# 89bio

## Powerful Science Meaningful Medicines Changing Lives

Nasdaq: ETNB

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## **Corporate Highlights**



## Advancing Pegozafermin in Clinical Development

INDICATION	TRIAL	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
MASH	<b>ENlighten</b> fibrosis	Phase 3 trial in F2	2/F3: Histology & Ou	tcomes – Ongoing	
Therapy & PRIME designations	<b>ENlighten</b>	Phase 3 trial in F4	4: Histology & Outco	omes – Ongoing	
SHTG	ENtrust	Phase 3 trial – To	pline data expected	in 2025	

## Pegozafermin is an FGF21 Analog Optimally Engineered to Balance Efficacy and Long Dosing Interval



	FGF21	Pegozafermin
RECEDTOR	EC <sub>50</sub> (nM)	EC <sub>50</sub> (nM)
RECEPTOR	Mean ± S.D.	Mean ± S.D.
KLB	nd	nd
KLB/FGFR1	4.5 ± 1.0	0.3 ± 0.07
KLB/FGFR2	4.5 ± 0.9	$1.1 \pm 0.4$
KLB/FGFR3	1.8 ± 0.3	$1.2 \pm 0.4$
KLB/FGFR4	nd	nd

nd – not determined; rhFGF19 EC\_{50} at FGFR4 = 1.7  $\pm$  0.4

- Proprietary glycoPEGylation technology commercially validated with approved products
- Increases half-life of native FGF21 (<2 hours) to 55-100 hours based on single ascending dose study
- Composition of matter patent expires in 2038, assuming no patent term extensions



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## **Opportunity in MASH**





## Pegozafermin Offers Potential Best-in-Class Therapeutic for Advanced MASH





## ENLIVEN Trial Evaluated Weekly (QW) and Every-Two-Week (Q2W) Dosing in Non-cirrhotic Patients



### **PRIMARY ENDPOINTS**

- ≥1-stage fibrosis improvement with no worsening of MASH<sup>1</sup>
- MASH resolution with no worsening of fibrosis<sup>2</sup>

### KEY SECONDARY EFFICACY ENDPOINTS

- ≥2-point change in NAS with no worsening of fibrosis
- Non-invasive liver markers (liver fat, liver injury, fibrosis markers)

<sup>1</sup>Improvement in liver fibrosis by ≥1 stage and no worsening of steatohepatitis defined as no increase in NAS for ballooning, inflammation, or steatosis (FDA draft guidance). <sup>2</sup>Resolution of steatohepatitis is defined as absent fatty liver disease or isolated or simple steatosis without steatohepatitis and a NAS score of 0-1 for inflammation, 0 for ballooning and any value for steatosis (FDA draft guidance).

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\*Some placebo patients were re-randomized in the extension phase to receive pegozafermin.

NAS, NAFLD Activity Score; MRI-PDFF, Magnetic resonance imaging-estimated proton density fat fraction; QW: Every week; Q2W: Every 2 weeks

## Pegozafermin Demonstrated Statistical Significance on Fibrosis Improvement at 30mg QW and 44mg Q2W Dose



### Treatment with PGZ Delays Progression to Cirrhosis

- In the placebo group,
   7 of 37 (19%) of the F3 patients progressed
- In the pooled PGZ group, 6 of 69 (9%) of the F3 patients progressed

\*Relative risk presented is calculated by dividing the drug response by placebo response. Relative risk calculated using statistical methods show similar results. Source: Full Analysis Set; multiple imputation analysis via Cochran-Mantel-Haenszel (CMH) test stratified by type 2 diabetes mellitus (T2DM) status (yes vs. no) and fibrosis stage (F2 vs. F3).

### Comparative Clinical Data in Non-Cirrhotic Patients ≥1 Stage Fibrosis Improvement with No Worsening of MASH

In absence of H2H studies, drug response as a multiple of placebo offers robust window for cross-trial comparisons by controlling for variability amongst readers and consensus methods

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	Pegoza FG	ifermin F21		Efrux FG	ifermin GF21		Rezd TR-β A	liffra <sup>1</sup> Agonist	Semaglutide GLP-1	Tirzej GLP-	oatide 1/GIP	Survoo GLP-1/G	dutide Iucagon	Den F	nifanstat FASN	VK2 TR-β <i>F</i>	2809 Agonist
	Phas 24 W 3 reade	se 2b /eeks er panel	Phas 24 W 2 rea	e 2b eeks ders	Pha 96 W 2 rea	se 2b /eeks aders	Pha 52 W 2 rea	ise 3 /eeks aders	Phase 2 72 Weeks 2 readers	Pha 52 W 2 rea	se 2 /eeks aders	Pha 48 W Single	se 2 'eeks reader	Ph 52 Singl	ase 2b Weeks le reader	Phase 52 W	e 2b eeks
Relative Risk Drug response as multiple of placebo response*	3.5	3.6	2.0	2.0	1.9	3.1	1.7	1.9	1.3	1.7	1.7	2.0	1.8		2.1	1	.5
Fibrosis Improvement (Placebo- adjusted)	19%	20%	19%	, 21%	22%	51%	10%	12%	10%	21%	21%	19%	15%	1	16%	17	7%
	30mg QW (n=66)	44mg Q2W (n=51)	28mg (n=38)	50mg (n=34)	28mg (n=26)	50mg (n=28)	80mg (n=316)	100mg (n=321)	0.4mg (n=56)	10mg (n=47)	15mg (n=48)	4.8mg (n=72)	6mg (n=74)	5 (1	50mg n=81)	Comi (n=:	bined 137)

\*Relative risk, or drug response as multiple of placebo response, is calculated by dividing drug response by placebo response

<sup>1</sup>≥1 stage fibrosis improvement with no worsening of NAS. Fibrosis improvement by ≥ 1 stage with no worsening of NAFLD activity score.

Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

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## Pegozafermin Demonstrated Statistical Significance on MASH Resolution at All Doses



• Relative risk presented is calculated by dividing the drug response by placebo response. Relative risk calculated using statistical methods show similar results.
• Source: Full Analysis Set; multiple imputation analysis via Cochran-Mantel-Haenszel (CMH) test stratified by T2DM status (yes vs. no) and fibrosis stage (F2 vs. F3).

## Pegozafermin Demonstrated Statistical Significance on the Combined Endpoint of Fibrosis Improvement and MASH Resolution



Source: Full Analysis Set; multiple imputation analysis via Cochran-Mantel-Haenszel (CMH) test stratified by T2DM status (yes vs. no) and fibrosis stage (F2 vs. F3).

MRI-PDFF responder defined as ≥30% reduction in liver fat content; ALT responder defined as ≥17U/L reduction.

\*\*\*p<0.001 versus placebo.

## Pegozafermin Demonstrated Robust Liver Fat Reduction with High Responder Rates by MRI-PDFF



<sup>1</sup>Analysis via mixed model repeated measure (MMRM). <sup>2</sup>Analysis via Cochran-Mantel-Haenszel (CMH) test stratified by T2DM status (yes vs. no) and fibrosis stage (F2 vs. F3). MRI-PDFF Analysis Set in patients with >10% liver fat at baseline. \*\*\*p<0.001 versus placebo

## Pegozafermin Demonstrated Significant Improvements in Markers of Liver Injury/Inflammation (ALT and AST)





<sup>1</sup>ALT normalization defined as patients with ALT ≥30 U/L at baseline (n=133) with end-of-study ALT <30 U/L. Source: Full Analysis Set: Analysis via mixed model with repeated measure (MMRM). Data presented as LS Means. \*\*\*p<0.001 versus placebo.

## Pegozafermin Demonstrated Significant Reductions in Non-Invasive Markers (NITs) of Liver Inflammation and Fibrosis



Source: Full Analysis Set for FibroScan and PRO-C3 assessments and MRI-PDFF analysis set for cT1, Analysis via MMRM for cT1 and PRO-C3, ANCOVA for VCTE. A patient is

designated a cT1 responder with ≥80 msec reduction as compared to baseline. cT1 analysis was performed at sites where available.

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001 versus placebo.

## Pegozafermin Demonstrated Significant Improvements on Non-Invasive Markers (NITs) for Fibrosis



Source: Full Analysis Set. NITs reported as LS means with changes from baseline (absolute or %) \*\*\*p<0.001 versus placebo.

Long-term Treatment with Pegozafermin Results in Sustained Improvements over a Wide Range of Liver NITs

	Placebo Week 24 (n=42)	Placebo Week 48 (n=35)	30mg QW Week 24 (n=66)	30mg QW Week 48 (n=50)	44mg Q2W Week 24 (n=51)	44mg Q2W Week 48 (n=45)
MRI-PDFF	-6%	-11%	-56%	-60%	-60%	-47%
ALT	0%	-11%	-42%	-42%	-32%	-35%
AST	-2%	-4%	-39%	-39%	-34%	-36%
Pro-C3	+6%	+2%	-18%	-15%	-17%	-14%
FAST	-3%	-1%	-56%	-59%	-57%	-51%
VCTE (kPa)	-0.1	-0.8	-2.8	-2.9	-1.5	-1.3
ELF score	+0.2	+0.1	-0.3	-0.3	-0.3	-0.4



WEEK 24 WEEK 48

# Pegozafermin Offered Additive Benefits to GLP-1 Therapy in Patients with MASH through Week 48



- 37 patients in ENLIVEN were on GLP-1 therapy at baseline – 25 received pegozafermin, 12 received placebo
- Patients on GLP-1 were on stable doses for a minimum of six months with most patients on semaglutide or dulaglutide; most of these patients were also on additional diabetes medications
- Patients had comparable baseline characteristics across groups and relative to full study population



### **KEY RESULTS**

Pegozafermin on top of GLP-1 therapy showed the following versus GLP-1 plus placebo at week 24 and week 48:

- Improved Fibrosis
- Reduced Liver Fat
- Improved Liver Health
- Acceptable Tolerability Profile

GLP1

Greater Benefits on Fibrosis Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 24





WEEK 24 GLP1 Greater Benefits on Metabolic Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 24



Source: Full Analysis Set. Adiponectin reported as LS mean change from baseline; HbA1c reported as median change (absolute) from baseline; MRI-PDFF and TG reported as median percent change from baseline. Post-hoc analysis

WEEK 24 GLP1

## Pegozafermin Offers a Promising Profile in Patients with Compensated MASH Cirrhosis (F4)



- ENLIVEN enrolled 14 MASH stage F4 patients of which 12 patients\* had follow-up biopsies at week 24
- Patients had baseline characteristics generally reflective of a well-compensated cirrhotic population



### **KEY RESULTS**

- 45% of pegozafermin-treated patients had fibrosis improvement ≥1 stage without worsening of MASH
- Improvements in NITs of fibrosis, liver injury, and liver fat were observed through week 48
- Safety and tolerability profile in F4 was similar to the F2/F3 population

## Pegozafermin Achieved Fibrosis Improvement Without Worsening of MASH in 45% of Patients with F4 Fibrosis at Baseline



## Pegozafermin Has Demonstrated Preliminary Evidence of Fibrosis Regression in Patients with F4 Fibrosis\*



\* If approved



Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

## NIT Results over 48 Weeks in F4 Patients From ENLIVEN Demonstrated Consistent Benefit



### **PGZ-Treated Patients (n=12)**

Parameter	24 weeks	48 weeks				
Liver Fibrosis and Inflammation						
ELF (units)	-0.3	-0.5				
FAST	-46%	-42%				
VCTE (kPa)	-2.7	-1.1				
Pro-C3	-5%	-20%				
FIB-4	-11%	-16%				
Liver Injury						
ALT (%)	-53%	-58%				
AST (%)	-31%	-38%				

### High correlation between NIT responders and fibrosis improvement

### Pegozafermin Was Well Tolerated Across All Patients In ENLIVEN Most TEAEs were Grade 1 and Grade 2

### Drug-related TEAEs in ≥10% of patients Through 48 Weeks

Preferred Term	Placebo (n=50)	15mg QW (n=21)	30mg QW (n=72)	44mg Q2W (n=57)
Diarrhea	3%	24%	17%	9%
Nausea	1%	14%	21%	18%
Injection site erythema	4%	14%	14%	5%
Injection site rash	2%	0	10%	4%
Increased appetite	2%	10%	13%	5%

• At week 48, no statistically significant or clinically meaningful changes were observed in blood pressure, bone biomarkers or DXA with PGZ 30 mg QW or 44 mg Q2W relative to placebo.

	Placebo	15mg QW	30mg QW	44mg Q2W
Drug-related AEs leading to discontinuation	0	5%ª	6% <sup>b</sup>	4% <sup>c</sup>
Drug-related Serious Adverse Event (SAE)	0	0	0	2% <sup>c</sup>

Related discontinuations: a Diarrhea [15 mg QW]; b Diarrhea [30 mg QW]; Nausea [30 mg QW]; Diarrhea [30 mg QW]; ISR erythema [30 mg QW]; Charreatitis [44 mg Q2W]; Nausea [44 mg Q2W].



# ENLIGHTEN-Fibrosis: Phase 3 trial in Non-cirrhotic MASH (F2-F3) is Ongoing



### HISTOLOGY PORTION FOR ACCELERATED APPROVAL

- Co-primary Endpoints:
- One-point improvement in fibrosis with no worsening of MASH
- MASH resolution with no worsening of fibrosis
- Duration: 52 weeks
- **Patients:** Subset of the ~1,000 patients

### **OUTCOMES PORTION FOR FULL APPROVAL**

- Primary Endpoint: Patients are expected to continue to be treated beyond the 52-week assessment through outcomes to support full approval in F2-F3 patients
  - Progression to cirrhosis expected to comprise most outcome events
- Patients: ~1,000 patients

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ENlighten

in Non-cirrhotic

**MASH** patients

# ENLIGHTEN-Fibrosis: Potential for success on both histology and clinical outcomes for F2/F3 MASH

### **HISTOLOGY**

- FGF21 analogs have demonstrated robust fibrosis regression at both week 24 and over longer time frames
- Pegozafermin demonstrated fibrosis improvement at week 24 and maintenance of NITs at week 48
  - Biopsy at month 12 in a Phase 3 trial may show even more robust effect
- Robust statistical design to determine a clinically meaningful delta

### **OUTCOMES**

- Build on strong fibrosis regression and NIT data demonstrated from ENLIVEN
- Encouraging clinical outcomes data from Intercept's REGENERATE Phase 3 trial
  - Despite modest, ~10% fibrosis delta, Ocaliva<sup>®</sup> had a trend (p=0.04) to clinical outcome benefit\*
- ~20% fibrosis delta for PGZ at week 24, bodes well especially given the potential for improved response with longer treatment
- Phase 3 is well-powered for outcomes; REGENERATE validated that progression to cirrhosis is the primary outcomes event

# ENLIGHTEN-Cirrhosis: First FGF21 Analog to Enter Phase 3 Study in Compensated Cirrhosis (F4)



### HISTOLOGY PORTION FOR ACCELERATED APPROVAL

- Primary Endpoint: Regression of fibrosis from F4 to an earlier stage of fibrosis
- **Duration:** 24 months
- **Patients:** Subset of the 760 patients

### **OUTCOMES PORTION FOR FULL APPROVAL**

- Primary Endpoint: Clinical outcomes composite to support full approval in the U.S. and in Europe, across F2-F4 patients
  - Modifications to some outcome definitions to allow trial to reach final number of events quicker, and therefore potentially accelerate timeline to readout
- Patients: Approximately 760 patients\*

ENlighten

in

Compensated

Cirrhotic (F4) MASH patients

## ENLIGHTEN-Cirrhosis: Potential for Success on Histology and Outcomes

### HISTOLOGY

- FGF21 analogs have demonstrated greatest degree of benefit in fibrosis regression
- Consistent response in fibrosis & NITs across F3 and F4 to support potential for robust fibrosis benefit
- Enroll/select patients with early F4 disease more likely to show fibrosis regression
- Follow-up biopsy at 24 months
  - Expected to be sufficient time to allow PGZ to work
  - Could reduce placebo biopsy noise
- Robust statistical design to determine a clinically meaningful delta

### **OUTCOMES**

- Build on strong fibrosis regression and NIT data from ENLIVEN
- Enroll/select additional patients with the right profile to increase event rates
- Modified outcome definitions to increase event rate
- Rigorous endpoint assessment
- Robust statistical design to determine a clinically meaningful delta

## Potential to Address Substantial Needs in MASH with Advanced Fibrosis and Cirrhosis

### Large patient population with significant health risks

- The market for F2-F3 and F4 MASH is estimated to impact ~15M patients by 2035 in the US with equivalent number in the EU
  - The prevalence of F2-F3 MASH and compensated cirrhotic MASH (F4) may potentially reach ~10.7M and ~3.6M respectively in 2035, net of impacts from GLP-1-based therapies<sup>1</sup>
  - While the wide adoption of GLP-1 based therapies may reduce MASH prevalence, the eligible pool of diagnosed patients may increase due to new MASH-specific therapies

### Significant market opportunity for pegozafermin

- We believe we are uniquely positioned to meet the needs of MASH patients with advanced fibrosis (primarily F3) and compensated cirrhosis (F4)
  - Potent anti-fibrotic drugs such as pegozafermin is expected to be the preferred option to treat advanced MASH versus metabolic therapies that reduce fat and indirectly improve liver health over time
  - Clinical data show additive benefits to GLP-1 based therapies, and we believe support combination use
- Large market is likely to support therapies with different mechanisms of action (MOA) and multiple therapies within a specific mechanism (similar to T2DM or LDL therapeutic area) – no MOA is currently a "cure" for MASH

## Pegozafermin Positioned to Address Advanced MASH



## Advanced MASH (F2/F3) Represents a Significant Market



## Market Opportunity in Compensated F4 Patients Expected to Grow



#### Pegozafermin – Potential Usage in Multiple Settings with GLP-1 Based on Treatment History, Fibrosis Stage and Comorbidities **Future Treatment Decision-making PRIOR GLP-1** in MASH Patients **IIIUSTRATIVE EXPOSURE?** Yes, discontinued Yes, ongoing No Does patient have Degree of fibrosis? Why did patient discontinue? T2D / obesity? Yes No Degree of fibrosis? No sustained Limited Advanced Other (e.g. cost, Limited Advanced benefit/poor poor compliance) tolerability Tolerability concerns? Yes No Add NASH Tx Start NASH Start NASH Start GLP-1 + Start NASH Continue GLP-1 Case-by-case Start GLP-1<sup>1</sup> Specific Tx to GLP-1 **Specific Tx** NASH Combo Specific Tx **PEGOZAFERMIN TARGET**



<sup>1</sup>To re-evaluate fibrosis progression after 6 – 12 months to assess need for NASH-specific Tx. HCP: Healthcare Provider; T2D: Type 2 Diabetes; Tx: Treatment. Source: Physician Interviews; ClearView Analysis.

## Pegozafermin Expected to Garner Significant Market Share In F3 Patients



FGF21s garner ~45% market share, with ~2/3<sup>rd</sup> gained by PGZ

 PGZ benefit/risk profile and fewer injections make it preferred FGF21

 ~50% of usage in combination with GLP-1

Total GLP-1 usage (combo + mono): ~65%



^F4 shares only tested change if pegozafermin had FDA approval in F4 patients and assumes uptake in "other FGF21" due to benefit of being in the same class; research did not show profiles or assume approvals for other agents. Source: Primary research with 35 Hep/GIs, September 2023.

## Pegozafermin Expected to Garner Significant Market Share In Compensated F4 Patients



\*\*Includes no pharmacologic treatment, clinical trials and existing non-approved agents like vitamin E or pioglitazone

^F4 shares only tested change if pegozafermin had FDA approval in F4 patients and assumes uptake in "other FGF21" due to benefit of being in the same class; research did not show profiles or assume approvals for other agents. Source: Primary research with 35 Hep/GIs, September 2023.

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## Opportunity in Severe Hypertriglyceridemia (SHTG)





### Pegozafermin Could Offer an Important New Treatment Option for SHTG Topline results expected in 2025

### Large growing patient population with significant health risks; overlap with MASH patient population

- Increasing TG levels increase risk of acute pancreatitis, cardiovascular disease and all-cause mortality
- Emerging evidence of the cardiovascular (CV) benefit associated with TG reduction in patients with CV risk factors

### Significant market opportunity for agent with broad metabolic benefits

- Pegozafermin has a unique selling proposition that is meaningful to prescribers more effective triglyceride reduction with improvements in liver fat and other metabolic measures
- Analyst consensus peak year sales estimated to be ~\$1 billion (US only)

### Clinical program substantially de-risked

- Phase 3 ENTRUST trial initiated; design similar to positive Phase 2 ENTRIGUE design with same primary endpoint
- Agency alignment on trial design and regulatory path; exploring alternatives for a more efficient path to registration

### SHTG program is synergistic with the MASH program

- Development: Leverages safety database across the two programs to minimize spend across total program
- Commercial: Leverage sales force and infrastructure costs
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## ENtrigue – Phase 2 SHTG Trial Design



**KEY INCLUSION CRITERIA** 

- TG ≥500mg/dL and ≤2,000mg/dL
- Background therapy: statins and/or prescription fish oil and/or fibrates OR none

### **PRIMARY ENDPOINT**

 Primary endpoint: % Change in TGs from baseline

### **KEY SECONDARY ENDPOINTS**

- Lipids: non-HDL-C, HDL-C, Apo-B
- Liver fat (MRI-PDFF)
- Glycemic control

Magnetic Resonance Imaging – Proton Density Fat Fraction QW, once-weekly; Q2W, once every two weeks. Safety analysis set, n=85 (patients who received at least 1 dose) Full analysis set, n=82 (patients with at least 1 post-baseline TG assessment) MRI analysis set n=23 (patients with baseline and end of treatment MRIs)

## Pegozafermin Significantly Reduced Triglycerides Across All Dose Groups



QW: Every week; Q2W: Every 2 weeks



## Pegozafermin Showed Significant Decrease in Triglycerides on Top of Background Therapy

Median % Change in Triglycerides from Baseline at Week 8



prescription fish oils, and fibrates



## Pegozafermin Showed Significant Decrease in Triglycerides at Different Threshold Levels



Analysis via unstratified Chi-square Test comparing the individual PGZ groups vs placebo. \* p<0.05; \*\* p<0.01; \*\*\* p<0.001 vs. placebo

TG Responders defined as patients who achieve TG <500 mg/dL

## Pegozafermin Demonstrated Clinically Meaningful Improvements in Key Marker of CV Risk for SHTG



# Pegozafermin Demonstrated Significant Improvement on Key Co-morbidities for SHTG Patients



\*p <0.05 vs. placebo MDL Angleris Satura university placebo based on ANCOVA anglesis

MRI Analysis Set; p value vs placebo based on ANCOVA analysis

## Pegozafermin Demonstrated Favorable Safety/Tolerability Profile in Phase 2 Study

- Pooled pegozafermin treatment related Adverse Events (AEs) observed in ≥7.5% of patients were:
  - Nausea (10%), diarrhea (9%) and injection site reaction (9%) vs placebo (0%)
  - All Gastrointestinal (GI) AEs were Grade 1 or 2
- No Grade 3 or higher AEs
- No treatment-related SAEs; 2 treatment-related discontinuations at 27mg QW (both Grade 2)
- No tremor or hypersensitivity AEs reported
- No adverse effects on blood pressure or heart rate

## Phase 3 ENTRUST Trial Design



### **KEY INCLUSION CRITERIA**

- TG ≥500mg/dL and ≤2,000mg/dL
- Stable background lipid modifying therapy\*

### **PRIMARY ENDPOINT**

 Percent change from baseline in fasting TGs at Week 26 vs. placebo

### **KEY SECONDARY ENDPOINTS**

 Liver fat by MRI-PDFF, Various lipids, HbA1c at Week 26 vs. placebo, TGs at Week 52 vs. placebo

## SHTG Represents a Large Population with High Unmet Need





## Pegozafermin Delivers on Key Attributes for Successful SHTG Therapy



Pegozafermin has Similar TG Effects and Added Metabolic Benefits with No Increase in LDL-C when Compared to APO-C3 Inhibitor

	Pegozafermin ENTRIGUE <sup>1</sup>	Plozasiran (ARO-APO-C3) SHASTA-2 <sup>2</sup>
Endpoint	27mg QW placebo-adjusted	50mg Q12W placebo-adjusted
TG	-53%	-57%
% Patients with TG<500	46%	37%
Liver fat by MRI-PDFF <sup>3</sup>	-32%	Not reported
HDL-C	+35%	+58%
Non-HDL-C	-29%	-20%
LDL-C	+1%	+59%
Аро-В	-17%	-6%
Glycemic control	Demonstrated beneficial effect on glycemic control	Worsening glycemic control reported as AE: 19% vs 12% placebo

<sup>1</sup>Bhatt, Bays, Miller et al. ENTRIGUE. Nature Medicine, 2023.

<sup>2</sup>AHA 2023: Gaudet, D; ARO-APOC3, an Investigational RNAi Therapeutic, Silences APOC3 and Reduces TG to Near Normal Levels in Patients with SHTG: SHASTA-2 Study Results <sup>3</sup>ENTRIGUE topline data presentation, June 2022.

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## **Corporate Highlights**



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## Appendix

## **Experienced Management Team Positions 89bio for Success**



## Pegozafermin Exhibits Highly Potent FGF Receptor Agonism



Pegozafermin has the potential to reproduce the beneficial metabolic effects of native FGF21

	<u> </u>		
EC <sub>50</sub> (nM)	EC <sub>50</sub> (nM)		
Mean ± S.D.	Mean ± S.D.		
nd	nd		
4.5 ± 1.0	0.3 ± 0.07		
4.5 ± 0.9	$1.1 \pm 0.4$		
1.8 ± 0.3	$1.2 \pm 0.4$		
nd	nd		
	EC <sub>50</sub> (nM) Mean ± S.D. nd 4.5 ± 1.0 4.5 ± 0.9 1.8 ± 0.3 nd		

nd – not determined; rhFGF19 EC<sub>50</sub> at FGFR4 =  $1.7 \pm 0.4$ 

\* Receptor agonism measured in L6 cells expressing  $\beta$ -klotho and either FGF Receptor 1c, 2c, 3c, or 4 via pERK functional assay \*\* Figures represent data from a single experiment; Table represents mean data from multiple experiments

## **ENLIVEN Baseline Characteristics Well Balanced Across Dose Groups**

<b>Parameter</b> Mean or %	<b>Placebo</b> (n=71)	<b>15mg QW</b> (n=21)	<b>30mg QW</b> (n=73)	<b>44mg Q2W</b> (n=57)	Total (n=222)
Age (years)	56	55	55	55	56
Female	55%	43%	69%	65%	61%
BMI (kg/m²)	38	38	35	36	37
Type 2 Diabetes	69%	86%	62%	61%	66%
Fibrosis Stage (% F3)	66%	43%	64%	53%	60%
NAFLD Activity Score	5.0	4.8	5.3	5.2	5.1
Liver Fat Content (MRI-PDFF)	16.7%	15.8%	16.7%	15.8%	16.4%
Liver Stiffness (VCTE, kPa)	14.1	11.2	12.5	13.2	13.0
PRO-C3 (ng/mL)	50	62	54	52	53
ALT (U/L)	50	61	60	56	56
AST (U/L)	41	48	47	42	44
HbA1c, overall population (%)	6.6	7.0	6.6	6.7	6.7
Triglycerides (mg/dL)	170	186	175	165	172

Baseline characteristics were consistent in full analysis set (n=192) and the safety set (n=222)

Source: Randomized Analysis Set.

DIO ALT, alanine aminotransferase; AST, aspartate aminotransferase; NAFLD, nonalcoholic fatty liver disease; PRO-C3, N-terminal type III collagen propeptide; VCTE, Vibration-controlled transient elastography. 53

## **ENLIVEN** Patient Disposition and Analysis Sets



ENLIVEN Used Objective Biopsy Reading Methodology Designed to Reduce Histology Scoring Biases and Variability



- Pathologists underwent protocol-specific harmonization training before and during trial
- Pathologists were blinded to patient, treatment and sequence
- >99% of final scores determined by a priori established algorithm, versus resolving disagreements via interreader discussion

## Pre-Specified ITT Analysis Confirms Robustness of Primary Efficacy Results

### ITT (missing data = non-responder); (n=192) at Week 24

	30mg QW	44mg Q2W			
Fibrosis improvement without worsening of MASH					
Effect Size (placebo-adjusted)	15%	16%			
p-value	0.019	0.015			
MASH resolution without worsening of fibrosis					
Effect Size (placebo-adjusted)	17%	20%			
p-value	0.0019	0.0009			



# Pegozafermin Demonstrated Meaningful Reductions in HbA1c (ENLIVEN)



### Change in HbA1c from Baseline at Week 24

Source: Full Analysis Set for either overall population or FAS with baseline HbA1c  $\geq$ 6.5%. Analysis via MMRM. \*p<0.05, \*\*p<0.01 versus placebo.

# Pegozafermin Demonstrated Meaningful Changes in Serum Lipids (ENLIVEN)

#### **Triglycerides** Non-HDL Cholesterol HDL Cholesterol 0% 0% 0% 20% 14%\*\*\* -6% -10% 10% -10% **6%**\* -20% 0% -7% -7% -3% -27%\*\*\* -30% -10% -10% 30mg QW 44mg Q2W Placebo 30mg QW 44mg Q2W Placebo Placebo 30mg QW 44mg Q2W n=61 n=66 n=51 n=61 n=66 n=51 n=61 n=66 n=51

### Percent Change in Serum Lipids from Baseline at Week 24

Source: Full Analysis Set. Analysis via van Eltren Test for triglycerides (reported as median) and mixed model with repeated measure (MMRM). Patients with missing week 24 triglycerides are excluded from the non-parametric analysis.

Non-HDL-cholesterol and HDL Cholesterol (reported as LS means) with changes from baseline (absolute or %) as dependent variables.

Independent Patient Confirmation of Pegozafermin Treatment Effect Placebo Patients Showed Robust Benefits Upon Crossing Over to Pegozafermin



Parameter	Main Study Placebo n=19	Extension Phase 30mg QW n=19
MRI-PDFF	-21%	-63%
ALT	-2%	-32%
AST	-2%	-31%
PRO-C3	+8%	-17%
FAST	-14%	-53%
VCTE (kPa)	-0.7	-2.4
ELF score	+0.1	-0.2

### **Change from Baseline**

19 patients were re-randomized from placebo to 30mg QW at week 24 and continued through week 48



Sustained Benefits on Fibrosis Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 48



**WEEK 48** 

GLP1

Sustained Benefits on Metabolic Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 48



WEEK 48 GLP1 Pegozafermin Showed Consistent and Significant Benefit in Achieving Fibrosis Improvement Across Prespecified Subgroups

### Pegozafermin 30mg QW Proportion Achieving Fibrosis Improvement

BL T2DM: Yes BL T2DM: No BL Fibrosis stage: F2 BL Fibrosis stage: F3 BL MRI-PDFF: <Median (16%) BL MRI-PDFF: ≥Median (16%) BL ALT: Normal BL ALT: >ULN BL NAS score: <Median (5) BL NAS score: ≥Median (5)



### Pegozafermin 44mg Q2W

Proportion Achieving Fibrosis Improvement



### Est. proportion difference (95% CI)

Source: Full Analysis Set



ALT, alanine aminotransferase; BL, baseline; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NAS, Nonalcoholic fatty liver disease Activity Score; MASH, nonalcoholic steatohepatitis; Q2W, every 2 weeks; QW, once weekly; T2DM, type 2 diabetes mellitus; ULN, upper limit of normal.

# Comparative Profile of FGF21 Analogs in NASH – Safety/Tolerability at Latest Timepoints

	Pegozafe	rmin (PGZ)	Efruxifer	min (EFX)
	48 \	weeks	96 v	veeks
	30mg QW	44mg Q2W	28mg QW	50mg QW
	n=72	n=57	n=40	n=43
Treatment-related Adverse Events (key terms)				
Diarrhea	17%	9%	40%	37%
Nausea	21%	18%	30%	33%
Increased appetite	13%	5%	18%	23%
Injection site erythema	14%	5%	20%	16%
Injection site bruising	3%	4%	15%	7%



## Data from Cohort 7 Support Pegozafermin's Impact in F4 Patients

### Histology data - Fibrosis improvement ≥ 1 stage without worsening of MASH ranged from 17% to 57%

Parameter	PGZ Treated Patients (n=6)
Liver Fibrosis	
VCTE (kPa)	-3.8
FAST (%)	-78.5%
Pro-C3 (%)	-25.5%
Liver Injury	
ALT (%)	-50.7%
AST (%)	-48.7%

Data presented as means for Cohort 7 F4 patients

Safety and tolerability were similar to what has been observed in the non-cirrhotic patient population



## Learnings from the Obeticholic Acid MASH Phase 3 Program: Comparison of Single Central Reader vs. 3-Panel Consensus

### Improvement of Fibrosis by $\geq$ 1 Stage without Worsening



#### **Original Analysis** Consensus Method Read 25-Percent Responders 20-NS NS 11.2 8.0 6.5 5 3.5 Placebo OCA 10 mg OCA 25 mg Placebo OCA 10 mg OCA 25 mg (N=311) (N=312) (N=308) (N=311) (N=312) (N=308)

### **OBSERVATIONS:**

- Placebo response for MASH resolution is >2 fold higher with single reader vs 3-panel consensus
- Placebo response similar to ENLIVEN study for both fibrosis improvement and for MASH resolution

### IMPLICATIONS:

- 3-panel consensus highlights treatment delta but dampens absolute response
- 3-panel consensus methodology can reproduce low placebo response in phase 3 trial

### Resolution of MASH with No Worsening of Liver Fibrosis

## Over 60% of T2D Patients Prefer or Strongly Prefer Every-Two-Week Injections



- Every-two-week dosing provides opportunity for physicians to optimize therapy to patient preference
- Compliance is important in treatment for chronic, asymptomatic diseases

# The Perception of GLP-1 Therapy in Advanced MASH is Mixed Due to Lack of Fibrosis Improvement and Difficult Tolerability Profile



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Lack of fibrosis improvement, difficult tolerability profile, and weight gain after discontinuation make physicians wary of using incretins as a monotherapy for the treatment of MASH, especially for patients with advanced fibrosis. Need for direct anti-fibrotic agents still exists.

### PATIENT PERCEPTIONS OF INCRETINS

- Perceived to be highly effective for weight loss
  - Minority mention no known impact on MASH yet
- Injections not perceived as painful or barrier
- Experience difficult side effects, primarily GI
  - Benefit trade-off positive; some ultimately forced to discontinue due to severity

### HCP PERCEPTIONS OF INCRETINS

- Felt to be efficacious
- High GI-related side effect led to discontinuation rate ~15-30%
- Payer coverage for obesity drugs a challenge (potentially to change over time)

## Prescribers Believe Pegozafermin has the Strongest Liver & MASH Clinical Activity and Favorable Tolerability Profile



### **BENEFITS**

### NEUTRAL

#### DRAWBACKS

(SC)

**Liver-related clinical activity is strongest** (esp. Hep/GIs): Fibrosis improvement; MASH resolution, liver stiffness, ALT reduction and MRI-PDFF is impressive

Favorable tolerability profile



Combination with GLP-1s is appealing given trial includes those on GLP-1s



Other metabolic benefits are nice to have, but less relevant (Hep/GI)



Patients will accept injectables for efficacy - once every 2 weeks is preferred



Few PCPs and Endos would like to see more improvement on HbA1c and weight loss



Some PCPs prefer to refer MASH treatment to liver specialists

