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## Pegozafermin Phase 2b (ENLIVEN) Topline Results in Nonalcoholic Steatohepatitis (NASH)

**Nasdaq: ETNB**

Powerful Science
Meaningful Medicines
Changing Lives

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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, or intentions relating to product candidates, potential market opportunities, patient acceptance of pegozafermin, estimates of market size, the potential clinical benefit, effect on the histology and safety and tolerability profile of pegozafermin (formerly BIO89-100), the clinical potential of pegozafermin, potential indications for pegozafermin, the anticipated dosing regimen for pegozafermin, if approved, the timing of regulatory meetings or discussions, 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. 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 under the caption "Risk Factors" and elsewhere in such report and in other subsequent disclosure documents filed with the U.S. Securities and Exchange Commission.

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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.

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# Pegozafermin – A Potentially Differentiated and Foundational NASH Drug

**Statistically Significant Results on Fibrosis Improvement and NASH Resolution**

- Fibrosis improvement – 3.5x and NASH resolution – 12-14x placebo rate

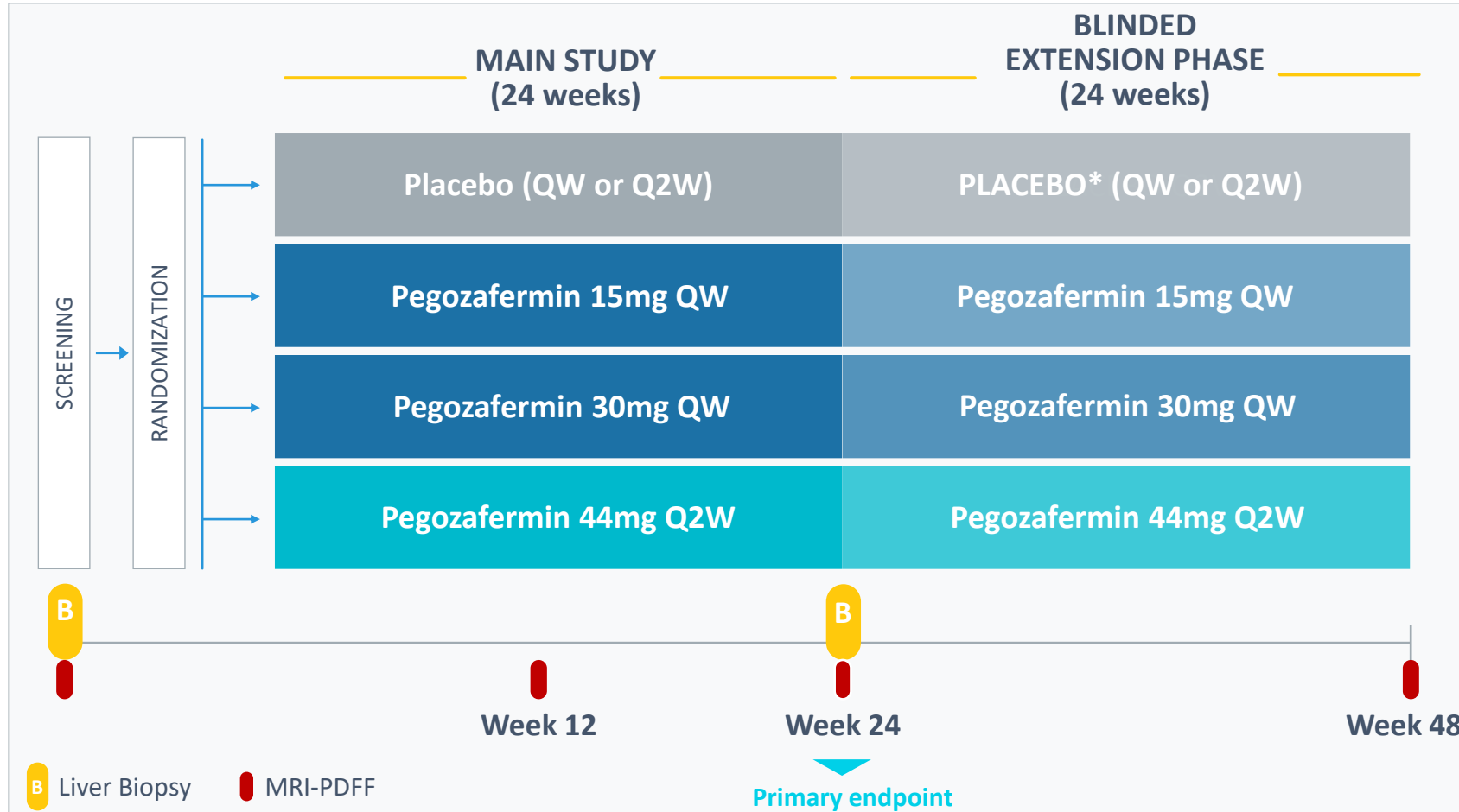**Significant Results with Weekly and Every-Two-Week Dosing on Both Endpoints**

- Only drug in the category pursuing this optionality

**Favorable Safety and Tolerability Profile**

**Rigorous Trial Increases Our Confidence in Phase 3**

- FDA guidance on endpoints and analysis; Rigorous biopsy reading methods; Large study

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# ENLIVEN Trial Design

| | MAIN STUDY (24 weeks) | BLINDED EXTENSION PHASE (24 weeks) |
|---|---|---|
| | Placebo (QW or Q2W) | PLACEBO* (QW or Q2W) |
| | Pegozafermin 15mg QW | Pegozafermin 15mg QW |
| | Pegozafermin 30mg QW | Pegozafermin 30mg QW |
| | Pegozafermin 44mg Q2W | Pegozafermin 44mg Q2W |

SCREENING → RANDOMIZATION →

Week 12   Week 24   Week 48

**Primary endpoint**

**B** Liver Biopsy    **▮** MRI-PDFF

## PRIMARY ANALYSIS POPULATION

- F2-F3 NASH; NAS ≥4

### PRIMARY ENDPOINTS

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

### KEY SECONDARY EFFICACY ENDPOINTS

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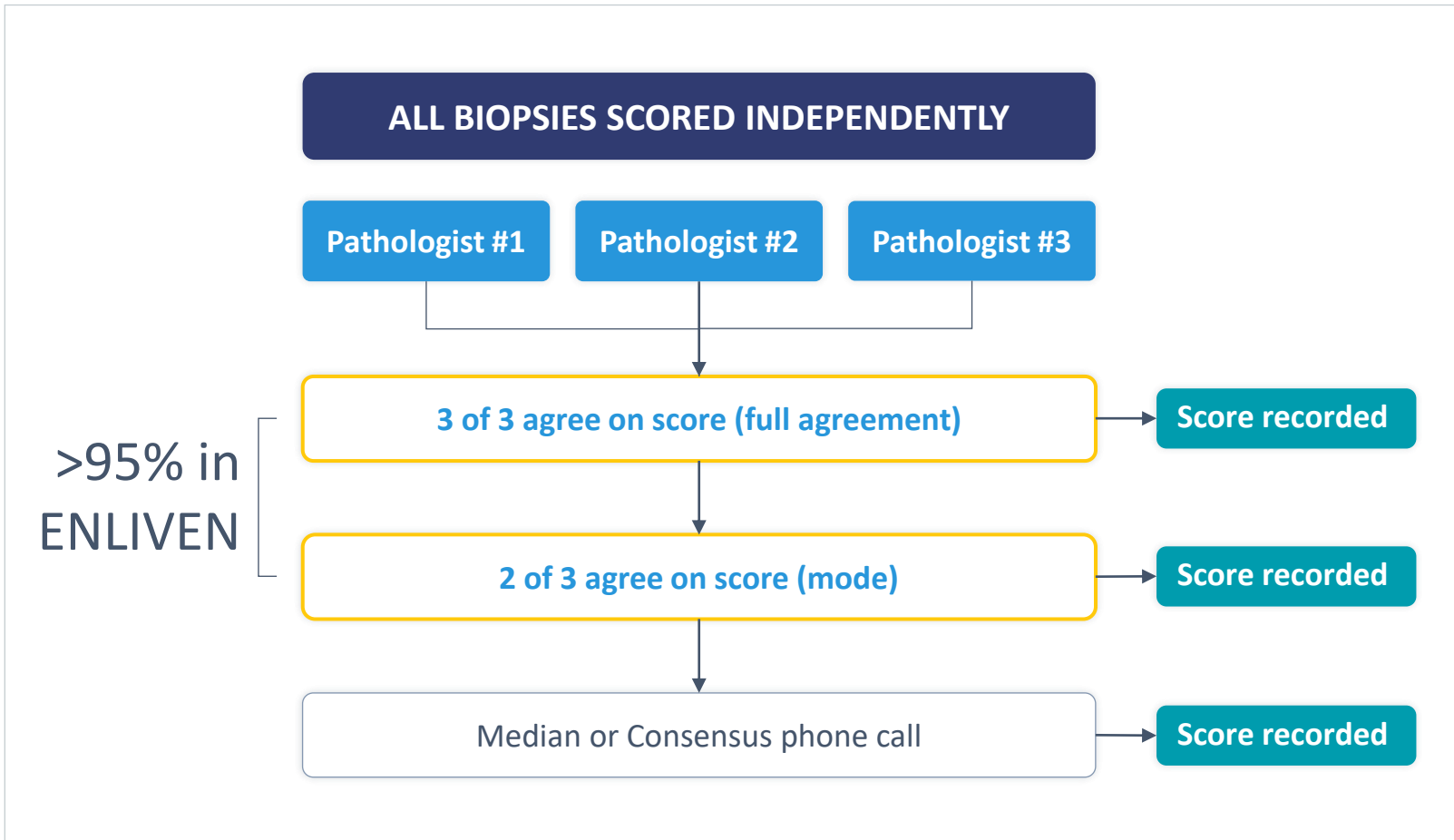- Non-invasive liver markers (liver fat, liver injury, fibrosis markers)

# Rigorous Biopsy Reading Method Designed to Identify Drug Effect



**ALL BIOPSIES SCORED INDEPENDENTLY**

| Pathologist #1 | Pathologist #2 | Pathologist #3 |

**>95% in ENLIVEN**

**3 of 3 agree on score (full agreement)** → Score recorded

**2 of 3 agree on score (mode)** → Score recorded

Median or Consensus phone call → Score recorded

- All biopsies scored independently by three pathologists (on 4 components of NASH-CRN criteria)
- Pathologists underwent protocol-specific harmonization training before and during trial
- Pathologists were blinded to subject, treatment and sequence

▶ **Designed to reduce impact of individual reader bias and inter-reader variability**

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# Patient Disposition and Analysis Sets



Analysis Sets were prospectively defined
Completer Analysis Set = FAS subjects with biopsies at both baseline and Week 24 (n=164).
MRI-PDFF Analysis Set = all subjects in FAS with baseline and at least one post-baseline MRI-PDFF assessment (n=181).
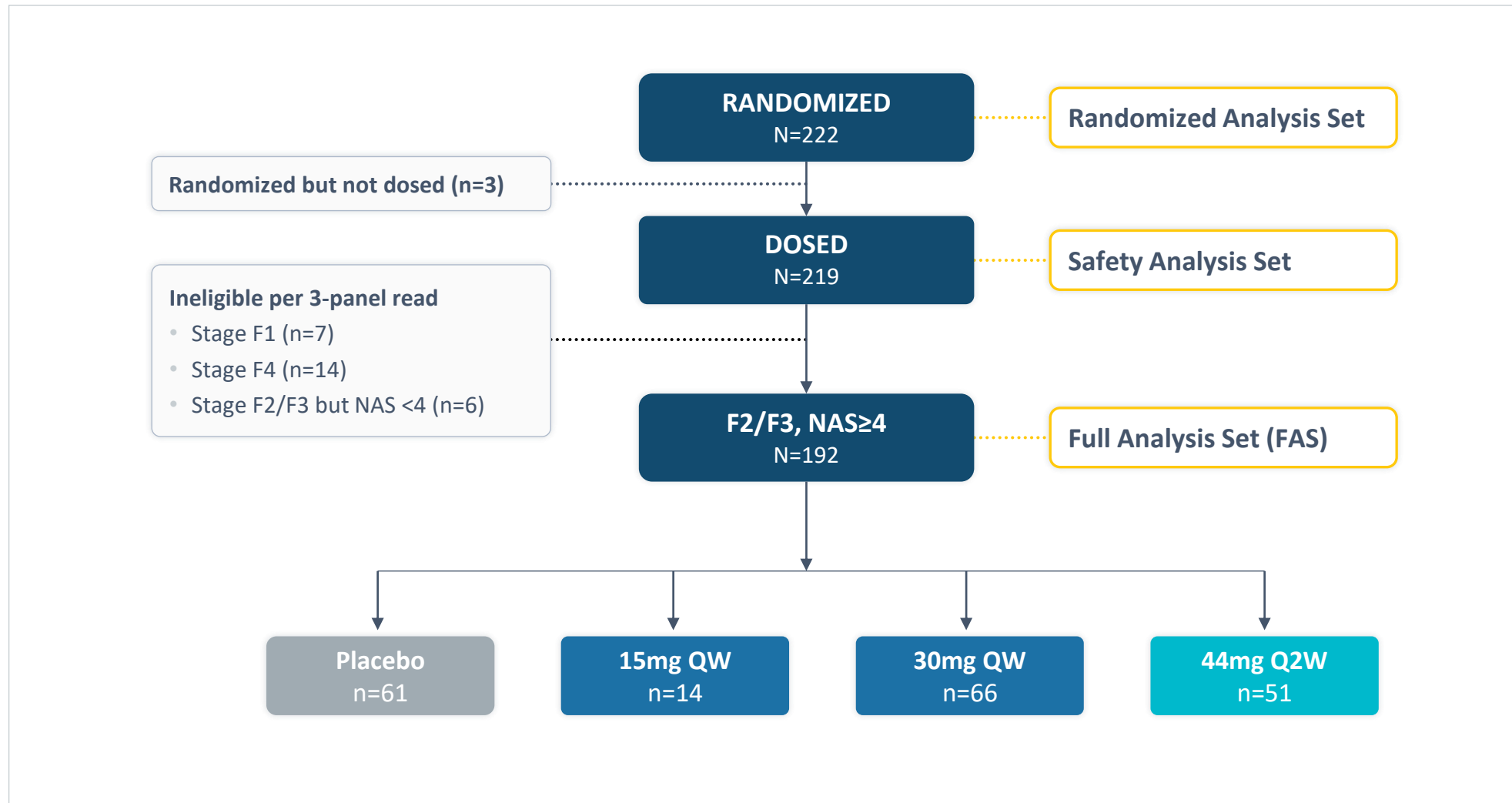
# Baseline Characteristics Well Balanced Across Dose Groups

| Parameter<br>Mean or % | Placebo<br>(n=71) | 15mg QW<br>(n=21) | 30mg QW<br>(n=73) | 44mg Q2W<br>(n=57) | Total<br>(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 |

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# Pegozafermin Demonstrated Statistical Significance on Fibrosis Improvement with Weekly and Every-Two-Week Dosing
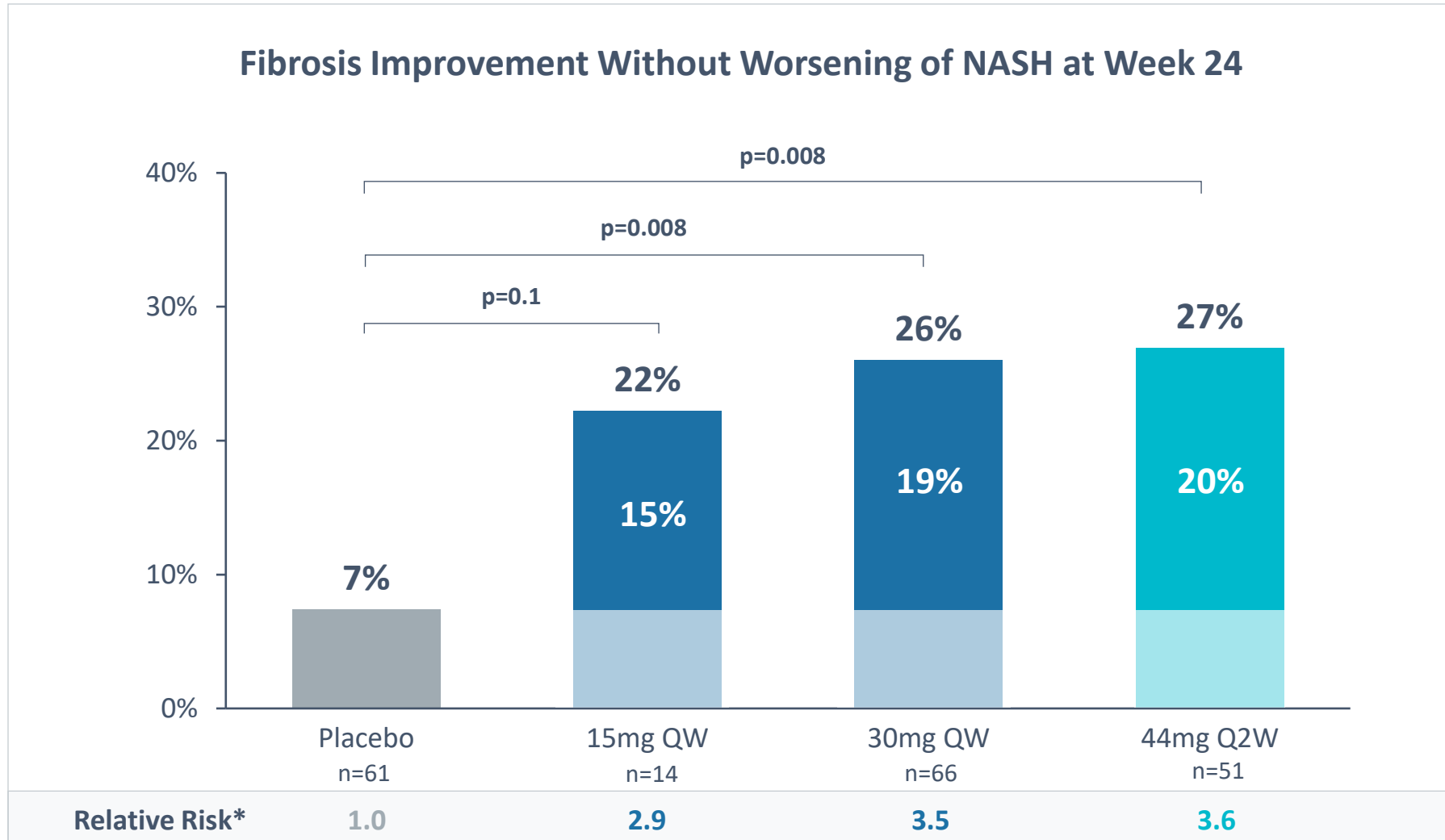


**Fibrosis Improvement Without Worsening of NASH at Week 24**

| | Placebo | 15mg QW | 30mg QW | 44mg Q2W |
|---|---|---|---|---|
| | n=61 | n=14 | n=66 | n=51 |
| **Relative Risk*** | 1.0 | 2.9 | 3.5 | 3.6 |

Relative risk is calculated by dividing drug response by placebo response

# Pre-Specified Additional Analyses Confirm Robustness of Primary Efficacy Results

**Fibrosis Improvement Without Worsening of NASH at Week 24**

|  | 30mg QW | 44mg Q2W |
|---|---|---|
| **Completer Analysis Set (n=164)** | | |
| Effect Size (placebo-adjusted) | 19% | 20% |
| p-value | 0.009 | 0.008 |
| **Intent-to-treat (ITT; missing data = non-responder); (n=192)** | | |
| Effect Size (placebo-adjusted) | 15% | 16% |
| p-value | 0.019 | 0.015 |

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Source: FAS for ITT and Completer Analysis Set

# Clinical Data in Pre-Cirrhotic Patients

*≥1 Stage Fibrosis Improvement with No Worsening of NASH (placebo-adjusted)*
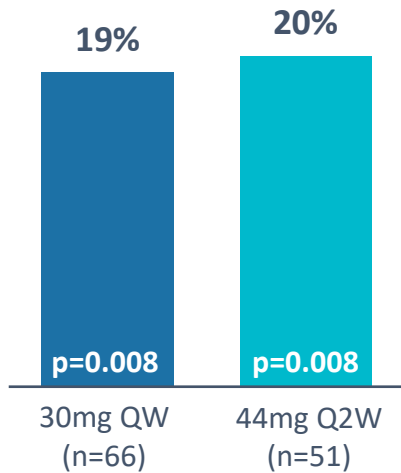
| | 89bio | | Intercept | Madrigal Pharmaceuticals | | inventiva | | novo nordisk | ak2ro | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Pegozafermin** Phase 2b \| 24 weeks Multiple Imputation[1] | | **Ocaliva** Phase 3 \| 72 weeks | **Resmetirom[2]** Phase 3 \| 52 weeks | | **Lanifibranor** Phase 2b \| 24 weeks | | **Semaglutide** Phase 2 \| 72 weeks | **Efruxifermin** Phase 2b \| 24 weeks Completers Analysis | |
| **Drug response as multiple of placebo response*** | 3.5 | 3.6 | 2.3 | 1.7 | 1.9 | 1.1 | 1.6 | 1.3 | 2.0 | 2.0 |
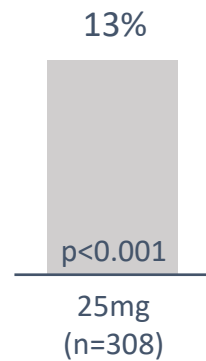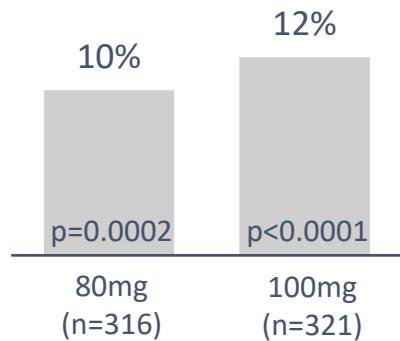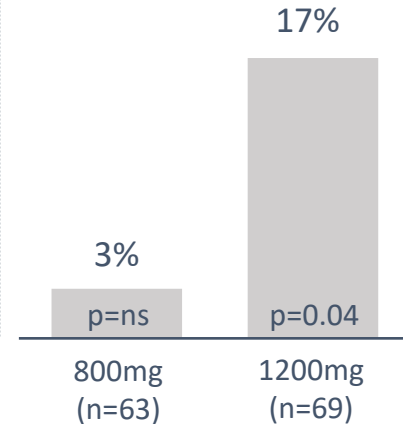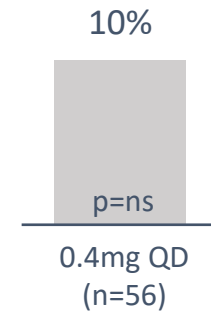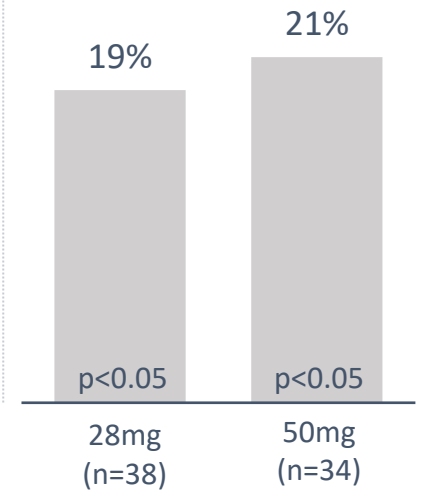
**Bar chart values:**

| | 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 QD (n=56) | 28mg (n=38) | 50mg (n=34) |
|---|---|---|---|---|---|---|---|---|---|---|
| % | 19% | 20% | 13% | 10% | 12% | 3% | 17% | 10% | 19% | 21% |
| p-value | p=0.008 | p=0.008 | p<0.001 | p=0.0002 | p<0.0001 | p=ns | p=0.04 | p=ns | p<0.05 | p<0.05 |

*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

**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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# Descriptive Analysis Data of Cirrhotic (F4) Patients from ENLIVEN

**Fibrosis Improvement Without Worsening of NASH[1] at Week 24**
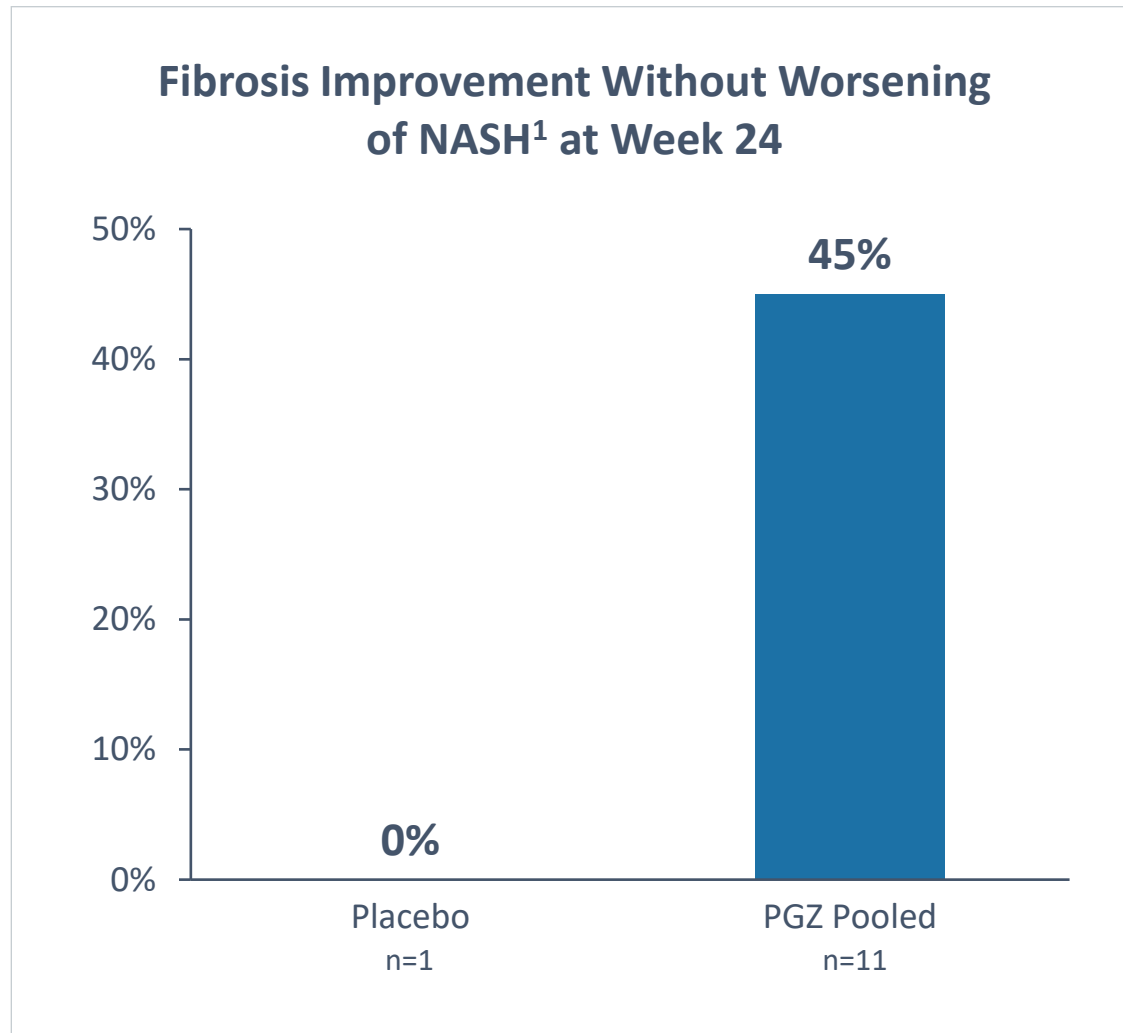


- 5/11 patients had fibrosis improvement without worsening of NASH[1]

- An additional 4 patients had fibrosis improvement only (9/11 total treated patients)

**12/14 F4 patients enrolled in ENLIVEN had follow-up biopsies at week 24**

[1]Improvement in liver fibrosis by ≥1 stage and no worsening of steatohepatitis defined as no increase in NAS for ballooning, inflammation, or steatosis.

# Pegozafermin Demonstrated Statistical Significance on NASH Resolution at All Doses
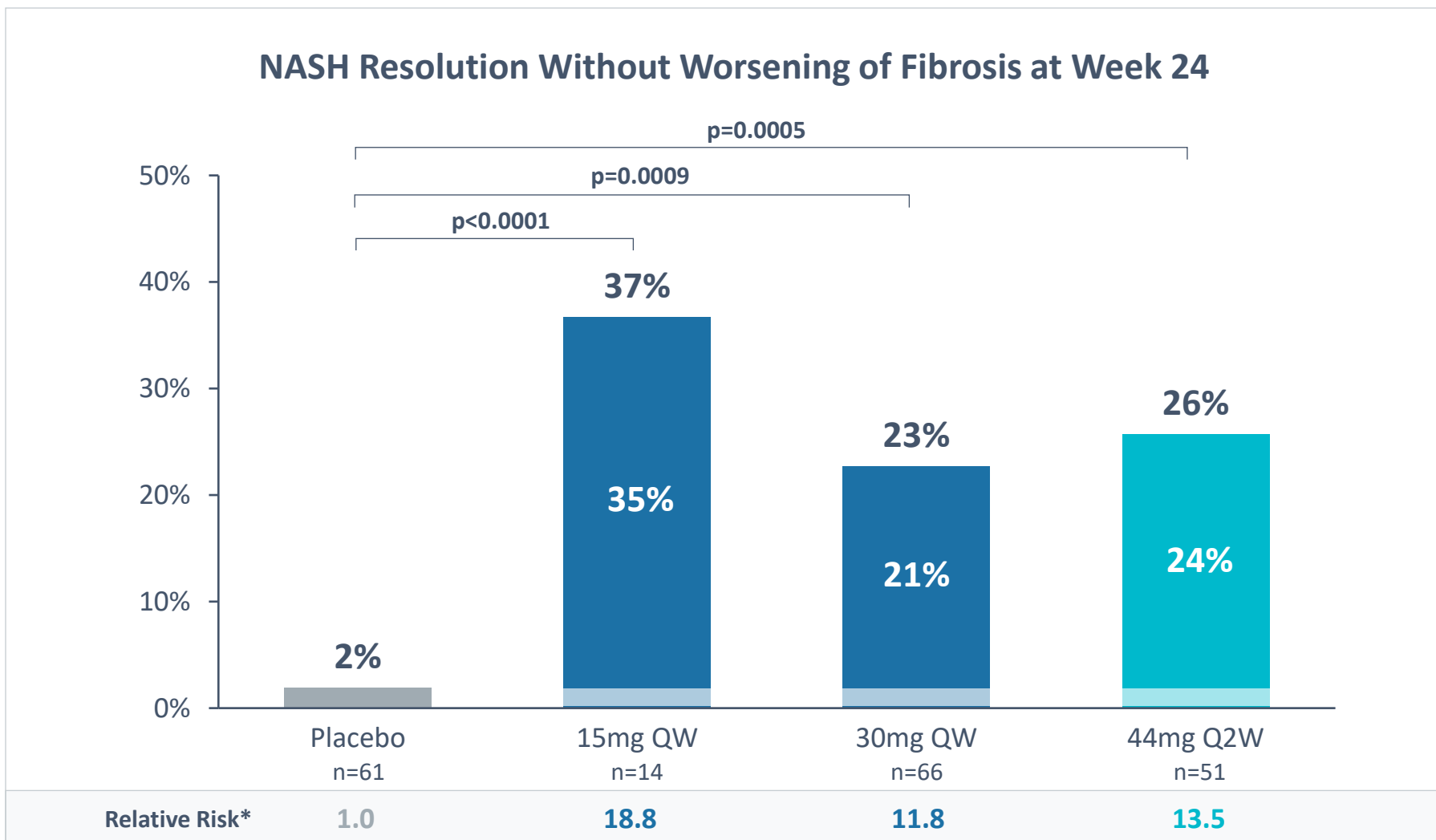
## NASH Resolution Without Worsening of Fibrosis at Week 24



| | Placebo n=61 | 15mg QW n=14 | 30mg QW n=66 | 44mg Q2W n=51 |
|---|---|---|---|---|
| Relative Risk* | 1.0 | 18.8 | 11.8 | 13.5 |

Bar values:
- Placebo: 2%
- 15mg QW: 37% (35%)
- 30mg QW: 23% (21%)
- 44mg Q2W: 26% (24%)

p<0.0001 (Placebo vs 15mg QW)
p=0.0009 (Placebo vs 30mg QW)
p=0.0005 (Placebo vs 44mg Q2W)

Relative risk is calculated by dividing drug response by placebo response

# Pre-Specified Additional Analyses Confirm Robustness of Primary Efficacy Results

**NASH Resolution Without Worsening of Fibrosis at Week 24**

|  | 30mg QW | 44mg Q2W |
|---|---|---|
| **Completer Analysis Set (n=164)** | | |
| Effect Size (placebo-adjusted) | 21% | 24% |
| p-value | 0.0009 | 0.0004 |
| **ITT (missing data = non-responder); (n=192)** | | |
| Effect Size (placebo-adjusted) | 17% | 20% |
| p-value | 0.0019 | 0.0009 |

# Clinical Data in Pre-Cirrhotic Patients
## *NASH Resolution with No Worsening of Fibrosis*

| | **89bio** | | Intercept | Madrigal Pharmaceuticals | | inventiva | | novo nordisk | akero | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **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 |



Bar chart — NASH resolution rates:
- **Pegozafermin** (89bio): 30mg QW (n=66): **21%**, p=0.0009; 44mg Q2W (n=51): **24%**, p=0.0005
- **Ocalivia** (Intercept): 25mg (n=308): 3%, p=ns
- **Resmetirom** (Madrigal): 80mg (n=316): 16%, p<0.0001; 100mg (n=321): 20%, p<0.0001
- **Lanifibranor** (inventiva): 800mg (n=63): 17%, p=0.039; 1200mg (n=69): 26%, p=0.002
- **Semaglutide** (novo nordisk): 0.4mg (n=56): 44%, p<0.001
- **Efruxifermin** (akero): 28mg (n=38): 32%, p<0.01; 50mg (n=34): 61%, p<0.001

\* Drug response as multiple of placebo response is calculated by dividing drug response by placebo response
[1] Results same for Completer Analysis Set
[2] NASH resolution with ≥2 point reduction in NAS and no worsening of fibrosis
**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.**
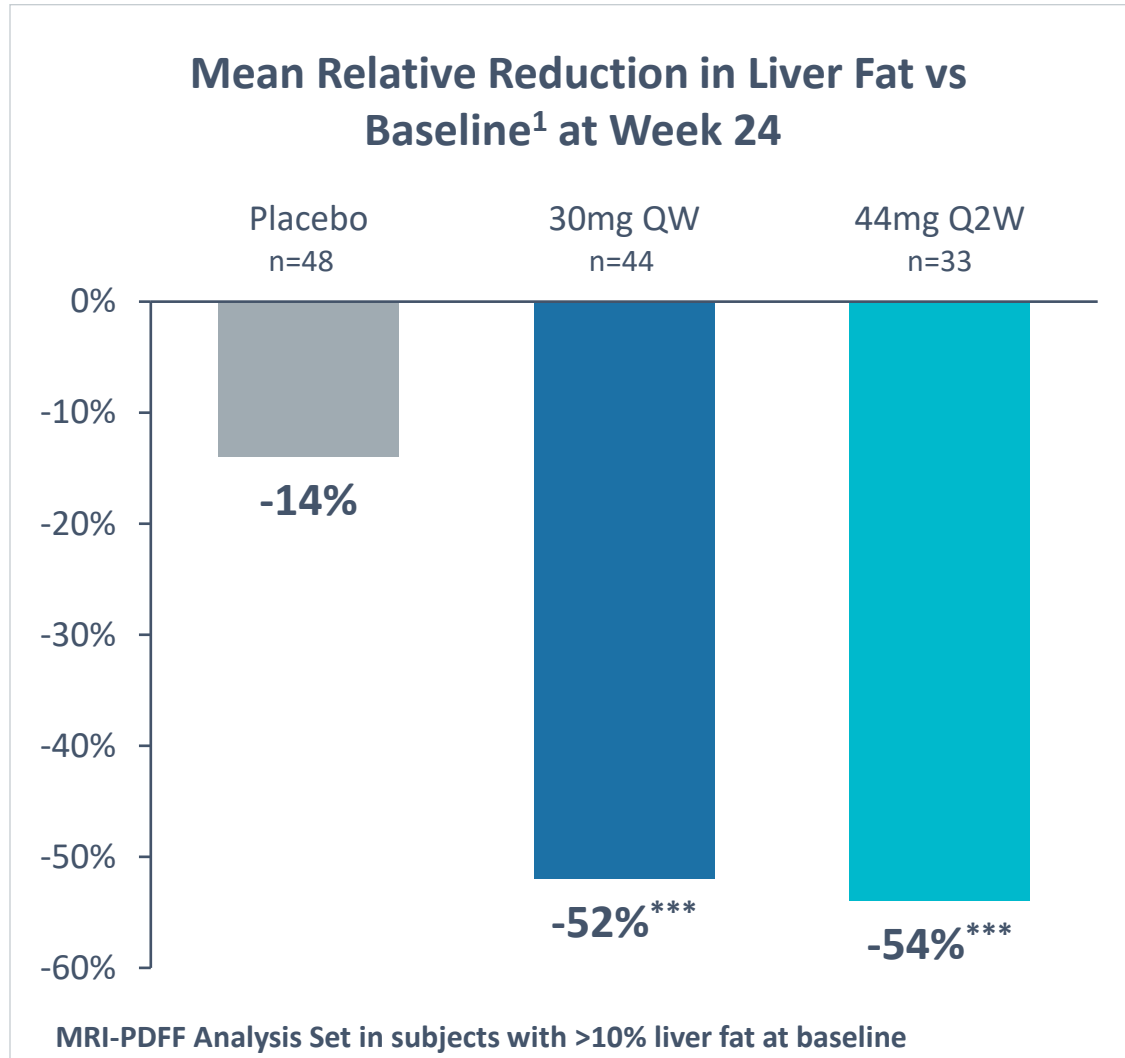
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# Pegozafermin Demonstrated Statistical Significance on ≥2-point NAS Improvement

**≥2-point NAS Improvement and no Worsening of Fibrosis[1] at Week 24**
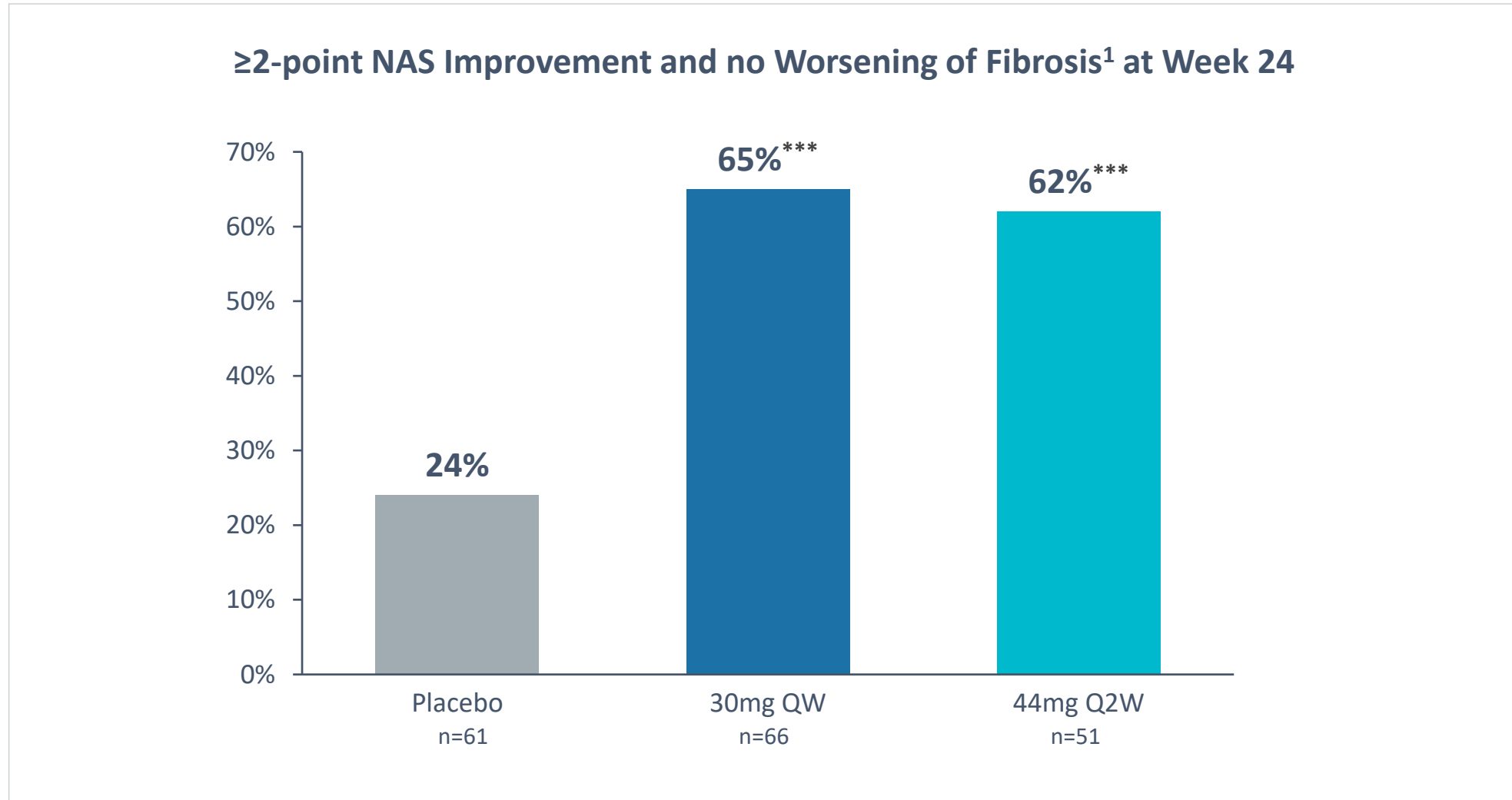


Results for the 15mg QW dose: 37%

[1] Full Analysis Set. Analysis via Cochran-Mantel-Haenszel (CMH) test stratified by T2DM status (yes vs. no) and fibrosis stage (F2 vs. F3)
***p<0.001 versus placebo.

# Pegozafermin Demonstrated Robust Liver Fat Reduction with High Responder Rates by MRI-PDFF at Week 24

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

| | Placebo n=48 | 30mg QW n=44 | 44mg Q2W n=33 |
| --- | --- | --- | --- |

- Placebo: -14%
- 30mg QW: -52%***
- 44mg Q2W: -54%***

**MRI-PDFF Analysis Set in subjects with >10% liver fat at baseline**

## Proportion of Patients Achieving ≥50% Reductions in Liver Fat[2] at Week 24

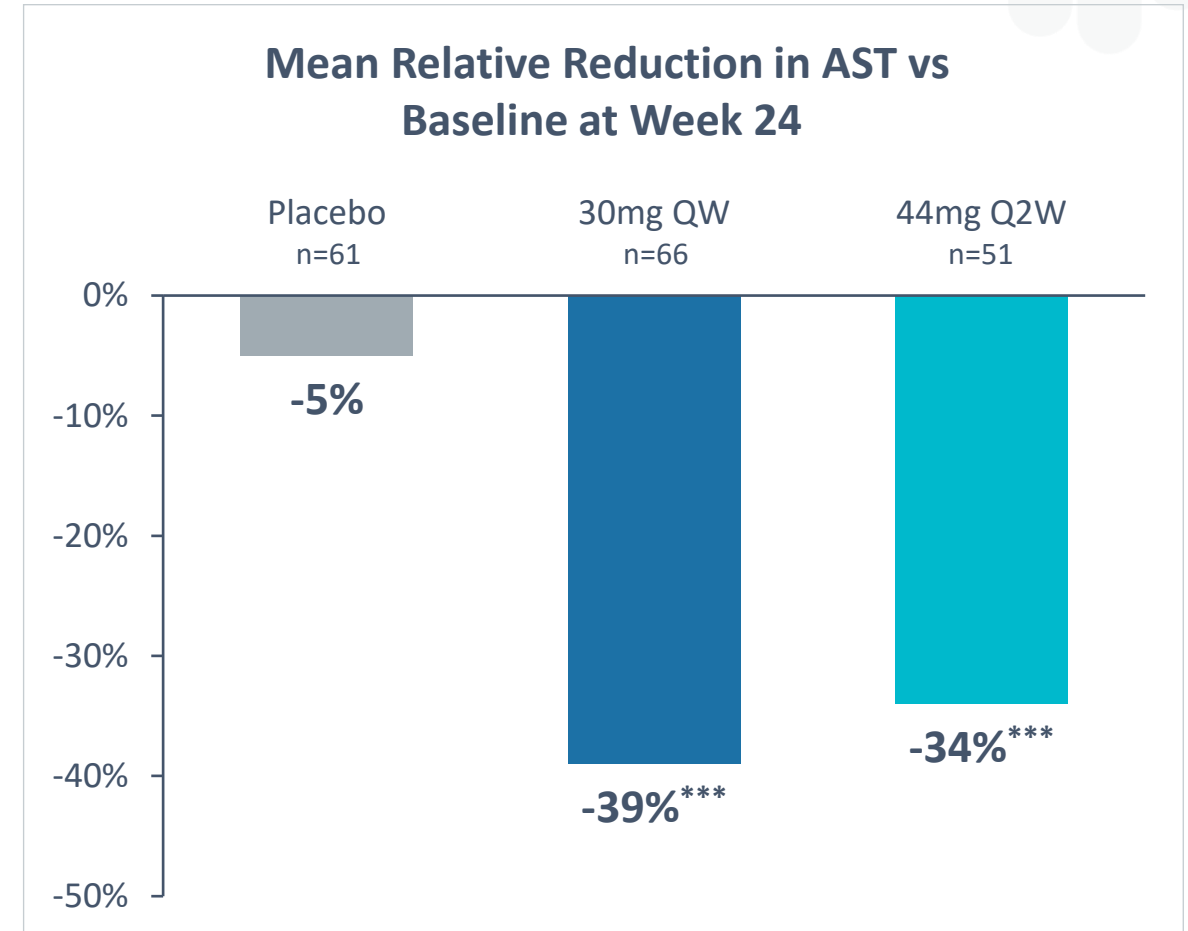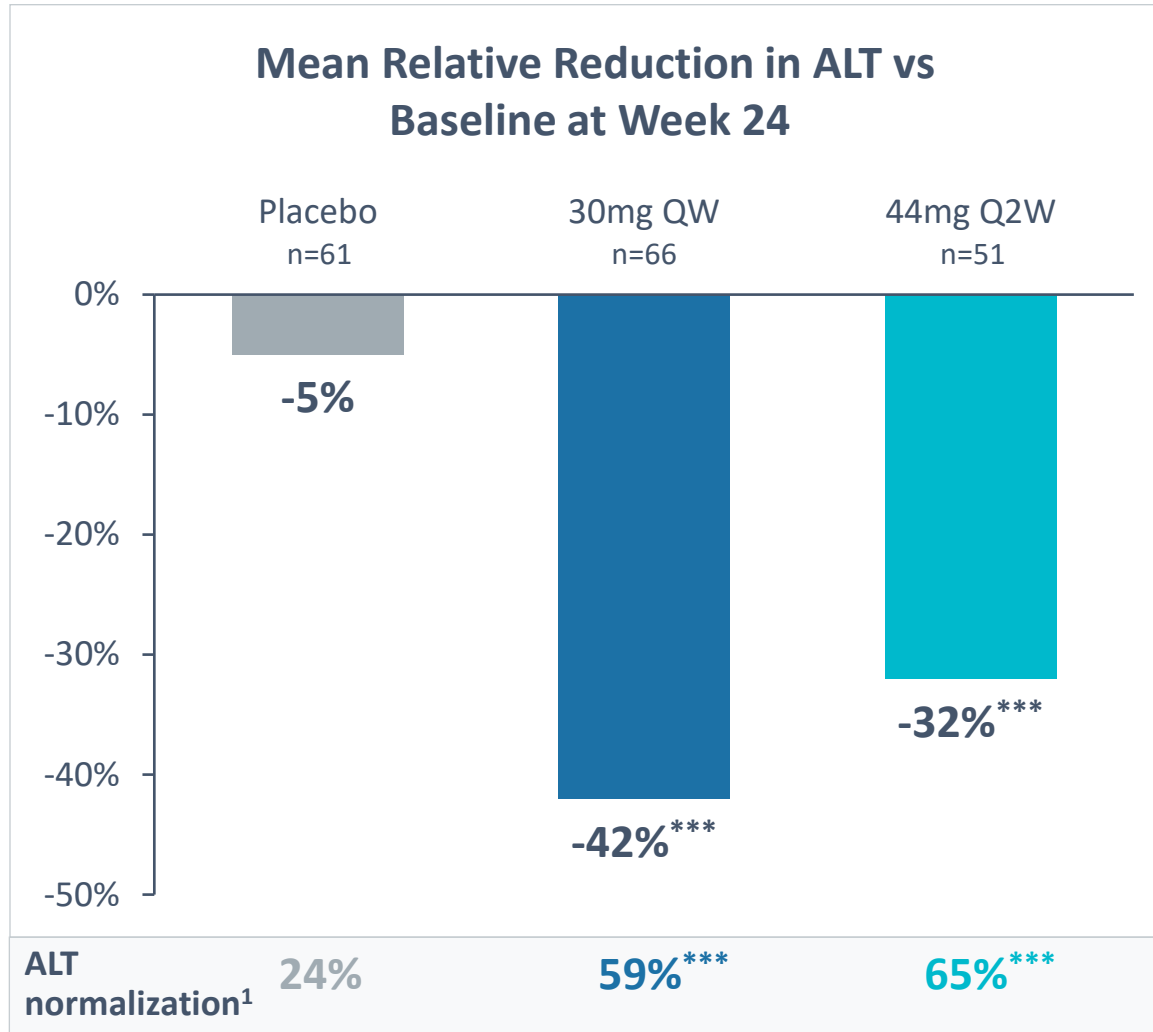| Placebo (n=48) | 30mg QW (n=44) | 44mg Q2W (n=33) |
| --- | --- | --- |
| 13% | 66%*** | 67%*** |

Results for the 15mg QW dose: -33% (n=12; p=ns)

[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).
***p<0.001 versus placebo

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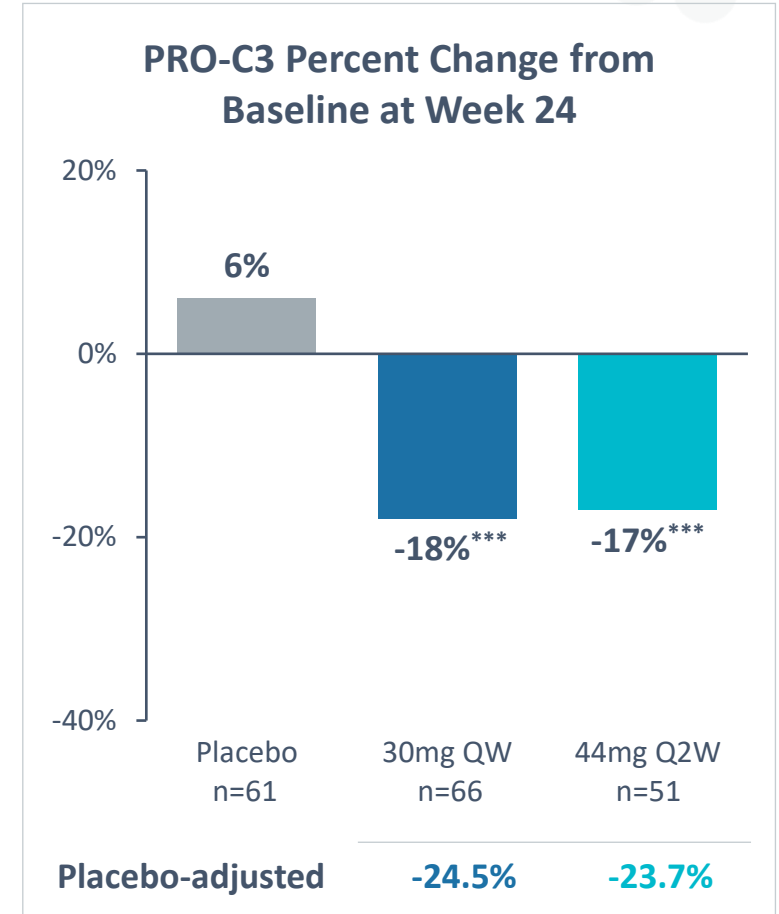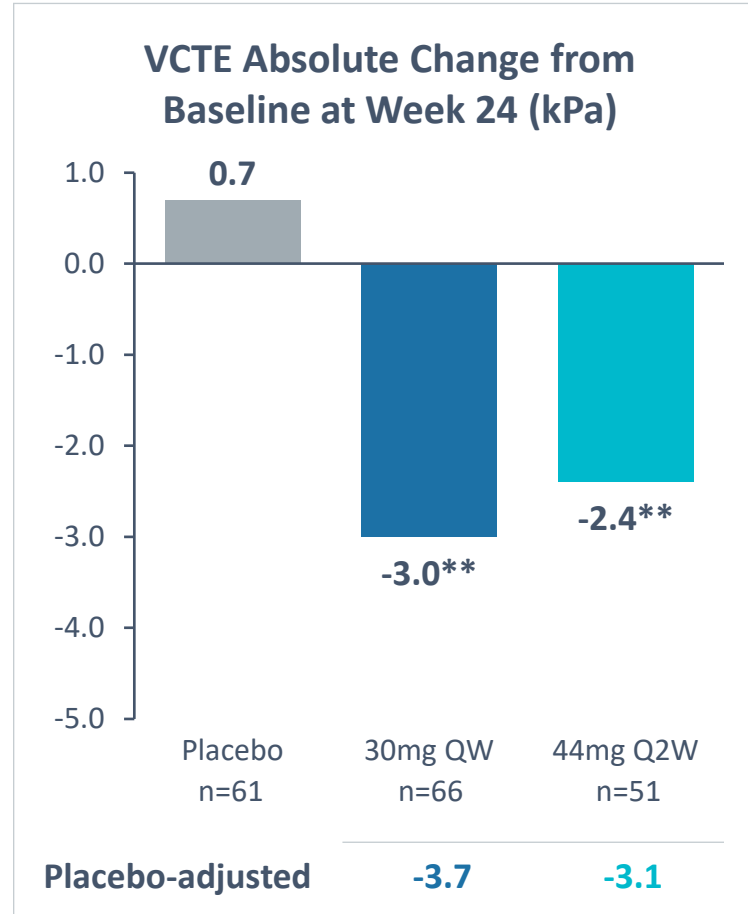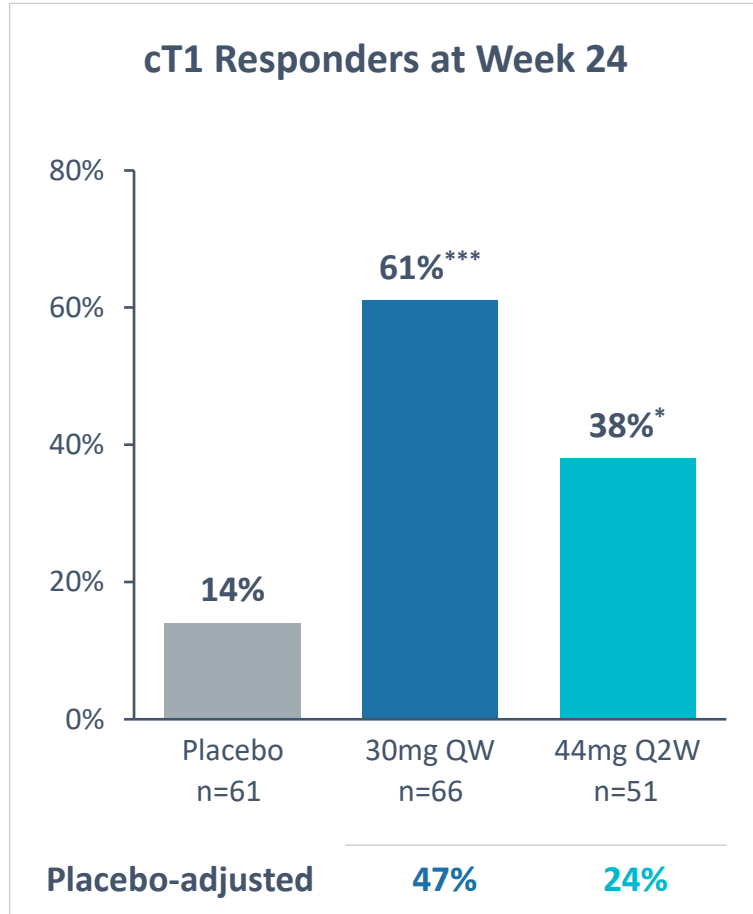
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# Pegozafermin Demonstrated Significant Improvements in Markers of Liver Injury (ALT and AST)



**Mean Relative Reduction in ALT vs Baseline at Week 24**

| Placebo n=61 | 30mg QW n=66 | 44mg Q2W n=51 |
|:---:|:---:|:---:|
| -5% | -42%*** | -32%*** |

**ALT normalization[1]**

| 24% | 59%*** | 65%*** |
|:---:|:---:|:---:|

**Mean Relative Reduction in AST vs Baseline at Week 24**

| Placebo n=61 | 30mg QW n=66 | 44mg Q2W n=51 |
|:---:|:---:|:---:|
| -5% | -39%*** | -34%*** |

ALT Results for the 15mg QW dose: -38% (n=14; p<0.01)

[1]ALT normalization defined as patients with ALT ≥30 U/L at baseline (n=133) with end-of-study ALT <30 U/L.

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



**cT1 Responders at Week 24**

| | Placebo n=61 | 30mg QW n=66 | 44mg Q2W n=51 |
|---|---|---|---|
| | 14% | 61%*** | 38%* |
| **Placebo-adjusted** | | 47% | 24% |

**VCTE Absolute Change from Baseline at Week 24 (kPa)**

| | Placebo n=61 | 30mg QW n=66 | 44mg Q2W n=51 |
|---|---|---|---|
| | 0.7 | -3.0** | -2.4** |
| **Placebo-adjusted** | | -3.7 | -3.1 |

**PRO-C3 Percent Change from Baseline at Week 24**

| | Placebo n=61 | 30mg QW n=66 | 44mg Q2W n=51 |
|---|---|---|---|
| | 6% | -18%*** | -17%*** |
| **Placebo-adjusted** | | -24.5% | -23.7% |

Results for the 15mg QW dose: cT1 40% (n=10; p=ns); VCTE -1.6 kPa (n=14; p=ns); PRO-C3 -5% (n=14; p=ns).

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.
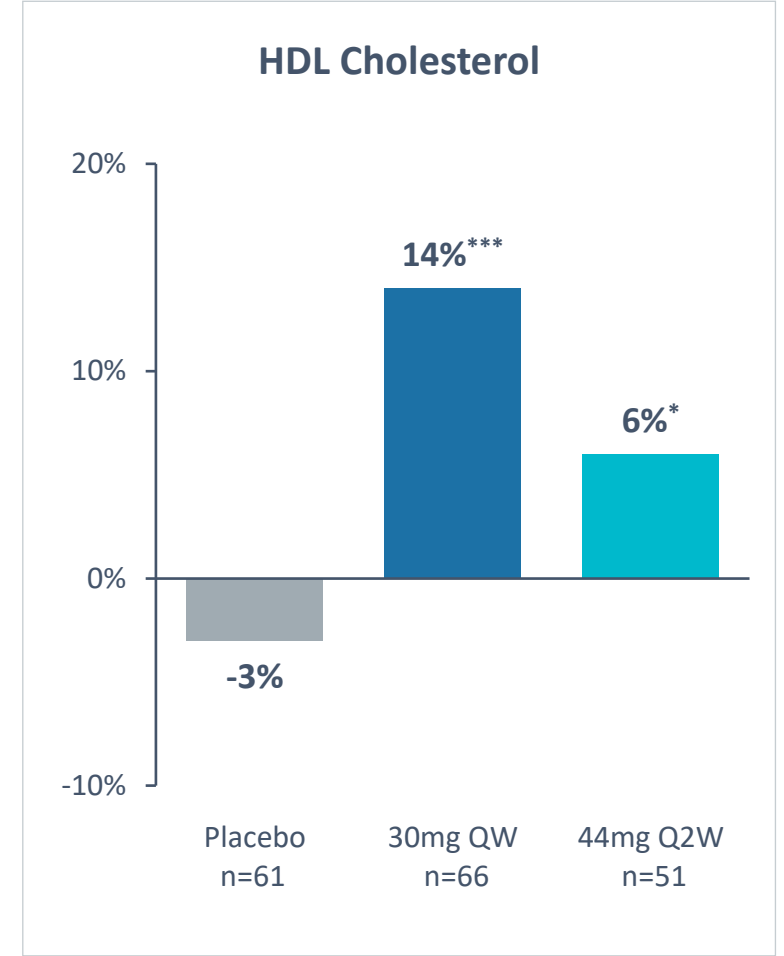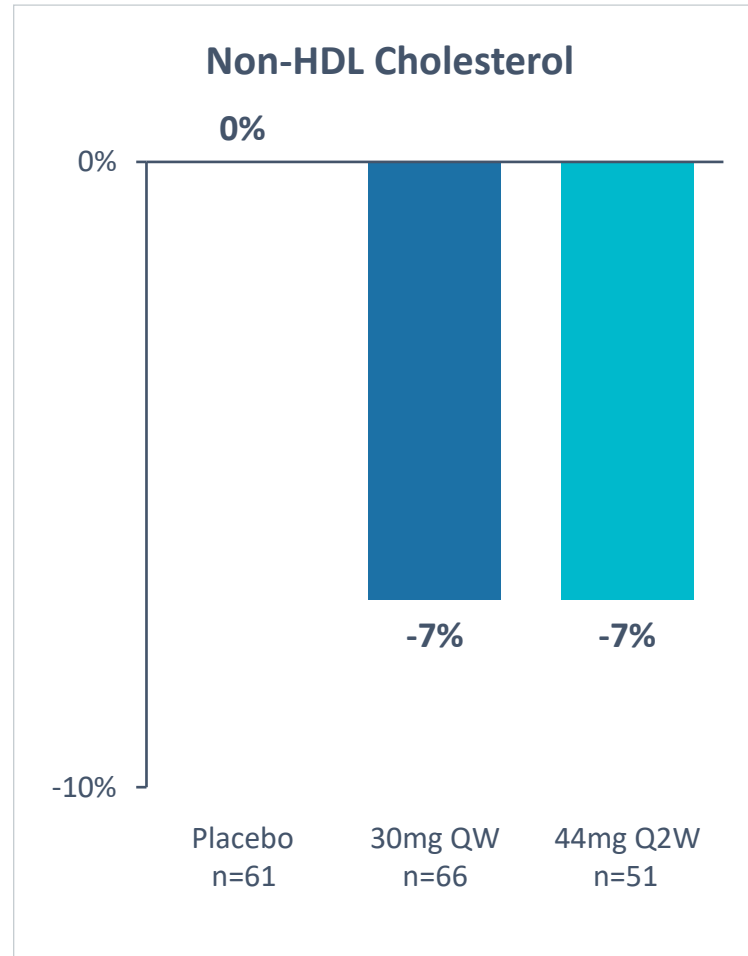
# Pegozafermin Demonstrated Meaningful Reductions in HbA1c

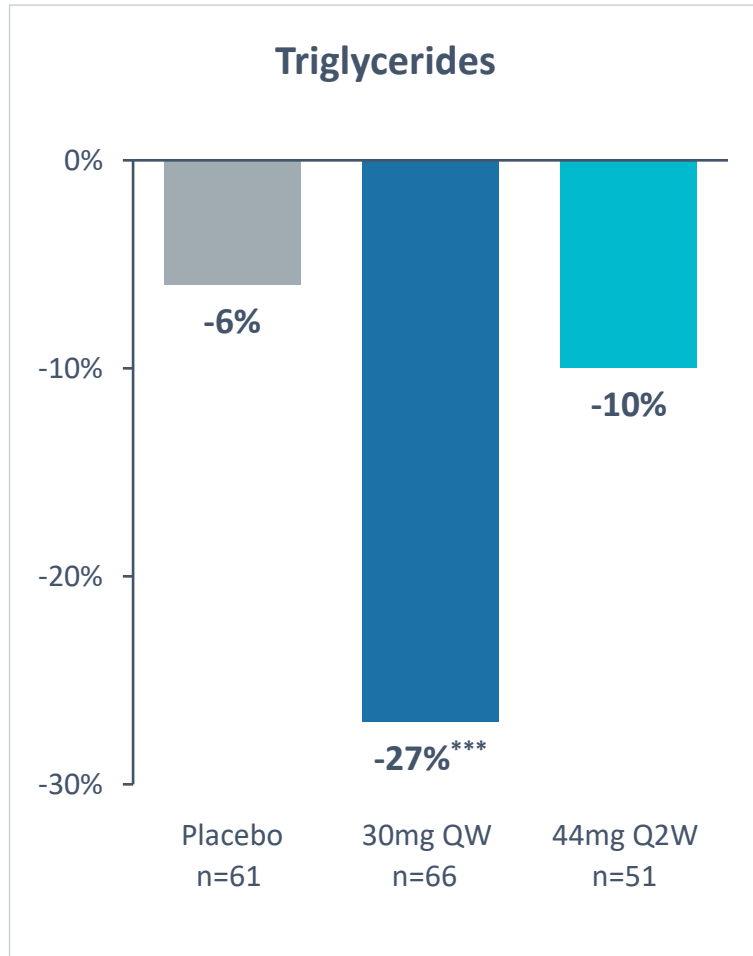**Change in HbA1c from Baseline at Week 24**

**Total Population**



**Baseline HbA1c ≥6.5%**
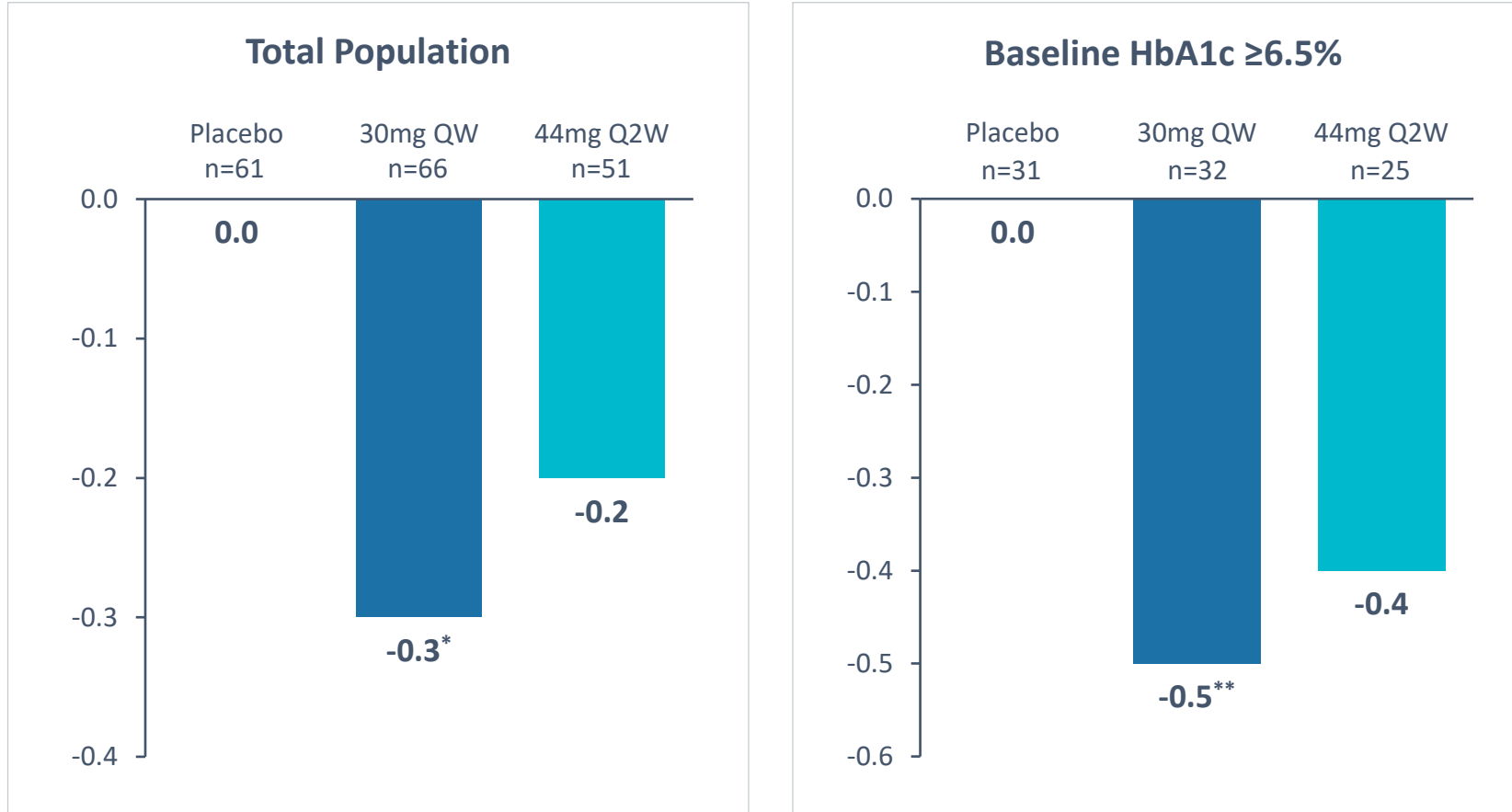
# Pegozafermin Demonstrated Meaningful Changes in Serum Lipids

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

# Pegozafermin Was Well Tolerated Across Doses
## *Low incidence of treatment-related TEAEs*

**Drug-related TEAEs in ≥10% of patients**

| Preferred Term | Placebo (n=69) | 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 | 3% | 14% | 14% | 5% |
| Injection site rash | 1% | 0 | 10% | 4% |
| Increased appetite | 0 | 10% | 13% | 5% |

Most TEAEs were grade 1 or 2. No tremor reported.

| | Placebo | 15mg QW | 30mg QW | 44mg Q2W |
|---|---|---|---|---|
| Drug-related AEs leading to discontinuation | 0 | 5%[a] | 6%[b] | 2%[c] |
| Drug-related Serious Adverse Event (SAE) | 0 | 0 | 0 | 2%[c] |

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]; [c] Pancreatitis [44 mg Q2W].
Unrelated discontinuations: Angina [placebo]; Colon CA [30 mg QW]; COVID-19 [30 mg QW].

# Pegozafermin – A Potentially Differentiated and Foundational NASH Therapy

**PEGOZAFERMIN**

- FGF21 - promising mechanism
- Significant histology changes (Fibrosis improvement and NASH resolution)
- Broad metabolic benefits
- Favorable Safety and Tolerability profile
- Every-two-week dosing
- Liquid formulation prefilled syringe
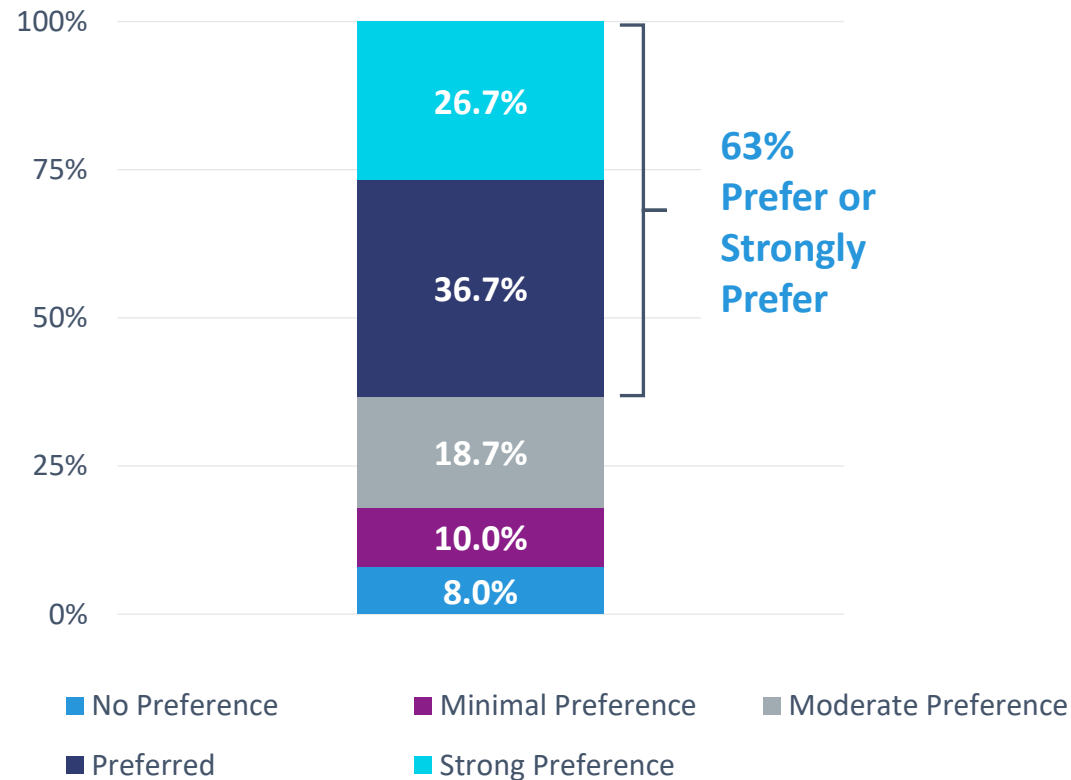- Rigorous Phase 2b trial = Increased confidence in Phase 3
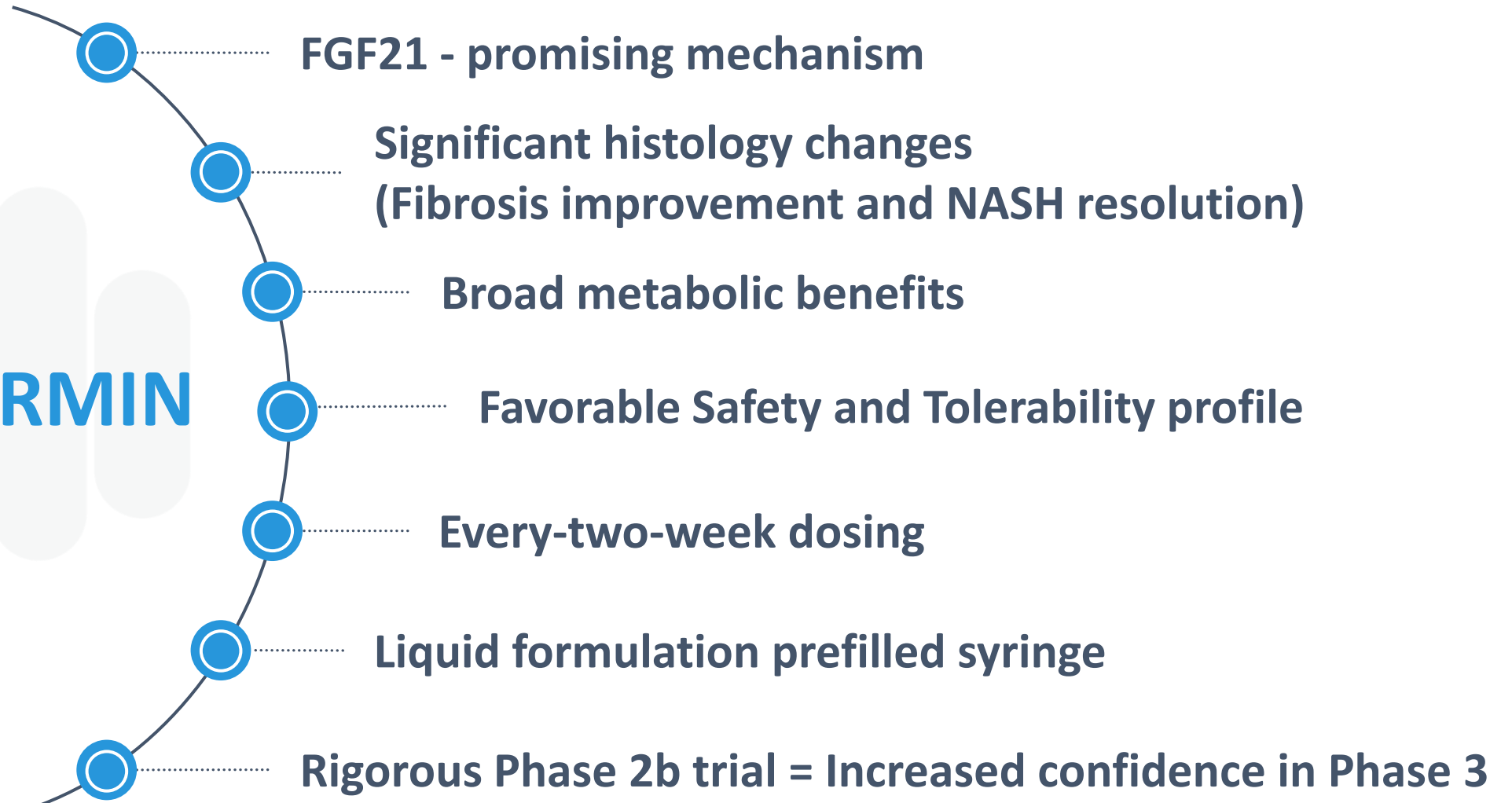
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# APPENDIX

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

**Preference of Every-Two-Week Injections Over Weekly Injections**



| Category | % |
|---|---|
| Strong Preference | 26.7% |
| Preferred | 36.7% |
| Moderate Preference | 18.7% |
| Minimal Preference | 10.0% |
| No Preference | 8.0% |

**63% Prefer or Strongly Prefer**

Legend:
- No Preference
- Minimal Preference
- Moderate Preference
- Preferred
- Strong Preference

- 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.