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Powerful Science
Meaningful Medicines
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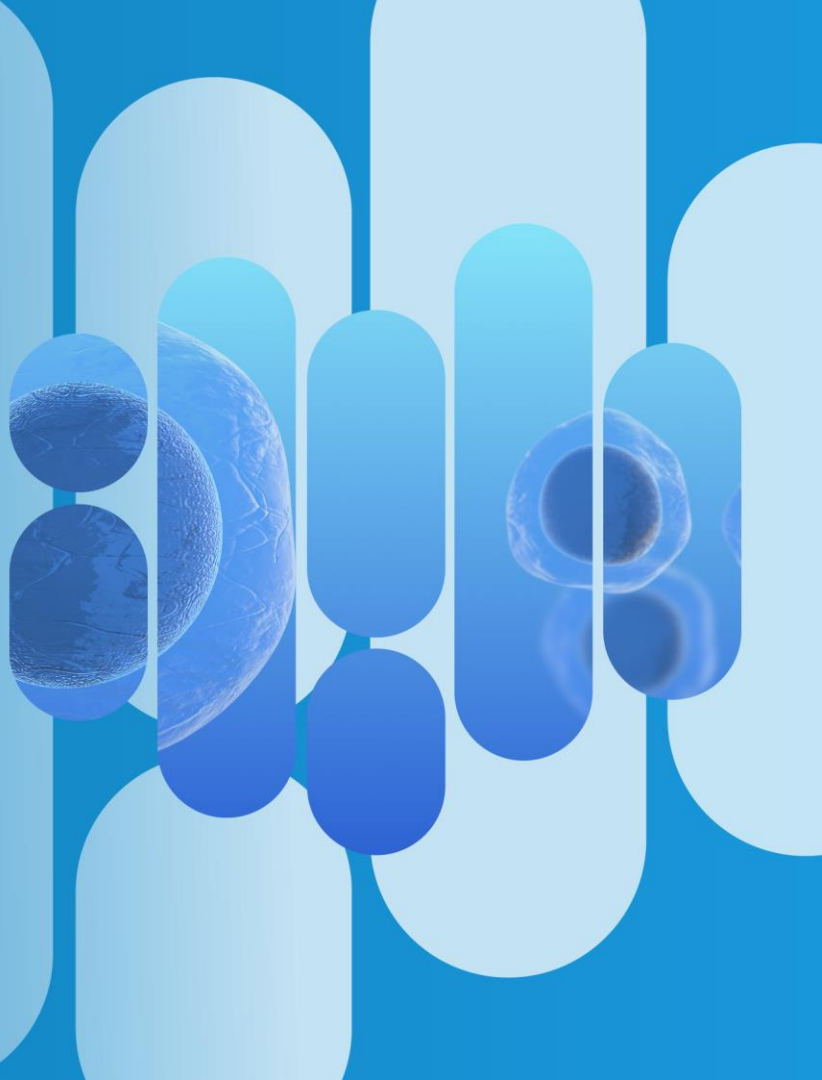
Nasdaq: ETNB

March 2024



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This presentation contains “forward-looking statements” within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties and are based on estimates and assumptions. Other than statements of historical facts, all statements included in this presentation are forward-looking statements, including statements concerning our plans, objectives, goals, strategies, future events, plans or intentions relating to product candidates, potential market opportunities, estimates of market size, estimates of market growth, estimates of market share, the potential clinical benefit, complementary benefits to other therapies, effect on histology and safety and tolerability profile of pegozafermin (formerly BIO89-100), the clinical potential of pegozafermin, potential indications for pegozafermin, the association of clinical data with potential clinical benefit in other indications, the anticipated timing, design, endpoints, and conduct of our future and ongoing clinical trials for pegozafermin, the timing of anticipated milestones, the timing of regulatory meetings, the timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated product development efforts and our liquidity and capital resources, including our cash position. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “plan” or the negative of these terms, and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in this presentation including those described more fully our most recent Form 10-K and Form 10-Q under the caption “Risk Factors” and elsewhere in such report and in other subsequent disclosure documents filed with the SEC.

We cannot assure you that we will realize the results, benefits or developments that we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our business in the way expected. Forward-looking statements are not historical facts, and reflect our current views with respect to future events. Given the significant uncertainties, you should evaluate all forward-looking statements made in this presentation in the context of these risks and uncertainties and not place undue reliance on these forward-looking statements as predictions of future events. All forward-looking statements in this presentation apply only as of the date made and are expressly qualified in their entirety by the cautionary statements included in this presentation. We disclaim any intent to publicly update or revise any forward-looking statements to reflect subsequent events or circumstances, except as required by law.

We obtained the industry, market and competitive position data used throughout this presentation from our own internal estimates and research, as well as from industry and general publications, and research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of the industry and market, which we believe to be reasonable. In addition, while we believe the industry, market and competitive position data included in this presentation is reliable and based on reasonable assumptions, we have not independently verified any third-party information, and all such data involve risks and uncertainties and are subject to change based on various factors. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

This presentation discusses product candidates that are under preclinical or clinical evaluation and that have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory authority. Until finalized in a clinical study report, clinical trial data presented herein remain subject to adjustment as a result of clinical site audits and other review processes. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

Corporate Highlights

Potential Best-in-Class FGF21 in two Phase 3 programs, each of which represents a significant market opportunity*

Metabolic dysfunction-associated steatohepatitis (MASH) Program

- Strong fibrosis data with favorable tolerability and dosing convenience[1]
- Positive long-term data; additive benefits in patients on background GLP-1 therapy
- Regulatory alignment on Phase 3 program including potentially accelerated approval using histology in non-cirrhotic (F2-F3) and cirrhotic (F4) patients
- ENLIGHTEN-Fibrosis initiated, ENLIGHTEN-Cirrhosis expected to initiate in 2Q24

Severe Hypertriglyceridemia (SHTG) Program

- Substantially de-risked Phase 3 with topline data anticipated in 2025

Strong balance sheet with ~579 million in cash[3]

Intended commercial product presentation available; composition of matter patent expires in 2038[2]

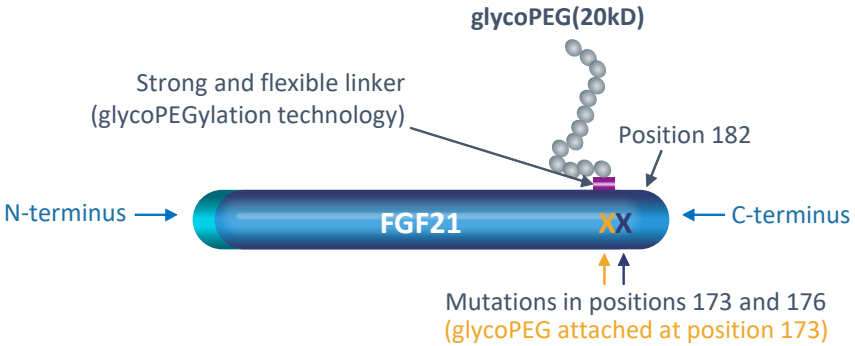
Highly experienced leadership team with track record of execution

[1] Efficacy comparison based on relative risk ratios and not based on head-to-head results
[2] Patent expiration date excludes any patent term extension or new patents
[3] $578.9 million in cash and cash equivalents as of December 31, 2023; excludes in-the-money warrants of approximately $50 million that expire on June 30, 2024
* If approved

Advancing Pegozafermin in Clinical Development

INDICATION	TRIAL	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
MASH *Breakthrough Therapy designation*	ENlighten fibrosis	Phase 3 trial in F2/F3: Histology & Outcomes – Initiated			
	ENlighten cirrhosis	Phase 3 trial in F4: Histology & Outcomes – 2Q24			
SHTG	ENtrust	Phase 3 trial – Ongoing			

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



RECEPTOR	FGF21	Pegozafermin
	EC_{50} (nM)	EC_{50} (nM)
	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 ± 0.4
KLB/FGFR3	1.8 ± 0.3	1.2 ± 0.4
KLB/FGFR4	nd	nd

nd – not determined; rhFGF19 EC_{50} at FGFR4 = 1.7 ± 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
- Low nanomolar potency against FGF receptors 1c, 2c, 3c, similar to native FGF21
- Composition of Matter patent expiring in 2038

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* Receptor agonism measured in L6 cells expressing β-klotho and either FGF Receptor 1c, 2c, 3c, or 4 via pERK functional assay
** Table represents mean data from multiple experiments

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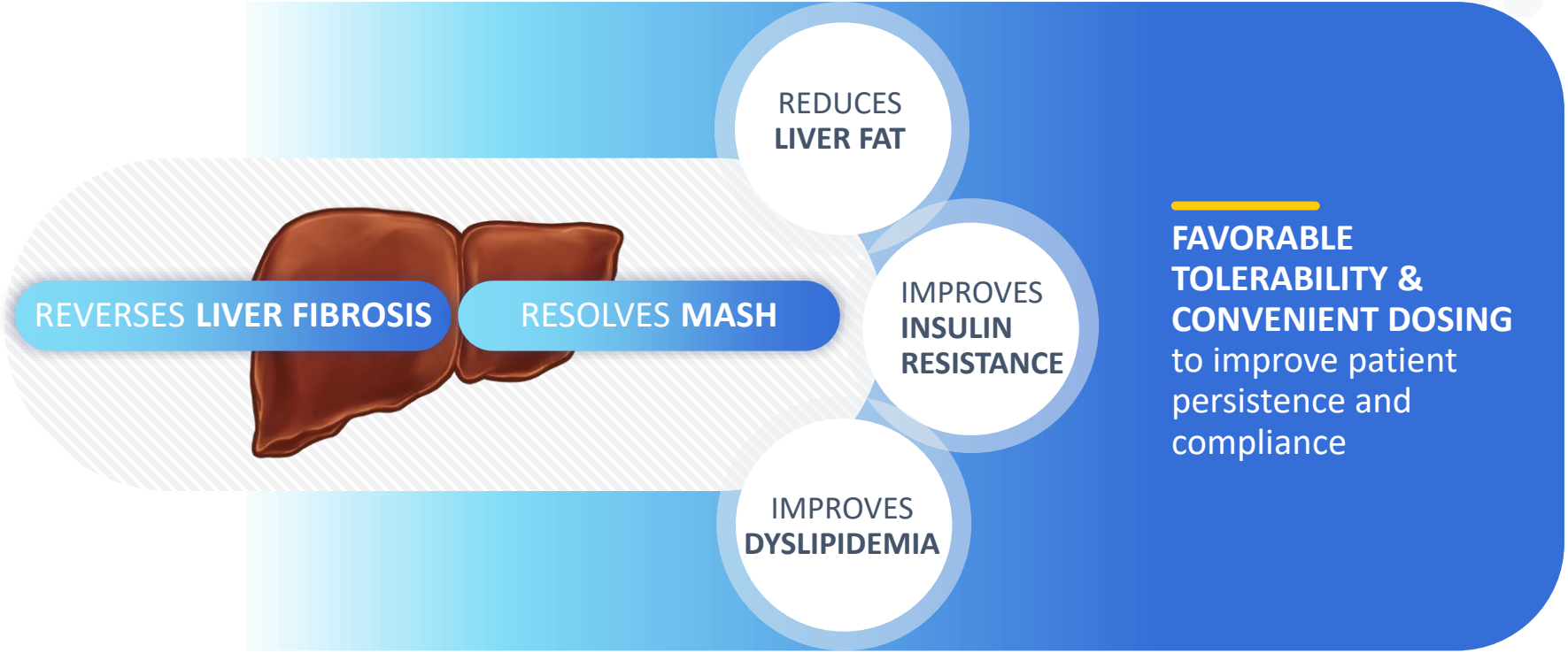
Opportunity in MASH

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



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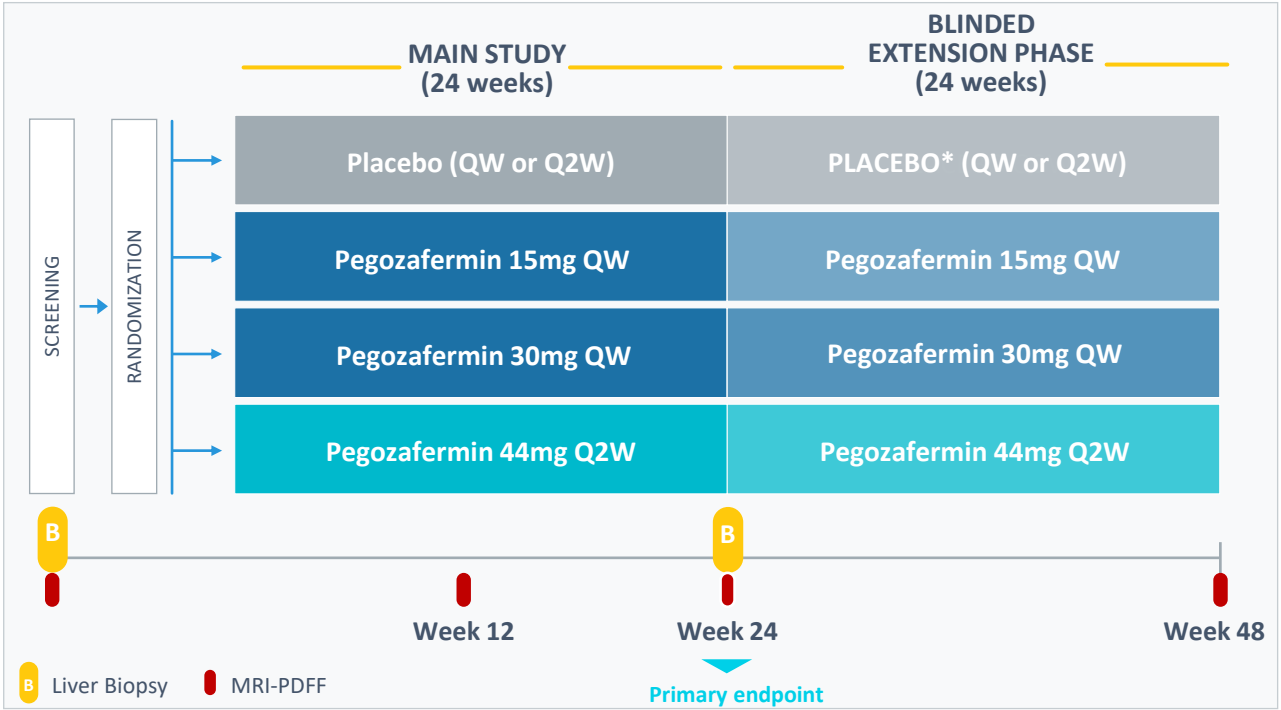
ENLIVEN Trial Evaluated Weekly (QW) and Every-Two-Week (Q2W) Dosing in Non-cirrhotic Patients



PRIMARY ENDPOINTS

- ≥1-stage fibrosis improvement with no worsening of MASH[1]
- MASH resolution with no worsening of fibrosis[2]

KEY SECONDARY EFFICACY ENDPOINTS

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

[1]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).
[2]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).
*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

Baseline Characteristics Well Balanced Across Dose Groups

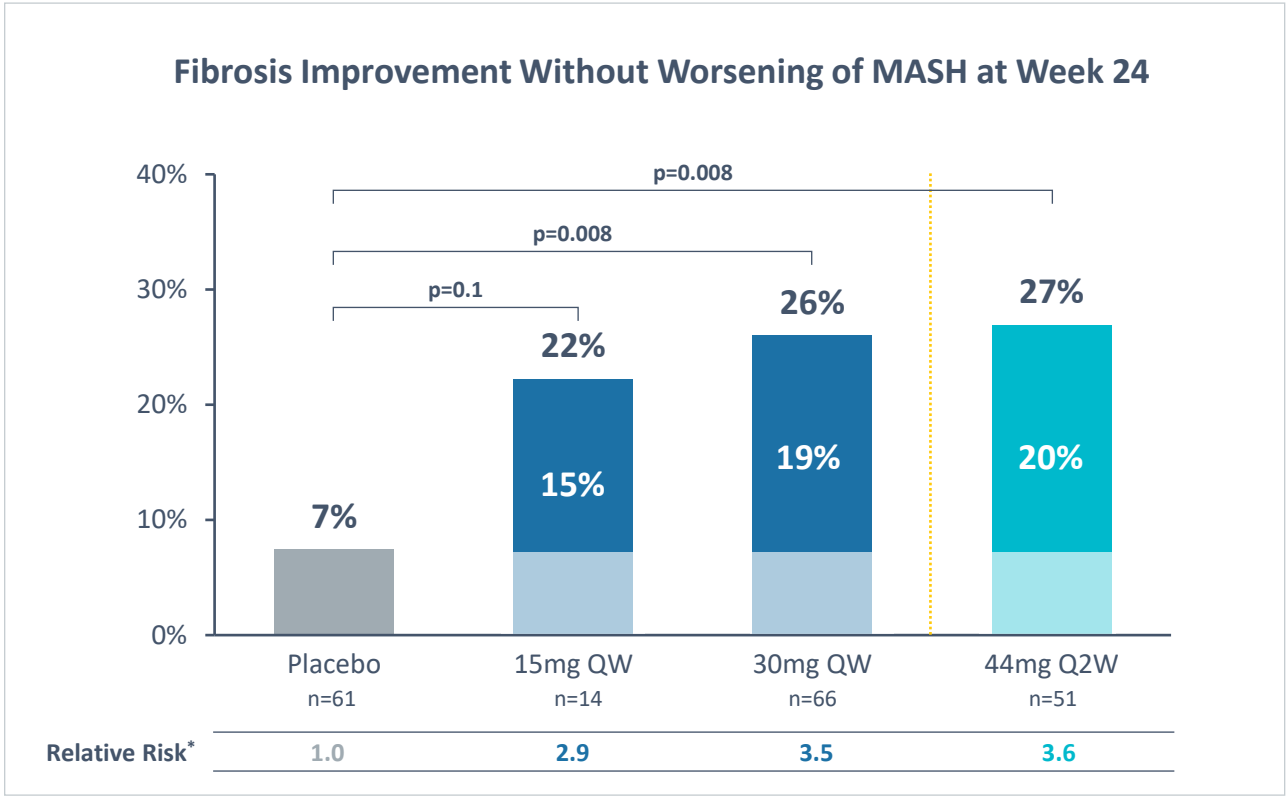
Parameter Mean or %	Placebo (n=71)	15mg QW (n=21)	30mg QW (n=73)	44mg Q2W (n=57)	Total (n=222)
Age (years)	56	55	55	55	**56**
Female	55%	43%	69%	65%	**61%**
BMI (kg/m^2)	38	38	35	36	**37**
Type 2 Diabetes	69%	86%	62%	61%	**66%**
Fibrosis Stage (% F3)	66%	43%	64%	53%	**60%**
NAFLD Activity Score	5.0	4.8	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.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; NAFLD, nonalcoholic fatty liver disease; PRO-C3, N-terminal type III collagen propeptide; VCTE, Vibration-controlled transient elastography.

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

WEEK 24



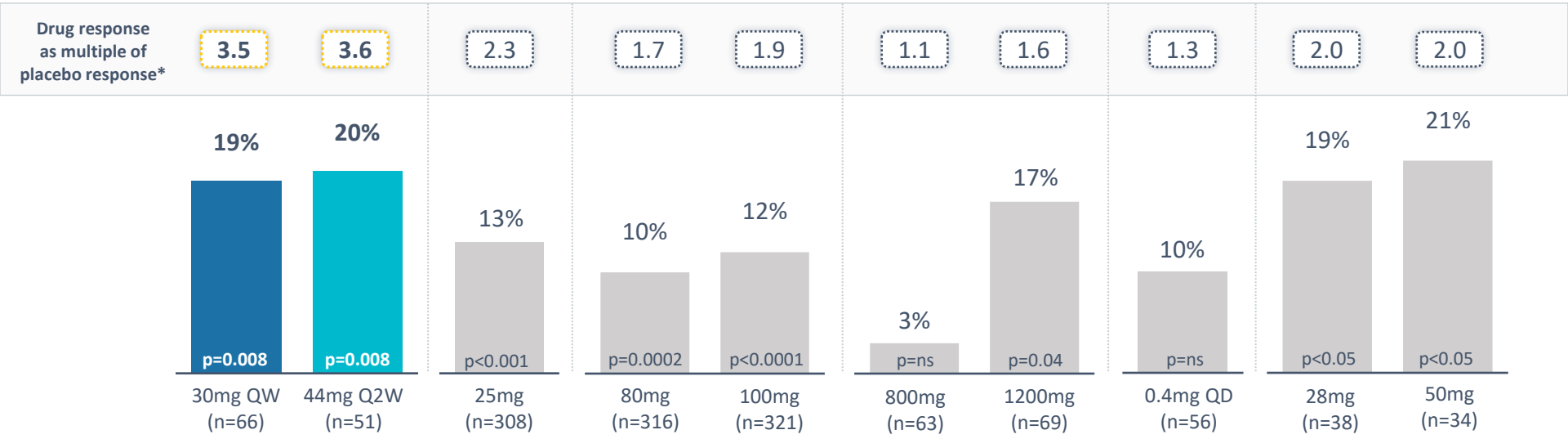
Treatment with PGZ Delays Progression to Cirrhosis

- 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 (placebo-adjusted)



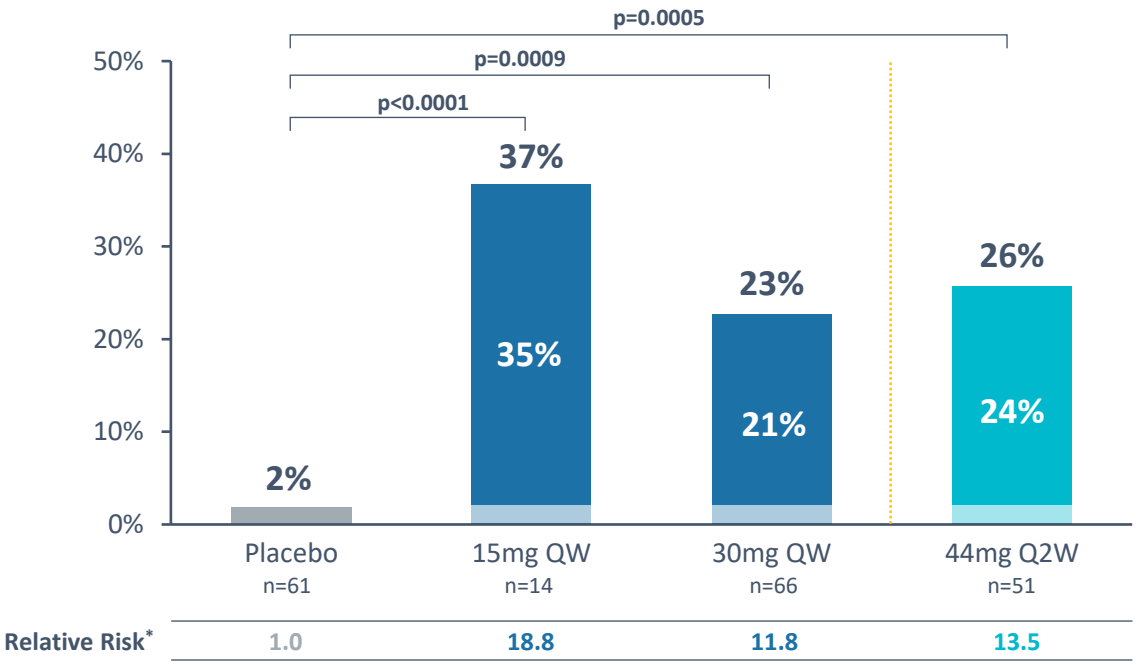
*Drug response as multiple of placebo response is calculated by dividing drug response by placebo response

[1]Results same for Completer Analysis Set; [2] ≥1 stage fibrosis improvement with no worsening of NAS; [†]Program discontinued; ns= not significant

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.

Pegozafermin Demonstrated Statistical Significance on MASH Resolution at All Doses

WEEK 24



* 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).

Comparative Clinical Data in Non-Cirrhotic Patients

MASH Resolution with No Worsening of Fibrosis

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	Pegozafermin	Ocalivia[†]	Resmetirom[2]	Lanifibranor	Semaglutide	Efruxifermin
	Phase 2b | 24 weeks Multiple Imputation[1]	Phase 3 | 72 weeks	Phase 3 | 52 weeks	Phase 2b | 24 weeks	Phase 2 | 72 weeks	Phase 2b | 24 weeks Completers Analysis
Drug response as multiple of placebo response*	**11.8**	**13.5**	1.9	2.6	3.0	1.7	2.1	3.5	3.1	5.1
	21%	**24%**	3%	16%	20%	17%	26%	44%	32%	61%
	p=0.0009	**p=0.0005**	p=ns	p<0.0001	p<0.0001	p=0.039	p=0.002	p<0.001	p<0.01	p<0.001
	30mg QW (n=66)	44mg Q2W (n=51)	25mg (n=308)	80mg (n=316)	100mg (n=321)	800mg (n=63)	1200mg (n=69)	0.4mg (n=56)	28mg (n=38)	50mg (n=34)

* Drug response as multiple of placebo response is calculated by dividing drug response by placebo response

[1] Results same for Completer Analysis Set; [2] MASH resolution with ≥2 point reduction in NAS and no worsening of fibrosis

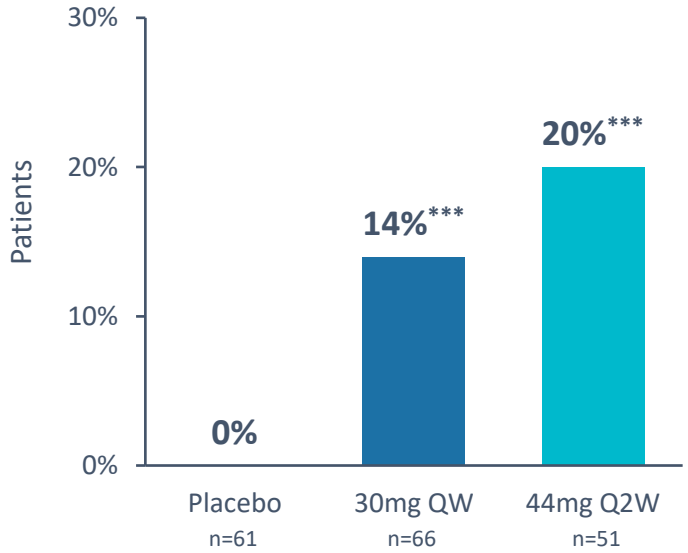
[†]Program discontinued

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.

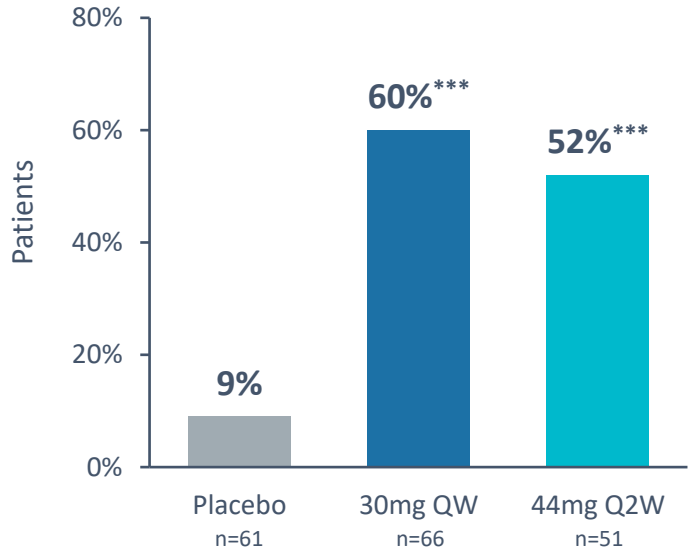
Pegozafermin Demonstrated Statistical Significance on the Combined Endpoint of Fibrosis Improvement and MASH Resolution

WEEK 24

Both Fibrosis Improvement and MASH Resolution at Week 24



≥2-Point Improvement in NAS and MRI-PDFF Response and ALT Response



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.

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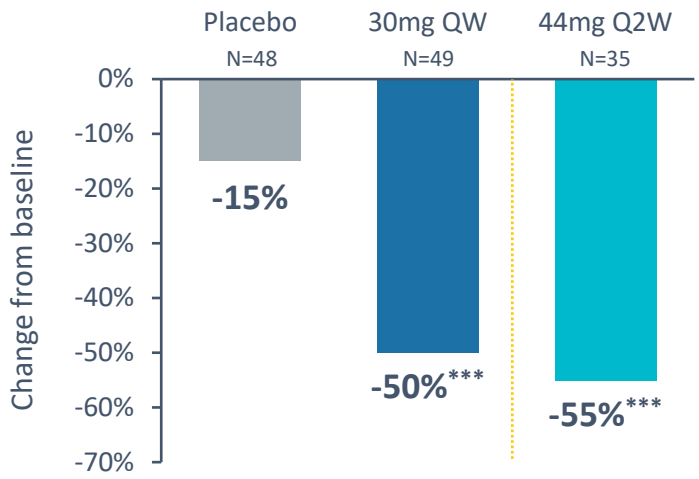
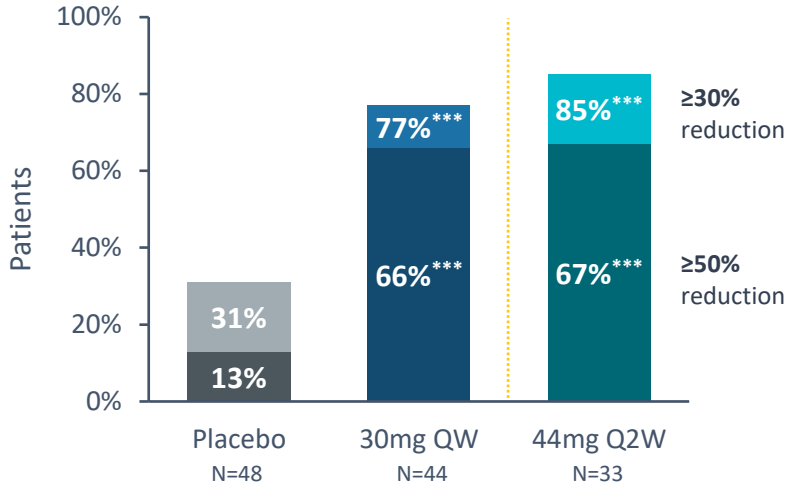
Pegozafermin Demonstrated Robust Liver Fat Reduction with High Responder Rates by MRI-PDFF

WEEK 24

Mean Relative Reduction in Liver Fat vs Baseline[1] at Week 24



Patients Achieving ≥30% and ≥50% Reduction in Hepatic Fat Fraction Versus Baseline[2]

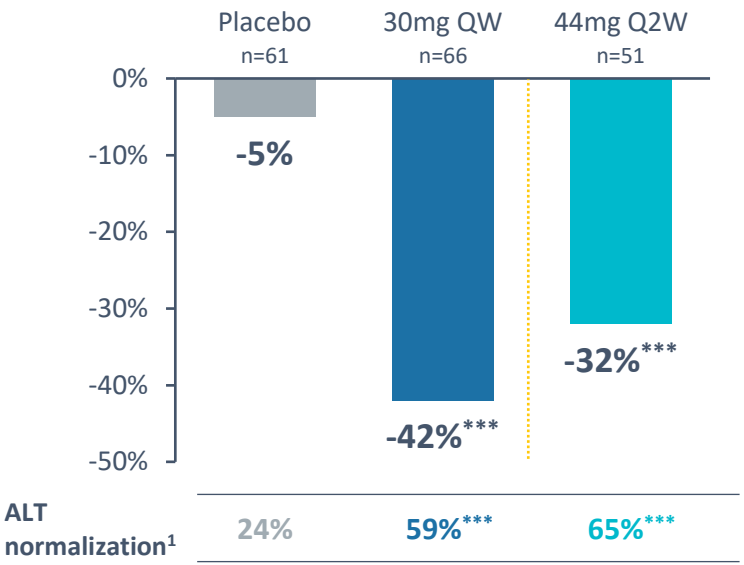


[1]Analysis via mixed model repeated measure (MMRM). [2]Analysis via Cochran-Mantel-Haenszel (CMH) test stratified by T2DM status (yes vs. no) and fibrosis stage (F2 vs. F3).
MRI-PDFF Analysis Set in patients with >10% liver fat at baseline.
***p<0.001 versus placebo

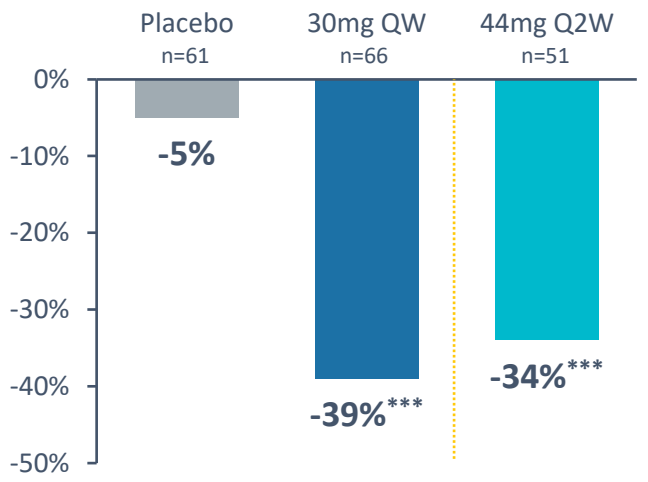
Pegozafermin Demonstrated Significant Improvements in Markers of Liver Injury/Inflammation (ALT and AST)

WEEK 24

Mean Relative Reduction in ALT vs Baseline at Week 24



Mean Relative Reduction in AST vs Baseline at Week 24



[1]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.

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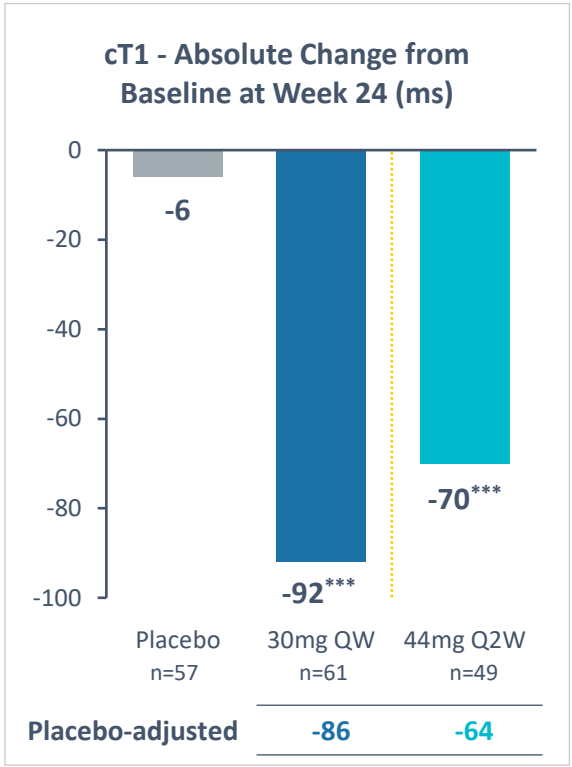
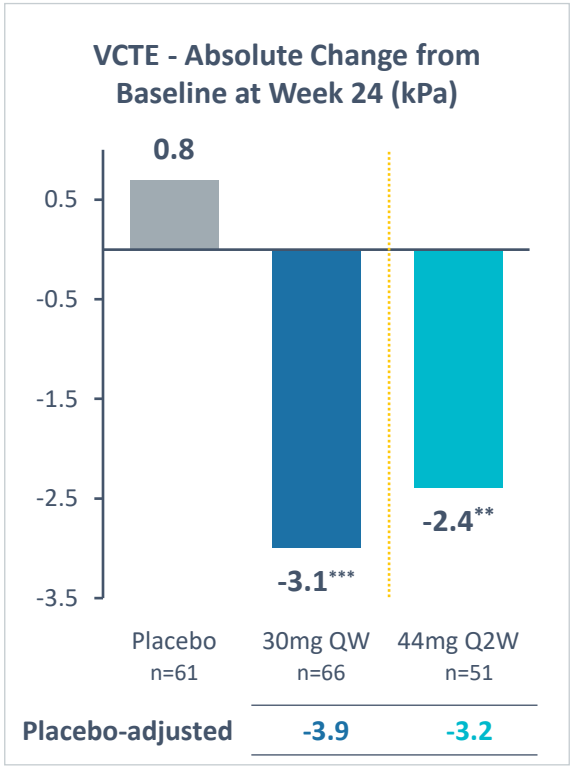
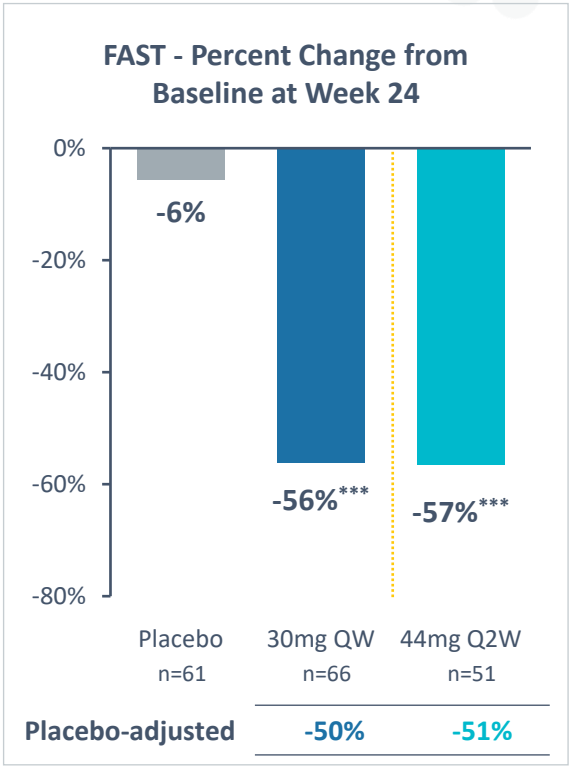
Pegozafermin Demonstrated Significant Reductions in Non-Invasive Markers (NITs) of Liver Inflammation and Fibrosis

WEEK 24



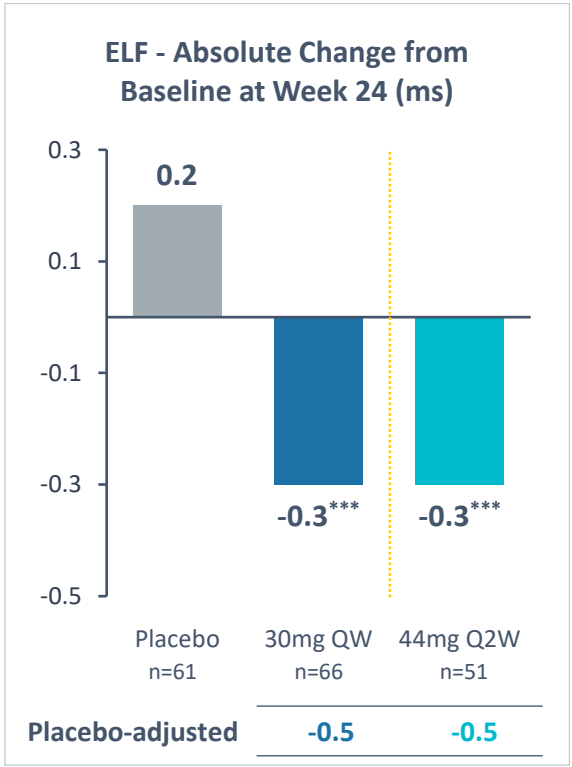


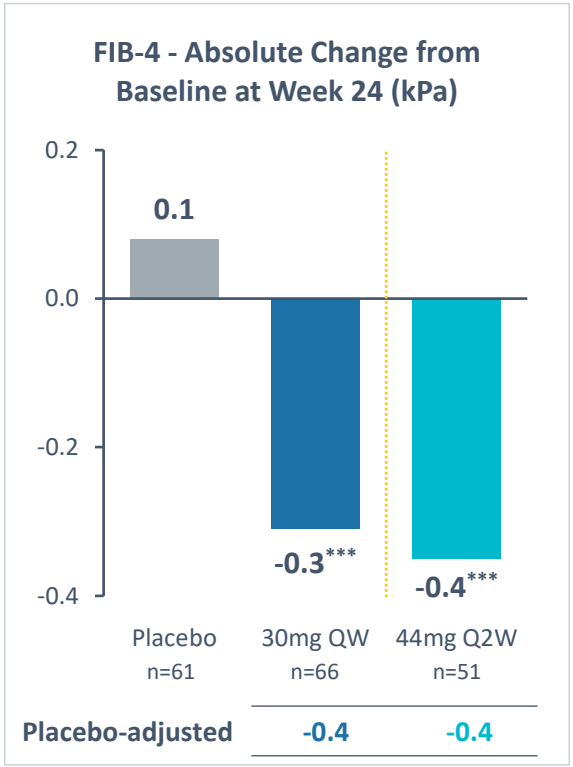


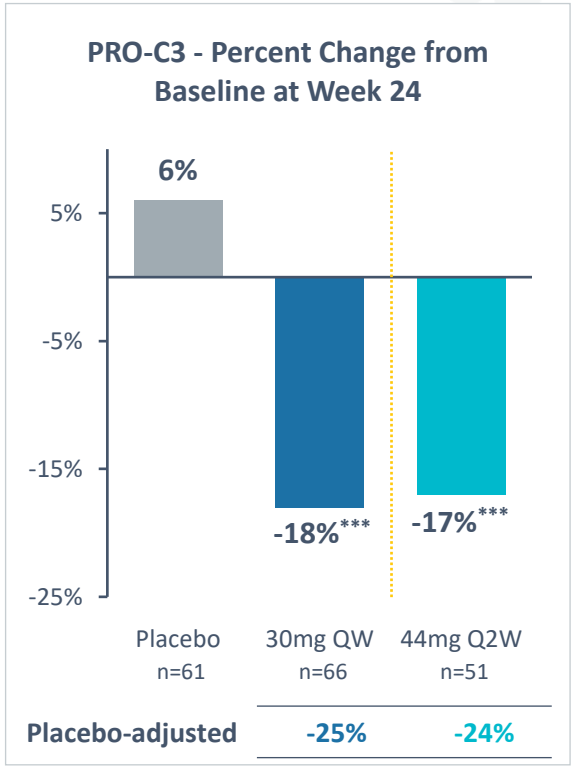
Source: Full Analysis Set for FibroScan and PRO-C3 assessments and MRI-PDFF analysis set for cT1, Analysis via MMRM for cT1 and PRO-C3, ANCOVA for VCTE. A patient is designated a cT1 responder with ≥80 msec reduction as compared to baseline. cT1 analysis was performed at sites where available.
*p<0.05, **p<0.01, ***p<0.001 versus placebo.

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

WEEK 24







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

WEEK 24
WEEK 48

	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

Full Analysis Set; preliminary data
LS mean change from baseline except for MRI and VCTE which are medians. VCTE n=139 at week 24; n=121 at week 48
MRI-PDFF in patients with >10% liver fat at baseline (n=108 at week 24; n=92 at week 48)

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Independent Patient Confirmation of Pegozafermin Treatment Effect

Placebo Patients Showed Robust Benefits Upon Crossing Over to Pegozafermin

WEEK 48

Change from Baseline

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

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

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Mean change from baseline except for VCTE which is median
MRI-PDFF in patients with >10% liver fat at baseline (n=17); Full Analysis Set

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

GLP1

BACKGROUND

- Results from 37 patients in ENLIVEN who 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

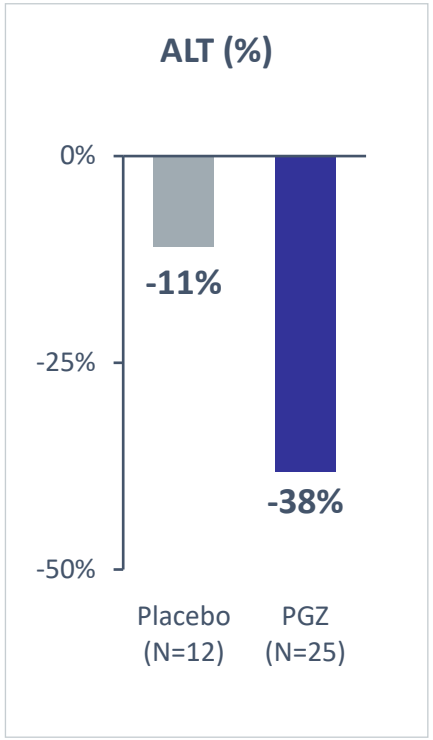
KEY RESULTS

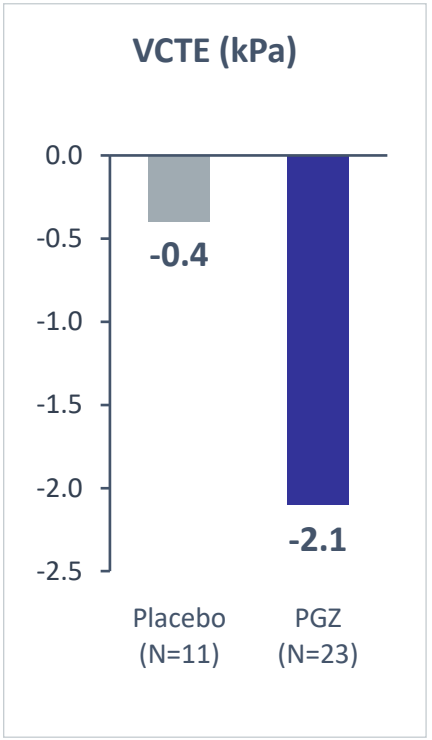
Pegozafermin on top of GLP-1 therapy showed the following versus GLP-1 plus placebo at week 24 and week 48:

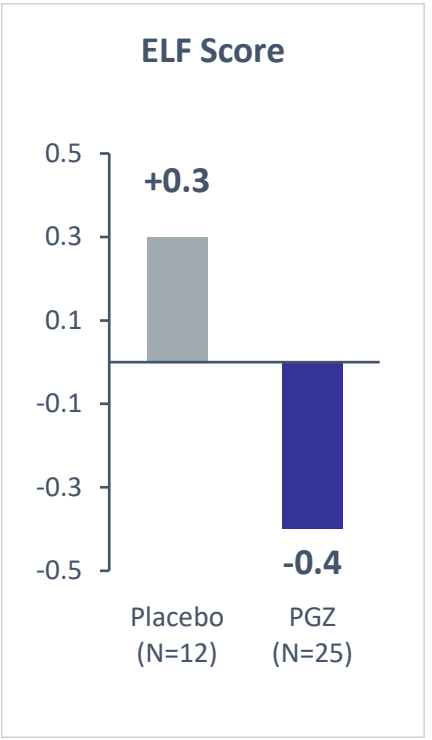
- Improved Fibrosis
- Reduced Liver Fat
- Improved Liver Health
- Acceptable Tolerability Profile

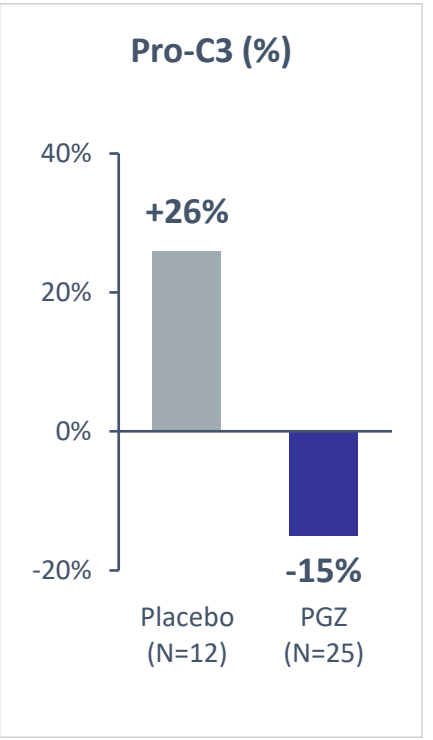
Greater Benefits on Fibrosis Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 24

WEEK 24
GLP1





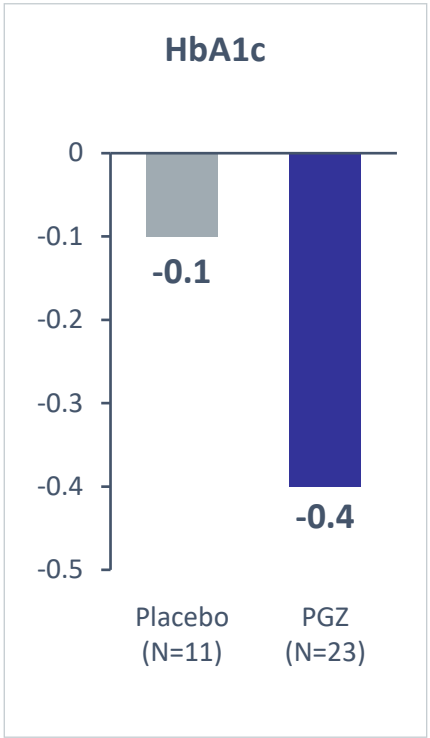


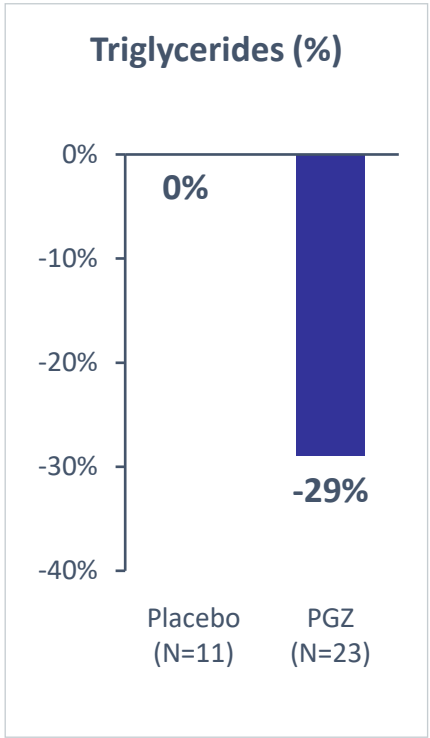


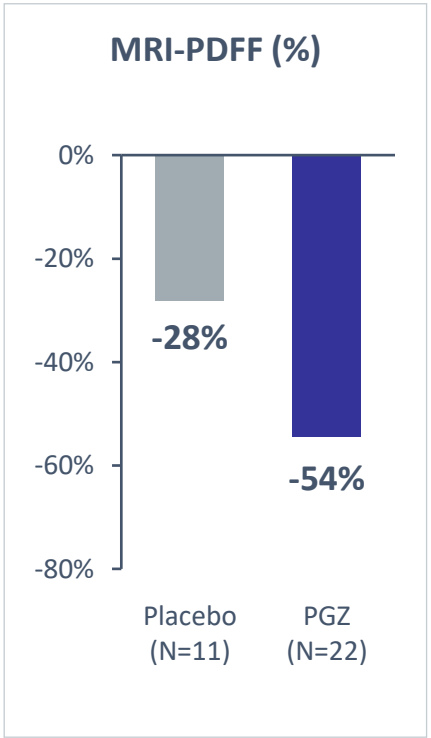
Source: Full Analysis Set. ELF, ALT and Pro-C3 reported as LS mean change from baseline; VCTE reported as median change (absolute) from baseline.
Post-hoc analysis

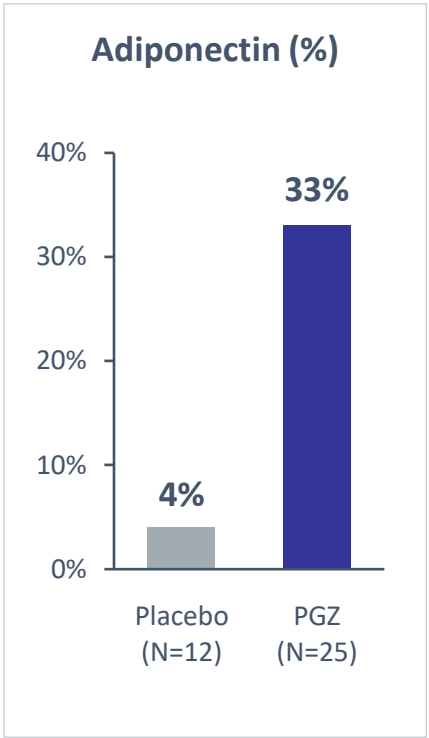
Greater Benefits on Metabolic Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 24

WEEK 24
GLP1





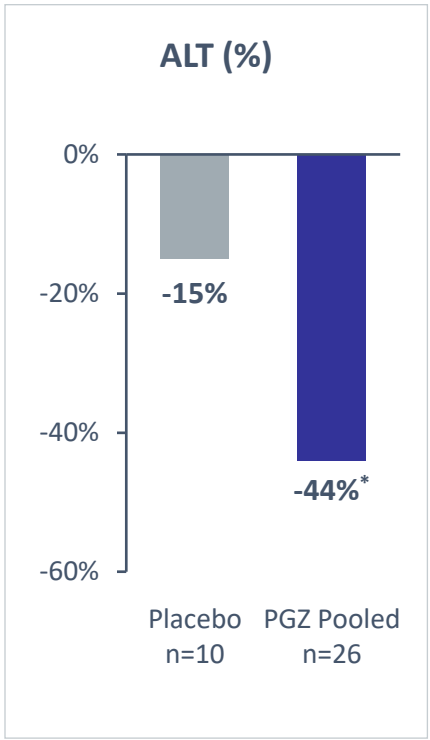


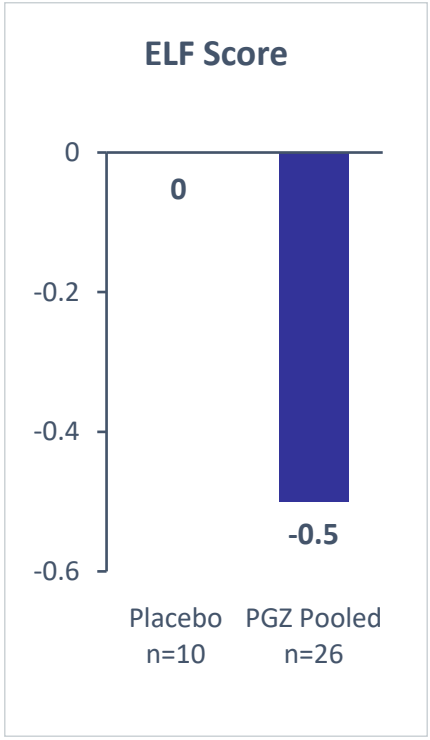


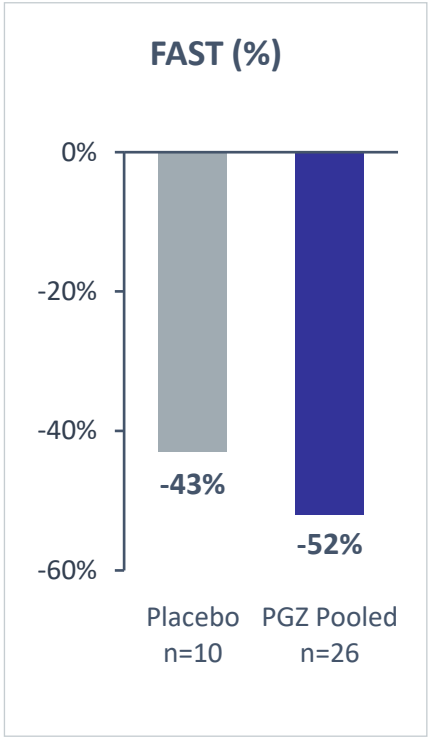
Source: Full Analysis Set. Adiponectin reported as LS mean change from baseline; HbA1c reported as median change (absolute) from baseline; MRI-PDFF and TG reported as median percent change from baseline. Post-hoc analysis

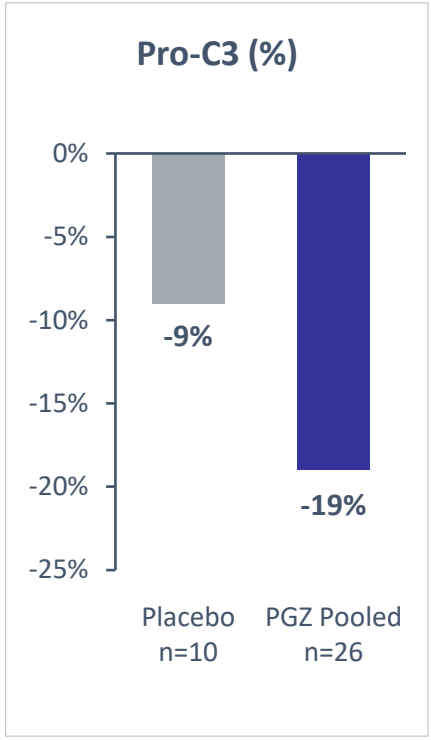
Sustained Benefits on Fibrosis Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 48

WEEK 48
GLP1









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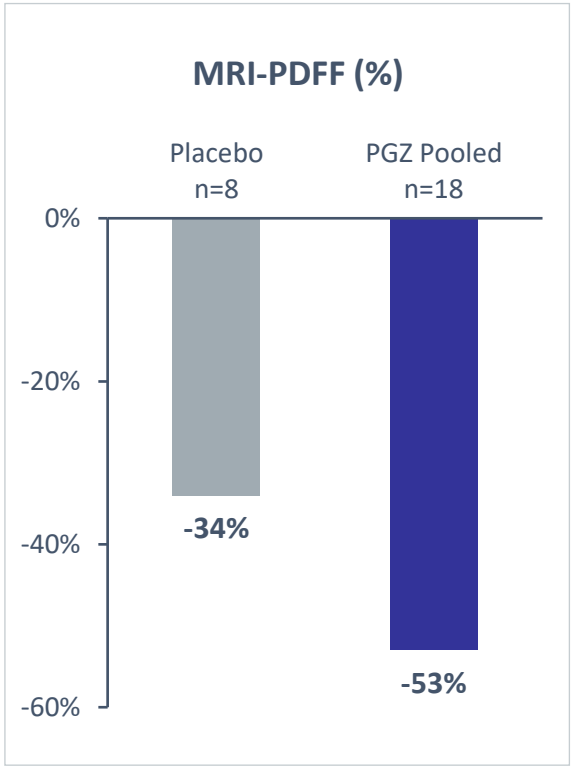
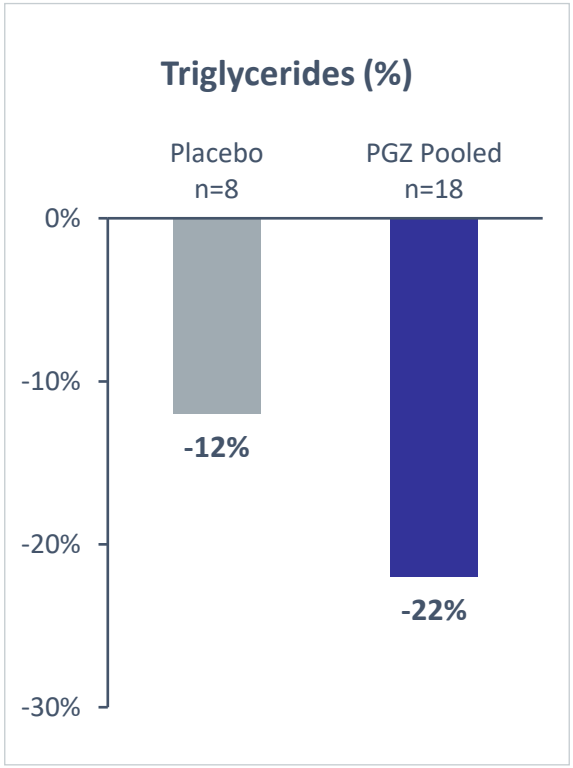
Source: Extension Full Analysis Set. ELF, ALT, FAST and Pro-C3 reported as LS mean change from baseline. *p<0.05 versus placebo. Post-hoc analysis.

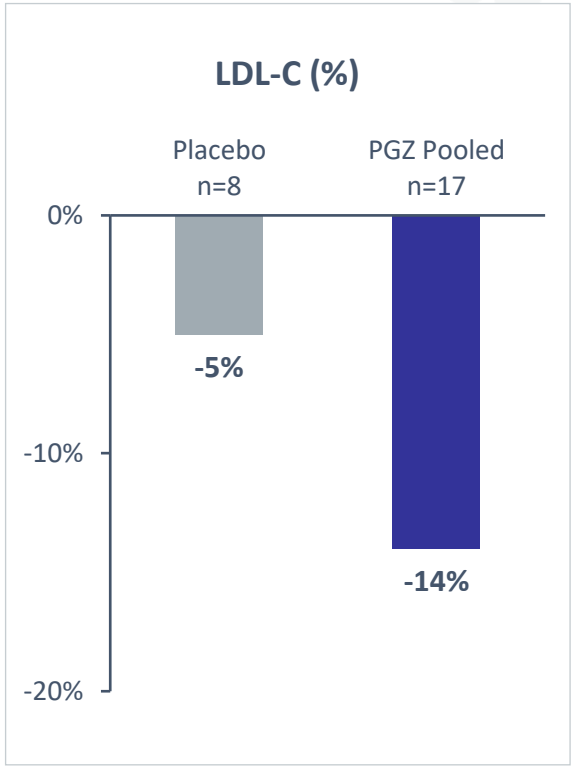
Sustained Benefits on Metabolic Markers Were Observed with Pegozafermin vs. Placebo in Patients on Background GLP-1 Therapy at Week 48

WEEK 48

GLP1







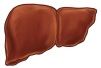
Source: Extension Full Analysis Set. TG, and LDL-C and MRI-PDFF reported as median percent change from baseline. Post-hoc analysis

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

F4

BACKGROUND

- 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

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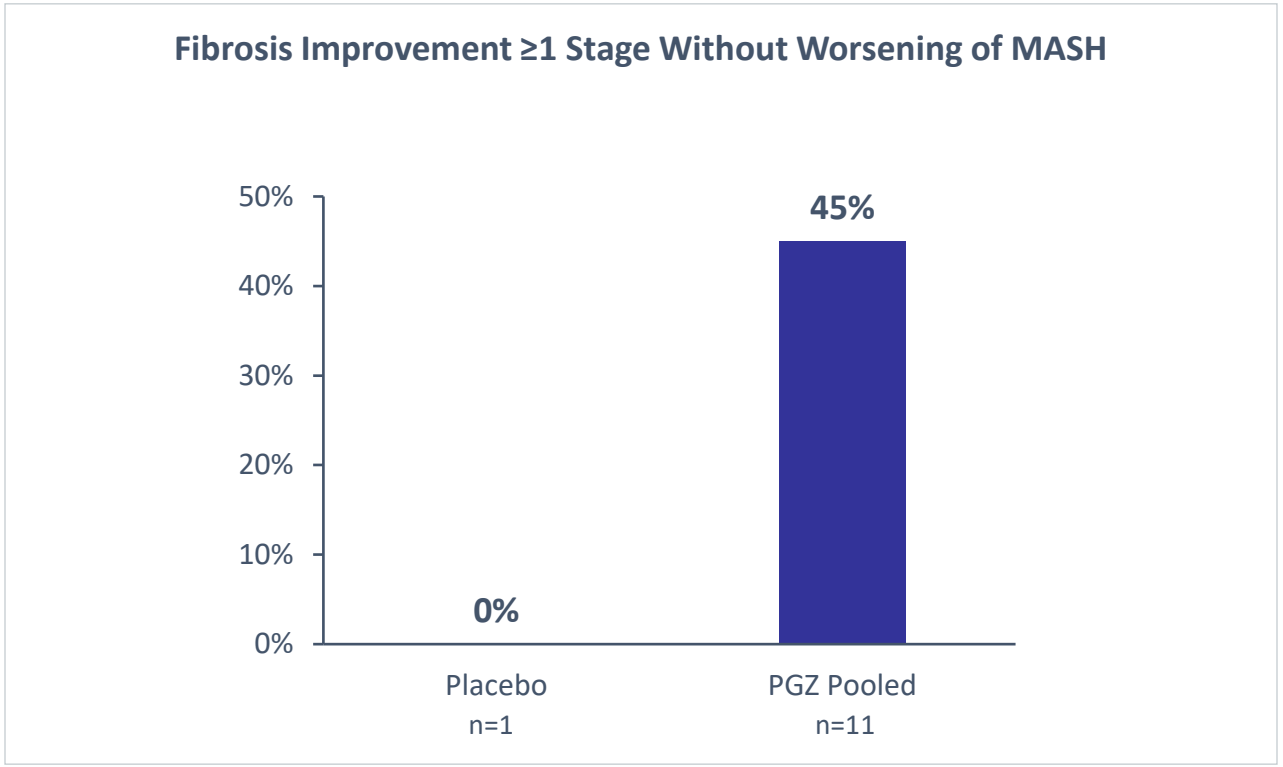
*N=1 on placebo and N=11 PGZ (all doses)

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

WEEK 24

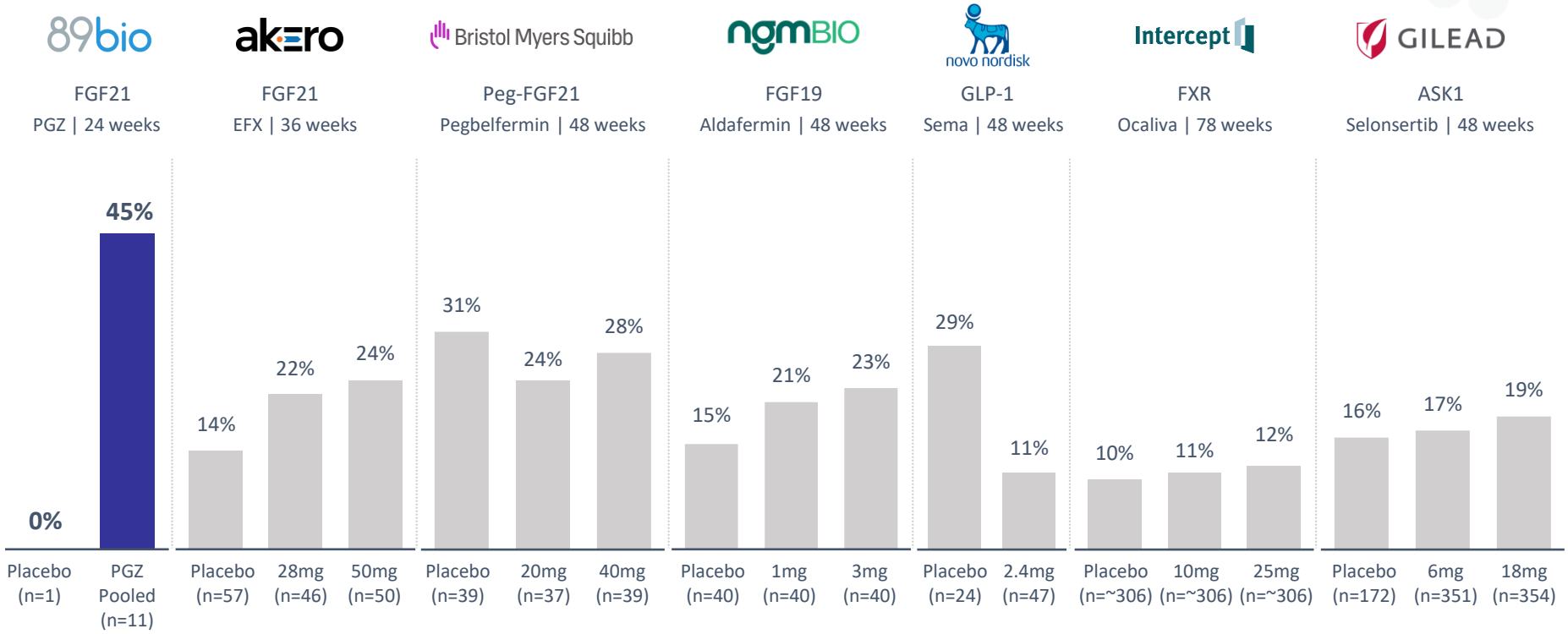
F4



- Pegozafermin treatment led to fibrosis improvement ≥1 stage in 9/11 treated patients (82%)
- Pegozafermin treatment led to fibrosis improvement with no worsening of ballooning and inflammation in 7/11 treated patients

12/14 cirrhotic patients enrolled in ENLIVEN had follow-up biopsies at week 24 (11 treated patients and 1 placebo patient).

Pegozafermin Has Demonstrated Preliminary Evidence for Potential Best-in-Category 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

WEEK 24
WEEK 48
F4

	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 (AASLD 2023)

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Data presented as LS means for ALT, AST, FAST, Pro-C3, FIB-4 and ELF and as medians for the other parameters

Pegozafermin Was Well Tolerated Through 48 Weeks

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	4%	24%	17%	9%
Nausea	0%	14%	21%	18%
Injection site erythema	4%	14%	14%	5%
Injection site rash	2%	0	10%	4%
Increased appetite	2%	10%	14%	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.

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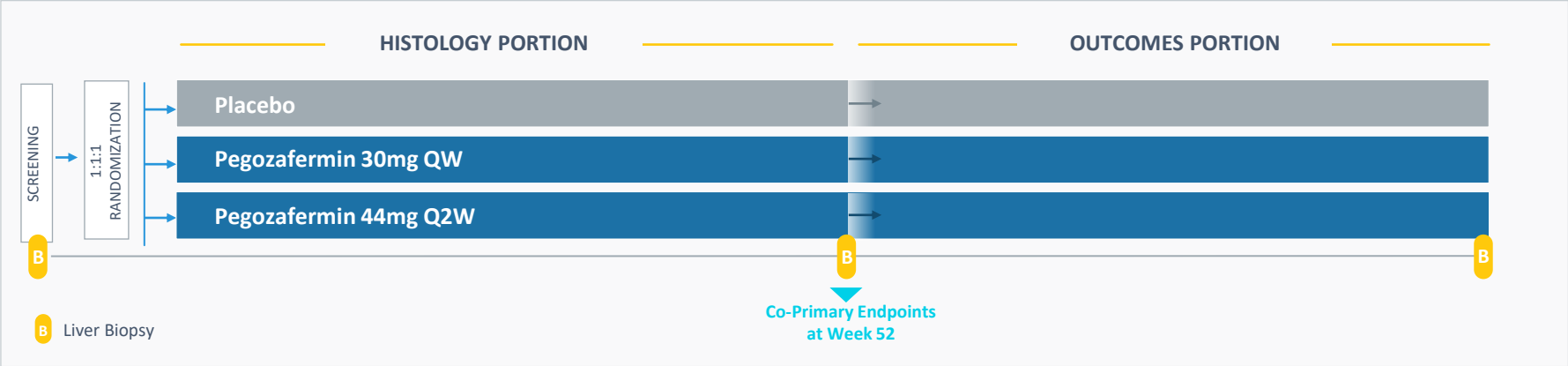
Detailed safety and tolerability presented in Loomba et al, NEJM 2023

Source: Safety Analysis Set. AE table cutoff ≥10% of patients for placebo, 30mg QW and 44mg Q2W doses. Bone biomarkers were CTX and P1NP.

ENLIGHTEN-Fibrosis: Phase 3 trial in Non-cirrhotic MASH (Fibrosis Stage F2-F3) Initiated in 1Q24



ENlighten fibrosis

in Non-cirrhotic MASH patients

HISTOLOGY PORTION FOR ACCELERATED APPROVAL

- Co-primary endpoints assessed at week 52:
  - One-point improvement in fibrosis with no worsening of MASH
  - MASH resolution with no worsening of fibrosis

OUTCOMES PORTION FOR FULL APPROVAL

- 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

Approximately 1,000 patients will be enrolled. A subset of the patients will be assessed for the histology portion

Safety Database: Regulatory alignment on size of safety database including data from the ongoing SHTG Phase 3 program

Drug Presentation: Liquid formulation in pre-filled syringe (planned commercial presentation; stable at 2-8 C)

ENLIGHTEN-Cirrhosis: Phase 3 in Compensated Cirrhotic (F4) MASH is Expected to Initiate in 2Q24

ENlighten cirrhosis

in compensated cirrhotic MASH patients

DESIGN/DOSE	Randomized, double-blind, placebo-controlled trial of **pegozafermin 30mg QW**
HISTOLOGY PORTION FOR ACCELERATED APPROVAL	**Primary endpoint:** regression of fibrosis from F4 to an earlier stage of fibrosis **Duration:** 24 months, with potential to assess earlier based on the evolving clinical and regulatory landscape
OUTCOMES PORTION FOR FULL APPROVAL	• Patients continue to clinical outcomes to support full approval 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

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

Large patient population with significant health risks

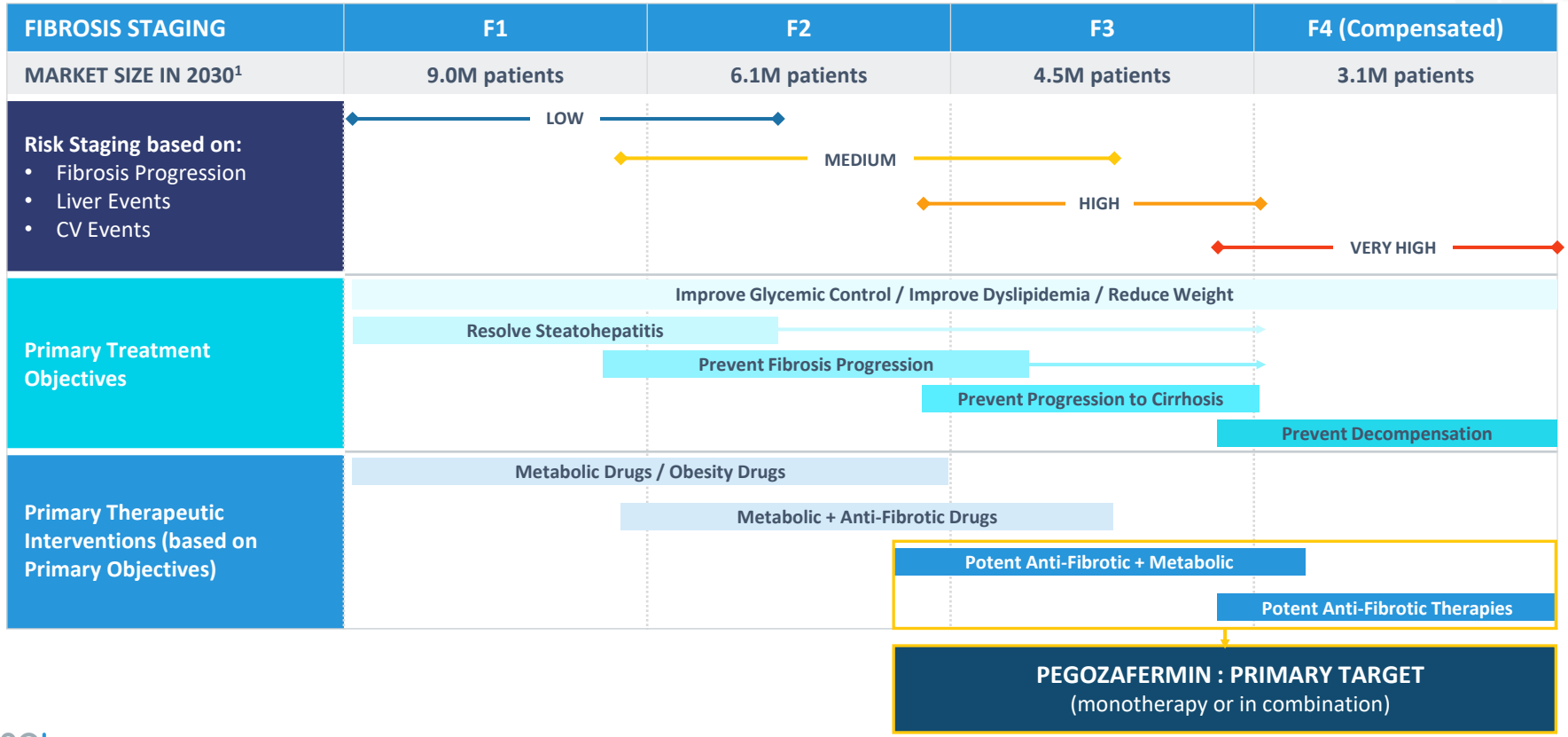
- MASH is estimated to impact ~27M patients by 2030 in the US with equivalent number in EU
  - Advanced fibrosis (F3) and cirrhotic patients (F4) are expected to reach 4.5M and 3.1M respectively in 2030[1]

Significant market opportunity for pegozafermin

- 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 will likely 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 therefore 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

1. Source: Estes C et al. Hepatol 2018

Pegozafermin Positioned to Address Advanced MASH



1. Source: Estes C et al. Hepatol 2018.

Pegozafermin Offers a Highly Differentiated Profile

Pegozafermin differentiates on key attributes for an effective advanced MASH therapy

1. **EFFICACY:** Strongest fibrosis data[1]; robust metabolic data; additional benefits when added to GLP-1
2. **SAFETY AND TOLERABILITY:** Best-in-class (FGF21) tolerability profile
3. **DOSING:** Convenience of every-two-week injections (26 fewer annual injections)

FGF21s have the opportunity to dominate the advanced MASH market

- Best-in-category mechanisms have multiple successful drugs with the same MOA (e.g. GLP-1 RAs, Anti-TNF)

MASH commercialization considerations

- Target audience (US): ~7,300 hepatology providers
- Payers: Premium pricing for advanced fibrosis (incl. cirrhotic)

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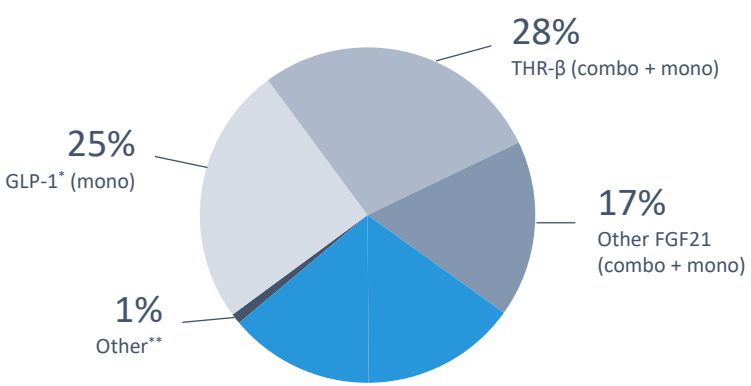
1. Based on cross-trial comparison of fibrosis between different therapies in clinical development for MASH; no head-to-head clinical trials have been conducted
Source: Primary research with US payers, October 2020

Based on Market Research, Pegozafermin Expected to Garner Significant Market Share

*Usage expected to be in combination with GLP-1 therapy**

EXPECTED PRESCRIBING AMONGST HEP/GI PHYSICIANS *(% treated MASH patients)*

F3

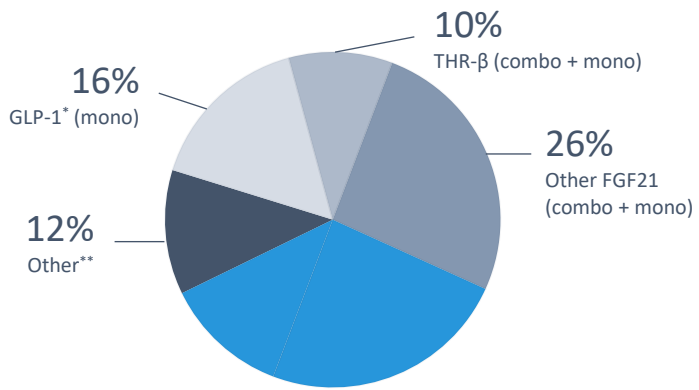


29% Total PGZ

(**15%** mono + **14%** combo with GLP-1*)

Total GLP-1* (mono + combo) | **65% (25% + 40%)**

Compensated F4^



36% Total PGZ

(**24%** mono + **12%** combo with GLP-1*)

Total GLP-1* (mono + combo) | **46% (16% + 30%)**

- In F2, pegozafermin expected to garner 23% market share, and ~70% of patients expected to be on GLP-1

*Includes currently approved GLP-1s & 2nd generation incretins; **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 greater than $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 to approval

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

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

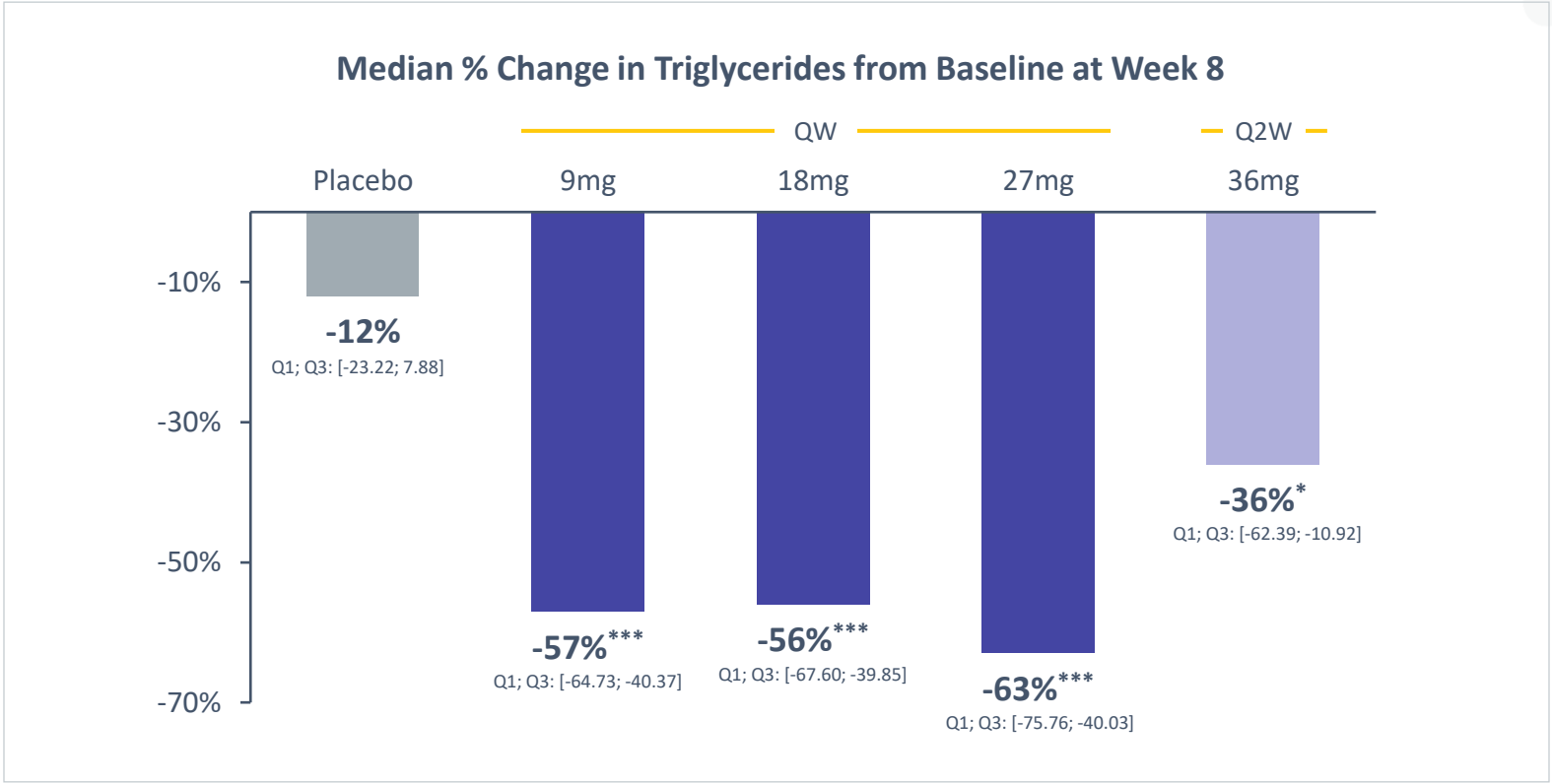
- Primary endpoint: % Change in TGs from baseline

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 Reduces Triglycerides Across All Dose Groups

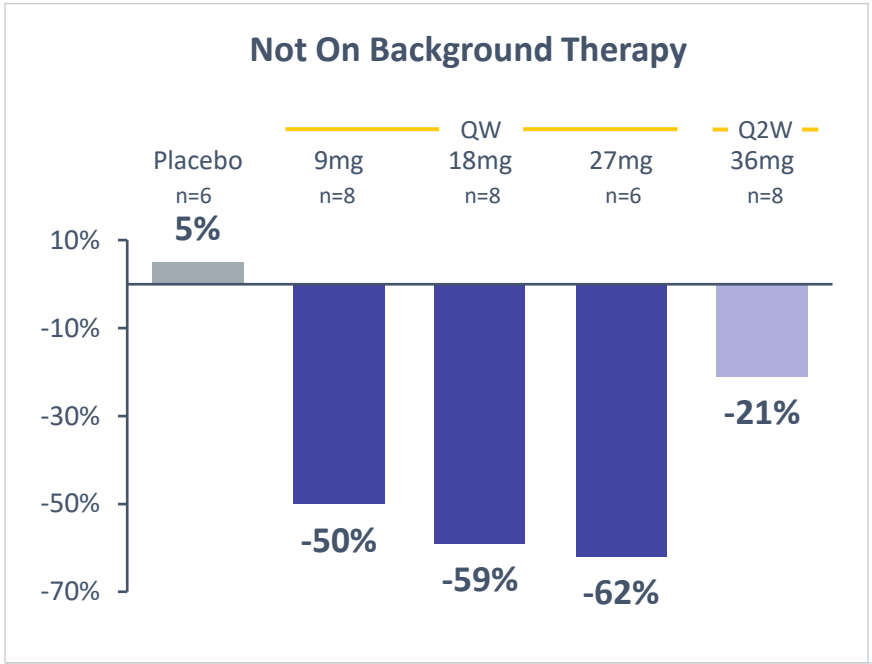


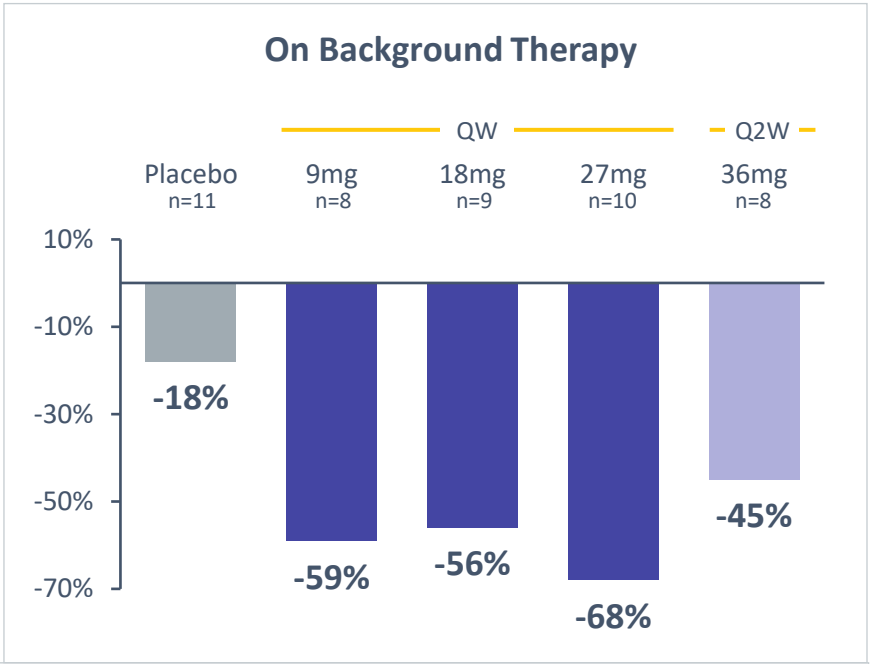
QW: Every week; Q2W: Every 2 weeks

p value vs placebo for change from baseline based on Wilcoxon Rank-Sum Test
Full Analysis Set; * p<0.05; ** p<0.01; *** p<0.001 vs. placebo

Pegozafermin Shows Significant Decrease in Triglycerides on Top of Background Therapy

Median % Change in Triglycerides from Baseline at Week 8

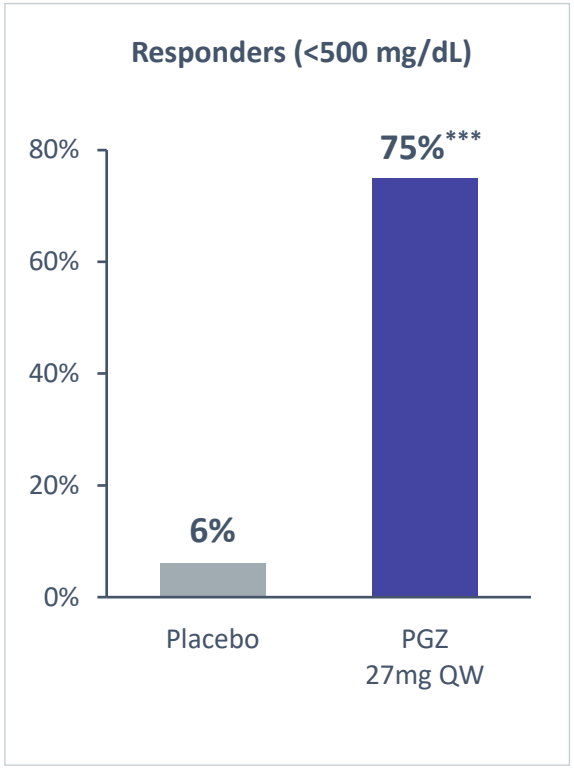


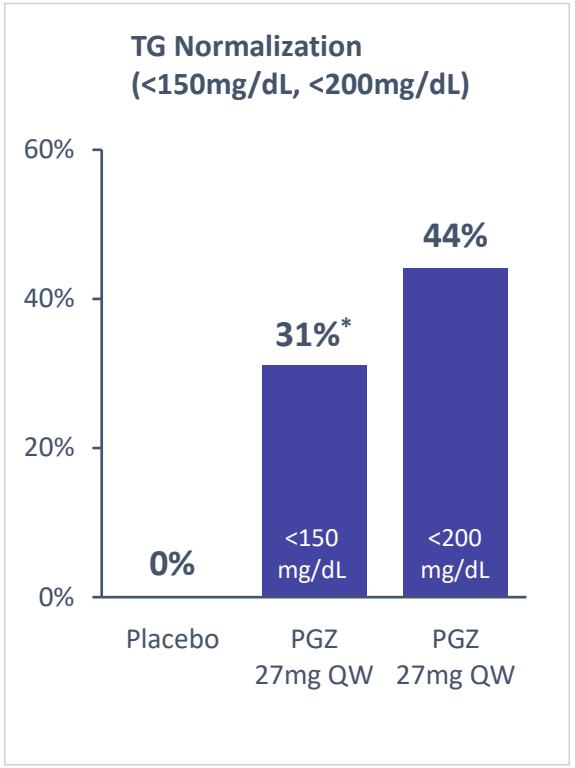


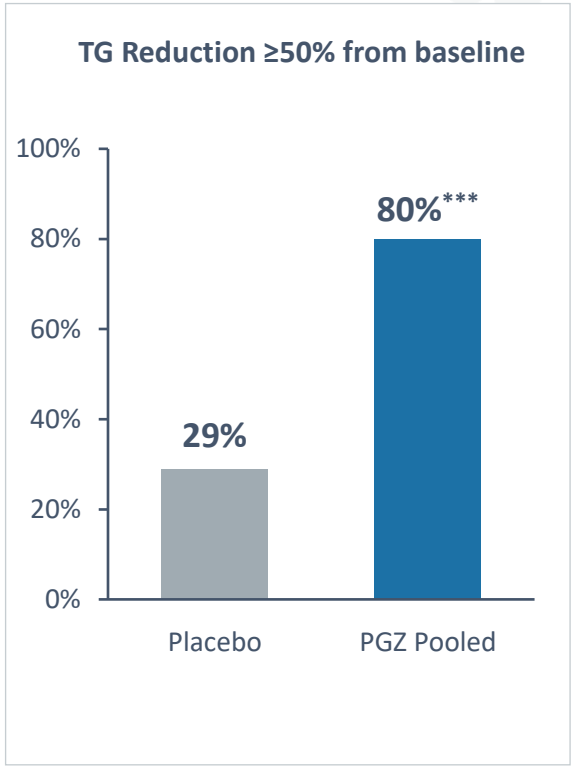
Results are consistent with data from patients on background therapy of statins or statin combos, prescription fish oils, and fibrates

Background therapy defined as concomitant lipid-modifying therapy
Full Analysis Set

Pegozafermin Shows Significant Decrease in Triglycerides at Different Threshold Levels

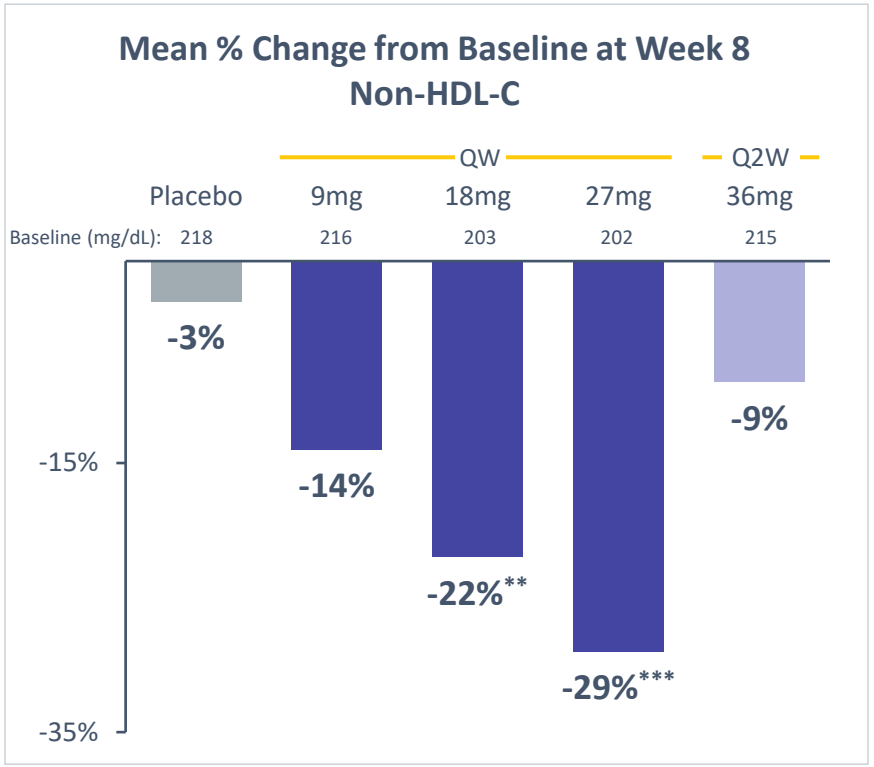


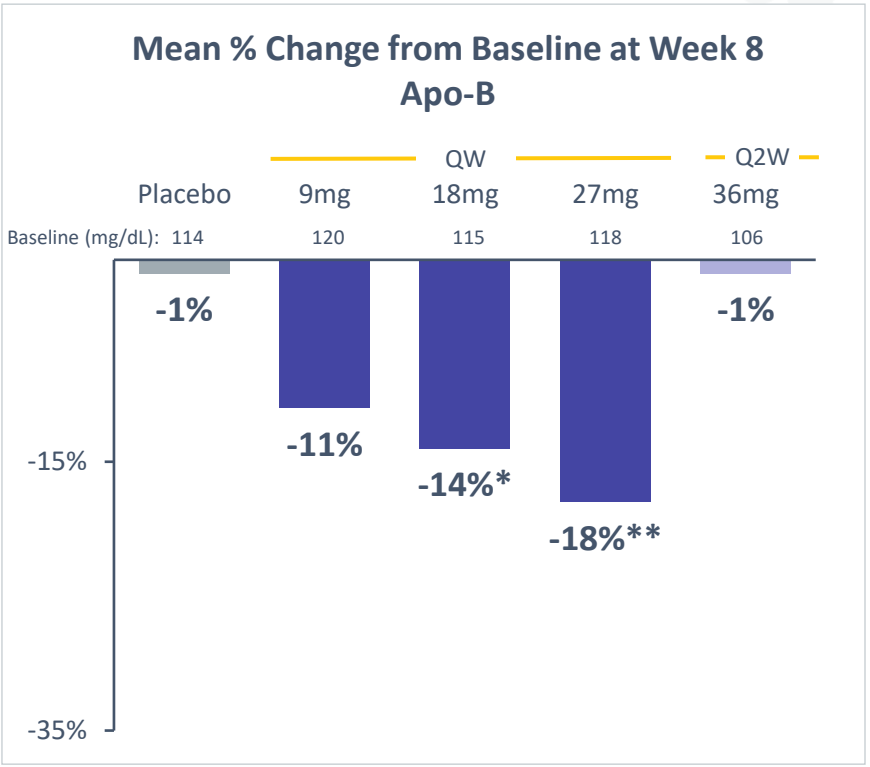




Analysis via unstratified Chi-square Test comparing the individual PGZ groups vs placebo. * p<0.05; ** p<0.01; *** p<0.001 vs. placebo
TG Responders defined as patients who achieve TG <500 mg/dL
Full Analysis Set

Pegozafermin Demonstrated Clinically Meaningful Improvements in Non-HDL-C and Apo-B – Key Marker of CV Risk

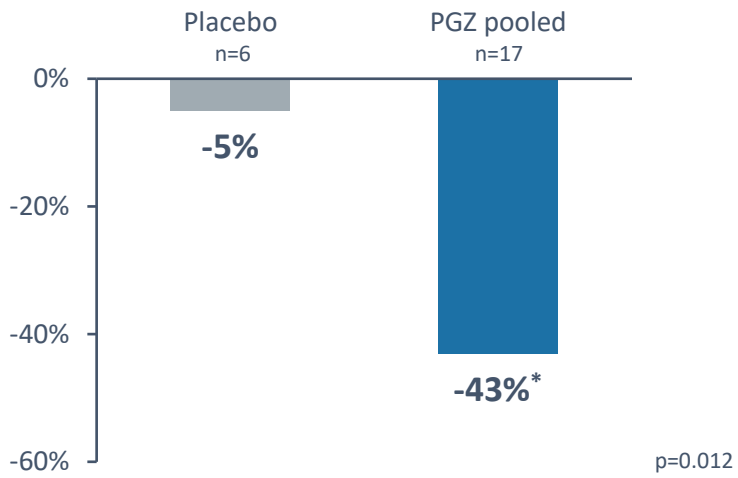




Full Analysis Set; * p<0.05; ** p<0.01; *** p<0.001 vs. placebo based on MMRM analysis

Pegozafermin Demonstrated Significant Improvement on Key Co-morbidities in SHTG – Liver Fat and Glycemic Control

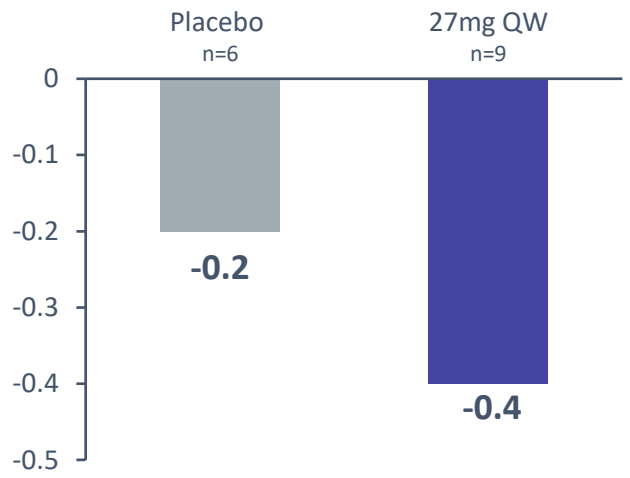
Mean Relative Reduction in Liver Fat vs Baseline at Week 8



HIGH RESPONDER RATES

≥30% Reduction in liver fat: 88% *vs 0% in placebo*

Absolute Change in HbA1c at Week 8 Patients with Baseline HbA1c ≥6.5%



HbA1c: Mean Baseline 27 mg QW: 7.48%; Week 8: 7.08%

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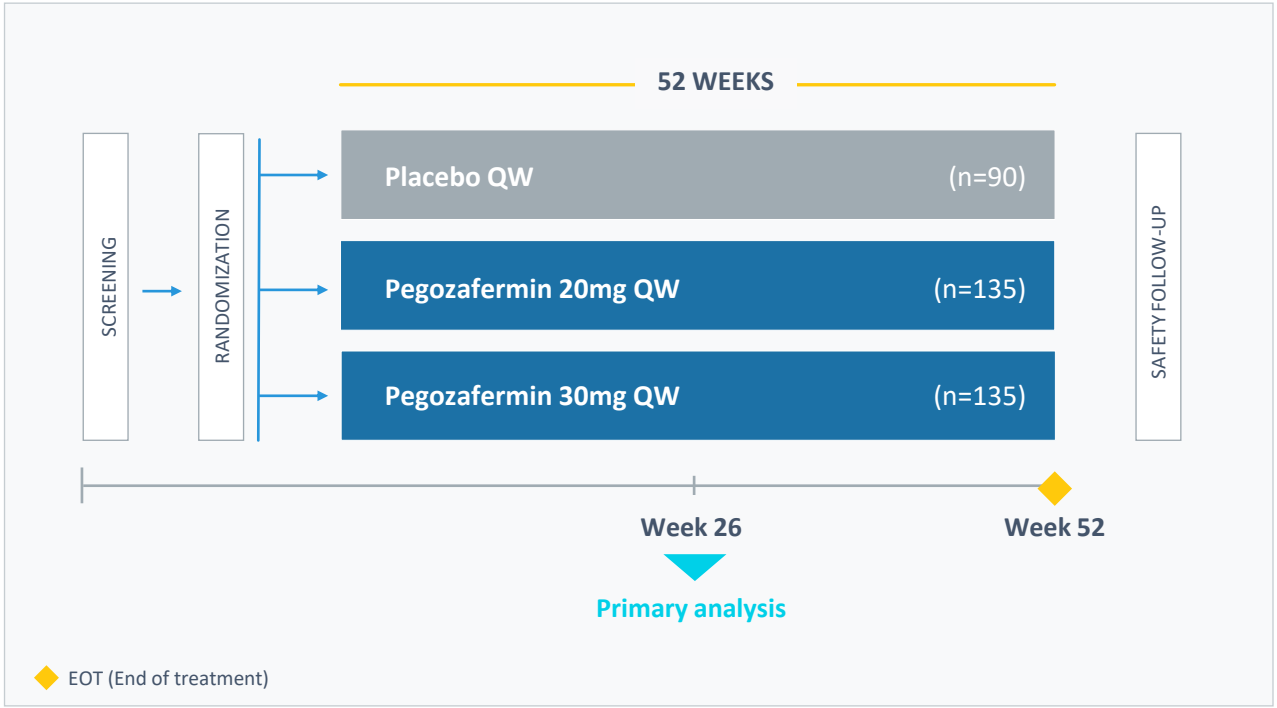
Post-hoc analysis of patients with follow-up MRI-PDFF ≤21 days from date of last dose in 27mg QW cohort demonstrated a 63% mean relative reduction from baseline
*p <0.05 vs. placebo
MRI Analysis Set; p value vs placebo based on ANCOVA analysis

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

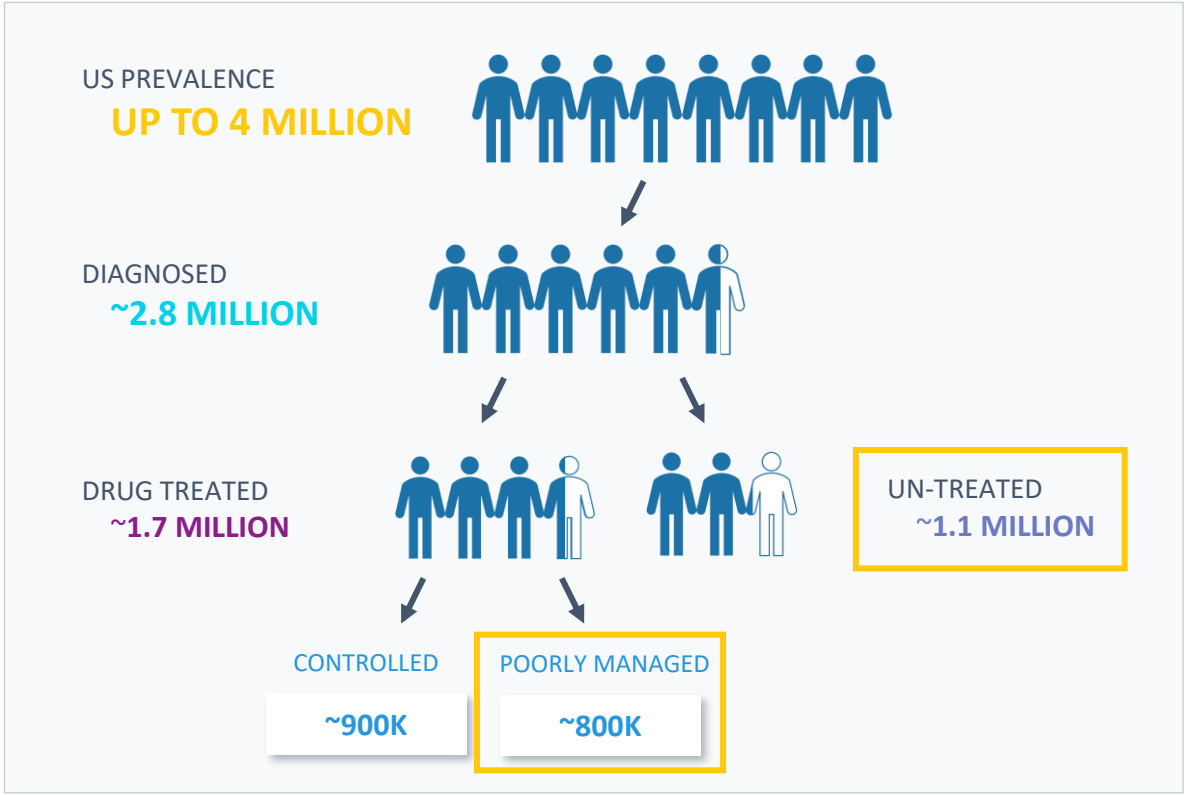
- Percent change from baseline in fasting TGs at Week 26 vs. placebo

KEY SECONDARY ENDPOINTS

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

89bio *Not all patients may be on background lipid modifying therapy

SHTG Represents a Large Population with High Unmet Need



Co-morbidity	Prevalence in SHTG population
Fatty Liver Disease (NAFLD)	Up to 100%
Type 2 diabetes/Prediabetes	Up to 70%
Dyslipidemia	Up to 65%

Pegozafermin profile is unique and compelling to physicians because of potential for metabolic benefits

PEGOZAFERMIN TARGET POPULATION

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Pegozafermin Delivers on Key Attributes for Successful SHTG Therapy

MINOR INFLUENCE — MODEST INFLUENCE — MAJOR INFLUENCE

Hierarchy of Attributes for SHTG Therapy

RoA/Dosing

- RoA and dosing were seen as the least influential

Clinical Outcomes

- Physicians noted that clinical outcomes are not required to drive utilization in SHTG

Safety/Tolerability

- Lesser impact on treatment decisions compared to efficacy

Metabolic Endpoints

- Viewed as additive benefits
- Liver fat, HbA1c, and weight loss most important

TG Endpoints

- Most influential endpoint to drive use
- Significant efficacy over SoC will drive utilization

PEGOZAFERMIN ATTRIBUTES

- Generally well-tolerated
- 43% mean relative reduction in liver fat[1]
- 0.4% absolute reduction in HbA1c[2]
- 63% reduction in TG from baseline[2]
- 80% of patients achieved TG<500mg/dL[1]

Physician Enthusiasm for Metabolic Endpoints

Liver fat reduction

Decrease in HbA1c

[1]Pooled pegozafermin data at week 8
[2]27mg pegozafermin data at week 8
RoA: Route of Administration.
Source: Physician Interviews; ClearView Analysis, 2022.

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

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

[1]Bhatt, Bays, Miller et al. ENTRIGUE. Nature Medicine, 2023.
[2]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
[3]ENTRIGUE topline data presentation, June 2022.

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.

Corporate Highlights

Potential Best-in-Class FGF21 in two Phase 3 programs, each of which represents a significant market opportunity*

Metabolic dysfunction-associated steatohepatitis (MASH) Program

- Strong fibrosis data with favorable tolerability and dosing convenience[1]
- Positive long-term data; additive benefits in patients on background GLP-1 therapy
- Regulatory alignment on Phase 3 program including potentially accelerated approval using histology in non-cirrhotic (F2-F3) and cirrhotic (F4) patients
- ENLIGHTEN-Fibrosis initiated, ENLIGHTEN-Cirrhosis expected to initiate in 2Q24

Severe Hypertriglyceridemia (SHTG) Program

- Substantially de-risked Phase 3 with topline data anticipated in 2025

Strong balance sheet with ~579 million in cash[3]

Intended commercial product presentation available; composition of matter patent expires in 2038[2]

Highly experienced leadership team with track record of execution

[1] Efficacy comparison based on relative risk ratios and not based on head-to-head results
[2] Patent expiration date excludes any patent term extension or new patents
[3] $578.9 million in cash and cash equivalents as of December 31, 2023; excludes in-the-money warrants of approximately $50 million that expire on June 30, 2024
* If approved

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Appendix

Experienced Management Team Positions 89bio for Success

Rohan Palekar

CEO

CEO, CCO experience

Commercial, strategy, and R&D experience

Otsuka AVANIR PHARMACEUTICALS MEDIVATION J&J

Hank Mansbach, MD

CMO

20+ years biopharma and R&D leadership in clinical development and medical affairs

ultragenyx MEDIVATION VALEANT Pharmaceuticals International, Inc. gsk

Ryan Martins

CFO

CFO, Strategy/IR, finance, sell-side experience

REVOLUTION MEDICINES ultragenyx pharmaceutical Jefferies CHIRON LEHMAN BROTHERS LAZARD BARCLAYS

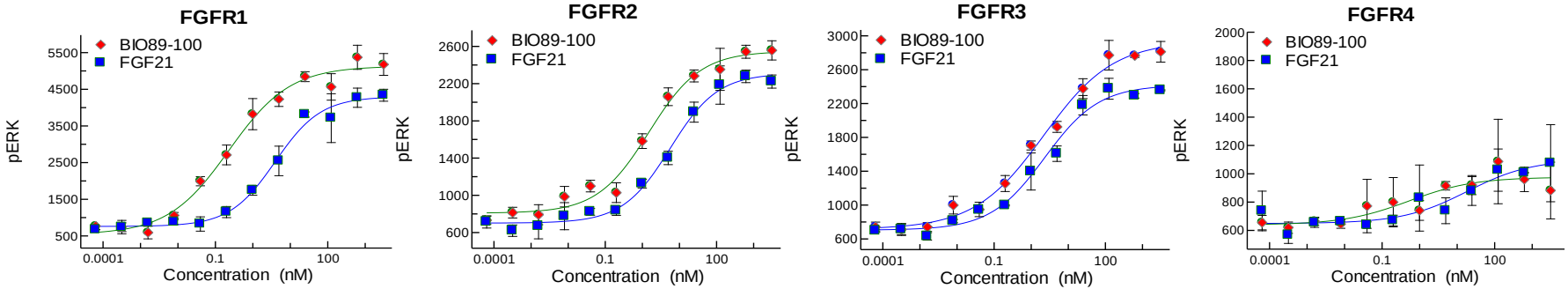
Quoc Le-Nguyen

CTO & Head of Quality

20+ years biopharma and leadership in technical operations, product supply, and quality

Aduro NOVARTIS BIOMARIN BAYER

Pegozafermin Exhibits Highly Potent FGF Receptor Agonism



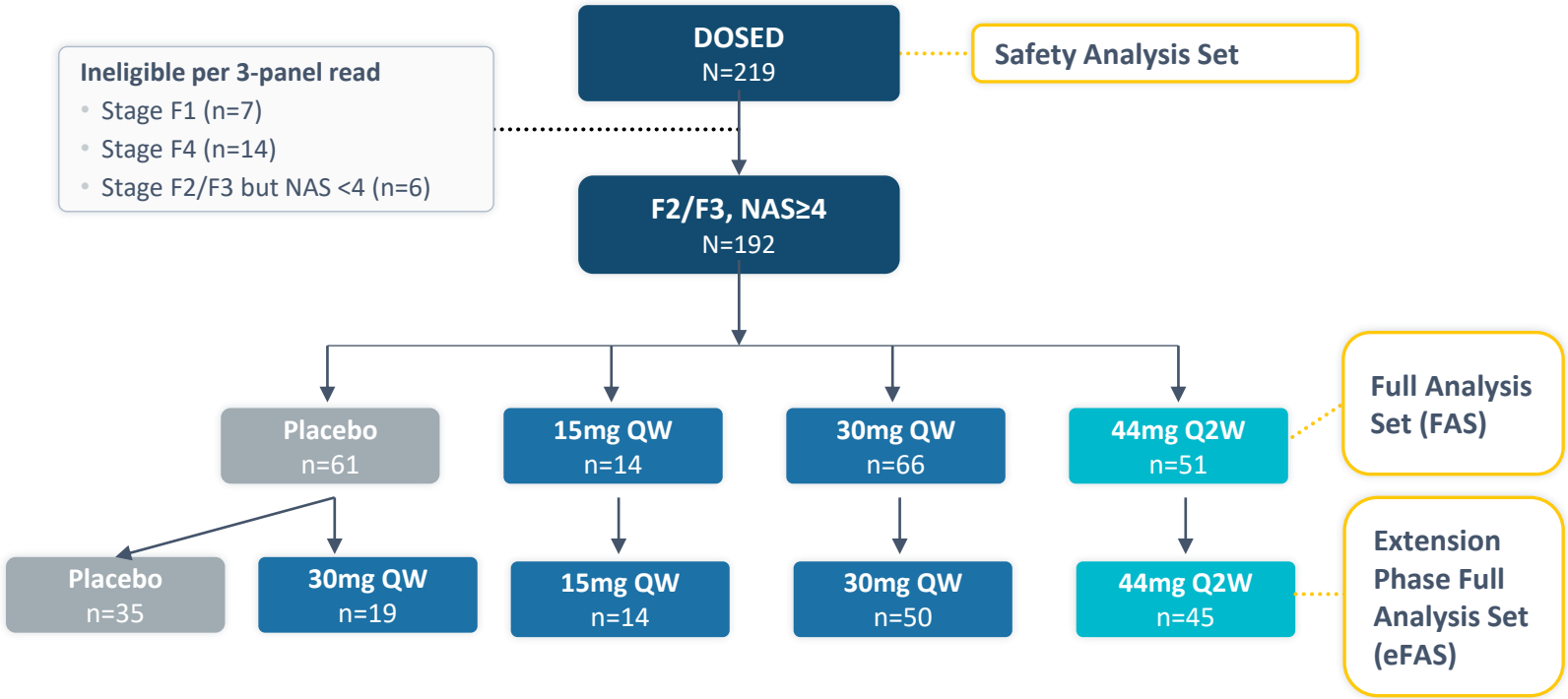
Pegozafermin has the potential to reproduce the beneficial metabolic effects of native FGF21

RECEPTOR	FGF21	Pegozafermin
	EC_{50} (nM)	EC_{50} (nM)
	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 ± 0.4
KLB/FGFR3	1.8 ± 0.3	1.2 ± 0.4
KLB/FGFR4	nd	nd

nd – not determined; rhFGF19 EC_{50} at FGFR4 = 1.7 ± 0.4

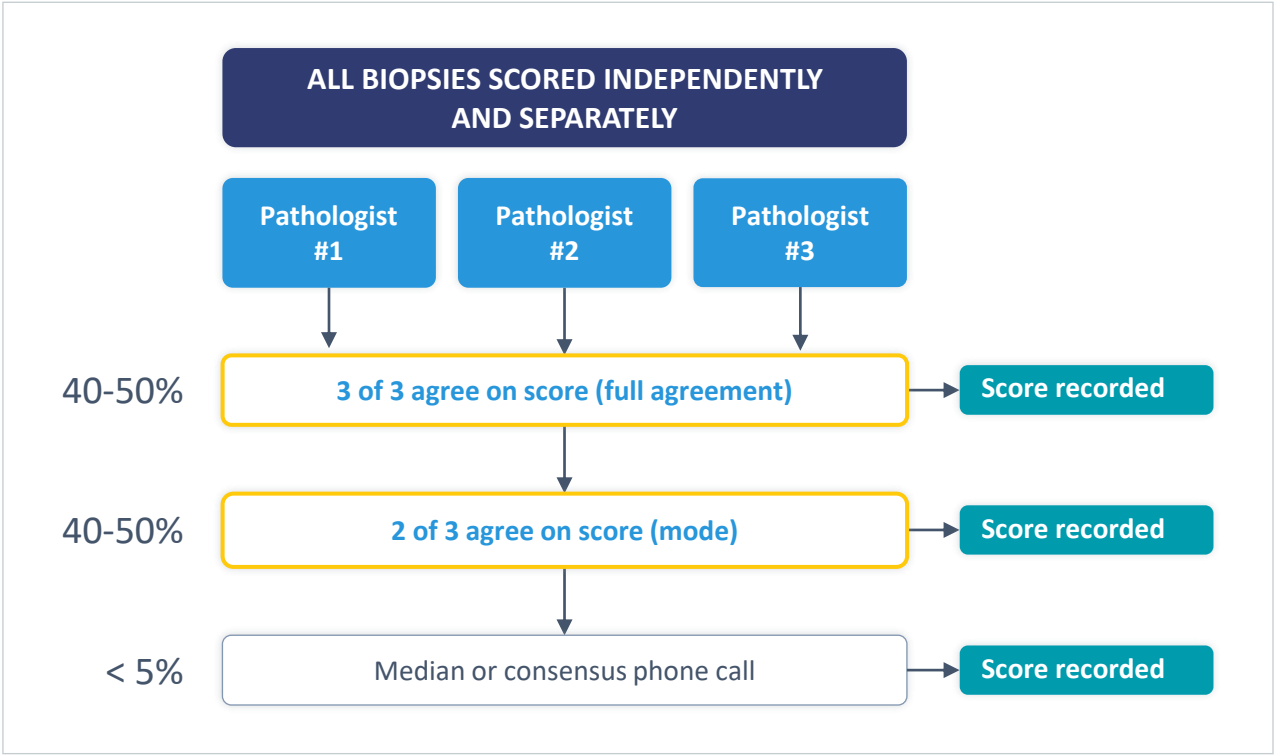
* Receptor agonism measured in L6 cells expressing β-klotho and either FGF Receptor 1c, 2c, 3c, or 4 via pERK functional assay
** Figures represent data from a single experiment; Table represents mean data from multiple experiments

ENLIVEN Patient Disposition and Analysis Sets



Analysis Sets were prospectively defined
MRI-PDFF Analysis Set = all patients in FAS with baseline and at least one post-baseline MRI-PDFF assessment (n=181).

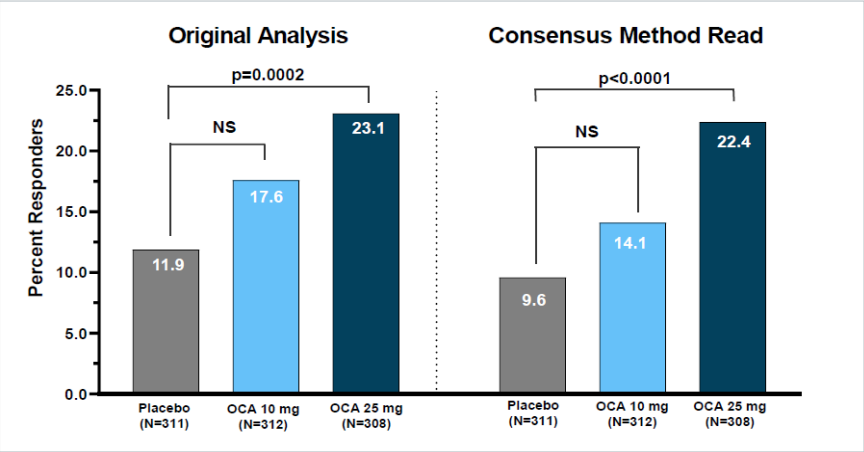
ENLIVEN Used Objective Biopsy Reading Methodology Designed to Reduce Histology Scoring Biases and Variability



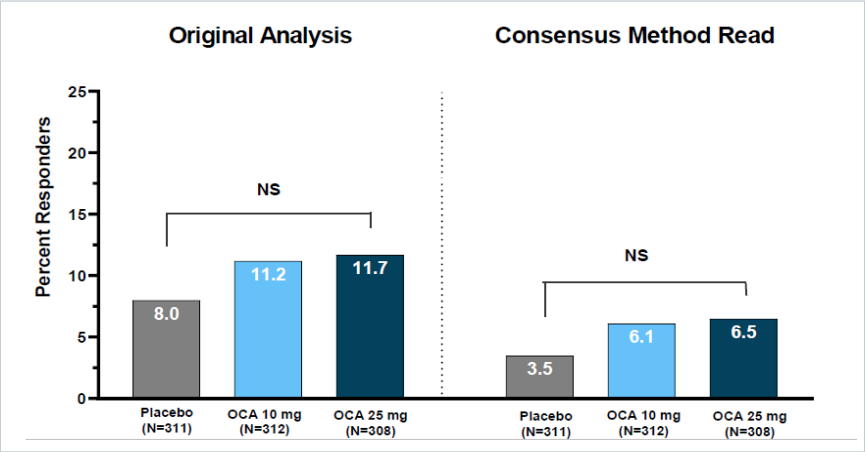
- Pathologists underwent protocol-specific harmonization training before and during trial
- Pathologists were blinded to patient, treatment and sequence
- >99% of final scores determined by a priori established algorithm, versus resolving disagreements via inter-reader discussion

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

Improvement of Fibrosis by ≥ 1 Stage without Worsening MASH



Resolution of MASH with No Worsening of Liver Fibrosis



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

89bio REGENERATE re-analysis topline, July 2022.

Pre-Specified ITT Analysis Confirms Robustness of Primary Efficacy Results

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

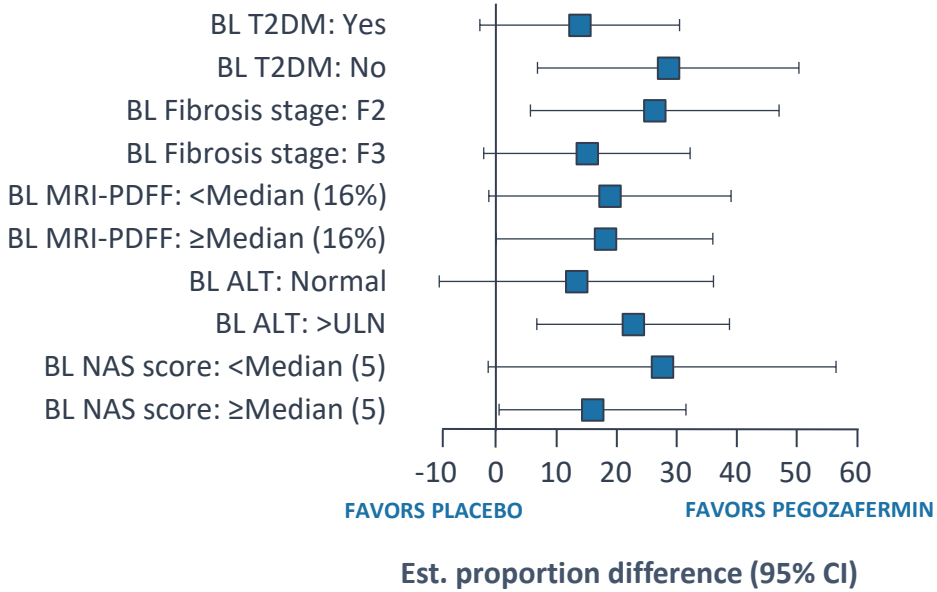
	30mg QW	44mg Q2W
Fibrosis improvement without worsening of MASH		
Effect Size (placebo-adjusted)	15%	16%
p-value	0.019	0.015
MASH resolution without worsening of fibrosis		
Effect Size (placebo-adjusted)	17%	20%
p-value	0.0019	0.0009

89bio Source: FAS

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

Pegozafermin 30mg QW

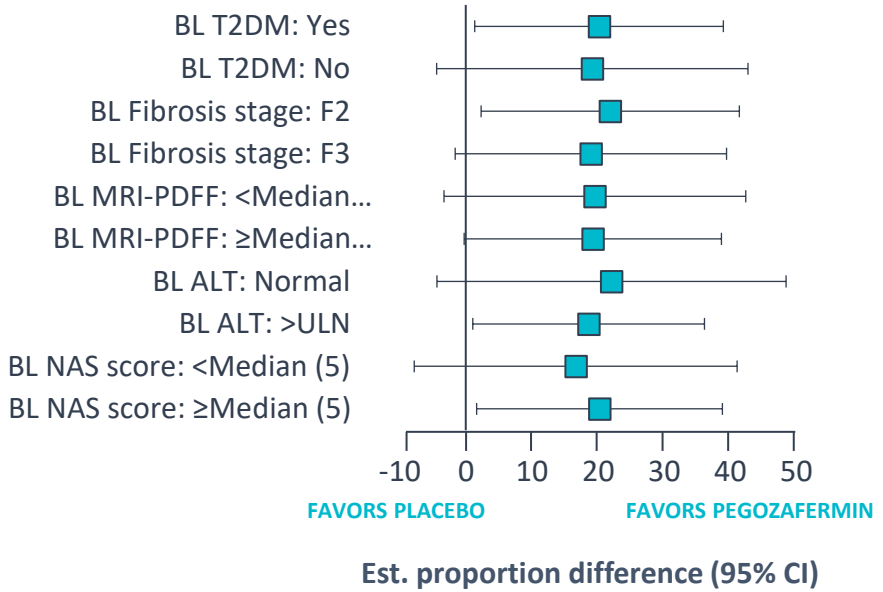
Proportion Achieving Fibrosis Improvement



Est. proportion difference (95% CI)

Pegozafermin 44mg Q2W

Proportion Achieving Fibrosis Improvement

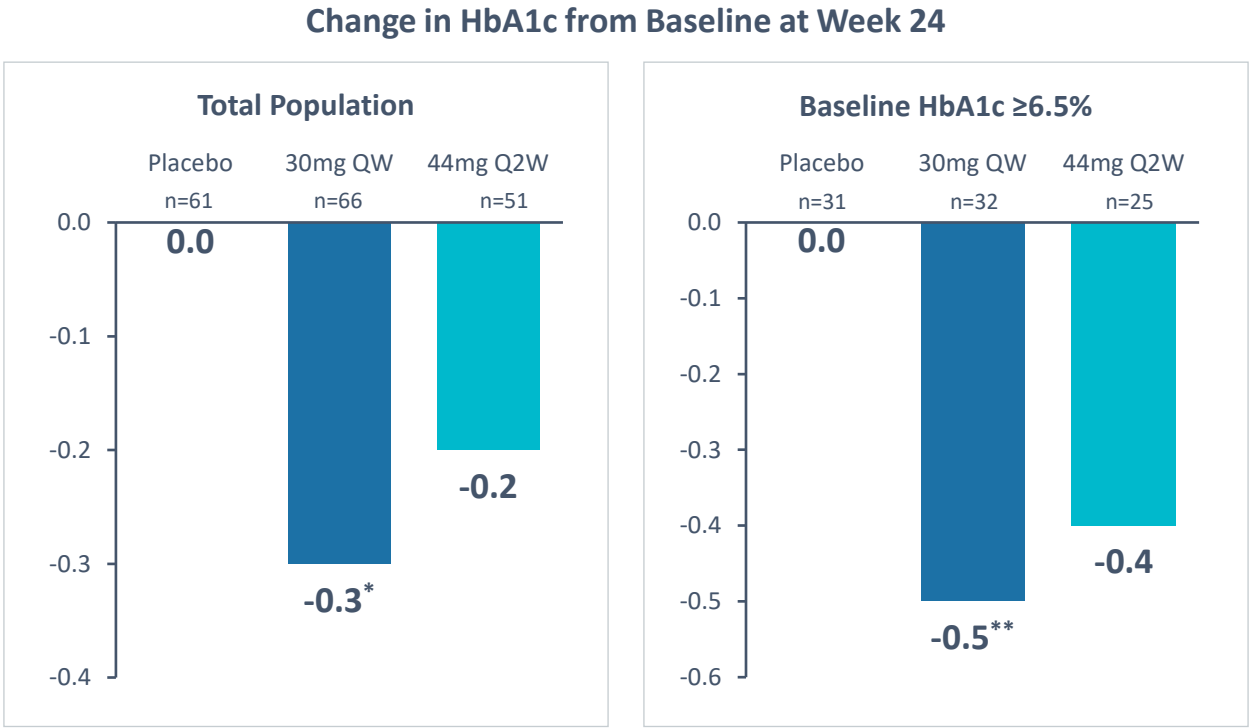


Est. proportion difference (95% CI)

Source: Full Analysis Set

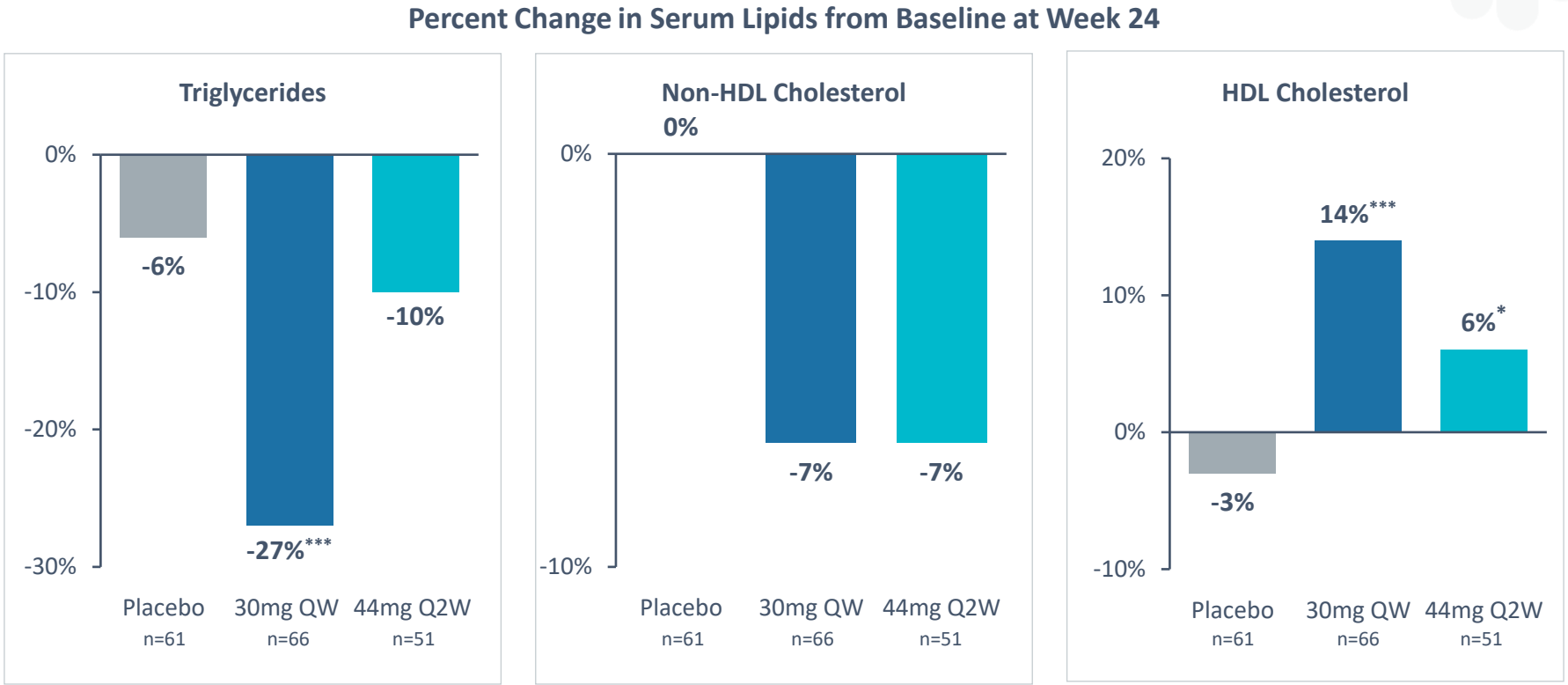
ALT, alanine aminotransferase; BL, baseline; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NAS, Nonalcoholic fatty liver disease Activity Score; MASH, nonalcoholic steatohepatitis; Q2W, every 2 weeks; QW, once weekly; T2DM, type 2 diabetes mellitus; ULN, upper limit of normal.

Pegozafermin Demonstrated Meaningful Reductions in HbA1c (ENLIVEN)



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

Pegozafermin Demonstrated Meaningful Changes in Serum Lipids (ENLIVEN)



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

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

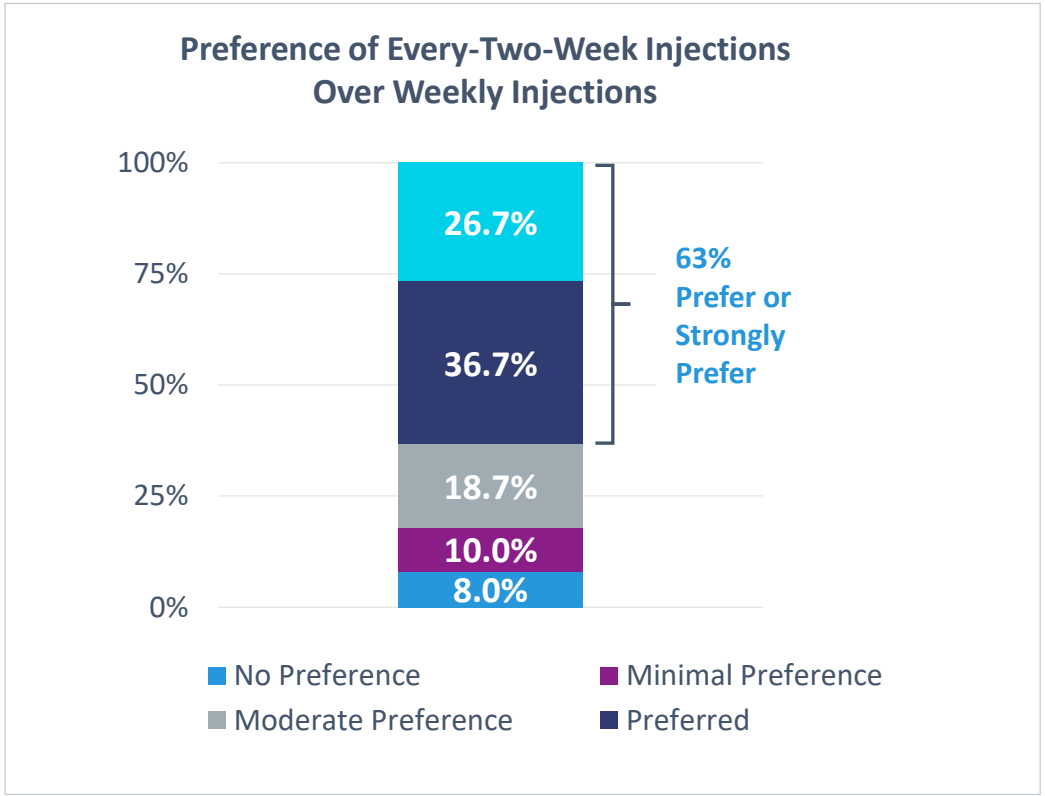
Histology data - Fibrosis improvement ≥ 1 stage without worsening of MASH ranged from 17% to 57%

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

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

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Source: primary market research with 150 people with type 2 diabetes, 2019.

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

INCRETIN PERCEPTIONS

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)**

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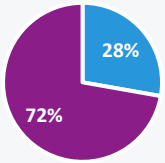
Sources: Primary research with 18 MDs (PCP, Endo, Hep, GI) and 15 patients, August 2023. Primary research with 35 Hep/GIs, September 2023.

Prescribers Believe Pegozafermin has the Strongest Liver & MASH-Relevant Efficacy with Good Safety Profile[1]



N=18
Includes all Hep/GIs

13 out of 18 MDs (72%) would be likely to prescribe pegozafermin, defined as a score of 8-10 out of 10

pegozafermin

PATIENT TYPES:

- **Most suitable: F3 and F4, though would use widely**
- **Less suitable:** F2 with T2DM (PCPs & Endo/Diabs)
- **Not suitable**: those who refuse injection (likely rare)

BENEFITS	NEUTRAL	DRAWBACKS
Liver-related efficacy is strongest (esp. Hep/GIs): Fibrosis improvement; MASH resolution, liver stiffness, ALT reduction and MRI-PDFF is impressive	**Other metabolic benefits are nice to have, but less relevant (Hep/GI)**	**Few PCPs and Endos would like to see more improvement on HbA1c and weight loss**
Safety: no major issues	**Patients will accept injectables for efficacy - once every 2 weeks is preferred**	**Some PCPs prefer to refer MASH treatment to liver specialists**
Combination with GLP-1s is appealing given trial includes those on GLP-1s		

1. Research based on profiles for FGF21 analogs, assuming no fibrosis benefit for resmetirom and incretins
Source: Primary research with 18 MDs (PCP, Endo, Hep, GI) and 15 patients, August 2023