



# Corporate Overview

May 2022

# Forward-looking statements

This presentation contains, in addition to historical information, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements relate to future events or future financial performance and use words such as “may,” “estimate,” “could,” “expect” and others. They are based on our current expectations and are subject to factors and uncertainties that could cause actual results to differ materially from those described in the statements.

These statements include those regarding potential therapeutic benefits of our drugs, expectations, plans and timelines related to our clinical trials, supporting activities, potential partnering opportunities and estimated spending for 2022 and beyond. Factors that could cause our actual performance to differ materially from those discussed in the forward-looking statements include, among others, our trials and supporting CMC information may be impacted by COVID-19.

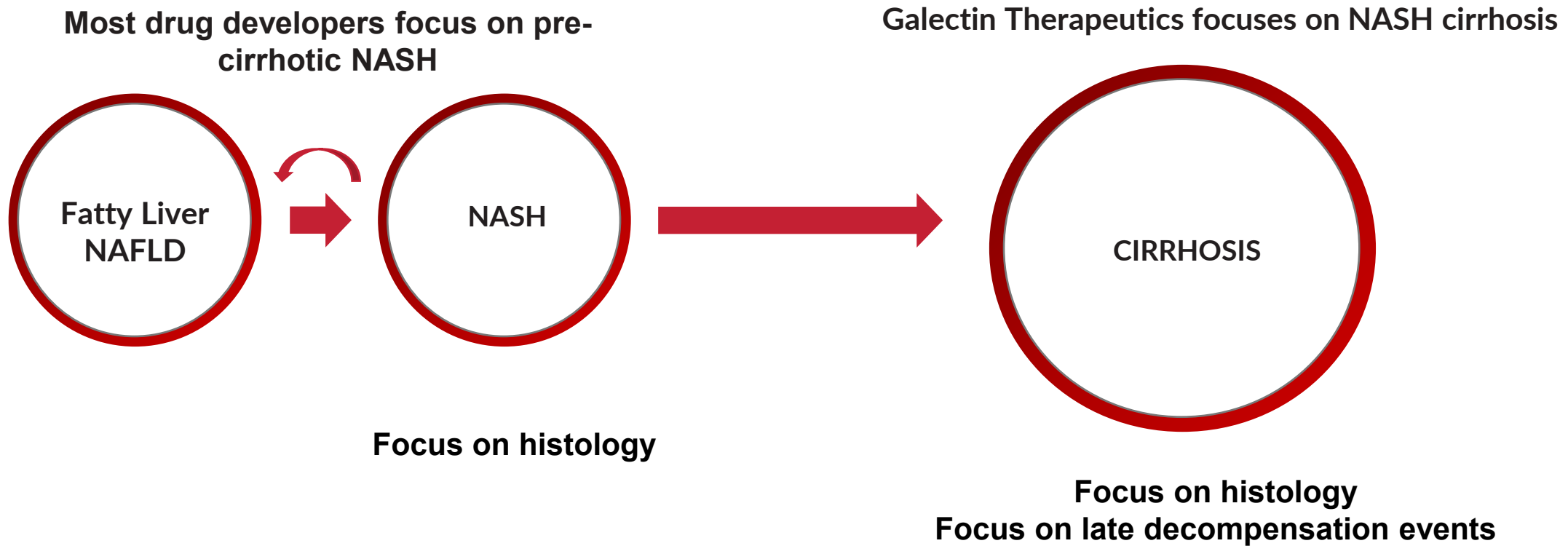
We may experience delays in our trials, which could include enrollment delays. Future phases or future clinical studies may not begin or produce positive results in a timely fashion, if at all, and could prove time consuming and costly. Plans regarding development, approval and marketing of any of our drugs are subject to change at any time based on the changing needs of our company as determined by management and regulatory agencies. Strategies and spending projections may change. We may be unsuccessful in developing partnerships with other companies or obtaining capital that would allow us to complete our clinical trials or further develop and/or fund any future studies or trials.

To date, we have incurred operating losses since our inception, and our future success may be impacted by our ability to manage costs and finance our continuing operations. For a discussion of additional factors impacting our business, see our Annual Report on Form 10-K for the year ended December 31, 2021, and our subsequent filings with the SEC. You should not place undue reliance on forward-looking statements. Although subsequent events may cause our views to change, we disclaim any obligation to update forward-looking statements. 2

# Galectin Overview



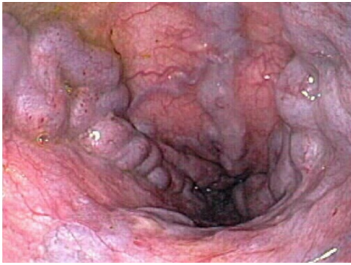
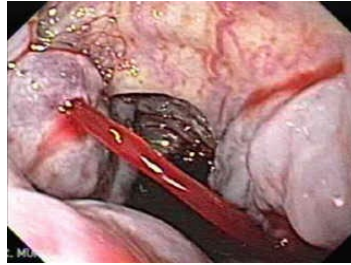
- Conducting an adaptively-designed Phase 2b/3 trial of **belapectin**, a potent galectin-3 inhibitor, for the prevention of esophageal varices in NASH cirrhosis (NAVIGATE)
- Strong, experienced management team
- **Belapectin** is a novel galectin-3 inhibitor that targets macrophages (a key driver in cirrhosis) and may improve multiple fibrotic diseases
- **Belapectin** efficacy observed in animal models and Phase 2 trial (NASH-CX)
- NASH-CX in patients with compensated cirrhosis and portal hypertension demonstrated that **belapectin** prevented the development of new esophageal varices in a population with a high degree of clinical unmet need with no available therapies and few in development
- **Belapectin** in combination with PD-1 inhibitor showed encouraging clinical response rate in difficult to treat cancers (e.g. head and neck cancer)
- **Belapectin** has a robust IP portfolio
  - Composition of matter for complex carbohydrates and/or methods of use in treatment of fibrosis, in combination cancer immunotherapy and other indications
  - Patent applications filed for small molecule galectin-3 inhibitors

# For a drug developer pre-cirrhotic NASH and NASH cirrhosis are different fields



**The only way forward is to think outside the box: innovate or stagnate !**

# The drug developer dilemma in cirrhosis: when to intervene?

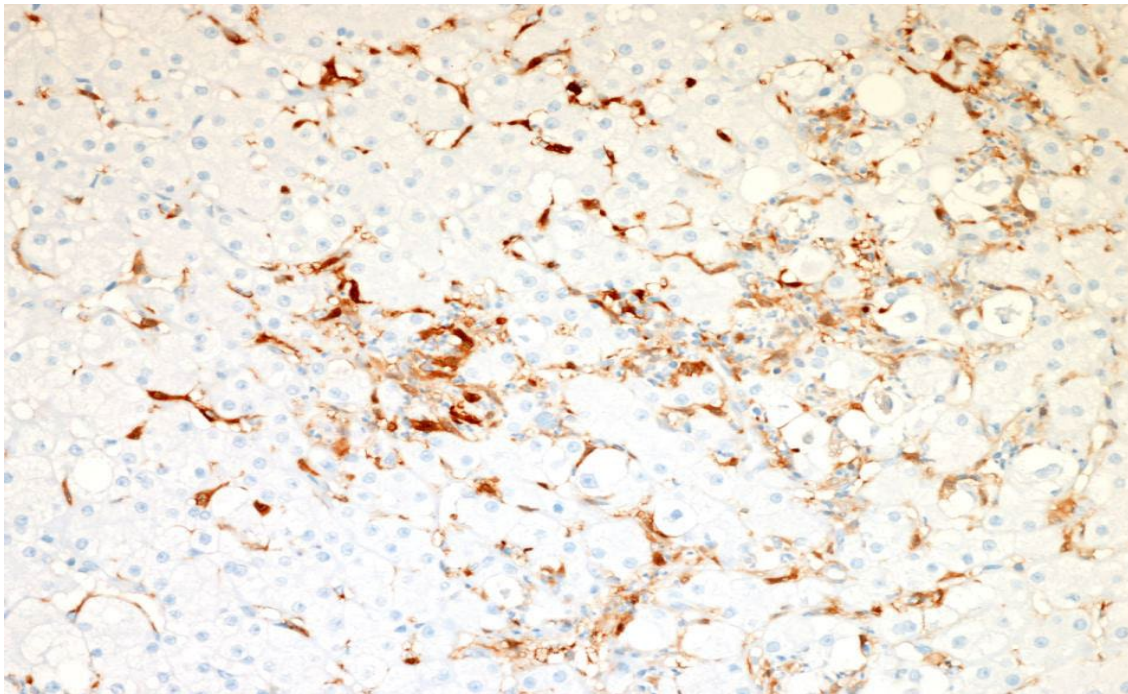
| Compensated cirrhosis  |   | Decompensated cirrhosis   |   |
|--|---|---|---|
| No Portal Hypertension   | Portal Hypertension   |   |   |
| No varices<br> | No varices<br> | Varices, small to large<br> | Varices Bleeding, ascites, encephalopathy<br> |
|  | ≥6  | HVPG <sup>1</sup> mm Hg   | >10   |
|  | One year mortality 1-3%   |   | One year mortality ~50%   |

<sup>1</sup> HVPG: Hepatic Venous Pressure Gradient

# The galectin-3 'fibrosome' and the role of activated macrophages

Galectin-3 binds to glycoproteins and form a lattice structure on cell surface and the inflammatory tissue microenvironment

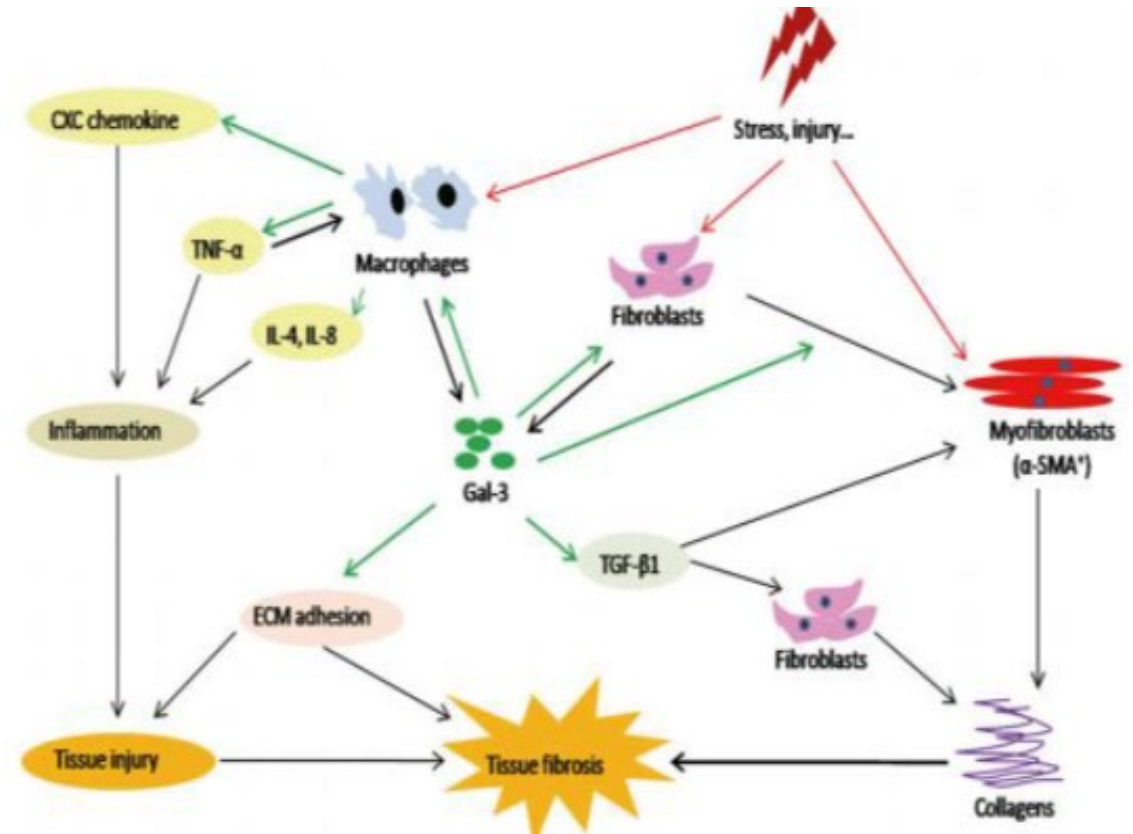
Galectin-3 expression is up-regulated in human fibrotic liver disease, and disruption of Galectin-3 can markedly reduce liver fibrosis



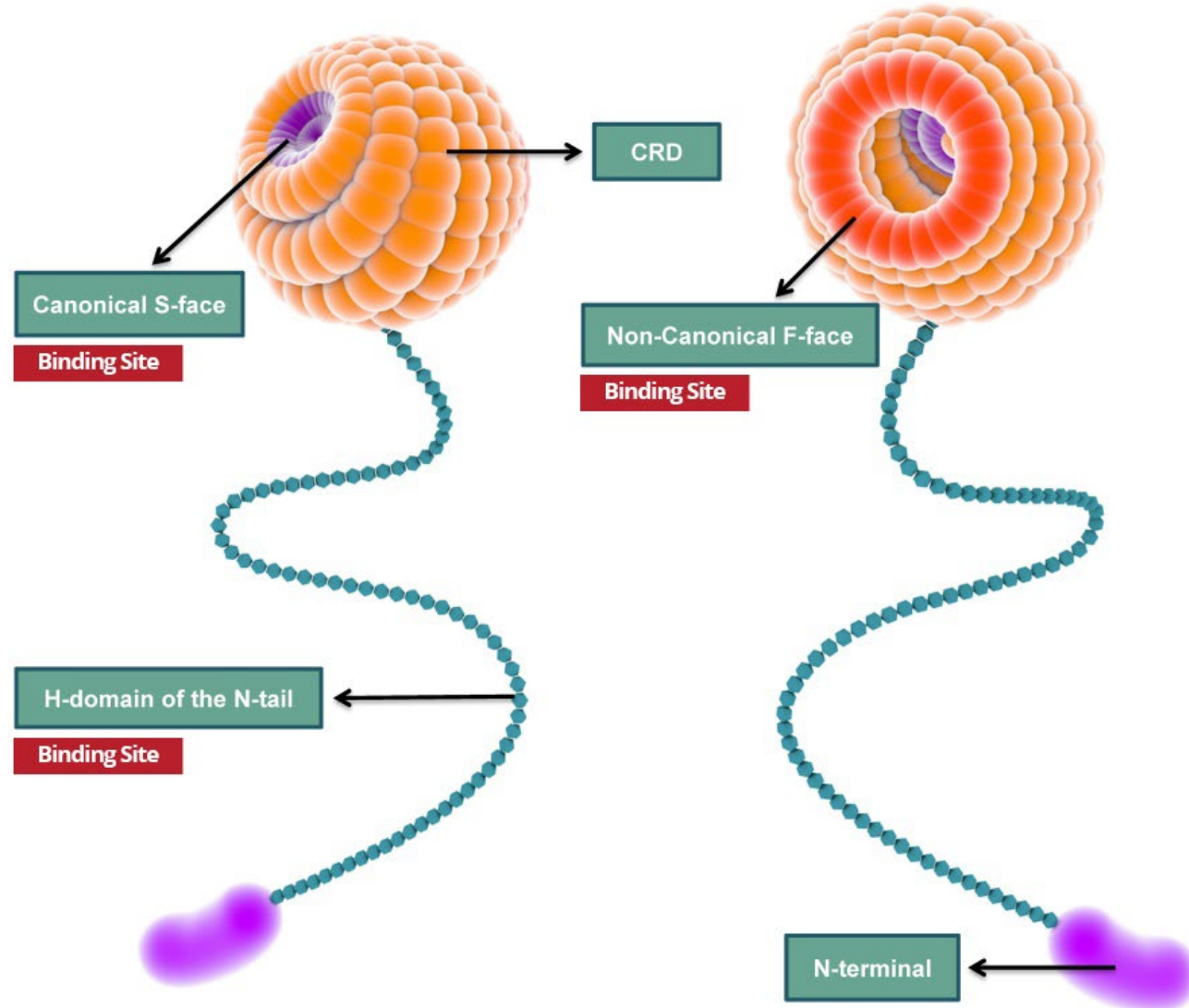
Activated liver macrophages stained with galectin-3<sup>1</sup>

1 Courtesy of Dr. Z. Goodman

## Central role of Gal-3 in multiple pathological processes



# Schematic representation of Galectin-3 a HEAD, with carbohydrate recognition domains, and a TAIL



**Belapectin binding sites**

Illustration by Medvisuals/Maartje Kunen

# Galectin-3: conformation and polymerization

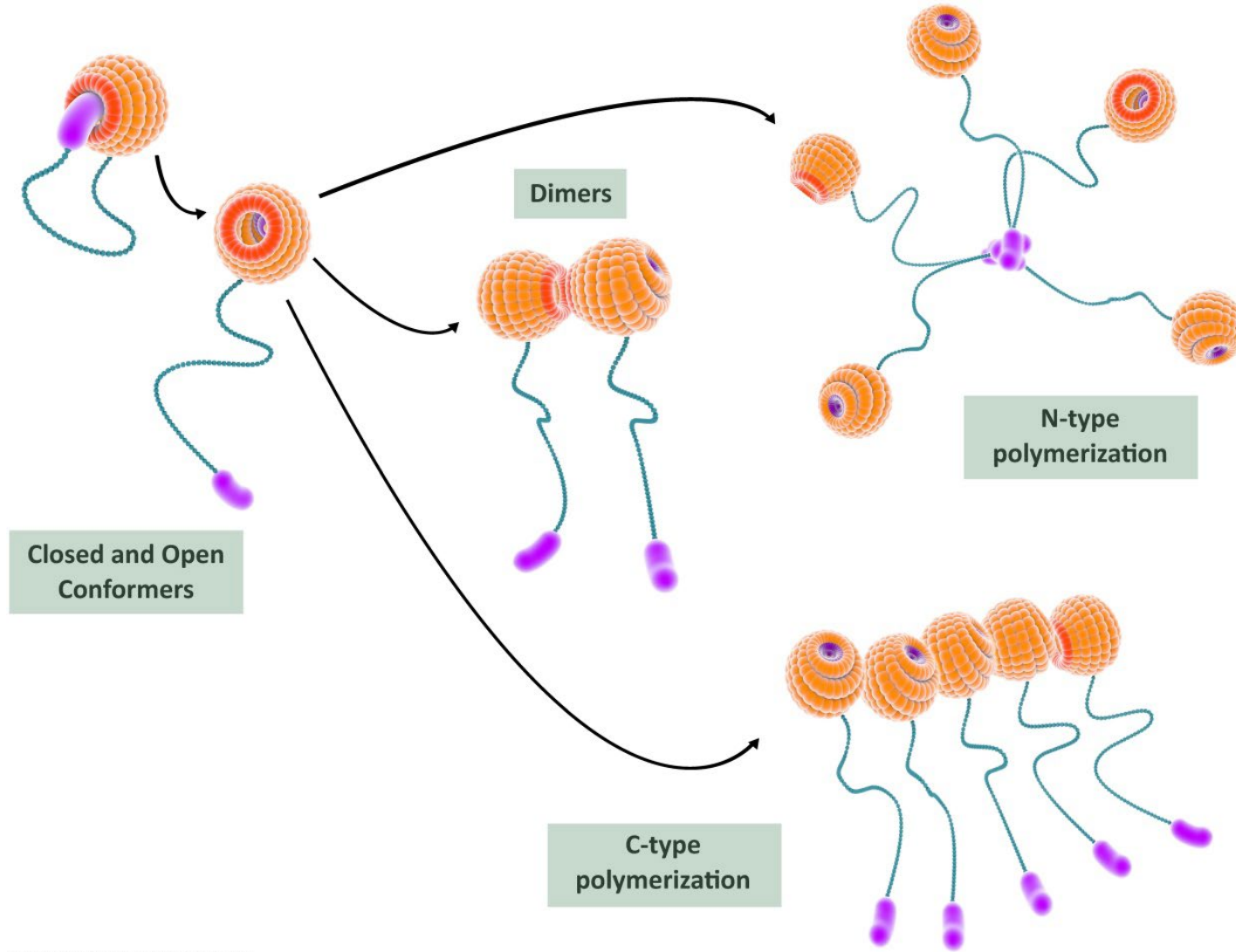


Illustration by Medvisuals/Maartje Kunen



# Belapectin a complex carbohydrate drug that inhibits galectin-3

- **In animal models of NASH (streptozotocin High-Fat Diet mice<sup>1</sup>) and fibrosis (thioacetamide treated rats<sup>2</sup>) belapectin was associated with:**
  - Decreases galectin-3 staining and galectin-3 expression in macrophages
  - Decreases NAFLD Activity Scores
  - Decreases collagen-1 expression, decreases hepatic collagen deposition (Sirius red), and decreases hepatic fibrosis (Ishak)
- **In toxicology studies, including monkeys, belapectin:**
  - Was well tolerated at high doses
  - Accumulated in macrophages with a residence time longer than in plasma
- **Belapectin was well tolerated and appeared safe in phase 1 and phase 2 clinical studies**
  - Carbohydrate-based molecules degraded by natural processes
  - No adverse safety signal identified
  - In a large phase 2 study with one year of biweekly infusion: dropout rate of 6%
  - Belapectin exposure does not appear to increase with higher degree of hepatic insufficiency
- **The phase 2 NASH cirrhosis study provided a proof of concept for efficacy, for the choice of a relevant clinical outcome (prevention of varices), and dose range selection**

<sup>1</sup> PLOS One 2013;8:e83481 <sup>2</sup> PLOS One 2013;8:e75351

# Randomized, double-blind, placebo-controlled phase 2b 162 NASH cirrhosis patients<sup>1</sup>

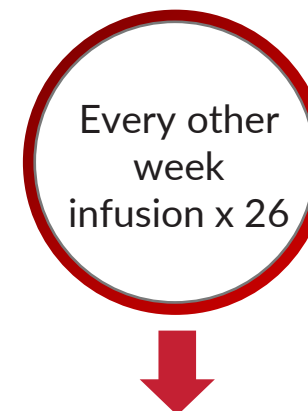
## Design

### Major inclusion criteria

- NASH cirrhosis (biopsy)
- Portal Hypertension: HVPG<sup>2</sup> ≥ 6 mmHg
- No cirrhosis complications
- No varices/varices (50:50)

| Endpoints           |                                    | Baseline | Week 54 |
|---------------------|------------------------------------|----------|---------|
| Primary endpoint    | Portal pressure: HVPG <sup>2</sup> | ✓        | ✓       |
| Secondary endpoints | Liver biopsy                       | ✓        | ✓       |
|                     | Varices (Endoscopy )               | ✓        | ✓       |
|                     | Cirrhosis decompensation           | ✓        | ✓       |

### Dosing and administration



| Treatment              | #Patients |
|------------------------|-----------|
| Placebo                | 54        |
| Belapectin 2 mg/kg LBM | 54        |
| Belapectin 8 mg/kg LBM | 54        |

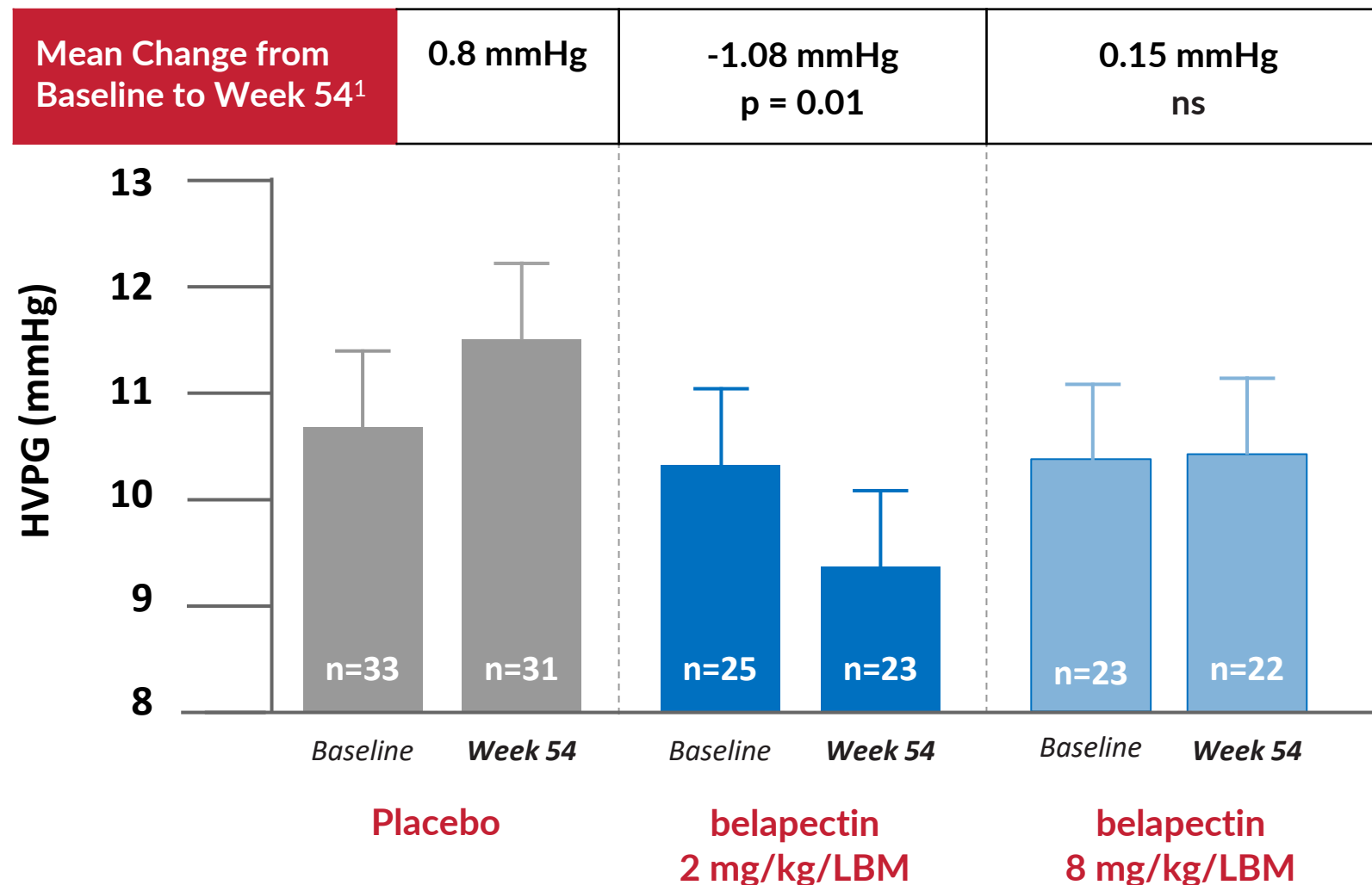
LBM – Lean Body Mass

<sup>1</sup> Chalasani et al. Gastroenterol 2020;158:1334-45

<sup>2</sup> HVPG = Hepatic Venous Pressure Gradient

# In patients without varice, belapectin 2 mg/kg LBM showed a statistically significant reduction in HVPG from baseline to week 54

Statistically significant effect of 2 mg/kg/LBM dose on change in HVPG at baseline



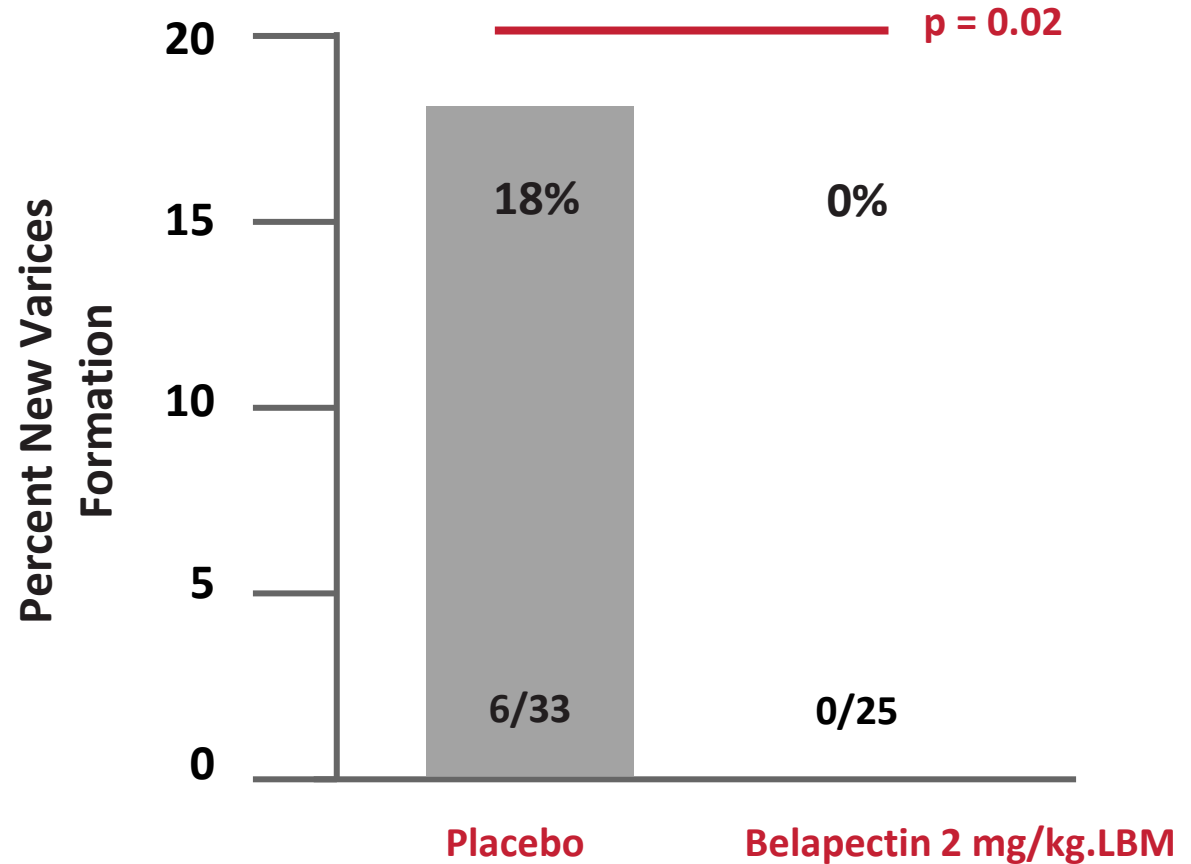
<sup>1</sup>ITT with LOCF, ANCOVA with LSD

Mean ± SEM

# Significantly fewer new varices on belapectin vs placebo

## No patients on 2 mg/kg.LBM developed new varices

Prevention of varices, a clinically relevant endpoint



<sup>1</sup> Chi Square

# **Belapectin demonstrated efficacy on a clinically meaningful endpoint where no current therapies exist**

- **Portal hypertension is a deleterious consequence of cirrhosis**
  - The dichotomy between compensated and decompensated cirrhosis is too restrictive and simplistic
  - What matters is whether portal hypertension is present or not
  - Increased portal pressure is associated with increased risk of decompensation and mortality
  - The increase in risk is a continuum of the same mechanism of action
  - Esophageal varices are the first clinical expression of portal hypertension, precede other complications of cirrhosis
- **For patients with portal hypertension who have not yet developed varices, there are no specific therapies available**
  - For a liver drug, the earlier the intervention to treat portal hypertension the more chance to be successful
  - Beta-blockers are for advanced portal hypertension (extra-hepatic vascular component)
  - Practice guidelines do not recommend beta-blockers for the prevention of esophageal varices
- **The phase 2 study provided a proof of concept for efficacy and for selecting the prevention of esophageal varices as a relevant clinical efficacy outcome**
- **Belapectin was safe and well tolerated in phase 2, at doses up to 8 mg/kg LBM**

# Next step: NAVIGATE belapectin's seamless, adaptive study

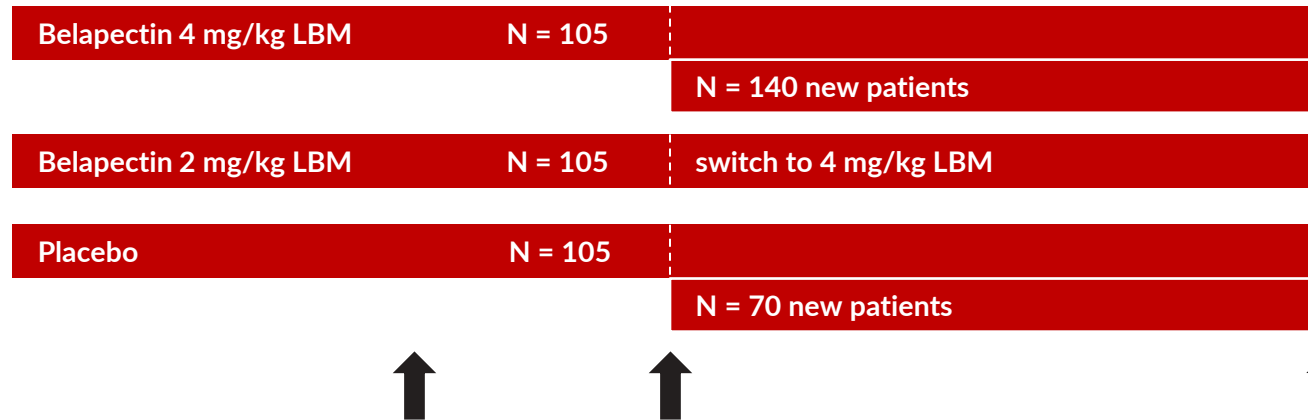
Screening →

18-Month  
Phase 2b

18-Month  
Phase 3

## Key Eligibility Criteria:

- 1). Nash cirrhosis
- 2). No varices on EGD
- 3). CTP Scores  $\leq 7$
- 4). Portal hypertension:
  - Thrombocytopenia
 Or at least 2
  - AST/ALT  $> 1$
  - Spleen  $\geq 14$  cm
  - Collaterals by imaging
  - Stiffness  $\geq 20$  kPa



Sample size re-estimation

Interim Analysis to Inform Phase 3  
1° endpoint: development of new varices

## Final Analysis

1° endpoint: development of new varices

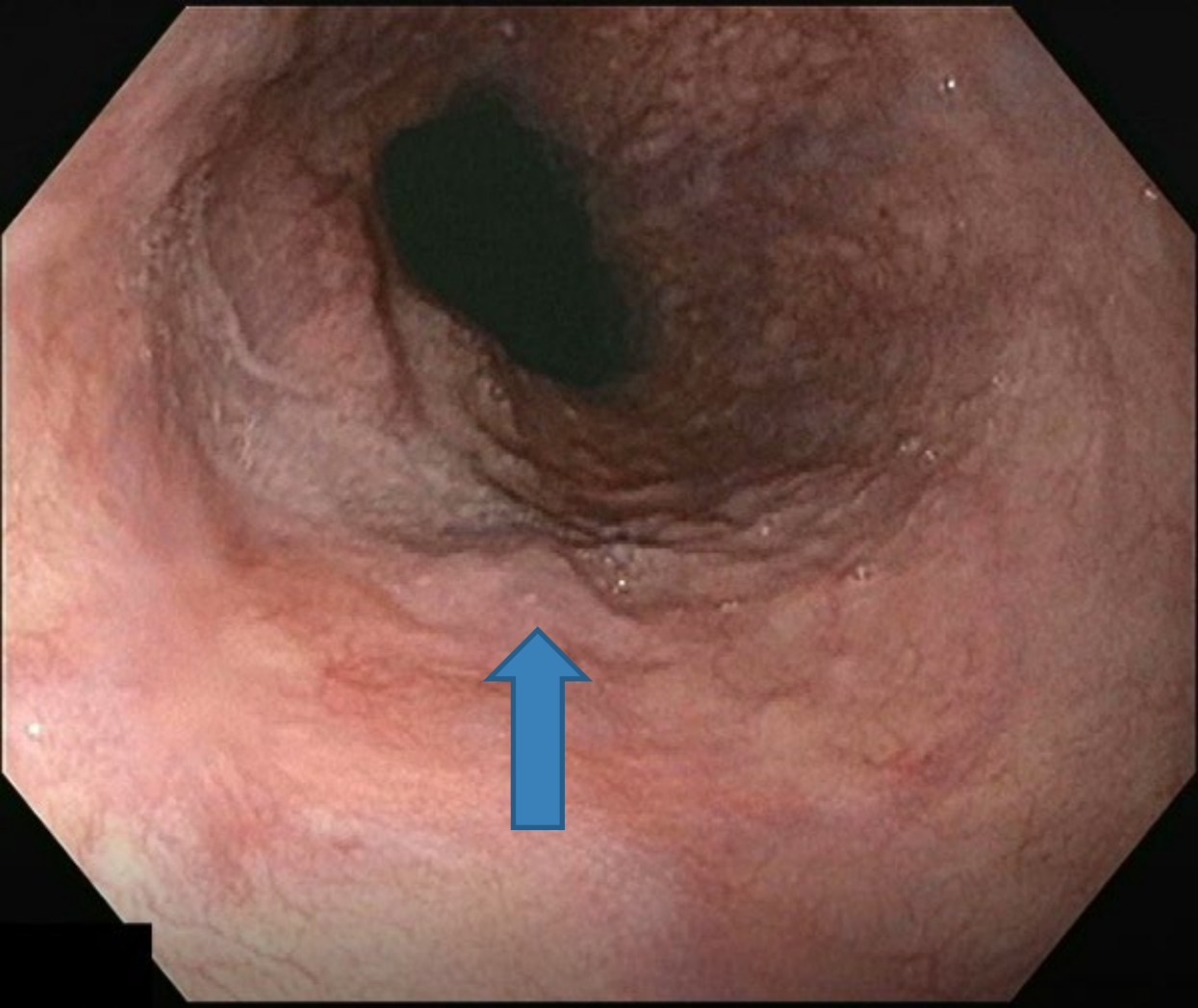
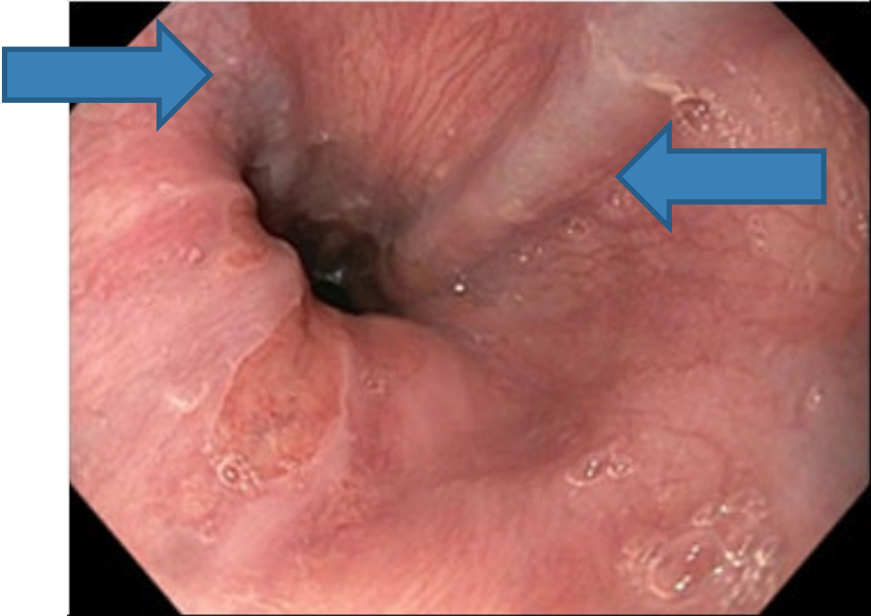
### 2° endpoints:

- Hepatic decompensation events
- All-cause mortality
- Proportion of patients with large varices or red wales
- Varices requiring treatment
- MELD  $\geq 15$
- Liver transplant
- Non-invasive biomarkers

## NAVIGATE update

- Recruitment ongoing
- Current objective: randomize approximately 315 patients in part 2b
- Approximately 130+ sites, 15 countries, 5 continents
- No systematic liver biopsies required
- Pre-screening on portal hypertension clinical criteria
- Central review of esophago-gastro-endoscopies
- Interim analysis phase 2b expected ~Q2 2024

# Esophageal varix





# Esophageal varices



# Belapectin Oncology Data Overview

- **Belapectin** activity demonstrated in tumor-bearing mice models (sarcoma, mammary carcinoma, and prostate adenocarcinoma)<sup>1</sup>
- **Belapectin** good tolerance, apparent safety, and efficacy demonstrated in a phase 1 study<sup>2</sup> and a phase 1 extension study in metastatic melanoma (MM) and head and neck squamous cell carcinoma (HNSCC):
  - Investigator-sponsored IND in collaboration with Galectin Therapeutics.
  - **Belapectin** used in combination with anti-PD-1 (Keytruda®, pembrolizumab).
  - Objective response observed in 50% of MM (7/14) and 33% of HNSCC (2/6) patients.
  - Extension in more advanced patients: 56% stable disease in MM (5/9) and 40% in HNSCC (2/5).
  - Combination is associated with fewer immune adverse events than expected.
  - Combination shows good tolerance and appears safe with no dose-limiting toxicity.
  - Combination significantly increases effector memory T-cell activation and reduces M-MDSCs in responders vs. non-responders.
  - Increased baseline expression of Gal3<sup>+</sup> tumor cells and PD-1<sup>+</sup>CD8<sup>+</sup> T cells in the periphery and higher serum trough levels of pembrolizumab correlate with clinical response.
- **Conclusion:** Clinical efficacy and safety proof of concept in combination with PD-1 inhibitor achieved.

<sup>1</sup> Sturgill ER *et al.* OncoImmunol 2021;10:e1892265 <sup>2</sup> Curti B. J Immunother Cancer 2021;9:e002371

# Summary of Belapectin Drug Development Program

- **NASH Cirrhosis is a major unmet medical need with a large potential market**
  - NASH-CX is the first positive phase 2 clinical data in a subset of patients without esophageal varices
  - Belapectin was safe and well-tolerated, improved portal pressure, and reduced development of varices
  - Galectin Therapeutics is competitively well positioned in the industry
  - Large, experienced global CRO conducting the NAVIGATE trial
  - First Patient randomized August 2020; Interim Analysis Data analysis expected 2Q-2024
  
- **Combination cancer immunotherapy with PD-1 inhibitor**
  - Galectin-3 important in cancer immunity, blocking it with belapectin showed encouraging early clinical results: Objective response in 50% of Metastatic Melanoma and 33% of advanced Head and Neck cancer.
  - Extension cohort showed positive results in partial response or stable disease (56% in 5 of 9 melanoma patients and 40% in 2 of 5 head and neck patients). The frequency and severity of toxicities related to pembrolizumab, notably immune-mediated adverse events, was less than anticipated
  - Potential to improve efficacy and safety of cancer immunotherapy
  - Plan to file IND for head and neck cancer in 2022.