

Galectin Therapeutics Corporate Overview January 2025



### **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 2024 and beyond. Factors that could cause our actual performance to differ materially from those discussed in the forward-looking statements include, among others, that our trials and supporting CMC information may be impacted by a resurgence of COVID-19 or a similar outbreak of an infectious disease.

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, 2023, 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.



### **Investment Highlights**

Developing galectin-based therapeutics to improve the lives of patients with chronic liver diseases and cancer

**Focused Pipeline** 

MASH Cirrhosis

Belapectin is a novel, potent, galectin-3 inhibitor with Fast Track Designation Low toxicity as a carbohydrate-based molecule which is degraded by natural processes Patent protection through 2032

Only company to <u>exclusively</u> focus on treatment for MASH cirrhosis and portal hypertension Significant efficacy observed in cirrhotic patients without varices Promising NAVIGATE topline results at 18 month read out, ≥40% reduction in new varices vs placebo in ITT; significantly lower incidence of new varices in per protocol population

Oncology (Combination Therapy)

Encouraging clinical response in difficult-to-treat cancers in combination with checkpoint inhibitor IND filed and approval to proceed received from FDA (Head & Neck cancer)



### **Highly Experienced Leadership Team**



JOEL LEWIS Chief Executive Officer & President Financial executive with over 25 years of management experience in a taxation, restructuring, acquisition, and private equity ventures.



JEFF KATSTRA VP, CMC / Pharmaceutical Development Highly experienced in pharmaceutical development of novel formulations and medicines with advanced manufacturing techniques and bringing them to approval.



KHURRAM JAMIL, M.D. Chief Medical Officer Have two decades of expereince leading drug development across various stages of clinical trials in the pharmaceutical industry. Led multiple new drug application filings and secured approvals from several regulatory agencies.



JESSICA KOPACZEWSKI Senior Director, Clinical Operations Over 25 years diverse experience in the pharmaceutical research industry supporting global study operations from site to personnel management.



JACK W. CALLICUTT Chief Financial Officer Over 32 years of public and private company experience including more than a decade of audit, tax and SEC registrant experience with a major accounting firm.



SETH ZUCKERMAN Senior Director, Biostatistics Over 28 years of experience working in the pharmaceutical industry in clinical data and trial management with 23 years as statistician.



SUE THORNTON VP Regulatory Affairs More than 20 years of domestic and international drug development experience encompassing all aspects of global Regulatory Affairs and Quality Assurance.



**EZRA LOWE, Ph.D.** VP, Clinical and Preclinical Pharmacology Extensive experience in clinical pharmacology, drug metabolism, and pharmacokinetics with various drug formats and across therapeutic areas, leading to 10 different global drug approvals.



### **Laser-Focused Pipeline**

Clinical Program		Development Stage				
Drug	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Fibrosis						
	MASH Cirrebosis and Dortal					

Belapectin	Belapectin	MASH Cirrhosis and Portal Hypertension	

#### Cancer Immunotherapy (Combination therapy)

Belapectin + Keytruda	Melanoma + Head / Neck Cancer			

Oral Galectin-3 Inhibitors

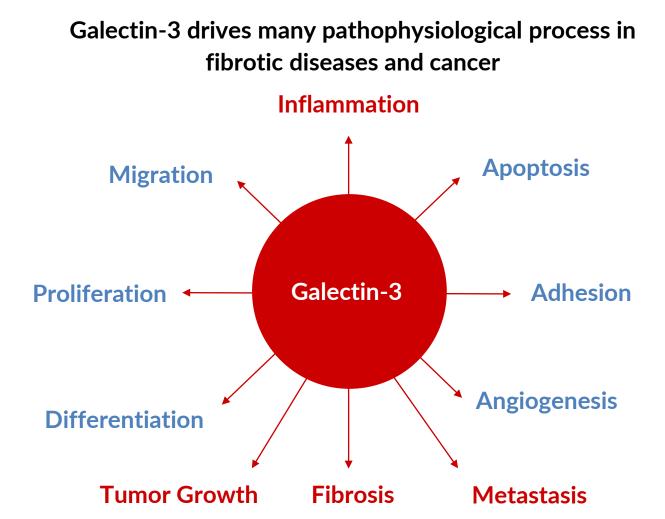
Discovery program to identify subcutaneous forms of carbohydrates			
and oral small molecules			
and oral small molecules			

# **Galectin-3 is a Promising Therapeutic Target in Inflammatory and Fibrotic Diseases**<sup>1,2</sup>

Galectin 3 is part of the galectin family of sugar-binding proteins that act as a "molecular glue", it is:

- Predominantly produced by activated macrophages
- Involved in a wide number of biological and pathological processes

Galectin-3 recruits macrophages to injury sites and promotes chronic inflammation by activating proinflammatory pathways





# Belapectin: a Proprietary Galectin-3 Inhibitor with Low Toxicity and Anti-fibrotic Activity

#### **Belapectin Preclinical Data:**

In animal models of MASH (streptozotocin High-Fat Diet mice<sup>1</sup>) and cirrhosis (thioacetamide treated rats<sup>2</sup>) belapectin was associated with decreased:

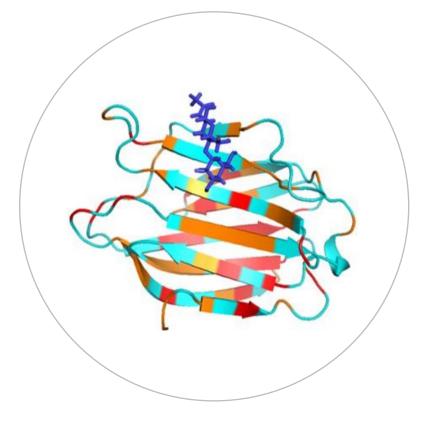
- Galectin-3 staining and galectin-3 expression in macrophages
- NAFLD Activity Scores
- Collagen-1 expression
- Hepatic collagen deposition
- Hepatic fibrosis
- Portal pressure

#### In toxicology studies, including monkeys, belapectin:

- Was well-tolerated even at high doses
- Accumulated in macrophages with a residence time longer than in plasma

Belapectin is a polysaccharide polymer comprising galacturonic acid, galactose, arabinose, rhamnose and smaller amounts of other sugars







# **MASH Cirrhosis**



# MASH Cirrhosis Represents a Significant Market Opportunity in the U.S. with No FDA-Approved Treatment



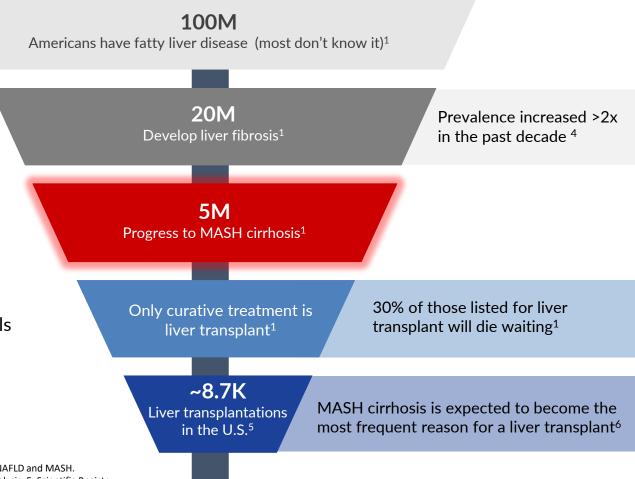
Metabolic dysfunction-associated steatohepatitis (MASH), previously known as non-alcoholic steatohepatitis (NASH), is characterized by fat accumulation, inflammation and fibrosis of the liver<sup>1</sup>

3%-5% of the global population is estimated to be affected by MASH, though the disease is considered to be underdiagnosed<sup>2</sup>

There are genetic predisposition to MASH, yet certain health conditions put patients at increased risk:<sup>3</sup>

- Being overweight or obese
- Having hypertension, high cholesterol or high triglyceride levels
- Having type 2 diabetes, insulin resistance or prediabetes

#### Addressable market in the U.S.



1. Fatty Liver Foundation. https://www.fattyliverfoundation.org/#gsc.tab=0. .2. Sherif ZA, et al. *Dig Dis Sci*. 2016;61(5):1214-25. 3. NIDDK. NAFLD and MASH. https://www.niddk.nih.gov/health-information/liver-disease/nafld-nash/symptoms-causes. 4. Datamonitor Healthcare. MASH Disease Analysis. 5. Scientific Registry of Transplant Recipients. OPTN/SRTR 2021 Annual Data Report: Liver. https://srtr.transplant.hrsa.gov/annual\_reports/2021/Liver.aspx. 6. Stepanova M, et al. *Hepatol Commun*. 2022;6(7):1506-1515.

# Belapectin is a Novel Therapy with First- and Best-in-Class Potential in MASH Cirrhosis



#### **United States Estimates<sup>1</sup>**



Patients with compensated MASH cirrhosis in 2024



Patients with compensated cirrhosis and portal hypertension with no varices in 2024



Peak belapectin sales in U.S.

#### 3<sup>rd</sup> Party Market Opportunity Assessment Suggests<sup>1</sup>

Potential 50-100% Adoption Rate

Limited current treatment options:

- Cirrhotic management focuses on stabilization and delaying progression
- Management directed towards comorbidities

Highly favorable perception of belapectin indication, MoA and safety by HCPs

Payers believe in the high unmet need in MASH cirrhosis

A significant unmet need exists for MASH compensated cirrhosis patients with portal hypertension due to disease severity and risk of decompensation



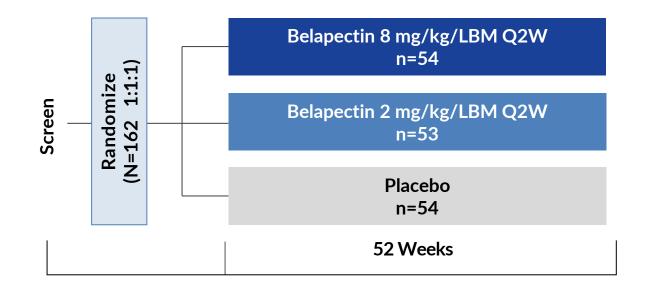
### When to Intervene in Cirrhosis- before its too late!

	Decompensated cirrhosis		
No Portal Hypertension		Portal Hypertension	
No varices	No varices Varices, small to large   Image: Image interval and image in		Varices Bleeding, ascites, encephalopathy
≥6 HVPG <sup>1</sup> mm Hg >10			
	One year mortality 1	One year mortality ~50%	

There are no approved therapies to reverse portal hypertension once it develops in MASH Cirrhosis

# Phase 2b Study of Belapectin in Patients with MASH Cirrhosis: GT-026 Trial





#### Main inclusion criteria

- · MASH cirrhosis (biopsy)
- Portal Hypertension: HVPG  $\geq$  6 mmHg
- · No cirrhosis complications
- No varices/varices (50:50)

#### **Primary endpoint**

 Portal pressure (HPVG) change from baseline to Week 54

#### Secondary endpoints at Week 54

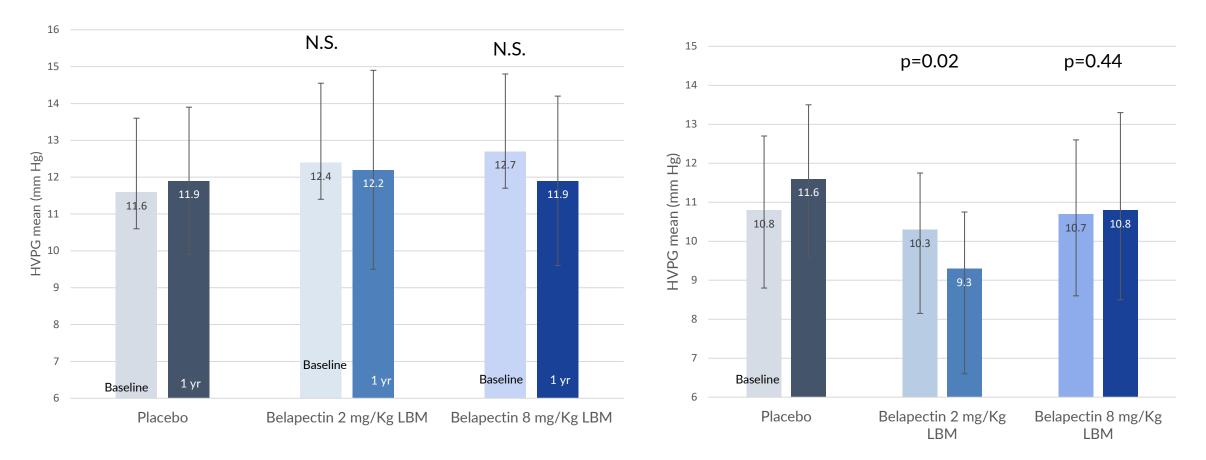
- Liver biopsy
- Varices (esophago-gastric endoscopy)
- Cirrhosis decompensation



## Belapectin Impact on HPVG at One Year<sup>1,\*</sup>

ITT Population

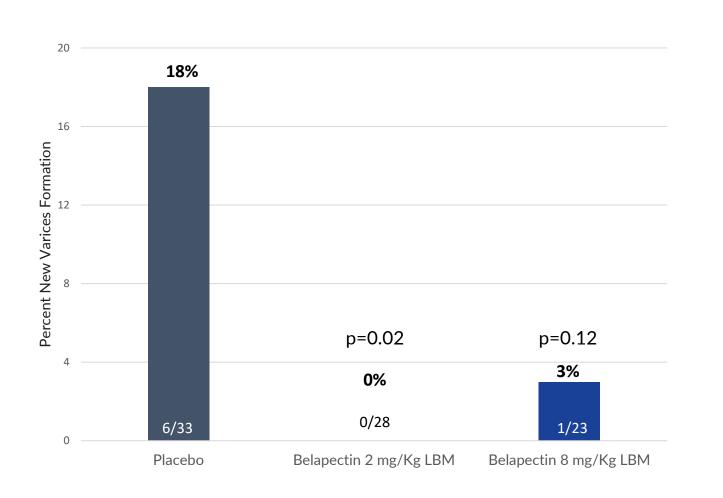
Subjects with no varices at baseline



HVPG = Hepatic Venous Pressure Gradient; LBM=lean body mass, N.S.=non significant. \*ITT with LOCF, ANCOVA with baseline as covariate and treatment as factors, Bonferroni-Holm.

1. Chalasani N, et al. Gastroentrol. 2020;158:1334-45.

## Belapectin Reduces Emergence of Varices in Patients with Galectin MASH Cirrhosis<sup>1,\*</sup>

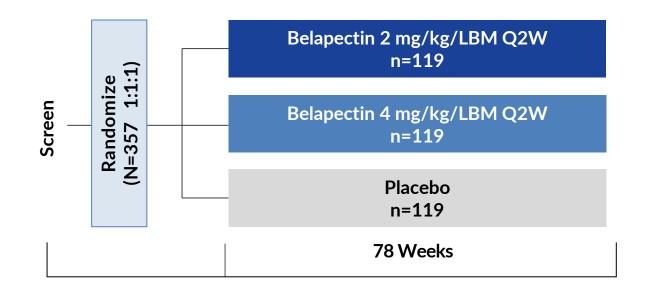


Significantly fewer new varices on belapectin vs placebo

*No patients* on <u>2 mg/kg/LBM</u> developed new varices

Belapectin demonstrated efficacy on a clinicallymeaningful endpoint where no current therapies exist

# NAVIGATE Trial: Belapectin for Prevention ofGalectiVarices in Patients with MASH cirrhosis and Portal Hypertension



#### **Patient Population**

- MASH cirrhosis
- Diagnosis of Portal Hypertension using Baveno criteria

(via non-invasive markers as per latest guidelines)

EGDs assessed via central review by multiple blinded reviewers.

Originally the NAVIGATE trial was designed as an adaptive Phase 2b/3 trial for 36-month duration. However, based on FDA feedback, the Company made the decision to analyze the stage 1 (18 month) as stand-alone clinical trial.



# NAVIGATE Study: Patient Population and Efficacy Endpoints

#### Key inclusion criteria

MASH cirrhosis

No varices on EGD

CTP Scores <7

Portal hypertension:

- Thrombocytopenia or at least
- AST/ALT > 1
- Spleen ≥ 14 cm
- Collaterals by imaging
- Stiffness ≥ 20 kPa

#### Primary endpoint

- Development of new varices (composite strategy) in ITT population-
  - 1. Number of subjects with varices
  - Subject with intercurrent events (ICE\*)
  - 3. Subject with missing EGDs and no ICE
- Pre-defined per protocol population-
  - Development of new varices per protocol

#### Secondary endpoint

Hepatic decompensation events

All-cause mortality

Proportion of patients with large varices or red wales

Varices requiring treatment

MELD ≥ 15

Liver transplant

Non-invasive biomarkers

ALT=alanine aminotransferase ; AST=aspartate transaminase; CTP=Child-Turcotte-Pugh; MELD=model for end-stage liver disease.

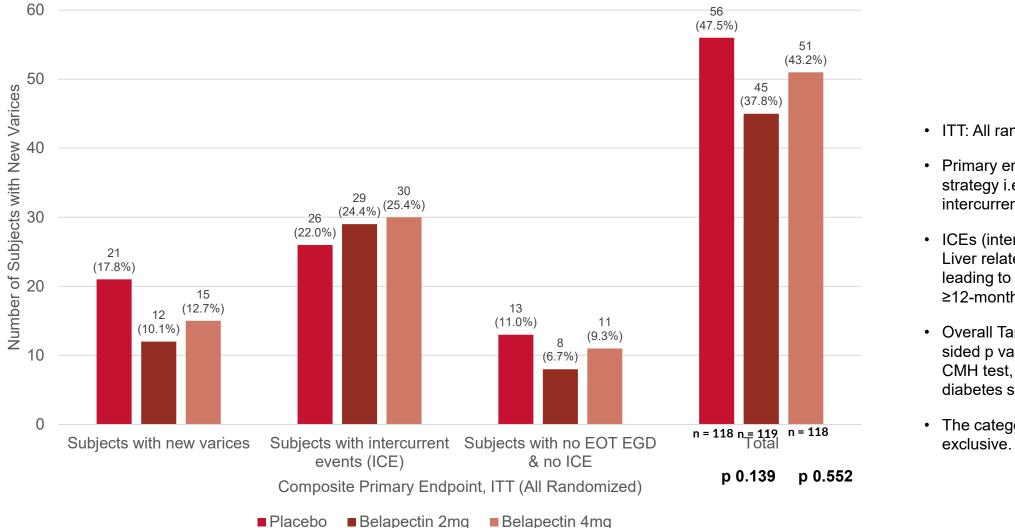
\*Intercurrent events include; Liver related clinical events, any AE leading to discontinuation, TIPS; ≥12-month use of GLP-1 or NSBB

#### Baseline demographics Table 14.1.3.1



Baseline Demographics and Clinical Characteristics (n=355)				
	Placebo (N = 118)	2mg/kg LBM (N = 119)	4mg/kg LBM (N = 118)	
	Mean (Standard Deviation)	Mean (Standard Deviation)	Mean (Standard Deviation)	
Age (years)	60.4 (8.50)	60.6 (8.82)	59.0 (9.14)	
Gender (female), n	72 (61.0)	75 (63.0)	83 (70.3)	
Ethnicity (Hispanic), n	34 (28.8)	39 (32.8)	33 (28.0)	
Race (white), n	104 (88.1)	107 (89.9)	111 (94.1)	
Weight (kg)	94.2 (21.68)	98.1 (24.30)	94.6 (20.95)	
BMI (Kg/m²)	33.82 (6.467)	34.88 (6.683)	34.53 (6.223)	
Hypertension	89 (75.4)	89 (74.8)	82 (69.5)	
Type 2 Diabetes	80 (67.8)	79 (66.4)	79 (66.9)	
HbA1C %	6.4 (1.27)	6.3 (1.13)	6.4 (1.09)	
Alanine Aminotransferase (ALT), U/L	46.3 (29.92)	38.9 (26.88)	39.7 (20.22)	
Aspartate Aminotransferase (AST), U/L	46.7 (23.52)	41.8 (24.40)	43.6 (21.90)	
Platelets (per μL)	130.1 (39.66)	127.6 (48.39)	136.4 (53.62)	
Liver Stiffness Measurement (kPa)	24.22 (12.179)	24.63 (13.548)	25.67 (13.196)	
Spleen (cm)	13.79 (2.750)	13.97 (2.602)	13.87 (2.436)	
MELD Score	7.6 (1.65)	7.9 (2.46)	7.5 (1.55)	
Child Pugh Score	5.1 (0.29)	5.1 (0.31)	5.0 (0.18)	
Statins (n)	49 (41.5)	55 (46.2)	47 (39.8)	
GLP-1 agonist (n)	24 (20.3)	26 (21.8)	27 (22.9)	

#### **NAVIGATE 18-month Primary Analyses Result**



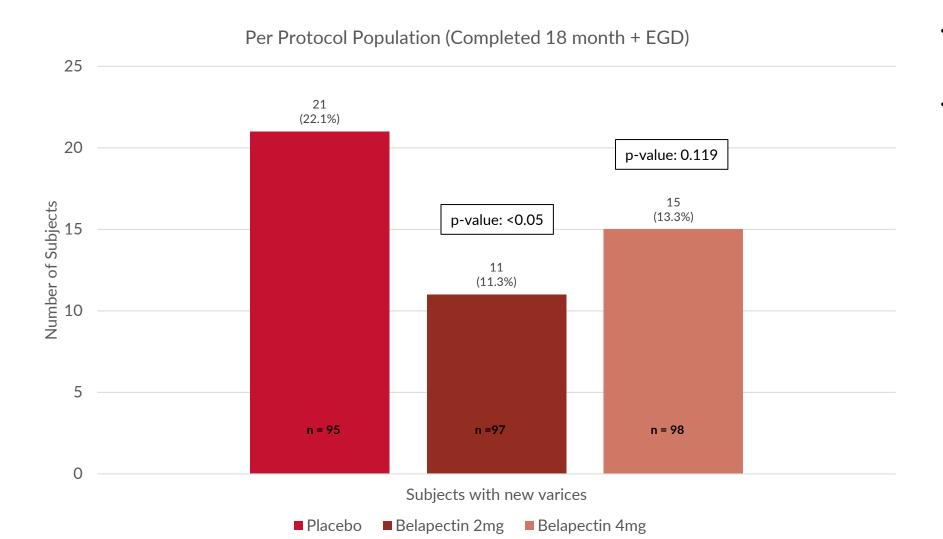
• ITT: All randomized subjects

Galectin G

- Primary end point composite strategy i.e. new varices and or intercurrent events or drop out
- ICEs (intercurrent events) include; Liver related clinical events, AE leading to discontinuation, TIPS; ≥12-month use of GLP-1 or NSBB
- Overall Target Significance level 2sided p value of 0.05; p: 0.048, using CMH test, stratified by Type 2 diabetes status at randomization.
- The categories are not mutually exclusive.

#### **NAVIGATE 18-month Primary Analyses Result**

#### Per protocol population





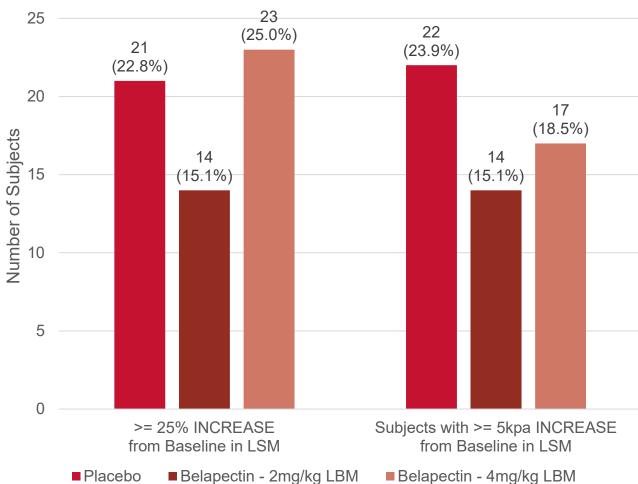
- Per Protocol: All ITT subjects who completed 18 months of treatment and an end of treatment (EOT) EDG
- Overall Target Significance level 2sided p value of 0.05; using CMH test, stratified by Type 2 diabetes status at randomization.

#### Categorical Changes in Liver Stiffness Measure LSM (kPa) Baseline to 18 month Per-Protocol (N = 277) Table 14.2.5.1.1.3



		<u>Belapectin</u>		
	Placebo (N = 92)	2mg/kg LBM (N = 93)	4mg/kg LBM (N = 92)	
Baseline LSM Value (kPA)				
Mean (SD)	23.3 (11.1)	22.9 (10.6)	24.4 (11.8 )	
Median	22.4	21.5	23.4	
W78/EOT LSM Value (kPa)				
Mean (SD)	22.5 (13.6)	21.2 (12.9)	22.8 (13.8)	
Change from Baseline in W78/EOT LSM Value (kPa)				
Mean (SD)	-0.8 (11.8)	-1.7 (9.7)	-1.5 (12.6)	
% Change from Baseline in W78/EOT LSM Value (kPa) *				
Mean %	9.9	-4.3	9.3	

\* Percentage change calculated for each individual subject



#### Categorical Changes in ELF Score- Baseline to 18 months Per-Protocol Table 14.2.5.1.2.2 (N: 275)



22

20 (23.2%)

(21.5%)

Subjects with ELF Value <= 9.8

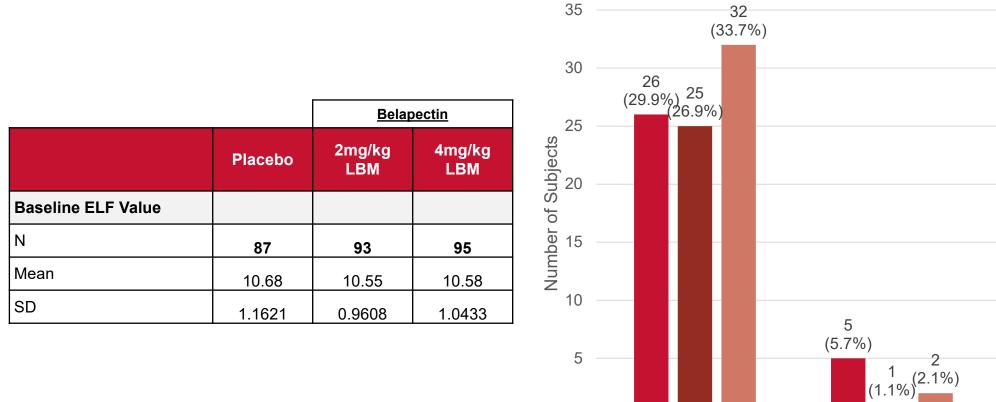
11

(12.6%)

Belapectin - 4mg/kg LBM

ELF Value >= 13

Belapectin - 2mg/kg LBM



ELF Enhanced Liver Fibrosis Score- combined for HA, PIIINP and TIMP-1

ELF: Risk of disease progression. < 9.8 Low risk, ≥11.3 mid risk, highest risk ≥13

0

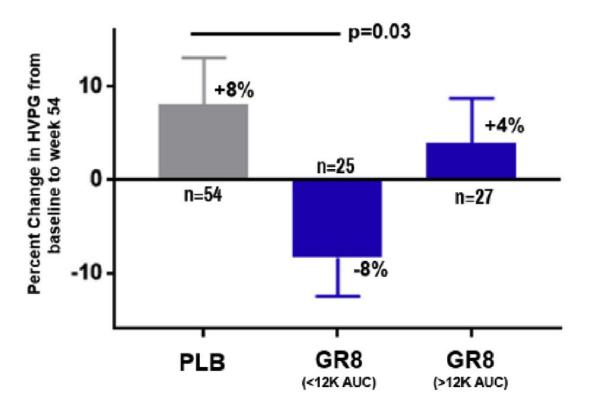
ELF Value >= 11.3

Placebo



# Lack of Dose Response at Higher Doses of Belapectin in GT-026 were also observed in NAVIGATE trial

- Based on findings from preclinical and clinical trials to date, Belapectin likely demonstrates target-mediated drug disposition (TMDD)
- Once Galectin-3 binding sites within macrophages are saturated, additional drug molecules do not enhance efficacy
- Higher doses may exceed the macrophage-specific uptake mechanisms, resulting in altered drug distribution and clearance
- Higher drug concentrations have been associated with reduced efficacy, as observed in the GT-026 cohort, where subjects receiving 8 mg/kg (with higher AUC) exhibited lower pharmacodynamic (PD) effects.
- Similar PK profile shown by monoclonal antibodies and interferon among other agents.
- 2 mg/kg dose demonstrated consistent and most optimum efficacy response
- Similar PK-PD effects were observed across the GT-026 trial and the NAVIGATE 18-month results



Chalasani et al. Gastroenterology 2020; 158: 1334-1345

#### Summary of safety results



- Similar proportion of subjects <u>discontinued the study treatment</u> in each arm due to Adverse Events: 7 (5.9%) in the Placebo arm, 6 (5.0%) in the Belapectin 2 mg/Kg arm and 9 (7.5%) in the Belapectin 4 mg/Kg arm.
- Similar proportion of subjects <u>discontinued the study</u> due to Adverse Events: 7 (5.9%) in the Pbo, 5 (4.2%) in 2 mg/Kg arm and 8 (6.7%) in the Belapectin 4 mg
  - One subject in each arm discontinued the study due to death
- No Adjudicated Drug-Induced Liver Injury (DILI) Events.
- Similar proportion of subjects reported Treatment-Emergent Adverse Events TEAEs across 3 cohorts: 112 (94.9%) in Pbo, 116 (97.5%) in 2 mg and 116 (96.7%) in 4 mg
- Similar proportion of subjects reported Treatment-Emergent Serious Adverse Events (TESAEs) across 3 cohorts: 23 (19.5%) in Pbo, 27 (22.7%) 2 mg and 25 (20.8%) 4 mg

#### **Assessment of Results**



- Belapectin 2 mg reduced varices incidence by 43.2% compared to placebo in the overall population; results were not statistically significant (ITT).
- In the per-protocol population (18-month treatment + end-of-treatment EGD), the reduction was **48.9%**.
  - Initial sample size assumed **52.5**% lower varices incidence with Belapectin vs. placebo.
  - Per-protocol population (18-month treatment + EGD) parallels evaluable biopsy results in MASH trials.
  - Non-diabetic subjects showed better responses, aligning with trends in MASH interventions (Belapectin 2 mg: 11.1% vs. placebo: 29.4%, n=70).
- Following reasons likely contributed to missing statistical significance;
  - Fewer recorded varices than expected; mid-study sample size re-estimation based on composite endpoint, not varices.
  - Shorter treatment duration; primary analysis at 18 months instead of 36 months.
  - Higher dropout rate (18.3% observed vs. 10% expected), mostly during COVID and first 4 months.
- These risks were accepted, leading to unblinding at 18 months instead of completing the 36-month trial.

\*Power of a trial roughly equates to the probability of seeing a statistically significant result - all else being equal



- 2 mg dose demonstrated a meaningful reduction in the development of new esophageal varices in patients with MASH cirrhosis and portal hypertension validating the findings observed in GT-026 trial.
- Non-invasive markers provide supportive evidence showing a lower incidence of disease progression 36month categorical changes in the 2 mg group compared to placebo in LSM and ELF data.
- Belapectin exhibits a clean and favorable safety profile; low rate of discontinuation due to AEs, no drug related SAEs.
- Analyses for 18-month data ongoing; 36-month data from available patients; biomarker data expected by end of first quarter.
- Prevention of varices in this high-unmet-need population is a recognized clinical need, and we believe an acceptable regulatory endpoint; FDA accepted central EGD reading.
- The distinct MOA of belapectin as Galectin 3 inhibitor positions it as a favorable and complementary candidate for combination therapy in MASH cirrhosis.
- Exploring partnership opportunities

. Chalasani N, et al. Gastroentrol. 2020;158:1334-45

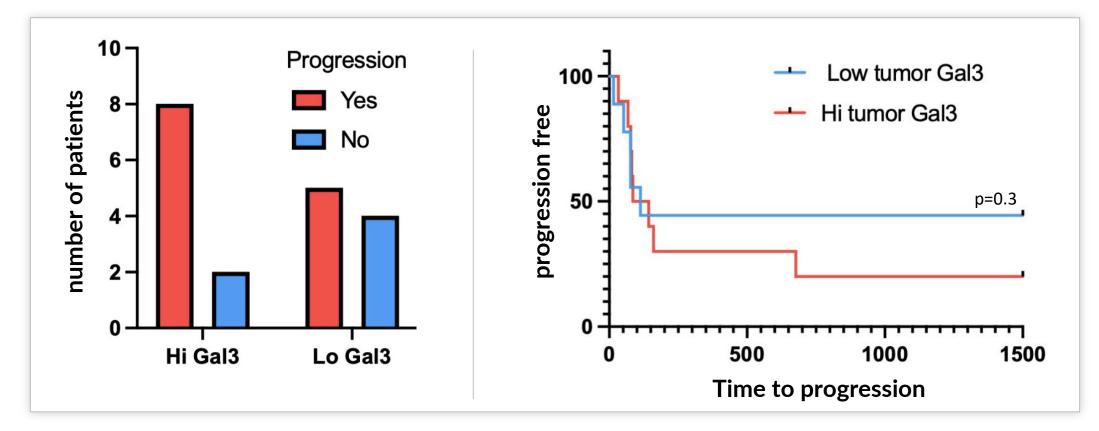
# Cancer Immunotherapy Program (Belapectin + checkpoint inhibitor)



# Higher Galectin-3 Tumor Levels are Associated with Metastatic Melanoma Progression



Number of patients with or without progressive disease in hi/lo Galectin-3 expression in metastatic melanoma



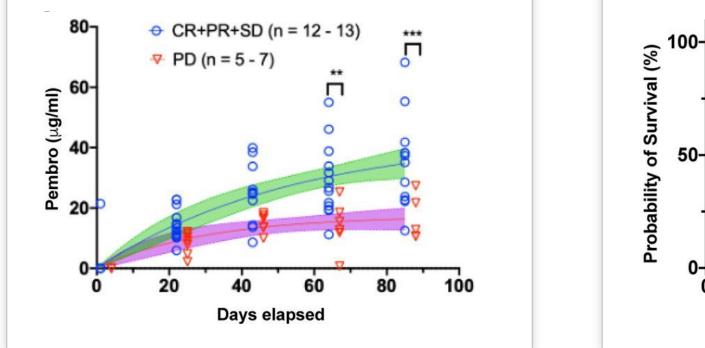
#### \*\*p<0.01, \*\*\*p<0.001.

CR=complete response; HNSCC=head and neck squamous cell carcinoma; MM=metastatic melanoma; PD=progressive disease; PR=partial response; SD=stable disease. 1. Greisen SR, et al. J Immunother Cancer. 2024;12(10):e009952.

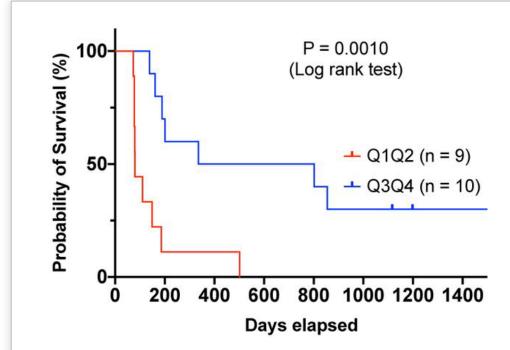
# Reduced PD-1 Clearance Correlates with Better Survival in Patients with MM and HNSCC



Serum trough levels of pembrolizumab in patients with disease control or progressive disease<sup>1</sup>



Increased progression-free survival in patients with higher trough level of pembrolizum<sup>1,\*</sup>



# Increased trough levels of belapectin and pembrolizumab correlated with better clinical outcome including progression free survival in patients with MM and HNSCC

\*Patients were grouped based on the trough levels of pembrolizumab at day 43: Q1Q2 (below population mean) and Q3Q4 (above population mean). \*\*p<0.01, \*\*\*p<0.001.

CR=complete response; HNSCC=head and neck squamous cell carcinoma; MM=metastatic melanoma; PD=progressive disease; PR=partial response; SD=stable disease. 1. Curti B. J Immunother Cancer. 2021;9:e002371.

# Belapectin in Combination with Pembrolizumab Showed Clinical Efficacy and Safety in Phase 1<sup>1</sup>

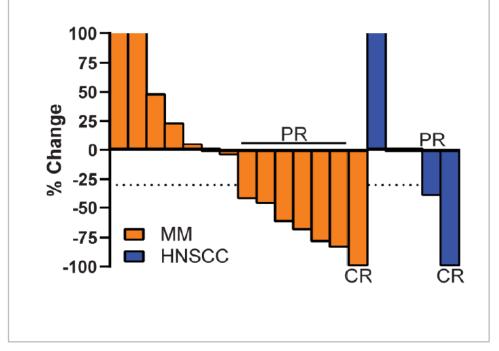


#### Phase 1 (Investigator-Initiated) of belapectin + pembrolizumab (Keytruda<sup>®</sup>)

- Objective response observed in 50% of MM (7/14) and 33% of HNSCC (2/6) patients
- Extension in more advanced patients showed stable disease in 56% MM (5/9) and 40% in HNSCC (2/5)
- Combination treatment was well tolerated with no doselimiting toxicity observed
- Fewer immune adverse events than expected
- Increased baseline expression of Gal3<sup>+</sup> tumor cells, periphery PD-1<sup>+</sup>CD8<sup>+</sup> T cells and reduced clearance of pembrolizumab correlated with clinical response

# IND filed and approval to proceed received from FDA (Head and Neck cancer)

#### Objective response to belapectin+pembrolizumab therapy at Day 85





### **Investment Highlights**

Developing galectin-based therapeutics to improve the lives of patients with chronic liver diseases and cancer

Focused Pipeline	Belapectin is a novel, potent, galectin-3 inhibitor with Fast Track Designation Low toxicity as a carbohydrate-based molecule which is degraded by natural processes Patent protection through 2032
MASH Cirrhosis	Only company to <u>exclusively</u> focus on treatment for MASH Cirrhosis and Portal Hypertension Consistent and promising results for prevention of varices in 2 mg dose across GT-026 and NAVIGATE trials Biomarker data and longer-term outcomes data (36-month data) from available patients expected by end of Q1 2025
Oncology (Combination Therapy)	Encouraging clinical response in difficult-to-treat cancers in combination with checkpoint inhibitor IND filed and approval to proceed received from FDA (Head & Neck cancer)



# Thank you!