

ACLF Day @AASLD

NOVEMBER 11, 2023

Corporate
Presentation

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Towards a new GENFIT

Pascal PRIGENT, CEO

ACLF disease state

Dr Jennifer Lai (UCSF), MD, MBA

Q&A

GENFIT's approach to ACLF

Dr. Carol Addy, CMO & Dean Hum, CSO

ACLF market opportunity

R. Stolper & P-A André, IQVIA

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Towards a new GENFIT

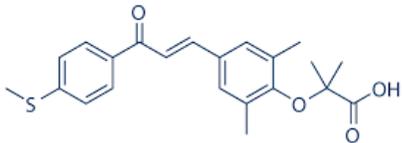


Inception & early years

1999

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

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



Clinical development in chronic liver diseases

Today

Development of **elafibranor in NASH/MASH¹** up to Phase 3

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.)



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)

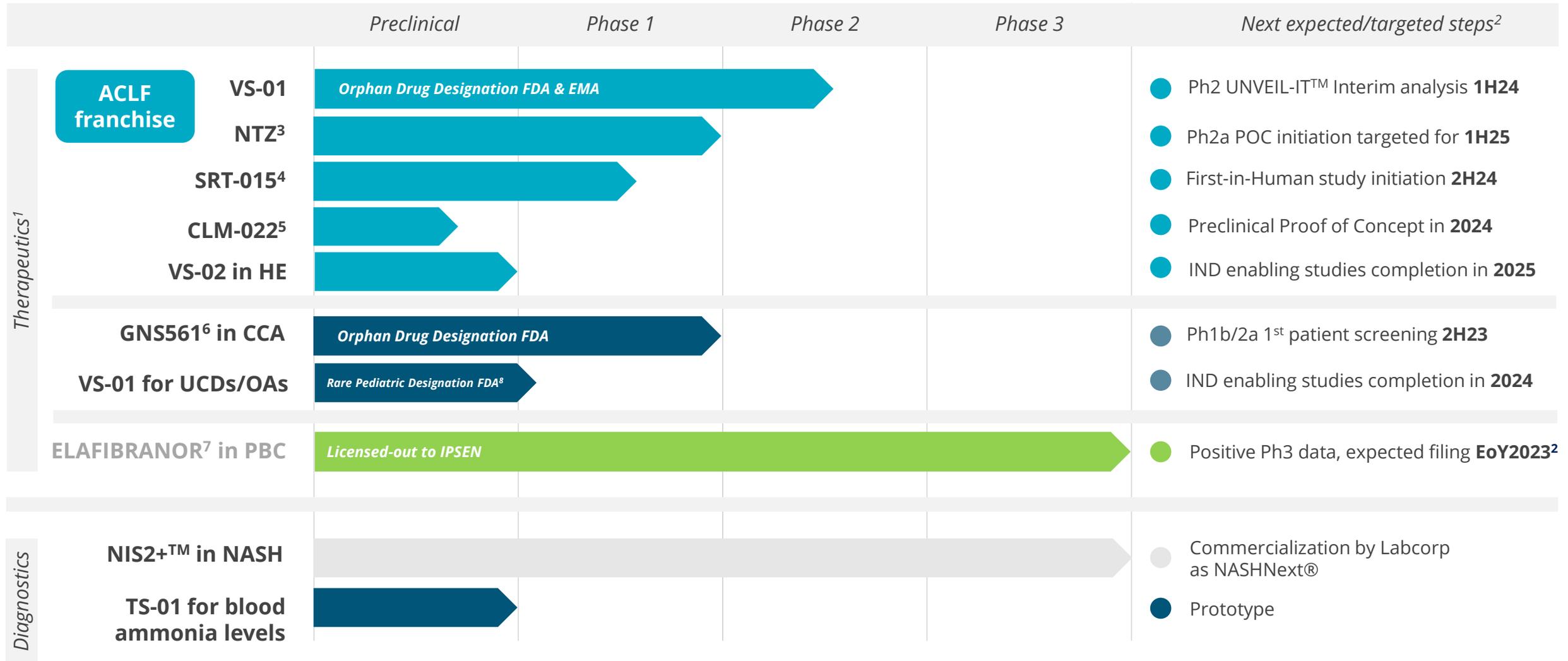
Other life-threatening liver diseases

- **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

Pipeline



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Pascal Prigent, CEO

Acute-on-Chronic Liver Failure (ACLF)

Jennifer C. Lai, MD, MBA

Transplant Hepatologist

Endowed Professor of Liver Health & Transplantation

University of California, San Francisco (UCSF)

- Acute-on-Chronic Liver Failure : Defined



...a potentially reversible condition in patients with chronic liver disease with or without cirrhosis that is associated with potential for multiple organ failure and high mortality within 3 months in the absence of treatment...

“

There is no direct therapeutic for ACLF.



SCOPE OF THE UNDERLYING
PROBLEM :
Chronic liver disease & cirrhosis

Chronic Liver Disease & Cirrhosis

11th most common cause of death

2 million deaths worldwide (~4% of deaths worldwide)

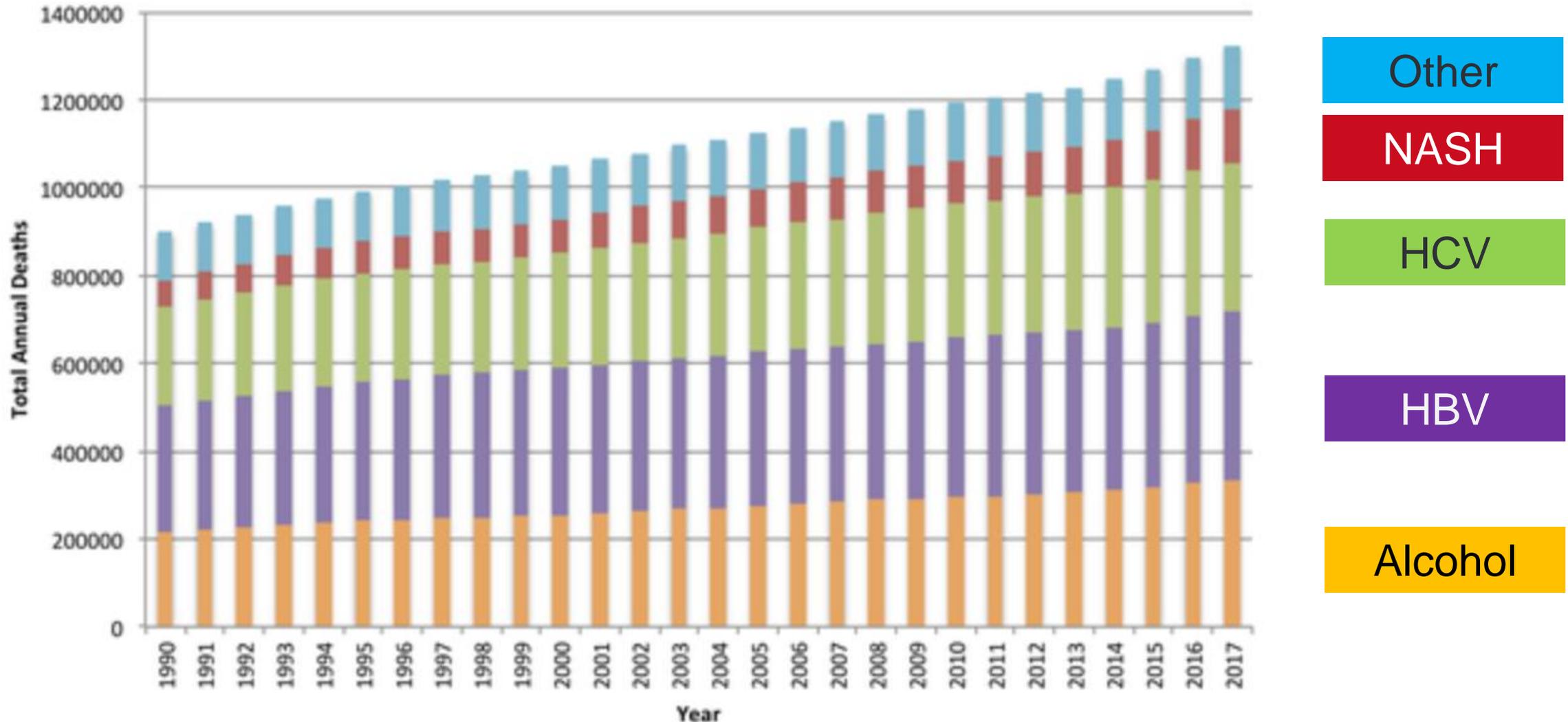
2 billion consume alcohol

At risk for alcohol-associated liver disease / cirrhosis

2 billion overweight/obese

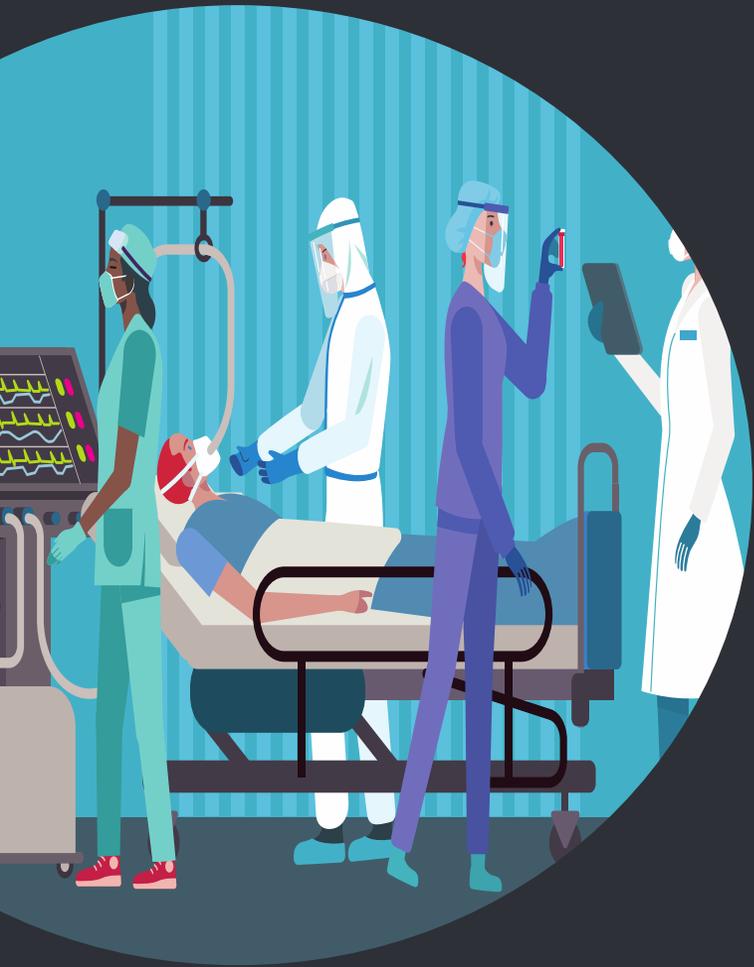
At risk for non-alcoholic fatty liver disease / cirrhosis

Deaths by liver disease etiology : RISING



Economic burden of chronic conditions in the U.S. : Cirrhosis and ACLF much higher!

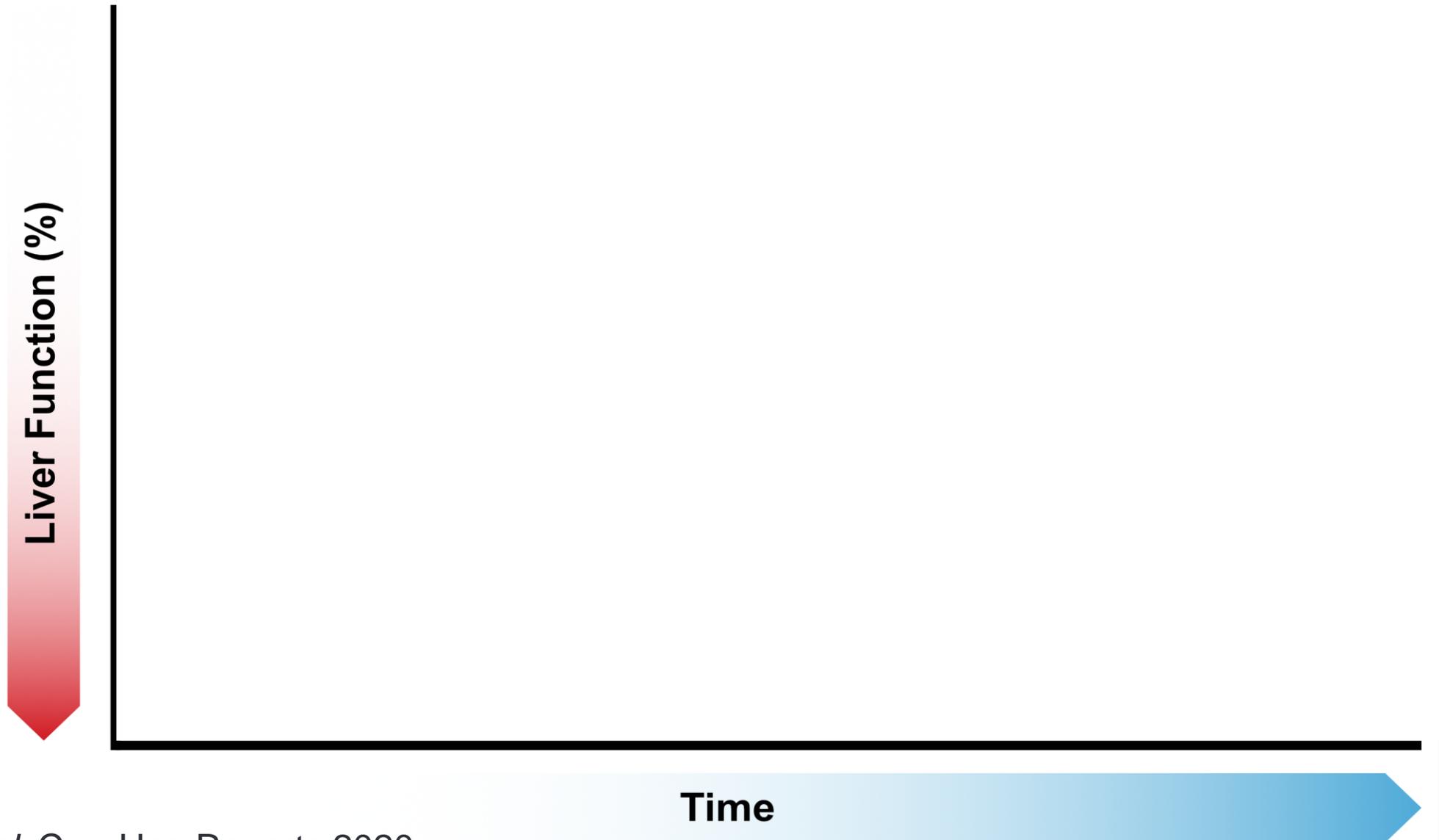
Chronic disease	Length of hospital stay	Inpatient mortality	Mean cost per hospitalization
Pneumonia	5 days	3.3%	\$7,581
Congestive heart failure	5 days	3.0%	\$8,315
Cerebrovascular disease	6 days	4.7%	\$8,117



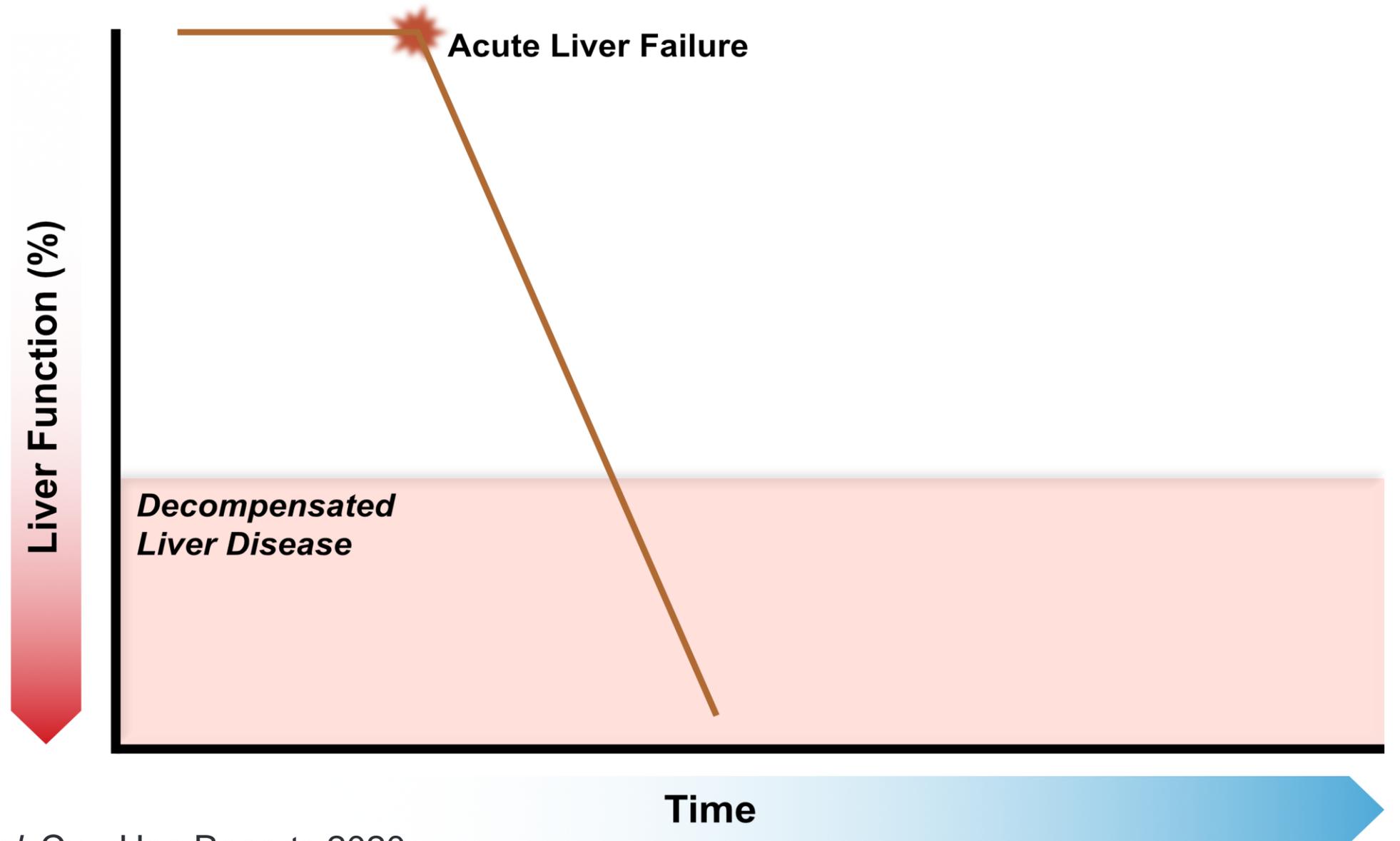
THE PATIENT :

Clinical Course & Features

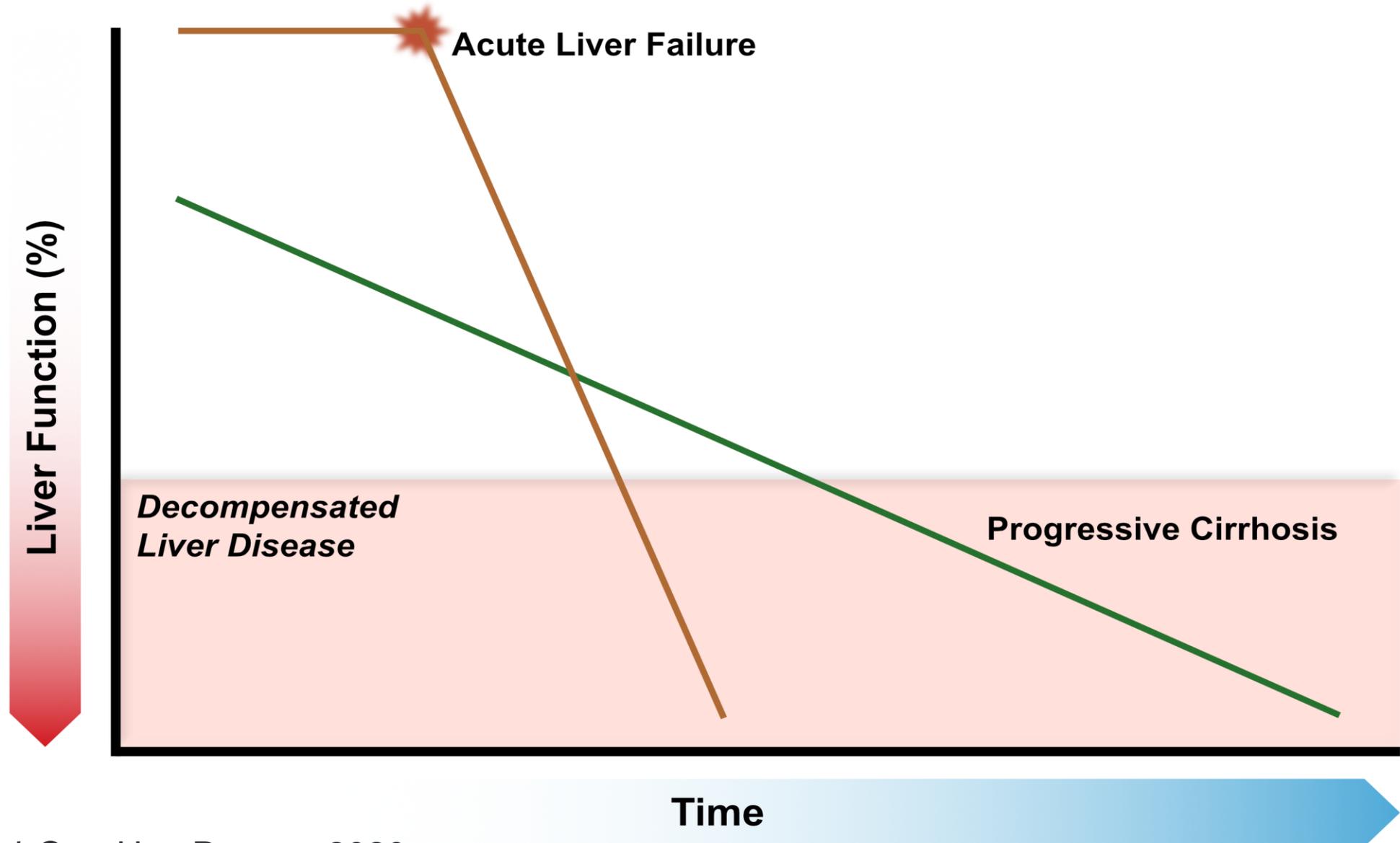
Trajectories of liver function in 3 common liver states



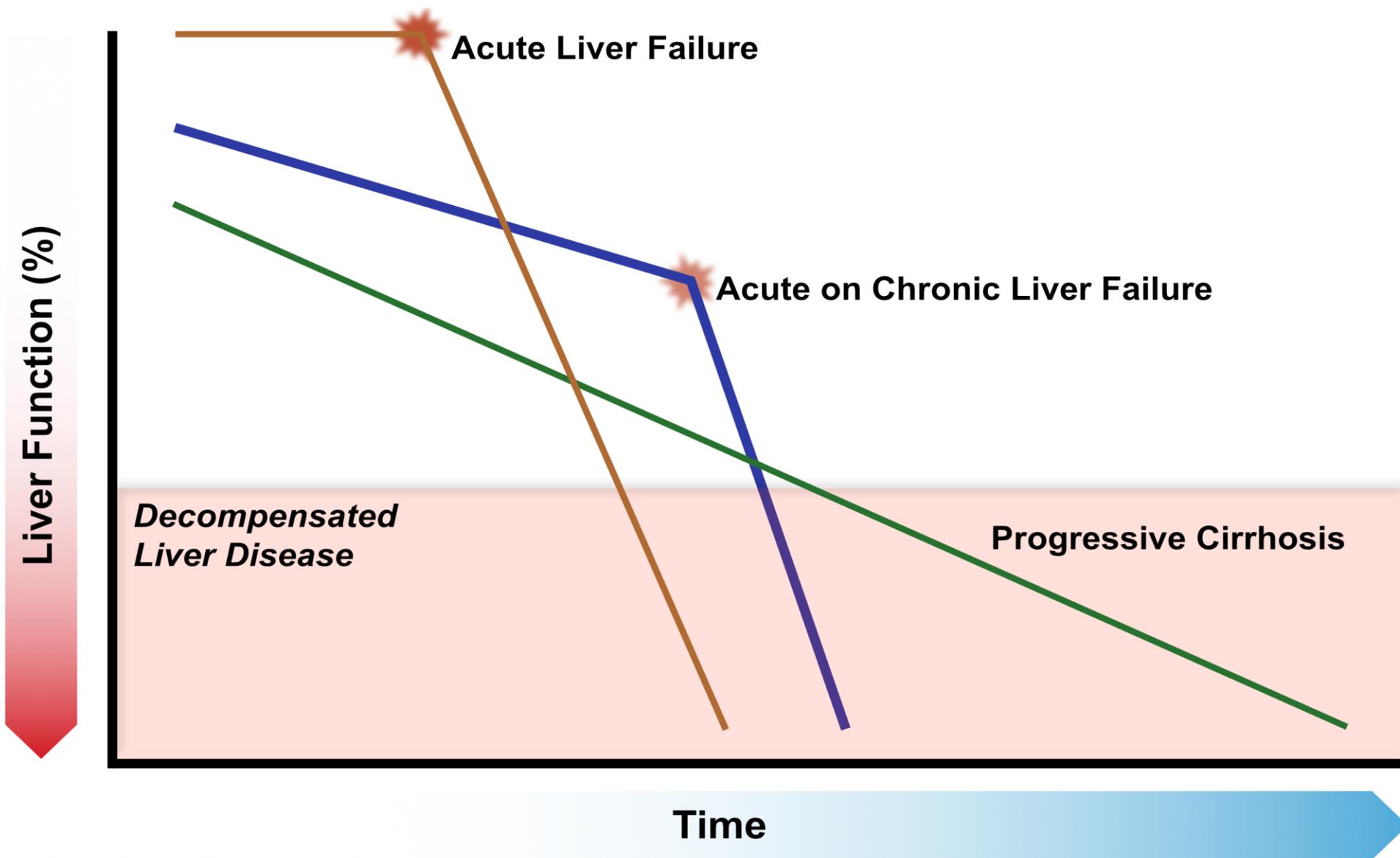
Trajectories of liver function in 3 common liver states



Trajectories of liver function in 3 common liver states



Trajectories of liver function in 3 common liver states



Clinical characteristics (U.S. cohort)

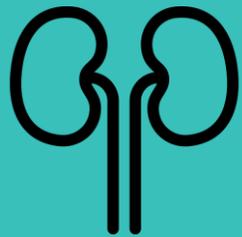
	n=1,031
Age (years)	57 (11)
Men	66%
Liver disease etiology	
Alcohol only	31%
HCV only	21%
Alcohol + HCV	15%
NASH	17%
Other	15%

Reason for admission	n=1,031
Bacterial infection	25%
GI bleed	16%
Hepatic enceph.	17%
Renal dysfxn	12%
Alcohol related	4%
Electrolytes abnl	3%
Other	23%

Role of prior hepatic decompensation

	n=417
No prior event	26%
<3 months prior	16%
3-12 prior	17%
>12 months prior	41%

Percent with *extra-hepatic* organ failure on admission



RENAL

50%



NEUROLOGIC

22%



CIRCULATORY

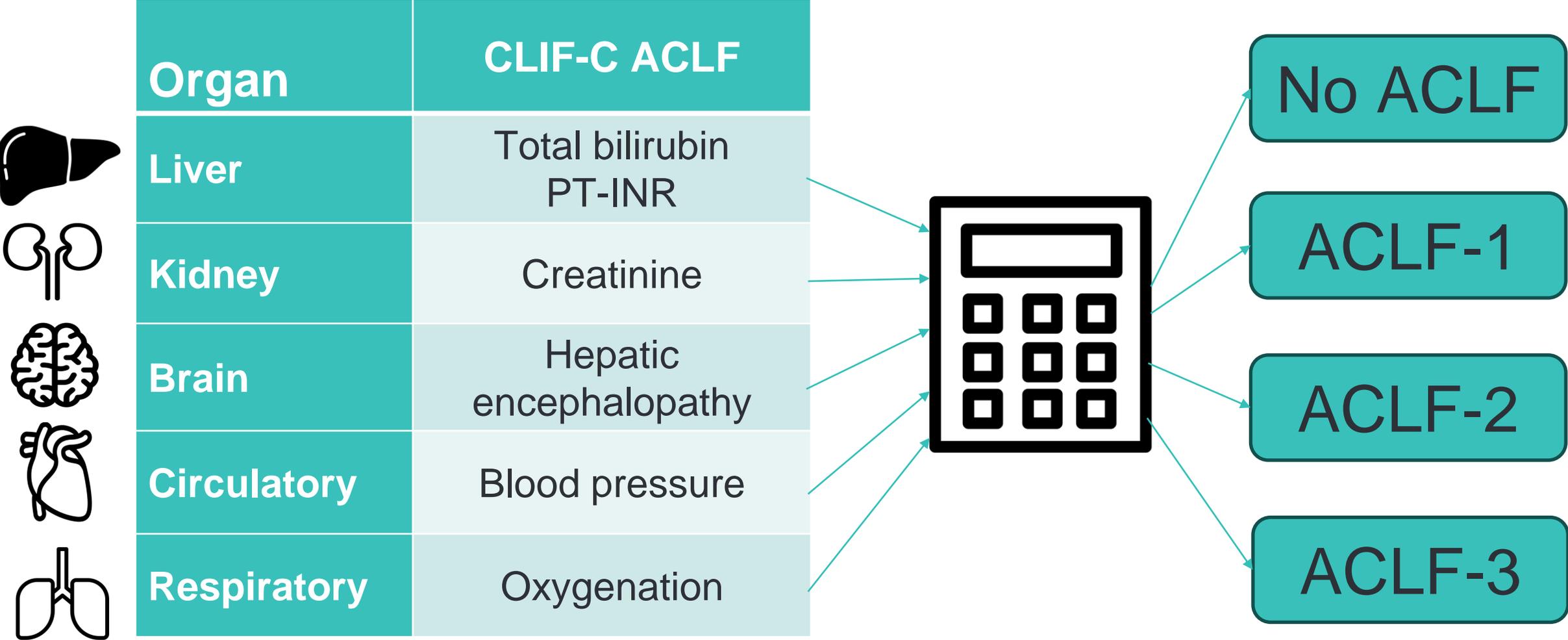
23%



RESPIRATORY

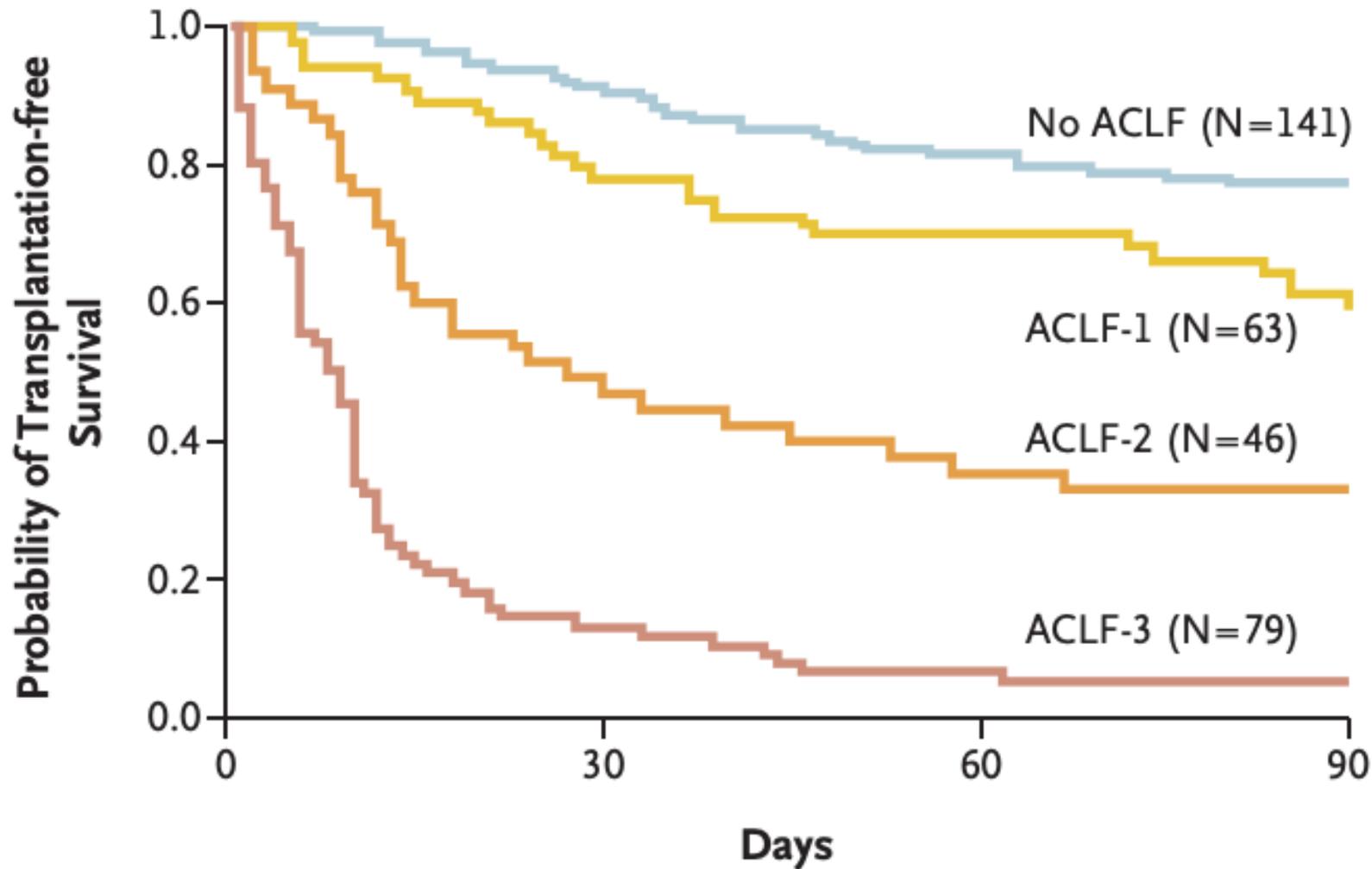
13%

Chronic Liver Failure Consortium (CLIF-C) ACLF



*CLIF-C ACLF = 10 x [0.33 x CLIF-Organ Failures + 0.04 x Age + 0.63 x ln(WBC)-2]

Probability of survival by ACLF severity



Increasing # / severity

The greater the number/severity of organ failures, the greater the risk of death.



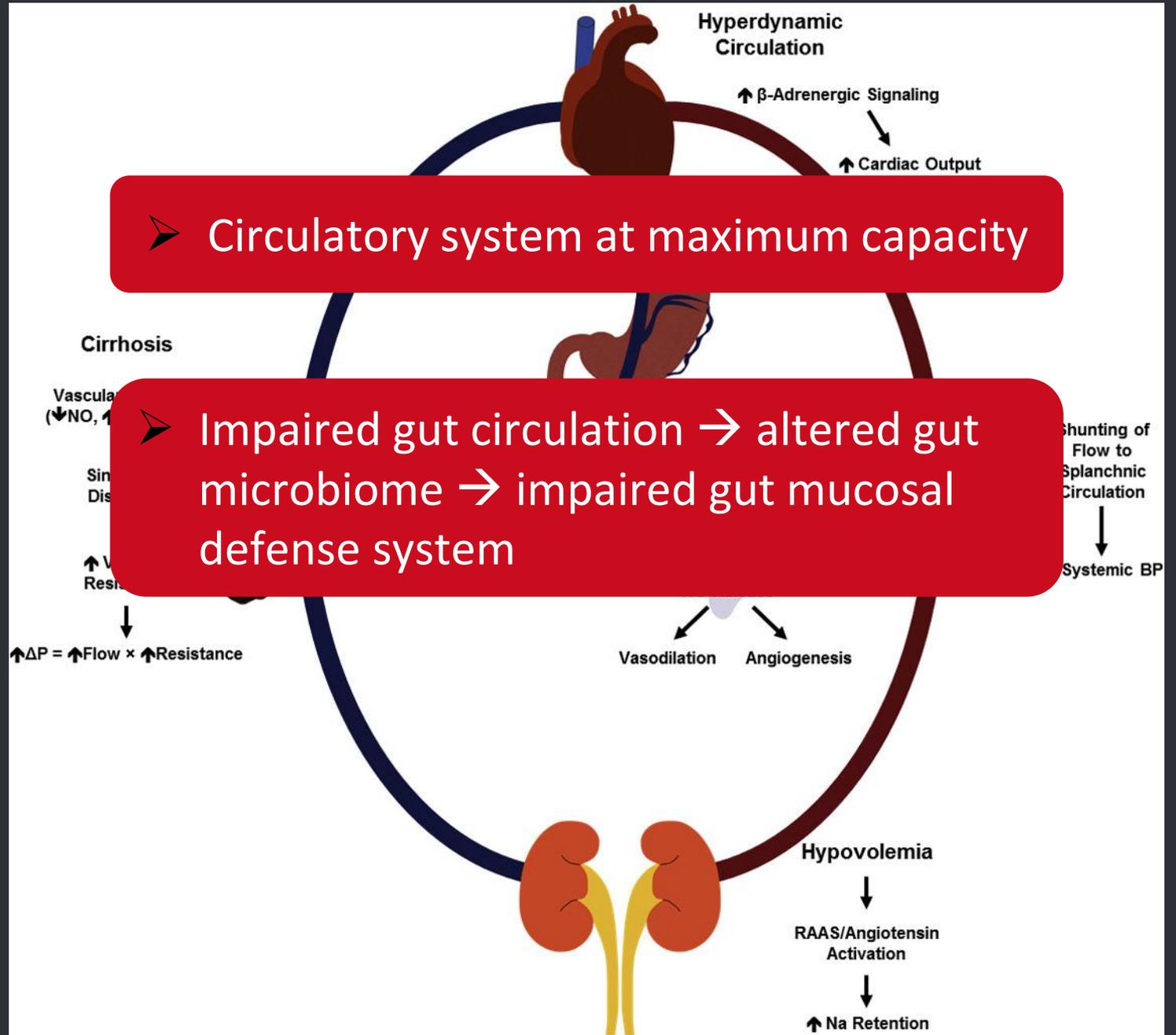
PATHOGENESIS :

Leading hypotheses and supporting data

The underlying condition

Portal hypertension 101

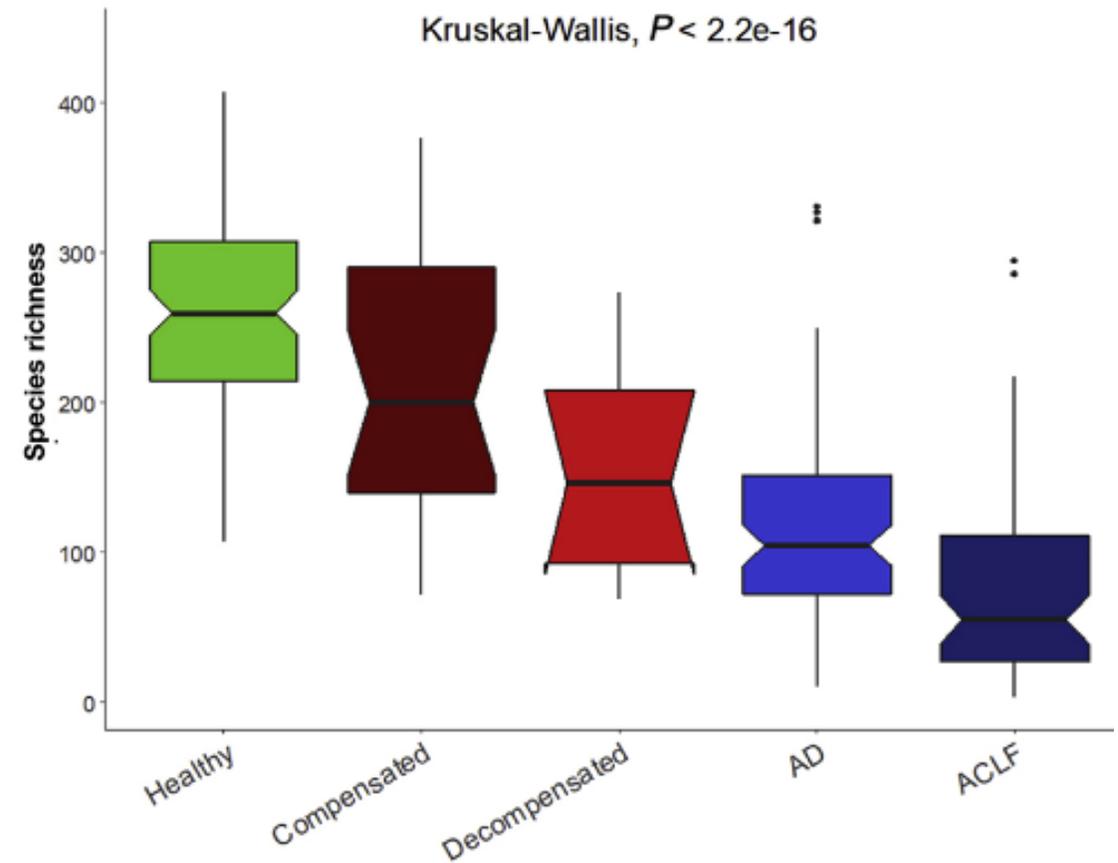
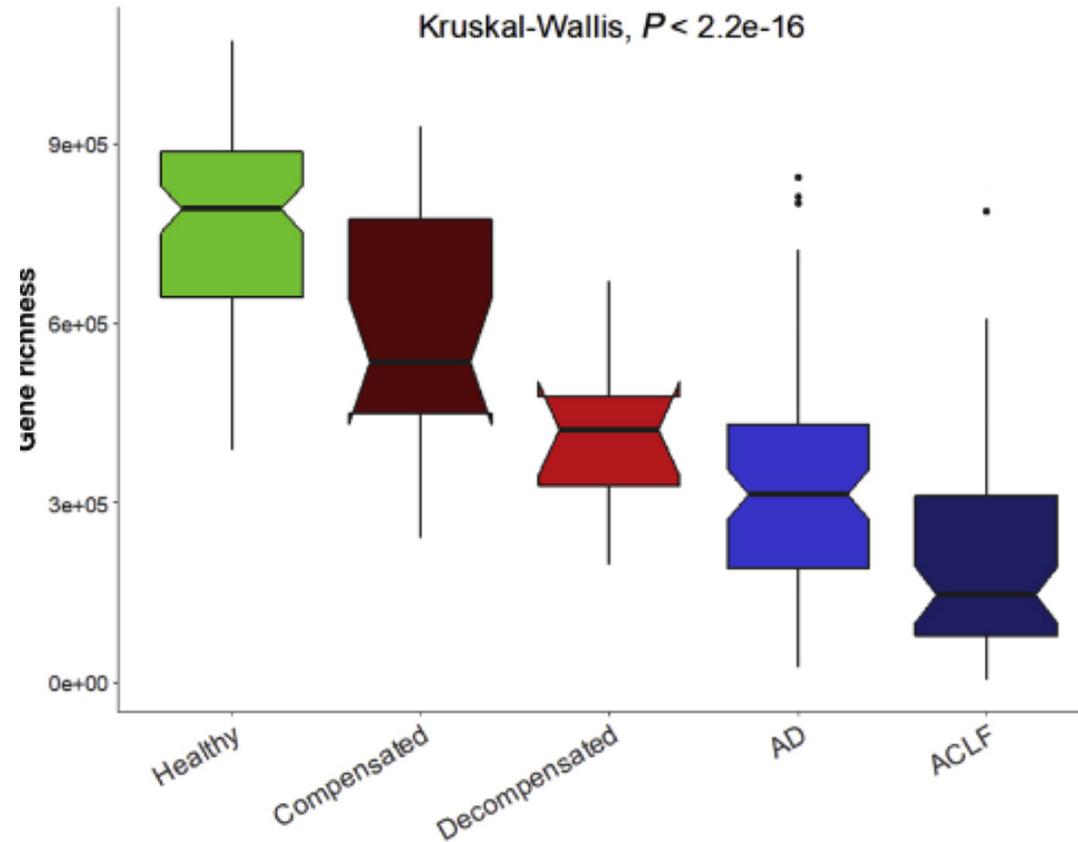
Simonetto DA, *et al.* Mayo Clinic Proc 2019.



➤ Circulatory system at maximum capacity

➤ Impaired gut circulation \rightarrow altered gut microbiome \rightarrow impaired gut mucosal defense system

Greater severity of liver disease is associated with less diverse microbiome

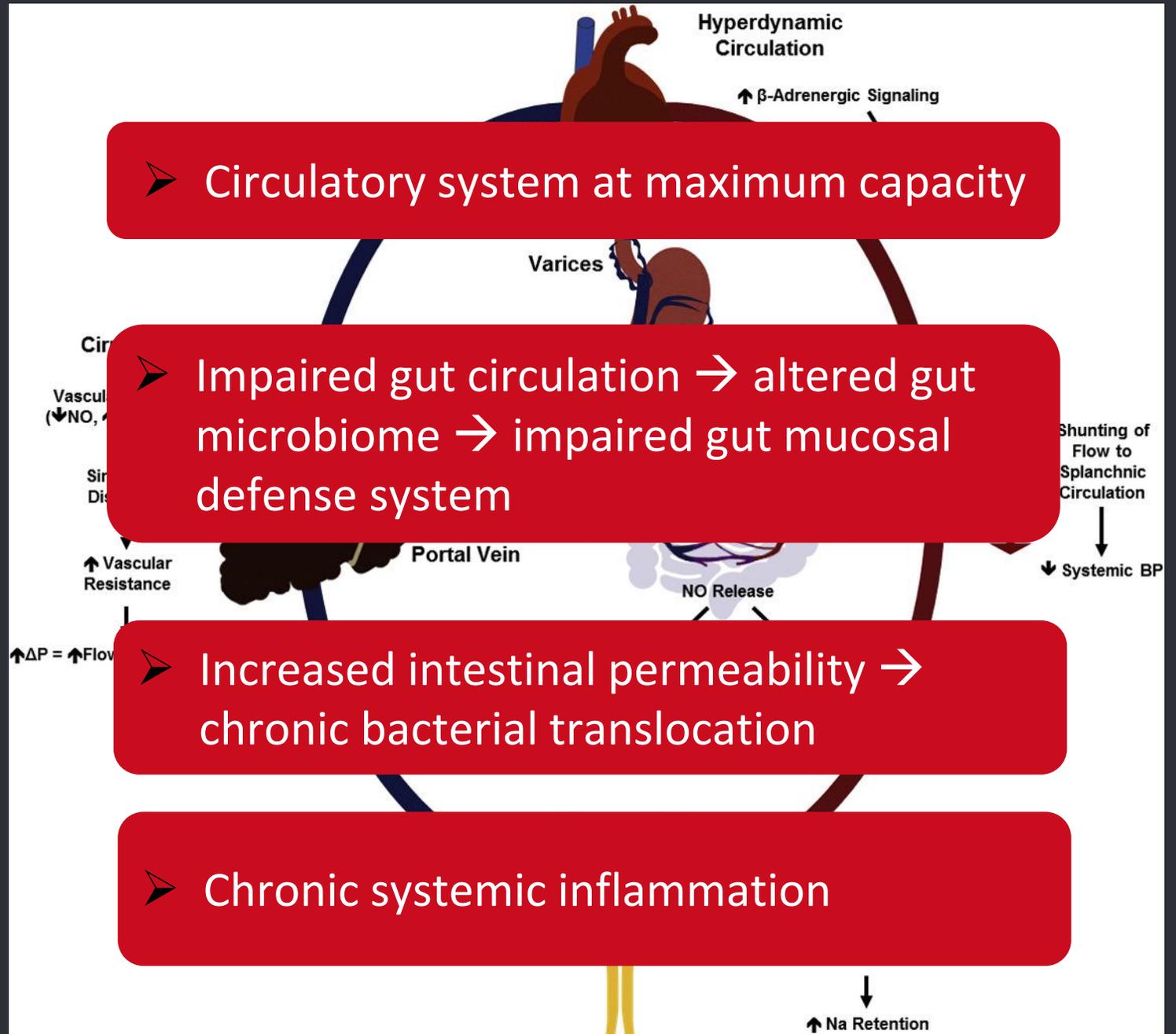


Is there a role for gut microbiota manipulation to improve ACLF outcomes?

The underlying condition

Portal hypertension 101

Simonetto DA, *et al.* Mayo Clinic Proc 2019.



The acute insult

Systemic inflammation hypothesis of ACLF

Exacerbation of portal hypertension

Acute precipitant

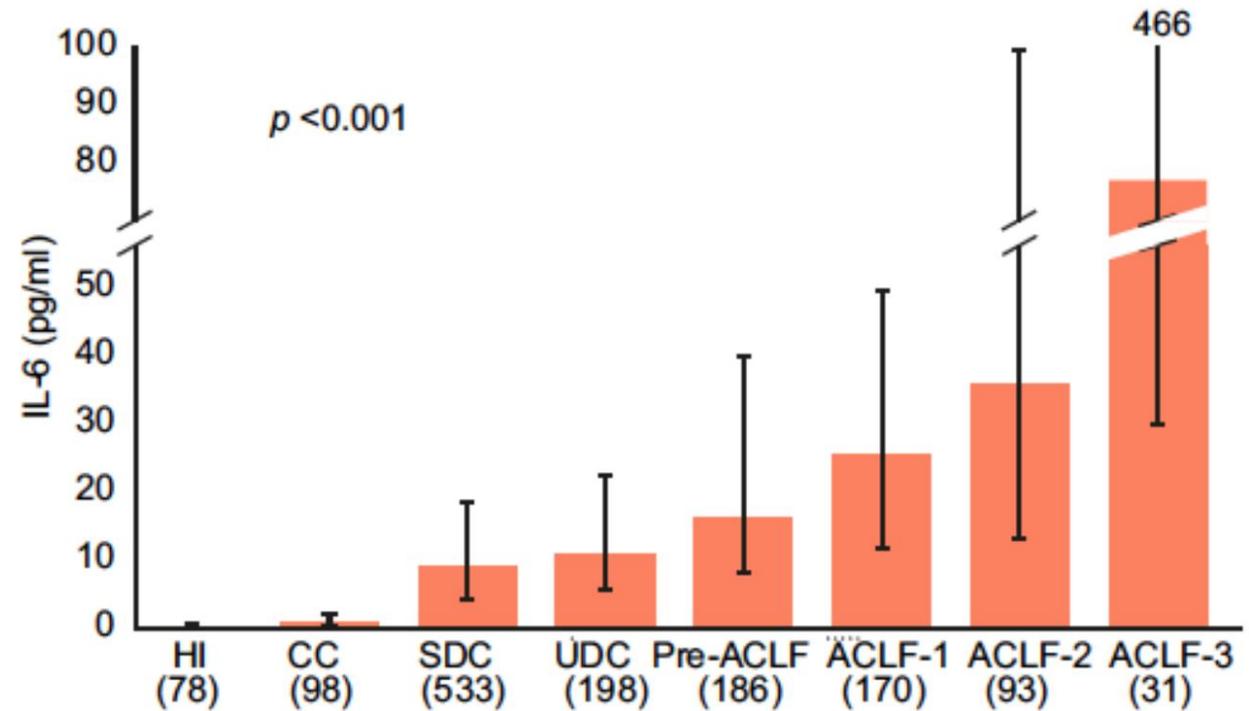
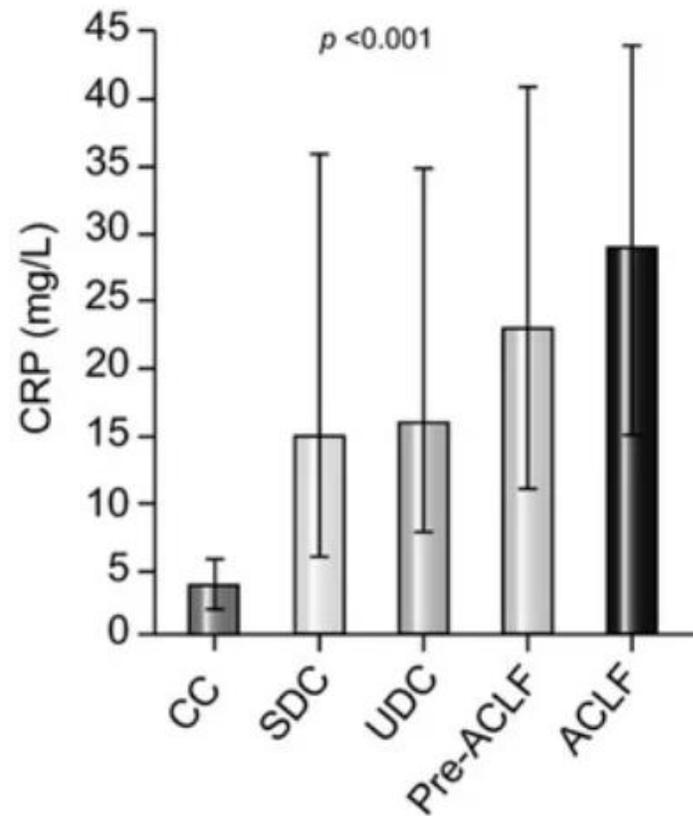
Excessive inflammatory reaction

Severe acute systemic inflammation and oxidative stress

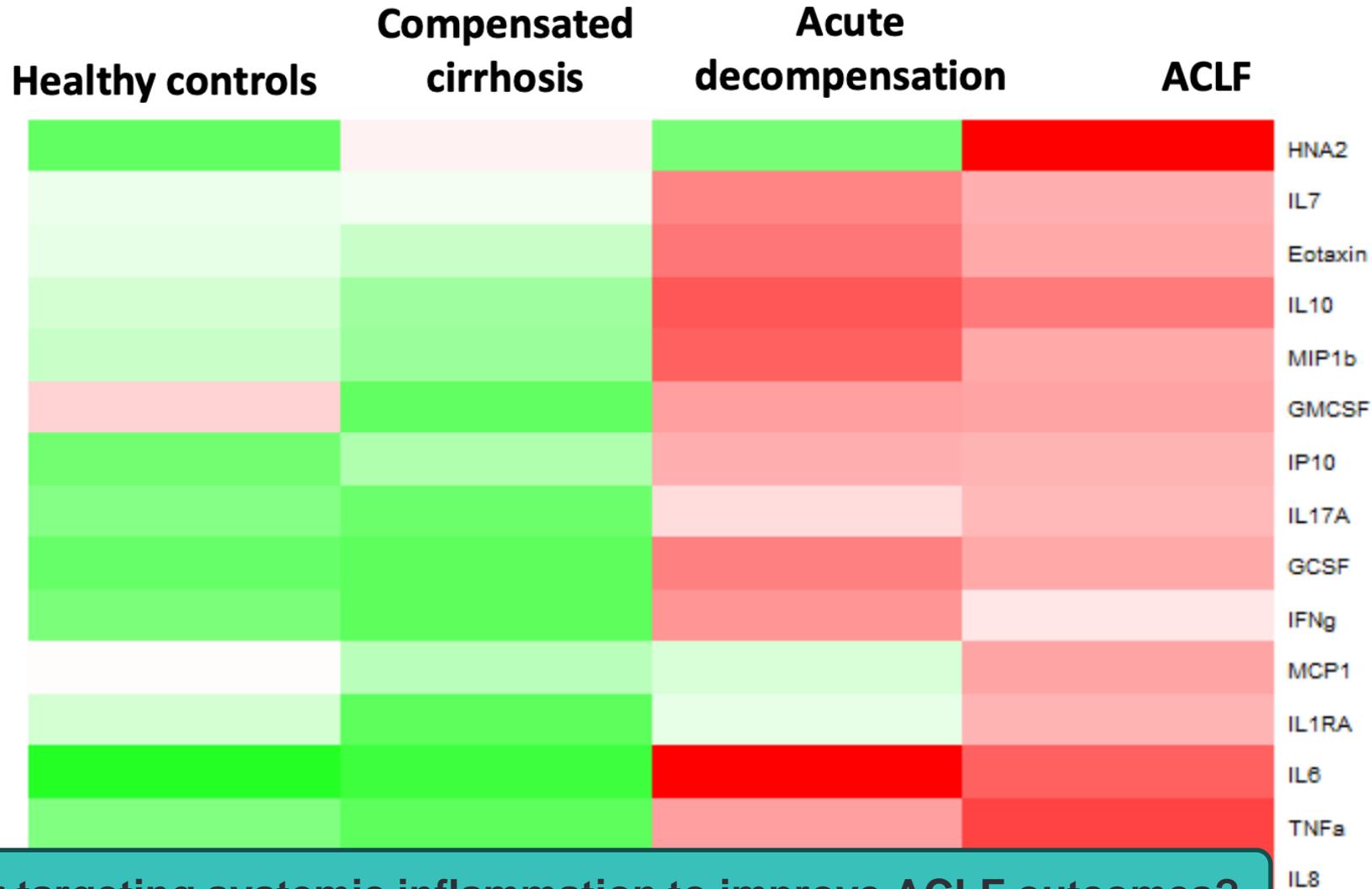
Acute on chronic systemic inflammation

Systemic inflammatory markers and risk of ACLF

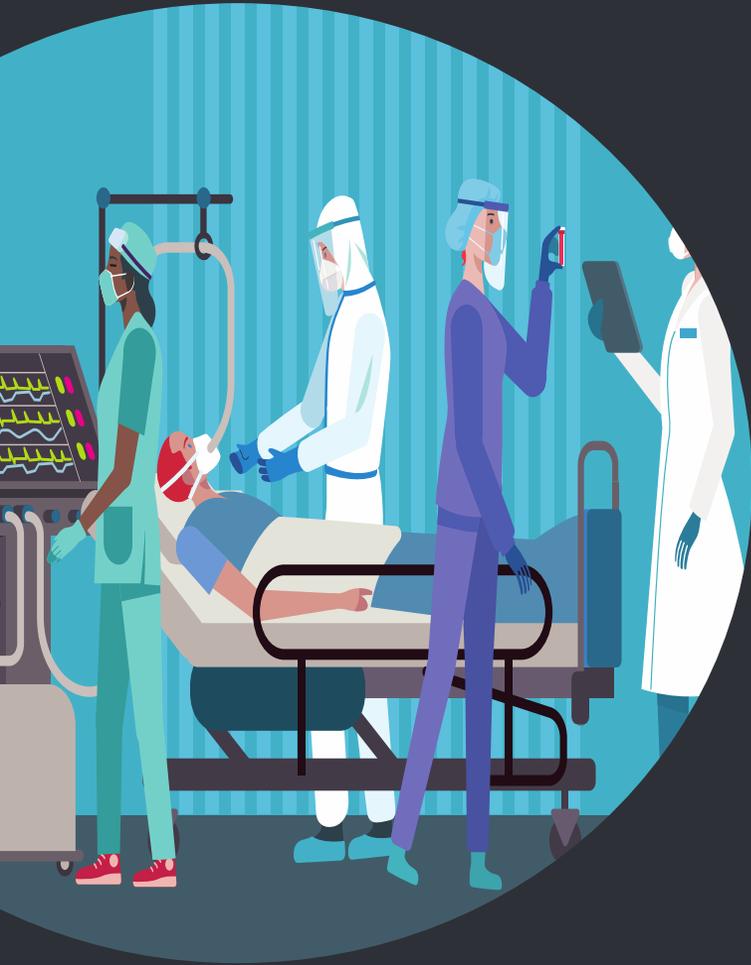
Escalating risk as systemic inflammatory markers increase



Systemic inflammatory markers are elevated



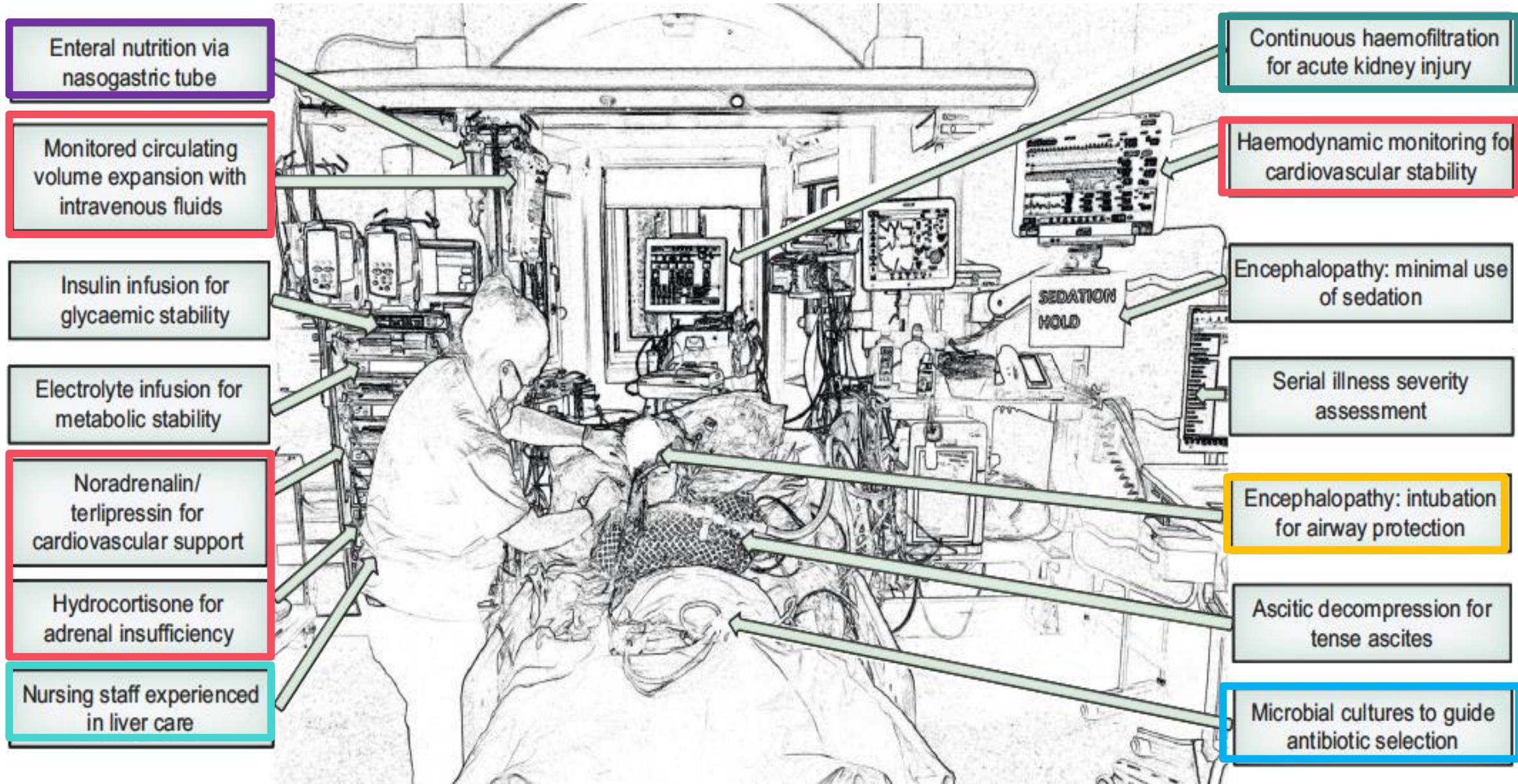
Is there a role for targeting systemic inflammation to improve ACLF outcomes?



AT THE BEDSIDE : Management

“

There is no direct therapeutic for ACLF.



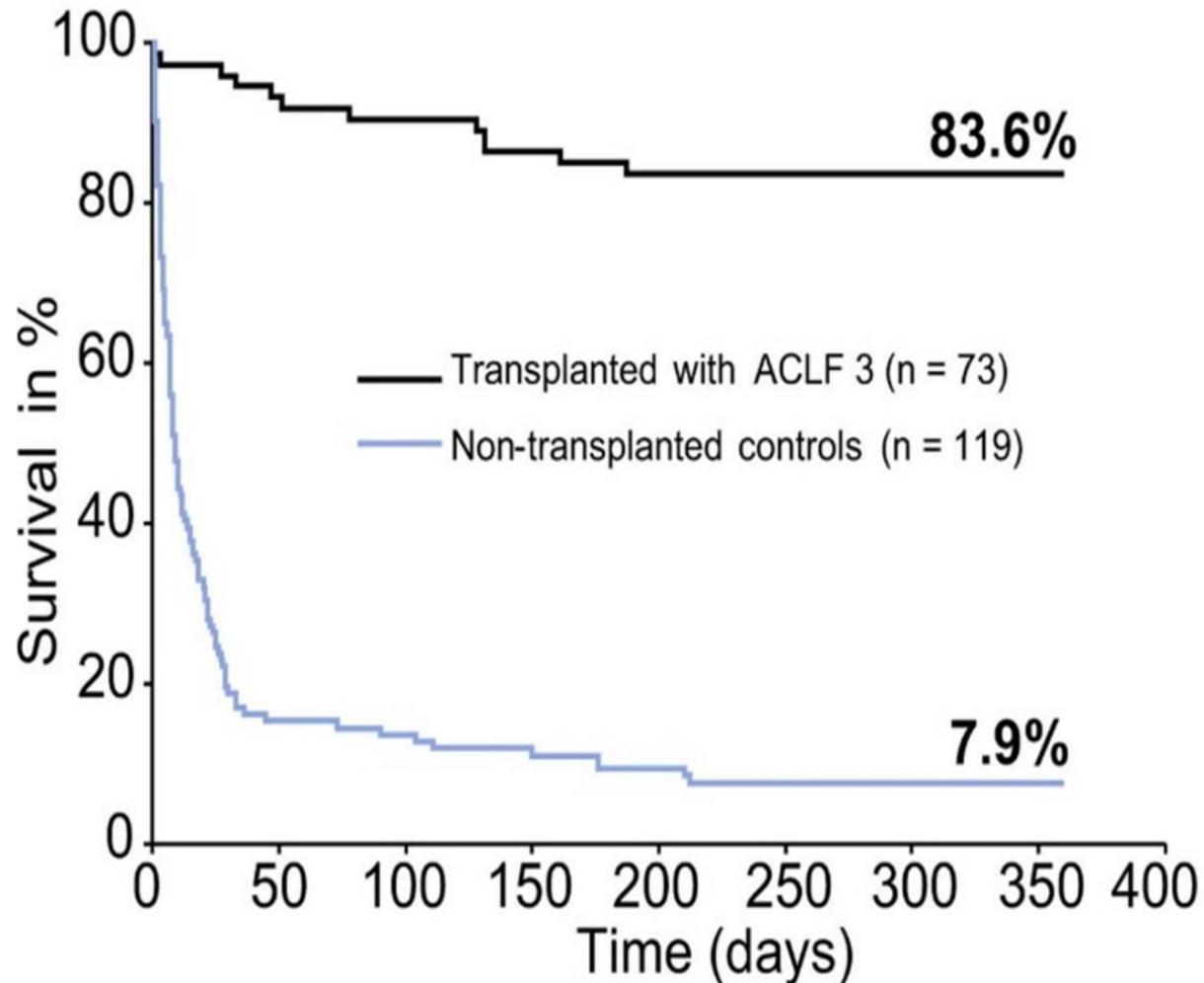
- GOAL OF TREATMENT : BUY TIME

Allow the
precipitant
to resolve

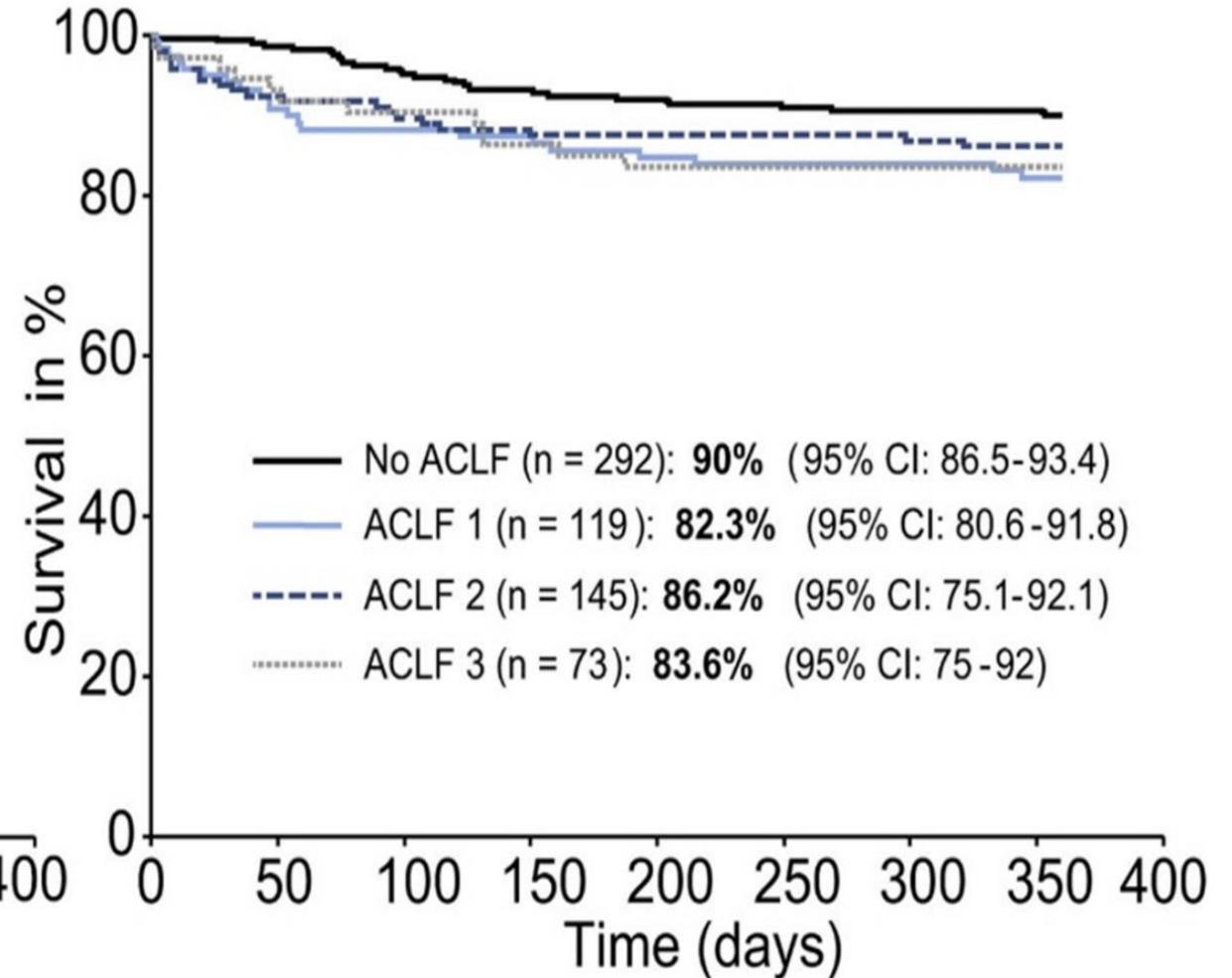
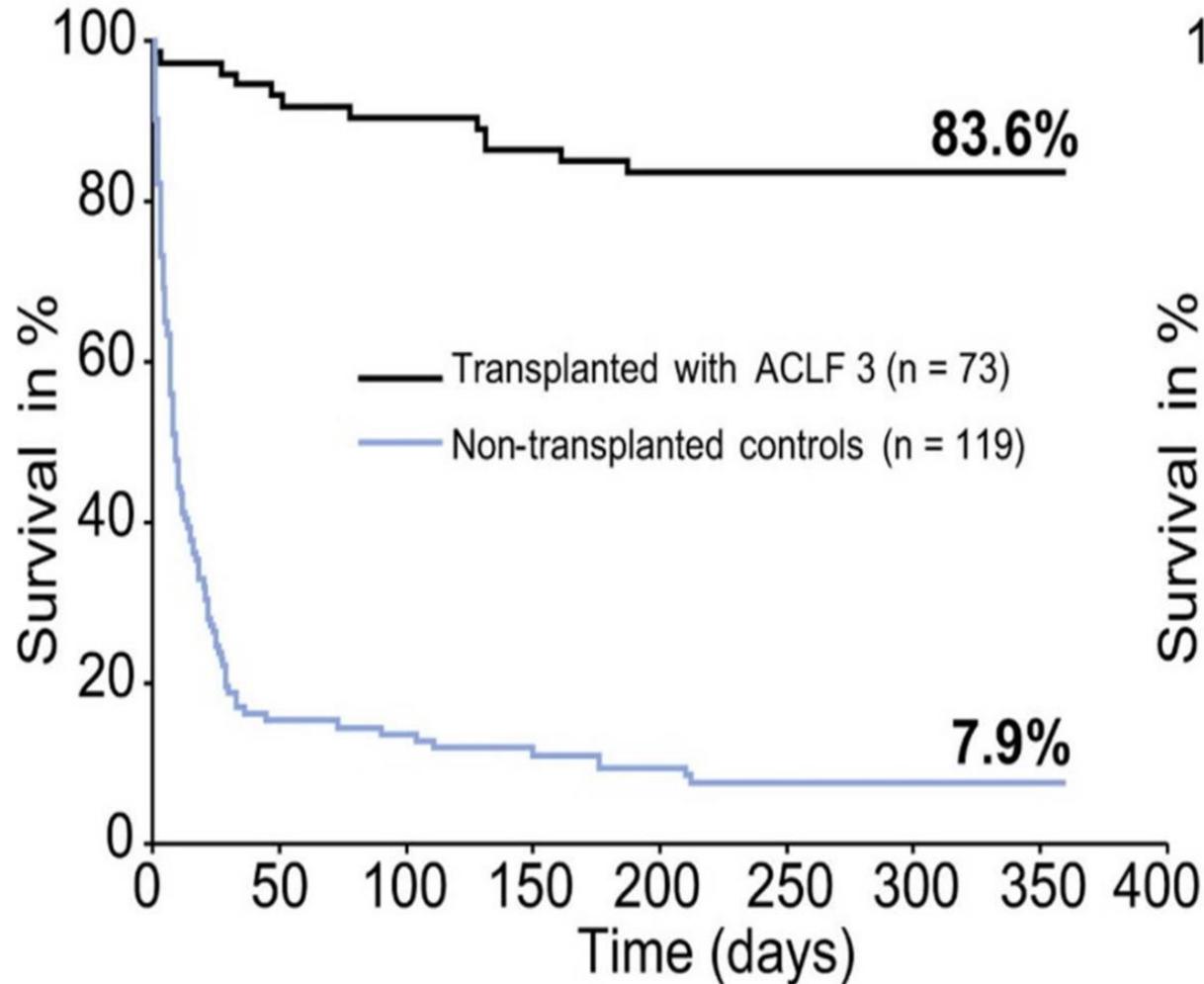
To allow
families to
say goodbye

To prepare
for liver
transplant

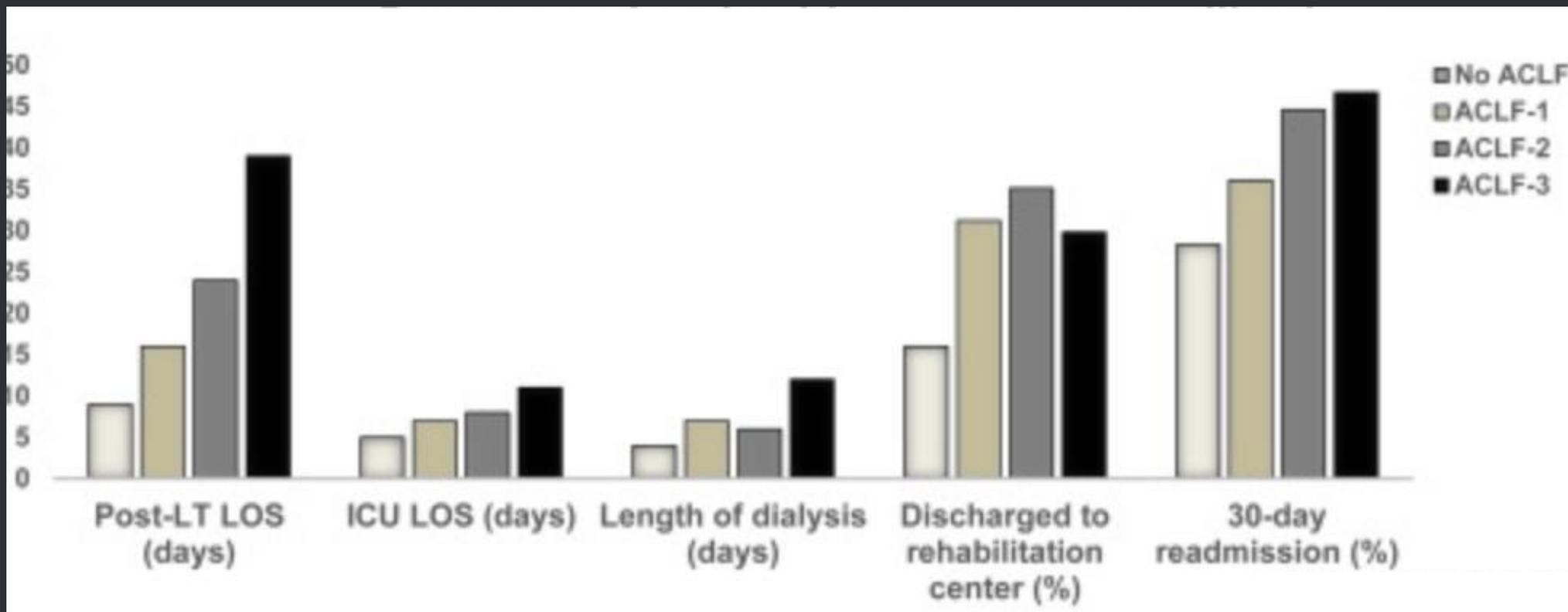
Survival is better with transplant than without



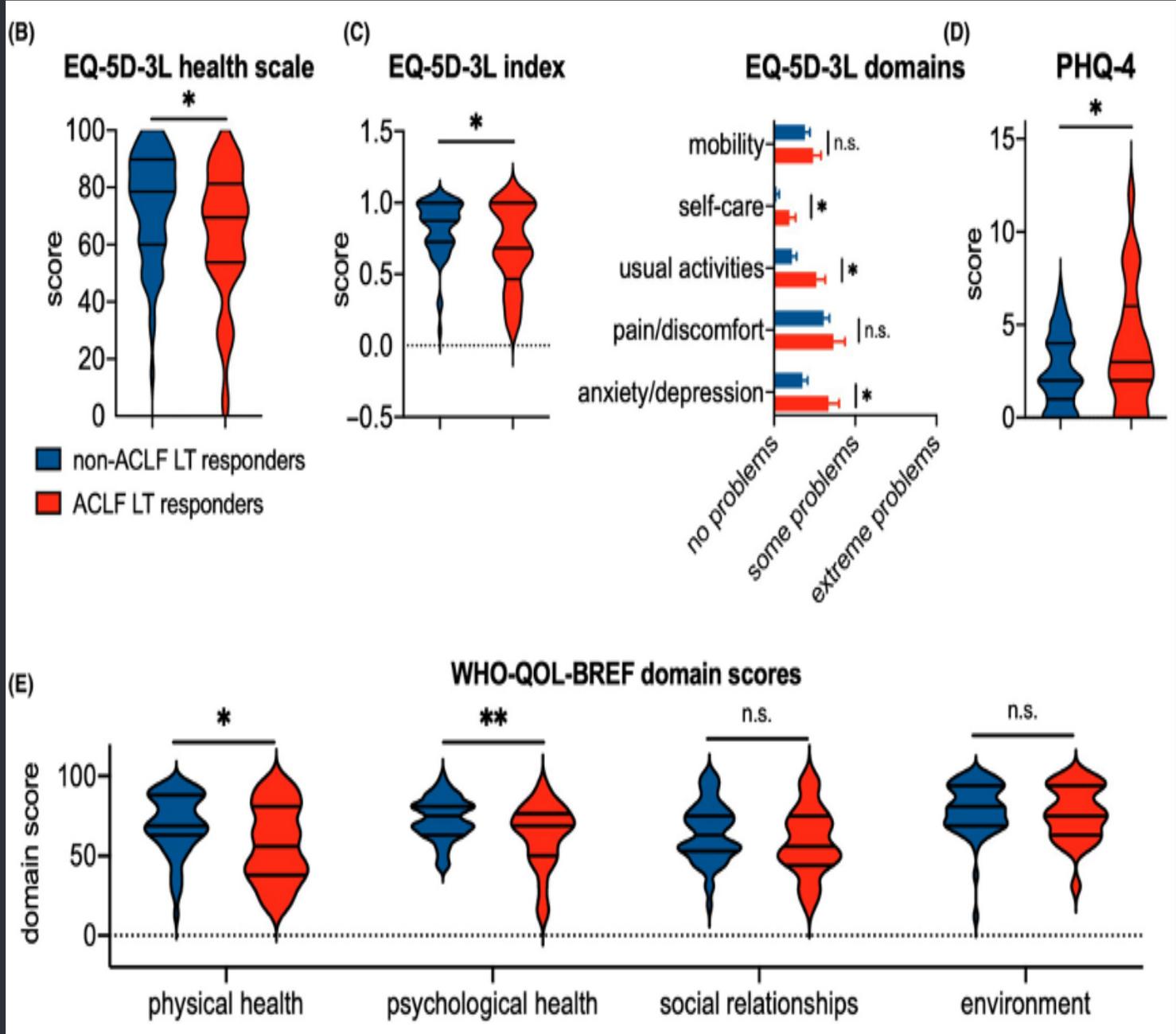
Transplant survival is acceptable in all ACLF grades



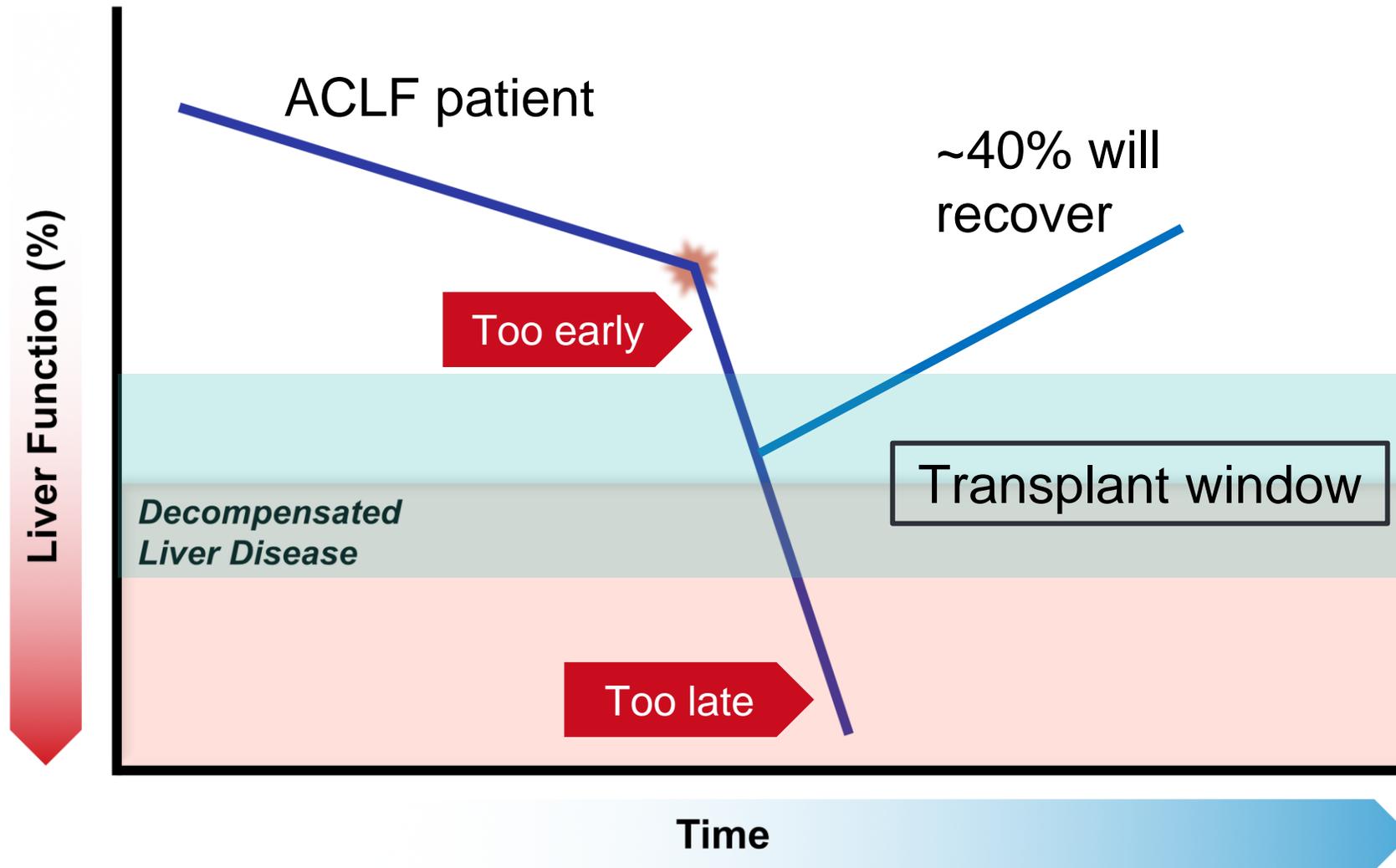
Post-transplant healthcare utilization increases by stage of ACLF



Post-LT
quality of life
is significantly
impaired



Narrow window for liver transplantation



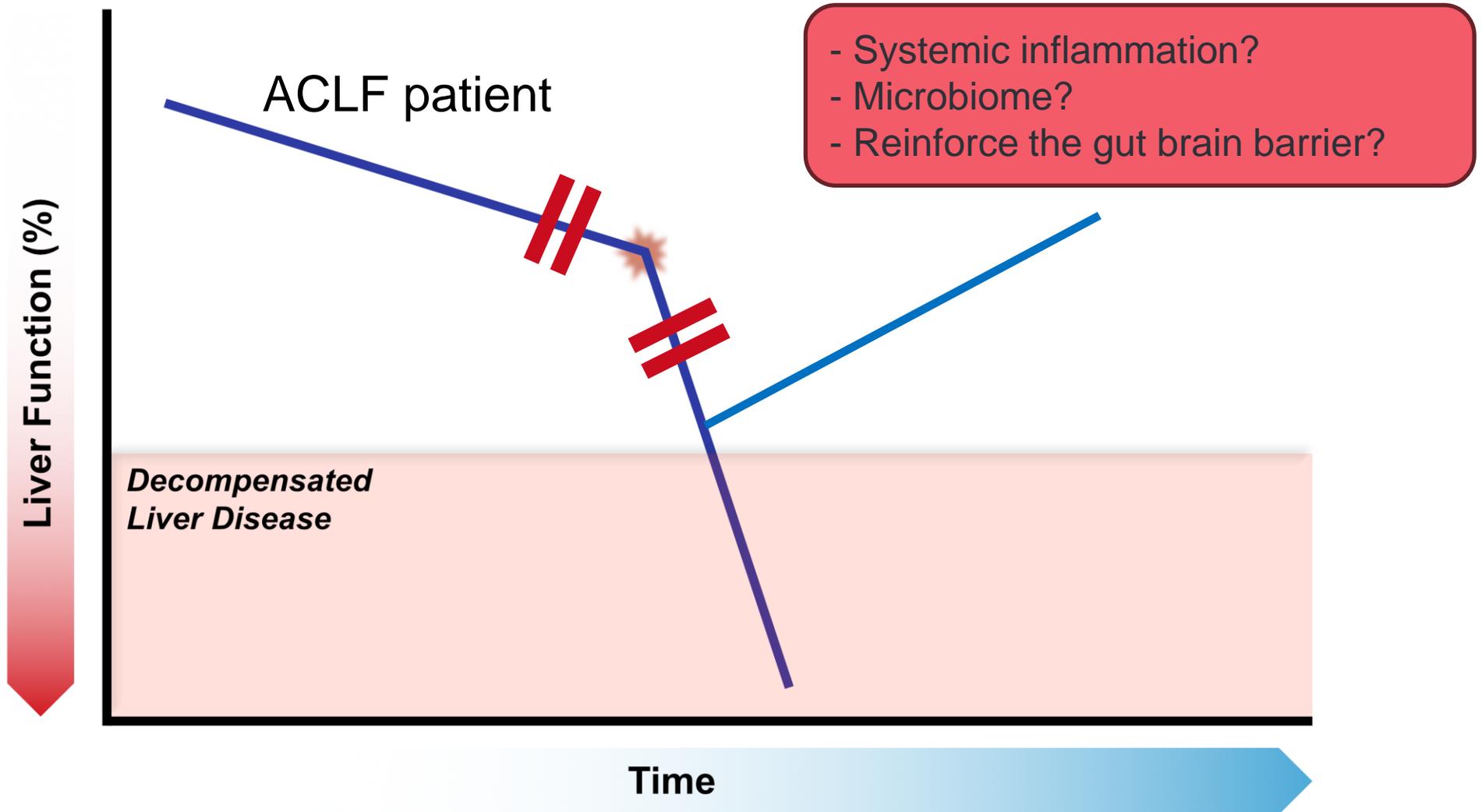
- ~4% of patients with cirrhosis are listed for liver transplant
- 1 in 4 patients listed for transplant die while waiting

Interventions other than liver transplantation :

Statements from the ACG ACLF guidelines

- Artificial liver support systems
“whether they provide any clinical benefit is unclear”
- Plasma exchange
“its effect in ACLF is unknown”
- Granulocyte colony stimulating factor
“we suggest against the use of G-CSF”
- Stem cell therapy
“evidence to support its use is currently insufficient”

The Opportunity





Key Points : ACLF (Disease state)

- ACLF is a highly lethal, resource-intensive condition that occurs in patients with chronic liver disease.
- Portal hypertension, altered microbiome, and systemic inflammation drive ACLF.
- There is no direct therapeutic for ACLF.
 - Liver transplantation, while effective, is limited due to narrow timing, low availability of organs, and poor access to high-level care.

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Questions & answers

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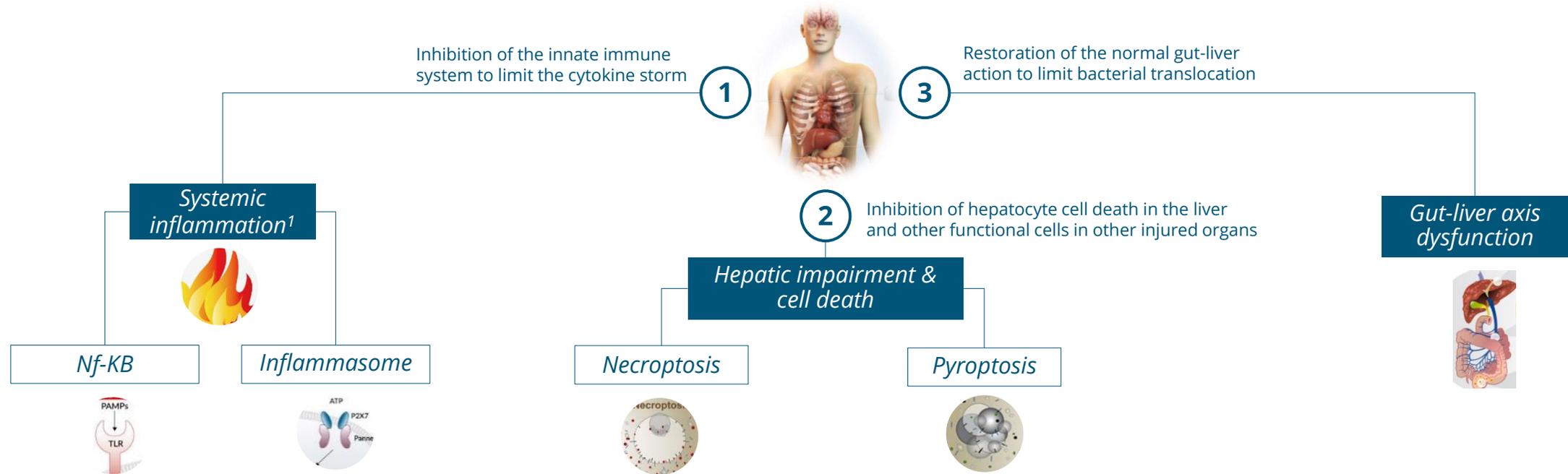
Q&A

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 shots** on goal
- 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

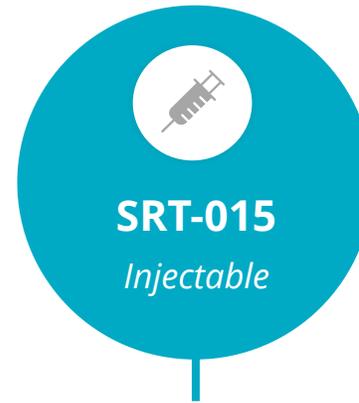
To drain out **ammonia** and **ACLF toxins** from the blood



Anti-inflammatory and anti-bacterial

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

[New formulation under development for dosing flexibility]



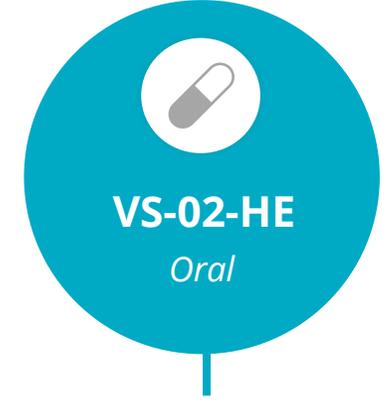
ASK1 inhibitor

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

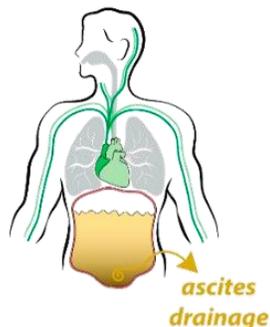
*Clinical Stage
Program in ACLF*



Extraction of Metabolites to Reduce Mortality

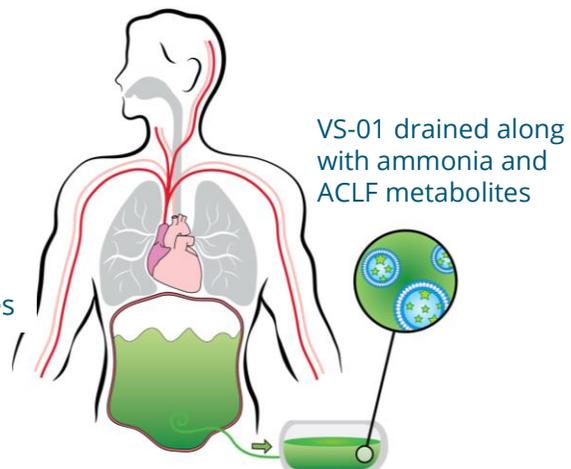
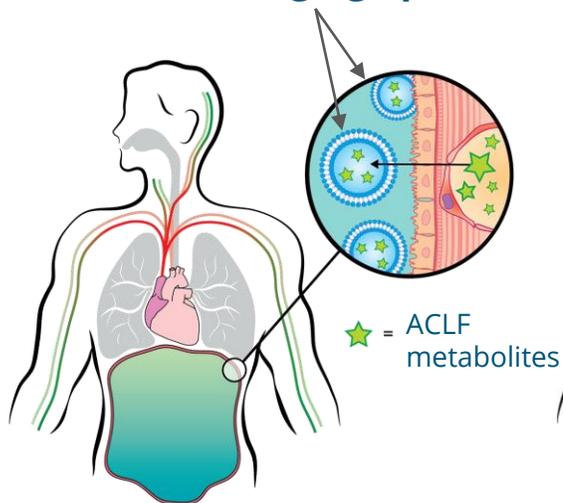
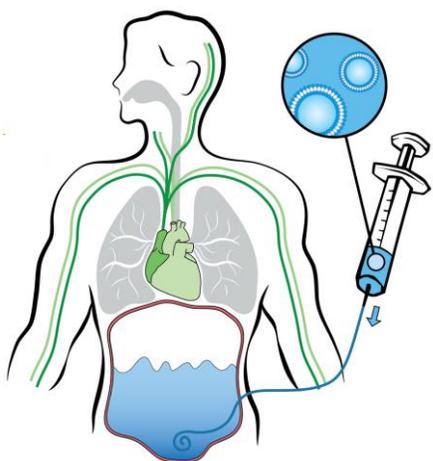
Standard of care

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**

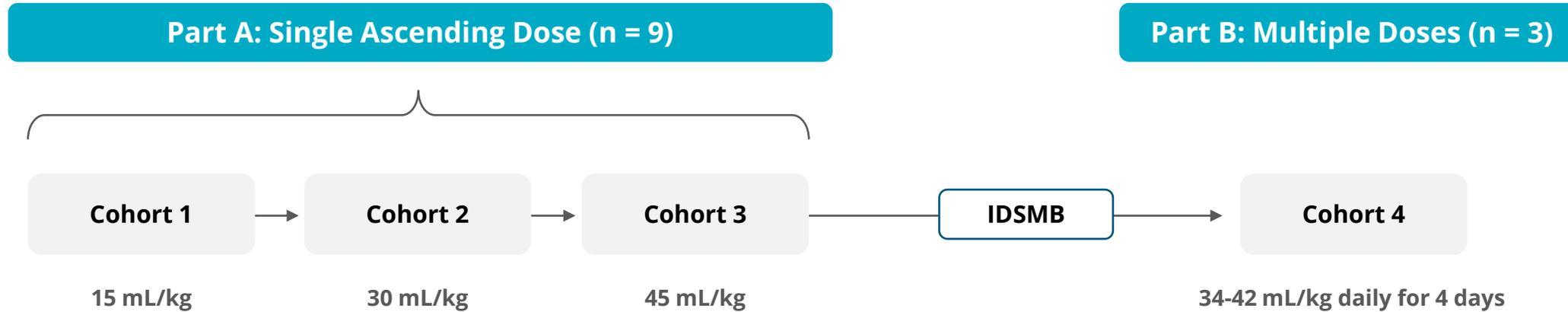


Targets **multiorgan support:** brain, liver, and kidney

— 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

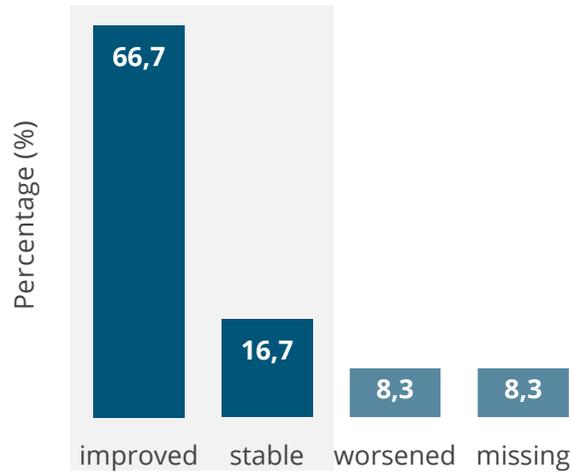
- ✓ Generally **safe** and **well tolerated**
- ✓ Promising **preliminary efficacy results**
- ✓ Confirmed **ease of *i.p.* administration**
- ✓ Data selected for **Clinical Hepatology Debrief** at AASLD 2021

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%**

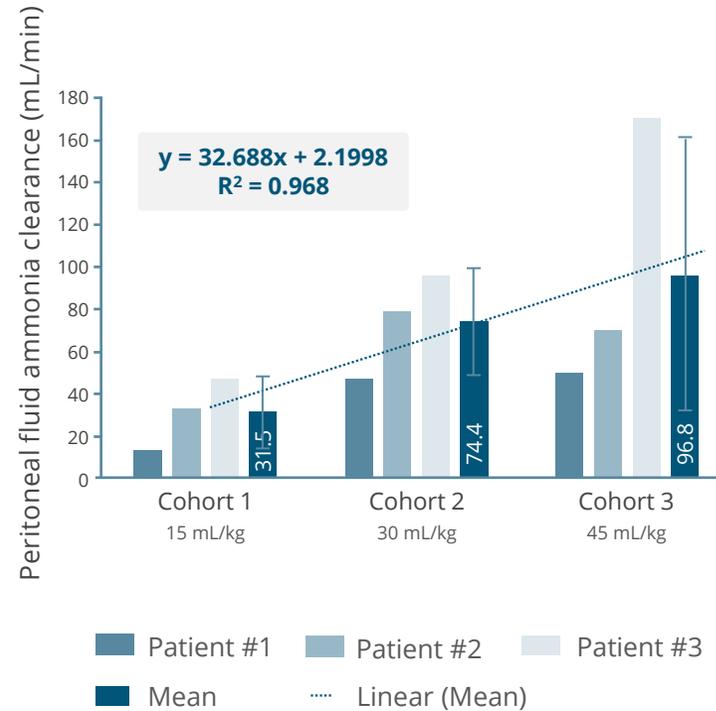


NO PATIENTS PROGRESSED TO ACLF



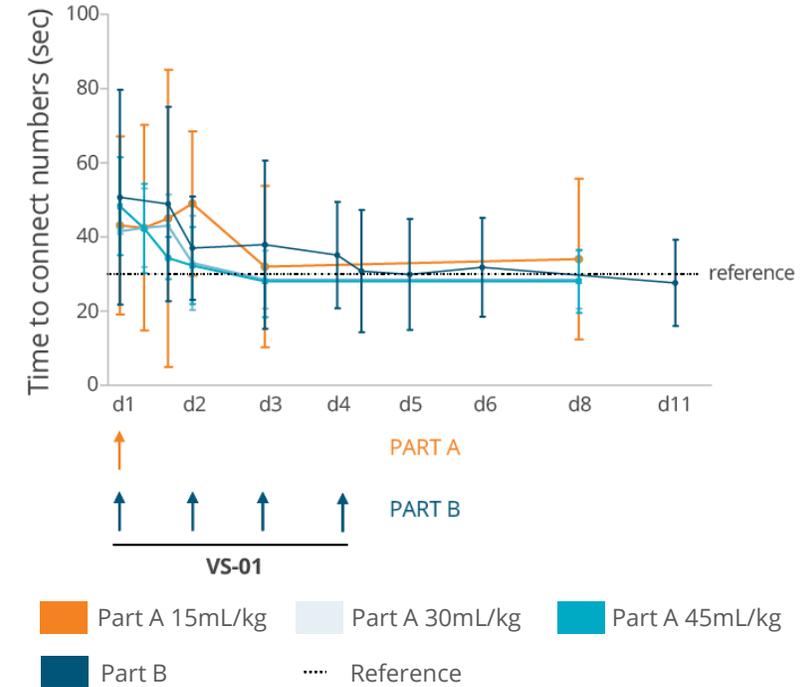
DOSE-DEPENDENT AMMONIA REMOVAL FROM THE BODY

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

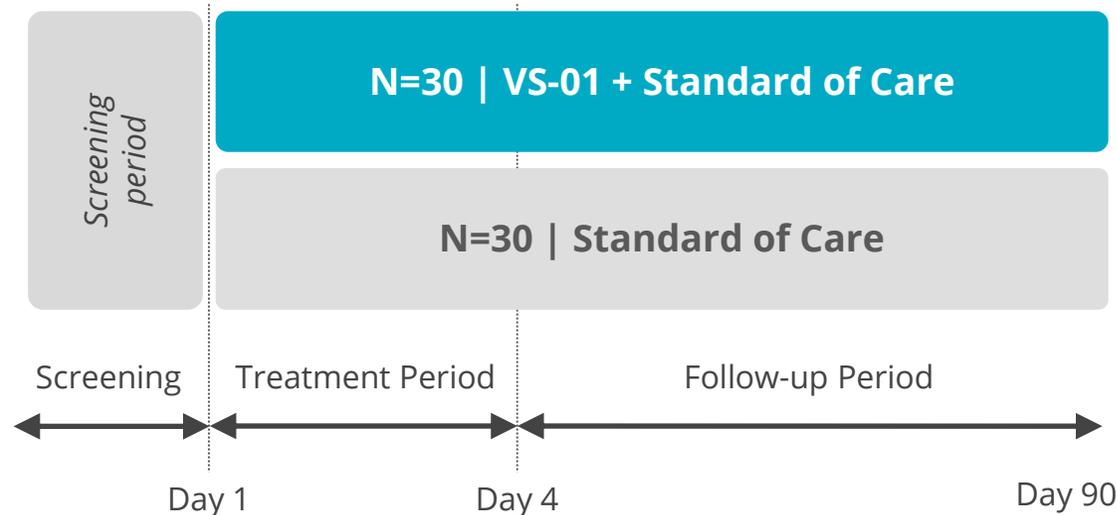
Adult patients with Acute-on-Chronic Liver Failure (ACLF) grade 1 and 2 and ascites

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

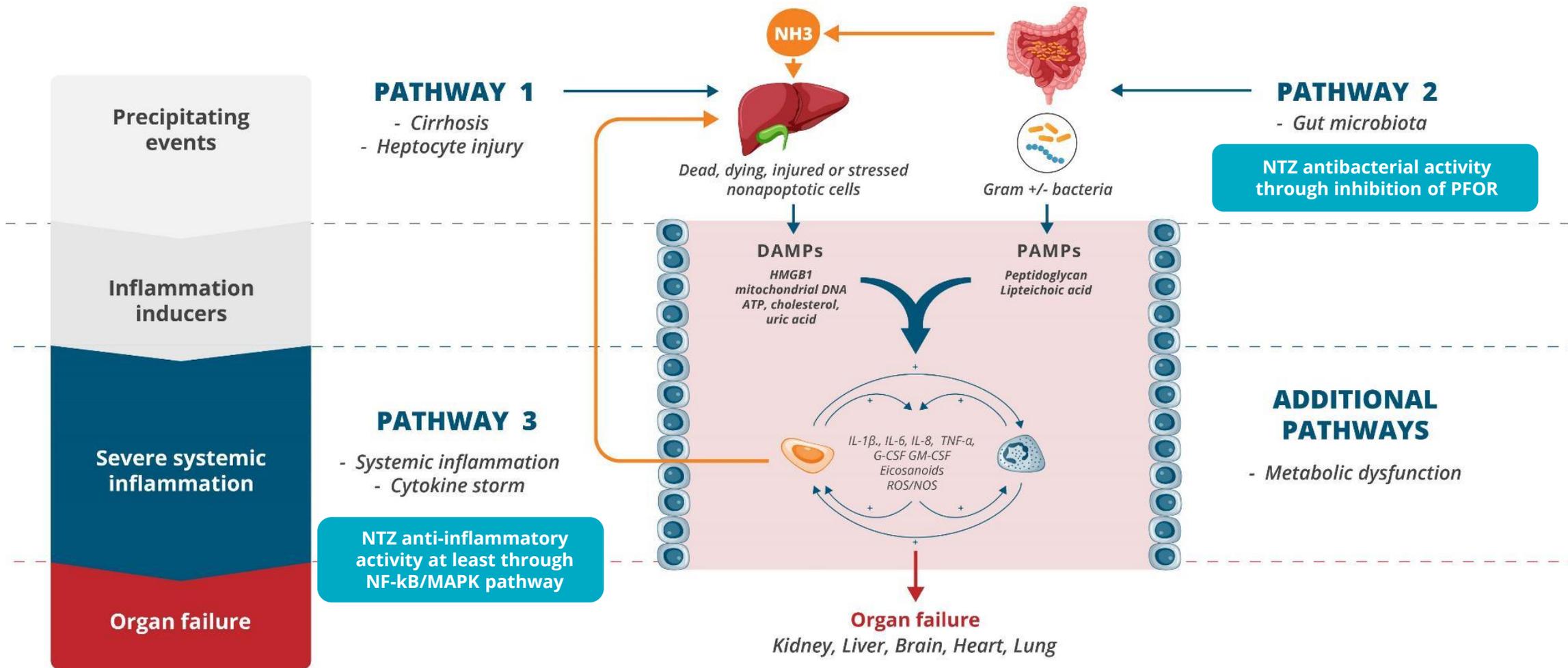
** www.efclif.com

NTZ

Clinical Stage Program in ACLF



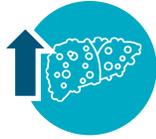
NTZ Impacts Multiple Pathways



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*



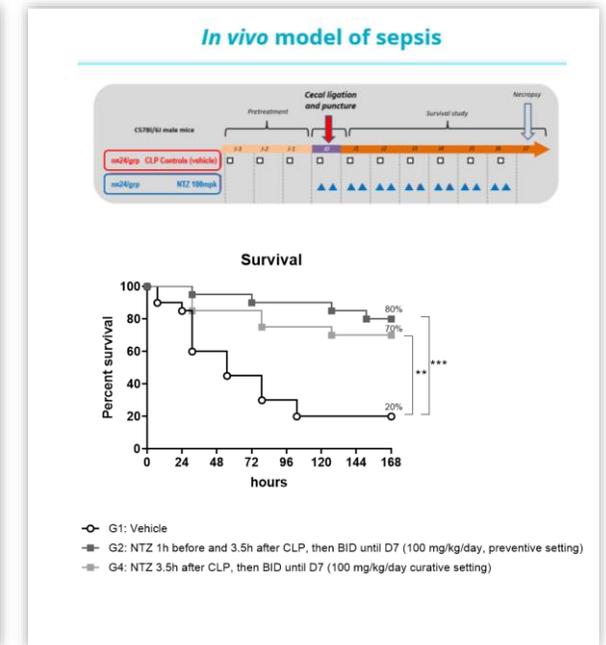
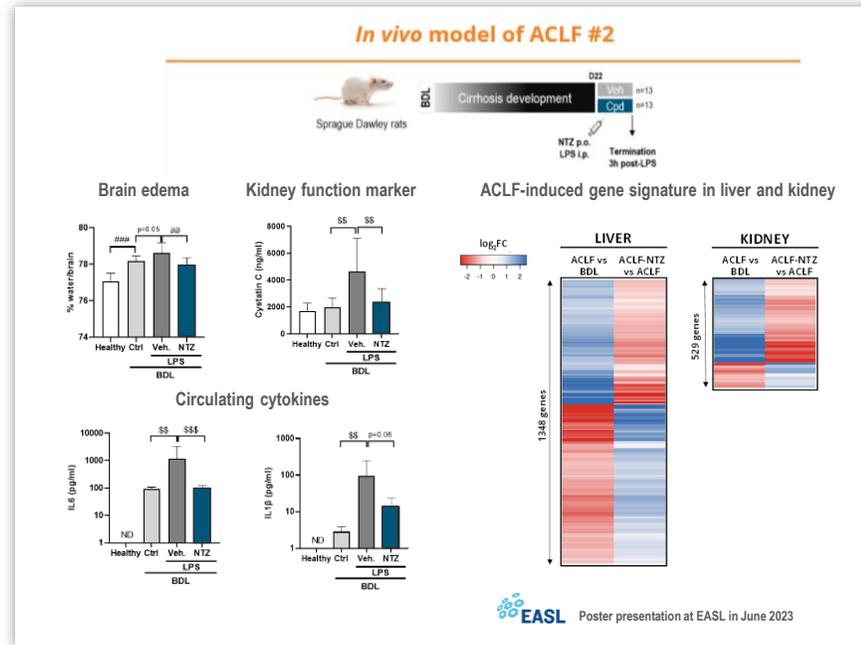
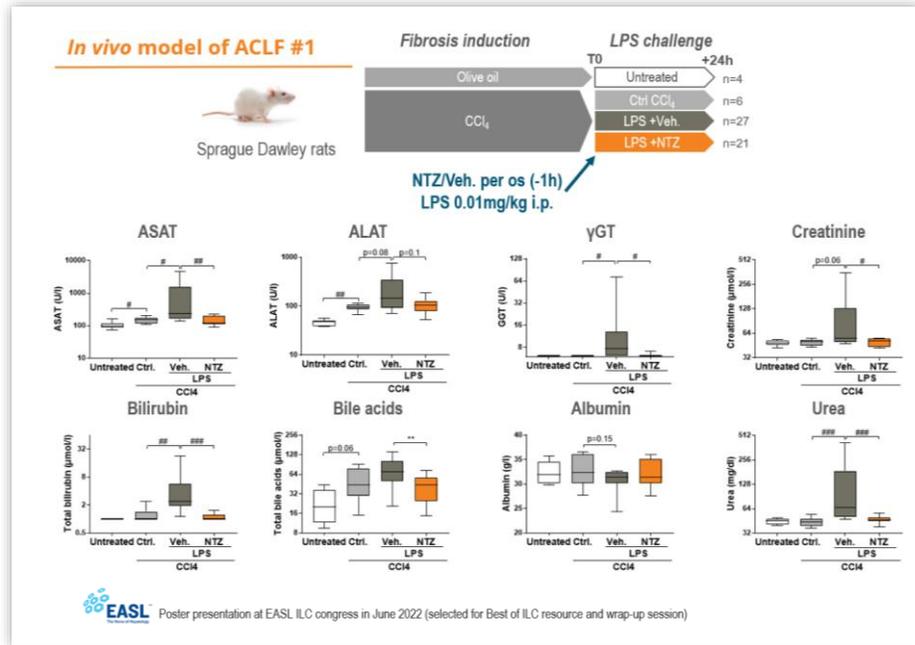
Alleviates liver and renal damages in a model of ACLF (CCL4+LPS)



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 indeed 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

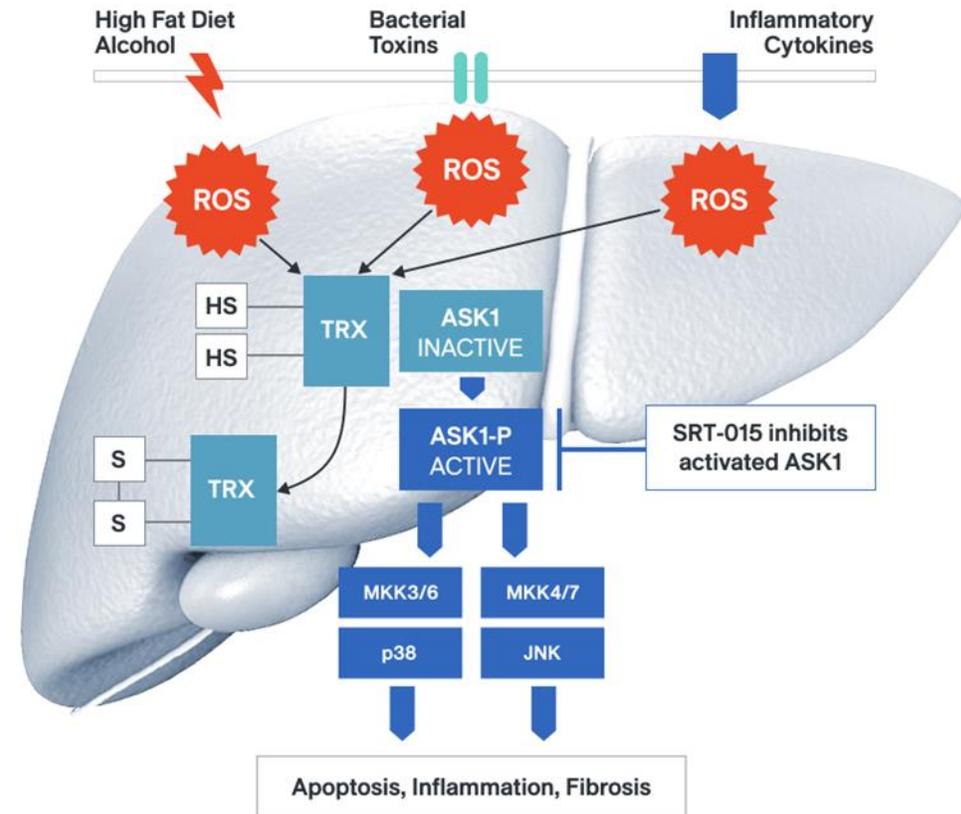


Targets inhibition of **cellular apoptosis, inflammation** and **fibrosis**

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**



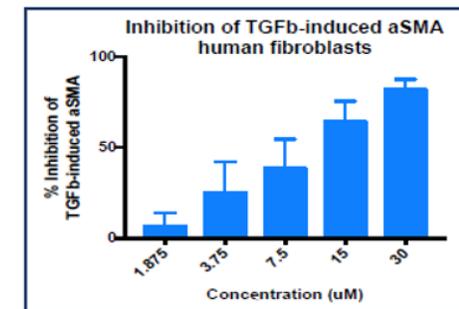
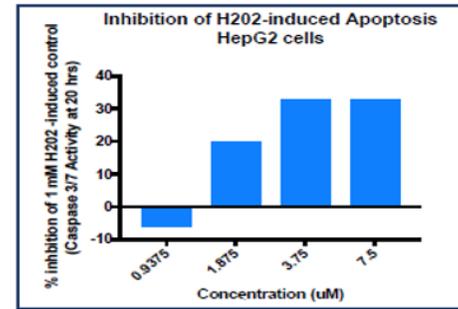
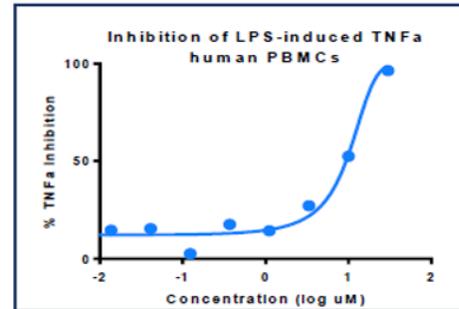
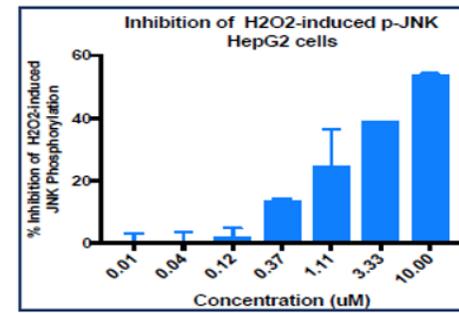
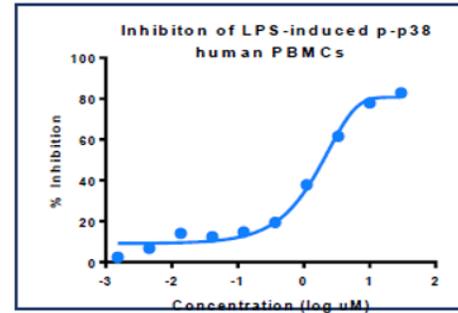
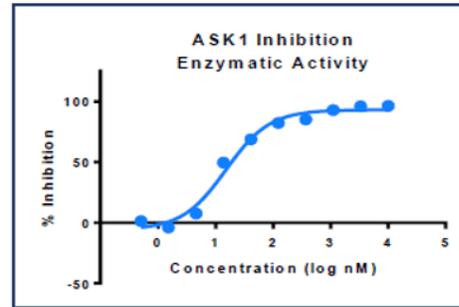
Target Engagement, MoA, Activity and Data Supporting Development in ACLF

Inhibits:

- Ask-1
- phosphorylation of p38
- phosphorylation of JNK

Activity:

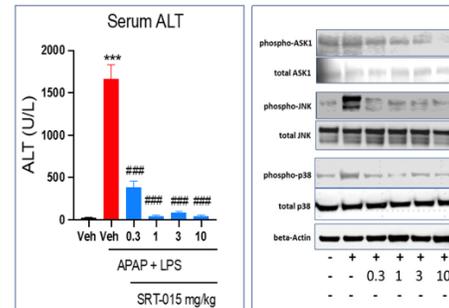
- Anti-inflammatory
- Anti-apoptotic
- Anti-fibrotic



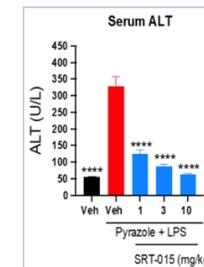
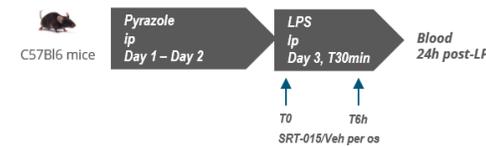
SRT-015 alleviates hepatic injury in a model of drug-induced liver injury, in association with reduction of phosphorylation of both JNK and ASK1

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**

=> ASK1 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 planned 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



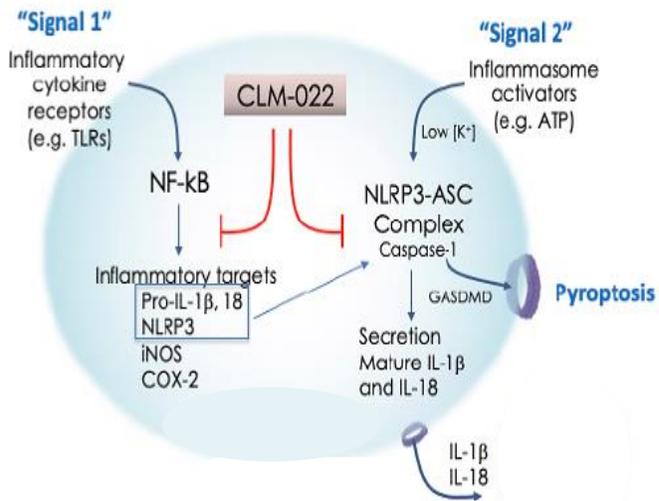
NLRP3
inflammasome
inhibitor

Preclinical

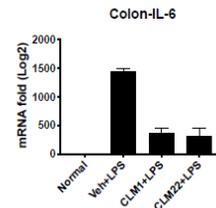
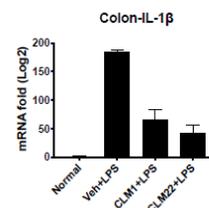
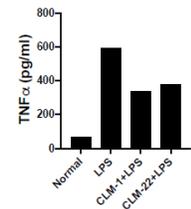
- Blocks NLRP3 inflammasome activated by ATP and Nigericin
- Blocks the endotoxin-induced production of inflammatory cytokines in an LPS sepsis model
- Blocks ASC speck formation at nanomolar concentrations
- Decreases IL-1 β secretion by macrophages stimulated with LPS and nigericin
- Protects against 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

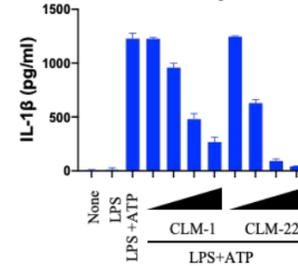
CLM-022: Dual Mode of Action



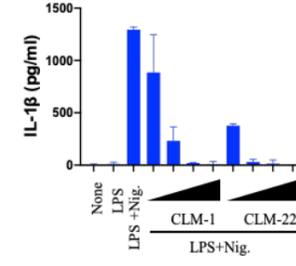
Serum TNF α levels



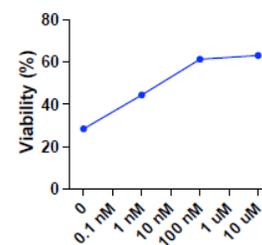
NLRP3 inflammasome activated by ATP



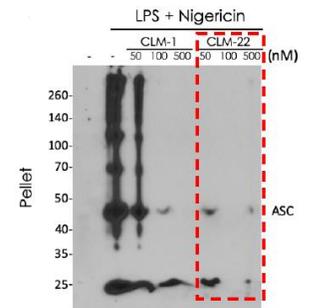
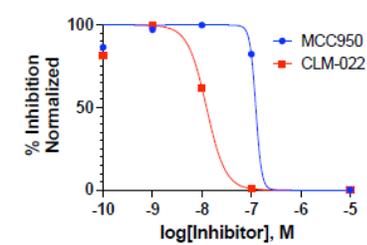
NLRP3 inflammasome activated by Nigericin



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



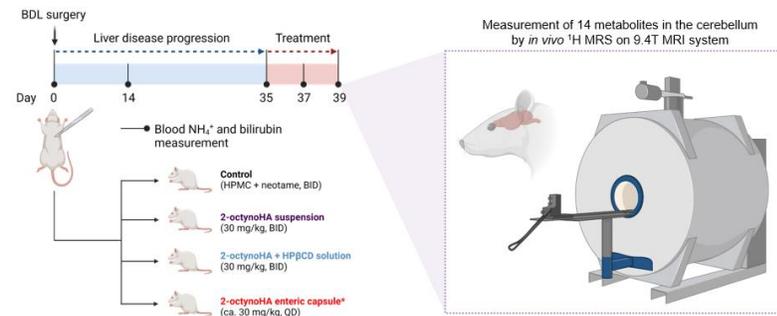
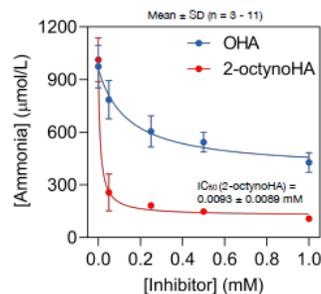
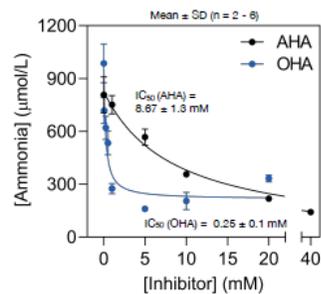
Urease inhibitor

Preclinical data

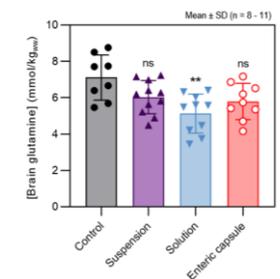
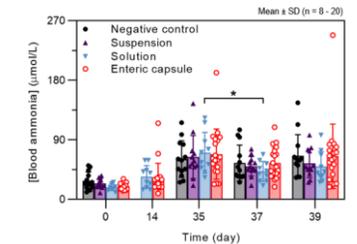
- Superior urease inhibitory activity in vitro
- Cytotoxicity and mutagenicity assessment (Ames test)
- Reduces plasmatic ammonia in a model of acute liver failure in rats
- Reduces plasmatic ammonia and brain glutamine in the bile duct-ligated model in rats

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)



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ACLF market opportunity

Robert Stolper & Pierre-Antoine André, IQVIA

Q&A

Highlights on newsflow

Pascal Prigent, CEO

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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



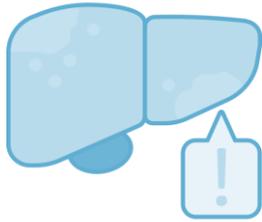
ACLF addressable market estimation



- 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

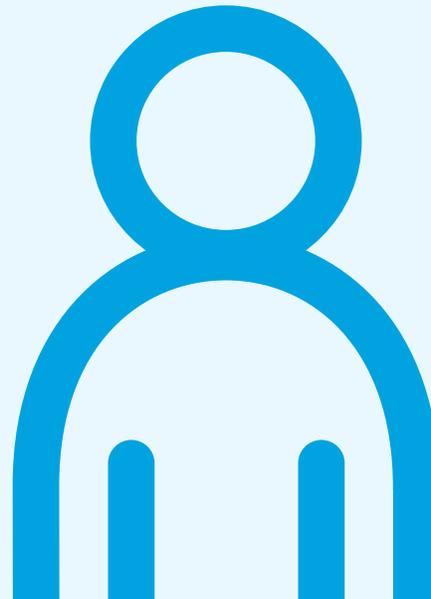
Life-threatening disease characterized by **acute decompensation** of chronic **liver** disease associated with multiple **organ failures** and high short-term mortality¹

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 \$

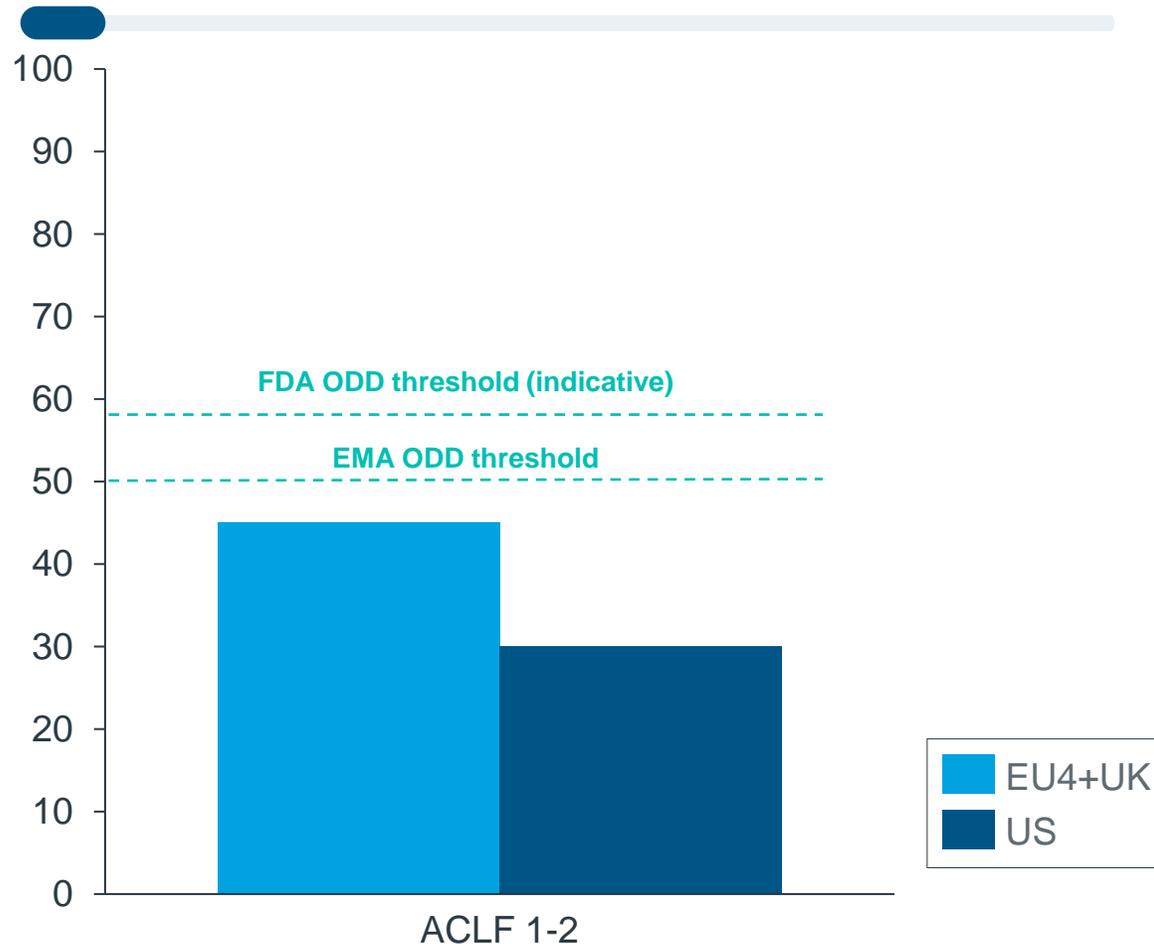
Estimated **annual cost burden** in US in 2021*
(a nearly 4-fold increase since 2011)*

*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

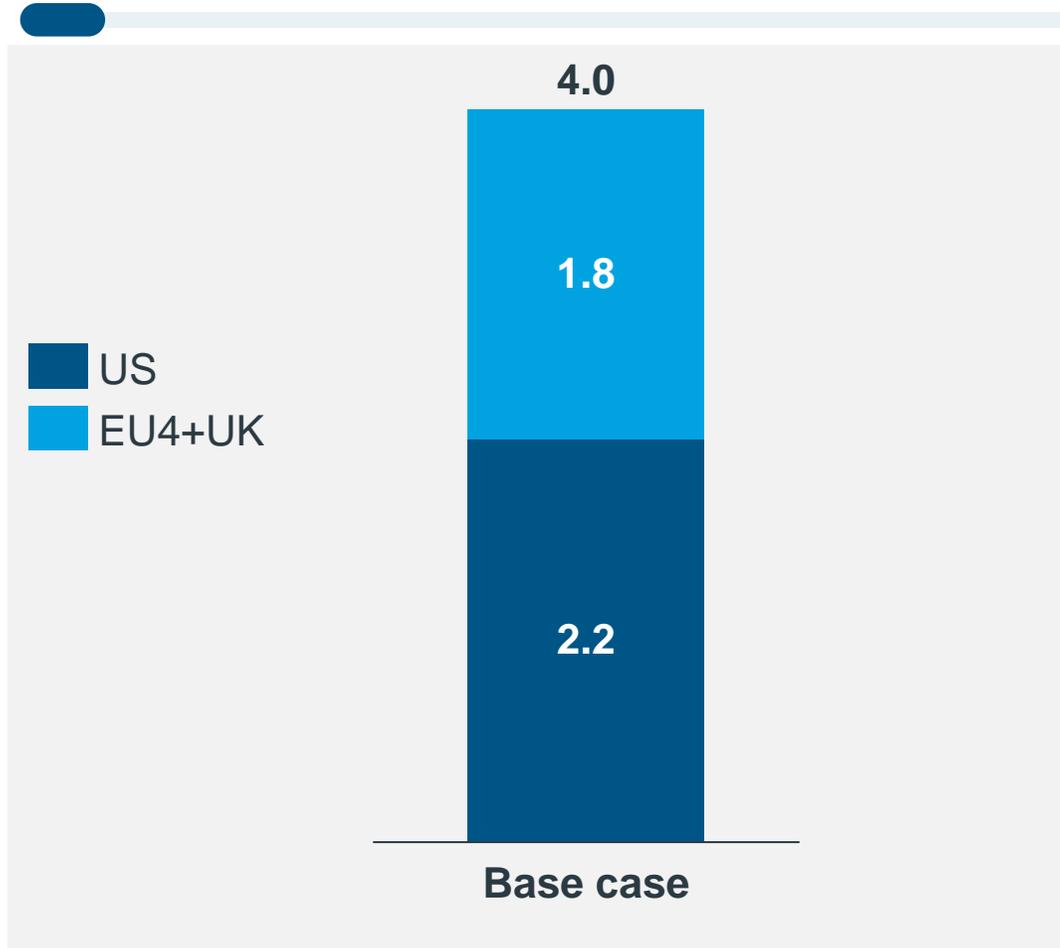
Analogues considered

- 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 (EU5) / 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 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

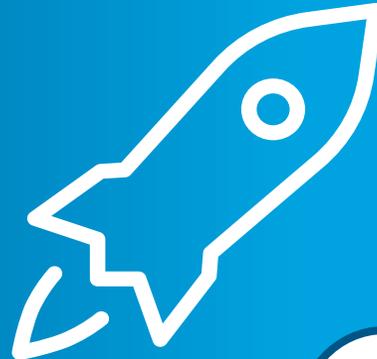
Assumptions / considerations

<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

Dr Jennifer Lai (UCSF), MD, MBA

Q&A

GENFIT's approach to ACLF

Dr. Carol Addy, CMO & Dean Hum, CSO

Q&A

ACLF market opportunity

R. Stolper & P-A André, IQVIA

Questions & answers

Highlights on newsflow

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ACLF market opportunity

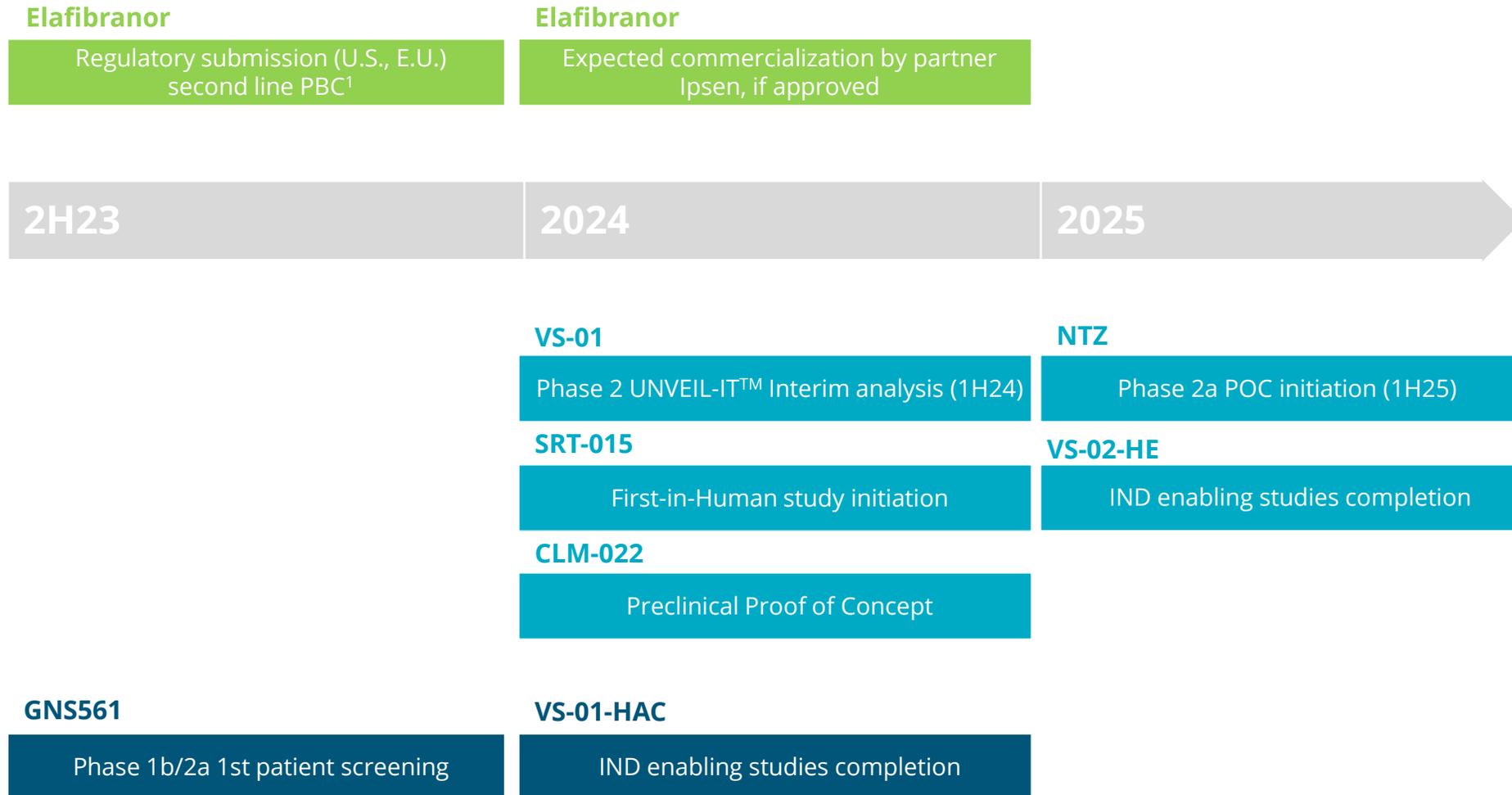
R. Stolper & P-A André, IQVIA

Q&A

Highlights on newsflow

Pascal Prigent, CEO

Highlights on newsflow



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

1: https://www.ipsen.com/websites/ipsen_com_v2/wp-content/uploads/2023/08/11114914/ipsen-investor-presentation-September-2023.pdf

THANK YOU

Corporate
Presentation