



Belapectin, a galectin-3 inhibitor, for the treatment of NASH cirrhosis

December 2020, NASH summit

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NASDAQ: GALT

www.galectintherapeutics.com

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.

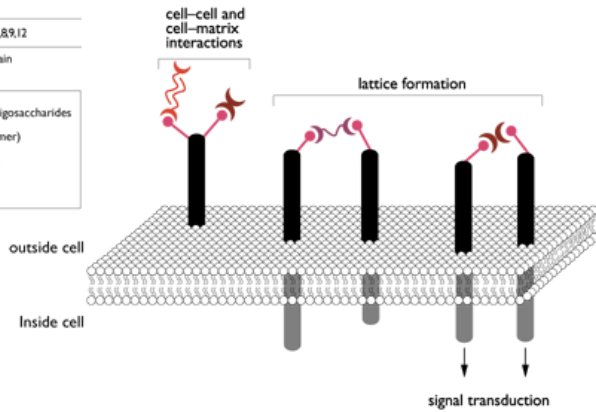
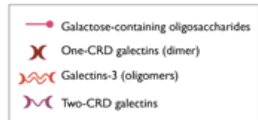
These statements include those regarding potential therapeutic benefits of our drugs, expectations, plans and timelines related to our clinical trials, supporting activities, potential partnering opportunities and estimated spending for 2020 and beyond. Factors that could cause our actual performance 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, 2019, 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.

Belapectin targets and disrupts the function of galectin-3, which plays a major role in the progression of fibrotic diseases

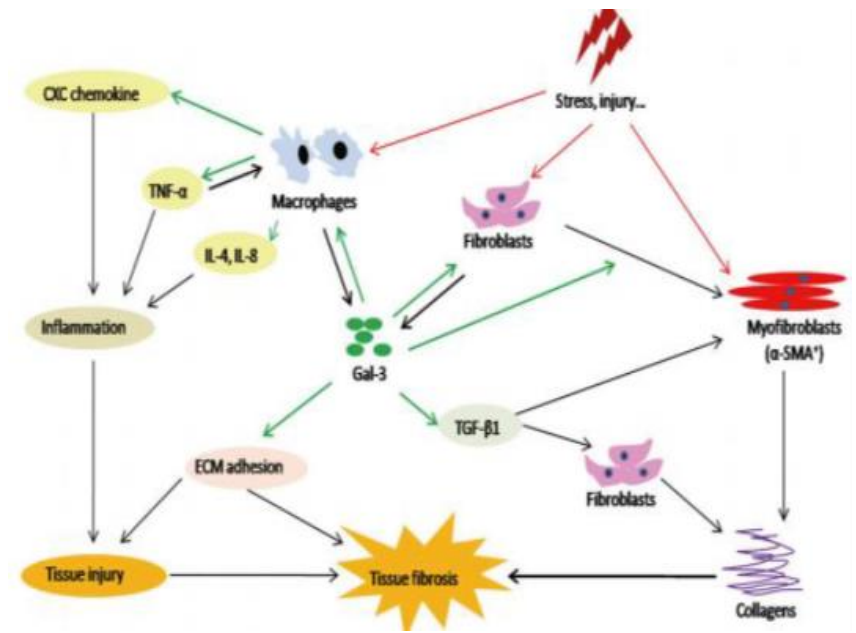
TYPE	STRUCTURE	GALECTIN
One-CRD		1,2,5,7,10,11,13,14,15
		3
Two-CRD		4,6,8,9,12



Galectin-3 has the ability to link glycoproteins to form a lattice structure on the cellular surface and promote cell-cell and cell-matrix interactions

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

Central role of Gal-3 in multiple pathological processes



* Henderson et al., PNAS, 2006.

Schematic representation of Galectin-3: a carbohydrate recognition domain and a tail

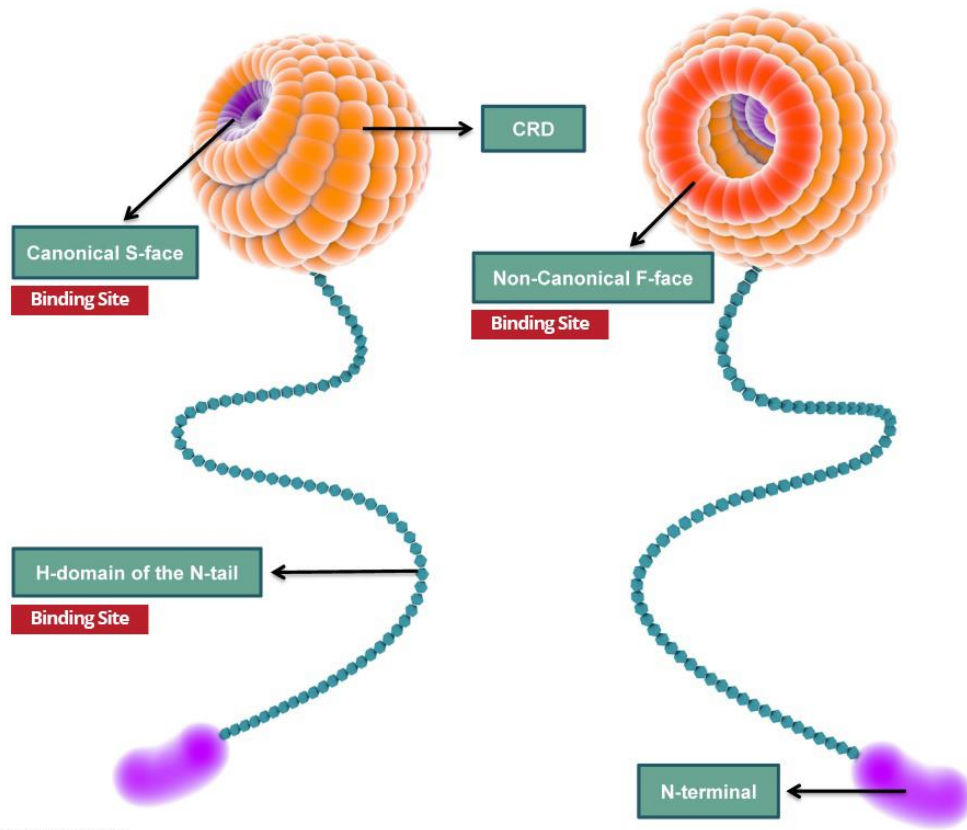


Illustration by Medvisuals/Maartje Kunen

Schematic representation of Galectin-3: unique conformation and polymerization.

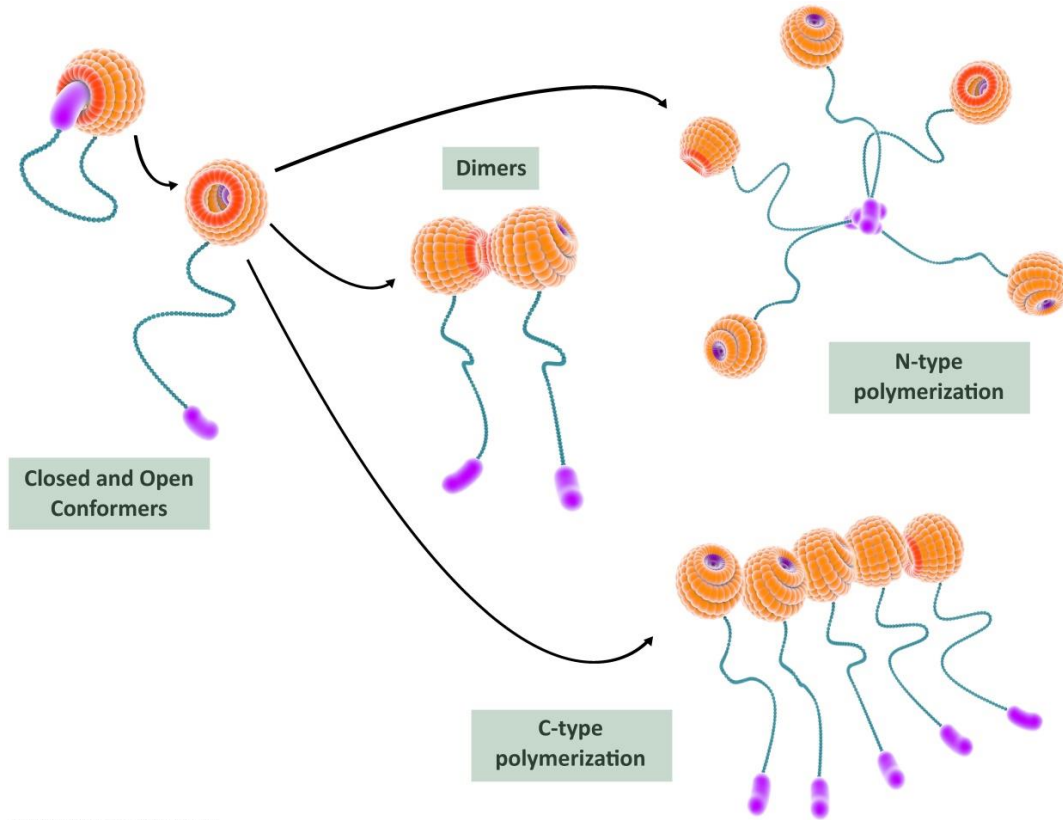
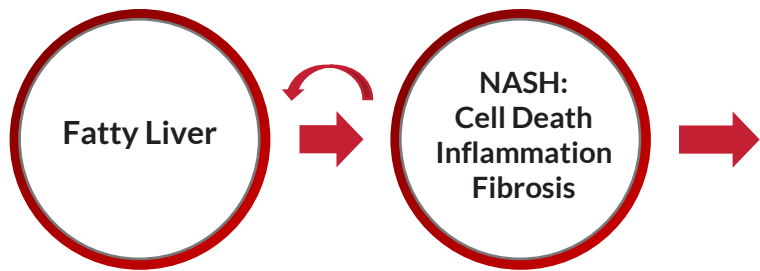




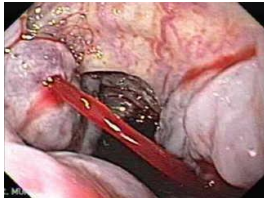
Illustration by Medvisuals/Maartje Kunen

There is currently no treatment for NASH cirrhosis, a progressive disease that may result in liver failure and increased mortality

The majority of companies are focused on pre-cirrhotic NASH



Few companies with Phase 2/3 trials in NASH cirrhosis

Compensated cirrhosis		Decompensated cirrhosis
Stage 1	Stage 2	Stage 3 and 4
No varices	Varices develop	Bleeding, ascites, encephalopathy
		
≥6	>10	>12
Portal pressure (mmHg)		
Low one year mortality (1-3%)		~50% one year mortality

Unlike many companies in the NASH space, Galectin is focusing on the *compensated cirrhotic* patients

Belapectin a complex carbohydrate drug that inhibits galectin-3

- **In animal models of NASH (streptozotocin High-Fat Diet mice¹) and fibrosis (thioacetamide treated rats²) belapectin was associated with:**
 - Decreases Galectin-3 staining and expression in macrophages
 - Decreases NAFLD Activity Scores
 - Decreases collagen-1 expression, decreases hepatic collagen deposition (Sirius red), and decreases hepatic fibrosis (Ishak)
 - Decrease portal pressure
- **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 specific signal identified
 - In a large phase 2 study over one year : dropout rate of 6%
- **The phase 2 NASH-CX in NASH cirrhosis provided an efficacy proof of concept and a rationale for selecting doses and primary efficacy primary outcome (prevention of varices)**

¹ PLOS One 2013;8:e83481 ² PLOS One 2013;8:e75351

NASH-CX: randomized, double-blind, placebo-controlled phase 2b in 162 NASH cirrhosis patients¹

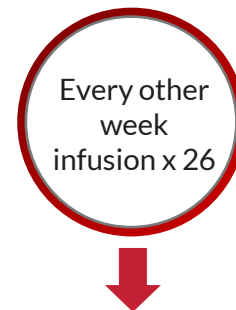
Phase 2b Trial design

Major inclusion criteria

- NASH cirrhosis (biopsy)
- HVPG² ≥ 6 mmHg
- No cirrhosis complications
- No or small varices (50:50)

Endpoints		Baseline	Week 54
Primary endpoint	Portal pressure: HVPG ²	✓	✓
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

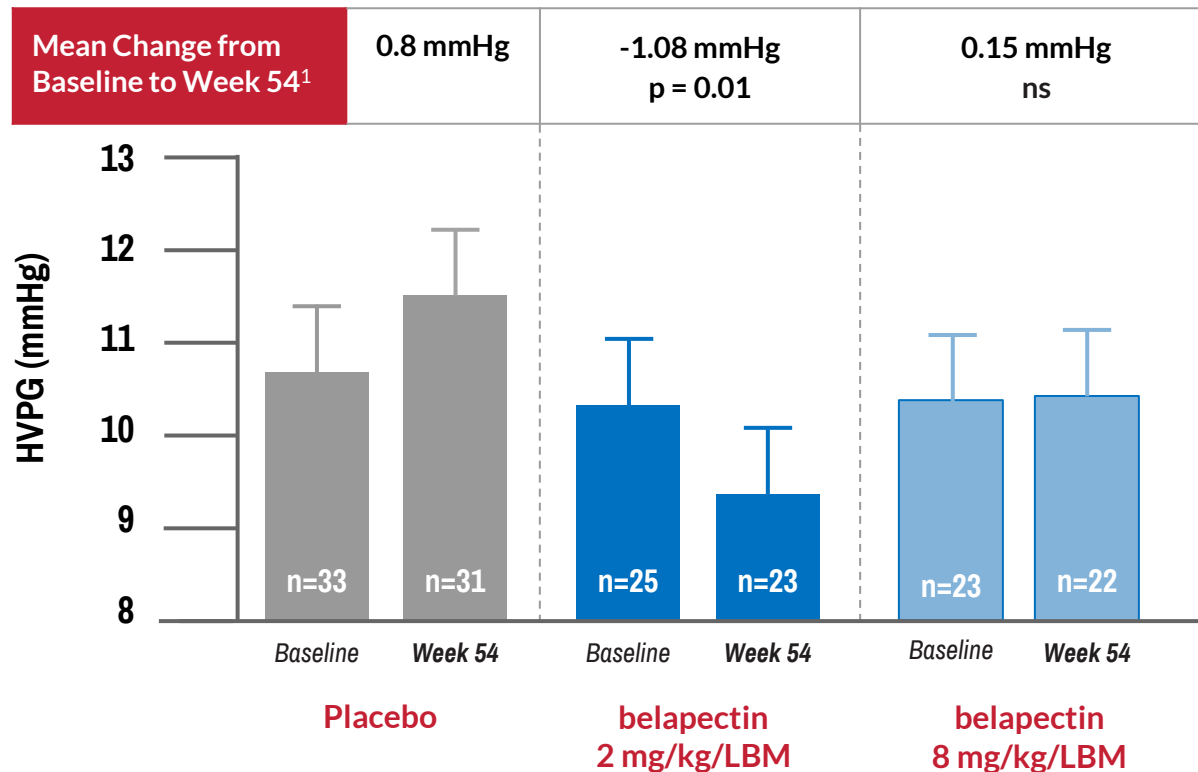
LBM – Lean Body Mass

¹ Chalasani et al. Gastroenterol 2020;158:1334-45

² 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 for

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



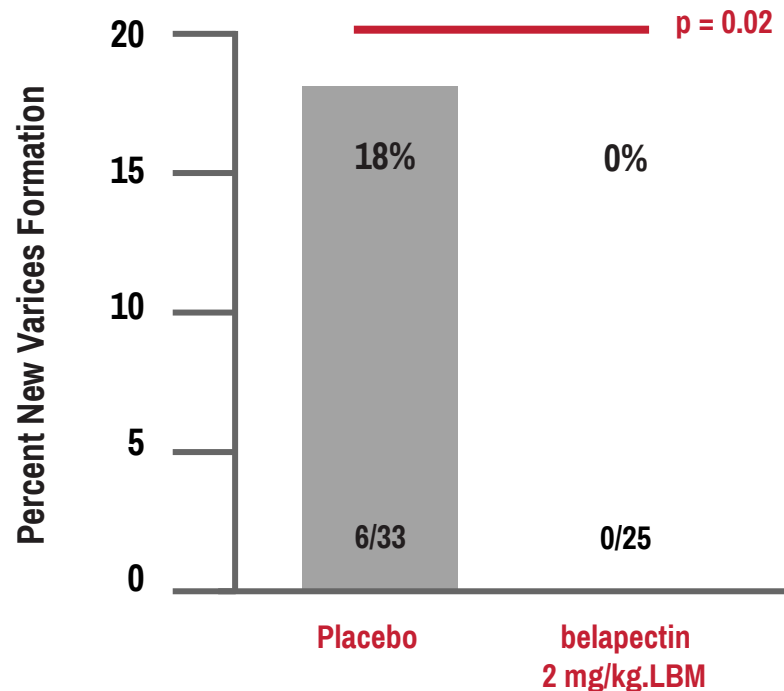
¹ITT with LOCF, ANCOVA with LSD

Mean ± SEM

Significantly fewer new varices on belapectin vs placebo

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

Trial hit a clinically relevant endpoint related to patient outcomes



¹ Chi Square

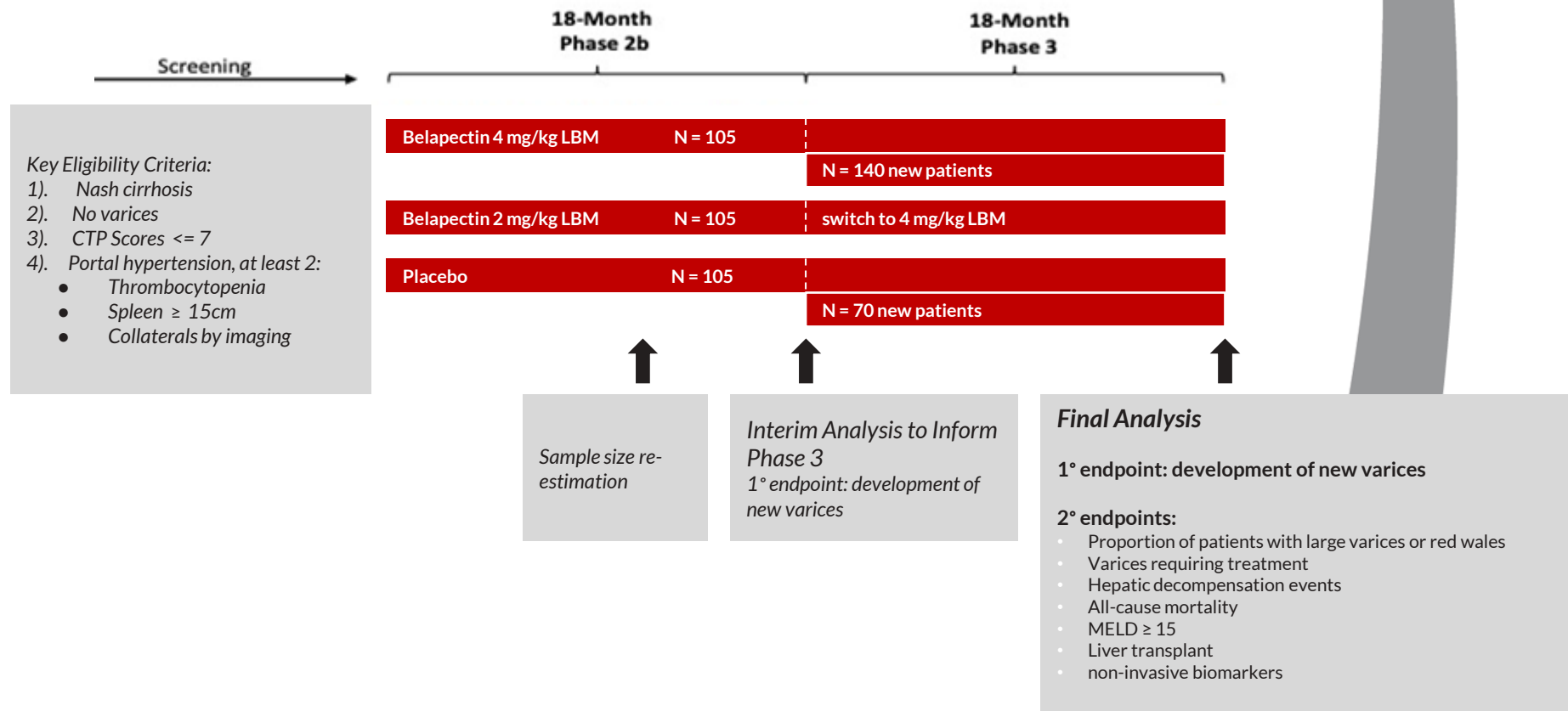
Belapectin demonstrated efficacy on a clinically meaningful endpoint where no current therapies exist

- **Portal hypertension is a deleterious consequence of cirrhosis and responsible for the majority of cirrhotic complications**
 - Portal pressure of ≥ 10 mmHg (HVPG) is associated with increased risk of decompensation and mortality
 - The increase in portal pressure and the development of varices are a continuum of the same mechanism of action
- **For patients with portal hypertension who have not yet developed varices, there are no specific therapies available**
 - Beta-blockers likely do not prevent development of varices/disease progression in early-stage cirrhosis patients (may improve outcomes in patients with portal hypertension and varices)
 - Practice guidelines do not recommend beta-blockers for the prevention of esophageal varice
 - No specific therapy to address fibrosis at the cirrhotic stage
- **Belapectin was safe and well tolerated in NASH-CX, at doses up to 8 mg/kg LBM**
- **The NASH-CX study provided a proof of concept for efficacy and for selecting the prevention of esophageal varices as a primary outcome to move forward**

Adaptively Designed Phase 2b/3 NASH-RX Study Overview

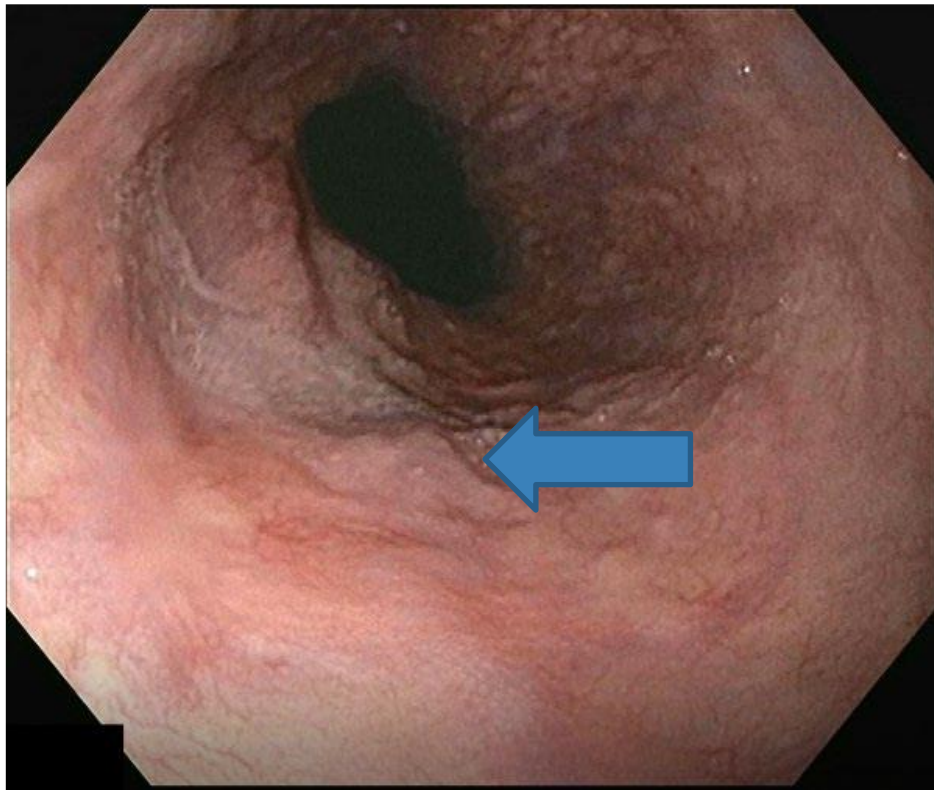
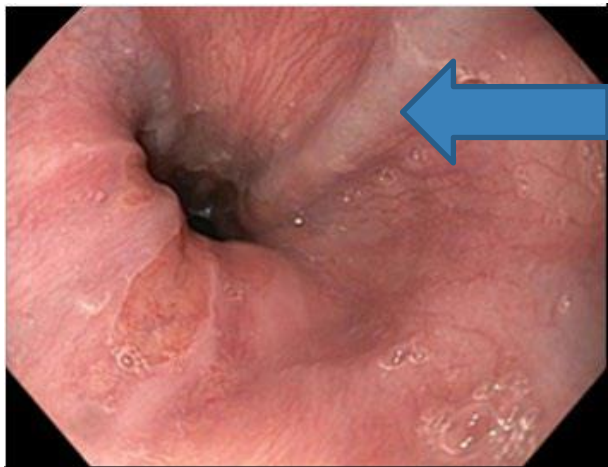
- NASH *cirrhosis*
 - Patients with NASH cirrhosis have the greatest immediate medical need
 - This population is not being addressed by most drug developers, who focus on the prevention of NASH cirrhosis using liver biopsies as an efficacy endpoint
 - We designed an innovative seamless, adaptive Phase 2b/3 study with leading NASH experts
- Progression to esophageal varices is a potential surrogate endpoint
- Progression to large varices is a component of a composite clinical endpoint
- Upper GI endoscopies are part of routine clinical practice to follow cirrhotic patients
- NASH cirrhosis patients with portal hypertension are at risk of developing esophageal varices which may bleed and are then life-threatening
- It is possible to identify portal hypertension clinically without having to perform invasive hemodynamic studies

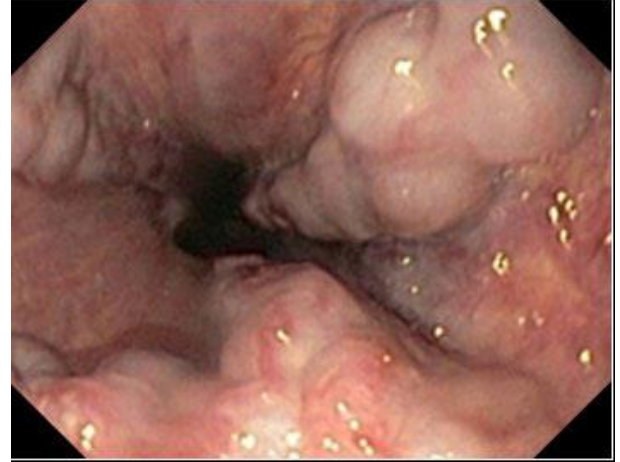
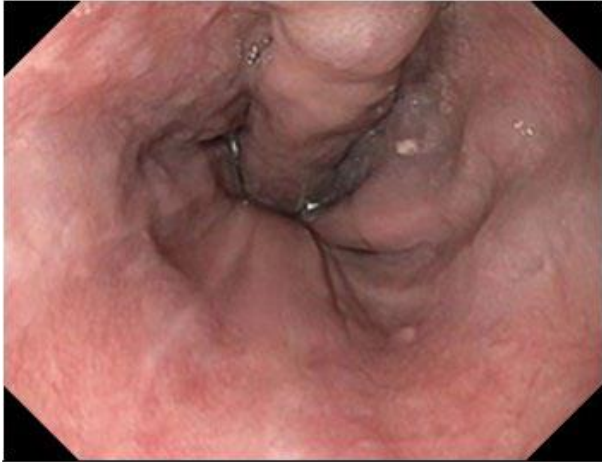
Belapectin Phase 2b/3 Adaptive Study Design



Belapectin Phase 2b/3 trial – NASH-RX summary

- First patient randomized August 2020
- ~130+ sites, 12 countries in North America, Europe, Asia and Australia
- Overall ~500 patients (~ 315 in phase 2b)
- Recruitment for phase 2b: ~ 12 – 14 months
- Key inclusion criteria
 - NASH cirrhosis (baseline or historical liver biopsy)
 - Clinical sign of portal hypertension (e.g., low platelet count, splenomegaly)
 - No esophageal varices (esophago-gastro endoscopy)
- Interim analysis phase 2b expected ~Q2 2023





Thank you