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A Global Disease,
A Pioneering Treatment

Cohort C Readout: 16-Week Study of EFX in Cirrhotic NASH Patients (F4)

March 22, 2021

SAFE HARBOR

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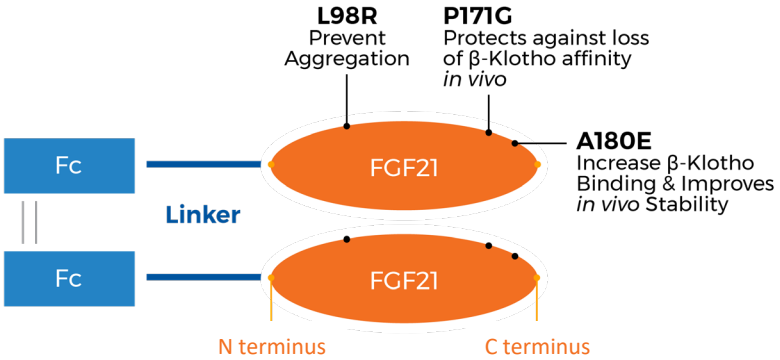
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company’s own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

EFRUXIFERMIN (EFX): BUILDING ON A STRONG FOUNDATION

EFX Engineering (ex-Amgen)

- Human FGF21 with 3 mutations fused to IgG1 Fc domain
- Half-life of 3-4 days: once-weekly dosing
- Balanced receptor potency comparable to native FGF21



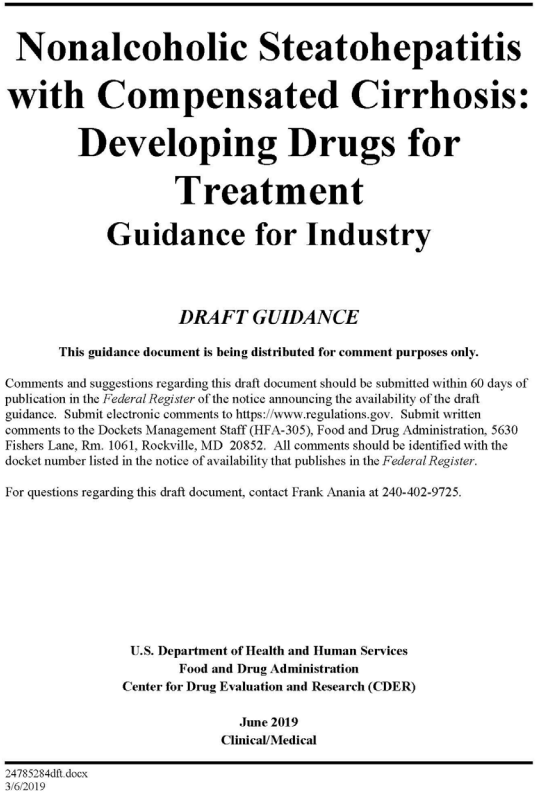
BALANCED Study (F1-F3): Improvements from Baseline

- ✓ Fibrosis Reversal
- ✓ NASH Resolution
- ✓ Liver Fat
- ✓ ELF and Pro-C3
- ✓ ALT, AST
- ✓ Lipoproteins
- ✓ HbA1c
- ✓ Weight Loss

EXPANDING EFX TO CIRRHOTIC PATIENT POPULATION (F4)

Developing Treatments for Cirrhotic (F4) NASH

- FDA draft guidance specific for F4 patients
- Projected ~3.5M US F4 patients in 2030
- FDA: *The goals of treatment for compensated NASH cirrhosis are to halt or slow progression of fibrosis, prevent clinical decompensation, reduce the need for liver transplantation, and improve survival*



Nonalcoholic Steatohepatitis with Compensated Cirrhosis: Developing Drugs for Treatment

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Frank Anania at 240-402-9725.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

June 2019
Clinical/Medical

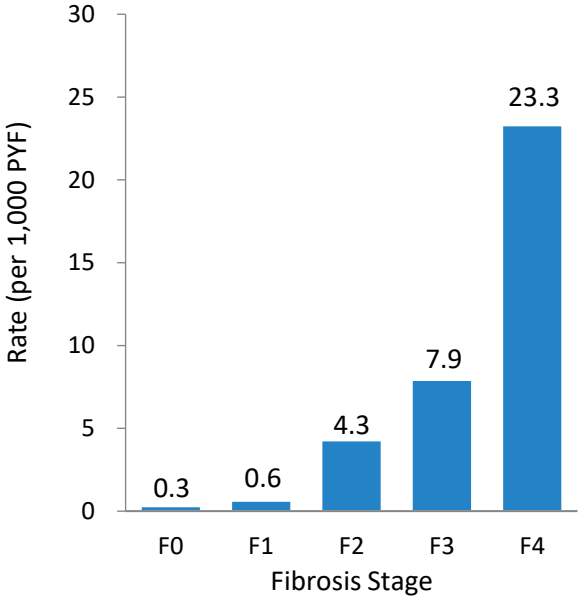
24785284dft.docx
3/6/2019

F4 NASH PATIENTS HAVE POOR PROGNOSIS

Liver-related mortality rate increases substantially from F3 to F4 fibrosis

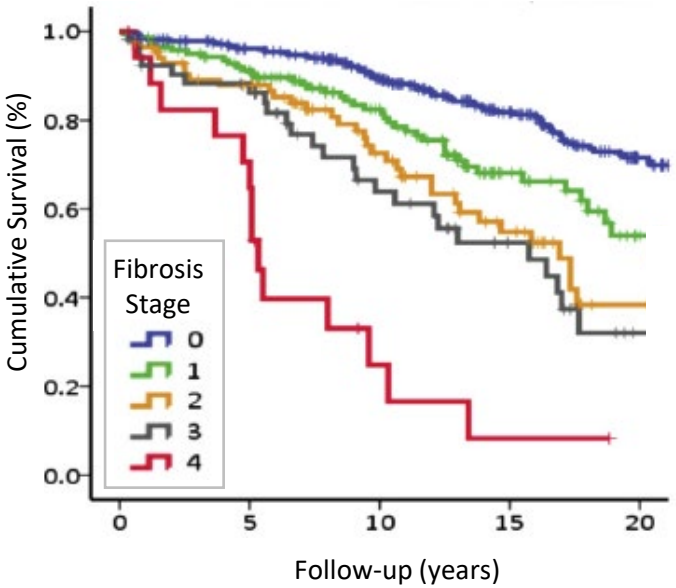
~60% 5-year mortality for F4 NASH patients absent transplant

Liver-Related Mortality



Dulai, PS et al. (2017) Hepatology 65:1557-65

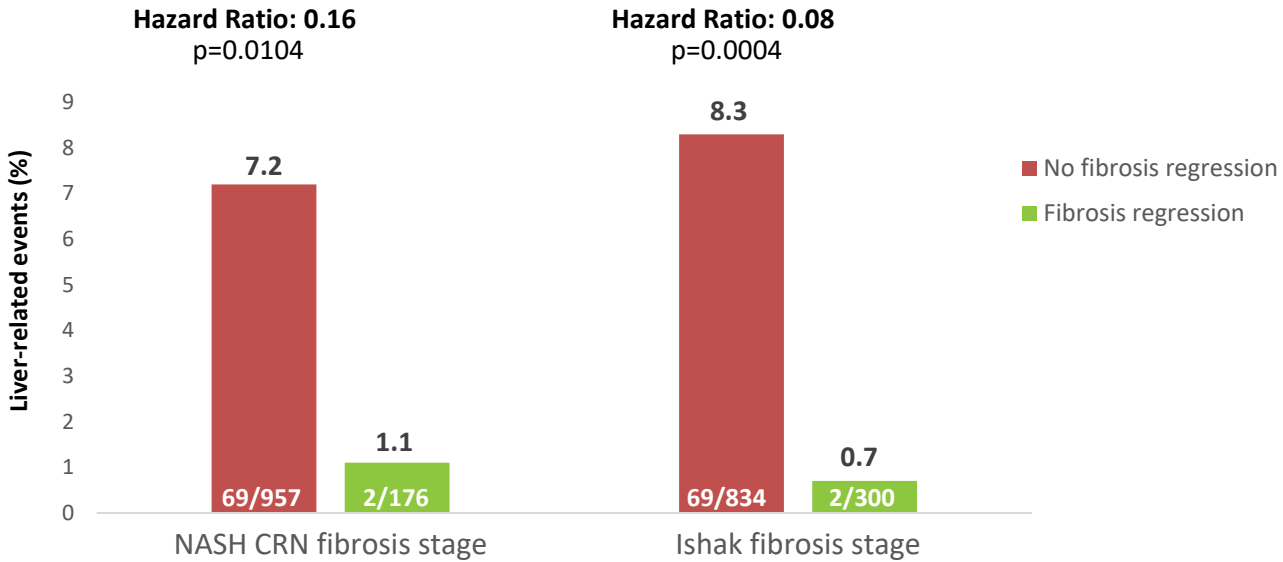
Survival Free of Liver Transplantation



Angulo, P et al. (2015) Gastroenterology 149:389-397

CIRRHOSIS REGRESSION IS ASSOCIATED WITH IMPROVED CLINICAL OUTCOMES

Pooled treatment groups from STELLAR 4 and simtuzumab cirrhosis study



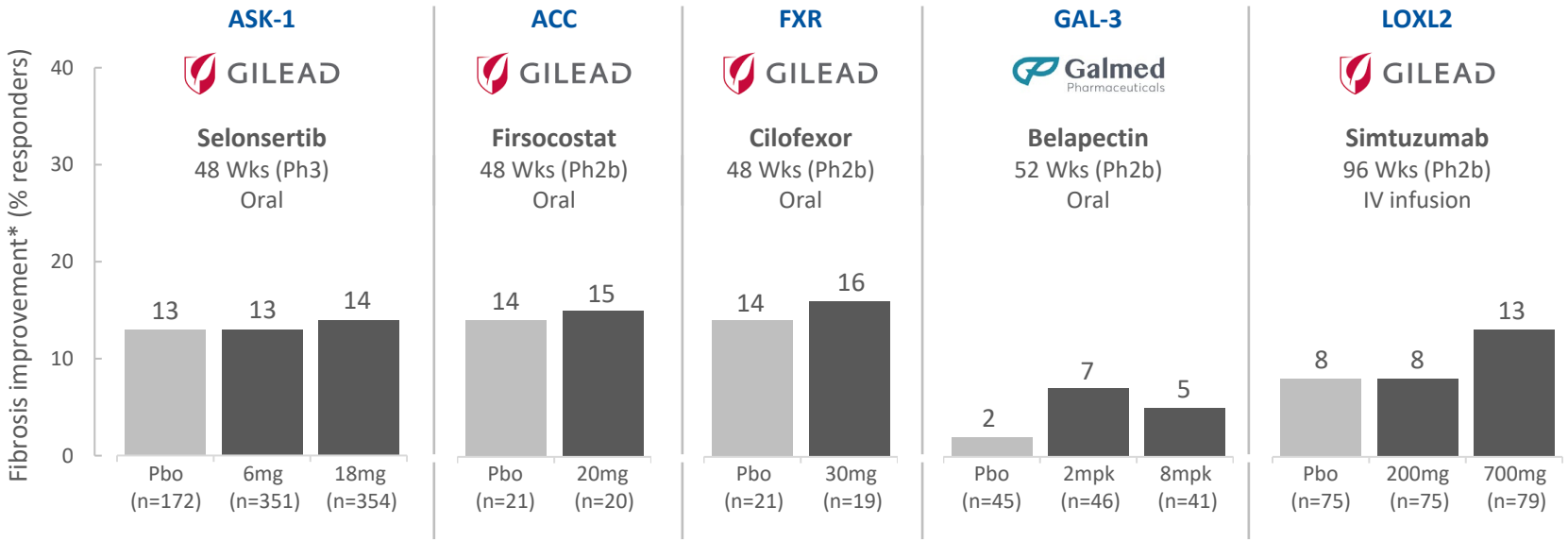
Cirrhosis regression observed in 16% of patients (treatment and placebo groups) over 48 weeks

Sanyal A, et al. AASLD TLMdX2020. #90

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.

SINGLE AGENT FIBROSIS IMPROVEMENT IN CIRRHOTIC NASH*

No investigational product has been successful in cirrhotic F4 NASH patients



** Results from all publicly reported NASH studies for single agents in F4 patients that reported either ≥ 1-stage fibrosis improvement (belapectin and simtuzumab) or ≥ 1-stage fibrosis improvement and no worsening of NASH (selonsertib, firsocostat and cilofexor)*

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.

Harrison, SH et al. (2020) J Hepatol 73(1):26-39; Loomba, R et al. (2020) Hepatol 73(2):625-43; Chalasani, N et al. (2020), Gastro 158:1334–45; Harrison, SH et al. (2018) Gastro 155:1140-53

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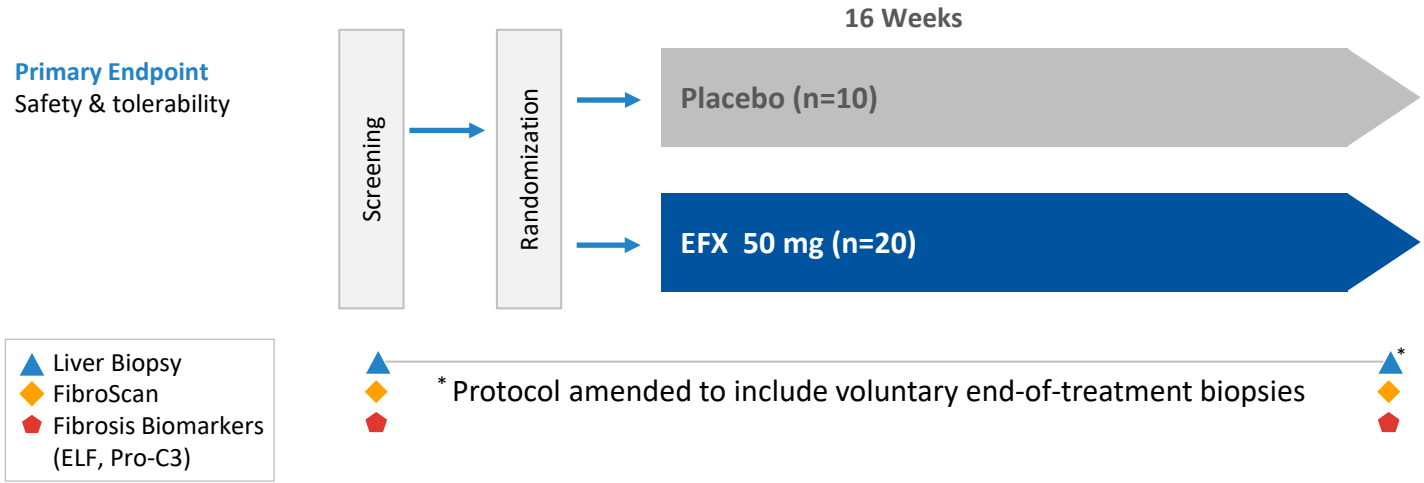
PHASE 2A EXPANSION COHORT C (F4) TRIAL DESIGN

BALANCED study included an expansion cohort, Cohort C, of patients with compensated cirrhosis (F4), Child-Pugh Class A; results to inform subsequent development in cirrhotic patients

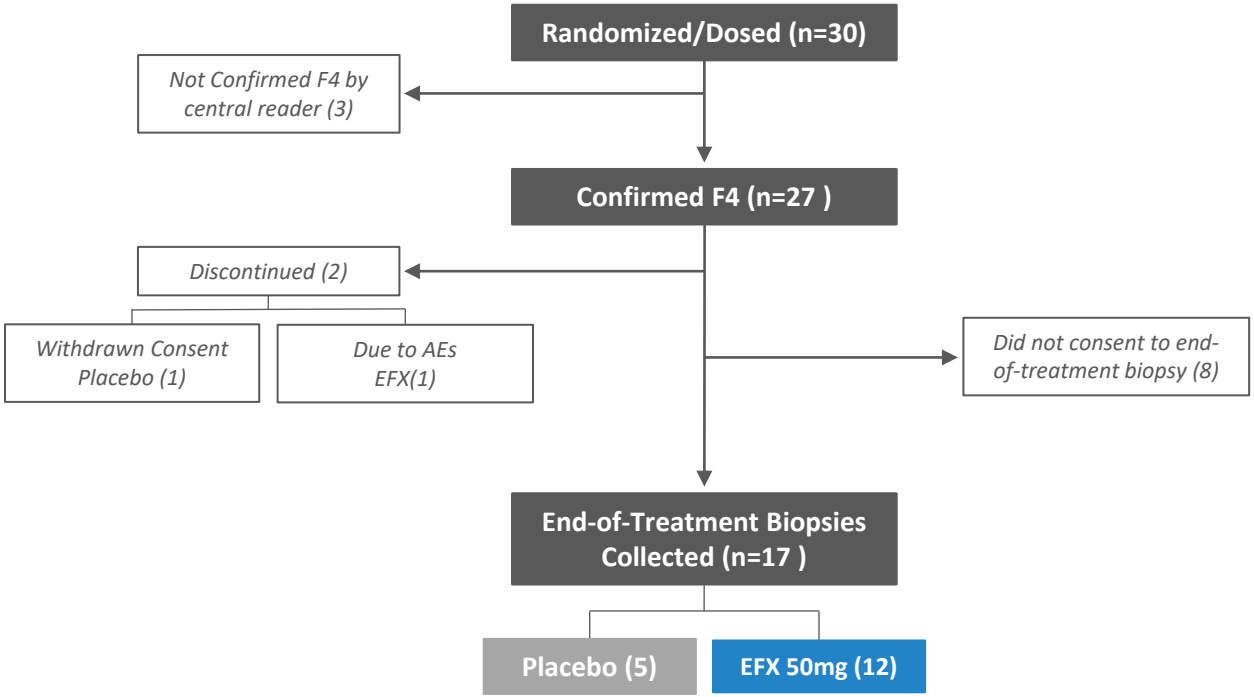


BASELINE DEMOGRAPHICS

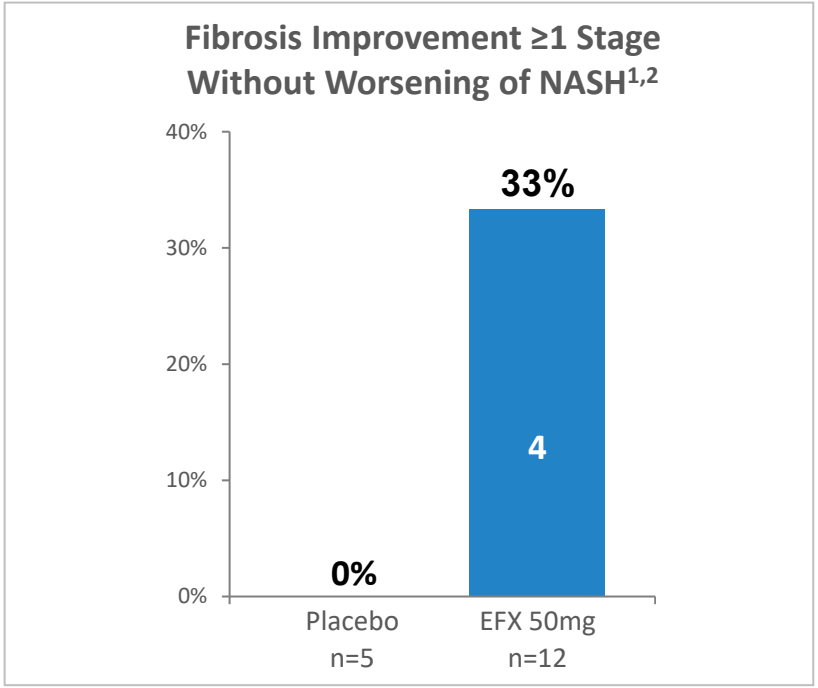
Parameter Mean	Placebo (n=10)	EFX 50mg (n=20)
Age (Years)	57.1	61.1
Sex (Male/Female)	7/3	4/16
Weight (kg)	119.1	97.9
Alanine Aminotransferase (ALT) (U/L)	32.7	31.7
Aspartate Aminotransferase (AST) (U/L)	28.9	31.4
HbA1c (%)	6.5	6.1
% Type 2 Diabetes	50	50
Triglycerides (mg/dL)	121.7	134.6
Liver Stiffness (kPA)	25.8	22.1
ELF Score	9.7	10.4
Pro-C3 (µg/L)	22.6	25.6

Source Data: Full Analysis Set (all subjects who were randomized into the study);
Topline preliminary data

PATIENT DISPOSITION



HIGHEST REPORTED RATE OF FIBROSIS IMPROVEMENT IN CIRRHOTIC NASH PATIENTS, AFTER ONLY 16 WEEKS



[1] No increase in NAS for ballooning, inflammation, or steatosis
[2] Study not powered to assess statistical significance of changes in histological endpoints

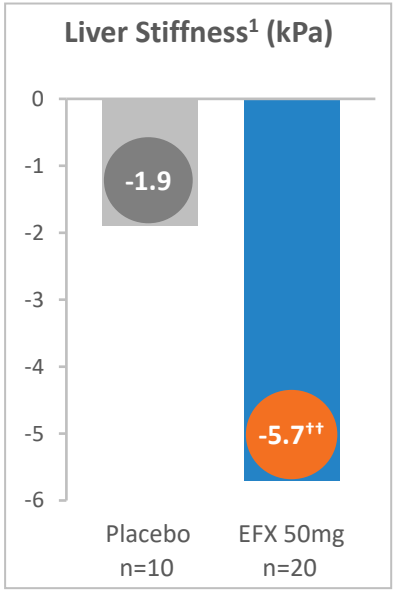
Biopsy Reading

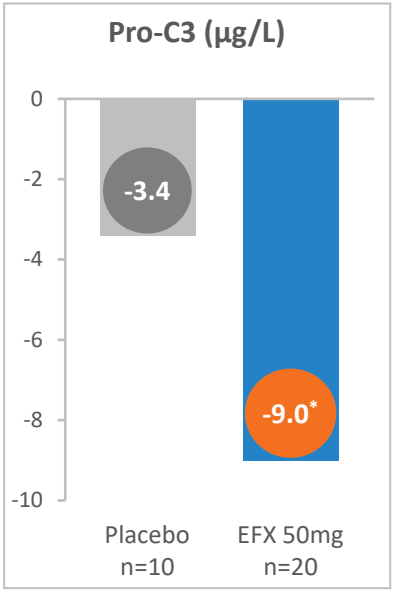
- All baseline and end-of-treatment biopsies were read by a single NASH-CRN pathologist
- All biopsies were read blinded to both treatment assignment and patient
- Baseline biopsies were read independently of end-of-treatment biopsies, in random fashion and not paired

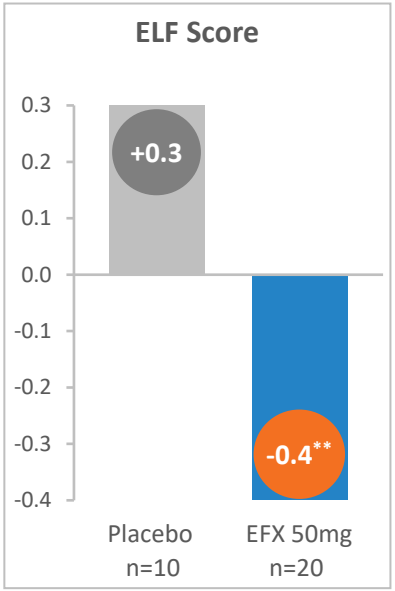
Source Data: Liver Biopsy Analysis Set (all subjects confirmed by central reader as F4 at baseline with Week 16 liver biopsy results); *Topline preliminary data*

NON-INVASIVE MARKERS OF FIBROSIS PROVIDE SUPPORT FOR HISTOLOGY RESULTS

LS Mean Change From Baseline to Week 16







[1] Measured by FibroScan

†† p<0.01, versus baseline (ANCOVA)

* p<0.05, versus placebo (ANCOVA)

** p<0.01, versus placebo (ANCOVA)

Source Data: Biomarker Analysis Set (all subjects with baseline and interpretable on study measure of ELF or pro-C3, respectively); Liver Stiffness Analysis Set (all subjects with baseline and interpretable on-study measure of Liver Stiffness); *Topline preliminary data*

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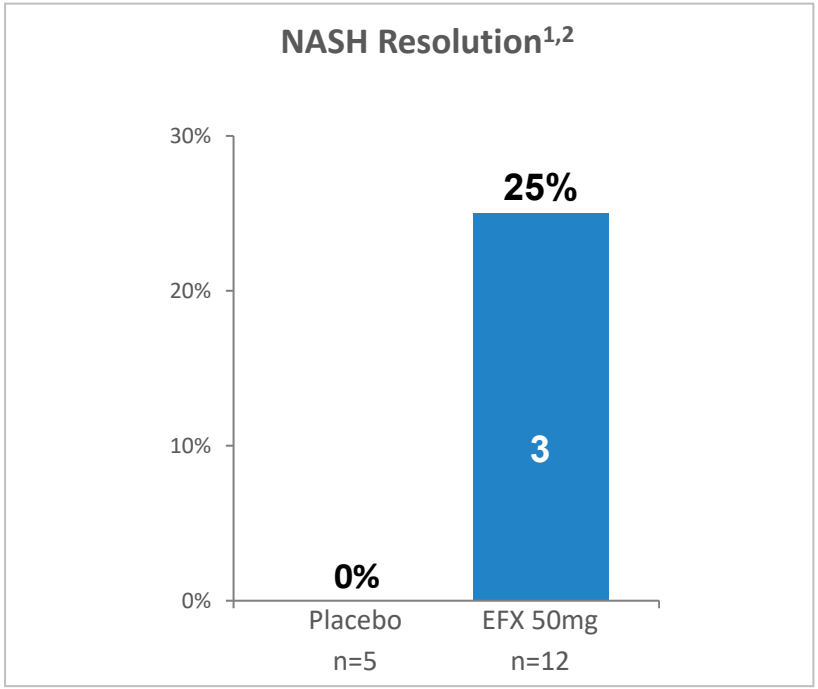
HIGH RATE OF NASH RESOLUTION, AFTER ONLY 16 WEEKS



[1] NAS score of 0 or 1 for lobular inflammation and a score of 0 for ballooning
[2] Study not powered to assess statistical significance of histological endpoints

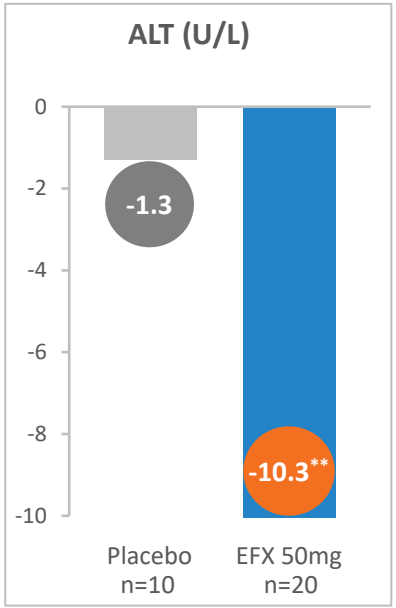
7 of 12 (58%) EFX patients achieved fibrosis improvement* or NASH resolution, compared to 0 of 5 (0%) placebo patients

* Improvement of one-stage fibrosis and no worsening of NASH (there was no overlap among patients who achieved fibrosis improvement without worsening of NASH (n=4) and other patients who achieved NASH resolution (n=3))

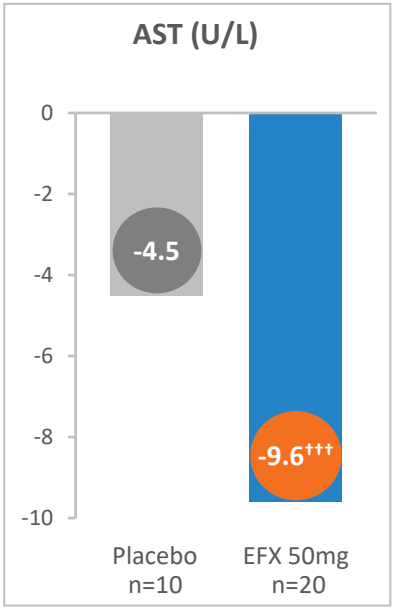
Source Data: Liver Biopsy Analysis Set; *Topline preliminary data*

REDUCTIONS IN MARKERS OF LIVER INJURY

LS Mean Change from Baseline to Week 16



** p<0.01, versus placebo (ANCOVA)



††† p<0.001, versus baseline (ANCOVA)

Source Data: Full Analysis Set; *Topline preliminary data*

SAFETY OVERVIEW

	Placebo (N=10)	EFX 50mg (N=20)
Study Discontinuations	1[a]	1[b]
Serious Adverse Events (SAE)	1[c]	0
Deaths	0	0

[a] Withdrawal of consent
[b] abdominal distension, constipation, diarrhea, pruritus
[c] pulmonary embolism

Source Data: F4 Safety Set (all subjects confirmed by central reader as F4 at baseline who received at least one dose of study drug); *Topline preliminary data*

TOLERABILITY OVERVIEW

Most Frequent (>15%) Drug-Related AEs	Placebo (N=10)	EFX 50mg (N=17)
Diarrhea	1 (10%)	7 (41%)
Nausea	1 (10%)	5 (29%)
Injection site reaction	0	5 (29%)
Injection site erythema	0	4 (24%)
Headache	0	3 (18%)

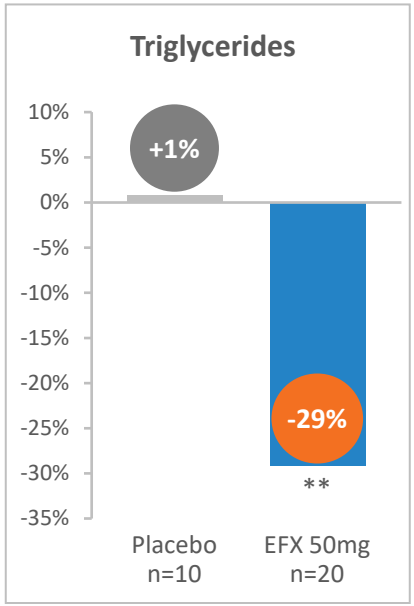
Key Observations

- Encouraging tolerability given population with more advanced disease
- All injection site AEs Grade 1
- No reports of tremor

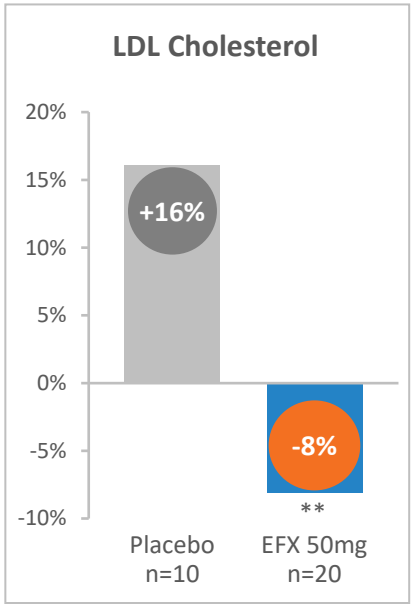
Source Data: F4 Safety Set; *Topline preliminary data*

IMPROVED LIPOPROTEIN PROFILE

LS Mean Change From Baseline to Week 16 (%)



** p<0.01, versus placebo (ANCOVA)



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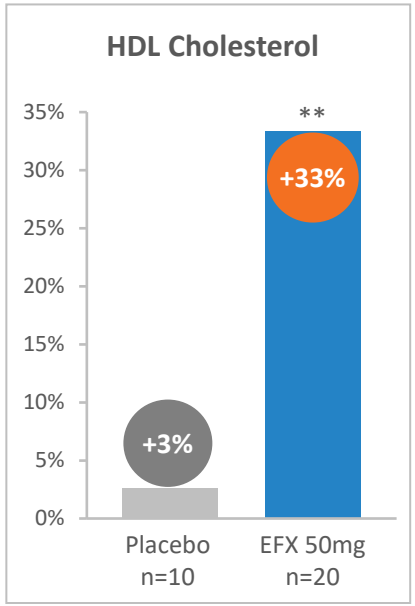
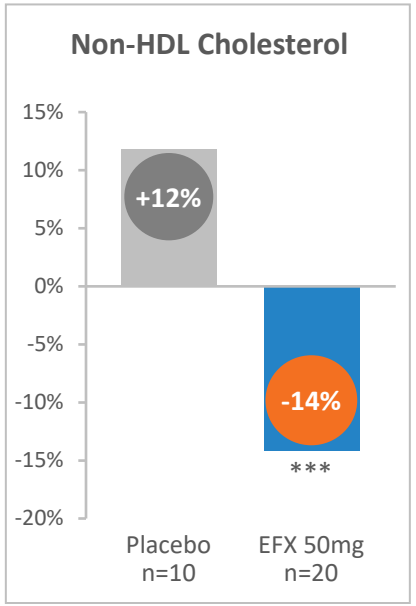


** p<0.01, versus placebo (ANCOVA)

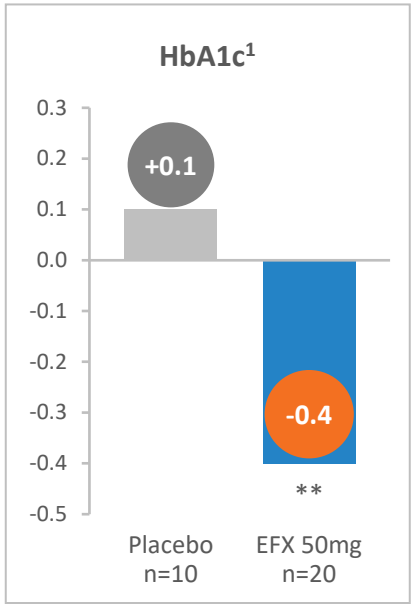


*** p<0.001, versus placebo (ANCOVA)

Source Data: Full Analysis Set; *Topline preliminary data*

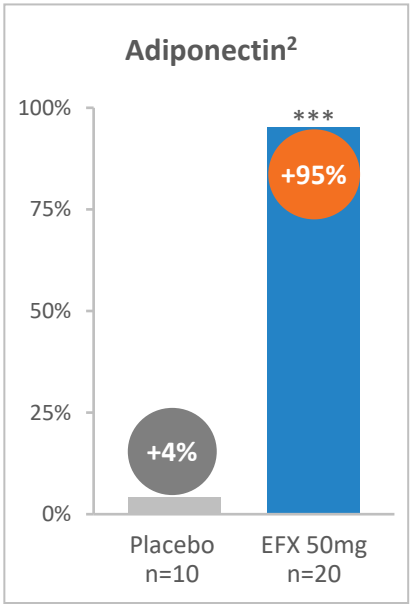
IMPROVED GLYCEMIC CONTROL; TREND TOWARD WEIGHT LOSS

LS Mean Change From Baseline to Week 16 (%)



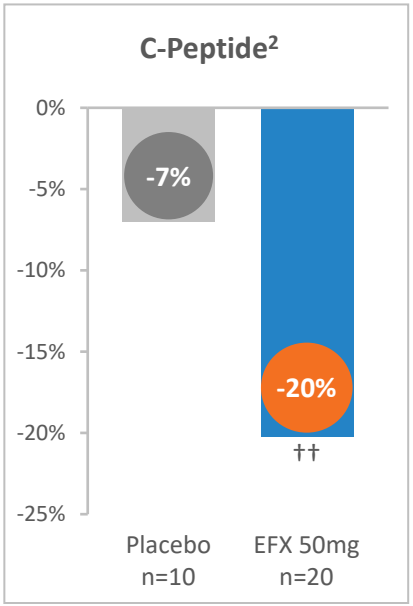
[1] Absolute change from baseline, %

** p<0.01, versus placebo (ANCOVA)



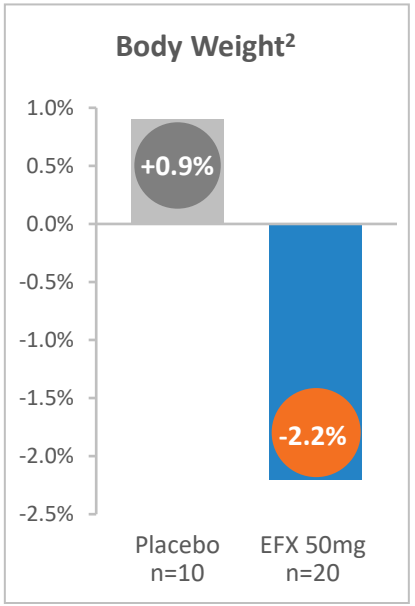
[2] Relative percent change from baseline

*** p<0.001, versus placebo (ANCOVA)



[2] Relative percent change from baseline

†† p<0.01, versus baseline (ANCOVA)

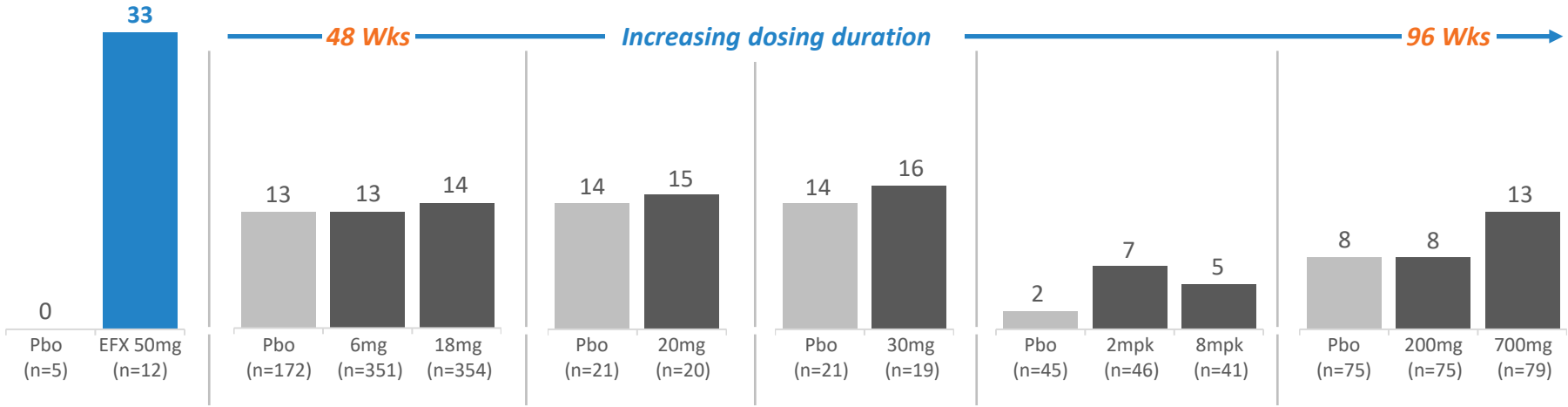


[2] Relative percent change from baseline

Source Data: Full Analysis Set; *Topline preliminary data*

EFX F4 RESULTS IN CONTEXT: FIBROSIS IMPROVEMENT*

Fc-FGF21	ASK-1	ACC	FXR	GAL-3	LOXL2
akero	GILEAD	GILEAD	GILEAD	Galmed Pharmaceuticals	GILEAD
Efruxifermin 16 Wks (Ph2a) SC Injection	**Selonsertib** 48 Wks (Ph3) Oral	**Firsocostat** 48 Wks (Ph2b) Oral	**Cilofexor** 48 Wks (Ph2b) Oral	**Belapectin** 52 Wks (Ph2b) Oral	**Simtuzumab** 96 Wks (Ph2b) IV infusion



** Results from all publicly reported NASH studies in F4 patients reporting either ≥ 1-stage fibrosis improvement (belapectin and simtuzumab) or ≥ 1-stage fibrosis improvement and no worsening of NASH (selonsertib, firsocostat and cilofexor); numerical values represent percent responders*

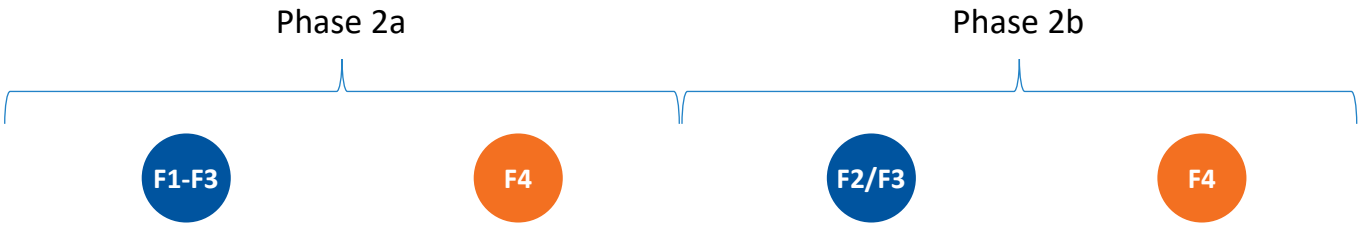
Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. No head-to-head clinical trials have been conducted.

INTERPRETING THE RAPID REVERSAL OF FIBROSIS OBSERVED IN CIRRHOTIC NASH PATIENTS (F4) TREATED WITH EFX

- Fibrosis reversal in cirrhotic patients (F4), two-stage improvement of fibrosis in F2/F3 patients, and corroborating non-invasive markers of fibrosis improvement likely reflects direct anti-fibrotic activity
- Fibrosis reversal is especially advantageous for cirrhotic patients who face high risk of mortality and severe morbidity

- Addressing underlying NASH disease drivers may indirectly contribute to fibrosis reversal for F1-F3 patients with adequate time for the liver to regenerate
- Redress of the underlying NASH disease drivers is necessary to sustain fibrosis reversal in F1-F4
- Supports broader metabolic improvements

NEXT STEPS FOR EFX: PARALLEL 2B TRIALS IN F2/F3 & F4



	BALANCED	Cohort C (Expansion of BALANCED)	HARMONY	SYMMETRY
Status	**Completed** (Readout Jun'20)	**Completed** (Readout Mar'21)	**Ongoing** (Initiated Feb'21)	**Expected to be initiated 2H'21**
Duration	16 Weeks	16 Weeks	24 Weeks	Under review
EFX Arms	28, 50, 70mg	50mg	28, 50mg	Under review
Placebo-Controlled	✓	✓	✓	✓

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NASDAQ: AKRO