



**akero**

**A Global Disease,  
A Pioneering Treatment**  
**Akero Therapeutics, Inc.**

*BALANCED Study Readout*

June 30, 2020



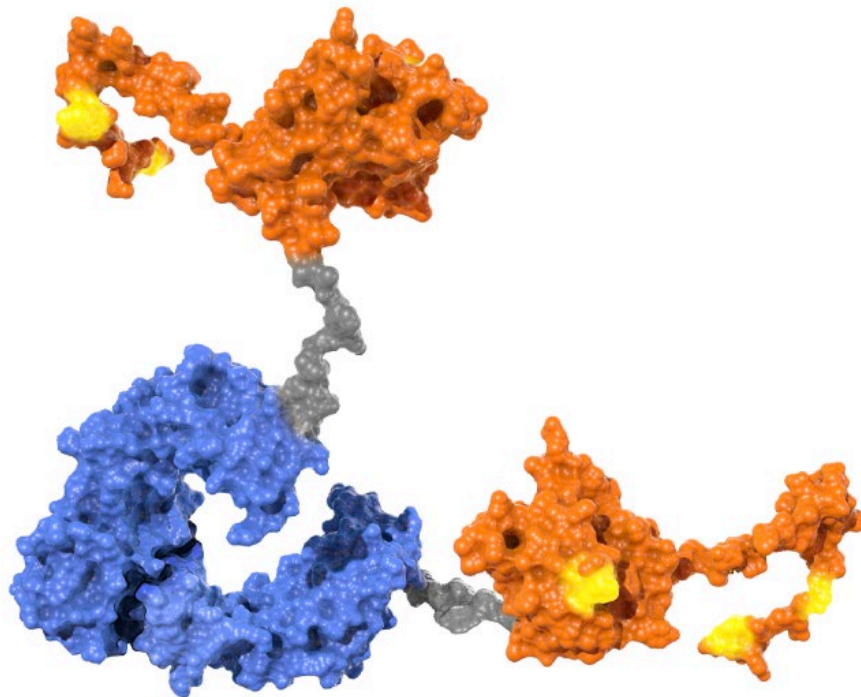
## SAFE HARBOR

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●  INTRODUCING EFRUXIFERMIN



Efruxifermin  
(EFX)

*e-FRUX-i-FER-min*

(Formerly AKR-001)

# SUBSTANTIAL HISTOLOGIC IMPROVEMENTS AFTER ONLY 16 WEEKS

## Histological Improvements

- Response rates for all EFX treated subjects who achieved at least a 30% liver fat reduction and had end-of-treatment biopsies (N=40):
  - **48%** NASH resolution without worsening of fibrosis
  - **48%** fibrosis improvement  $\geq 1$  stage without worsening of NAS
  - **28%** fibrosis improvement  $\geq 2$  stage
  - **28%** for combination of fibrosis improvement  $\geq 1$  stage and NASH resolution

## Safety & Tolerability

- EFX was generally well tolerated (N=79) with no discontinuations due to treatment-emergent adverse events (TEAEs) in 50mg dose group
- Most frequent TEAEs were transient mild/moderate gastrointestinal events
- No treatment- or dose-related effects on blood pressure, heart rate, or bone mineral density

## Improved Glycemic Control

- Significant improvements in HbA1c, HOMA-IR, C-Peptide, and Adiponectin

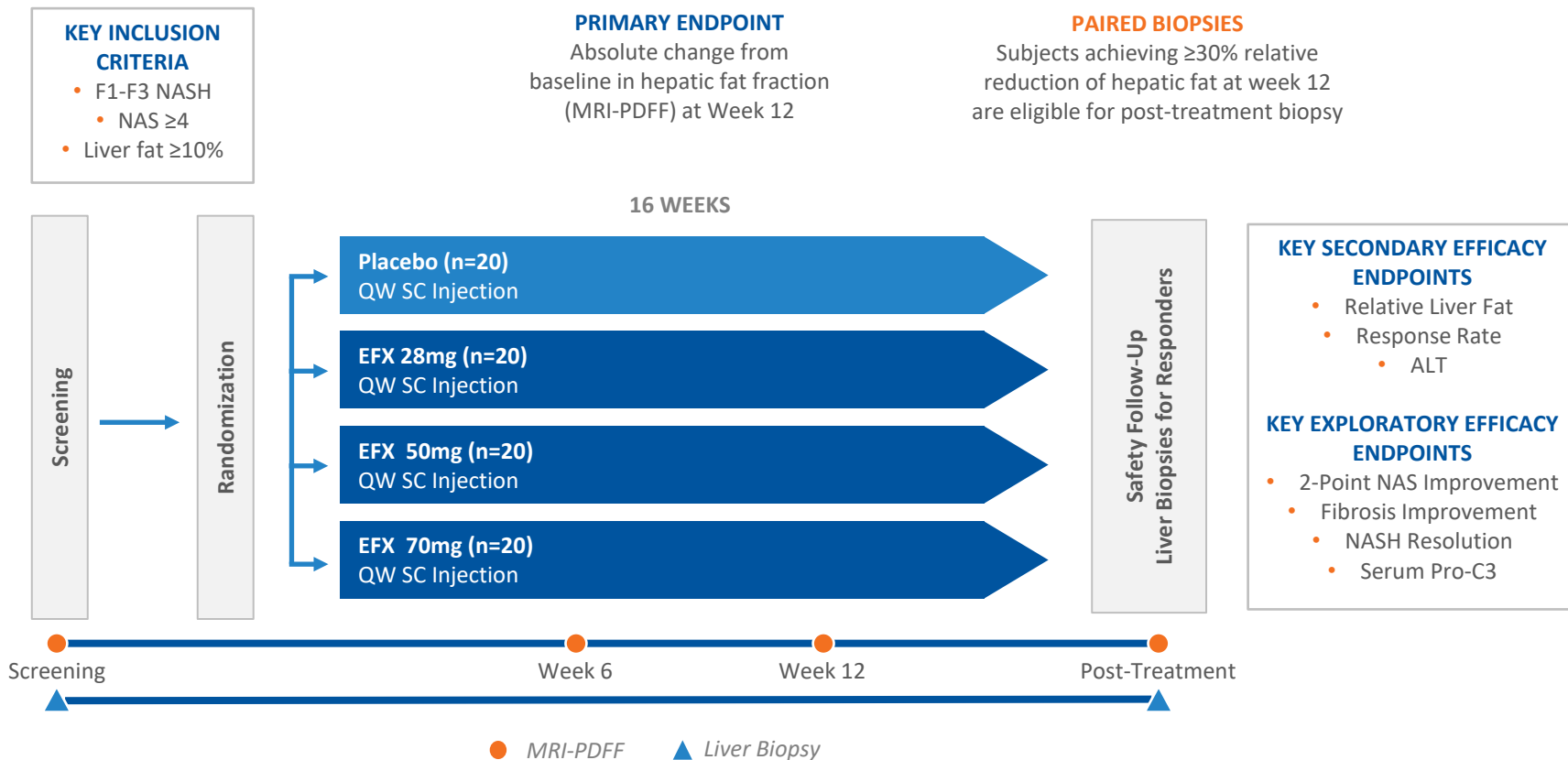
## Weight Loss

- Reductions seen across all groups

## Improved Dyslipidemia

- Significant improvements in triglycerides, HDL, and non-HDL cholesterol across all dose groups

# BALANCED STUDY TRIAL DESIGN

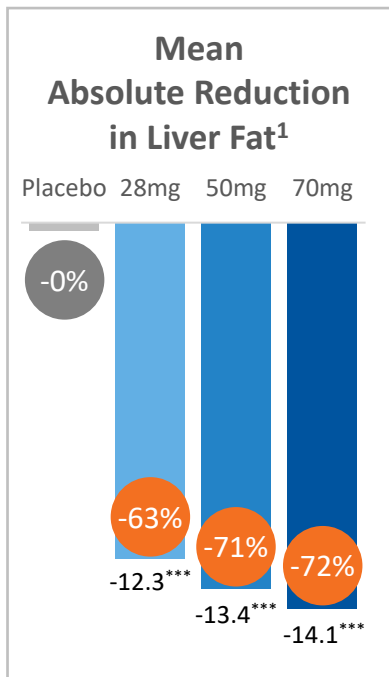


## BASELINE DEMOGRAPHICS

Parameter Mean	Placebo (N=21)	EFX 28mg (N=19)	EFX 50mg (N=20)	EFX 70mg (N=20)
Age (Years)	52	50	53	53
Sex (Male/Female)	6/15	9/10	10/10	9/11
Weight (kg)	99.6	108.2	103.6	103.1
BMI (kg/m <sup>2</sup> )	37.6	38.8	36.7	37.2
Liver Fat Content (% by MRI-PDFF)	19.3	21.4	18.3	19.4
NAFLD Activity Score (NAS)	5.1	5.6	5.1	5.6
Fibrosis Stage (% F2-F3)	62	63	65	65
Alanine Aminotransferase (ALT) (U/L)	50.7	62.5	53.4	56.8
Aspartate Aminotransferase (AST) (U/L)	38.6	41.1	35.4	44.6
% Type 2 Diabetes	67	37	50	50

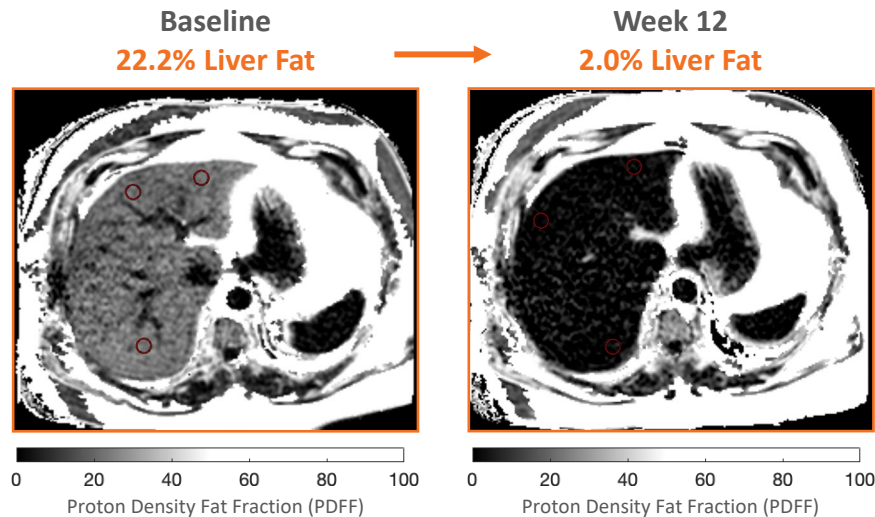
Analysis Set	N	Definition
Full Analysis Set (FAS)	N=80	All subjects who were randomized into the study
Safety Set (SS)	N=79	All subjects who received at least one dose of study drug.
MRI-PDFF Evaluable Analysis Set (MAS)	N=68	All FAS subjects who have Baseline and Week 12 hepatic fat fraction assessed by MRI-PDFF
Liver Biopsy Evaluable Analysis Set (BAS)	N=42	All responders who have Baseline and end-of-treatment liver biopsy results

# ● SUBSTANTIAL REDUCTIONS IN LIVER FAT AT WEEK 12 ACROSS ALL DOSE GROUPS



\*\*\* p<0.001, versus placebo

## MRI-PDFF Images for Subject 207-012 (50mg EFX)



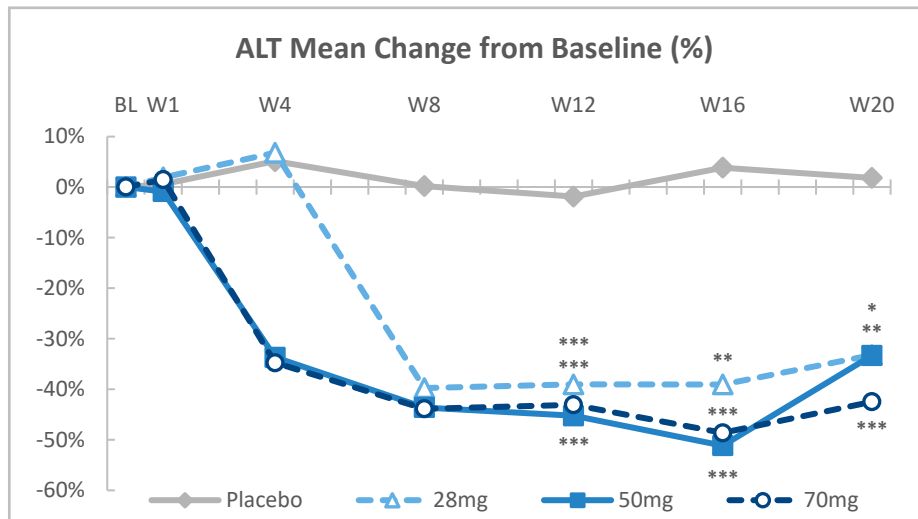
Analyzed with *LiverMultiScan*

## Response Rate<sup>2</sup>

Proportion of subjects who had a Week 12 MRI-PDFF showing  $\geq 30\%$  relative reduction

Placebo	10%
28mg	100%
50mg	100%
70mg	100%

# REDUCTION IN HEPATOCYTE STRESS AND COLLAGEN SYNTHESIS ACROSS ALL DOSE GROUPS



Similar dose-related improvements observed for AST, GGT, ALP

\* p<0.05, \*\* p<0.01, \*\*\* p<0.001, versus placebo  
(statistical significance tested only at Weeks 12, 16 and 20)

**Serum Pro-C3**

Mean Change from Baseline to Week 16

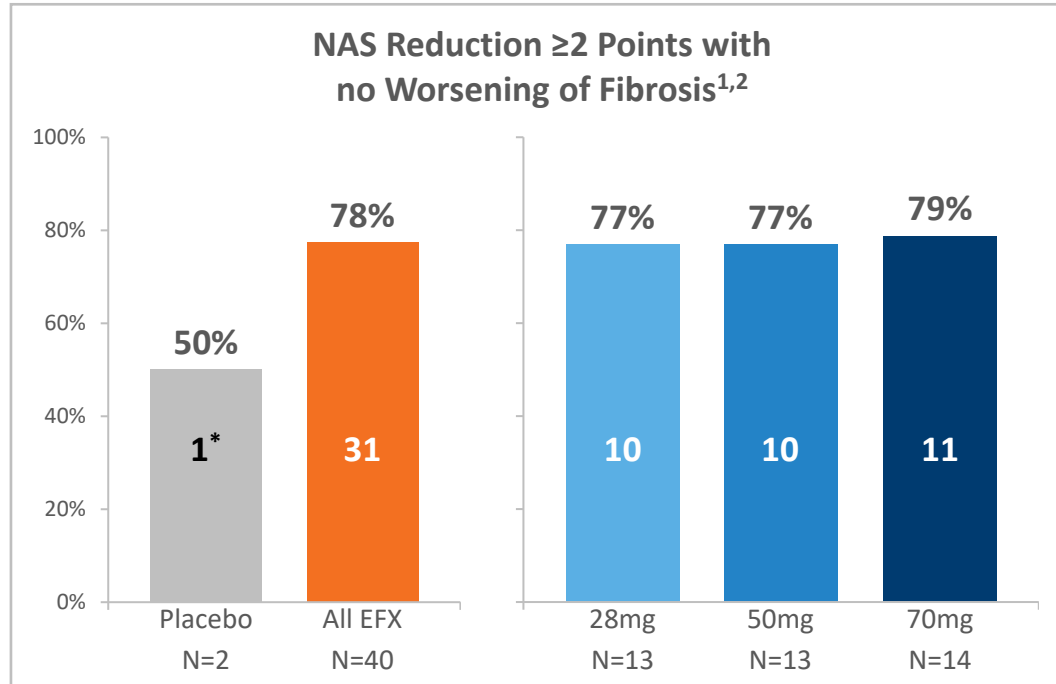
Placebo	+4%
28mg	-34%***
50mg	-27%**
70mg	-32%***

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





# CONSISTENT IMPROVEMENT IN STEATOHEPATITIS



<sup>1</sup> Endpoint recommended by FDA for Phase 2 clinical trials in NASH (F1-F3)

<sup>2</sup> Secondary and exploratory histological endpoints were not powered for statistical significance

\* A single placebo responder lost 25 pounds over 16 weeks (11% weight reduction)

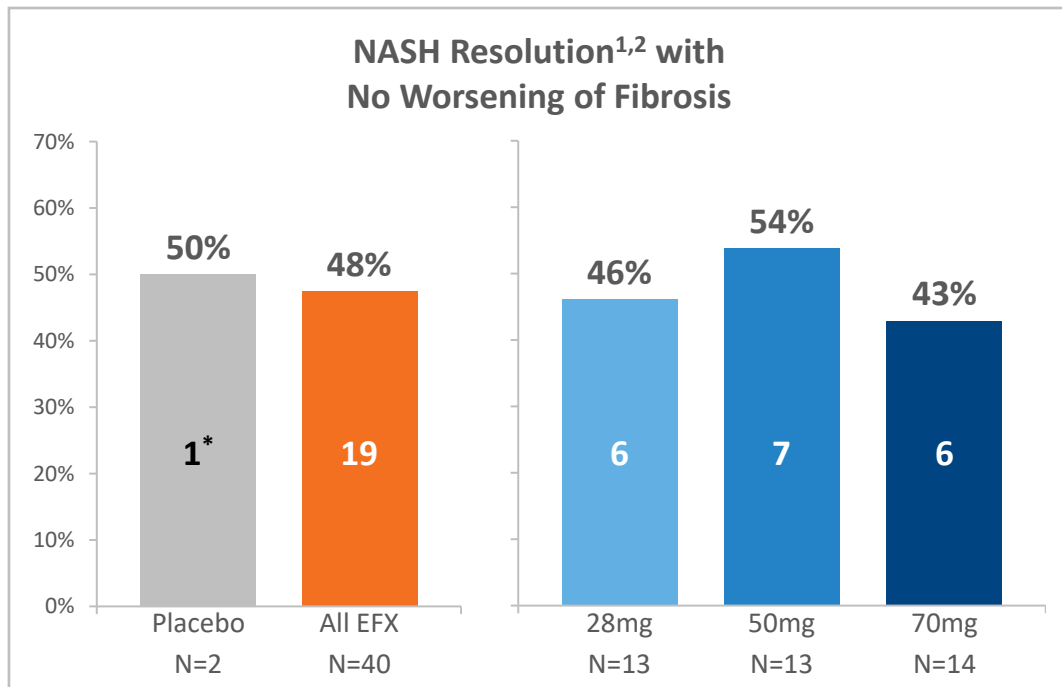
## Mean NAS Reduction

Change in NAS from Baseline after 16 weeks of dosing

Placebo	-2.5
28mg	-2.9
50mg	-3.1
70mg	-3.6

The placebo arm was enriched for NAS endpoints because only 10% of placebo patients met the MRI-PDFF responder definition and had an end-of-treatment biopsy

# HIGH RESPONSE RATES ON NASH RESOLUTION AFTER 16 WEEKS ACROSS ALL DOSES



<sup>1</sup> NAS score of 0 or 1 for lobular inflammation and a score of 0 for ballooning

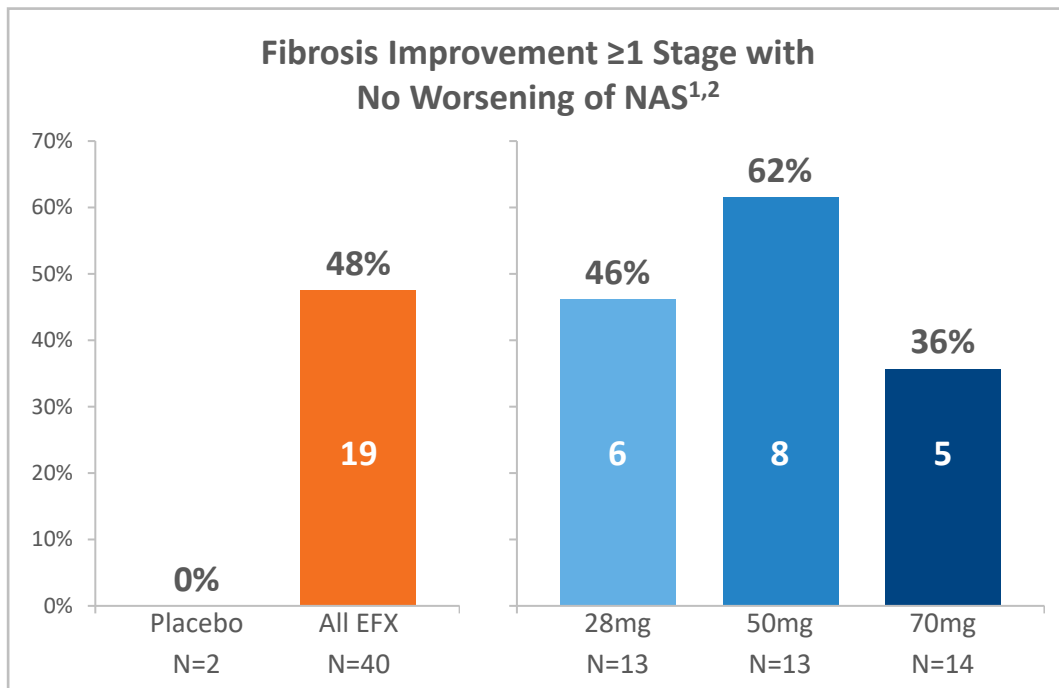
<sup>2</sup> Secondary and exploratory histological endpoints were not powered for statistical significance

\* A single placebo responder lost 25 pounds over 16 weeks (11% weight reduction)

## Biopsy Reading

- All baseline and end-of-treatment biopsies were centrally read by a single NASH-CRN pathologist
- Baseline biopsies were not re-read with end-of-treatment biopsies
- All biopsies were read blinded to both treatment assignment and patient

## HIGH RATES OF FIBROSIS IMPROVEMENT AFTER 16 WEEKS ACROSS ALL TREATED PATIENTS



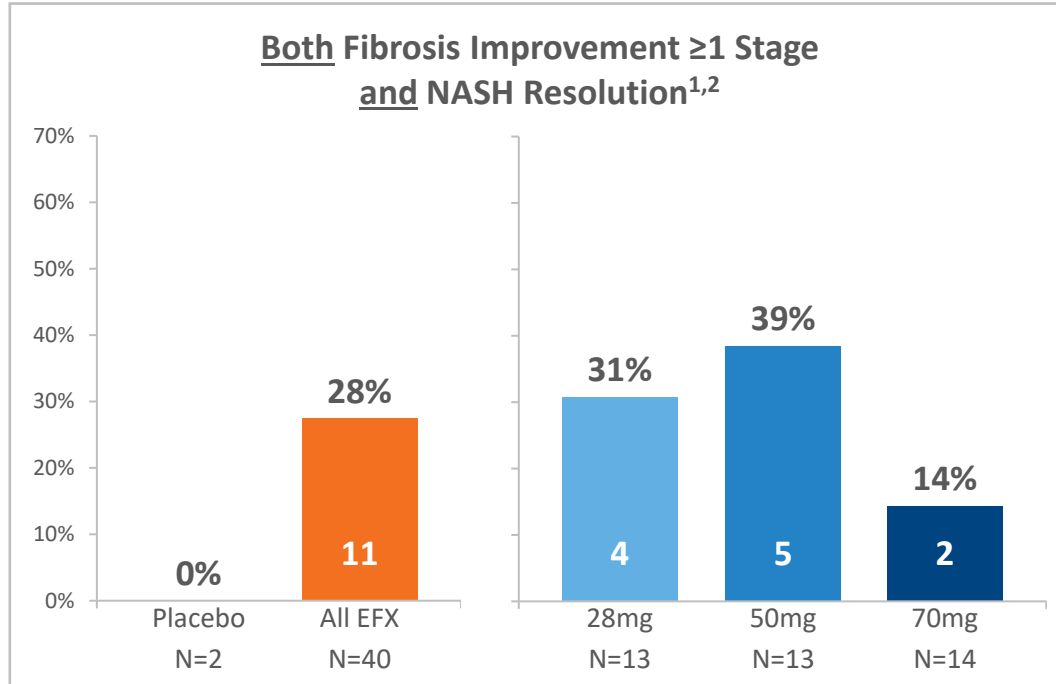
**$\geq 2$ -Stage Improvement in Fibrosis**

11 of 40 EFX patients (28%) had a  $\geq 2$ -stage improvement

<sup>1</sup> Improvement in liver fibrosis greater than or equal to one stage and no worsening of NASH (defined as no increase in NAS for ballooning, inflammation, or steatosis)

<sup>2</sup> Secondary and exploratory histological endpoints were not powered for statistical significance

# ENCOURAGING RESPONSE RATES FOR BOTH FIBROSIS IMPROVEMENT AND NASH RESOLUTION AFTER 16 WEEKS



<sup>1</sup> Subjects who achieve a NAS score of 0 or 1 for lobular inflammation and a score of 0 for ballooning AND Improvement in liver fibrosis greater than or equal to one stage

<sup>2</sup> Secondary and exploratory histological endpoints were not powered for statistical significance



## SAFETY OVERVIEW

Treatment-Emergent Adverse Event (TEAE) Classification	Placebo (N=21)	EFX 28mg (N=19)	EFX 50mg (N=19)	EFX 70mg (N=20)
TEAE Leading to Death	0	0	0	0
TEAE Leading to Discontinuation	1 <sup>a</sup>	2 <sup>b</sup>	0	4 <sup>c</sup>
Serious Adverse Event (SAE)	0	1 <sup>d</sup>	0	1

<sup>a</sup> Muscular Weakness & Myalgia; <sup>b</sup> Nausea, Vomiting & Dysgeusia; Panic Attack and Anxiety-Linked Tremor; <sup>c</sup> Dysphagia (Not Drug Related); Acute Pancreatitis (also an SAE); Vomiting; Fatigue & Nausea; <sup>d</sup> Related to pre-dosing liver biopsy

# DRUG-RELATED TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs)

Most Common (>10%) Drug-Related AEs *	Placebo (N=21)	All EFX (N=58)	EFX 28mg (N=19)	EFX 50mg (N=19)	EFX 70mg (N=20)
Diarrhea	2 (10%)	21 (36%)	5 (26%)	10 (53%)	6 (30%)
Nausea	0 (0%)	19 (33%)	6 (32%)	4 (21%)	9 (45%)
Increased appetite	1 (5%)	13 (22%)	4 (21%)	4 (21%)	5 (25%)
Vomiting	0 (0%)	9 (16%)	5 (26%)	2 (11%)	2 (10%)
Frequent bowel movements	0 (0%)	8 (14%)	3 (16%)	2 (11%)	3 (15%)
Abdominal pain	0 (0%)	7 (12%)	1 (5%)	3 (16%)	3 (15%)
Injection site erythema	0 (0%)	7 (12%)	2 (11%)	0 (0%)	5 (25%)
Injection site reaction	0 (0%)	6 (10%)	2 (11%)	1 (5%)	3 (15%)
Fatigue	2 (10%)	6 (10%)	0 (0%)	1 (5%)	5 (25%)

\*Across EFX dose groups

### Gastrointestinal Adverse Events:

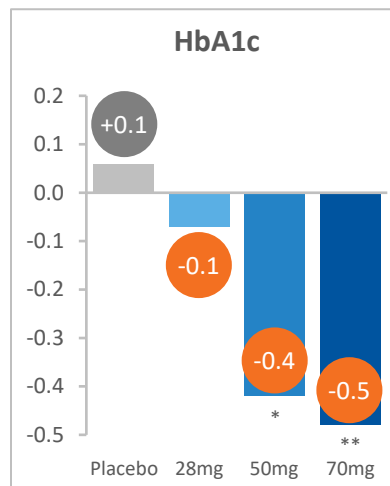
- Majority transient, Grade 1, with on-drug resolution
- Often single episodes
- Overall frequency decreased over treatment period
- No study discontinuations due to diarrhea

### No Treatment-Related Effects On:

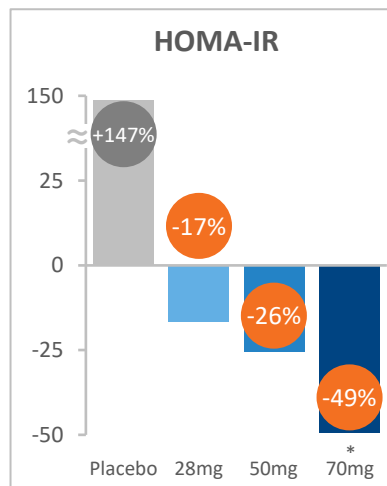
- Heart Rate
- Systolic Blood Pressure
- Diastolic Blood Pressure
- Bone mineral density

# CLINICALLY MEANINGFUL IMPROVEMENTS IN GLYCEMIC CONTROL AFTER 16 WEEKS

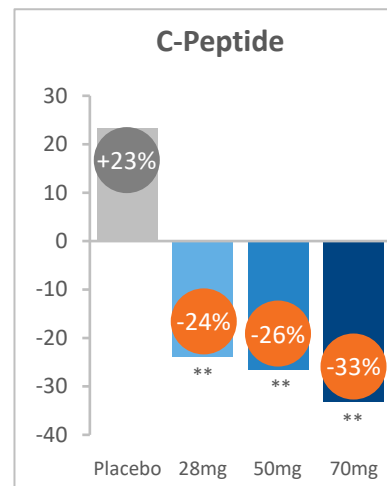
Mean Change From Baseline to Week 16 (%)<sup>1</sup>



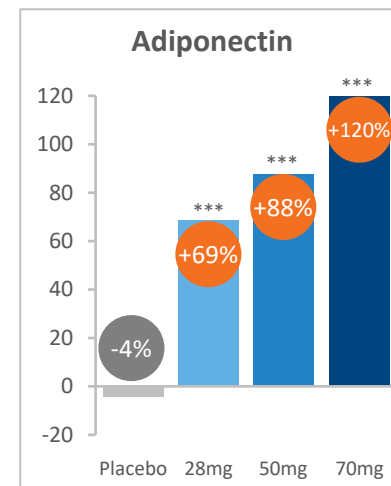
\* p<0.05, \*\* p<0.01, versus placebo



\* p<0.05, versus placebo



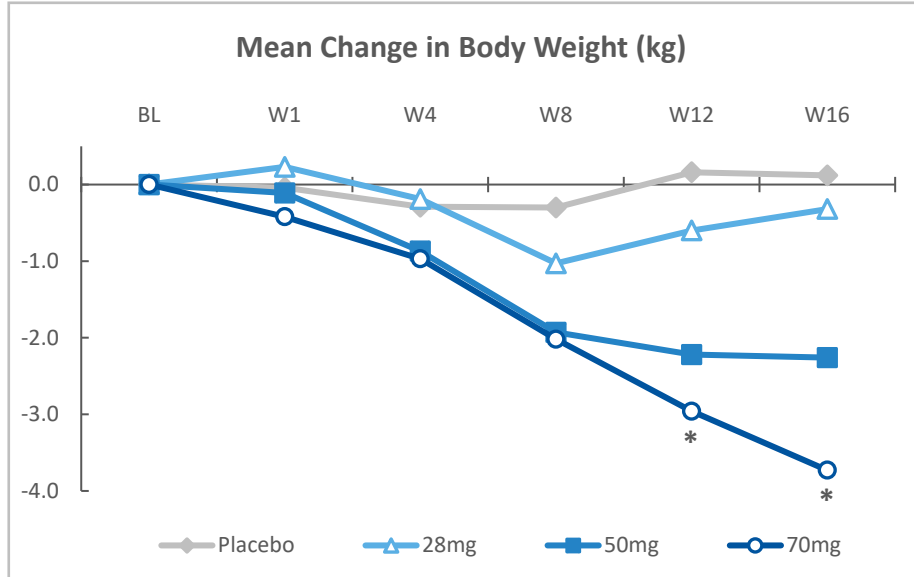
\*\* p<0.01, versus placebo



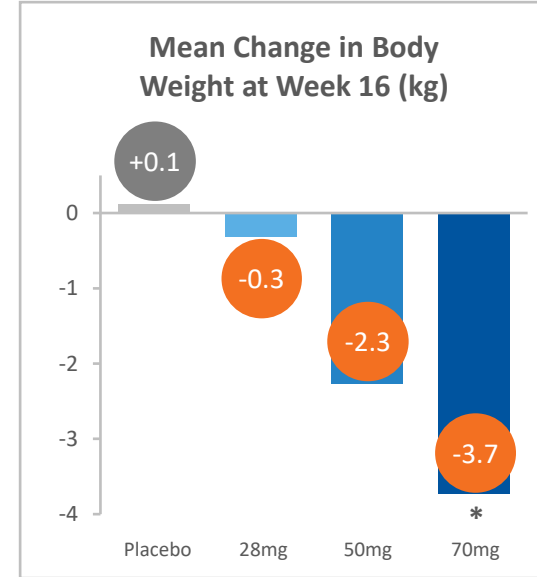
\*\*\* p<0.001, versus placebo

<sup>1</sup> HbA1c is presented in absolute percent change from baseline, whereas HOMA-IR, C-Peptide, and Adiponectin are presented in relative percent change from baseline

# WEIGHT LOSSES OBSERVED FOR ALL DOSE GROUPS: FIRST REPORT OF SIGNIFICANT WEIGHT LOSS FOR FGF21 CLASS



\* p<0.05, versus placebo  
(statistical significance tested only at Weeks 12 and 16)



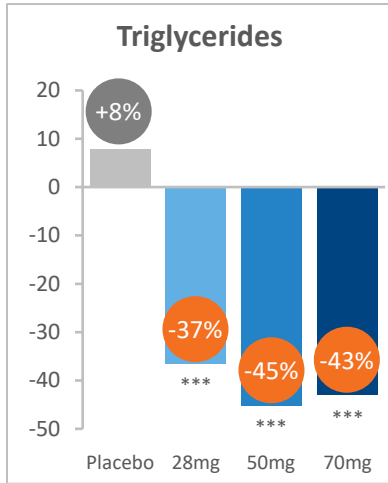
\* p<0.05, versus placebo



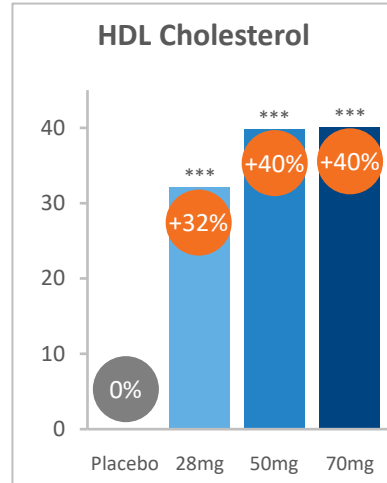


# IMPROVED LIPOPROTEIN PROFILE FOR CARDIOVASCULAR HEALTH

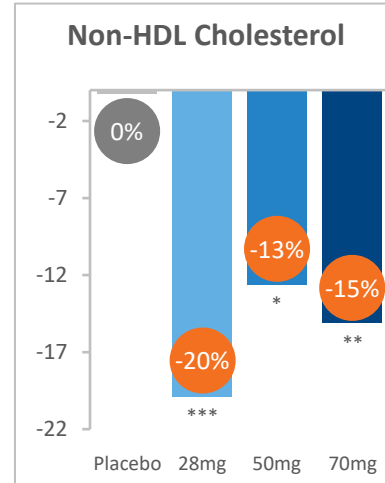
Mean Change From Baseline to Week 16 (%)



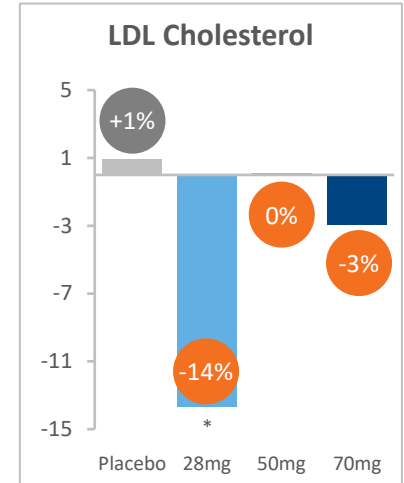
\*\*\* p<0.001, versus placebo



\*\*\* p<0.001, versus placebo



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



\* p<0.05, versus placebo

# DEVELOPMENT LANDSCAPE: NASH RESOLUTION

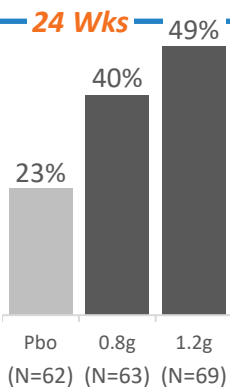
Proportion of Subjects with Resolution of NASH without Worsening of Fibrosis<sup>1</sup>

**akero**  
Efruxifermin  
16 Wks (Ph2a)  
Weekly Injection

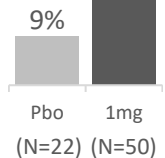


\* A single placebo responder lost 25 pounds over 16 weeks (11% weight reduction)

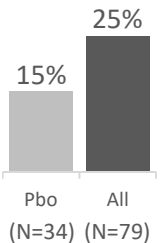
**inventiva**  
Lanifibranor  
24 Wks (Ph2b)  
Daily Oral



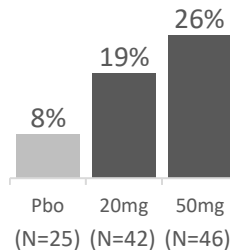
**NGM Bio**  
Aldafermin  
24 Wks (Ph2a)  
Daily Injection



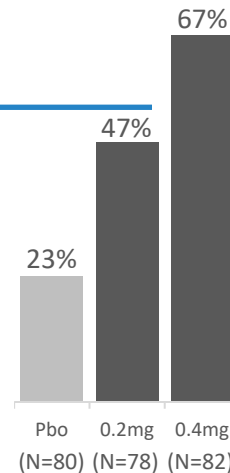
**Madrigal Pharmaceuticals**  
Resmetirom  
36 Wks (Ph2a)  
Daily Oral



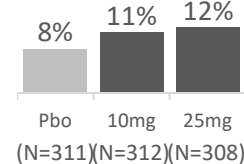
**CYMBAY**  
Seladelpar  
52 Wks (Ph2a)  
Daily Oral



**Novo Nordisk**  
Semaglutide  
72 Wks (Ph2b)  
Daily Injection



**Intercept**  
Ocaliva  
78 Wks (Ph3)  
Daily Oral



24 Wks → Increasing dosing duration → 78 Wks

Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. No head-to-head clinical trials have been conducted.

Inventiva (2020) June 16 Corporate Presentation; NGM Bio (2020) June 3 Corporate Presentation; Harrison, S et al. (2019) Lancet 394(10213):2012-24; CymaBay (2020) March 12 Press Release; Novo Nordisk (2020) June 19 R&D Investor Presentation; Younossi Z et al. (2019) Lancet 394(10215):2184-96. All trademarks are the property of their respective owners.

# DEVELOPMENT LANDSCAPE: FIBROSIS IMPROVEMENT

Proportion of Subjects with  $\geq 1$  Stage Improvement in Fibrosis without Worsening of NAS<sup>1</sup>

**akero**  
Efruxifermin  
16 Wks (Ph2a)  
Weekly Injection

**inventiva**  
Lanifibranor  
24 Wks (Ph2b)  
Daily Oral

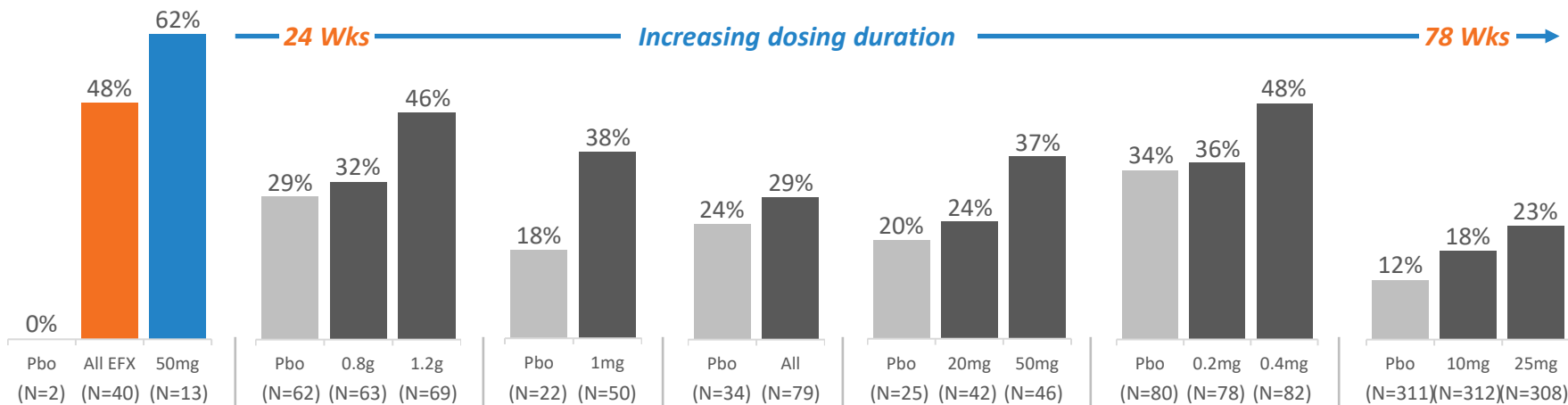
**NGM Bio**  
Aldafermin  
24 Wks (Ph2a)  
Daily Injection

**Madrigal**  
Pharmaceuticals  
Resmetirom  
36 Wks (Ph2a)  
Daily Oral

**CYMABAY**  
Seladelpar  
52 Wks (Ph2a)  
Daily Oral

**novo nordisk**  
Semaglutide  
72 Wks (Ph2b)  
Daily Injection

**Intercept**  
Ocaliva  
78 Wks (Ph3)  
Daily Oral

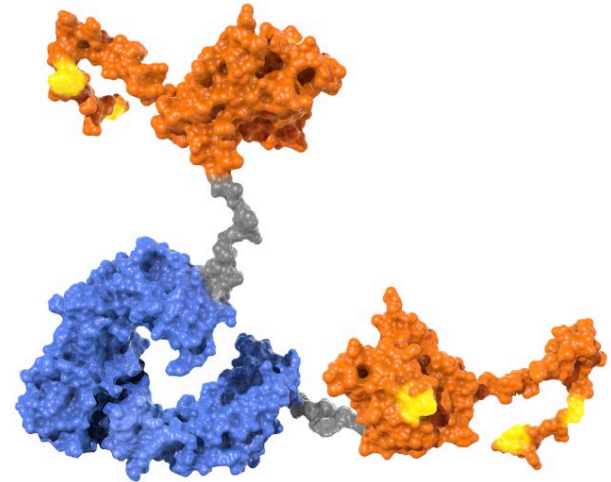


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## EFRUXIFERMIN: UNIQUE POTENTIAL AS A FOUNDATIONAL NASH MONOTHERAPY

- ✓ Unprecedented fibrosis improvement
- ✓ Unprecedented reductions in liver fat
  - Confirmed by NASH resolution
- ✓ Ameliorated dyslipidemia
  - No LDL cholesterol increase
- ✓ Improved glycemic control
- ✓ Weight loss at all doses
- ✓ Large, sustained reductions in ALT
- ✓ Few discontinuations due to AEs





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**A Global Disease,  
A Pioneering Treatment**

**NASDAQ: AKRO**