



## Corporate Overview

March 2019

Harold H. Shlevin, Ph.D.  
Chief Executive Officer

Jack W. Callicutt  
Chief Financial Officer

NASDAQ: GALT  
[www.galectintherapeutics.com](http://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 2019 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 not lead to positive outcomes or regulatory approval.

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, 2018, 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.

## Galectin Summary

- Galectin is advancing its lead compound, GR-MD-02 (belapectin), towards a Phase 3 trial in NASH Cirrhosis, First Patient ~ Fall, 2019
  - NASH market opportunity estimated to reach \$35 - \$40 Billion/Year by 2025\*
- Proven biological activity in both Phase 2b and animal trials
- Phase 3 ready asset – target starting Fall, 2019
- First randomized clinical trial of any drug to demonstrate statistically significant positive efficacy in compensated NASH cirrhosis without varices (NASH-CX trial)
- Demonstrated efficacy in a population with a high degree of clinical unmet need with no available therapies and few in development
- GR-MD-02 is protected by a strong and robust IP portfolio of 77 granted and 27 pending patents across a broad group of human diseases through at least 2033
  - ❖ Cover composition of matter for complex carbohydrate drugs and/or various methods of use in treatment of fibrosis and other relevant diseases.
- Experienced Leadership

\* Deutsche Bank "NASH – the next big global epidemic in 10 years?" July 14, 2014

## Galectin Phase 3 Trial – “NASH-RX”

- Investigating NASH cirrhosis, a condition that is more closely linked to liver failure and its life-threatening implications than earlier stages of NASH
- Have engaged leading NASH experts to provide advice and counsel to strengthen our plan for the NASH-RX Phase 3 clinical trial
- Type C Meeting with the FDA on February 6, 2019 discussed Galectin’s proposal for use of progression to varices as the primary surrogate endpoint moving forward
- FDA supports use of progression to varices as a potential surrogate endpoint and progression to large varices as a component of a composite clinical benefit endpoint pending additional requested information
  - ❖ NASH cirrhosis patients with portal hypertension are at risk of developing esophageal varices which may bleed and exhibit other decompensating events.
- Protocol is now in the process of finalization to provide meaningful clinical outcomes and address suggestions made by FDA
- First Patient First Visit target Fall, 2019; Top Line Data: Q4 2022

# Strong, experienced management team



**Harold H. Shlevin, Ph.D., CEO and President**

- Over 34 years of relevant experience
- Solvay Pharmaceuticals, CEO
- CIBA Vision Ophthalmics (n/k/a Novartis Vision), SVP & co-founder
- Tikvah Therapeutics, Founder and CEO
- CIBA-Geigy Pharmaceuticals



**Adam Allgood, Pharm D., Clinical Development**

- Over 30 years experience in clinical development, medical affairs & regulatory processes.
- UCB Inc., Abbott Laboratories, Solvay Pharmaceuticals



**Eli Zomer, PhD, Pharm Development**

- Over 34 years of relevant experience: Koor Biotechnologies, Charm Sciences, GlycoGenesis, HU Medical School (Jerusalem), and Harvard University



**Jack W. Callicutt, CFO**

- Over 27 years of relevant experience
- Reach Health, CFO,
- Vystar Corporation, CFO,
- Corautus Genetics, Deloitte



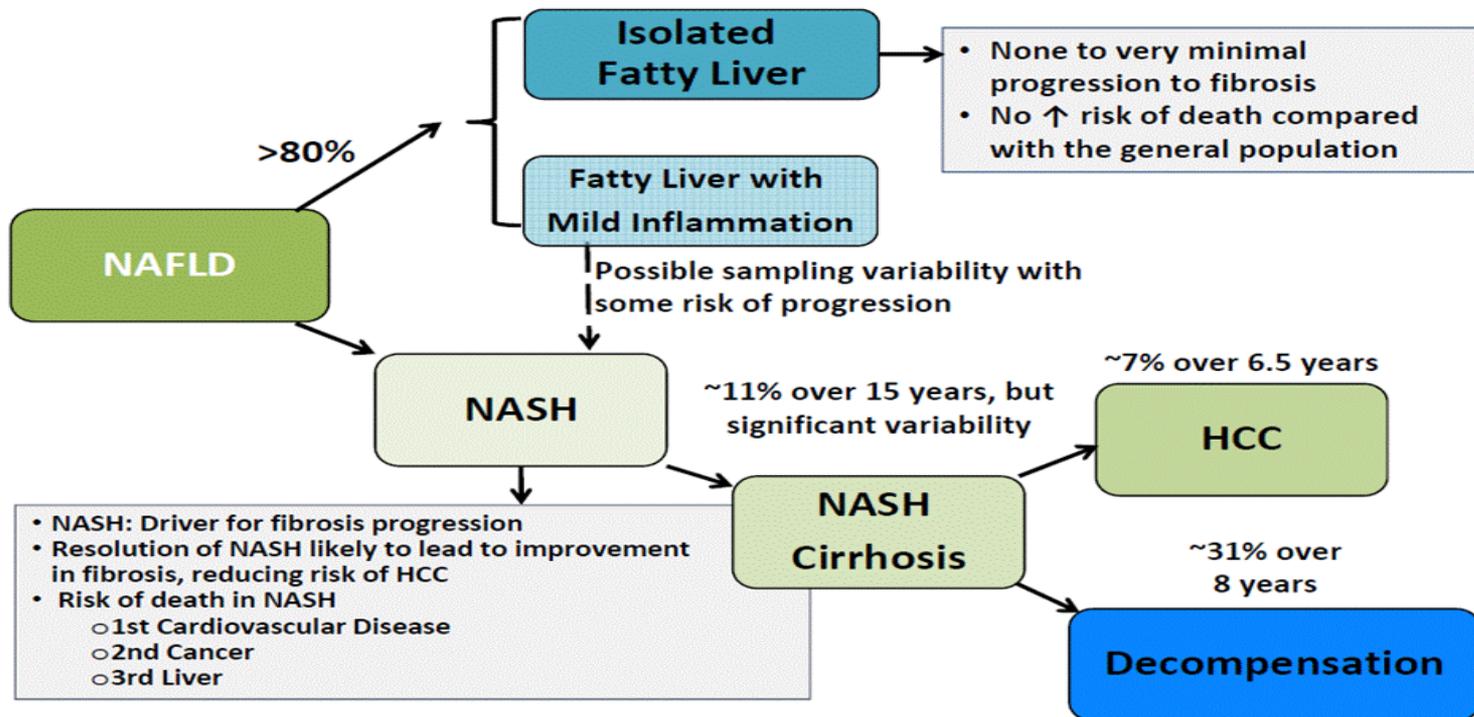
**Rex Horton, Regulatory**

- Over 29 years of experience; Director Regulatory Affairs at Solvay Pharmaceuticals and Chelsea Therapeutics; Georgia Institute of Technology
- Head of regulation, quality assurance and manufacturing

# Contents

- **General NASH Competitive Landscape**
- **NASH Cirrhosis and GR-MD-02**
  - **Phase 2b Results**
  - **Phase 3 plans**
- **Cancer Immunotherapy Combination**
- **Summary**

# NASH Disease Progression

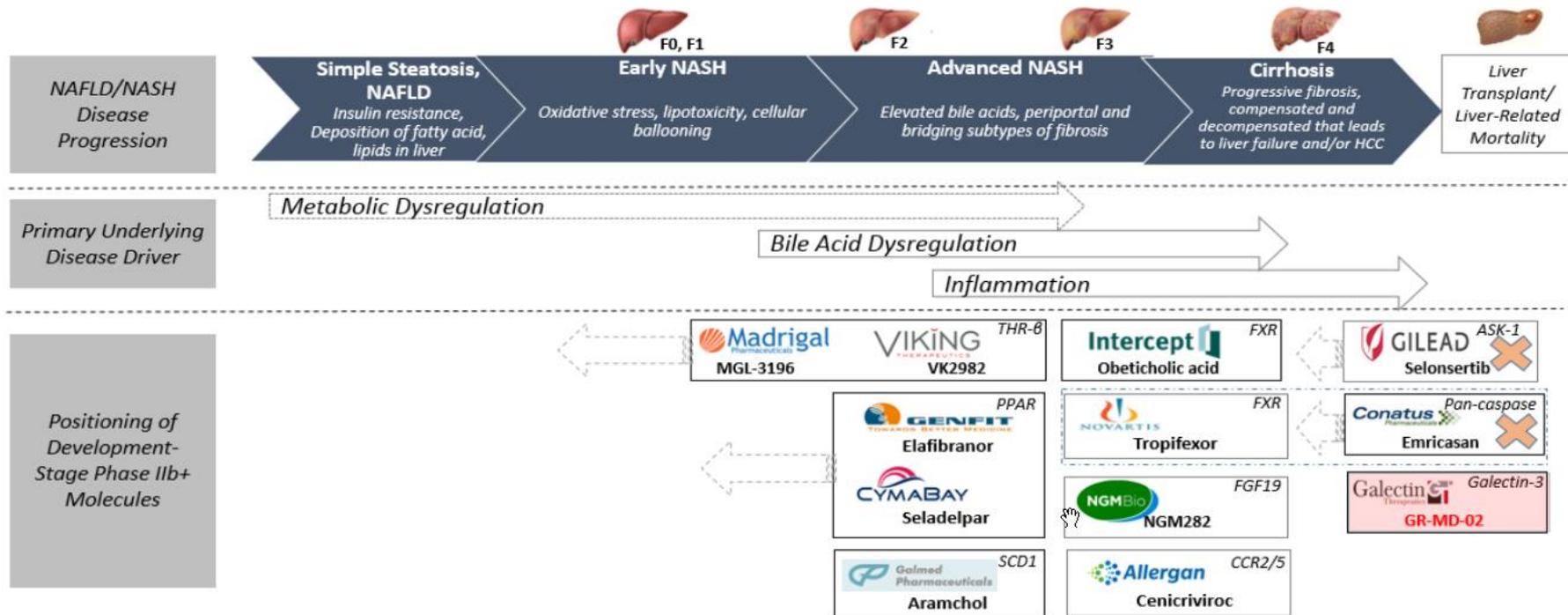


With permission from Torres DM, et al. *Clin Gastroenterol Hepatol.* 2012;10:837-858.

Source: Torres DM, et al. *Clin Gastroenterol Hepatol.* 2012;10:837-858.

# Industry Pipeline Is Relatively Less Crowded in Cirrhotic NASH

## GR-MD-02 Uniquely Positioned



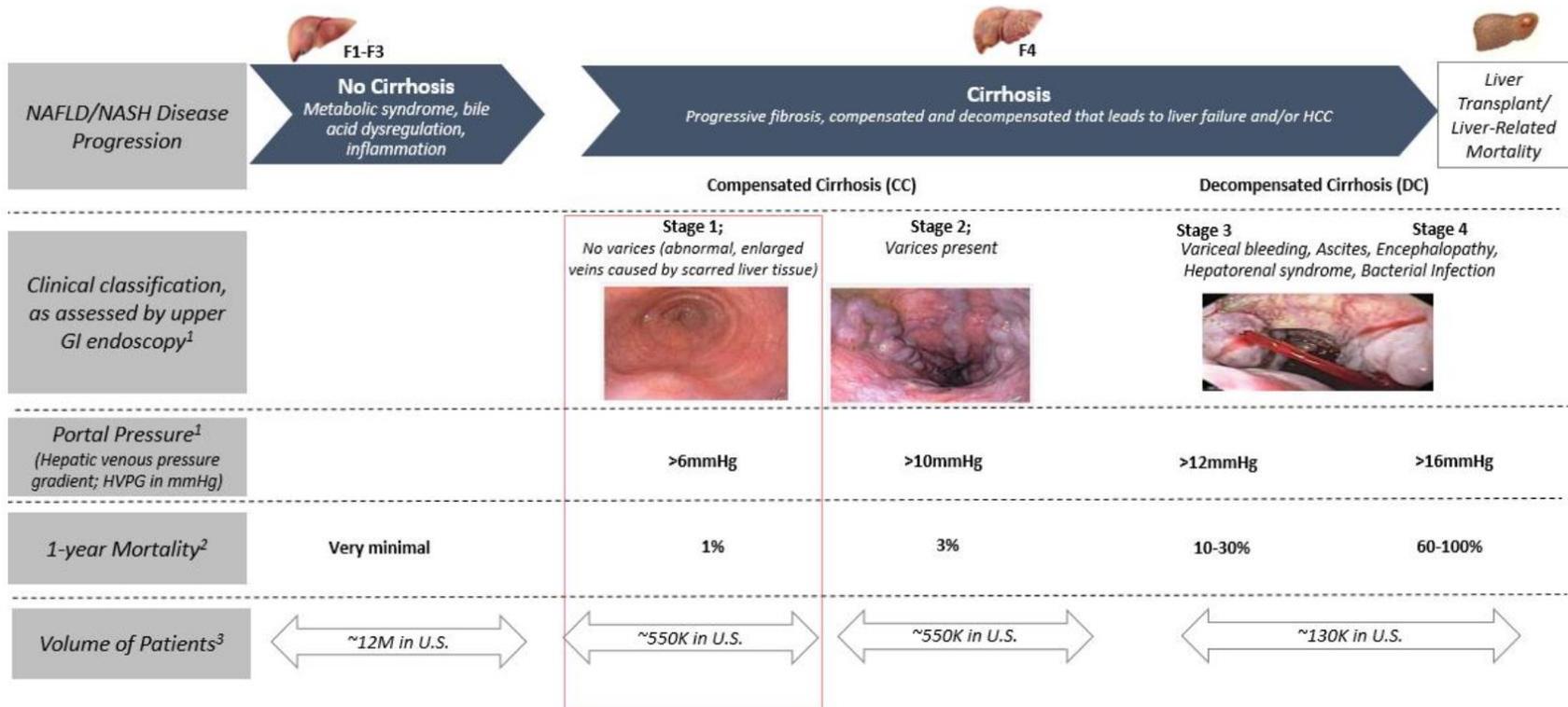
Source: B. Riley FBR Research, clinicaltrials.gov, and company filings

## Contents

- General NASH Competitive Landscape
- NASH Cirrhosis and GR-MD-02
  - Phase 2b Results
  - Phase 3 plans
- Cancer Immunotherapy Combination
- Summary

# Galectin is developing a compound for the most serious stages of the disease

## Target Patient Population for GR-MD-02 within the NASH Cirrhosis Disease Continuum



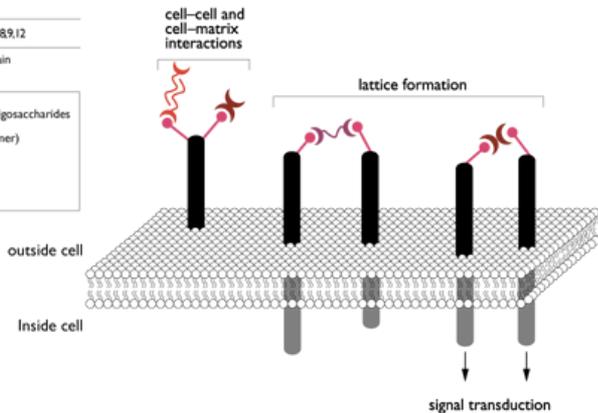
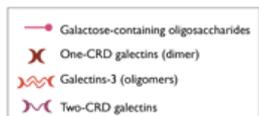
Source: (1): Garcia Tsao et al, AASLD Hepatology 2010, (2): Suk et al, Clinical and Molecular Hepatology 2014; (3); Estes et al, AASLD Hepatology 2018

Reprinted from: B Riley FBR Research, Feb., 2019

# GR-MD-02 targets and disrupts the function of galectin-3, which plays a major role in diseases that involve organ fibrosis

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

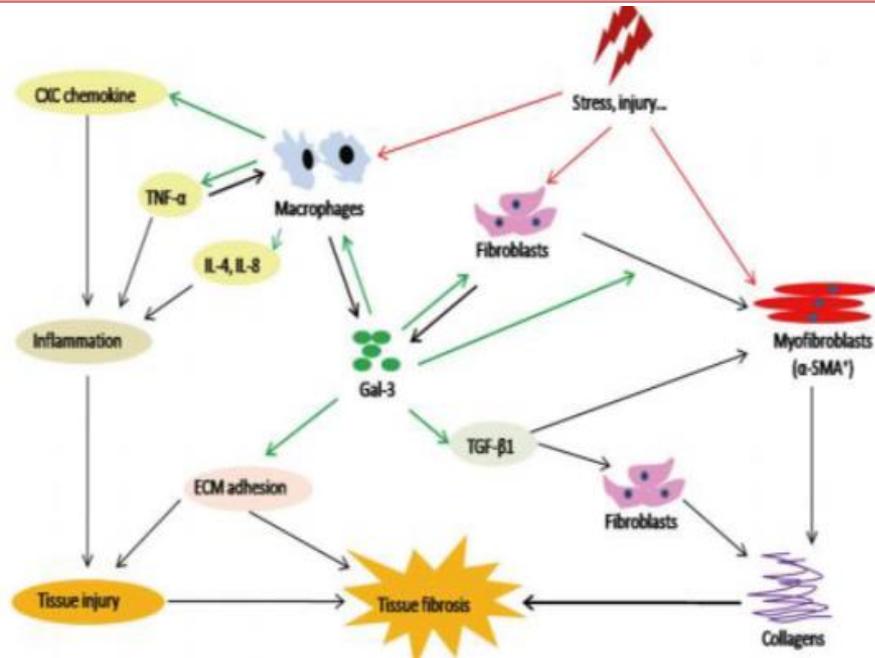
Carbohydrate Recognition Domain



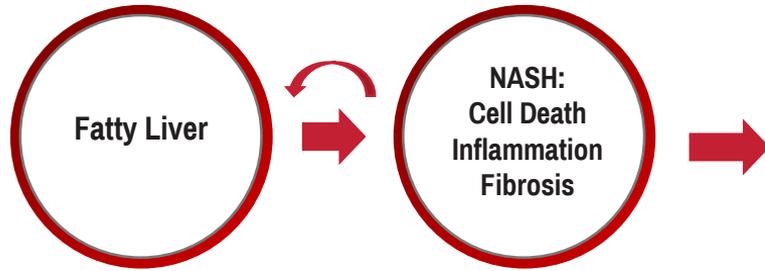
Galectin proteins' ability to dimerize creates the opportunity for galectins to link glycoproteins and form a lattice structure on the cellular surface and to promote cell-cell and cell-matrix interactions

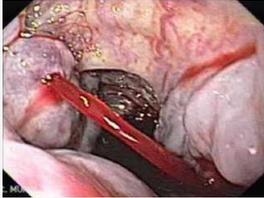
**Galectin-3 expression is up-regulated in established human fibrotic liver disease, and disruption of Galectin-3 can markedly reduce liver fibrosis (\*)**

## Central Role of Gal-3 in Multiple Pathological Processes



# There is currently no treatment for NASH cirrhosis, a progressive disease that can lead to significant mortality



Compensated Cirrhosis		Decompensated Cirrhosis
Stage 1	Stage 2	Stage 3 and 4
No Varices	Varices Develop	Bleeding, Ascites, Encephalopathy
		
≥6	>10	Portal Pressure (mmHg) >12
Low one year mortality (1-3%)		~50% one year mortality



The majority of companies are focused on pre-cirrhotic NASH



Few companies with Phase 2/3 trials in NASH cirrhosis

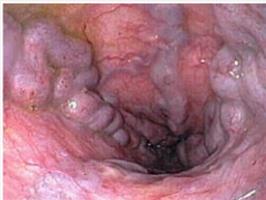
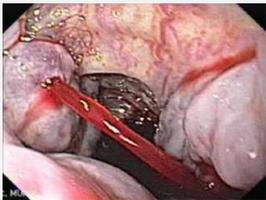
Unlike many companies in the NASH space, Galectin is focusing on the **compensated cirrhotic** patients

<sup>1</sup> Garcia-Tsao, G., Friedman, S., Iredale, J., Prinzani, M. *Hepatology*. 2010;51:14451449

# Patients with NASH cirrhosis without varices are at high risk for severe complications and have a high degree of unmet need

## Significance of Targeting NASH Cirrhosis without Varices:

- Once NASH progresses to cirrhosis, patients are at risk for severe complications, liver failure, and death and the condition is not reversible with lifestyle changes alone
- Presence/absence of varices is part of standard care for NASH patients and is easily assessed by endoscopy, and an important goal of treatment of patients with Stage 1 is to prevent progression to varices and complications
- The only currently available therapy for NASH cirrhosis is liver transplant when clinical progression is severe

Compensated Cirrhosis		Decompensated Cirrhosis
Stage 1	Stage 2	Stage 3 and 4
No Varices	Varices Develop	Bleeding, Ascites, Encephalopathy
		
≥6	>10	Portal Pressure (mmHg) >12
Low one year mortality (1-3%)		~50% one year mortality

Few companies with Phase 2/3 trials in NASH cirrhosis

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

<sup>1</sup> Garcia-Tsao, G., Friedman, S., Iredale, J., Prinzani, M. *Hepatology*. 2010;51:14451449

# NASH-CX was a randomized, double-blind, placebo-controlled phase 2b clinical trial that enrolled 162 NASH cirrhosis patients<sup>1</sup>

## Phase 2b Trial Design

### Major Inclusion Criteria

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

Endpoints		Baseline	Week 54
Primary Endpoint	Portal Pressure: HVPG <sup>2</sup>	✓	✓
Secondary Endpoints	Liver Biopsy <sup>3</sup>	✓	✓
	Endoscopy (varices)	✓	✓
	Complications <sup>4</sup>	✓	✓

### Dosing and Administration



Treatment	#Patients
Placebo	54
GR-MD-02 2 mg/kg	54
GR-MD-02 8 mg/kg	54

<sup>1</sup> Subjects were enrolled across 36 sites in the US

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

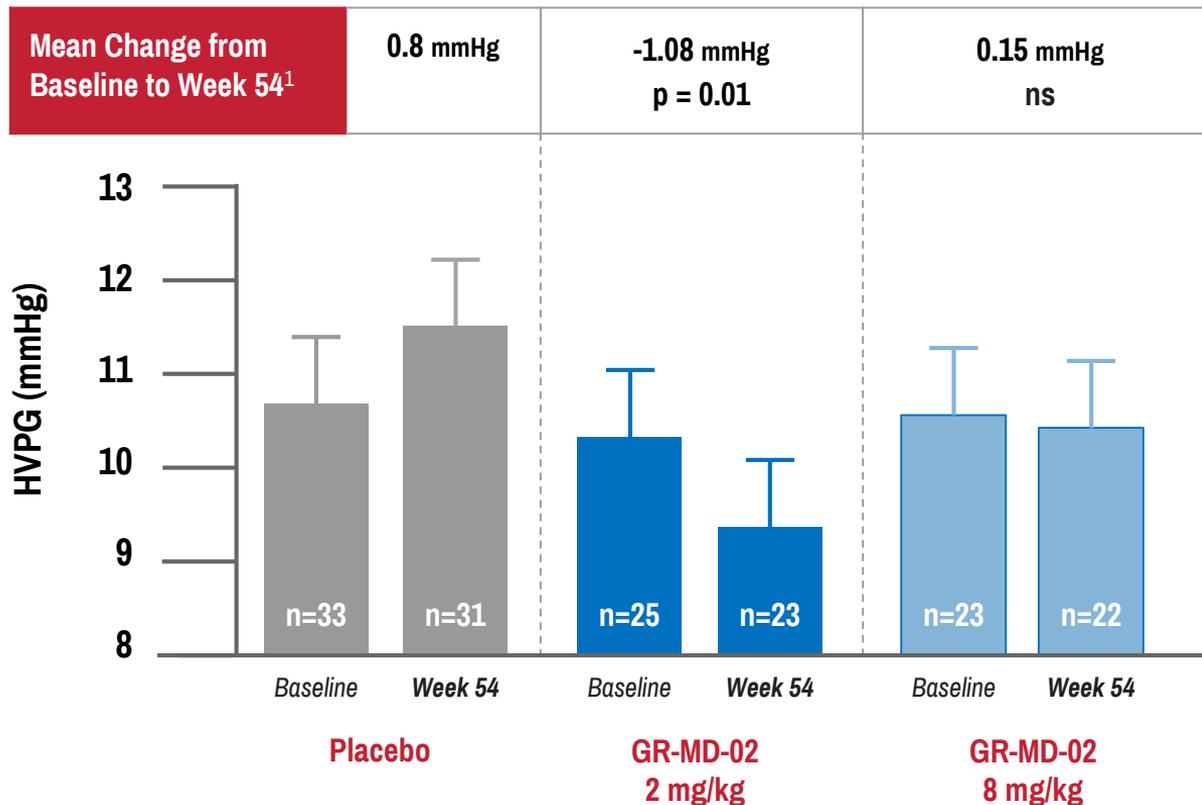
<sup>3</sup> Histologic staging & quantitative morphometry for collagen

<sup>4</sup> Liver-related complications (varices/bleeding, ascites, hepatic encephalopathy, liver-related death, or transplant)

[Additional trial data on website](#)

# The GR-MD-02 2 mg/kg group showed a statistically significant reduction in HVPG from baseline to week 54 for patients without varices

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



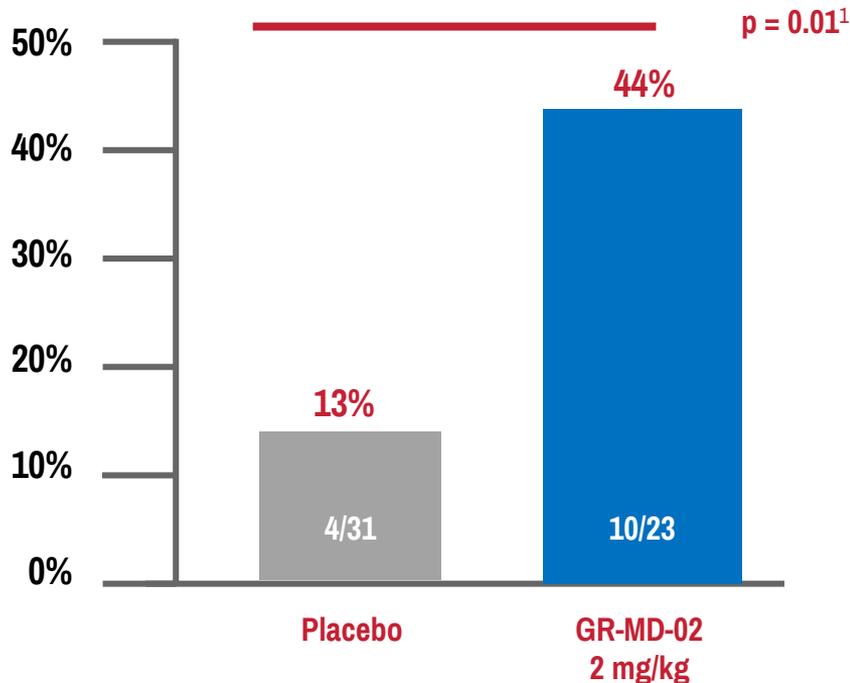
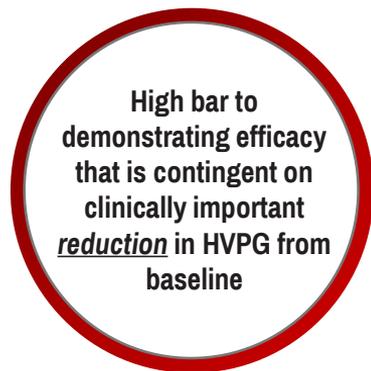
<sup>1</sup>ITT with LOCF, ANCOVA with LSD

Mean ± SEM

# 43% of patients without varices in the GR-MD-02 2mg/kg group showed a $\geq 2$ mmHg and $\geq 20\%$ decrease from baseline compared to 13% in the placebo group

## Percentage of Patients Who Had a Clinically Relevant Reduction in HVPG With:

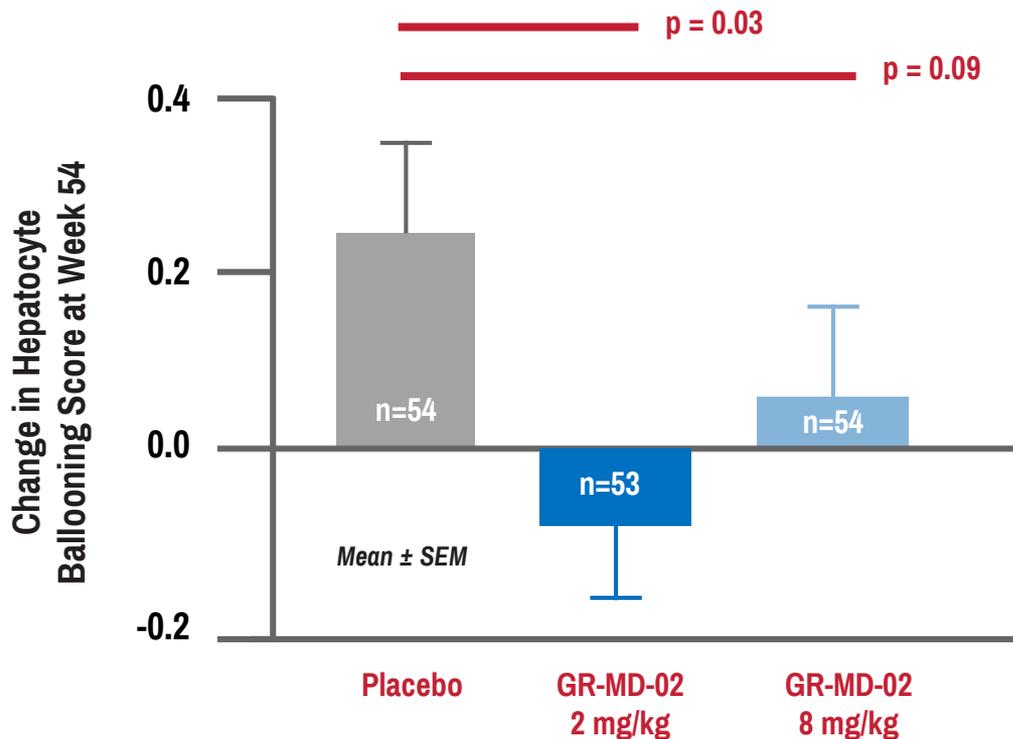
- $\geq 2$  mmHg Decrease From Baseline AND
- $\geq 20\%$  Decrease From Baseline



<sup>1</sup> Chi Square

# Patients in the 2 mg/kg treatment group showed statistically significant improvement of liver cell death on liver biopsy<sup>1</sup>

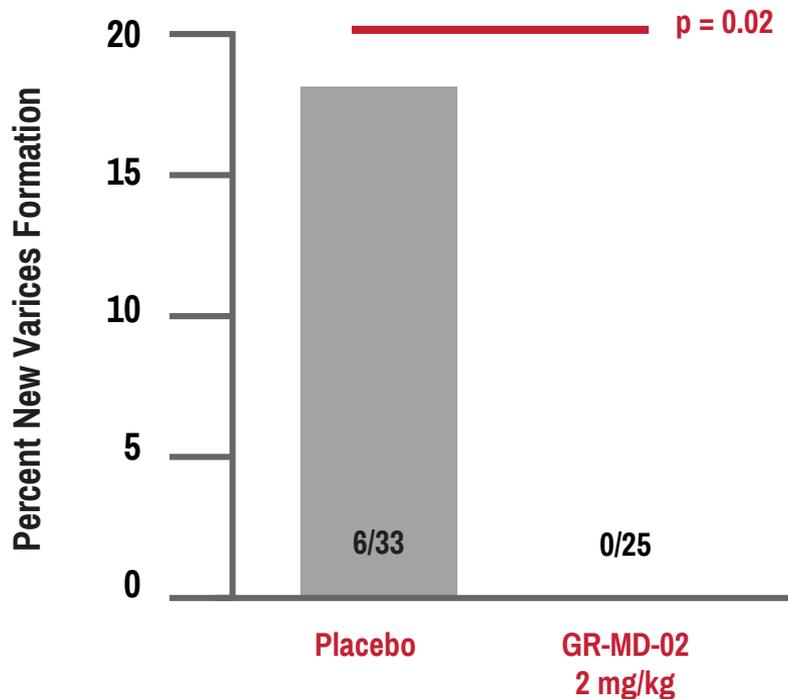
In the total population there was improvement in cell death, a critical feature of NASH



<sup>1</sup>ITT population

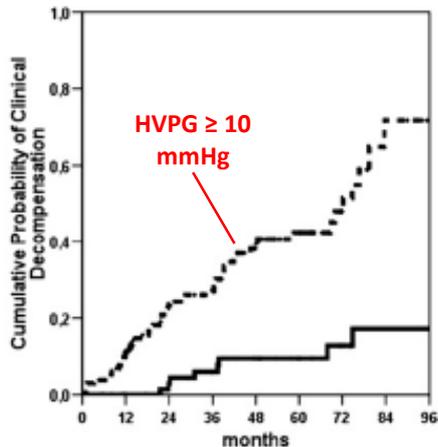
Ordinal Logistic Regression Analysis

# Significantly fewer new varices developed in treatment groups versus placebo, and no patients in the 2 mg/kg treatment group developed new varices



<sup>1</sup> Chi Square

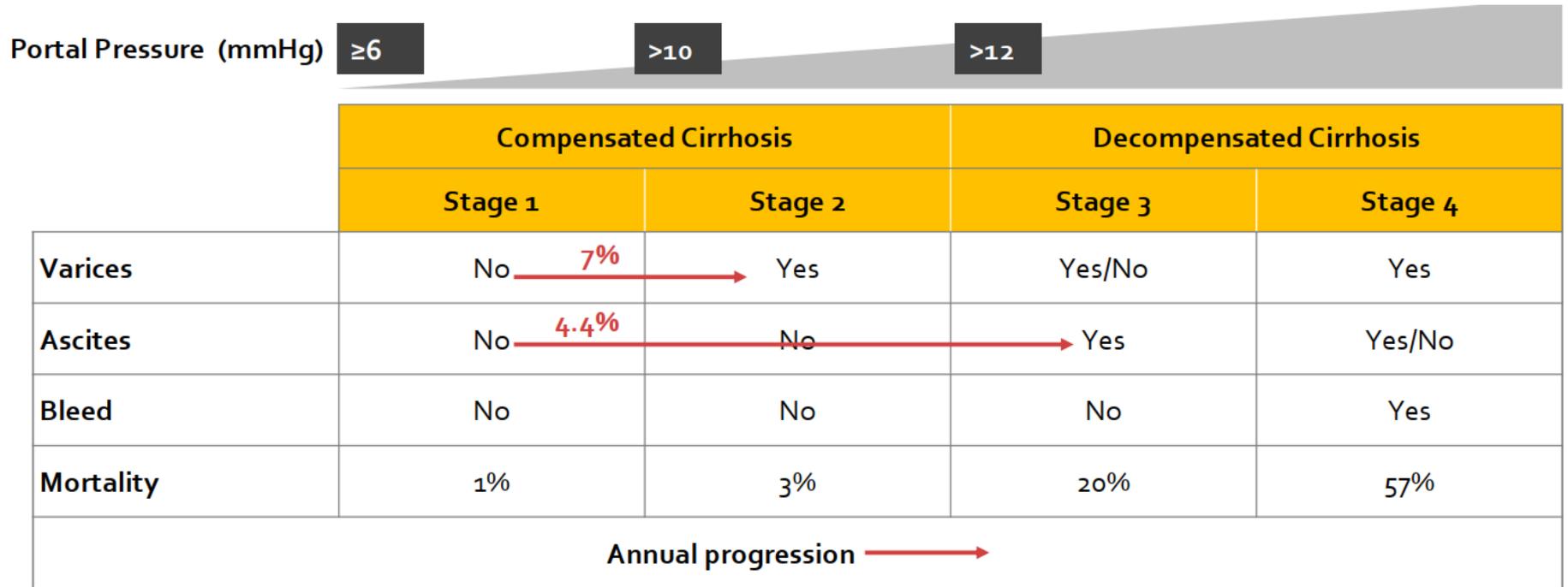
## GR-MD-02 has demonstrated efficacy in two clinically meaningful endpoints, where no current therapies exist



*Gastroenterology*, 2007;133:481–488

- **Portal hypertension (PH) is a critical, clinically important consequence of cirrhosis and responsible for the majority of associated complications**
  - Portal pressures of  $\geq 10$  mmHg are associated with increased risk of decompensation, varices, hepatocellular carcinoma, and 1-year mortality
  - For example, an HVPG  $\geq 10$  mmHg is associated with a 28% rate of varices development and a 20% rate of first decompensation at two years
  - Patients with an HVPG  $< 10$  mmHg have only a 10% chance of developing clinical decompensation (over median follow-up of 4 years)
- **For patients with compensated cirrhosis and PH without varices, there are no specific therapies indicated for reducing PH and/ or directly treating the underlying liver disease**
  - Beta-blockers are efficacious in improving outcomes in patients with portal hypertension and varices, but likely do not prevent development of varices/ slow disease progression in early stage cirrhosis patients
  - As a result, clinical guidelines in the US and EU do not recommend the use of beta-blockers for the prevention of variceal formation
- **Further, Compensated cirrhosis patients with no major complications carry a median survival of >12 years, but compensated patients with varices have a worse prognosis (3-fold higher one year mortality rates)**

# Portal Hypertension is the Main Driver of Decompensation



D'Aminco et. Al., J Hepatol 2006;44:217

## GR-MD-02 was safe and well-tolerated

- No differences between treatment groups in the number of patients with treatment emergent adverse events (AEs), grade 3/4 AEs, serious adverse events (SAE), or grade 3/4 laboratory abnormalities
- All but 2 SAEs were unrelated to study drug; 2 patients in 8 mg/kg group had SAEs that were possibly related to study drug <sup>1</sup>
- There was one death due to complications of a surgical procedure that was unrelated to study drug <sup>3</sup>
- There was a low patient dropout rate of 6% which suggests the drug was well tolerated and patients were adherent to the regimen (only one patient was removed from study for an AE possibly related to study drug <sup>2</sup> )

<sup>1</sup> Two SAEs were determined by the PI to be possibly related to study drug (transient ischemic attack and worsening of hyponatremia, both GR8); All others SAEs were felt to be unrelated to study drug

<sup>2</sup> *Possibly related to drug*: spasmodic cough (1); *Unrelated to study drug*: esophageal variceal bleeding (2), sepsis (1), pancreatitis (1)

<sup>3</sup> Pulmonary embolism following hernia repair surgery, judged to be unrelated to study drug

# Positive effects of GR-MD-02 shown in a subset of patients in the NASH-CX trial has allowed the company to reach its current Phase 3 development trajectory

*After incorporating advice and guidance from the FDA, Galectin announced on May 14, 2018 that the Company is proceeding with plans for a Phase 3 clinical trial program for GR-MD-02 in NASH cirrhosis*

*This plan is essentially complete and was discussed with FDA at a February 6 2019 meeting; additional input expected from CRO and others*



## *Phase 3 Trial Design*

### *Target Patient Population*

- Patients with NASH cirrhosis without esophageal varices*
- FDA indicated its support of the potential use of progression to varices as a surrogate endpoint and progression to large varices (or to small varices with a weal) as a component of a composite clinical benefit endpoint (subject to additional information)*

*Further details of the Phase 2b trial results are available on our website*

## Summary of GR-MD-02 in NASH Cirrhosis

- **NASH-CX is the first clinical trial to show positive results in compensated NASH cirrhosis without esophageal varices**
  - Clinically meaningful effect in reducing portal pressure in a subgroup of patients
  - Improvement in liver cell death, a key component of NASH
  - Reduction in the development of new esophageal varices
  - Drug was safe and well-tolerated
  - Following leadership meeting with FDA in May 2018, determined to be Phase 3-ready
  - FDA in Feb 2019 meeting indicated its support for *progression to varices as a surrogate endpoint and progression to large varices (or to small varices with a weal) as a component of a composite clinical benefit endpoint*
  - The presence of varices is part of Standard of Care for patients and can easily be assessed with endoscopy
  - 50% of cirrhotic NASH patients do not have varices when diagnosed
  - Further awareness of NASH will lead to early diagnosis which will increase the number of patients without varices
- **These results have propelled the development program to Phase 3 in consultation with Key Opinion Leaders (KOL) and FDA**

## Contents

- **General NASH Competitive Landscape**
- **NASH Cirrhosis and GR-MD-02**
  - **Phase 2b Results**
  - **Phase 3 plans**
- **Cancer Immunotherapy Combination**
- **Summary**

## Galectin Phase 3 Trial – “The NASH-RX” Overview

- The focus and goal of the therapeutic program is to establish the efficacy & assess safety & tolerability of GR-MD-02 compared to placebo in reducing the development and progression of esophageal varices in patients with NASH cirrhosis.
  - The results of the NASH-CX trial substantiate that, subject to confirmation in later stage clinical trials, this goal is achievable in a significant portion of the NASH cirrhosis patient population i.e. those NASH cirrhosis patients with portal hypertension at risk of developing esophageal varices which may bleed and /or exhibit other decompensating events.
- The trial design has been refined with external consultants and was sent out to several CROs for pricing, feasibility and other considerations. The selection of a large, global CRO with experience in international Phase 3 NASH trials is being finalized.
- Patients will be selected based on criteria commonly used in clinical practice to identify patients with portal hypertension who are at risk of developing esophageal varices.
  - Modified Baveno VI criteria (e.g., liver stiffness, platelet count, spleen diameter, and abdominal collaterals, etc.) to identify patients at risk of developing varices, plus confirmed NASH cirrhosis on biopsy
- Study design is optimized for an accelerated approval pathway

## Galectin Phase 3 Trial – “The NASH-RX” Highlights

- Parallel group, randomized, placebo-controlled, double-blinded, of either 2 mg/kg or 4 mg/kg GR-MD-02 or placebo administered by i.v. infusion every two weeks for two years to NASH Cirrhosis patients who did not have esophageal varices at baseline.
  - i. Surrogate Endpoint:* Proportion of patients in treatment groups who develop esophageal varices vs placebo after 2 years of treatment under an accelerated approval (Subpart H) pathway as a surrogate for the development of large varices
  - ii. Various secondary endpoints*
  - iii. Adjudication panels/Central Readers: Biopsy, EGD, HVPG, DSMB*
- Key study features:
  - Efficacy assessments will include upper endoscopy (EGD), liver biopsy, transient elastography (FibroScan), assessment for complications of cirrhosis, and serum/plasma biomarker tests, as well as HVPG measurement (in a subset of patients at selected sites), and others.
  - Primary inclusion criteria is based on using modified Baveno VI criteria plus biopsy confirmed NASH cirrhosis (stage 4), amongst other factors
  - Global CRO experienced in NASH Phase 3 studies
  - Use of NASH-specific site network to help assure timely site startup and enrollment

# Galectin Phase 3 Trial – “NASH-RX” Milestones

- **Next Steps:**
  - Complete final contract with CRO
  - Complete drug supply manufacturing
  - Contract for developmental and reproductive toxicology studies
- **Key clinical study milestones:**
  - Estimated First Patient ~ Fall, 2019
  - Global Study: ~120+ sites, rolling regulatory filings outside USA
  - Enrollment Period Estimated: ~ 1 year
  - Last Patient enrolled: Q3 - Q4, 2020
  - Primary inclusion criteria is based on using modified Baveno VI criteria plus biopsy confirmed NASH cirrhosis (stage 4), and other factors
  - Estimated Last Patient completion: Fall, 2022
  - Top Line Data: ~ Q4 2022

# Contents

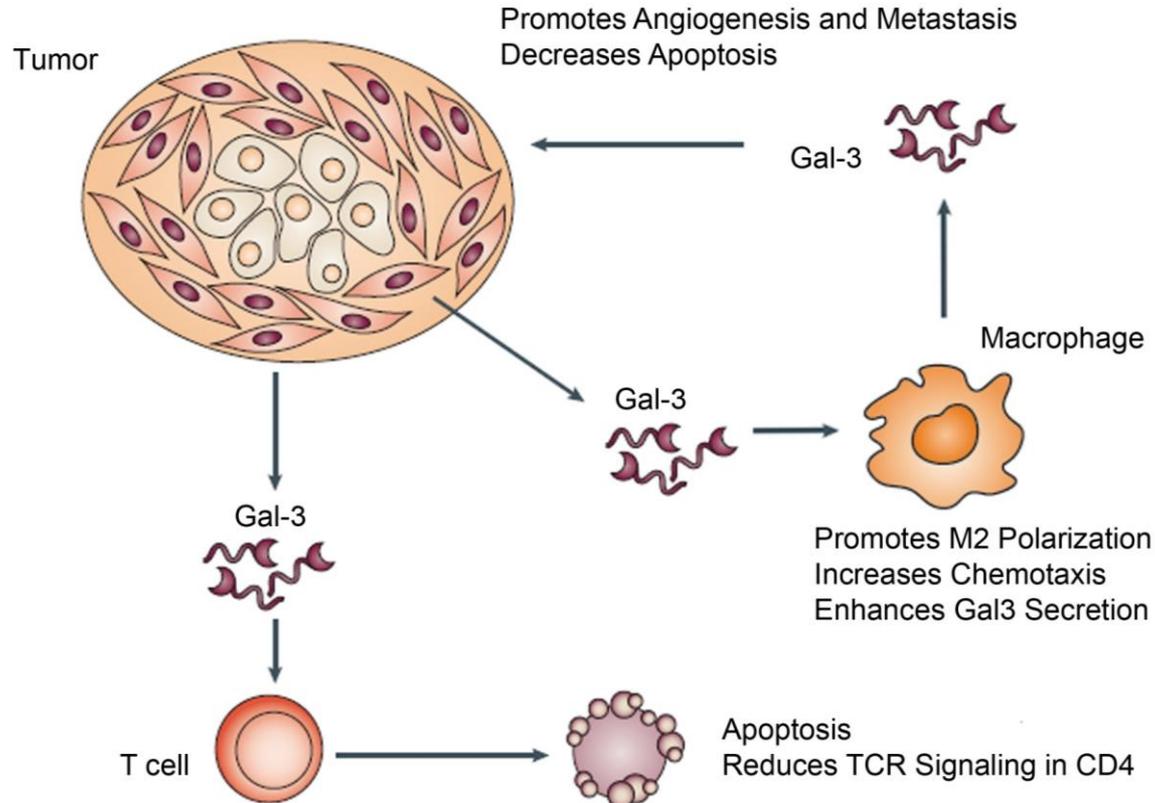
- **General NASH Competitive Landscape**
- **NASH Cirrhosis and GR-MD-02**
  - **Phase 2b Results**
  - **Phase 3 plans**
- **Cancer Immunotherapy Combination**
- **Summary**

## GR-MD-02 in Combination Cancer Immunotherapy

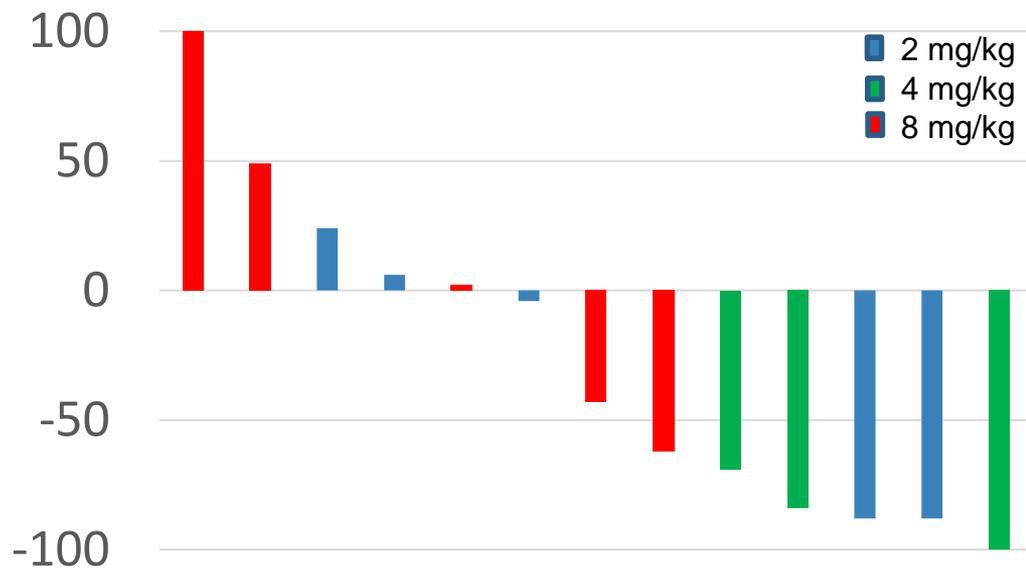
- **As a galectin-3 inhibitor, GR-MD-02 may represent a novel mechanism of action that is believed to be differentiated from the many other drugs being tested**
- **Potentially important advantages in combination immunotherapy**
  - Enhancement of activity with multiple agents and tumors (pre-clinical)
  - Potential novel and unique markers of anti-tumor activity
  - Encouraging enhancement of tumor response in phase 1 study
  - No increase adverse events when used in combination immunotherapy
- **Trial expansion planned for 2019**
- **Preclinical & Clinical work conducted at the Earl A. Chiles Research Institute of Providence Portland Medical Center**
  - **Preclinical Discoveries: Dr. William L. Redmond**
  - **Clinical: Dr. Brendan Curti, PI**

**Additional information available on website**

# Immune suppression via galectin-3

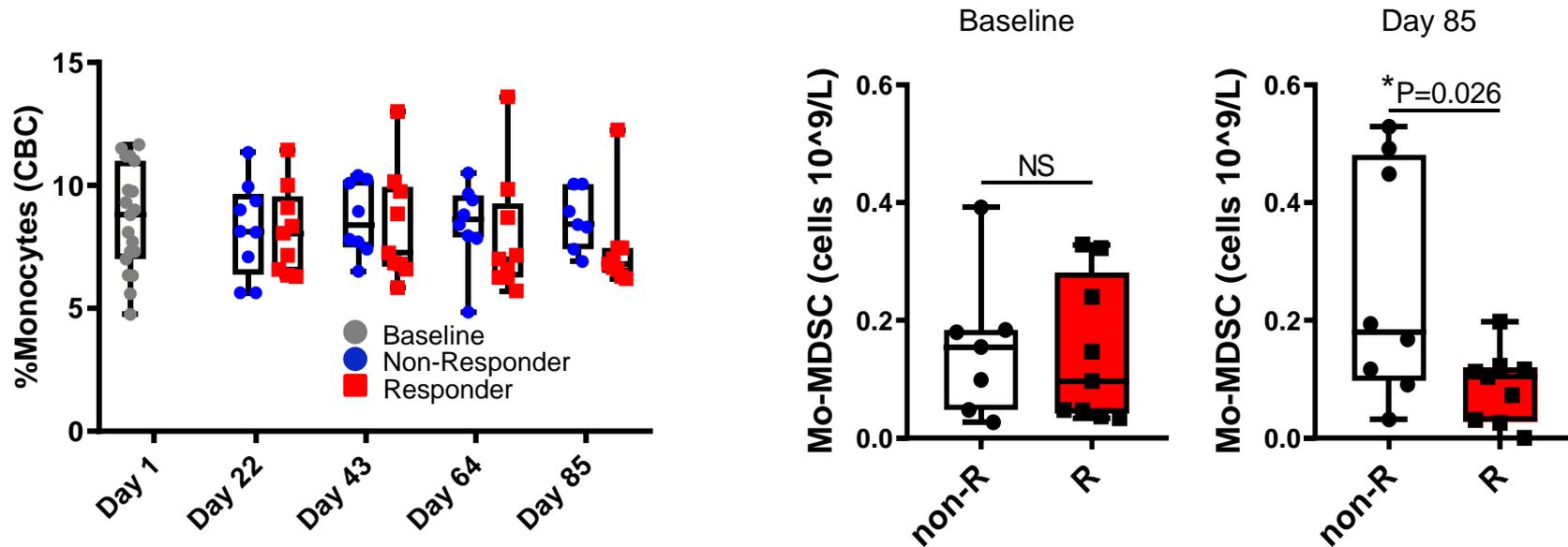


## Melanoma best response \*



\* Previously reported

## Responders to GR-MD-02/aPD-1 therapy have reduced Mo-MDSCs post-Tx \*



\* Data partially reported earlier

## Conclusions (clinical)

### Combination GR-MD-02/aPD-1 immunotherapy

- ✓ Combination therapy was safe and well-tolerated
- ✓ Favorable ORR (n=21 pts) compared to aPD-1 monotherapy

### Biomarkers of response

- ✓ Increased baseline expression of PD-1+ on effector CD8 T cells associated with response
- ✓ Reduced Mo-MDSCs post-treatment in responders
- ✓ Multiplex IHC analysis suggests potential correlation with Gal-3 expression and response

## Future Directions

- Additional analysis of biomarkers correlate with clinical response
  - flow cytometry and mIHC
- Expansion cohort (2019; 4 mg/kg GR-MD-02+pembro)
  - n=15 patients
  - 4 mg/kg dosing selected because immunological and anti-tumor responses were observed (and no increase in these at 8 mg/kg)
  - GR-MD-02 in patients with liver disease showed no enhanced biological effect at higher dose levels
  - No dose-limiting or severe adverse events at 4 mg/kg
- The expansion cohort will have continued GR-MD-02 dosing as long as pembrolizumab is administered
- Phase II trial: aPD-1 vs. GR-MD-02/aPD-1

## Contents

- NASH Cirrhosis
- Cancer Immunotherapy Combination
- Summary

# Summary of Drug Development Program

- **GR-MD-02 is a novel antigalectin-3 drug that may modulate the immune system and may improve multiple diseases**
- **NASH Cirrhosis is a major unmet medical need with a large potential market**
  - Galectin-3 is important in development of NASH cirrhosis
  - NASH-CX trial is first positive phase 2 clinical data in a subset of patients without esophageal varices
  - GR-MD-02 was safe and well-tolerated and improved portal pressure, aspects of liver biopsy, and reduced development of varices
  - GALT is competitively well positioned in the industry
  - FDA Meetings: EOP2 with FDA in May 2018; FDA meeting in Feb 2019 demonstrated support for proposed surrogate endpoint
  - Phase 3 study: First Patient ~ Fall 2019; Top Line Data Q4 2022
- **Combination cancer immunotherapy (Providence Cancer Institute)**
  - Galectin-3 important in cancer immunity with encouraging early clinical results
  - Large potential to improve results of cancer immunotherapy – trial continuing
- **GR-MD-02 has shown activity in moderate-to-severe plaque psoriasis**

# Summary of Drug Development Programs

- **Clinically meaningful improvement shown in Phase 2 study in primary program, NASH cirrhosis without varices**
  - First randomized clinical trial of any drug to demonstrate statistically significant positive efficacy in compensated NASH cirrhosis without varices
  - Demonstrated efficacy in a population with a high degree of clinical unmet need with no available therapies and few in development
  - *Phase 3 – First Patient ~ Fall, 2019*
- **Promising data in combination w/ market leading immuno-oncology agent, Keytruda®**
  - Investigator-initiated phase 1b clinical trial of GR-MD-02 in combination with Keytruda in advanced melanoma and other malignancies continuing
  - See [www.galactintherapeutics.com](http://www.galactintherapeutics.com) for further information
- **Demonstrated activity in patients with moderate-to-severe plaque psoriasis**
  - All 5 patients treated in phase 2a open label trial showed improvement in disease activity by an average of 50%
- **GR-MD-02 is protected by a strong and robust IP portfolio of granted and pending patents across a broad group of human diseases through at least 2033**

# Thank you for your attention

Harold Shlevin, PhD - CEO

[Shlevin@galactintherapeutics.com](mailto:Shlevin@galactintherapeutics.com)

Jack W. Callicutt – CFO

[Callicutt@galactintherapeutics.com](mailto:Callicutt@galactintherapeutics.com)

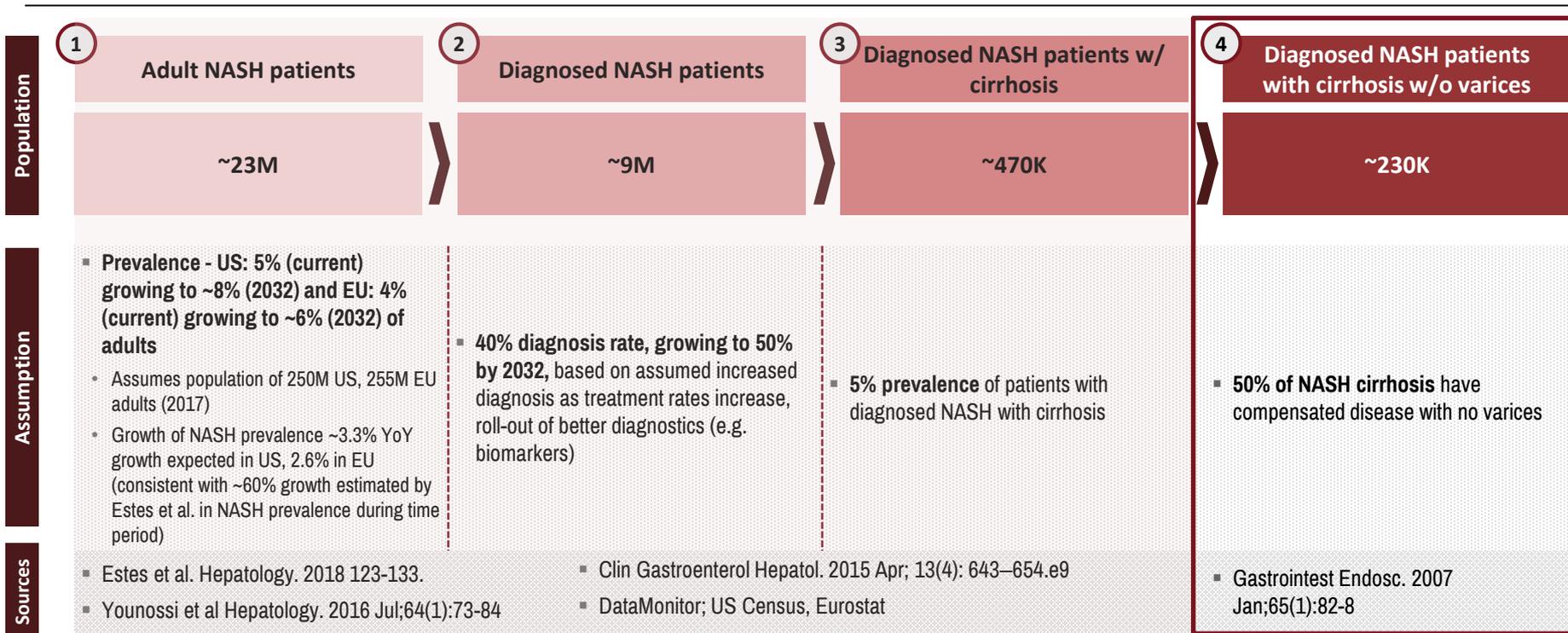
# Supplemental Slides

## **Additional Considerations**

- **Large Institutional Shareholder Converts Preferred to Common**
- **\$10 Million Line of Credit Unused yet and Extended until 2021**
- **Exalenz Bioscience uses Data Collected on GALT Trial for AASLD Presentation**
- **Encouraging Results from Phase 1B trial with Keytruda in Advanced Melanoma**

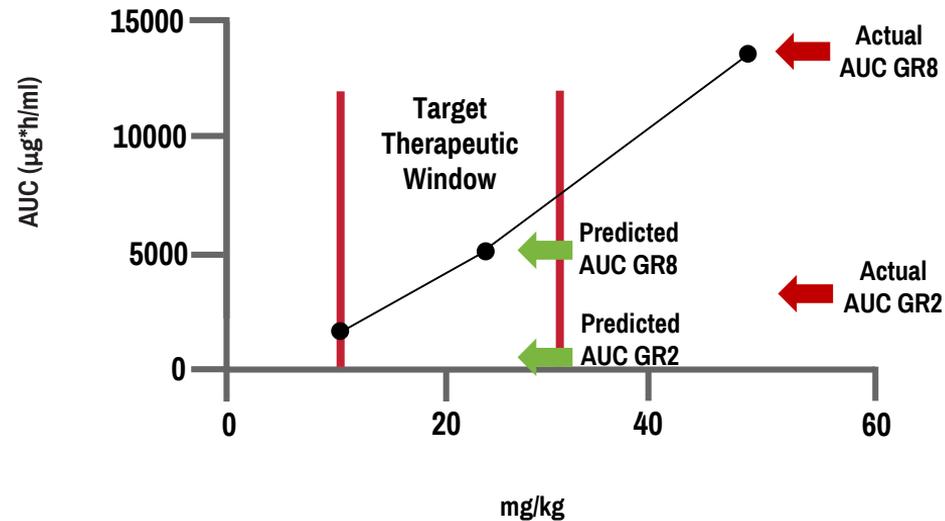
# GR-MD-02 targets the ~230,000 NASH patients with cirrhosis and without varices

## Addressable Patient Population (2018 estimates, US and EU5)



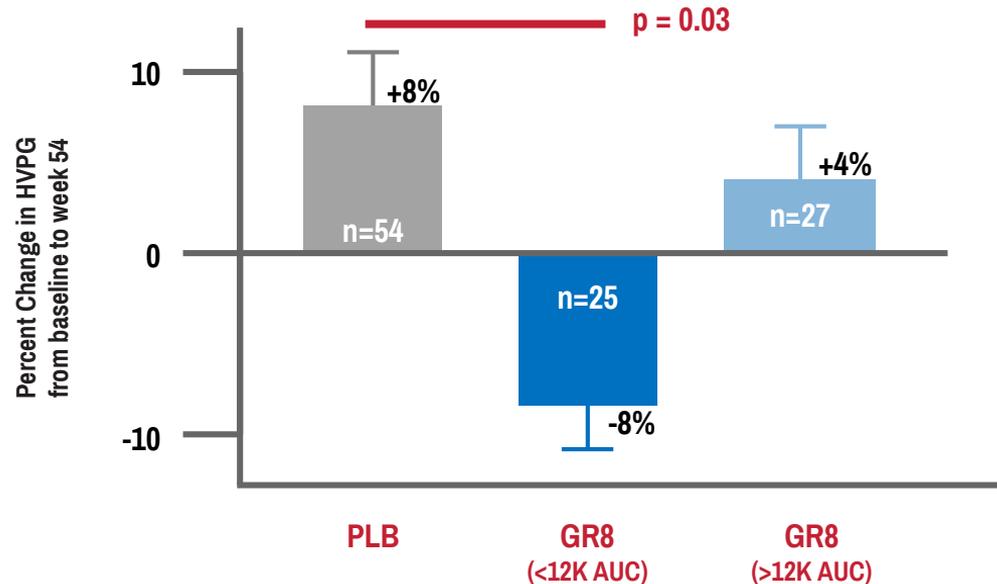
## Why is the GR2 dose better than GR8? PK May hold the key

This graph shows AUC versus dose for the mouse and the target therapeutic window from experiments I NASH mice. The dose chosen for the NAHS-CX study were informed from a phase 1 study in patients with NASH with advanced fibrosis. Predicted to be in the lower and higher range of therapeutic window. However, the actual AUCs for GR2 and GR8 were much higher in patients with NASH cirrhosis.



## Change in HVPG from Baseline to End of Study Using AUC Range Groups

This shows there is a significant difference from placebo in percent change of HVPG when compared to the GR8 (AUC<12K), but not when the AUC's in the GR8 treatment group at an AUC of 12K defines an upper range of the therapeutic window. Furthermore, this may explain why the GR2 dose was more effective in this study than the GR8 dose.



## PK-PD Correlation between Mouse and Human

A PK-PD relationship was developed based on experiments done in a mouse model of NASH<sup>1</sup>. AUCs for the GR2 dose and 8mg/kg GR-MD-02 dose were graphed with the mouse AUC values of 10, 30, 60, and 120mg/kg which were the doses used in the mouse NASH model. Also shown is the anti-inflammatory activity of each mouse dose as derived from the reduction in NASH mouse studies. In contrast, the AUCs of the GR8 dose straddle the AUC of 12,000, which is roughly the border where the anti-inflammatory activity in NASH mice begins to diminish.

