

- **Changes in gut microbiome (↑ pathobionts = “bad” bacteria)**
- **↑ Intestinal permeability to bacteria and/or bacterial PAMPs**
- **Translocation of bacteria and/or bacterial PAMPs to blood flowing to the liver**
- **↓ Function of the “hepatic filter”; bacteria and/or bacterial PAMPs reach systemic circulation**
- **Bacteria can cause infection & inflammation; isolated bacterial PAMPs can cause inflammation.**

Outline

- Cirrhosis & ACLF
- Defining ACLF
- Pathophysiology
- **Medical management**
- Liver transplantation
- Unmet needs

Key Points

- **Main principle: Diagnose acute precipitants & treat them urgently**
- **Provide supportive therapy in ICU**
- **Objective: Bridge to early liver transplantation**
- **No “pathophysiology-based” therapy available.**

Supportive Therapy

- **Cardiovascular: vasoconstrictors.**
- **Respiratory: mechanical ventilation.**
- **Brain: protective intubation if necessary; lactulose; albumin dialysis (MARS) if lactulose failure.**
- **Liver: 2 negative RCTs of extracorporeal MARS.**

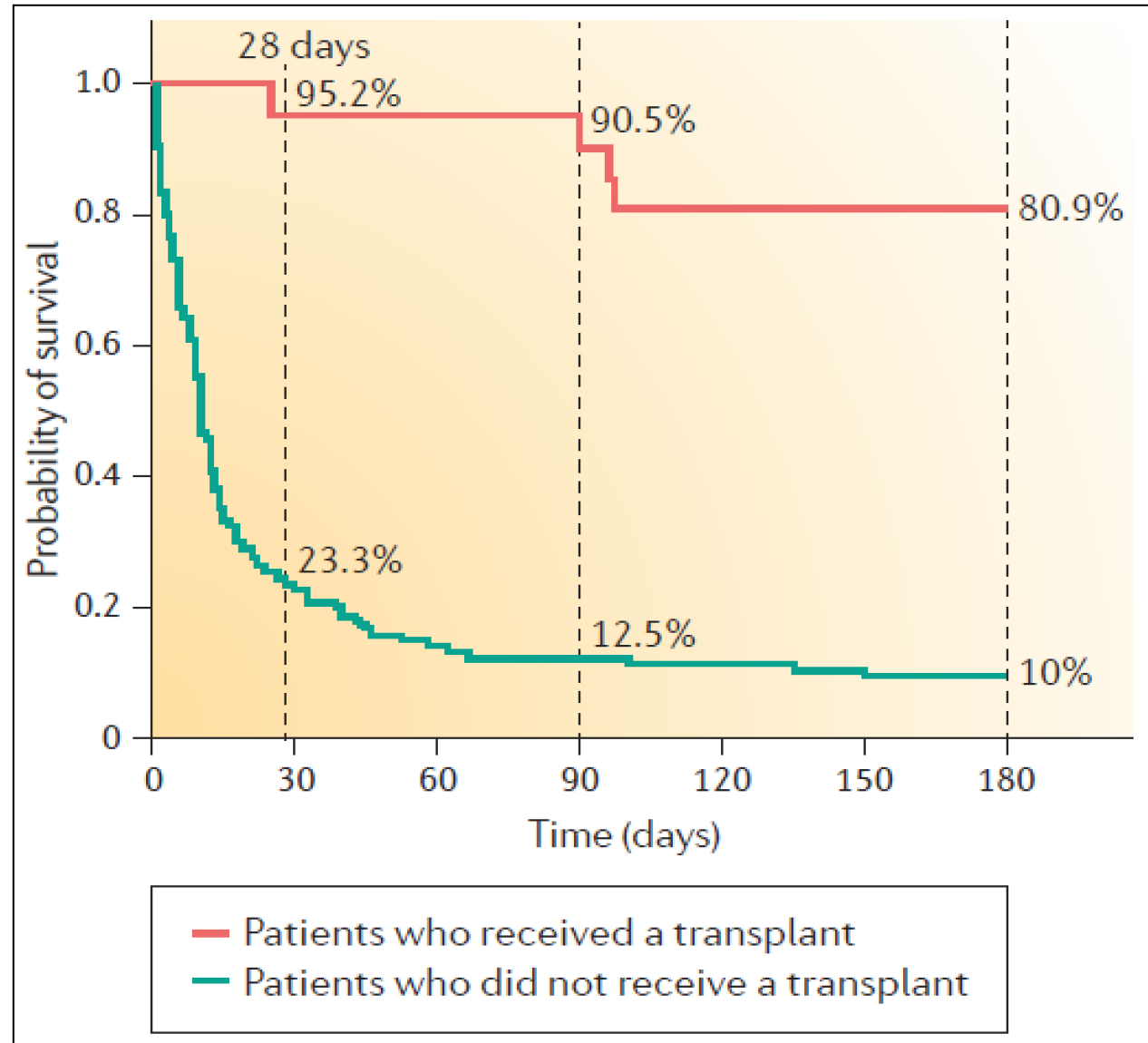
Other Interventions

- **Granulocyte colony-stimulating factor**
 - **No efficacy**
- **Plasma exchange**
 - **Trial recruiting**
- **Cell therapy**
 - **Under evaluation**

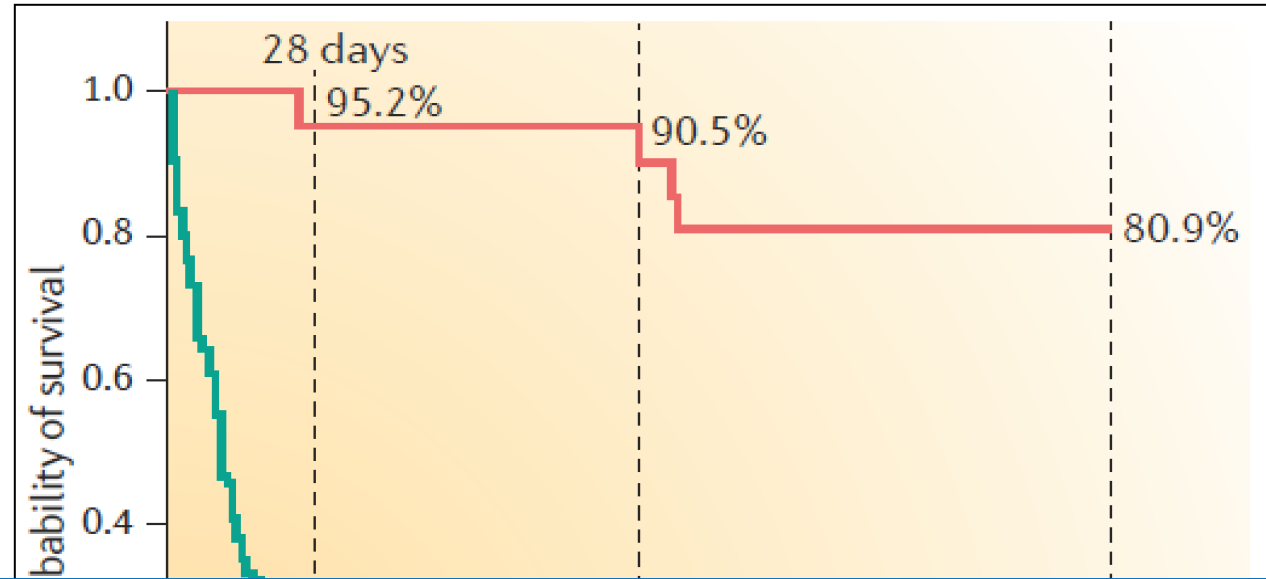
Outline

- Cirrhosis & ACLF
- Defining ACLF
- Pathophysiology
- Medical management
- **Liver transplantation**
- Unmet needs

Survival Among Patients with ACLF-2, -3 who Did or Did not Receive Early (<28 days) Liver Transplant



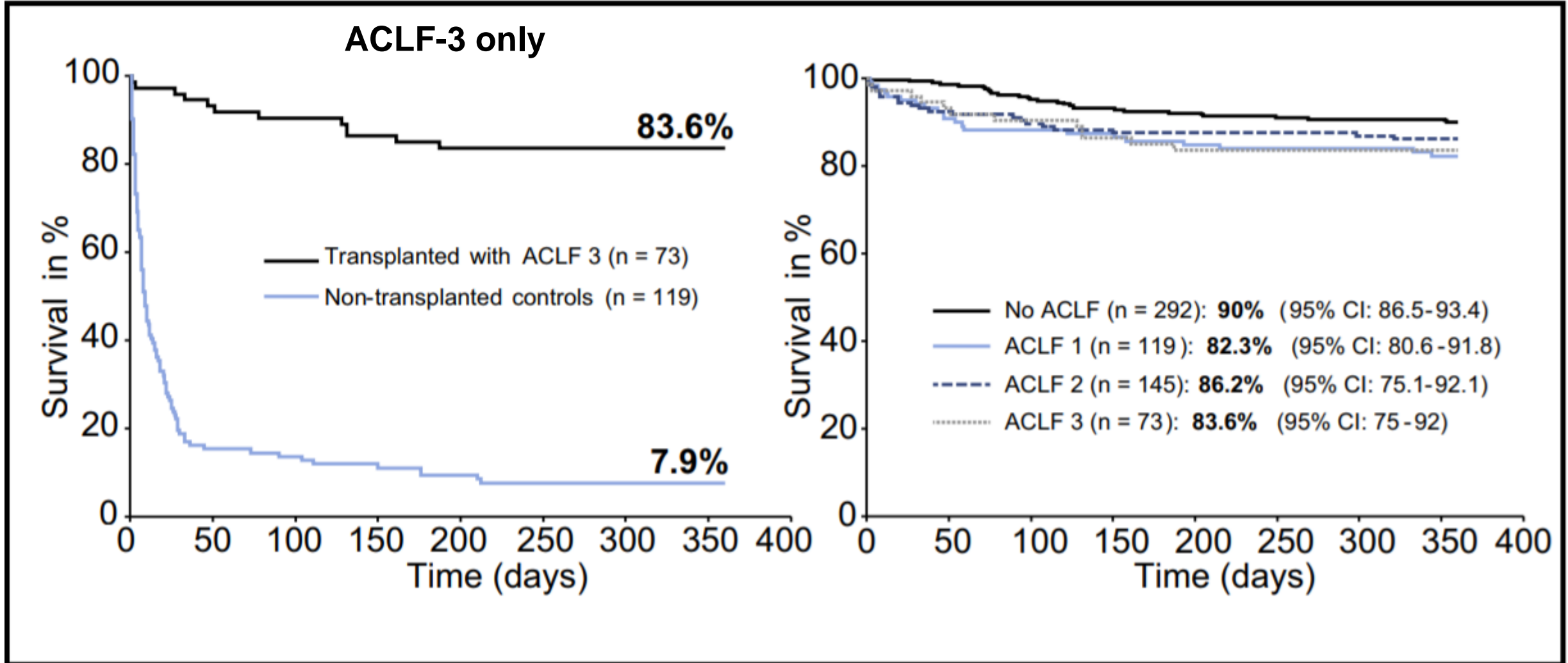
Survival Among Patients with ACLF-2, -3 who Did or Did not Receive Early (<28 days) Liver Transplant



Narrow window for liver transplantation

- Patients who received a transplant
- Patients who did not receive a transplant

Liver Transplantation in Patients with ACLF



Outline

- Cirrhosis & ACLF
- Defining ACLF
- Pathophysiology
- Medical management
- Liver transplantation
- **Unmet needs**

Targeting Bacterial/PAMP Translocation

- **Current approaches are based on antibiotics**
- **Restricted to few patients**
- **Major issues with antibiotic use
(emergence of multidrug-resistant bacteria)**
- **Alternative approaches: unmet need.**

Conclusions

- **ACLF is the most severe form of acutely decompensated cirrhosis**
- **Bacterial/PAMP translocation & systemic inflammation are key pathogenic mechanisms**
- **There is no “pathophysiology-based” therapy currently available**
- **Liver transplantation is effective but limited due to narrow time, organ shortage, poor access in high-level care.**

Towards a new GENFIT

Pascal Prigent, CEO

ACLF disease state

Pr. Richard Moreau, MD, Senior Scientist (Outstanding Grade) at INSERM

Questions & answers

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Towards a new GENFIT

Pascal Prigent, CEO

ACLF disease state

Pr. Richard Moreau, MD, Senior Scientist (Outstanding Grade) at INSERM

Q&A

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

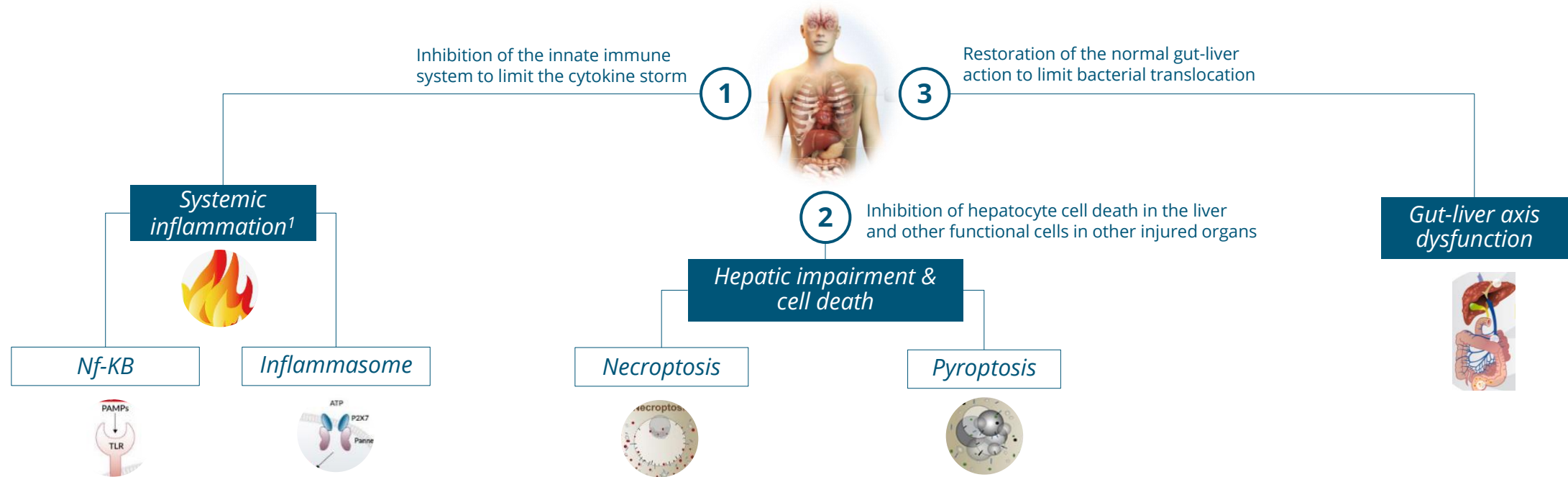
Q&A

Highlights on newsflow

Pascal Prigent, CEO

Building a targeted portfolio to address the unmet need that exists with current (not approved) Standard of Care in ACLF

Specific selection of strategic assets: based on pathophysiology¹ of ACLF, as defined by liver experts and consortiums such as EF-CLIF (European Foundation for the study of Chronic Liver Failure), to address most relevant pathways



ACLF patient management¹ (no drug approved)

1. Treating acute precipitants

- Antimicrobial therapy
- Corticosteroids for alcoholic hepatitis
- Acute variceal haemorrhage

2. Organ support

- Intravenous fluids
- Renal replacement therapy
- Extracorporeal liver support
- Liver transplantation

Benefits of a diversified pipeline targeting complementary/relevant pathways

- Explore more options for **patients**
- Provides **multiple opportunities** for success
- Allows exploration of potential synergies in **combinations**
- Offers possibility to apply key learnings across all programs, to **accelerate execution**

5 assets with complementary mechanisms of action targeting key pathways

We are developing a **diversified pipeline** to better address the **complexities of ACLF** and improve **treatment outcomes**



Liposomal-based technology

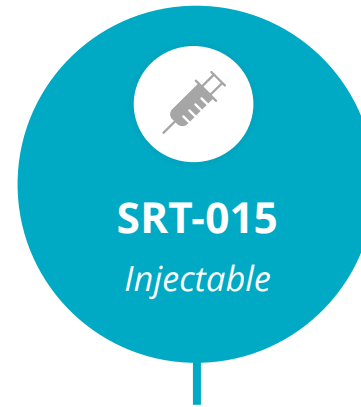
To drain out **ammonia** and **ACLF toxins** from the blood



Anti-inflammatory and anti-bacterial

To reduce **systemic inflammation** and impede **PAMPs release** and **bacterial translocation**

[New formulation under development for dosing flexibility]



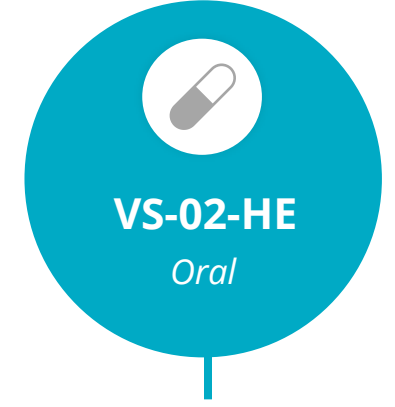
ASK1 inhibitor

To inhibit cell death **apoptosis**, **inflammation (liver-centricity)**, and **fibrosis**



NLRP3 inflammasome inhibitor

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



Urease inhibitor

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

VS-01

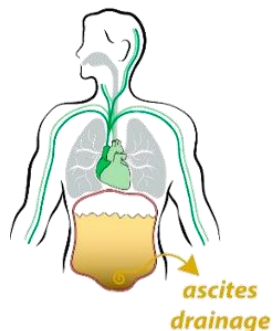
*Clinical Stage
Program in ACLF*



Extraction of Metabolites to Reduce Mortality

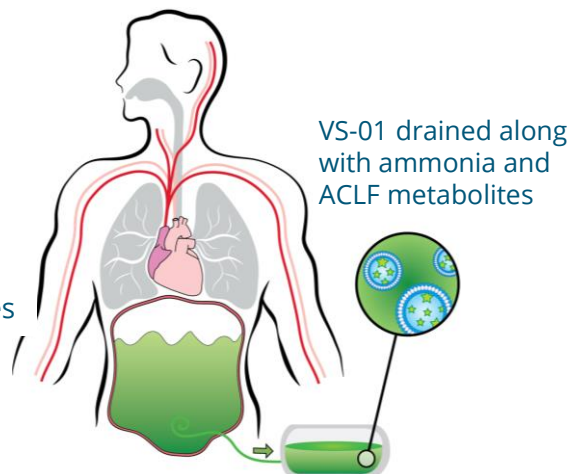
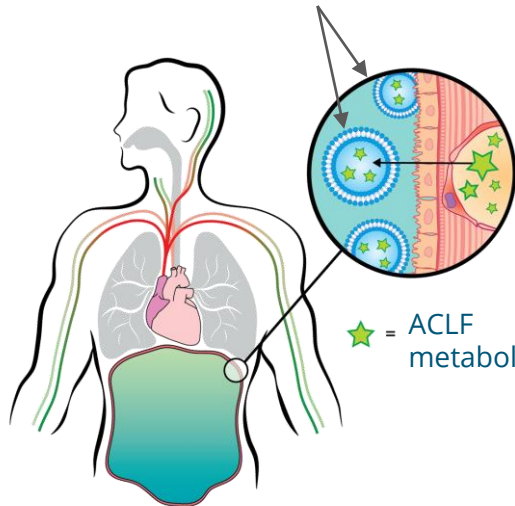
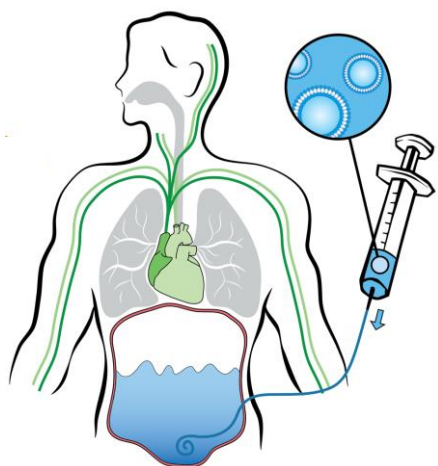
Standard of care

Ascites drainage



VS-01

VS-01 scavenging liposomes



Harnesses the intraperitoneal route of administration following paracentesis

VS-01 in brief

High unmet medical need in ACLF with **no approved treatment and 112'000 cases¹**



Targets **first-line treatment for ACLF** to **reverse** the disease



Delivered via **in-place peritoneal access catheter**

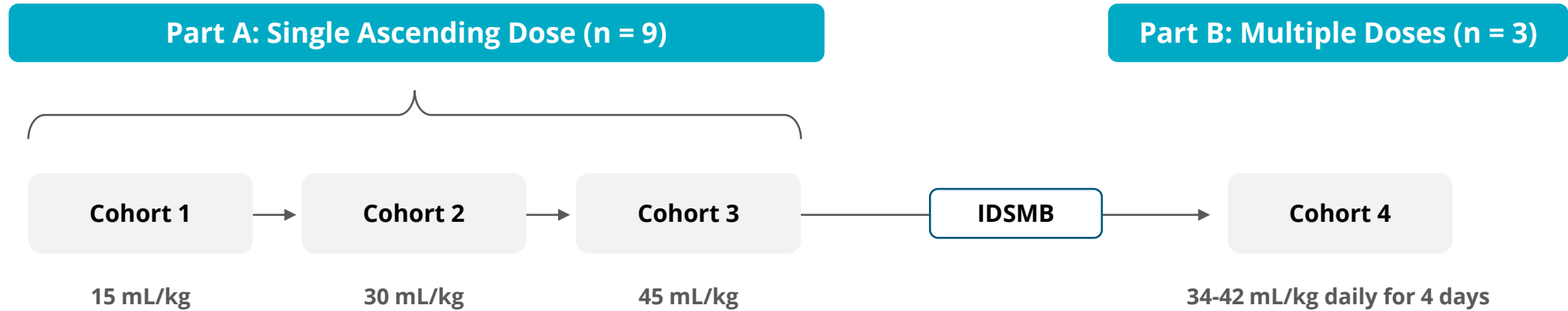


Targets **multiorgan support:** brain, liver, and kidney

— Early ACLF treatment may reduce —

- Length of hospital/ ICU stay
- Re-hospitalization
- Acute need of transplantation
- Healthcare and hospital costs

First in Human Study



DETAILS

- Study population (n=12):
 - Decompensated liver cirrhosis with
 - Ascites
 - Covert hepatic encephalopathy (minimal HE & HE 1)
- Principal investigator: Prof Dr Jonel Trebicka
- Clinical site:



OUTCOME

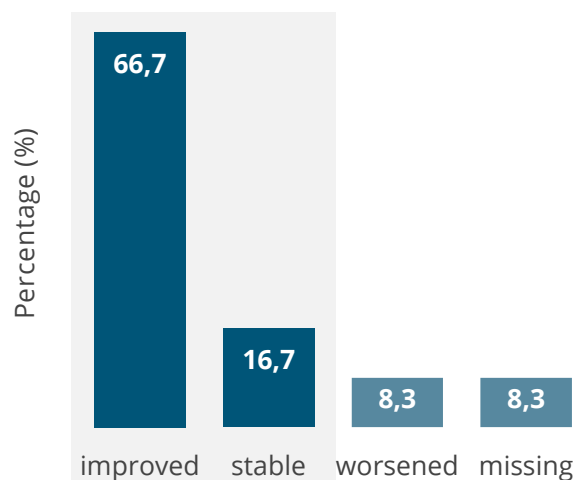
- ✓ Generally **safe** and **well tolerated**
- ✓ Promising **preliminary efficacy results**
- ✓ Confirmed **ease of *i.p.* administration**
- ✓ Data selected for **Clinical Hepatology Debrief** at AASLD 2021

Phase 1b Preliminary Efficacy Results on Liver & Brain Function

IMPACT ON OVERALL LIVER DISEASE SEVERITY

e.g., assessed by Child-Pugh Score (CPS)

Improved or stable disease: **83.4%**

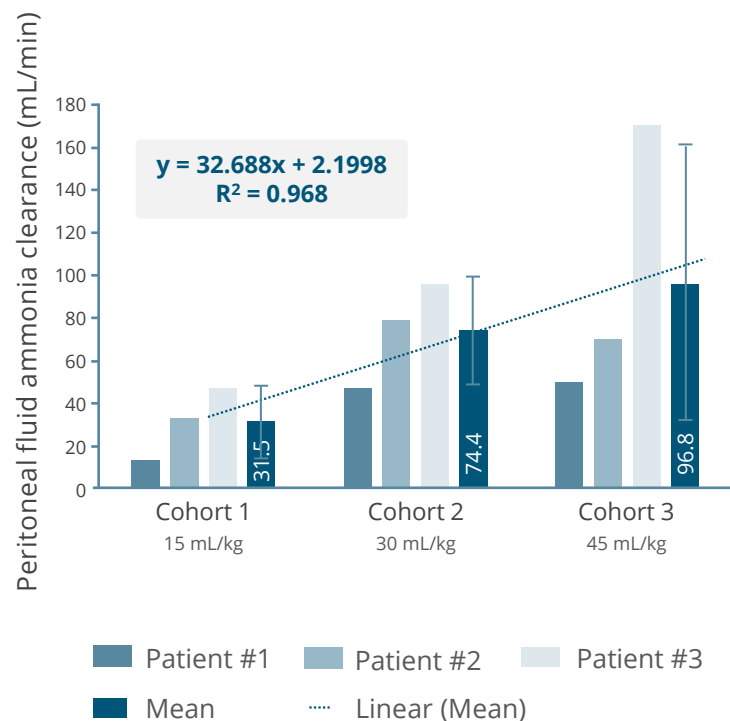


NO PATIENTS PROGRESSED TO ACLF



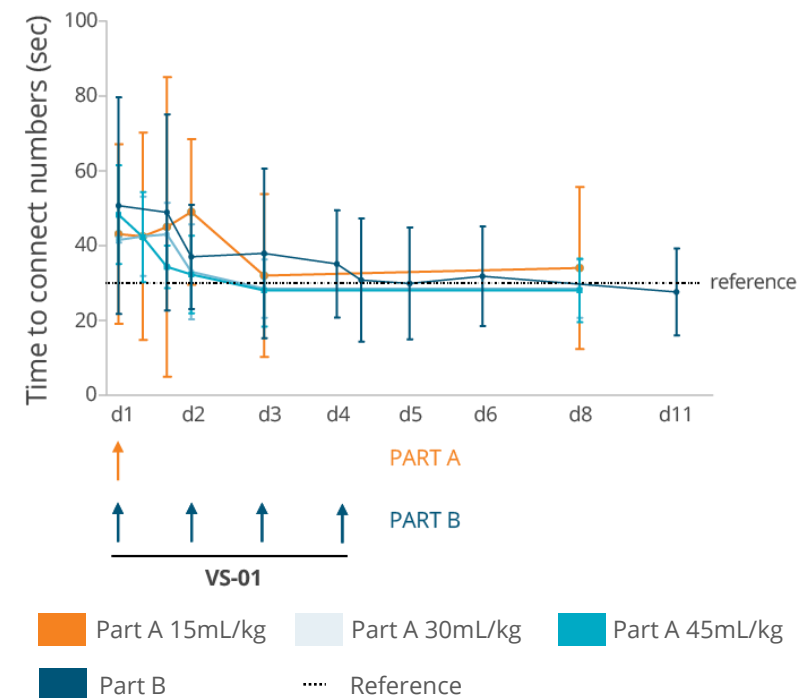
DOSE-DEPENDENT AMMONIA REMOVAL FROM THE BODY

Ammonia clearance increased with VS-01 dosage in peritoneal fluid



IMPROVEMENT IN PSYCHOMETRIC TESTS FOR HE

e.g., number connection test was performed faster



UNVEIL-IT™ Phase 2 Proof-of-Concept Trial

Phase 2a Proof Of Concept Study of VS-01 in Patients with Acute-on-Chronic Liver Failure

OPEN-LABEL

1:1 RANDOMIZED

CONTROLLED

MULTI-CENTER GLOBAL STUDY

INTERIM ANALYSIS*
TARGETED 1H2024

Patient Population

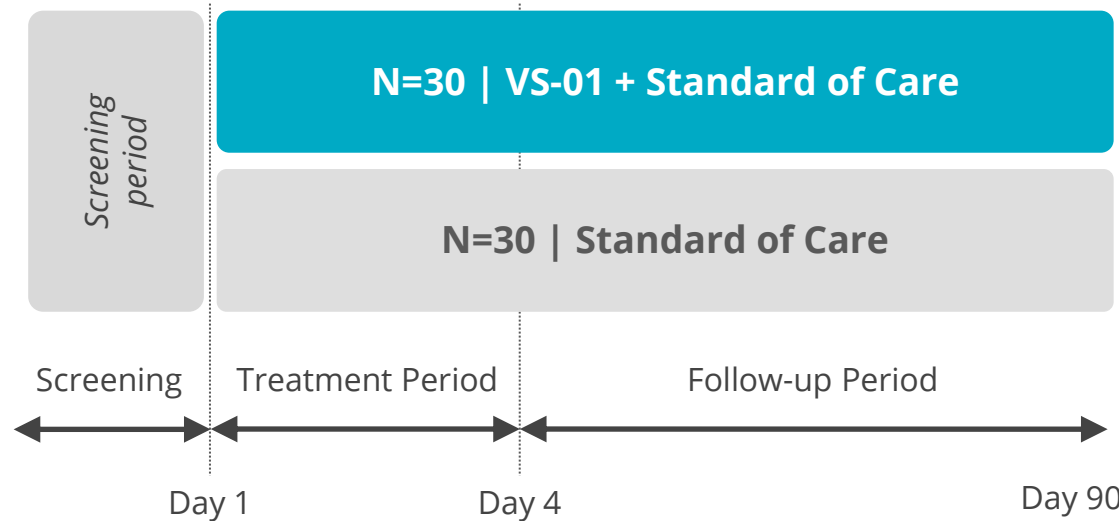
Adult patients with Acute-on-Chronic Liver Failure (ACLF) grade 1 and 2 and ascites

Number of Patients

~60

Number of Sites

50 (EU/US)



Primary Objective

Efficacy measured by CLIF-C ACLF score** at Day 7

Secondary Objectives

90 day - mortality
28 day - mortality
Time to death
ACLF grade change
Transplant-free survival
Safety and tolerability

*Interim analysis for the purpose of unblinded sample size re-estimation

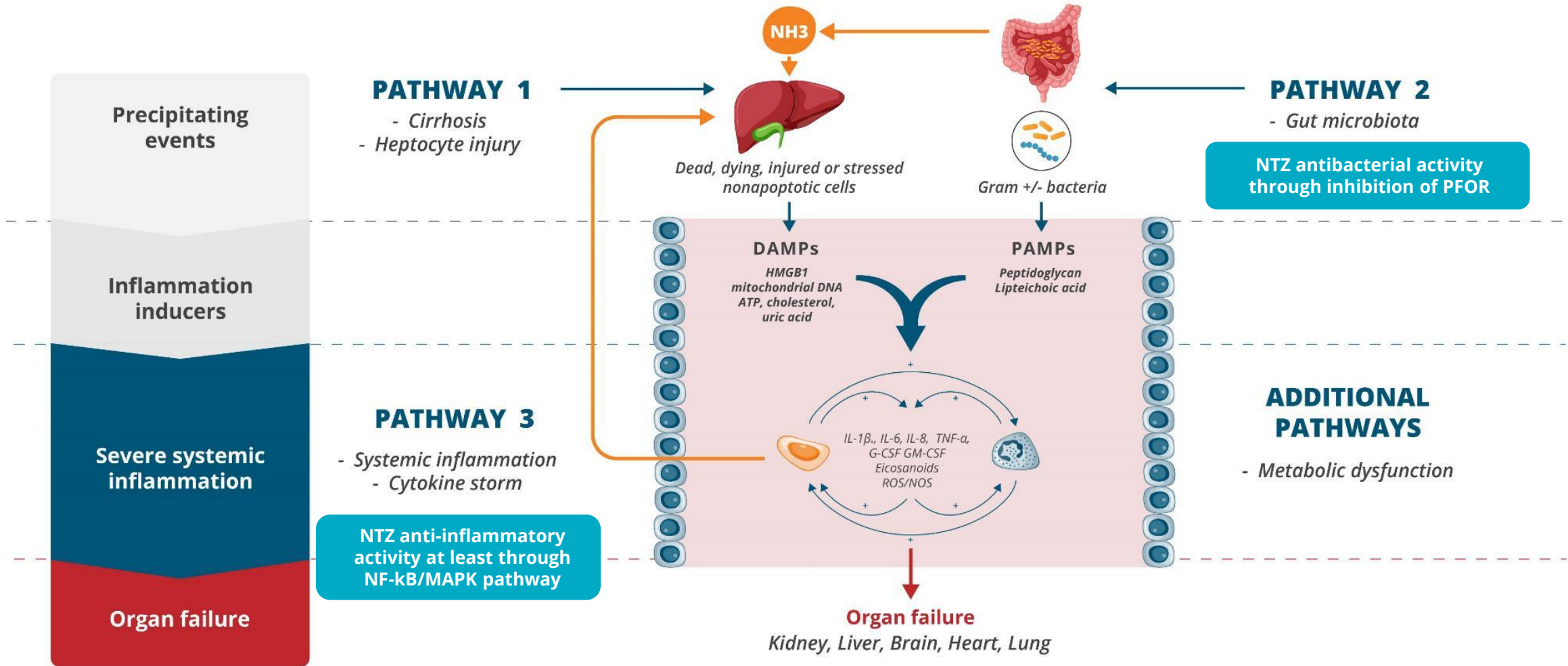
** www.efclif.com

NTZ

Clinical Stage Program in ACLF



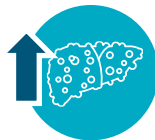
NTZ Impacts Multiple Pathways



Activity in Disease Models Support ACLF Clinical Development



Reduces LPS-induced inflammation in healthy rats*



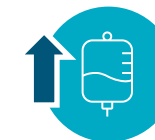
Beneficial effects on liver function markers (bil, alb) in models of cirrhosis*



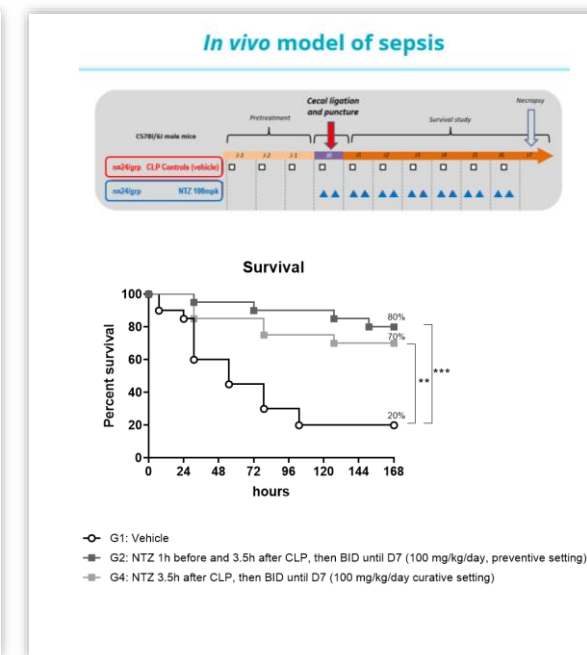
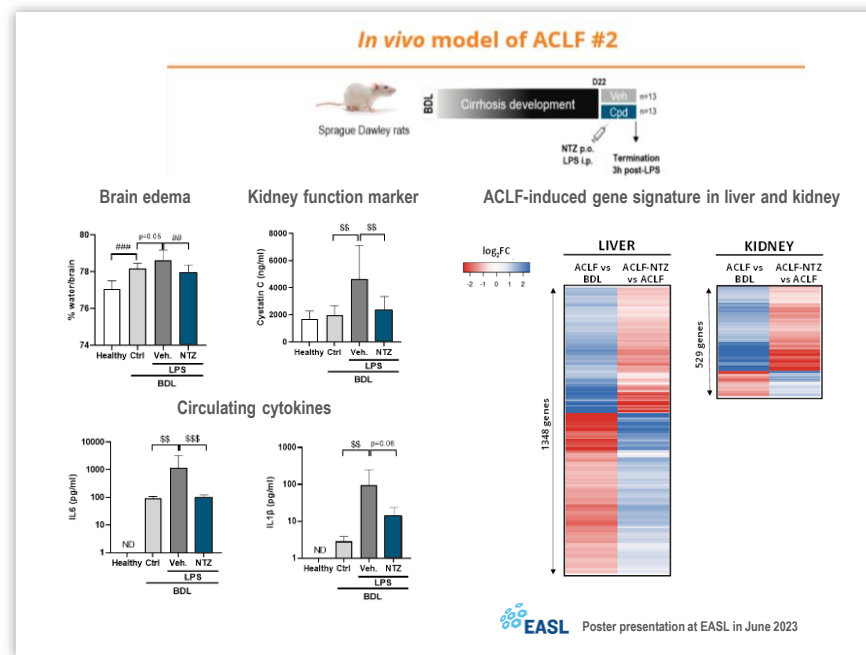
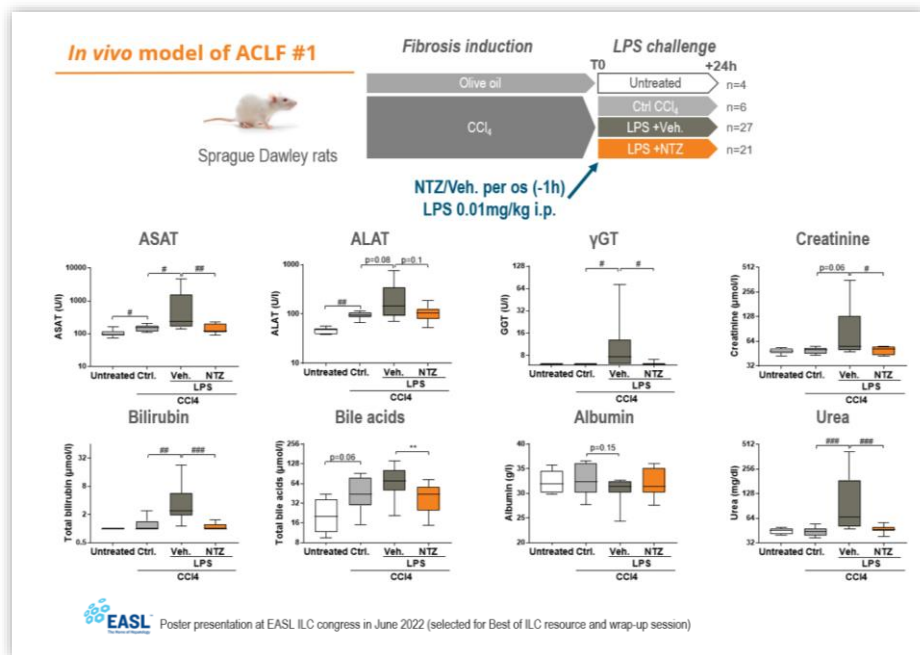
Alleviates liver and renal damages in a model of ACLF (CCL4+LPS)



Reduces brain edema, inflammation markers and reverses the ACLF-induced gene signature in a model of ACLF (BDL+LPS)



Improves survival in treatment models of **Sepsis** (CLP)



Completed Ph1 studies in subjects with hepatic impairment (HI) and renal impairment (RI)

An Open-label, Phase 1, Multiple-dose Study to Evaluate the **Pharmacokinetics and Safety of NTZ 500 mg twice daily for 7 days in Adult Subjects with Moderate & Severe Hepatic Impairment** and Adult Healthy Control Subjects

Design

- Moderate to Severe HI subjects vs healthy subjects
- 6-8 Subjects in each group
- Treatment period 7 days
- PK, safety, pharmacodynamics

Healthy control subjects (n=8)

Moderate hepatic impairment (n=8)

Severe hepatic impairment (n=8)

An Open-label, Phase 1, Multiple-dose Study to Evaluate the **Pharmacokinetics and Safety of NTZ 500 mg twice daily for 7 days in Adult Subjects with Mild, Moderate & Severe Renal Impairment** and Adult Healthy Control Subjects

Design

- Mild, Moderate and Severe RI subjects vs healthy subjects
- 8-10 Subjects in each group
- Treatment period 7 days
- PK and safety

Healthy control subjects (n=7-8)

Mild renal impairment (n=7-8)

Moderate renal impairment (n=7-8)

Severe renal impairment (n=7-8)

Development of a New Formulation, ahead of a Phase 1b/2a Proof-of-concept Targeted to Start in 1H25

New formulation under development

To permit **greater dosing flexibility** and ultimately better serve the ACLF patients:

- This population is known to have **impaired/organs failure**, and this new formulation will also permit to optimize safety and drug exposure in this patient population.
- Optimization of the future potential of NTZ, taking into account specific needs of the targeted patients.

Objectives of the POC

Phase 1b

- To evaluate safety and tolerability of NTZ across a range of doses in patients with ACLF
- To evaluate NTZ dose response relationship in patients with ACLF
- To select the optimal NTZ dose for evaluation in Phase 2a

Phase 2a

- To evaluate clinical outcomes in patients with ACLF following administration of NTZ
- To evaluate safety and tolerability of NTZ in patients with ACLF
- To evaluate NTZ PK/PD relationships in patients with ACLF

Patient Population: Patients with **ACLF1** or **ACLF2**

SRT-015

*Preclinical stage
program in ACLF*



An Injectable Formulation of ASK1 Inhibitor

SRT-015 in brief

ASK1 inhibitor

in-licensed from Seal Rock Therapeutics
in **acute liver diseases**



Injectable formulation

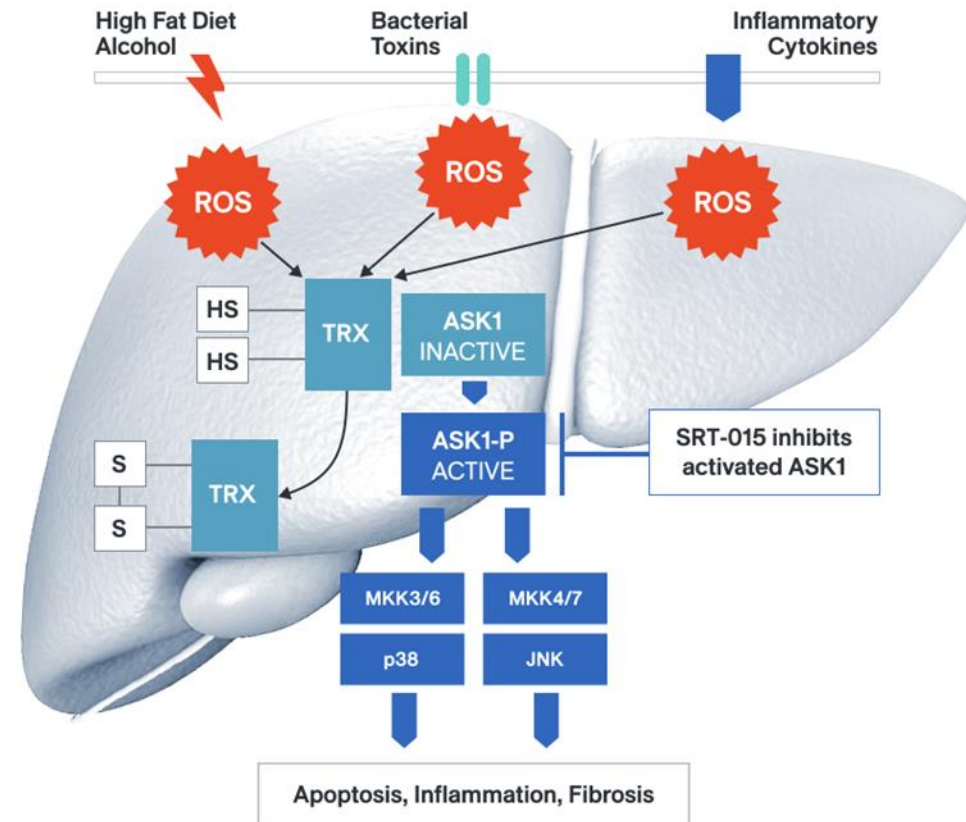


Targets inhibition of **cellular apoptosis, inflammation** and **fibrosis**

Scientific rationale

ASK1 inhibition has shown **several potentially beneficial effects** that may be relevant in ACLF

- > **Blocking LPS** (lipopolysaccharide) associated hyperinflammatory response
- > **Reducing the ROS** (Reactive Oxygen Species)-related immune response
- > **Reducing apoptosis**
- > **Reducing release of the proinflammatory cytokines**
- > **Reducing fibrosis**
- > **Protecting macrophage mitochondrial function**



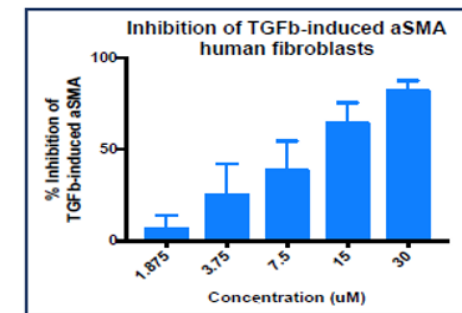
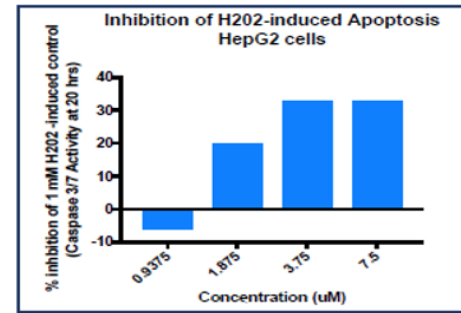
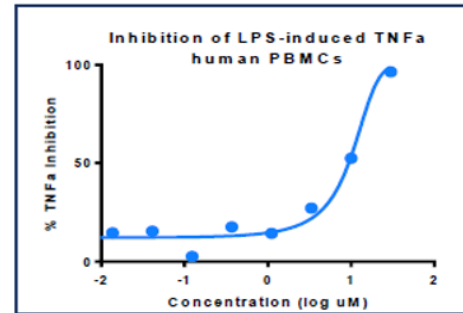
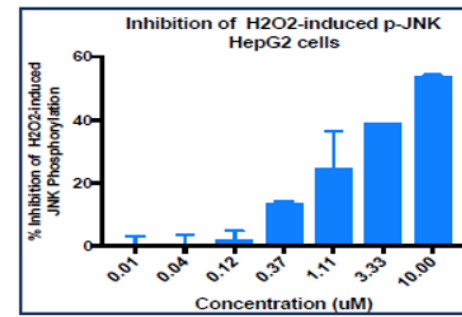
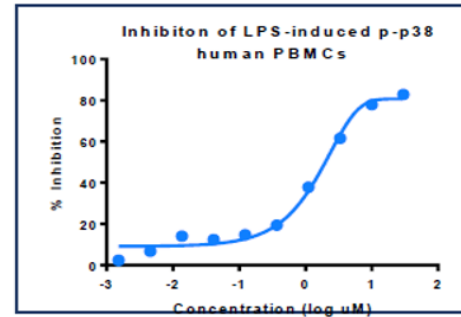
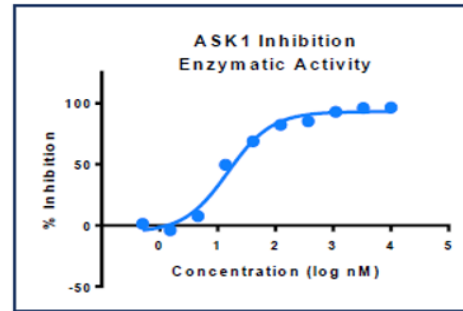
Target Engagement, MoA, Activity and Data Supporting Development in ACLF

Inhibits:

- ASK-1
- phosphorylation of p38
- phosphorylation of JNK

Activity:

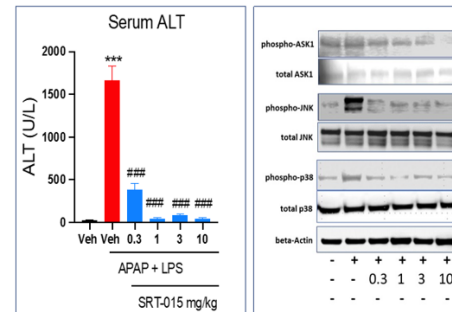
- Anti-inflammatory
- Anti-apoptotic
- Anti-fibrotic



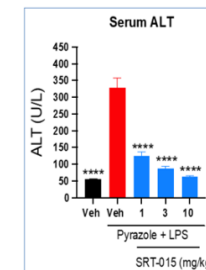
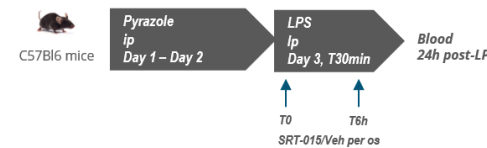
SRT-015 alleviates hepatic injury in a model of drug-induced liver injury, in association with reduction of phosphorylation of both JNK and ASK1

SRT-015 alleviates hepatic injury in a model of alcoholic hepatitis

In vivo APAP mouse model



In vivo Pyrazole-LPS mouse model



Similar preliminary data obtained using *iv* administration of SRT-015

Clinical Data Support Development in Liver Diseases

Multi-organ benefits of ASK1 modulation have been observed in **several animal models and clinical trials**¹



In **kidney diseases**

=> limits renal inflammation, apoptosis and fibrosis



In **liver diseases**

=> prevents hepatocyte death, inflammation and fibrosis



In **brain disorders**

=> ASK-1 modulation limits neurodegeneration



In **inflammatory diseases**

=> limits damaging immune responses



In **cardiopulmonary disease**

=> slows the onset of heart failure

- › SRT-015 has demonstrated **efficacy in multiple preclinical models**² of acute and chronic liver injury

- › SRT-015 phase 1 FiH trial³ completed in healthy volunteers, achieving **therapeutically relevant exposure with safety and tolerability profile** supportive of ongoing clinical investigation



Upcoming milestone
First-in-Human study targeted for 2H24

1. ASK1 inhibition: a therapeutic strategy with multi-system benefits: Journal of Molecular Medicine (2020)
2. <https://www.sealrocktx.com/science.html>
3. NCT04887038

CLM-022

*Preclinical stage
program in ACLF*



Supporting Evidence and Next Steps

CLM-022



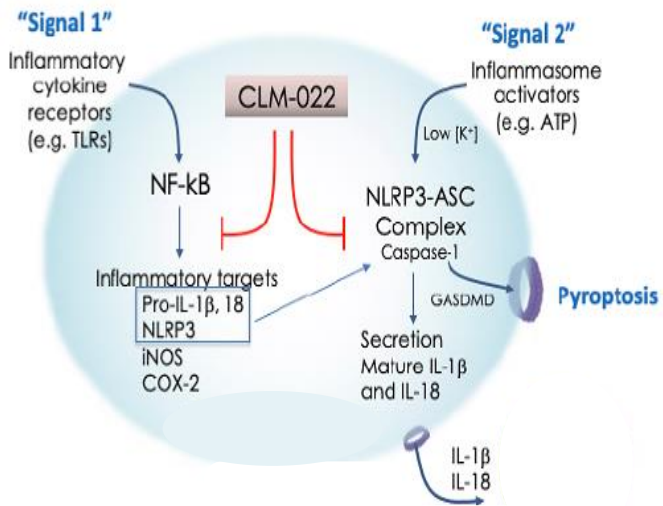
NLRP3
inflammasome
inhibitor

Preclinical

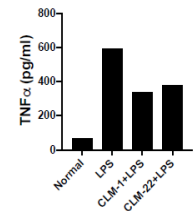
- Blocks NLRP3 inflammasome activated by ATP and Nigericin
- Blocks the endotoxin-induced production of inflammatory cytokines in an LPS sepsis model
- Blocks ASC speck formation at nanomolar concentrations
- Decreases IL-1 β secretion by macrophages stimulated with LPS and nigericin
- Protects against nigericin-induced pyroptosis in LPS-primed macrophages
- Active *in-vivo* in rodent preclinical models of sepsis and IBD.
- Well tolerated

Preclinical
Proof of Concept
in 2024

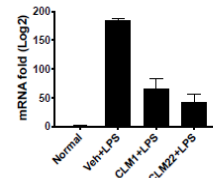
CLM-022: Dual Mode of Action



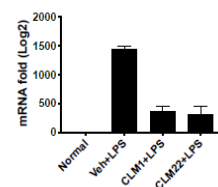
Serum TNF α levels



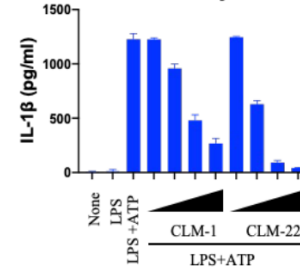
Colon-IL-1 β



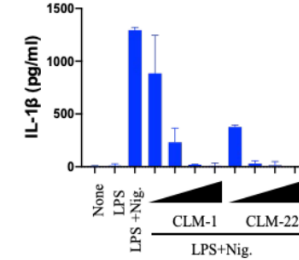
Colon-IL-6



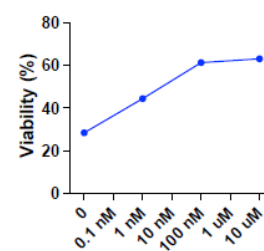
NLRP3 inflammasome activated by ATP



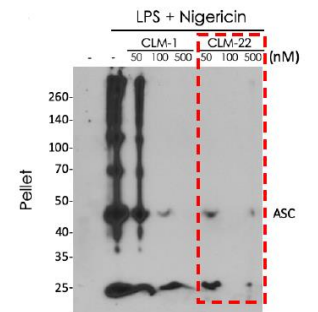
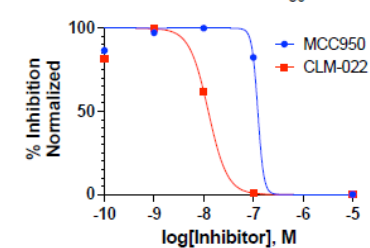
NLRP3 inflammasome activated by Nigericin



LPS+Nigericin w/ CLM-022



LDH release (IC₅₀)



VS-02-HE

*Preclinical program in
ACLF and its
complications*



Supporting Evidence and Next Steps

About HE

- Major complications of **advanced liver disease** and **portal hypertension**⁶
- **30-40% of patients with cirrhosis** will experience at least 1 episode⁵
- **Independent risk factor of mortality** in ACLF⁶

VS-02 in ACLF-HE



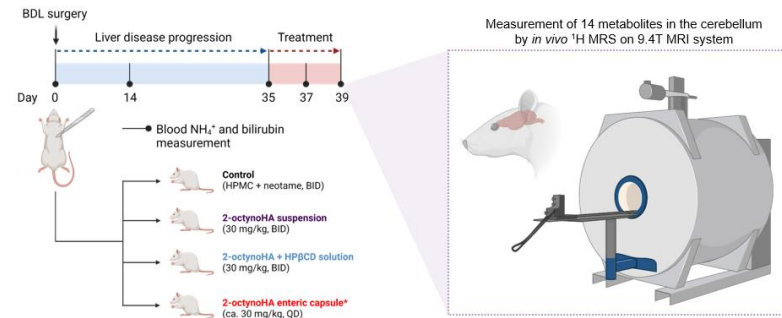
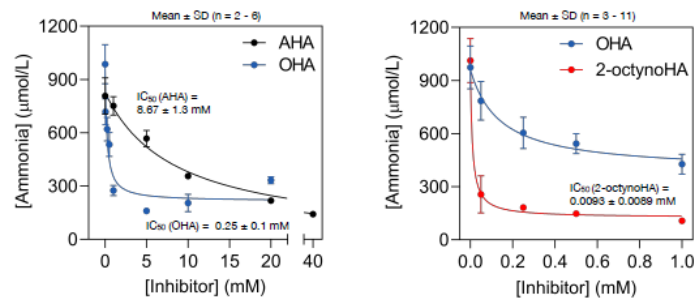
Urease inhibitor

Preclinical data

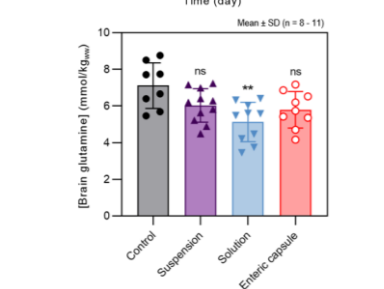
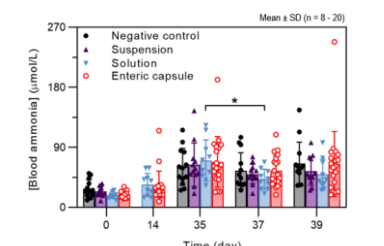
- Superior urease inhibitory activity in vitro
- Cytotoxicity and mutagenicity assessment (Ames test)
- Reduces plasmatic ammonia in a model of acute liver failure in rats
- Reduces plasmatic ammonia and brain glutamine in the bile duct-ligated model in rats

IND enabling studies completion in 2025

Urease inhibitory activity in the caecal content of Wistar rats



*Capsules (size 9h) were coated with 15% (w/w) Eudragit L100 solution for colonic delivery
 **Solution of 2-octynoHA was prepared using HPβCD (1:1, mol/mol)



Towards a new GENFIT

Pascal Prigent, CEO

ACLF disease state

MD, Senior Scientist at the National (French) Institute of Health (Inserm)

Q&A

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Disclaimer

- *IQVIA is not an “authorized person” for the purposes of the Financial Services and Markets Act 2000 (“FSMA”) and does not provide investment advice or carry on any other regulated activity under Part II of the FSMA 2000 (Regulated Activities) Order 2001.*
- *Projections and related information contained herein are made and provided subject to the assumptions, methodologies, caveats, and variables described in this report. Proprietary and third party Source on which analyses are conducted are reasonably believed to be reliable. No warranty is made as to the completeness or accuracy of such third party Source or Data.*
- *This report, in part or in whole, is not intended to constitute investment advice, and is not a recommendation to purchase or not purchase, an endorsement of, or an opinion as to the value of, any security or any investment instrument of our client or any other entity.*
- *As with any attempt to estimate future events, projections, conclusions, and other information included herein are subject to certain risks and uncertainties, and are not to be considered guarantees of any particular outcome.*
- *This report shall not be published, nor shall any public references to IQVIA be made regarding these services or this report, without IQVIA’s prior written approval, provided that, this report may be given to third party organizations as contemplated in the contract terms. When so provided, this report and the information herein must always be provided and used in its entirety, including this complete Disclaimer page.*
- *This report is subject to the IQVIA Standard Terms and Conditions.*

We conducted secondary market research / literature review to assess the commercial opportunity in ACLF

SCOPE



ACLF disease landscape



- Performed a **literature review and secondary market research** to understand:
 - Demographics and epidemiology / burden of disease with healthcare costs associated
 - Treatment algorithm
 - Competitive landscape
 - Expected future market events



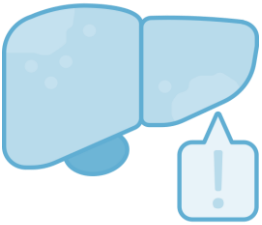
ACLF addressable market estimation



- Overall ACLF market size **estimated based on epidemiology and potential price point** from secondary market research

No detailed pricing primary market research was conducted. Estimation is not a forecast – calculations represent potential overall market size based on secondary research / literature review.

ACLF is a life-threatening disease involving multiple organs failure and characterized by short term mortality



Acute on chronic liver failure

Life-threatening disease characterized by **acute decompensation** of chronic **liver** disease associated with multiple **organ failures** and high short-term mortality¹

52-57

average age at diagnosis mostly driven by onset of alcohol related cirrhosis and/or hepatitis B or D^{5,6,7}

30%

Hospital readmission rate after 30 days since discharge¹



40-50%

mortality rate at 90 days for ACLF1 & ACLF2; and **up to 79% for ACLF3**^{2,3}

65%

of diagnosed patients are male^{5,6,7}

1) Shah NJ, et al. StatPearls (2022) 2) Moreau R et. al., Gastro, (2013); 3) Hernaez R, et al., Gut (2017); 4) IQVIA Analysis; 5) Kamath 2017; 6) Hernandez et al 2019; 7) Wong F, et al., Liver Transpl 2022; 8) Arroyo v., et al, J. Hepatol (2015)

Management of ACLF results in significant economic burden on healthcare systems, leading to a high need for innovative therapies

The burden of ACLF in numbers



52 000 \$

Average cost per hospitalization per patient in US¹



16 days

Average length of hospital stay¹
(vs 7 days for cirrhotic patients)



6.4 Bn \$

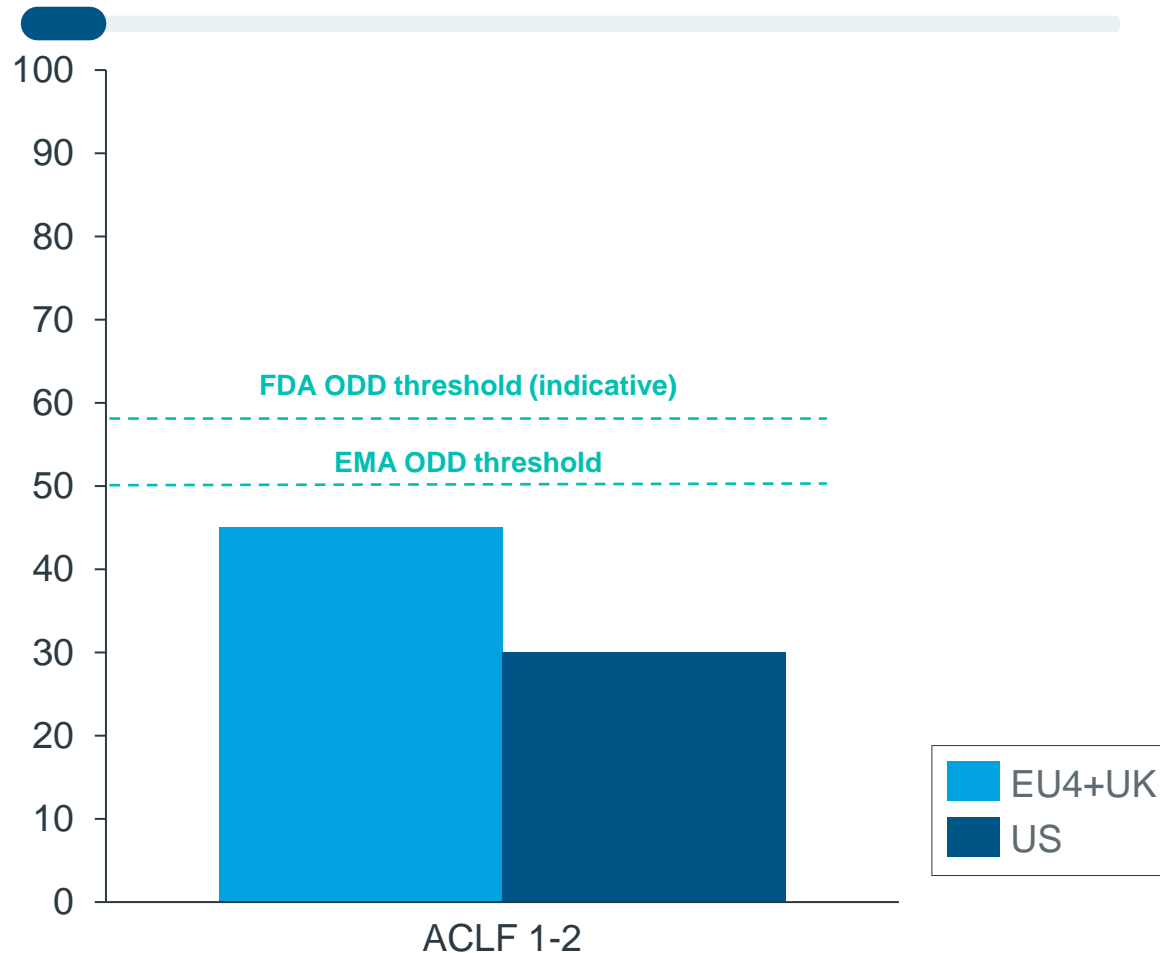
Estimated **annual cost burden** in US in 2021*
(a nearly 4-fold increase since 2011)*

*Note: Estimates based on triangulation of data from below mentioned publications and PMR interview (Desai et al, Clin Transl Gastroenterol. (2019); Hirode et al JAMA Netw Open. (2020); Hernaez et al, J Hepatol. (2019); Mezzano et al, Gut (2022); Moreau et al, Gastroenterology. (2013))

1) Kamath 2017; 2) Hernandez et al 2019 3);
Genfit –AASLD presentation - November 2023

ACLF has low epidemiology and could be eligible to orphan designation; aging population and launch of targeted Tx can increase diagnosis rate

Estimated current prevalence (1:100,000)



Notes:* Estimates based on triangulation of data from listed sources

Sources: 1. Moreau, R., et al., (2013) Supplemental Table 10; 2. Moreau, R., et al., (2013) CANONIC study Supplemental Table 10; 3. Allen MA et al., Hepatology (2016); 4. Internal Reference (PMR 2021); 5. Desai et al, Clin Transl Gastroenterol. (2019); 6. Hirode et al JAMA Netw Open. (2020); 7. Hernaez et al, J Hepatol. (2019); 8. Mezzano et al, Gut (2022); 9. Moreau et al, Gastroenterology. (2013);

Abbreviations: ACLF: Acute-on-chronic liver failure

Genfit -AASLD presentation - November 2023

Overview and future outlook

- In 2021, the **prevalence of ACLF is estimated to be ~294K** across the US, EU4 and UK¹
 - Approx. 45-52% of ACLF patients are grade 1 and 35% are grade 2^{2,3}
 - **Total addressable market** (for grade 1/2 ACLF patients) is estimated to be **~150K in EU4 & UK and 90K in US**
- Therefore, **therapies targeting ACLF are eligible for orphan drug designation** given low prevalence and lack of therapies

Note: while EMA and FDA ODD thresholds capture number of patients, the estimated ACLF prevalence refers to number of episodes rather than patients, thereby leading to potential overestimation of the disease prevalence

Several analogues were selected to estimate price range of upside potential, including one-off therapies for chronic disease and drugs for acute episodes

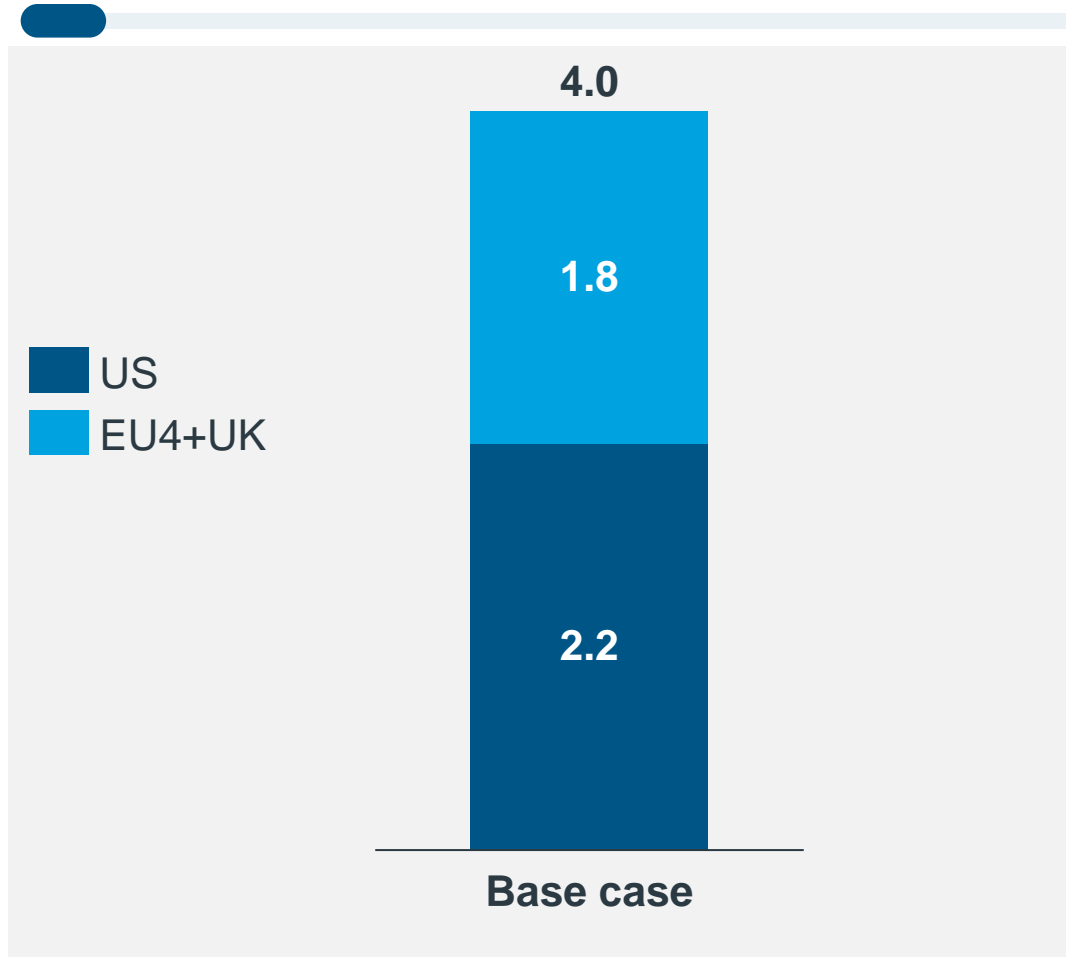
Analogues considered

- To identify relevant price range for the ACLF drugs, different analogues were considered
 - Type of rare disease (i.e. life threatening vs chronic)
 - Onset of acute episodes
 - Setting of treatment (hospitals vs out-patient care)
 - Benefit provided (significant mortality benefit vs slower progression over hard endpoint)
- IQVIA identified a 100-200k\$ in US as potential upside range for an upcoming ACLF therapy with mortality benefit targeting more severe patients

Analogue	MoA	Features	List Price (US)
Andexxa	Recombinant modified human factor Xa (FXa) protein	<ul style="list-style-type: none"> Adults with life threatening bleeds due to use of blood thinner therapies (apixaban and rivaroxaban) IV infusion by HCP Immediate, significant reverse blood thinning 	<ul style="list-style-type: none"> 25-50k\$ per treatment, depending on patient features
Cablivi	Monoclonal antibody	<ul style="list-style-type: none"> Treatment of acute episode in life threatening disease (i.e. acquired thrombotic thrombocytopenic purpura) Orphan drug Hospital setting Significantly reduced potentially fatal and serious disease related events 	<ul style="list-style-type: none"> 270k\$ per year
CAR – T cell	Chimeric Antigen Receptor	<ul style="list-style-type: none"> One off cycle for the treatment of acute/ severe conditions patients with blood cancer with limited life expectancy Mortality benefit over a sustained period of time 	<ul style="list-style-type: none"> 371k\$ average cost
Bylvay	Reversible inhibitor of ileal bile acid transporter	<ul style="list-style-type: none"> The first non-surgical treatment for severe itching (pruritus) in PFIC Orphan drug Highly significant sustained improvements in pruritus Small patient population (adult & pediatric) with high unmet need 	<ul style="list-style-type: none"> 385k\$ per year

Overall, grade 1-2 ACLF may represent a potential ~4 bn USD addressable market opportunity in the US and EU4+UK by 2030

Ballpark overall market size by 2030, bn USD¹















Assumptions / considerations

- **Prevalence: 150K (EU4 + UK) / 90k (US) for grade 1-2 ACLF patients²**
- **Drug price could amount to \$30-40k per patient in US and \$10-20k in EU** given the economic burden of hospitalizations and duration of treatment; the range was estimated based on:
 - Available robust data on hospitalization costs (i.e. 16 days average stay, 52k\$ average associated costs in US)
 - Likely price range for orphan drugs for life treating disease with uncertain mortality benefit over the target population
- **An upside scenario can be achieved** assuming the therapy provides significant mortality benefit for a restricted subpopulation (assuming 100-200k in US, 50-80k in EU price based on analogues assessment)
- **Potential upside of market opportunity (irrespective of price point):** ACLF incidence likely to slightly increase due to higher prevalence of lifestyle diseases, drug-induced liver injuries and raising disease awareness, market opportunity could be higher

Note: 1) Figures based on secondary research / literature review conducted in January 2023 – not a forecast and represents an estimated overall market size. No primary market research was conducted (e.g., pricing research); **2)** There is limited availability of recent US epi studies; lower prevalence vs EU is believed to be driven by differences in underlying population, Estimation includes compliance rate and gross-to-net price estimate

Detailed overview of assumptions used to estimate addressable market in 2030 in US & EU4+UK

Assumptions / considerations

<i>Input</i>	<i>Base</i>	<i>Upside</i>	<i>Rationale / Sources</i>
Prevalence	 ~100K  ~190		<ul style="list-style-type: none"> US: Hernaez, et al., J of Hepatol (2019) EU4+UK: Moreau, R., et al., (2013) Table 10;
<i>ACLF 1 prevalence</i> %	45%	45%	<ul style="list-style-type: none"> IQVIA Internal reference (PMR 2022); Moreau, R., et al., (2013) CANONIC study Supplemental Table 10
<i>ACLF 2 prevalence</i> %	35%	3%	
Total addressable market #	 ~90K  ~150K		
<i>Compliance</i> %	~75%	~75%	<ul style="list-style-type: none"> IQVIA expertise
Potential price	 ~40K  ~20K	 150K (subpop)  65K (subpop)	<ul style="list-style-type: none"> Base case: Hospitalization costs assessment and price of rare disease drugs without mortality benefit Upside case: Price of rare disease analogues with mortality benefit for a subpopulation with severe ACLF
<i>Gross to net</i> %	90%	90%	<ul style="list-style-type: none"> IQVIA expertise
2030 Addressable market (USD) \$	 2.2 Bn  1.9 Bn	 >4 Bn  >2.5 Bn	

Note: European countries in scope included only EU4+UK

ACLF is an attractive market opportunity with upside potential given significant unmet need for urgent treatment and easier clinical development

ACLF is an attractive opportunity for Biotechs to address an untapped patient population with high unmet need for urgent treatment



Possibility to **lead ACLF market growth** with **therapies** being **launched** at a **price** fully representing their **value**



Potential orphan designation **leading to easier clinical development**



Possibility to **consider commercialization on the condition** that industry collaborates with the scientific community to **increase disease awareness**

Towards a new GENFIT

Pascal Prigent, CEO

ACLF disease state

Pr. Richard Moreau, MD, Senior Scientist (Outstanding Grade) at INSERM

Q&A

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

Questions & answers

Highlights on newsflow

Pascal Prigent, CEO

Towards a new GENFIT

Pascal Prigent, CEO

ACLF disease state

Pr. Richard Moreau, MD, Senior Scientist (Outstanding Grade) at INSERM

Q&A

GENFIT's approach to ACLF

Dean Hum, Chief Scientific Officer – Meriam Kabbaj, Chief Technology Officer

ACLF market opportunity

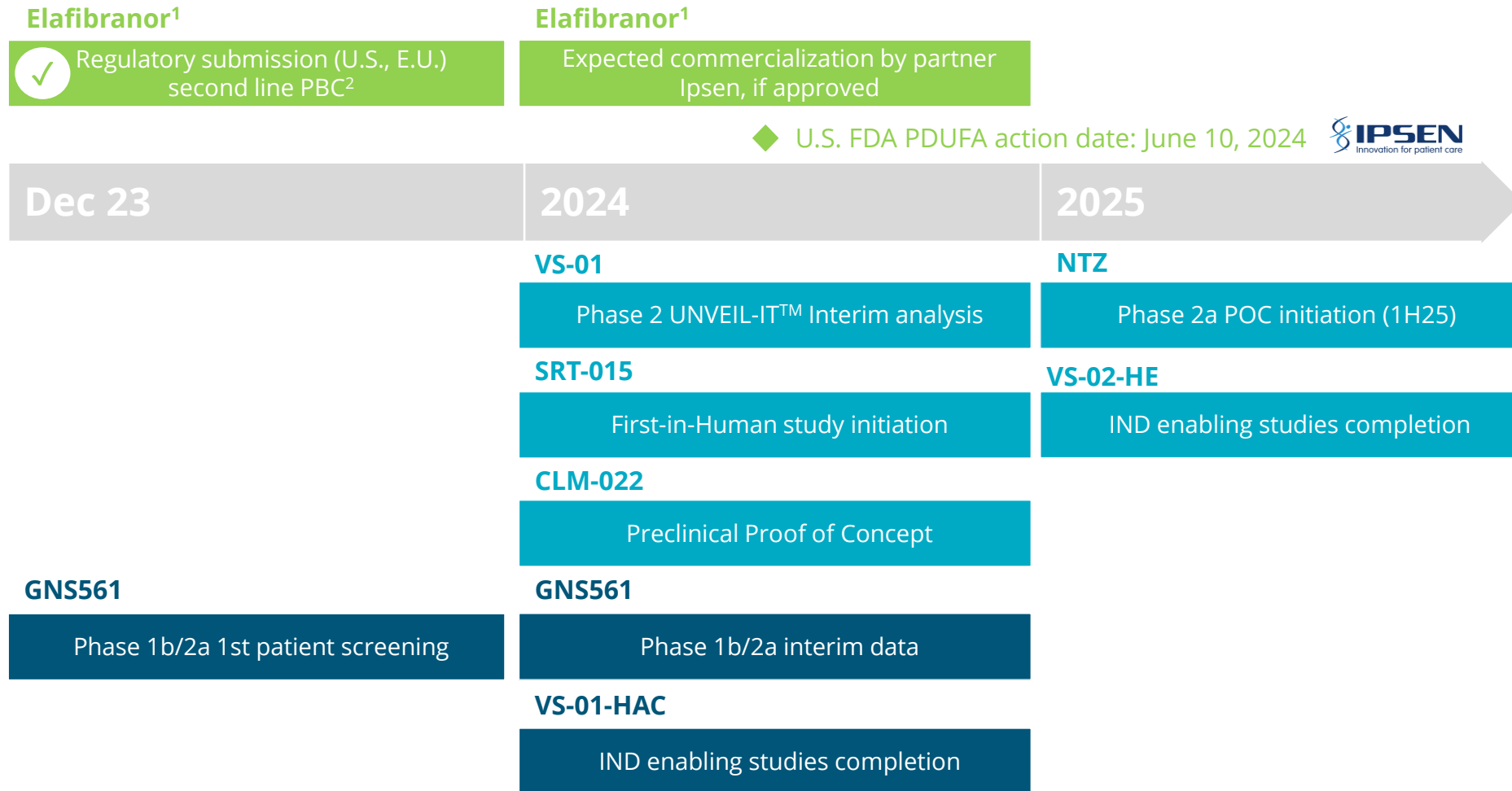
Pascal Caisey, Chief Operating Officer and Chief Commercial Officer

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Highlights on newsflow



These targeted timelines are indicative only (based on best estimates by management and current level of knowledge)

1: Elafibranor program has been out-licensed to partner in 2021 ([press release](#))
 2: <https://ir.genfit.com/news-releases/news-release-details/ipsen-confirms-us-fda-grants-priority-review-new-drug>

- ACLF (Acute On-Chronic Liver Failure)
- Other life-threatening liver diseases
- PBC (Primary Biliary Cholangitis)

THANK YOU

Corporate
Presentation