Corporate Presentation

November 2026

GENFIT
TOWARDS BETTER MEDICINE

Certified
B
Corporation

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This presentation contains certain forward-looking statements with respect to GENFIT, including, but not limited to, statements regarding the Company's cash runway, revenue growth, spending and path to profitability; potential royalties, milestone payments and additional royalty financing; the development, regulatory prospects and commercial potential of elafibranor; the development, reimbursement, adoption and commercialization of products based on NIS™ Technology, related market projections and GENFIT's revenue potential; and the advancement of its R&D programs, including anticipated clinical trial initiation and data readout timelines. The use of certain words, such as "believe", "potential", "expect", "target", "may", "will", "should", "could", "if" and similar expressions, is intended to identify forward-looking statements. Although the Company believes its expectations are based on the current expectations and reasonable assumptions of the Company's management, these forward-looking statements are subject to numerous known and unknown risks and uncertainties, which could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking statements. These risks and uncertainties include, among others, the uncertainties inherent in the Company's ability to advance its therapeutic programs and initiate and complete clinical trials; uncertainties relating to regulatory requirements and decisions, patient enrollment, clinical trial execution, safety findings, manufacturing and clinical supply; the possibility that findings from prior studies in other indications, preclinical research or ex vivo assays may not predict safety, efficacy or clinical benefit in patients with ACLF; uncertainties relating to the clinical utility, further validation, adoption and use of non-invasive MASH diagnostics, including for disease or treatment- response monitoring; changes in clinical practice, treatment uptake, reimbursement, access and applicable regulatory requirements; and the Company's dependence on partners and other third parties whose plans and activities may change. Those risks and uncertainties also include those discussed or identified in the Company's public filings with the AMF, including those listed in Chapter 2 "Risk Factors and Internal Control" of the Company's 2025 Universal Registration Document filed on April 3, 2026 (no. 26-0221) with the Autorité des marchés financiers ("AMF"), which is available on GENFIT's website (www.genfit.fr) and the AMF's website (www.amf.org), and those discussed in reports filed with the AMF or otherwise made public, by the Company, including the Half-Year 2026 Business and Financial Report. In addition, even if the results, performance, financial position and liquidity of the Company and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. These forward-looking statements speak only as of the date of publication of this press release. Other than as required by applicable law, the Company does not undertake any obligation to update or revise any forward-looking information or statements, whether as a result of new information, future events or otherwise. Links to third-party websites and materials, in particular those of Ipsen, are provided for convenience only. GENFIT is not responsible for the content of such materials and does not endorse or adopt any forward-looking statements contained therein.

Corporate Highlights

Two emerging revenue streams

Elafibranor

Partnership with Ipsen

- Covers all indications
- Iqirvo® launched in PBC in 2024[1,2]
- Upfront of €120M
- 8% equity stake
- Up to €360M milestones (potential €254.5M remaining[3,4])
- Tiered double-digit royalties of up to 20%
- Ipsen's peak sales estimates doubled from €500 to €1bn[5]

Royalty deal with HCRx

- Capped
- €160M received[3]
- Milestones excluded from the deal

MASH Diagnostics

NIS™ non-invasive diagnostic technology

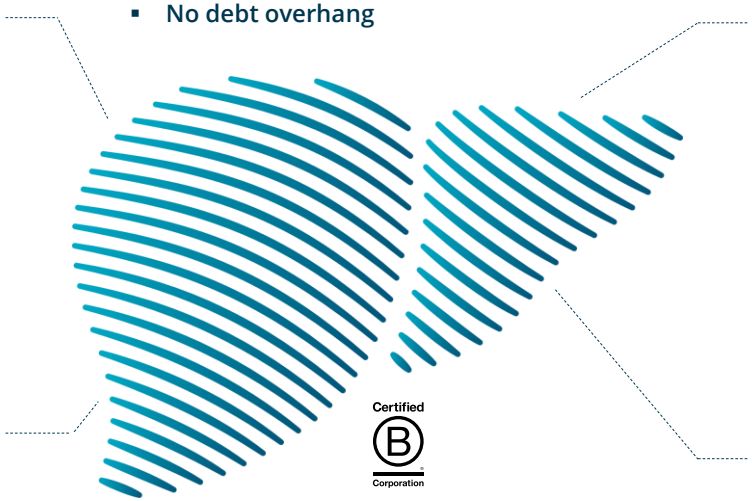
- NIS4® available in the U.S. through Labcorp NASHnext®[8]
- Next generation NIS2® recognized by independent consortia
- IVD launch for deployment at scale target in 2028

ABOUT GENFIT

- French biopharmaceutical company
- Euronext listed under "GNFT"
- 25+ years in liver diseases
- Focus on rare, severe liver diseases with high unmet medical need

FINANCIAL HIGHLIGHTS

- Cash position: €95.6M (3Q26)[6]
- Cash runway beyond 2028[7]
- Next financial update: end of February 2027
- No debt overhang



Several potential catalysts

Clinical Optionality

Phase 2 evaluating GNS561 in CCA

- Trial initiation: 4Q26
- Data expected 2H27

Phase 2 evaluating nangibotide in ACLF

- UPWARD trial inititation: 4Q26
- Data expected 2H27

Phase 2 evaluating nitazoxanide in ACLF

- Trial initiation: 4Q26
- Data expected mid-2027

Phase 3 evaluating elafibranor in PSC

- Led by partner Ipsen under the 2021 licensing agreement
- Data expected in 2031
- Additional financial benefits for GENFIT upon successful development and regulatory approval in this indication

Research Programs

Covering both ACLF and Oncology

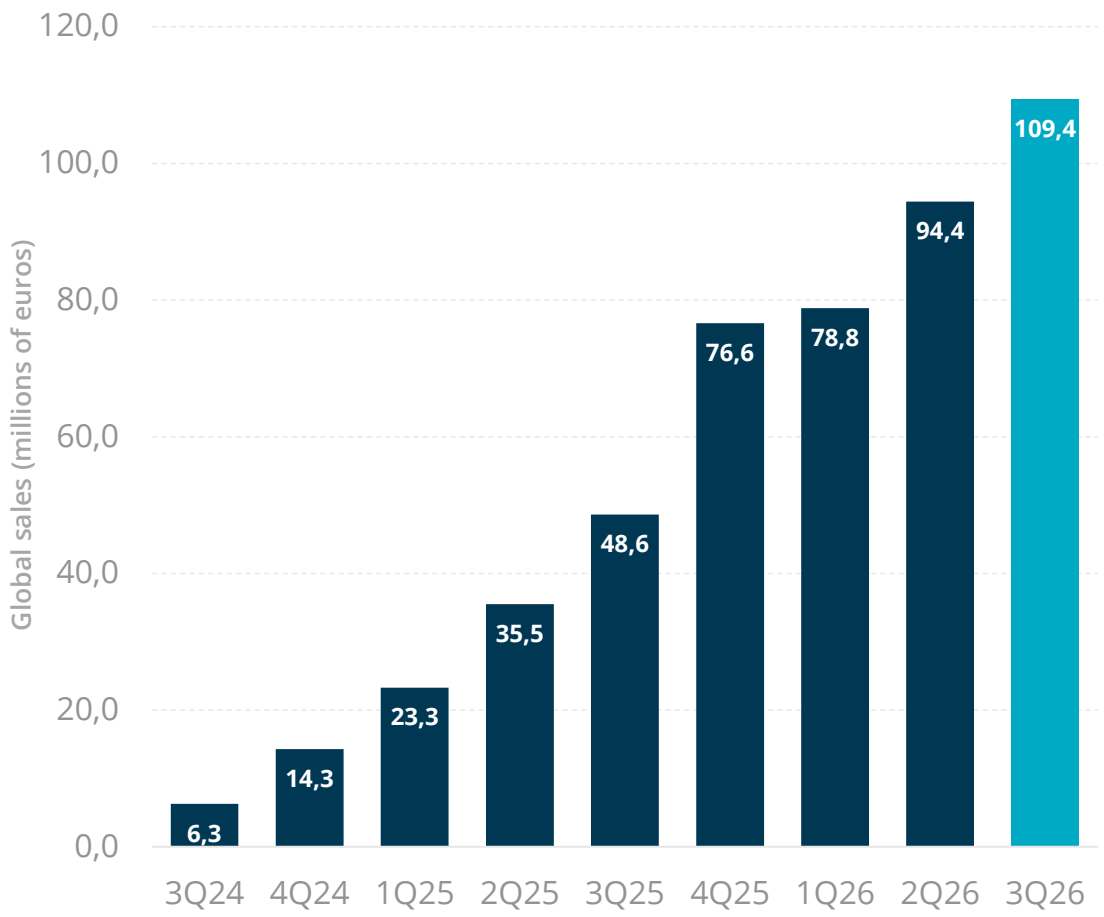
- Details to be provided as assets progress to clinical stage

PBC: Primary Biliary Cholangitis | CCA: Cholangiocarcinoma | ACLF: Acute-on-Chronic Liver Failure | PSC: Primary Sclerosing Cholangitis • 1. In-house from discovery to interim Phase 3 data readout, today commercialized by IPSEN - Approved in major markets including the US, Europe, and UK - PR - Ipsen and GENFIT enter into exclusive licensing agreement for elafibranor, a Phase III asset evaluated in Primary Biliary Cholangitis, as part of a long-term global partnership | 2. PR - January 2025,30 - GENFIT Announces Non-Dilutive Royalty Financing Agreement and Debt Overhang Resolution Plan | PR- GENFIT Reports First Quarter 2025 Financial Information | PR - GENFIT to receive a €26.5 million milestone payment following the approval of pricing and reimbursement of Ipsen's Iqirvo® in Italy | 3. PR - GENFIT to receive US$20M milestone after Ipsen's Iqirvo® exceeds the US$200M threshold in its first full year of net sales | 4. GENFIT Reports Full-Year 2025 Financial Results and Provides Corporate Update - This estimation is based on current assumptions and programs and does not include exceptional events. This estimation assumes (i) our expectation to receive significant future commercial milestone revenue pursuant to the license agreement with Ipsen and Ipsen meeting its sales-based thresholds and (ii) drawing down all additional installments under the Royalty Financing agreement with HCRx | 5. Source: Ipsen H1 2026 Results Presentation, July 2026. Information reported by Ipsen. GENFIT has not independently verified such information. Any forecasts, projections, expectations or other forward-looking statements referenced herein are those of Ipsen and do not constitute forecasts or expectations of GENFIT | 6. GENFIT Reports Third Quarter 2026 Financial Information and Provides Corporate Update | 7. This is based on current assumptions and programs and does not include exceptional events. This estimation assumes (i) our expectation to receive significant future commercial milestone revenue pursuant to the Ipsen Agreement and Ipsen meeting its sales-based thresholds and (ii) drawing down the third and final, optional installment under the Royalty Financing agreement | 8. GENFIT Announces U.S. Medicare Coverage and Future Reimbursement for NASHnext®, a Non-Invasive Diagnostic Technology to Identify Patients with At-Risk MASH

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Solid Commercial Performance from Ipsen in PBC

Iqirvo® sales (global, quarterly) since commercial launch[1]



Implications for GENFIT

IQIRVO® elafibranor 80 mg tablets

3Q sales
Q3'25 €48.6M → Q3'26 €109.4M
+125.4% CER

YTD sales
YTD'25 €107.4M → YTD'26 €282.6M
+170.8% CER

Cumulative milestone payments[2]	Cumulative royalties[3] since launch	Cumulative royalties[3] first 9 months 2026
€105.5M	€60.7M	€36.3M

Next financial update from Ipsen
11 February 2027
Full-year results & Q4 sales

Sales are reported in U.S. dollars (USD), while payments are made in euros (EUR). Currency conversion is performed in accordance with the contractually agreed exchange rate • 1. Source: Ipsen public disclosures. Commercial information has been derived from publicly available information released by Ipsen. GENFIT has not independently verified such information. Any forecasts, projections, expectations or other forward-looking statements referenced therein are those of Ipsen and do not constitute forecasts or expectations of GENFIT. Ipsen delivers outstanding sales growth in the first nine months of 2026 and further upgrades its full-year guidance • 2. €13.3M + € 48,7M + €43,5M | GENFIT Reports First-Half 2026 Financial Results and Provides Corporate Update | FDA New Drug Application and EMA Marketing Authorization Application accepted | First commercial sale of Iqirvo® in the US | Reimbursement in a 3rd European country – Italy | $200M threshold in its first full year of net sales • 3. Cumulative royalties received by GENFIT through 3Q26 | GENFIT Reports Third Quarter 2026 Financial Information and Provides Corporate Update

Ipsen's Updated Iqirvo® Peak Sales Guidance in PBC, Following Positive ELSPIRE Phase 3 Results

ELSPIRE Phase 3 study

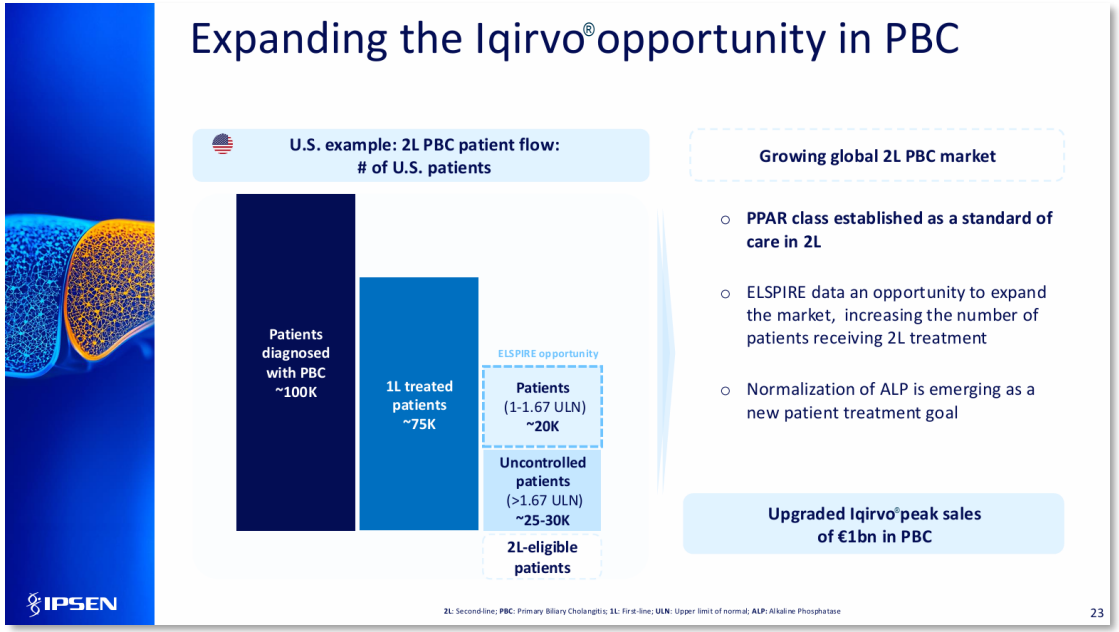
Press Release

July 13, 2026

IQIRVO® demonstrates statistically significant improvement in ALP normalization in patients with PBC in Phase IIIb ELSPIRE study

- The primary endpoint of ALP normalization was achieved in 85% of patients treated with IQIRVO® (elafibranor) vs 23% on placebo
- Normalization of ALP (≤1 ULN) is recognized as a key treatment goal for improved long-term prognosis and slowing disease progression in PBC[1,2,3]
- ELSPIRE evaluated IQIRVO in PBC patients with ALP 1–1.67 x ULN on or after UDCA treatment, having the potential to double the addressable population for IQIRVO where there are significant unmet needs

Updated peak sales guidance (July 2031)



New peak sales: €1bn in PBC

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Additional Potential for Elafibranor: Ipsen-Led ELASCOPE Phase 3 Trial Ongoing in PSC

Source: Ipsen Q3 2026 Results

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

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

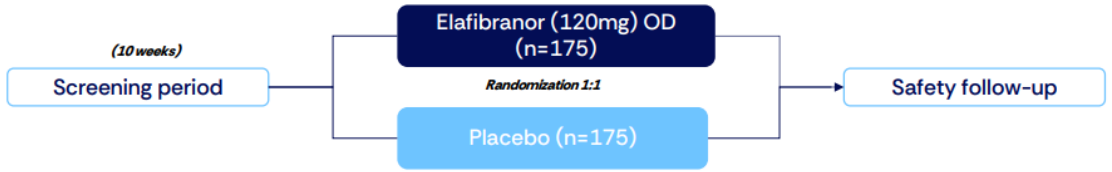
Should Iqirvo® ultimately receive regulatory approval for this indication, GENFIT would be eligible for additional milestone payments as well as additional double-digit royalties.

Data readout expected 2031 (clinicaltrial.gov)

Evaluating elafibranor in PSC

ELASCOPE: Phase III program initiated following positive Phase II data

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



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

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

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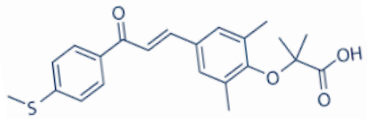
15 Years in MASH Have Built the Foundation for GENFIT's Diagnostic Strategy

Partnerships with pharma

Building R&D expertise through Big Pharma collaborations

A shift to in-house programs

Drug discovery of elafibranor and development in MASH



The turning point

Pivot to PBC and later CCA and ACLF Ipsen deal

Inception and early years

1999-2004

The MASH years

2005-2020

- GENFIT was among the first companies focusing on MASH
- Pioneering efforts in the Liver Forum (KOL, regulatory, patients)
- For over 15 years MASH was our primary focus

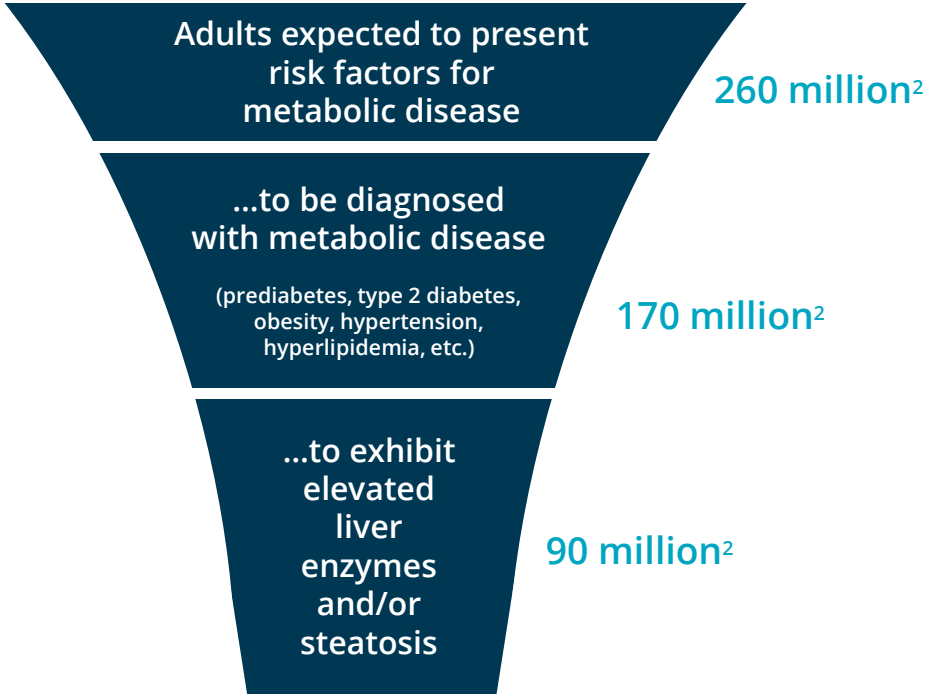
The reinvention

2020-2025

Today, MASH at an Inflection Point: Millions at Risk, and Bottleneck Shifting to Patient Identification & Disease Monitoring

Patient identification landscape

By 2033, Nearly 90 Million U.S. Patients in Care due to MASLD-related Risk Factors[1]



Why Now

- Resmetirom approval & blockbuster sales in year one
- Imminent entry of additional molecules, incl. GLP-1s

→ Bottleneck shifting from treatment availability to patient identification, disease stratification and long-term management

Shifting Physician & Market Behavior

Watch & Wait	→ Find & Treat
Passive Awareness	→ Broad identification & monitoring

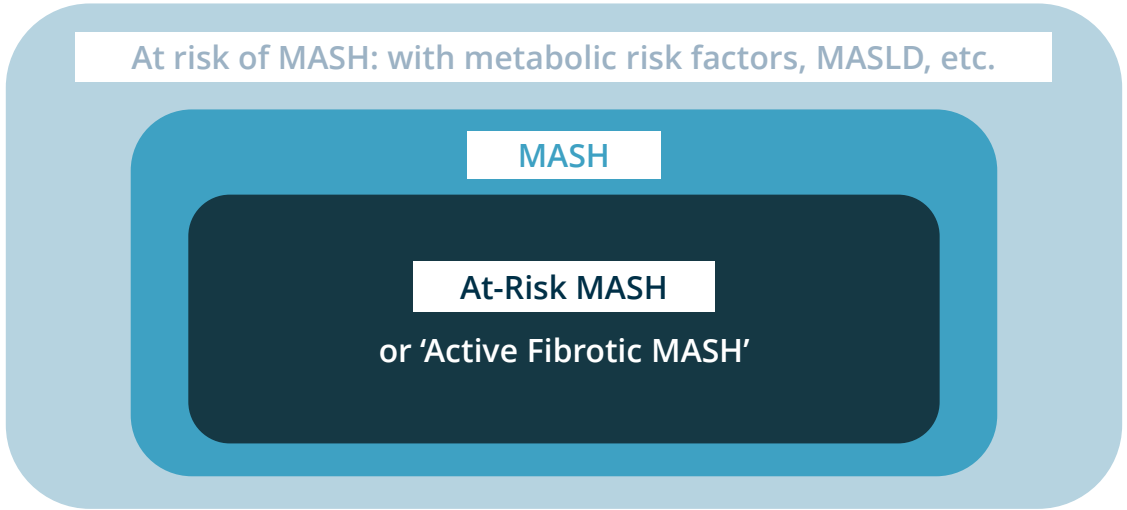
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1.MASLD: Metabolic dysfunction-Associated Steatotic Liver Disease • 2. Projections 2033, IQVIA research 2026

At-Risk MASH, or Active Fibrotic MASH: A Specific Stage of Interest in MASLD

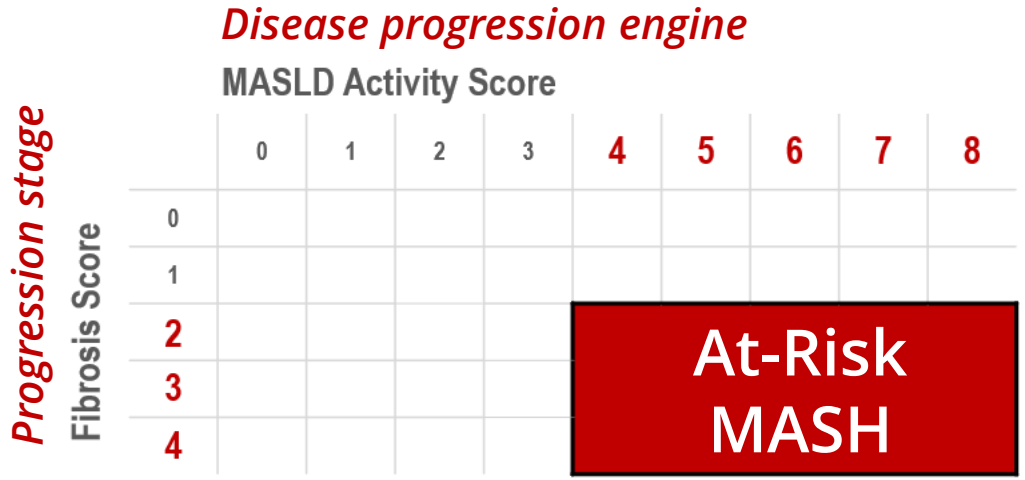
At-risk MASH ≠ At risk of developing MASH

Individuals with at-risk MASH generally have a higher risk of disease progression, all-cause mortality, cardiovascular disease and liver-related morbidity (i.e., liver cancer, decompensated cirrhosis)



At-risk MASH covers two key dimensions

It is critical to not only look at how far has the disease already progressed, through fibrosis, but also how fast it may be progressing, through disease activity



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This New MASH Care Paradigm Creates a Growing Need for Scalable, Reliable Diagnostic of At-Risk MASH

Earlier identification of At-Risk MASH can create value for key stakeholders across the entire care pathway

PATIENTS

Opportunity to change disease trajectory earlier

Act before progression to cirrhosis, while disease improvement remains a meaningful therapeutic objective

NON-LIVER SPECIALISTS

Make MASH actionable in routine care

Know who to test, what action to take and when referral to liver care is warranted

LIVER SPECIALISTS

See the right patients at the right time

Receive actionable, better-targeted referrals before advanced complications dominate management

PAYERS / HEALTH SYSTEMS

Target resources for greatest impact

Focus testing, specialist capacity and treatment on patients most likely to benefit from intervention

GENFIT Has Anticipated this Need Through a Decade of Development

Over the years, GENFIT leveraged its scientific expertise, extensive expert network and unique Phase 2 and Phase 3 tissue and blood sample datasets to develop a differentiated non-invasive technology addressing critical diagnostic and monitoring gaps

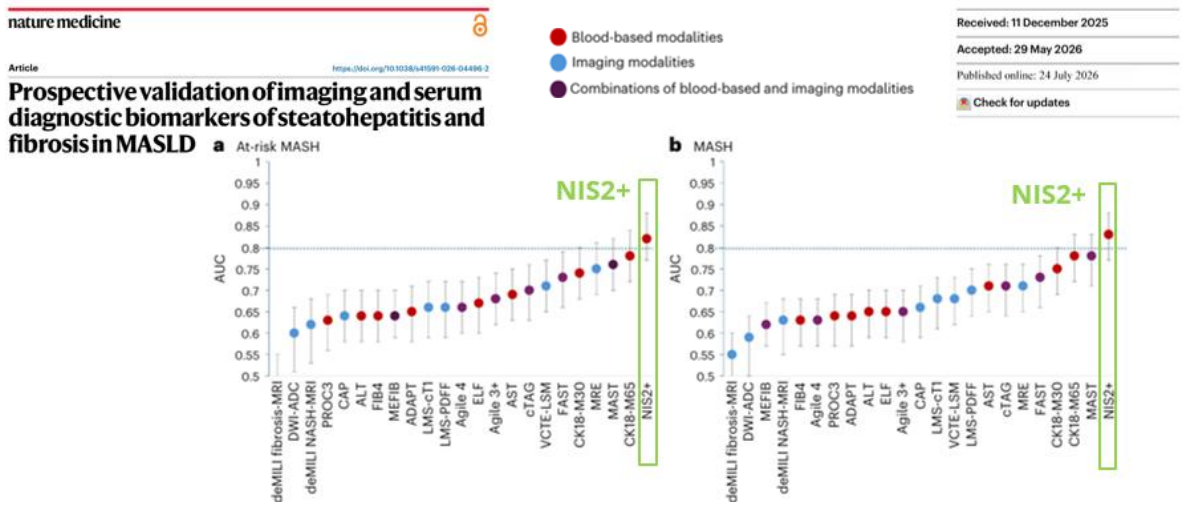
- Testing of hundreds of variables
- Selection of the most predictive variables
- Development of a unique algorithm
- Validation against independent cohorts
- Optimization for future industrialization
- Publications in several scientific journals
- Inclusion in several clinical trials — Phase 2, Phase 3
- Inclusion in international guidelines — EASL, EASL, EASO, AGA, ADA, KASL
- Recognition by Independent consortia — LITMUS
- Commercial availability[1] in the U.S. — labcorp
- First reimbursement[2] in the U.S. — Medicare
- Toward IVD 'In Vitro Diagnostic' — ...

1.via partner Labcorp, as a Laboratory Developed Test (LDT) ● 2: Medicare coverage for eligible U.S. patients

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This Development Journey Has Included Growing External Use and Recognition

LITMUS consortium[1] (Europe)



NIMBLE consortium[2] (U.S.)

nature medicine

Topline results from NIMBLE consortium, stage 1 (N=1073)[2]

	MASH		At-risk MASH		F stage ≥2	
	AUROC (95% CI)	*p* (vs ALT)	AUROC (95% CI)	*p* (vs ALT)	AUROC (95% CI)	*p* (vs FIB4)
ALT	0.678 (0.639, 0.717)		0.726 (0.694, 0.759)			
FIB4			0.704 (0.671, 0.737)		0.798 (0.768, 0.828)	
NIS4®	**0.832 (0.801, 0.864)**	< 0.001	**0.815 (0.786, 0.844)**	< 0.001	**0.874 (0.848, 0.899)**	< 0.001
ELF	-	-	-	-	0.828 (0.800, 0.857)	0.013
PROC3	-	-	-	-	0.809 (0.779, 0.839)	0.279
FibroM VCTE	-	-	-	-	0.841 (0.796, 0.886)	< 0.001

NIS4® utility has been recognized in a Stage 1 study[2] undertaken by the Non-Invasive Biomarkers of Metabolic Liver Disease (NIMBLE) initiative, with unique performances

†ELF data were not available for the ANGERS cohort (n=227). ‡VTCE data were not available for the RESOLVE-IT-DIAG cohort (n=475).

1. Harrison SA, Ratziv V, *et al. The lancet Gastroenterology & hepatology*, *5*(11), 970-985, 2020.
2. Sanyal A.J., *et al, Nature medicine*, *29*(10), 2656-2664, 2023

Included in Hepatology, Gastroenterology and Diabetology clinical guidelines

CLINICAL PRACTICE UPDATE — Gastroenterology

AGA Clinical Practice Update on the Role of Noninvasive Biomarkers in the Evaluation and Management of Nonalcoholic Fatty Liver Disease: Expert Review

Clinical Practice Guidelines — JOURNAL OF HEPATOLOGY

EASL–EASD–EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD)☆

European Association for the Study of the Liver (EASL)*, European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO)

CONSENSUS REPORT — Diabetes Care

Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) in People With Diabetes: The Need for Screening and Early Intervention. A Consensus Report of the American Diabetes Association

NIS4® for monitoring treatment response in independent publications from clinical trials

Lilly

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tirzepatide for Metabolic Dysfunction–Associated Steatohepatitis with Liver Fibrosis

AstraZeneca

Clinical Gastroenterology and Hepatology

Safety and Efficacy of Novel Incretin Co-agonist Cotadutide in Biopsy-proven Noncirrhotic MASH With Fibrosis

akero

THE LANCET Gastroenterology & Hepatology

Safety and efficacy of once-weekly efruxifermin versus placebo in non-alcoholic steatohepatitis (HARMONY): a multicentre, randomised, double-blind, placebo-controlled, phase 2b trial

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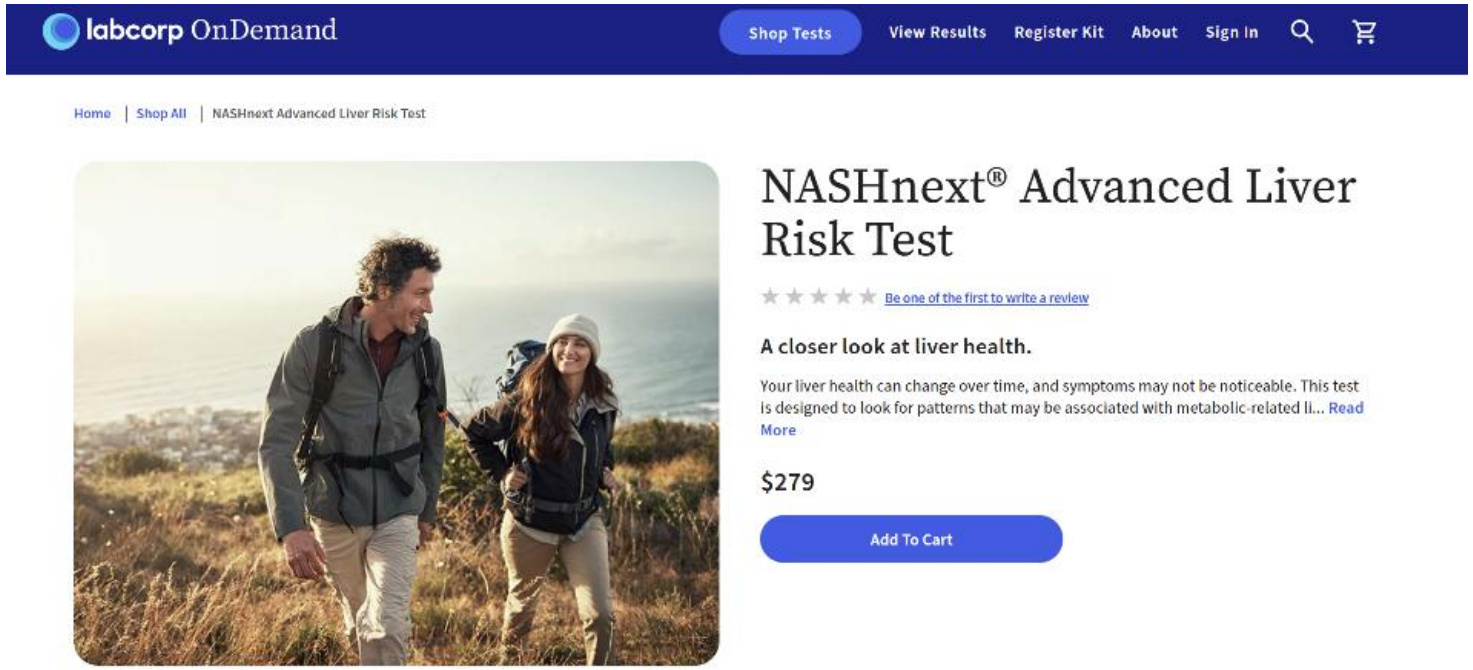
1. Nature Medicine | 2. Nature Medicine

The Journey Has Also Led to Clinical Availability Through Labcorp's NASHnext® as a Laboratory Developed Test (LDT)

Labcorp's NASHnext® LDT test available to millions of patients

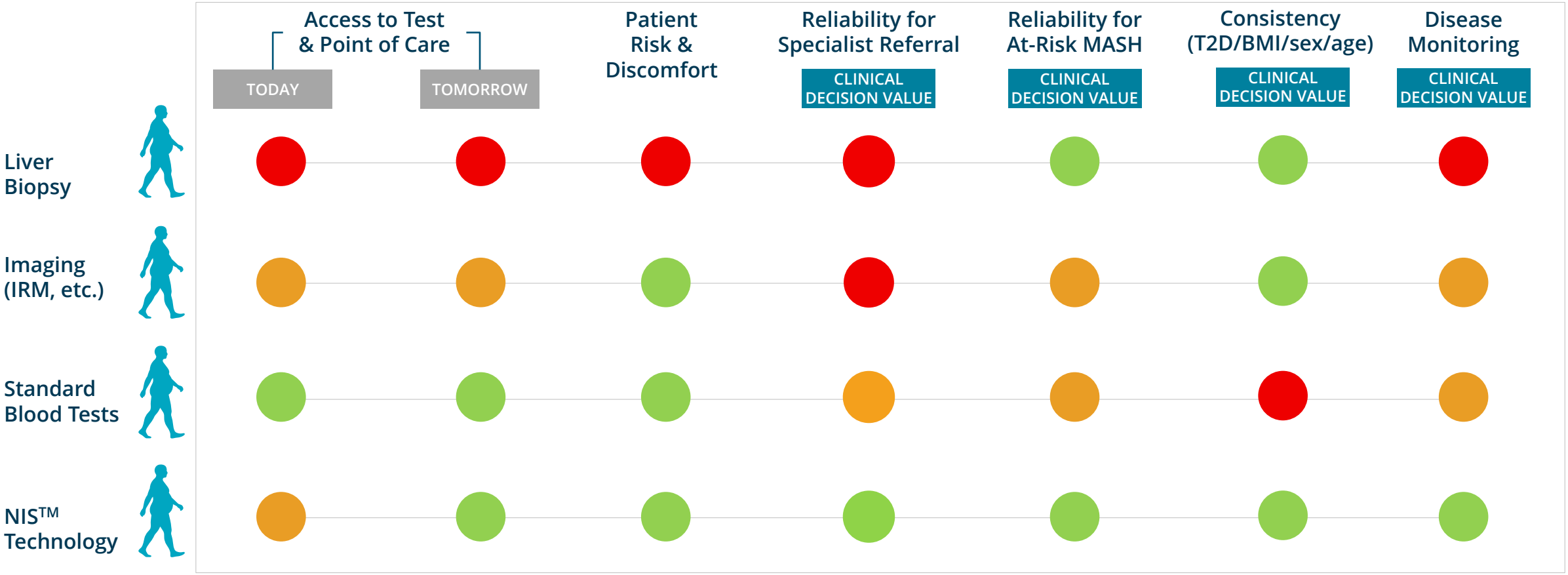
NASHnext® reimbursed by Medicare[1] under the Clinical Laboratory Fee Schedule, for patients who meet coverage criteria (effective from August 10, 2026)

This major milestone supports broader adoption and future coverage by private insurers



1. GENFIT Announces U.S. Medicare Coverage and Future Reimbursement for NASHnext®, a Non-Invasive Diagnostic Technology to Identify Patients with At-Risk MASH | GENFIT

Beyond the LDT, In Vitro Diagnostics (IVD) Is the Next Step Toward Use at Scale, Building on NIS™ Technology's Key Attributes



NIS™ Technology encompasses NIS4® and next-generation NIS2+® | NASHnext® (based on NIS4® technology) reimbursement by Medicare under the Clinical Laboratory Fee Schedule for Medicare patients who meet coverage criteria became effective on August 10, 2026 | NIS2+® is currently available in the United States through Labcorp as a Laboratory Developed Test (LDT). It has not been cleared or approved by the U.S. Food and Drug Administration (FDA) and is not CE marked in the European Union.

NIS™ Technology supports reliable specialist referral while retaining the access and scalability of a routine blood test

High / favorable Intermediate Low / unfavorable

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This table reflects GENFIT's management's perspective

IVD Could Expand the Estimated Peak Annual Laboratory Market Opportunity to ~$1.5B[1]

Base Case testing volumes across the patient journey

Diagnosis
1.7M
NIS2+ tests
~23%

+

Monitoring
5.7M
NIS2+ tests
~77%

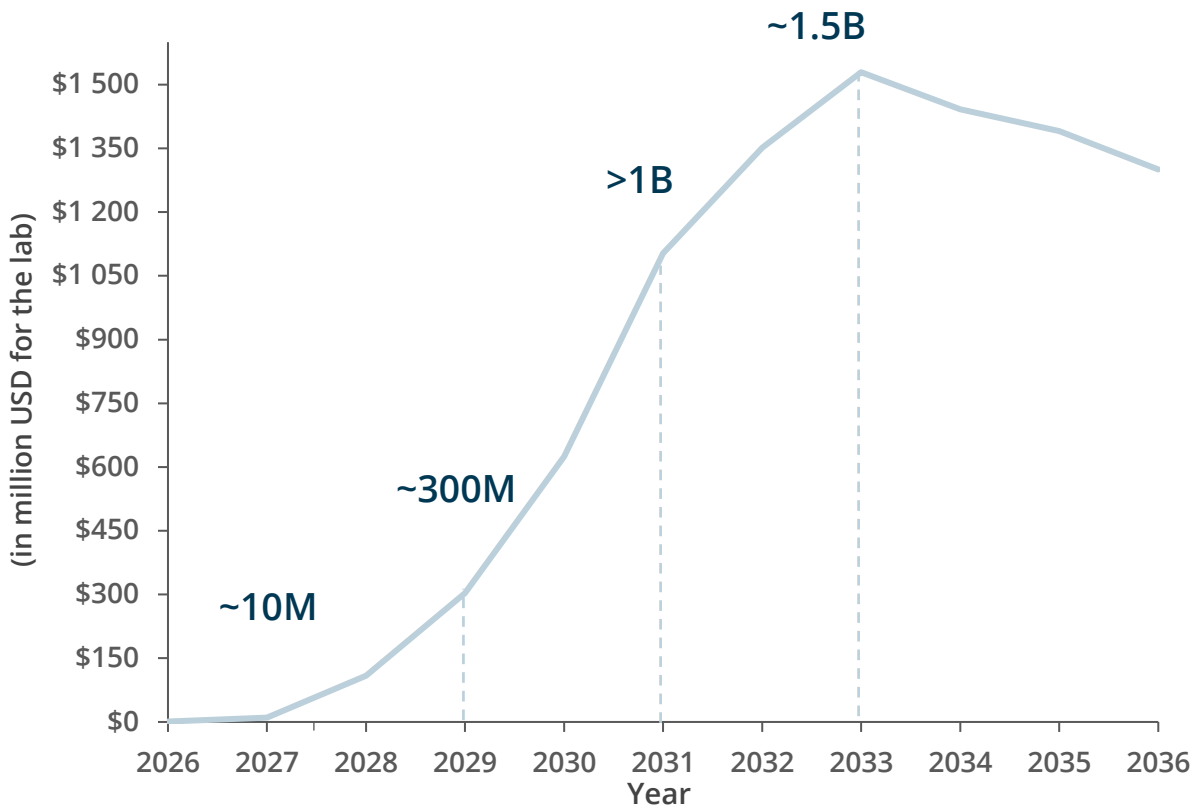
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Base Case Total
7.4M
NIS2+ volume

Volume peak year 2033 (U.S.)

IQVIA

NIS2+ Estimated Revenue to Partner Lab (LDT+IVD)



The diagnostics opportunity is no longer constrained by therapy availability, but by the ability to identify and manage eligible patients at scale

IQVIA

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1: IQVIA estimates 2026 / Laboratory Market Opportunity is not GENFIT revenue, which would be based on royalties from licensing fees | GENFIT Highlights Long-Term Commercial Opportunity for its MASH Diagnostics Technology | 2026.09.09 - GENFIT Highlights Long-Term Commercial Opportunity for its MASH Diagnostics Technology

Three In-House Phase 2 Programs, One External Phase 3 Program

In-house programs

Nangibotide in ACLF

Phase 2 initiation 2H26
Data readout 2027

Nitazoxanide in ACLF

Phase 2 initiation 2H26
Data readout 2027

GNS561 in CCA

Phase 2 initiation 2H26
Data readout 2027

External programs

Elafibranor in PSC

IPSEN

Phase 3 data readout (long term outcomes) 2031

GNS561
CCA
in combination

CCA, an Aggressive Liver Cancer Targeted via Autophagy Inhibition

DISEASE DESCRIPTION

Cholangiocarcinoma (CCA)
Liver malignancy develops in the bile ducts and can damage the liver and other organs

KRAS mutation
~30% of patients with CCA harbor KRAS mutations[1], which overactivate growth signaling pathways

THE UNMET MEDICAL NEED

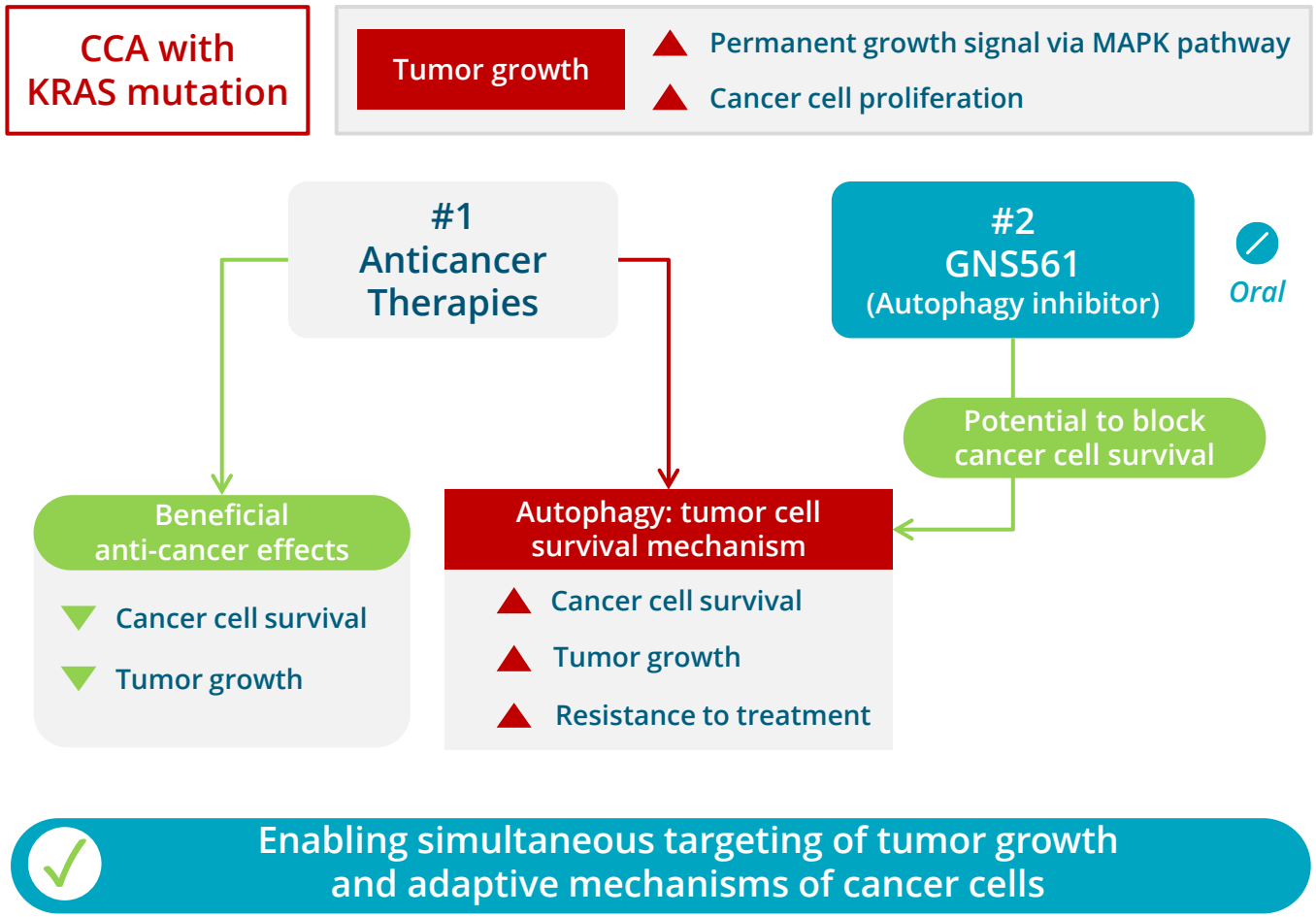
KRAS mutation is not addressed by current treatments

<20%
5-year survival from diagnosis without treatment[2]

30%
of patients present with resectable tumors[3], the primary treatment

10-12 months
to death on current standard of care[4] due to rapid tumor progression

MECHANISM OF ACTION



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SOC: Standard of care | 1. Banales et al., Cholangiocarcinoma 2020 | 2. Lamarca et al. 2021 | 3. Jesus M. Banales et al. 2020 | 4. Banales et al., Cholangiocarcinoma 2026

GNS561
CCA
in combination

Encouraging Preliminary Phase 1b Data Complement Preclinical Data

19
patients treated across several dose-escalation cohorts[1]

~50%
evaluable patients stable at Week 6[1]

PRECLINICAL DATA

- Mediated PPT1 inhibition, triggering cancer cell apoptosis
- Showed potent antitumor activity in several iCCA cell lines in mono therapy
- Improved chemotherapies efficacy in KRAS mutant cell line
- Strongly synergized with MEKi in several KRAS mutant CCA cell line

These findings support the rationale for targeting PPT1 with GNS561 in iCCA, particularly in KRAS-mutant tumors and in combination with MEK inhibitors

CLINICAL DATA[1]

On-going Phase 1b expanded to additional cohorts evaluating higher doses, as the Maximum Tolerated Dose (MTD) was not yet reached

SAFETY

- 19 patients enrolled across several dose-escalation cohorts[1]
- Overall favorable safety and tolerability profile[1]

EFFICACY SIGNALS

- ~50% of patients achieved disease stabilization at Week 6, who had all shown disease progression during previous treatment[1]
- One patient maintained Stable Disease up to Week 30[1]
- Tumor shrinkage in a subgroup of patients with the best response showing a 20% reduction approaching the partial response (PR) threshold[2]

Findings from preclinical models do not establish safety or efficacy in humans

As of June 2026 (sources: [1.] Press release GNS561 - June 23, 2026 - [2.] Press release GNS561 - December 10, 2025)

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Preclinical data: Brun et al., Invest New Drugs. 2019;37:1136–1145; Ansaldi et al., AASLD Poster 0352; Brun et al., Autophagy. 2022;18:678–694.

GNS561
CCA
in combination

Phase 2 Data Readout Expected 2H27

TARGET POPULATION

KEY INCLUSION CRITERIA
Patients with KRAS mutated CCA who have failed 1st line treatment therapy

~50 patients

~40 sites in 4 countries

Single arm with GNS561 at the Recommended Phase 2 Dose (RP2D)

In combination with a MEK inhibitor (trametinib)

Treatment duration:
Until disease progression or earlier discontinuation

ENPOINTS

Primary endpoint
Efficacy – objective response rate (ORR)

Secondary endpoint
Efficacy - progression free survival
Pharmacokinetics Pharmacodynamics
Safety and tolerability

Data Readout 2H27

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Nangibotide
ACLF
in monotherapy

ACLF, a High-Mortality Syndrome Targeted via the TREM-1 Inflammation Pathway

DISEASE DESCRIPTION



Acute-on-Chronic Liver Failure (ACLF)

Acute decompensation in patients with chronic liver disease triggered by a precipitating event leading to multiple organ failure[1]

THE UNMET MEDICAL NEED

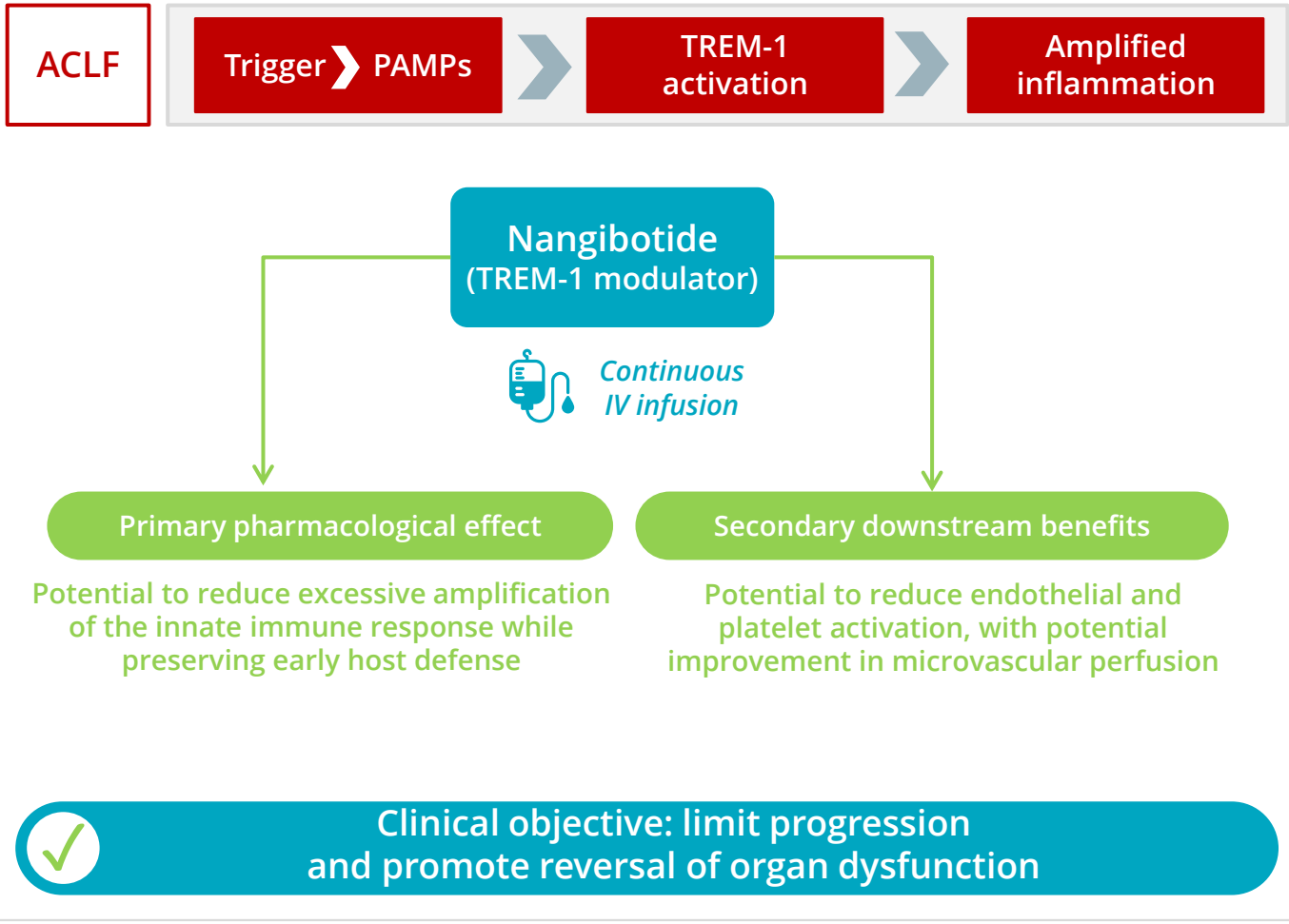
No approved drug

23-74%
mortality at 28 days[2]

1 in 4
of patients die while awaiting liver transplant[3]

~50%
mortality among patients admitted to the ICU[4]

MECHANISM OF ACTION



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1. Chronic liver disease: alcohol consumption, viruses, medications, metabolic dysfunctions, autoimmune & hereditary disease) | Precipitant: bacterial infection, alcohol consumption,... | Organ failure: liver, kidney, cerebral, heart, respiratory, coagulation, circulatory Wong F, et al. Liver Transpl 2022 | Arroyo V, et al. J Hepatol 2015 | Arroyo et al. NEJM 2020 | Jalan et al. J Hepatol 2015 | Moreau et al J Hepatol 2021 | Bernal W, et al. J Hepatol 2021 | PREDICT-study Trebicka, Fernandez, et al. J Hepatol 2021 | Trebicka J et al, Visceral Medicine 2018 | EASL- Clinical Practice Guideline on Decompensated Cirrhosis J Hepatol 2018 | Gustot T, et al. Hepatol 2015 | Arroyo V et al., Nat. Rev. Dis. Primers 2 2016 | Huang DQ, et al. Nat Rev Gastroenterol Hepatol 2023 | Gaspar R, et al. Dig Liver Dis 2019 • 2. Arroyo V et al., Nat. Rev. Dis. Primers 2. 2016 | 3. ACLF 2-3 - Gustot et al., CHANCE study, J Hepatol. 2026 | . Pereira R, Bagulho L, Cardoso FS. Rev Bras Ter Intensiva. 2020 | PAMPs: Pathogen-Associated Molecular Patterns

Nangibotide
ACLF
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Encouraging Data from Phase 2 Trials in Diseases Characterized by Systemic Inflammation and Multiorgan Failure

416
participants exposed across Phase 1 and Phase 2

−2.5 pts
greater SOFA reduction vs placebo at Day 5 in the elevated-TREM-1 subgroup

Day 28 mortality
Favorable trends in both septic shock and COVID19

PRECLINICAL DATA

HUMAN EX VIVO

Reduced:

- PAMPs-induced inflammatory mediators in human leukocytes
- human endothelial cell activation
- human platelets activation, supporting a potential effect on immunothrombotic & micro-thrombosis

SPECIES-SPECIFIC IN VIVO ANALOGUES

Species-specific TREM-1 pathway peptides:

- Improved survival in sepsis models across rodents, non-human primates and minipig
- Reported effects included systemic inflammation, haemodynamics and liver injury

INTERPRETATION FOR ACLF

- Human data supports target engagement & downstream biology
- Animal data support pathway relevance in severe systemic inflammation

The rationale is strongest for infection-triggered ACLF with marked systemic inflammation

Findings from preclinical models do not establish safety or efficacy in humans

CLINICAL DATA

SAFETY

In total, 416 participants exposed (0.03-6 mg/kg/h by continuous IV infusion)

- Phase 1: 21 healthy participants
- Phase 2a: 37 participants with septic shock
- Phase 2b: 239 participants with septic shock (ASTONISH)
- Phase 2: 119 participants with COVID-19 (ESSENTIAL)

Overall, AE profile described as similar to placebo; no safety signal identified

EFFICACY SIGNALS

SEPTIC SHOCK: 118 patients with high sTREM-1 (62 expose to 1.0 mg/kg/h by continuous IV infusion)

- 2.5-point greater reduction in SOFA score versus placebo at Day 5
- Statistically significant improvements reported for respiratory, cardiovascular, and renal components
- Consistent favorable trends were reported across Day 28 mortality, Day 28 organ support-free status, ICU stay, and organ failure-free days

COVID-19: 219 patients (119 expose to 1.0 mg/kg/h by continuous IV infusion)

Nangibotide was associated with improved clinical status and lower Day 28 mortality

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Preclinical data: Boufenzer et al., Crit Care. 2012;16(Suppl 3):P49; Cuvier et al., Br J Clin Pharmacol. 2018;84:2270–2279; Inotrem preclinical studies
Clinical data: Inotrem trials. Cuvier et al., Br J Clin Pharmacol. 2018;84:2270–2279; François et al., Intensive Care Med. 2020;46:1425–1437; François et al., Lancet Respir Med. 2023;11:894–904; François et al., eClinicalMedicine. 2023;60:102013

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Phase 2* Data Readout Expected 2H27

UPWARD

TARGET POPULATION

KEY INCLUSION CRITERIA
Participant with ACLF grade 2
With bacterial infection
Adult male or female
participants <75 years of age

24 patients

~20 sites in 6 countries

2:1 randomization

Nangibotide continuous IV infusion + standard of care, N=16

Treatment duration: 3 to 7 days

Placebo continuous IV infusion + standard of care, N=8

ENPOINTS

Primary endpoint
Safety

Secondary endpoint
Pharmacokinetics

Exploratory endpoint
efficacy and potential
immunogenicity

Data Readout 2H27

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IV: intravenous; | N: number of participant | *Subject to regulatory approval

ACLF, a High-Mortality Syndrome Targeted via Reduction of Inflammation and Cell Death

DISEASE DESCRIPTION



Acute-on-Chronic Liver Failure (ACLF)
Acute decompensation in patients with chronic liver disease triggered by a precipitating event leading to multiple organ failure[1]

THE UNMET MEDICAL NEED

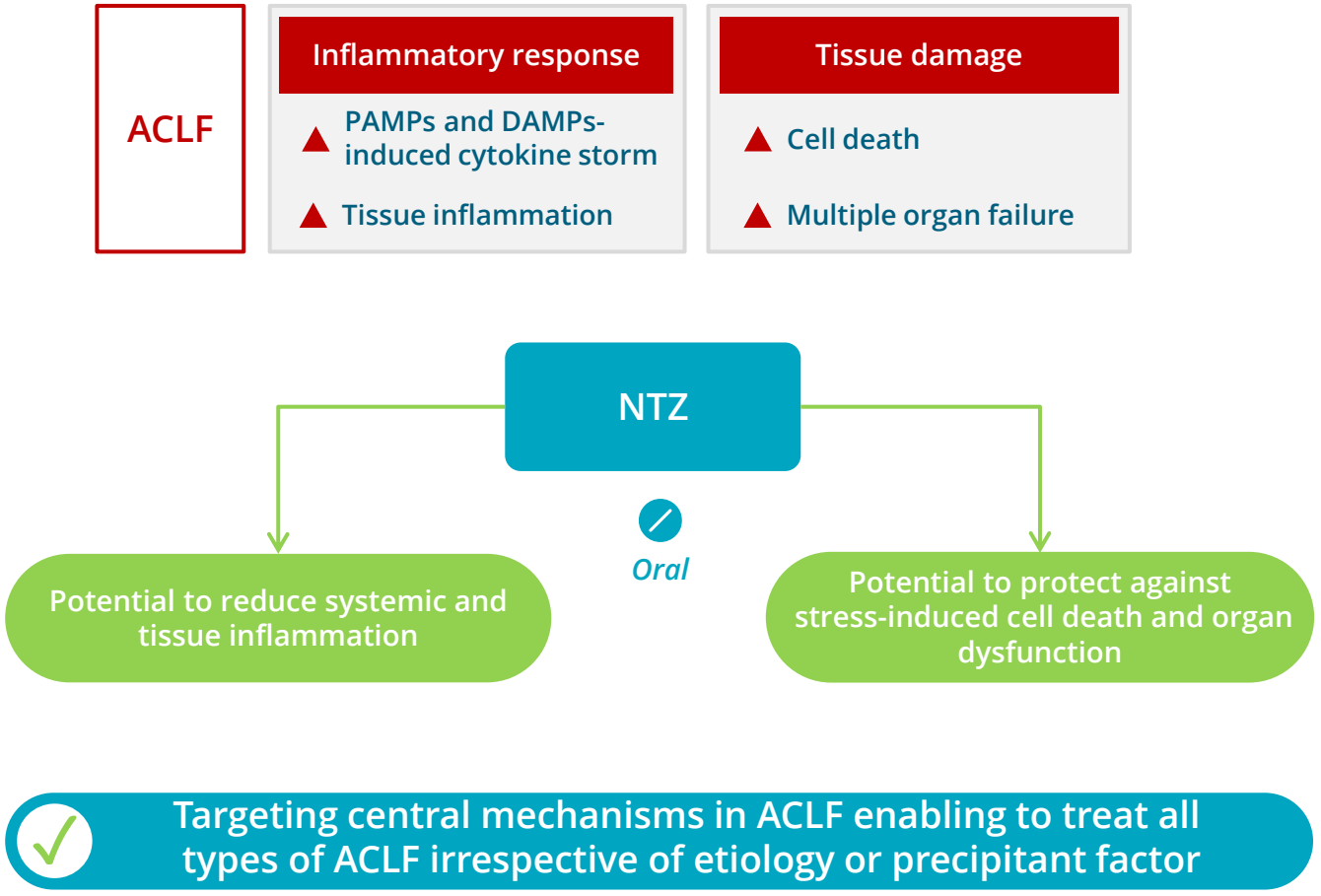
No approved drug

23-74%
mortality at 28 days[2]

1 in 4
of patients die while awaiting liver transplant[3]

~50%
mortality among patients admitted to the ICU[4]

MECHANISM OF ACTION



Targeting central mechanisms in ACLF enabling to treat all types of ACLF irrespective of etiology or precipitant factor

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1. Chronic liver diease: alcohol consumption, viruses, medications, metabolic dysfunctions, autoimmune & hereditary disease) | Precipitant: bacterial infection, alcohol consumption,... | Organ failure: liver, kidney, cerebral, heart, respiratory, coagulation, circulatory Wong F, et al. Liver Transpl 2022 | Arroyo V, et al. J Hepatol 2015 | Arroyo et al. NEJM 2020 | Jalan et al. J Hepatol 2015 | Moreau et al J Hepatol 2021 | Bernal W, et al. J Hepatol 2021 | PREDICT-study Trebicka, Fernandez, et al. J Hepatol 2021 | Trebicka J et al, Visceral Medicine 2018 | EASL- Clinical Practice Guideline on Decompensated Cirrhosis J Hepatol 2018 | Gustot T, et al. Hepatol 2015 | Arroyo V et al., Nat. Rev. Dis. Primers 2 2016 | Huang DQ, et al. Nat Rev Gastroenterol Hepatol 2023 | Gaspar R, et al. Dig Liver Dis 2019 • 2. Arroyo V et al., Nat. Rev. Dis. Primers 2. 2016 | 3. ACLF 2-3 - Gustot et al., CHANCE study, J Hepatol. 2026 | 4. Pereira R, Bagulho L, Cardoso FS. Rev Bras Ter Intensiva. 2020 PAMPs: Pathogen-Associated Molecular Patterns | DAMPs: Damage-Associated Molecular Patterns

Preclinical and Clinical Data Provide a Rationale for Further Investigation of Nitazoxanide in ACLF

102
patients across...

Phase 2 & 3
...published studies

67
participants in 2 GENFIT Phase 1 studies

PRECLINICAL DATA

- Decreased systemic inflammation in animal models, including in ACLF models
- Protected liver, kidney, lung & brain in rat models of ACLF by decreasing tissue damage
- Protected mice from mortality in a model of sepsis induced by gut leakage
- Prevented cell death via anti-apoptotic and anti- necroptotic effects
- Reduced PAMPs-induced inflammation

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

CLINICAL DATA

Three studies (Ph2, Ph2/3, Ph3) from the literature evaluated NTZ in 102 patients with hepatic encephalopathy and advanced liver disease provide supporting clinical data in a population resembling ACLF.

- NTZ was generally safe and well tolerated. Exposure of up to 24 weeks was associated mainly with mild gastrointestinal adverse events
- NTZ 500 mg BID showed signals of efficacy in treating and preventing hepatic encephalopathy, with favorable trends in MELD and Child-Pugh scores

Two Phase 1 studies performed by GENFIT evaluated NTZ 500 mg BID for 7 days in participants with hepatic or renal impairment, including severe hepatic impairment or renal impairment (67 participants exposed).

- NTZ was generally well tolerated, with no drug-related serious safety signals identified
- Participants with severe hepatic impairment showed decreases in interleukin-6 and total bilirubin following NTZ administration, consistent with findings from non-clinical studies

Findings from preclinical models do not establish safety or efficacy in humans

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Preclinical data: Legry V. et al., J Hepatol. 2022;77, THU528; Legry V. et al., J Hepatol. 2023;78, THU-342; Bobowski-Gerard M. et al., J Hepatol. 2024;80, WED-105; Bobowski-Gerard M. et al., Hepatology. 2024;80:880–881, abstract #1603; Bobowski-Gerard M. et al., J Hepatol. 2025;82:S170–S171; Bobowski-Gerard M. et al., Nephrol Dial Transplant. 2025;40(Suppl 3):gfaf116.132; Klein S. et al., EASL 2026, FRI-283 | Scientific posters: GENFIT – ACLF, NTZ • Clinical data: Abd-Elsalam et al J Clin Gastroenterol 2018, Elrakaybi et al., IJPSR, 2015, Glal et al., J Hepatobiliary Pancreat Sci. 2021; GENFIT Phase 1 studies NCT05116826 and NCT05368935; Harisseh et al., DDW 2023.

Nitazoxanide
ACLF
in monotherapy

Phase 2 Data Readout Expected Mid-2027

TARGET POPULATION

KEY INCLUSION CRITERIA
Participants with recent acute decompensation of liver cirrhosis with or without organ failure
High inflammatory baseline

16 patients

~10 sites in 4 countries

NTZ 500 mg BID + Standard of care, N=16

Treatment duration: 7 days

ENPOINTS

Primary endpoint
Safety

Exploratory endpoint
Efficacy based on disease progression, inflammatory profile and participants outcome

Data Readout Mid-2027

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TEAE: Treatment-Emergent Adverse Event | SAE: Serious adverse event

Exploring both ACLF and Oncology

ACLF

- Diversified set of mechanisms of action explored, based on the pathophysiology
- Along the full continuum (acute decompensation, hepatic encephalopathy, etc.)

Oncology

- Exploring other types of cancers, beyond cholangiocarcinoma
- Exploring other types of agents, beyond MEK inhibitors

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