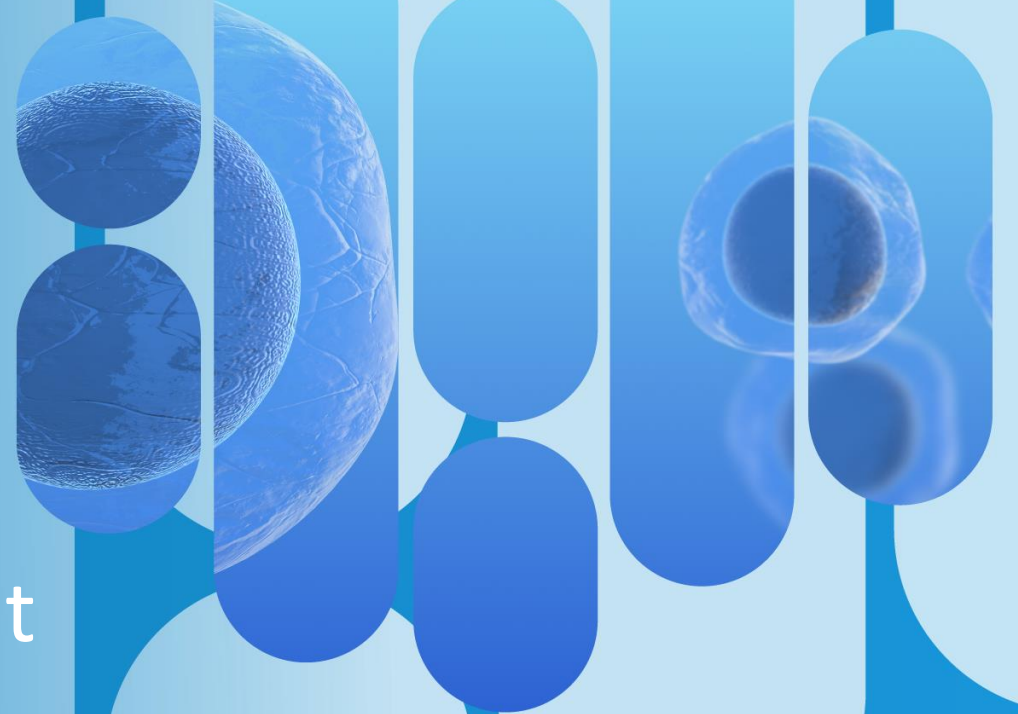


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**KOL Webinar on Metabolic
Dysfunction-Associated
Steatohepatitis (MASH)**

Pegozafermin's Anti-Fibrotic and
Metabolic Benefits for the Treatment
of MASH



Disclaimers

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, 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, including the topline results from ENTRUST Phase 3 trial in SHTG, 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 possibility of obtaining accelerated approval in MASH in advanced fibrosis (F2-F3), and compensated cirrhosis (F4) through an interim analysis based on histology. 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.

Today's Agenda



Introduction to Pegzofermin

Rohan Palekar, CEO

Non-cirrhotic (F2-F3) advanced MASH

Arun J. Sanyal, MBBS, MD

Compensated cirrhotic (F4) MASH

Arun J. Sanyal, MBBS, MD

Overview of ENLIGHTEN-Cirrhosis Trial

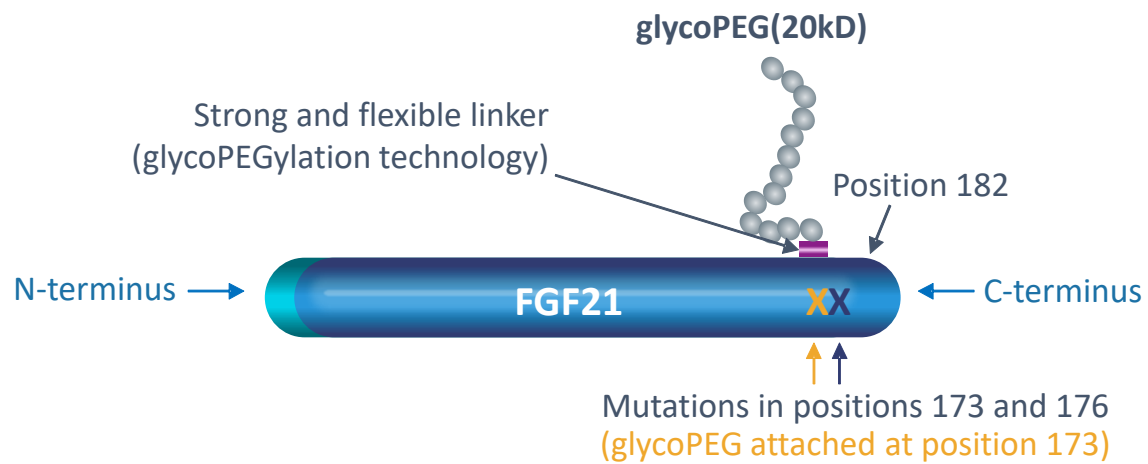
Hank Mansbach, MD, CMO

Pegzofermin's Commercial Opportunity

Rohan Palekar, CEO

Q&A

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



	FGF21	Pegozafermin
RECEPTOR	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 EC₅₀ 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
- Composition of Matter patent expiring in 2038

Pegozafermin Offers Potential Best-in-Class Therapeutic



ADVANCED MASH

REVERSES LIVER FIBROSIS
RESOLVES MASH



SHTG

REDUCES TRIGLYCERIDES

IMPROVES DYSLIPIDEMIA

REDUCES LIVER FAT

IMPROVES INSULIN RESISTANCE

FAVORABLE TOLERABILITY, CONVENIENT DOSING, AND COMMERCIAL PRESENTATION¹:
To improve patient persistence and compliance

Pegozafermin Could Offer an Important New Treatment Option with Significant Market Opportunities in MASH and SHTG



MASH | ADVANCED FIBROSIS PATIENTS

SHTG | SECOND-LINE THERAPY

CLINICAL

- Robust anti-fibrotic benefit
- Additive benefits to GLP-1 therapies

- Robust TG reduction on top of standard of care
- Substantially de-risked Phase 3 study

COMMERCIAL

- Large market will support multiple MOAs
- Cirrhotic patient market offers unique opportunity




- Large refractory market ~1M patients
- Potential best-in-category profile based on metabolic, lipid, and tolerability profile

BUSINESS

- Development and commercial synergies across program
- Three shots on goal provides diversification

Advancing Pegzofermin in Clinical Development



INDICATION	TRIAL	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
MASH <i>Breakthrough Therapy & PRIME designation</i>		Phase 3 trial in F2/F3: Histology & Outcomes – Ongoing			
		Phase 3 trial in F4: Histology & Outcomes – Initiated			
SHTG		Phase 3 trial – Topline data in 2025			

Speaker Introduction



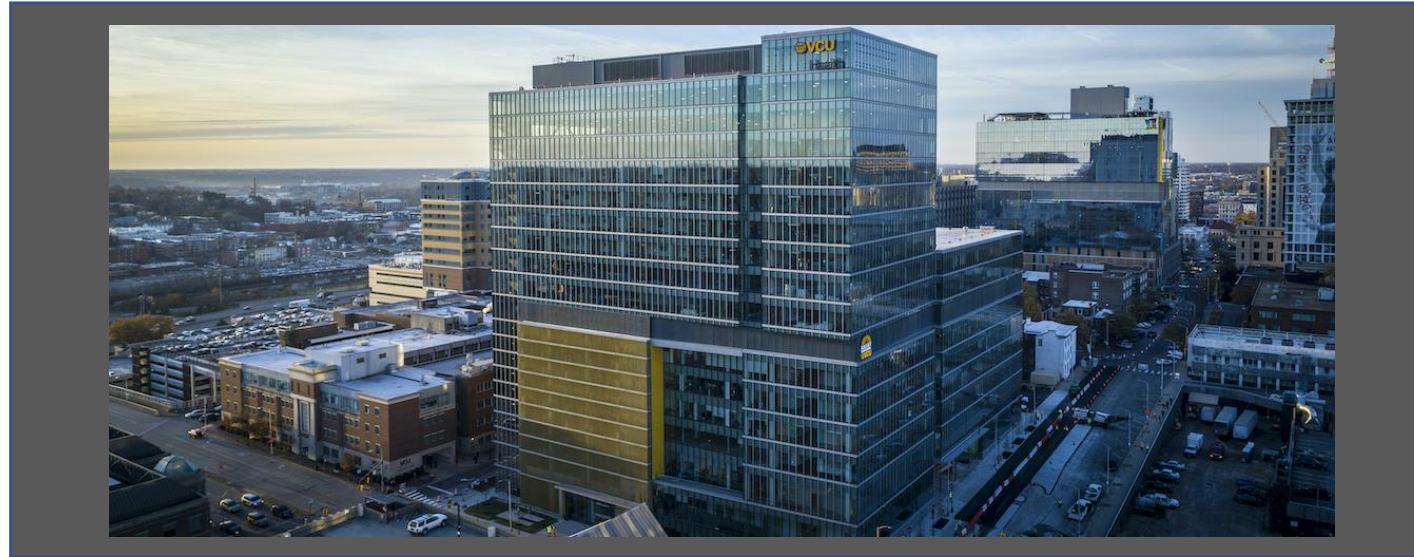
Arun J. Sanyal, MBBS, M.D.

Director of the Stravitz-Sanyal Institute for
Liver Disease and Metabolic Health, Virginia
Commonwealth University

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Treatment Considerations in Non-cirrhotic (F2-F3) Advanced Fibrosis MASH





Arun J. Sanyal MBBS MD

Z Reno Vlahcevic Professor of Medicine

Director, The Stravitz-Sanyal Institute for Liver Disease and Metabolic Health

VCU and VCU School of Medicine

Disclosures

I disclose the following financial relationship(s) with a commercial interest:

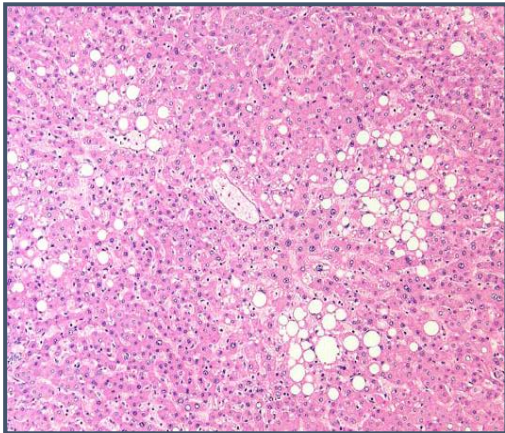
- Ownership interests: Durect, Tiziana, Genfit, Exhalenz, Northsea, Rivus, Inversago
- Consultant: Histoindex, Path AI, Pharmanest, Biocellvia,
- Consultant: 89Bio, Gilead, Intercept, Novartis, Novo Nordisk, Inventiva, Merck, Pfizer, Boehringer Ingelhiem, Bristol Myers Squibb, Eli Lilly, Genentech, Amgen, Alnylam, Regeneron, Thera Technologies, Madrigal, Salix, Malinckrodt, Gatehouse, Rivus, Siemens, Lipocine, Astra Zeneca, Akero, Foresite, Mitopower, Takeda
- Grant support to school: Gilead, Intercept, Novartis, Novo Nordisk, Inventiva, Eli Lilly, Genentech, Boehringer Ingelhiem, Bristol Myers Squibb

Wish I was there

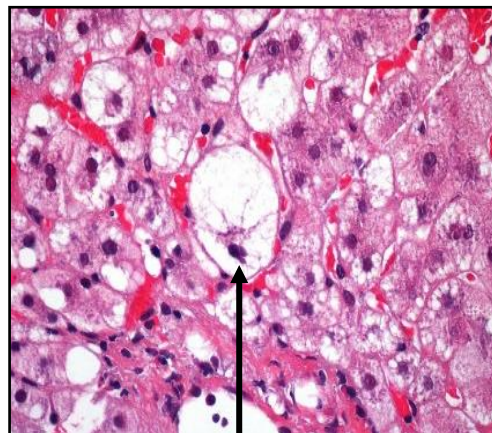


MASLD*—a progressive disease as described by pathologists

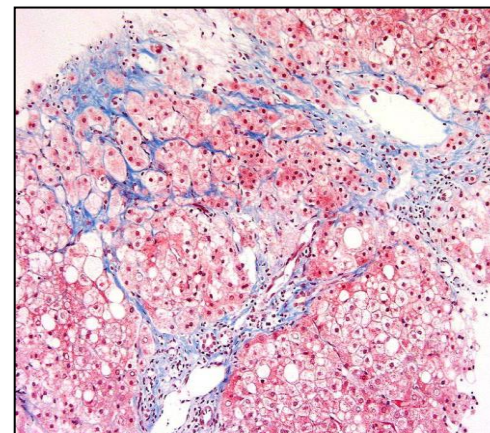
NAFL



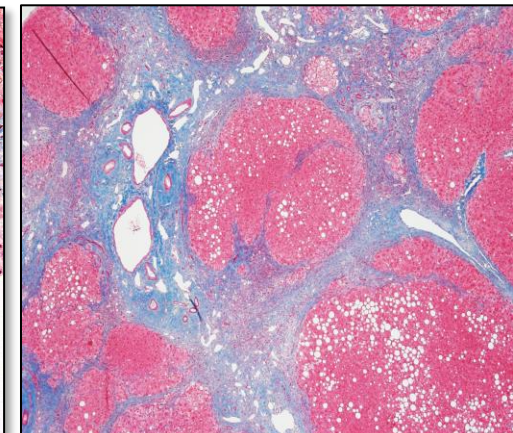
NASH



NASH with fibrosis



NASH Cirrhosis



Hepatocellular
ballooning

*In 2023, based on a multistakeholder consensus effort, the nomenclature for NAFLD and NASH were changed to MASLD and MASH. Rinella et al. *Hepatology* [78\(6\):p 1966-1986, December 2023.](#)

The MASLD pyramid—thinking through the floors

At what point will etiology specific vs decompensation related targets need to be attacked?



Cirrhosis
(N= 1 million)

Can disease activity and fibrosis both be decreased?



NASH (MASH)
Advanced fibrosis (F3/F4)
(N=2 million)

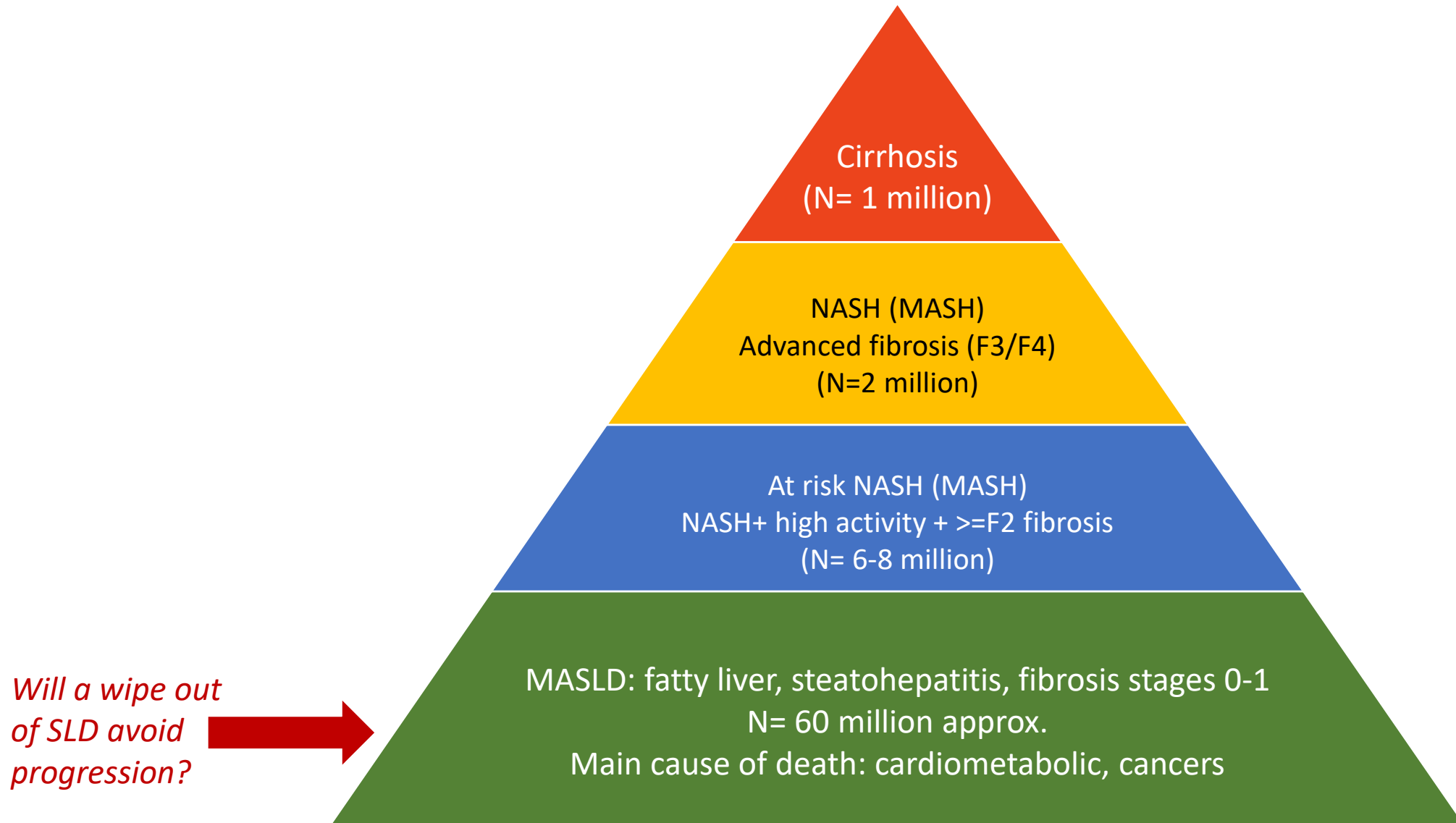
Will a wipe out of SLD avoid progression?



At risk NASH (MASH)
NASH+ high activity + \geq F2 fibrosis
(N= 6-8 million)

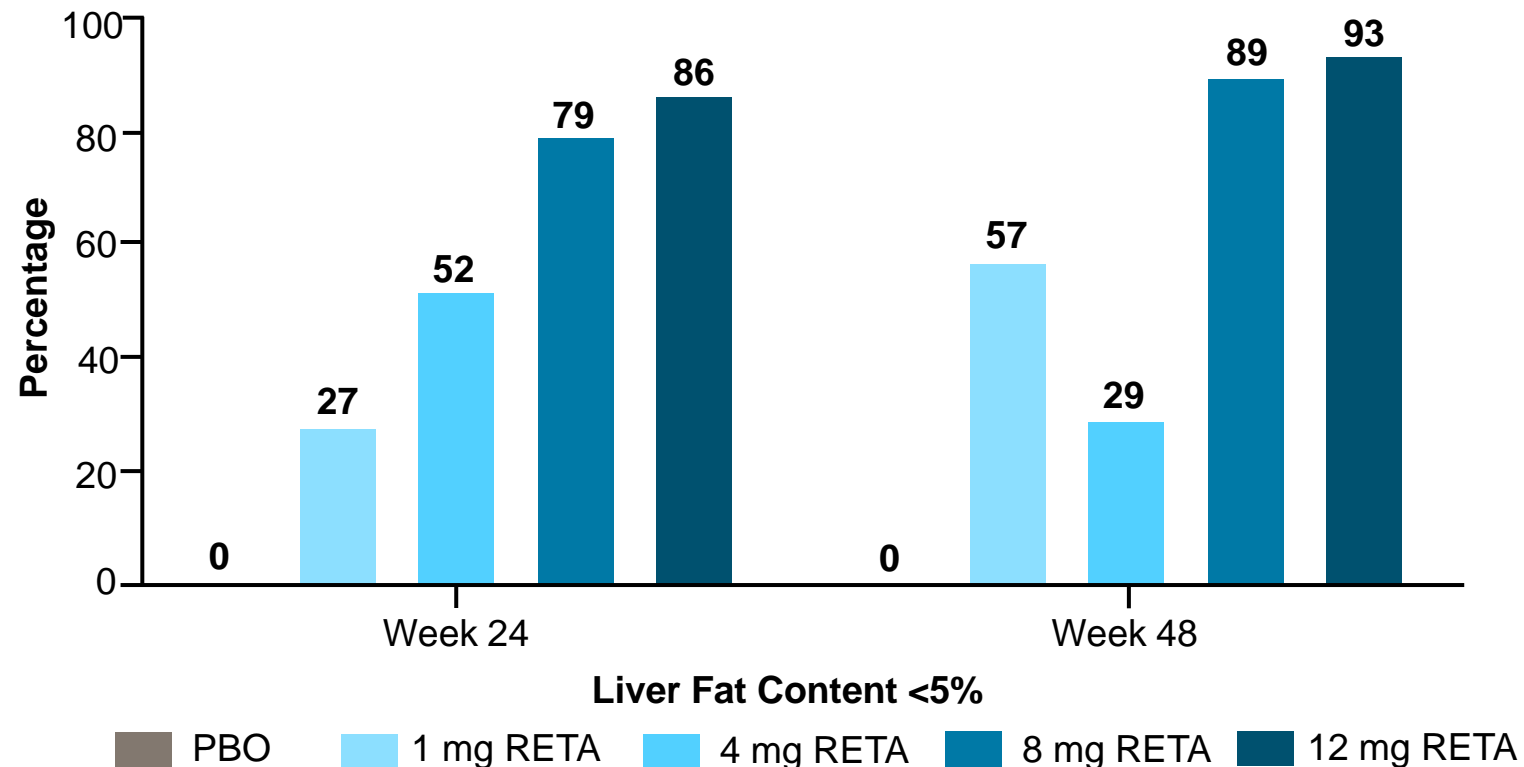
MASLD: fatty liver, steatohepatitis, fibrosis stages 0-1
N= 60 million approx.
Main cause of death: cardiometabolic, cancers

The MASLD pyramid—thinking through the floors



It is logical to hope that clearance of early stage MASLD with GLP-1 based therapies will stop injury-inflammation-fibrosis progression- but need data to establish this as a construct!

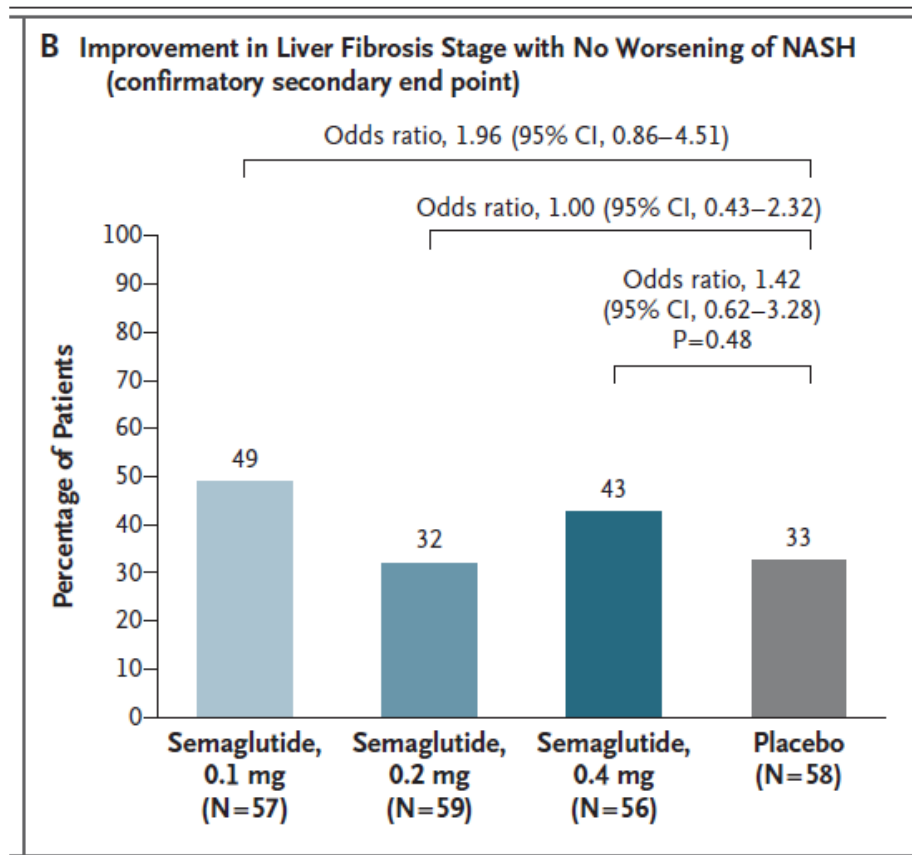
Proportion of Participants Achieving Liver Fat Content <5%^a



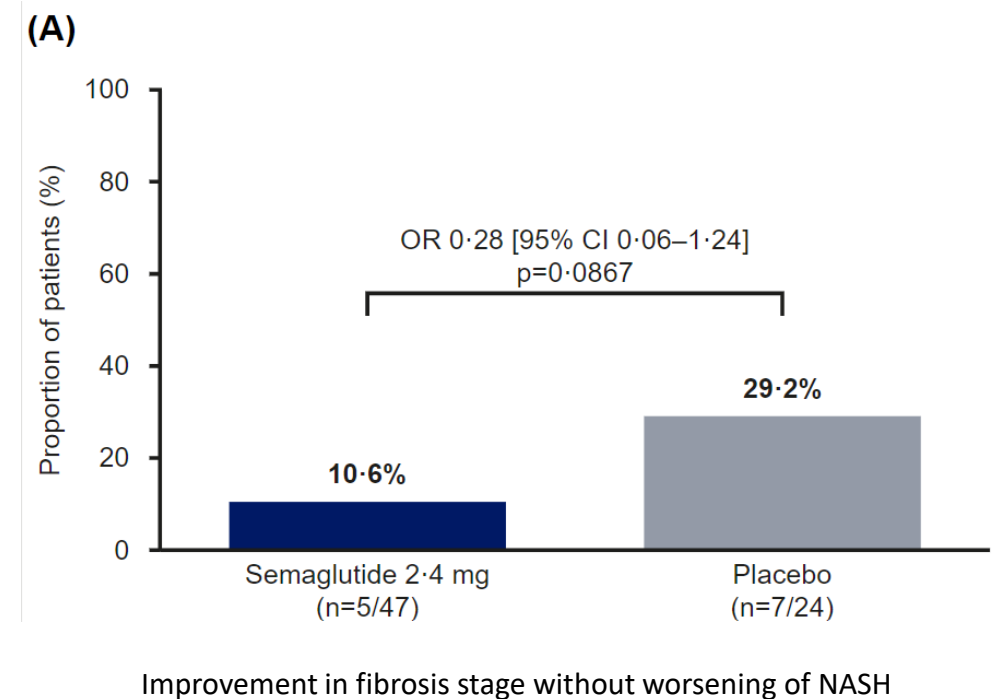
^aFewer participants had MRIs at Week 48 (n=8 [PBO], n=9 [1 mg RETA], n=9 [4 mg RETA], n=8 [8 mg RETA], n=9 [12 mg RETA]) compared to Week 24 (n=14 [PBO], n=16 [1 mg RETA], n=15 [4 mg RETA], n=17 [8 mg RETA], n=15 [12 mg RETA]). MRI=magnetic resonance imaging; NAFLD=non-alcoholic fatty liver disease; PBO=placebo; RETA=retatrutide.

Semaglutide did not show fibrosis improvement vs placebo in either F2-F3 nor F4 patients

F2- F3 patients

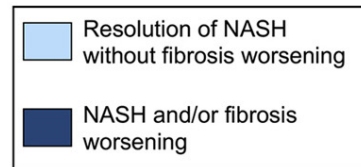
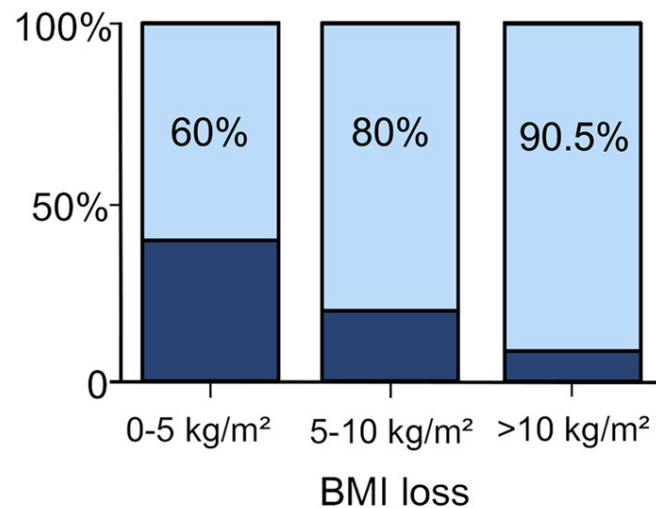


F4 patients

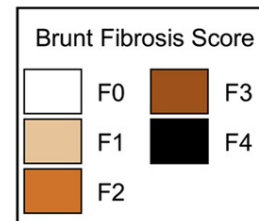
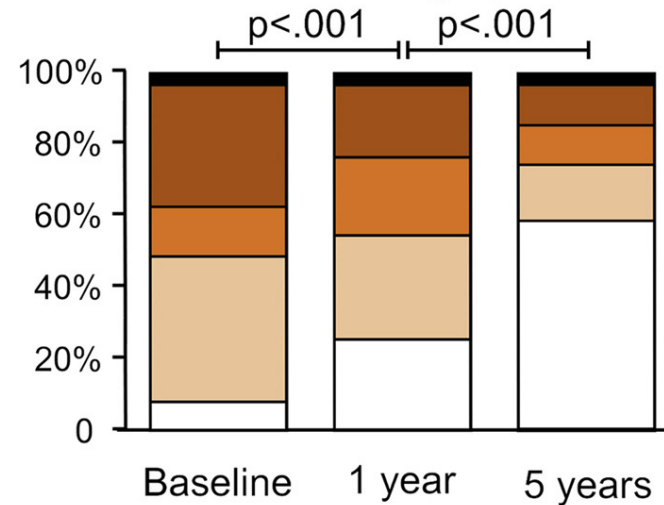


Weight loss does not improve advanced fibrosis

Resolution of NASH according to weight loss



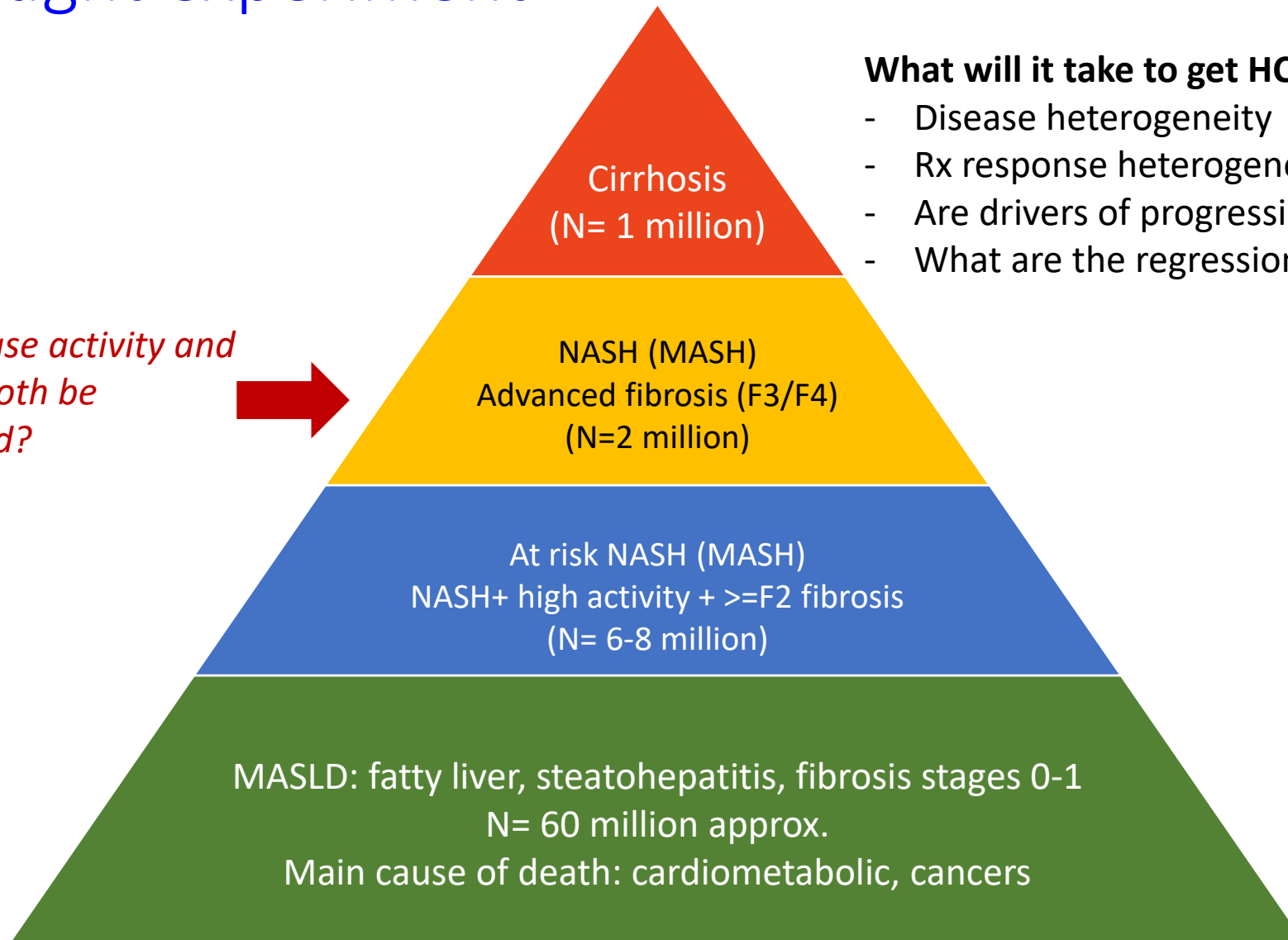
Evolution of Fibrosis after Bariatric Surgery



Are there collagen compartments that are differentially mobilizable?

How to optimize drug development for at risk MASH—a thought experiment

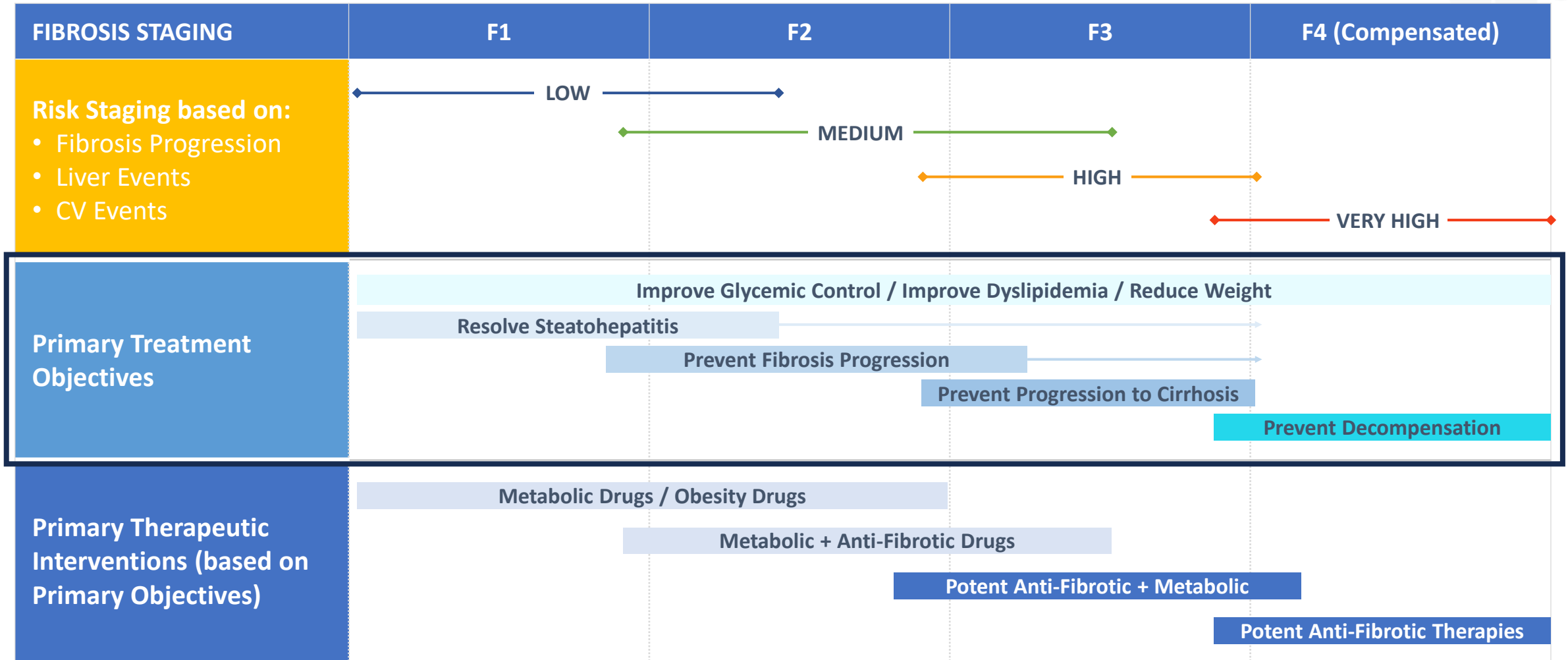
Can disease activity and fibrosis both be decreased?



What will it take to get HCV Rx-like benefits?

- Disease heterogeneity
- Rx response heterogeneity
- Are drivers of progression different at different levels
- What are the regression drivers

Treatment goals for MASH across fibrosis staging

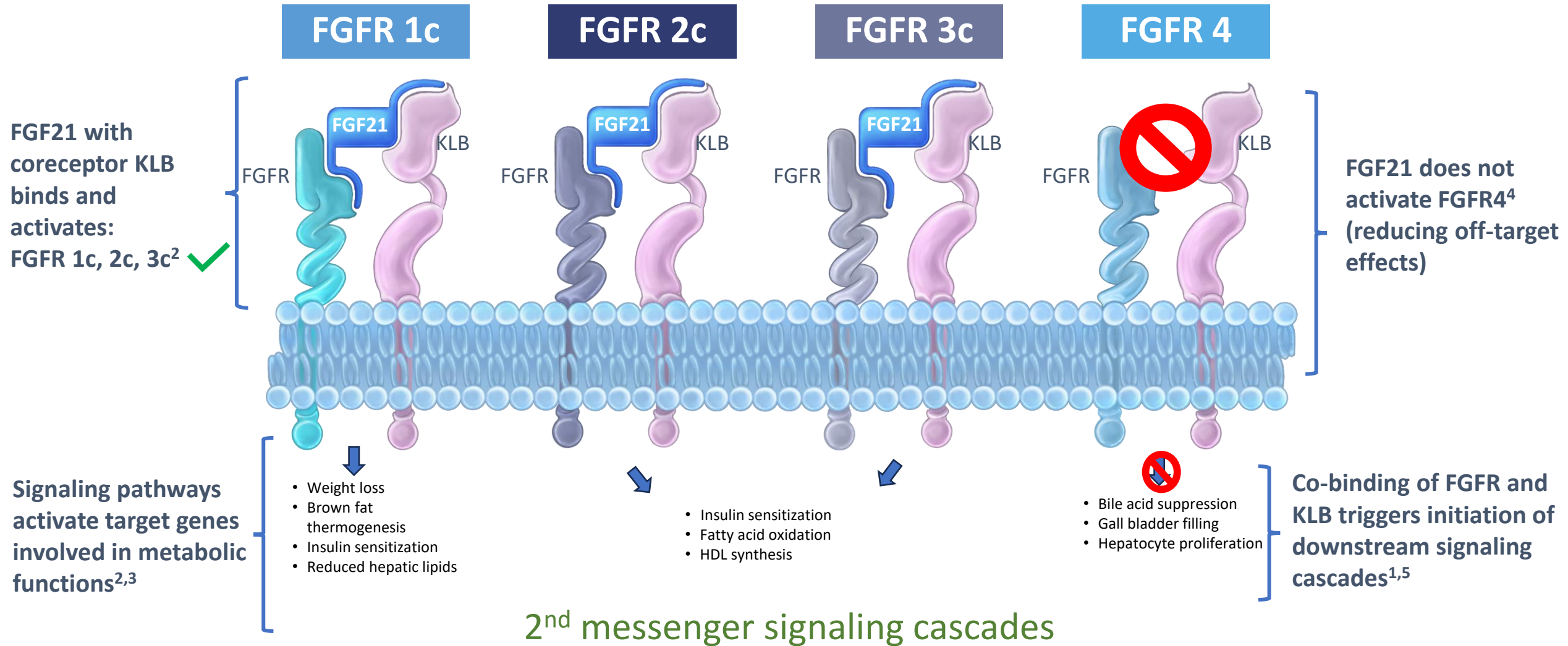


A look at the competitive landscape for at risk MASH

	Pan PPAR	FGF21	Thyroxine B-R	GLP-1
Weight	Gain	Loss	Neutral	Loss
LDL-C	Increase	Decrease	Decrease	Neutral
HDL-C	Increase	Increase	Neutral	Neutral
TG	Decrease	Decrease	Decrease	Neutral
MACE	Neutral	?	?	Improved
Stabilize GFR	?	?	?	Improved
Glycemic control	Improved	Neutral/Improved	Neutral	Improved
Improve activity	Yes	Yes	Yes	Yes
Improve fibrosis	Yes	Yes	Yes	Maybe

1. GLP-1 limited by nausea, up to 30% stop therapy but likely to be backbone Rx for Met S
2. 2nd gen FGF21 (PGZ and EFX) look very promising
3. TBR2 agonists first MOA to be approved
4. < 50% patients treated experience both improvement in activity and fibrosis

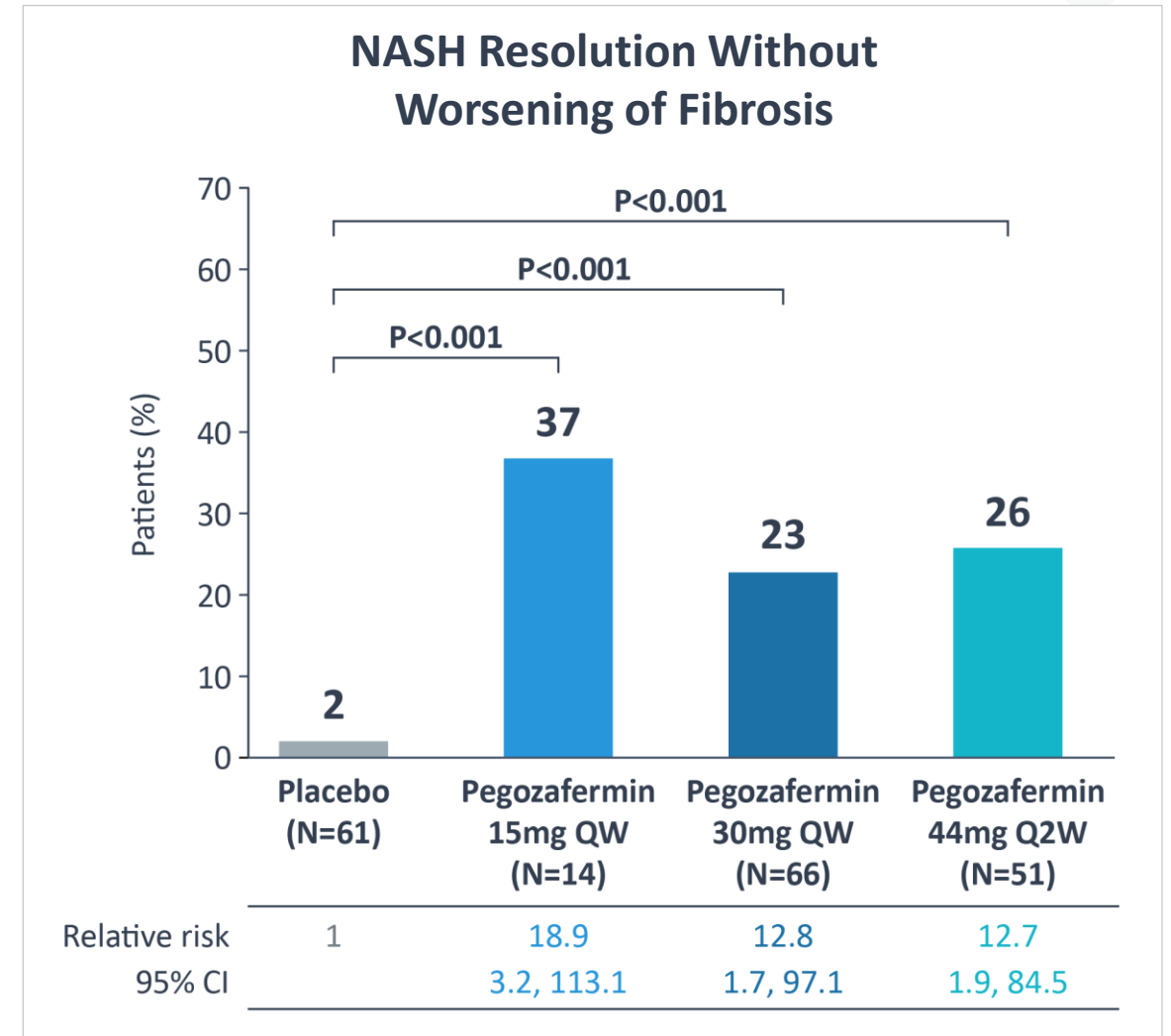
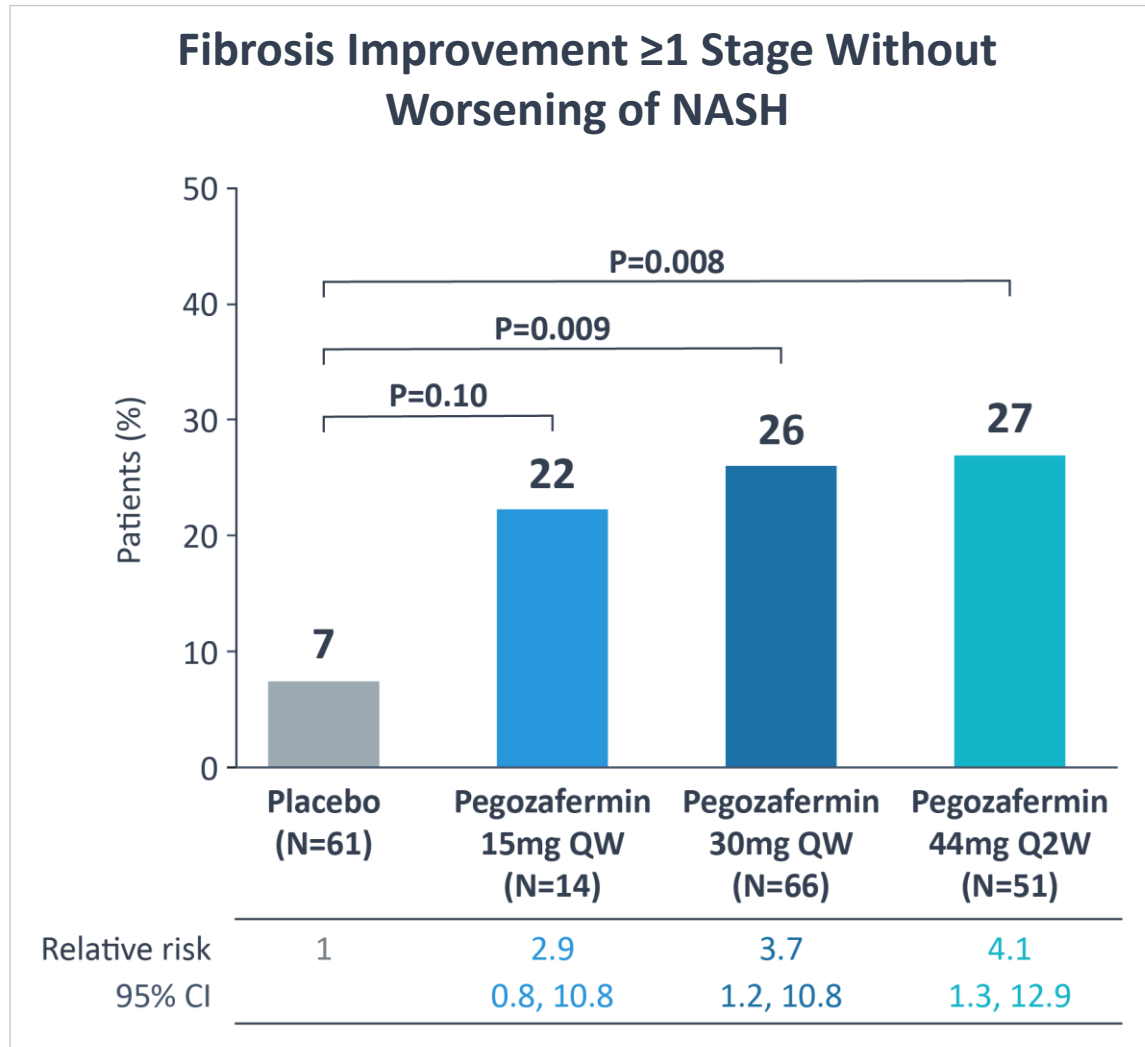
FGF21 acts via an FGF Receptor (FGFR) and the coreceptor KLB



1. Agrawal A, et al. *Mol Metabol.* 2018;13:45-55. 2. Sonoda J, et al. *Horm Mol Biol Clin Investig.* 2017;30(2):20170002. 3. Kwok KHM, Lam KSL. *Endocrinol Metab.* 2017;32(2):145-151. 4. Yang C, et al. *PLoS ONE.* 2012;7(3):e33870. 5. Kilkeny DM, Rocheleau JV. *Vitamins Hormones.* 2016;101:17-58.

FGF21, fibroblast growth factor 21.

Pegozafermin treatment led to a significant improvement on primary endpoints at week 24



Therapeutic landscape through the lens of fibrosis improvement

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Pegozafermin
Phase 2b | 24 weeks
Multiple Imputation¹

Intercept

Ocaliva[†]
Phase 3 | 72 weeks

Madrigal
Pharmaceuticals

Rezdiffra²
Phase 3 | 52 weeks

inventiva

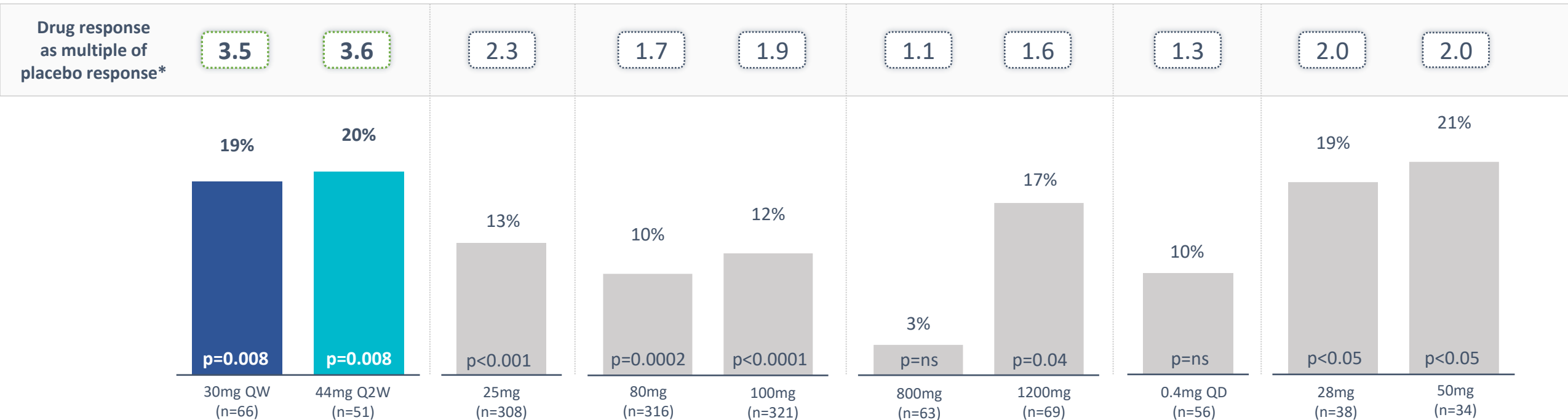
Lanifibranor
Phase 2b | 24 weeks



novo nordisk
Semaglutide
Phase 2 | 72 weeks

akero

Efruxifermin
Phase 2b | 24 weeks
Completers Analysis

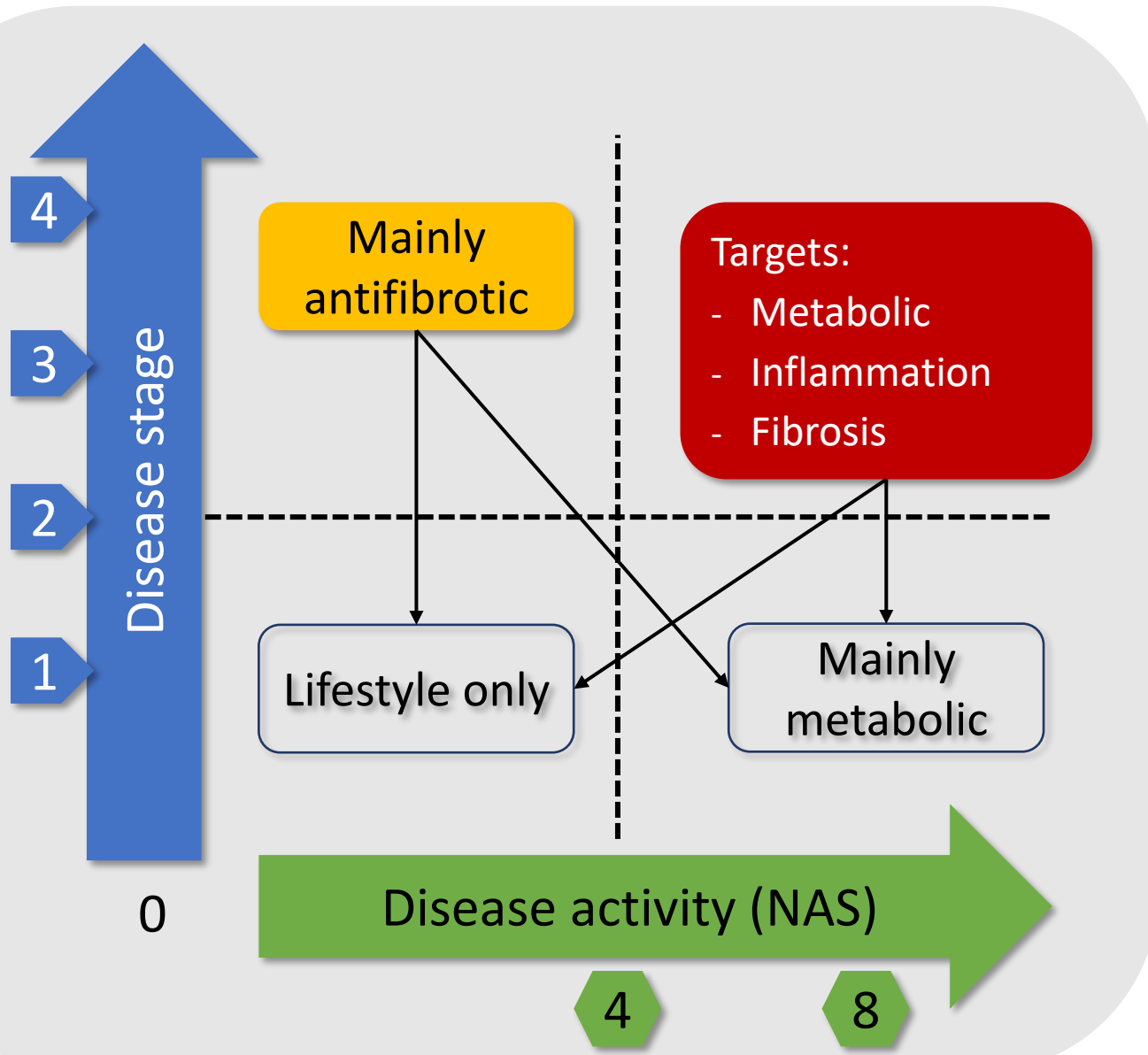


*Drug response as multiple of placebo response is calculated by dividing drug response by placebo response

¹Results same for Completer Analysis Set from 89bio Phase 2 ENLIVEN Trial; ²≥1 stage fibrosis improvement with no worsening of NAS. Fibrosis improvement by ≥ 1 stage with no worsening of NAFLD activity score.; [†]Program discontinued; ns= not significant

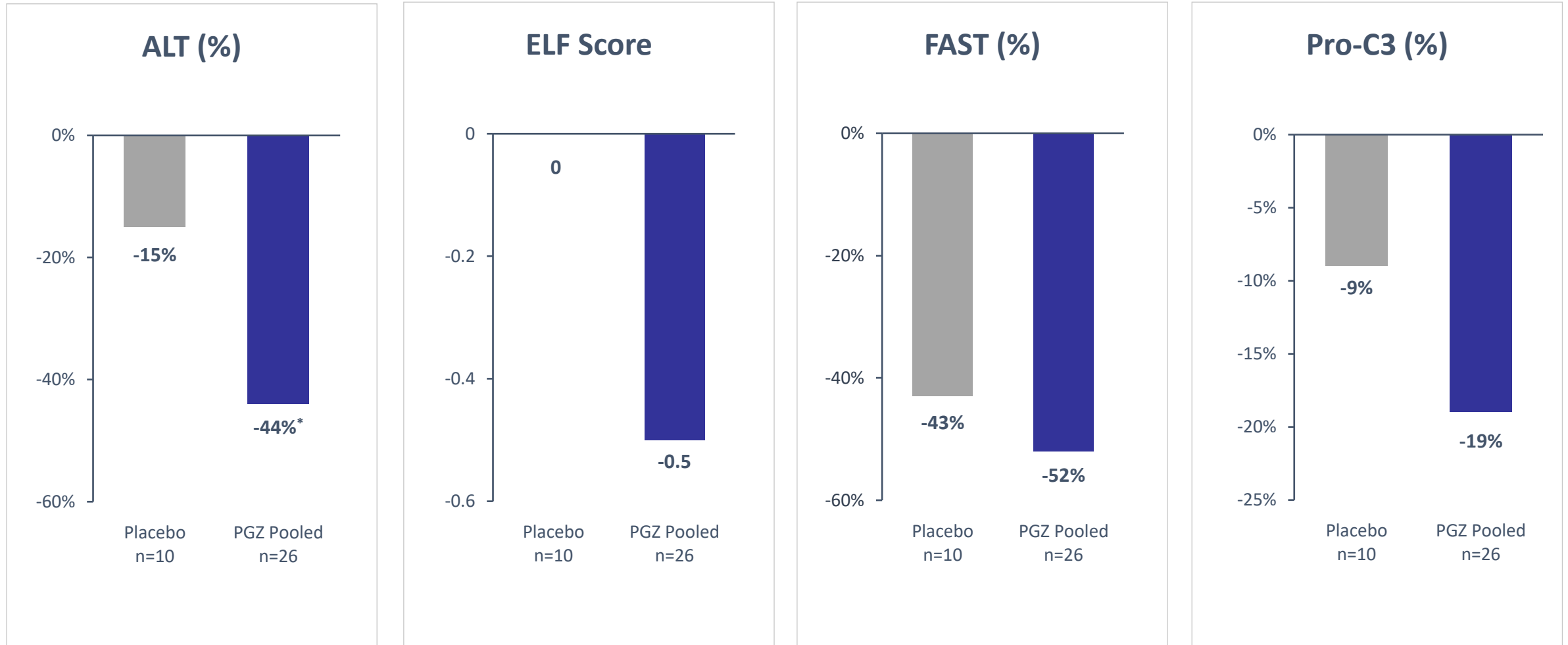
Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

Combination therapies- current approaches can be improved



- Population
- Relevant targets
- Relevant endpoints
- Booster strategies
- Ongoing combo trials:
 - Semaglutide + FGF21 (NCT # 05016882)
 - Semaglutide + fixed dose combo of cilofexor and firsocostat in cirrhosis (NCT #04971785)

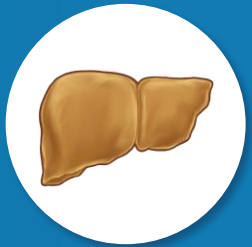
Sustained benefits on fibrosis markers were observed with pegozafermin vs. placebo in patients on background GLP-1 therapy at week 48



Source: 89bio Phase 2 ENLIVEN Trial, 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.

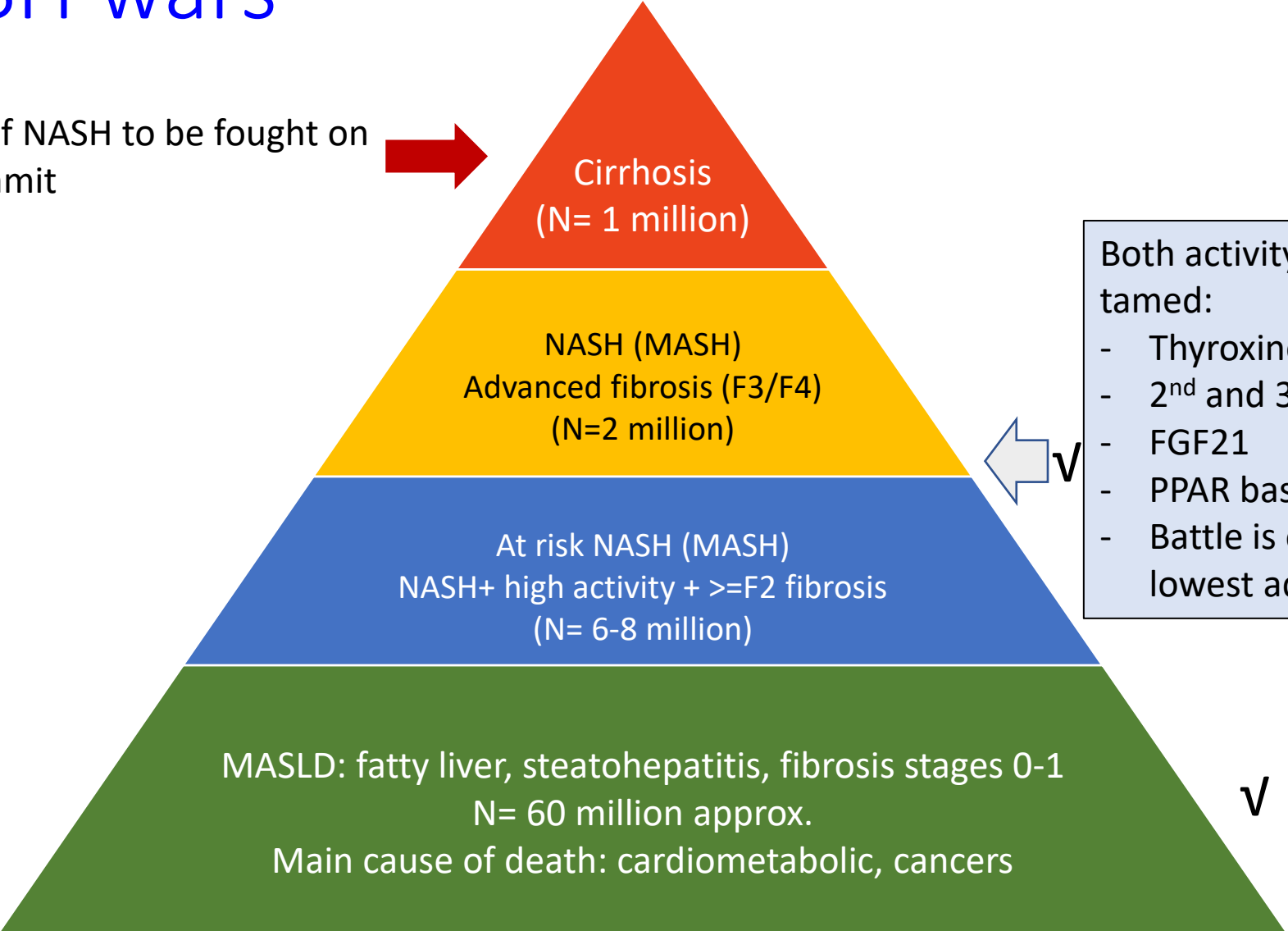
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Treatment Considerations in Compensated Cirrhosis (F4) MASH



NASH wars

Final Battle of NASH to be fought on cirrhosis summit



Both activity and fibrosis can be tamed:

- Thyroxine beta receptor agonists
- 2nd and 3rd gen GLP-1 based drugs
- FGF21
- PPAR based Rx
- Battle is on for best effect size and lowest adverse event profile

Treating root cause may reduce burden of disease substantially

Adapted from Estes et al, Hepatology 2018

Advanced fibrosis increases the hazard ratio for all-cause mortality, liver-related death and comorbidities

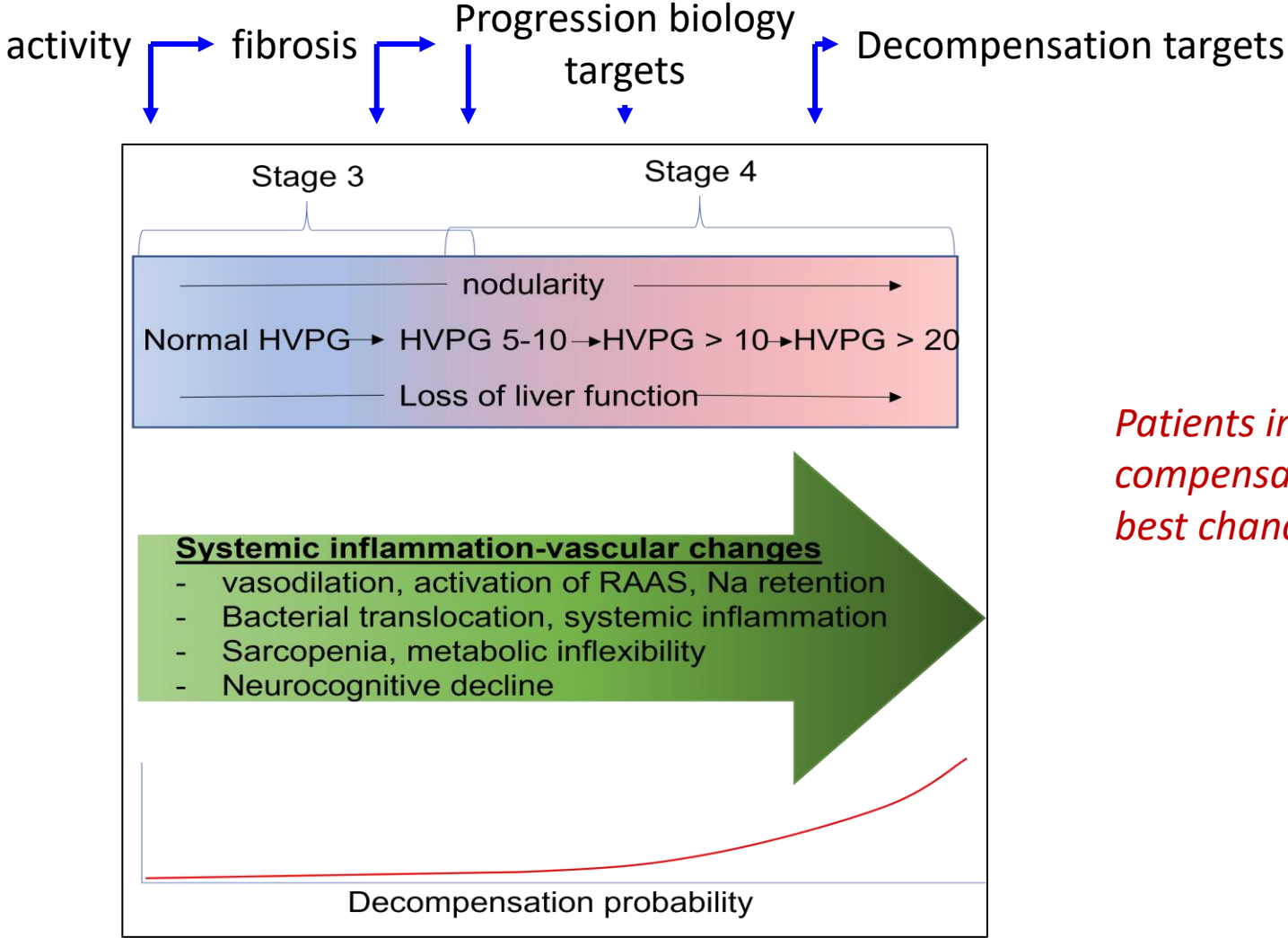


	Hazard Ratio for F3 vs F0-F2 (95% CI)	Hazard Ratio for F4 vs F0-F2 (95% CI)
Death from any cause	1.9 (0.9 - 3.7)	3.9 (1.8 - 8.4)
Liver-related death	5.8 (0.9 - 38.4)	12.7 (1.8 - 88.6)
Any hepatic decompensation event	18.7 (4.8 - 73.1)	36.1 (8.9 - 146.3)
MELD score ≥15	1.2 (0.6 - 2.3)	3.7 (1.8 - 7.3)
HCC	9.3 (1.4 - 61.8)	4.9 (0.4 - 63.2)

CI; confidence interval; eGFR, estimated glomerular filtration rate; F, fibrosis stage; HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease.

1. Sanyal AJ, et al. *N Engl J Med.* 2021;385:1559-1569. 5. Yamazaki H, et al. *Diabetes Care.* 2015;38(9):1673-1679.

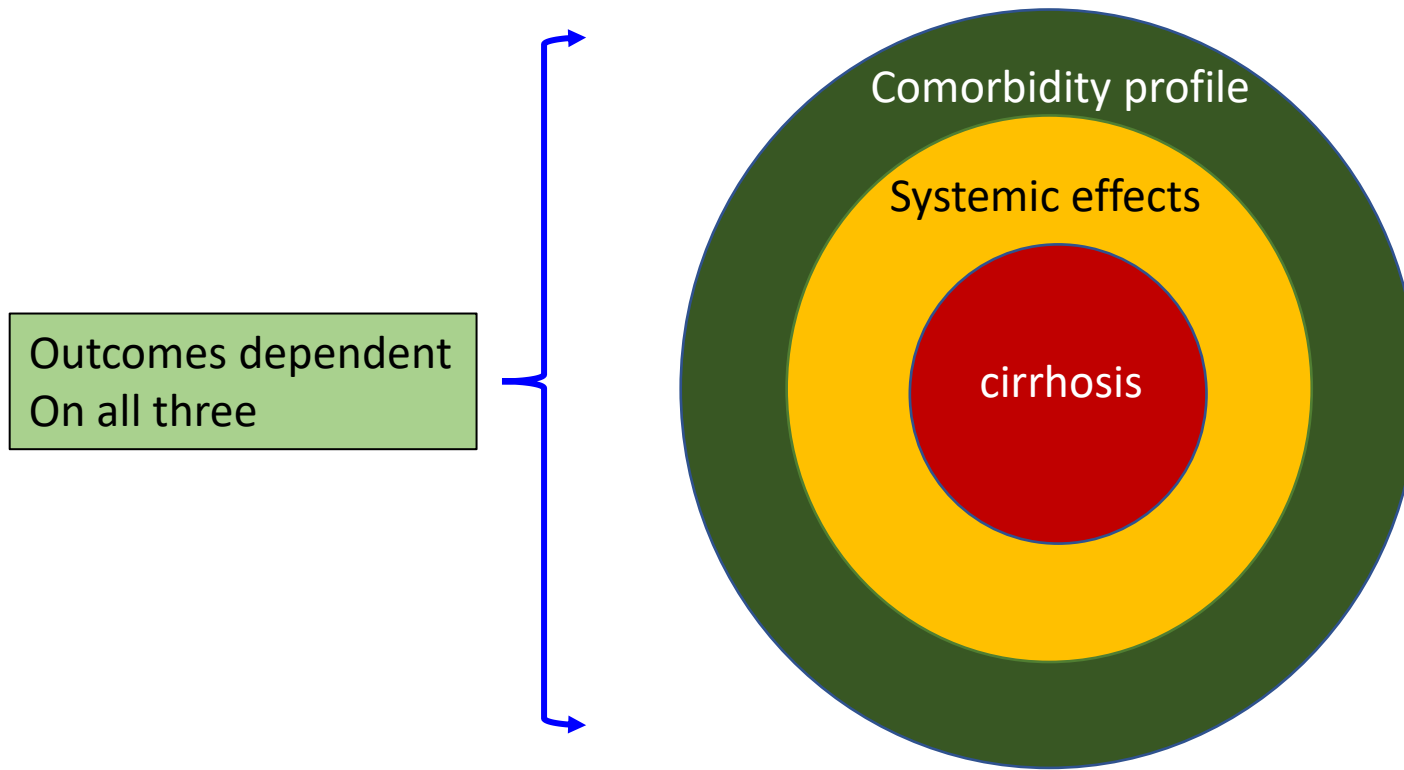
Selecting the Right patient



Patients in the earlier stages of compensated cirrhosis have best chance of fibrosis reversal

HVPG = hepatic venous pressure gradient

Selecting the Right Target



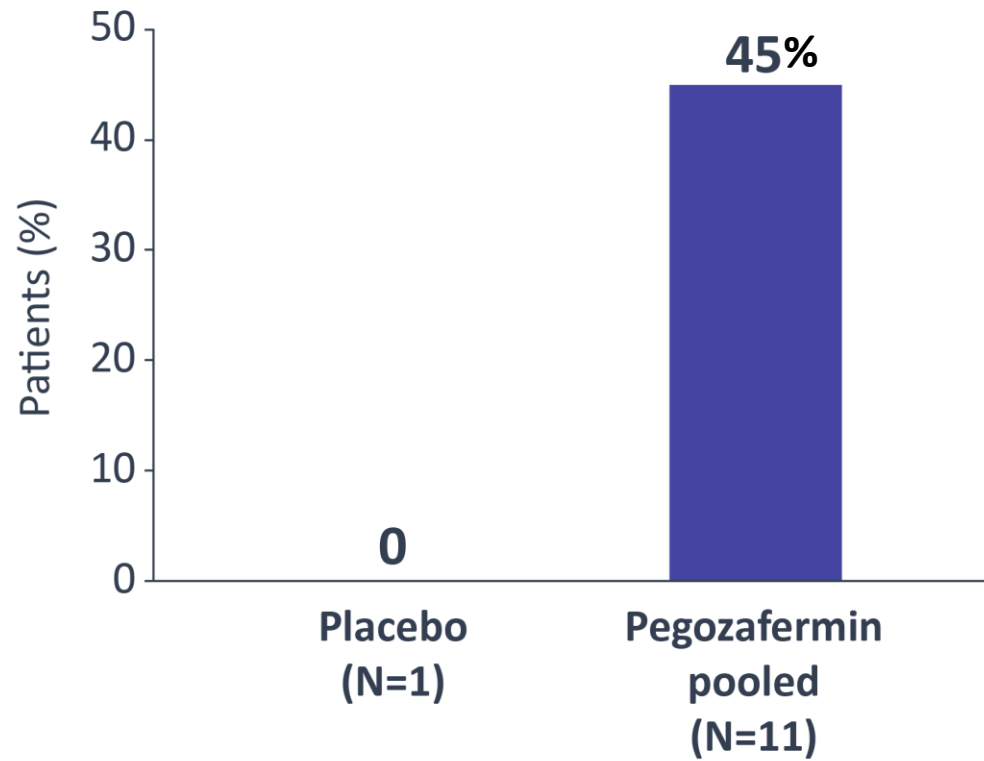
- Agents targeting systemic milieu may not be sufficient
- Targeting cirrhosis before systemic consequences of cirrhosis are well established may allow both elements to be resolved
- With progression to established vasodilation, systemic inflammation etc., simply targeting cirrhosis related drivers may not be sufficient
- Combination of upstream targets with cirrhotic progression drivers will be needed to prevent decompensation
- Since pathophysiology of ascites and HE are vastly different, patients closest to outcomes may be targeted approaches

Why FGF21 analogs may be the right target for MASH compensated cirrhosis

- Mechanism of action: direct liver anti-fibrotic effect and metabolic benefits
 - Suppresses Kupffer cell and hepatic stellate cell activation thus reducing inflammation and fibrogenesis
 - Reduces pro-fibrotic signaling
 - Continued suppression of metabolic insult to the liver [“liver healing”]
- Most robust & consistent fibrosis regression data and prevention of fibrosis progression in advanced fibrosis patients (F3 patients)
- Promising data in compensated cirrhotic patients in phase 2 studies
- In the right F4 patients, potent FGF21 analogs appear to be the best known target to show fibrosis regression and improvement in clinical outcomes

Pegozafermin: Fibrosis improvement without worsening of NASH in 45% of patients with F4 fibrosis at baseline

Fibrosis Improvement ≥ 1 Stage Without Worsening of NASH



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

Parameter	Mean Change from Baseline on Pegozafermin (n=12)
MRI-PDFF	-33%
ALT	-53%
AST	-31%
ELF	-0.4 units
cT1	-87 msec

Dramatic reduction in liver-related events in cirrhosis patients with fibrosis regression

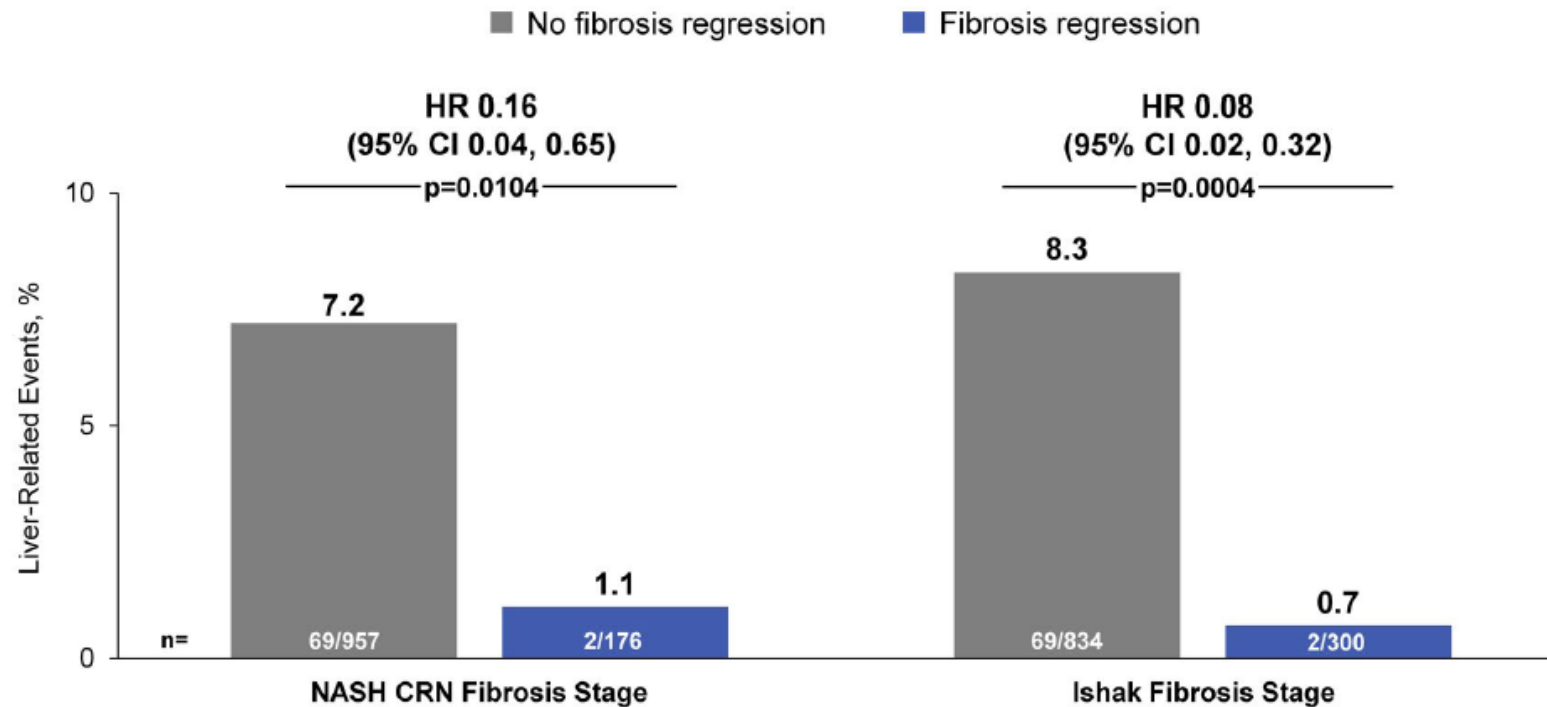
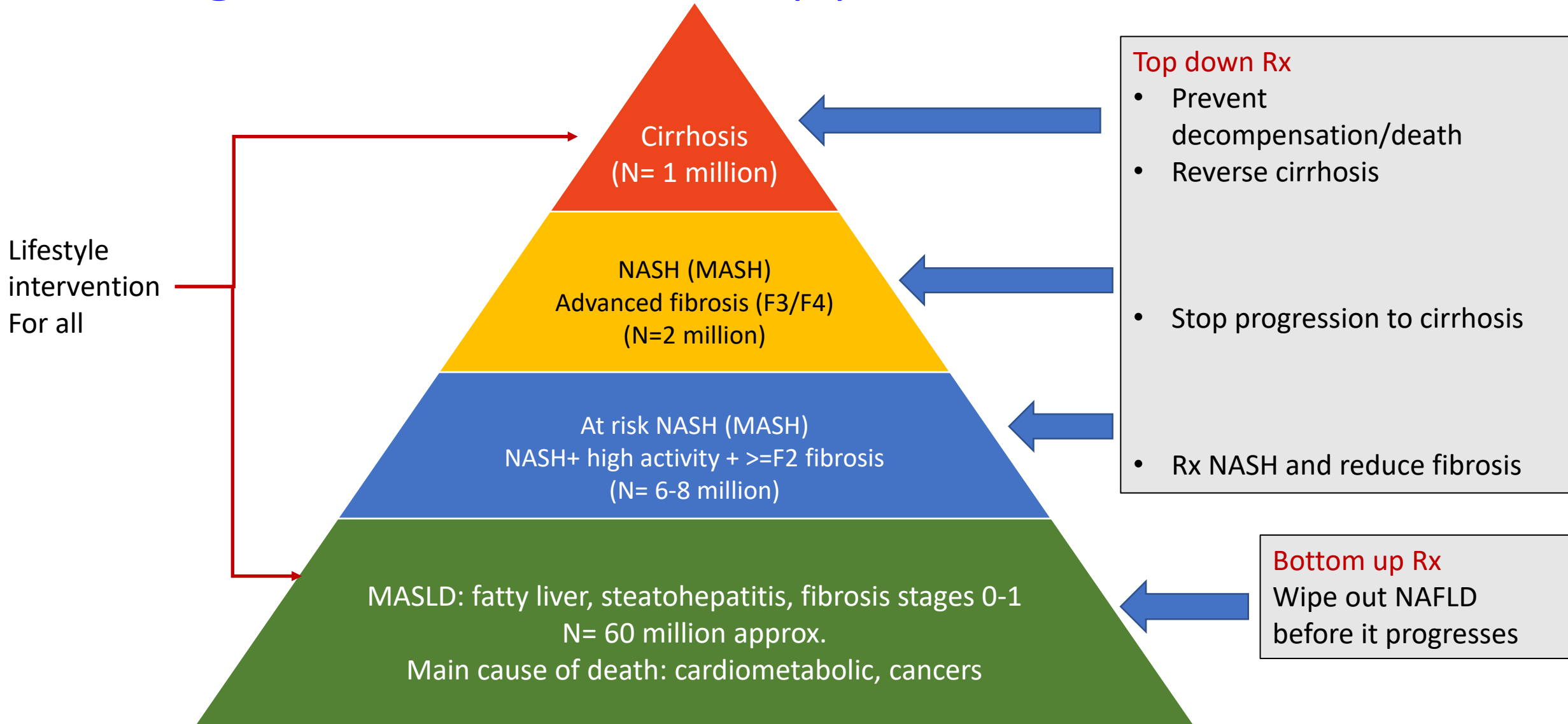


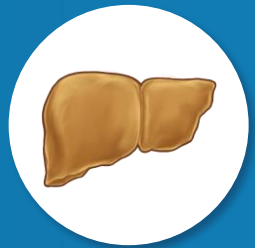
FIGURE 3 Association between fibrosis regression and liver-related clinical events. HR for clinical events with fibrosis regression vs. no fibrosis regression (reference). *p* values by Fisher's exact test

Taking down the MASLD pyramid

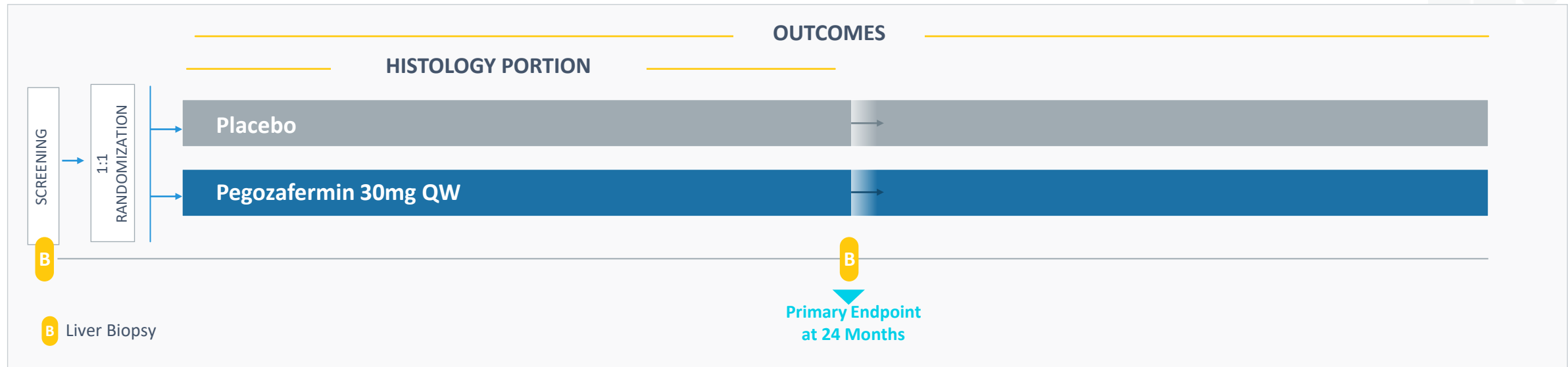


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Phase 3 ENLIGHTEN- Cirrhosis Trial in Compensated F4 MASH



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



ENlighten
cirrhosis
in Compensated
Cirrhotic (F4)
MASH patients

HISTOLOGY PORTION FOR ACCELERATED APPROVAL

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

OUTCOMES PORTION FOR FULL APPROVAL

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

ENLIGHTEN-Cirrhosis: Positioned for Success on Histology and Outcomes

HISTOLOGY

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

OUTCOMES

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

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Pegozafermin's Market Opportunity



FGF21s are the Preferred Class and Pegzofermin Offers the Most Favorable Overall Profile

KEY REASONS TO PRESCRIBE

- 1 **Reversal of fibrosis**
- 2 MASH resolution
- 3 Combinability
- 4 Improvement in other markers of cardiometabolic health

Well tolerated given chronic treatment

COMPETITIVE DIFFERENTIATION

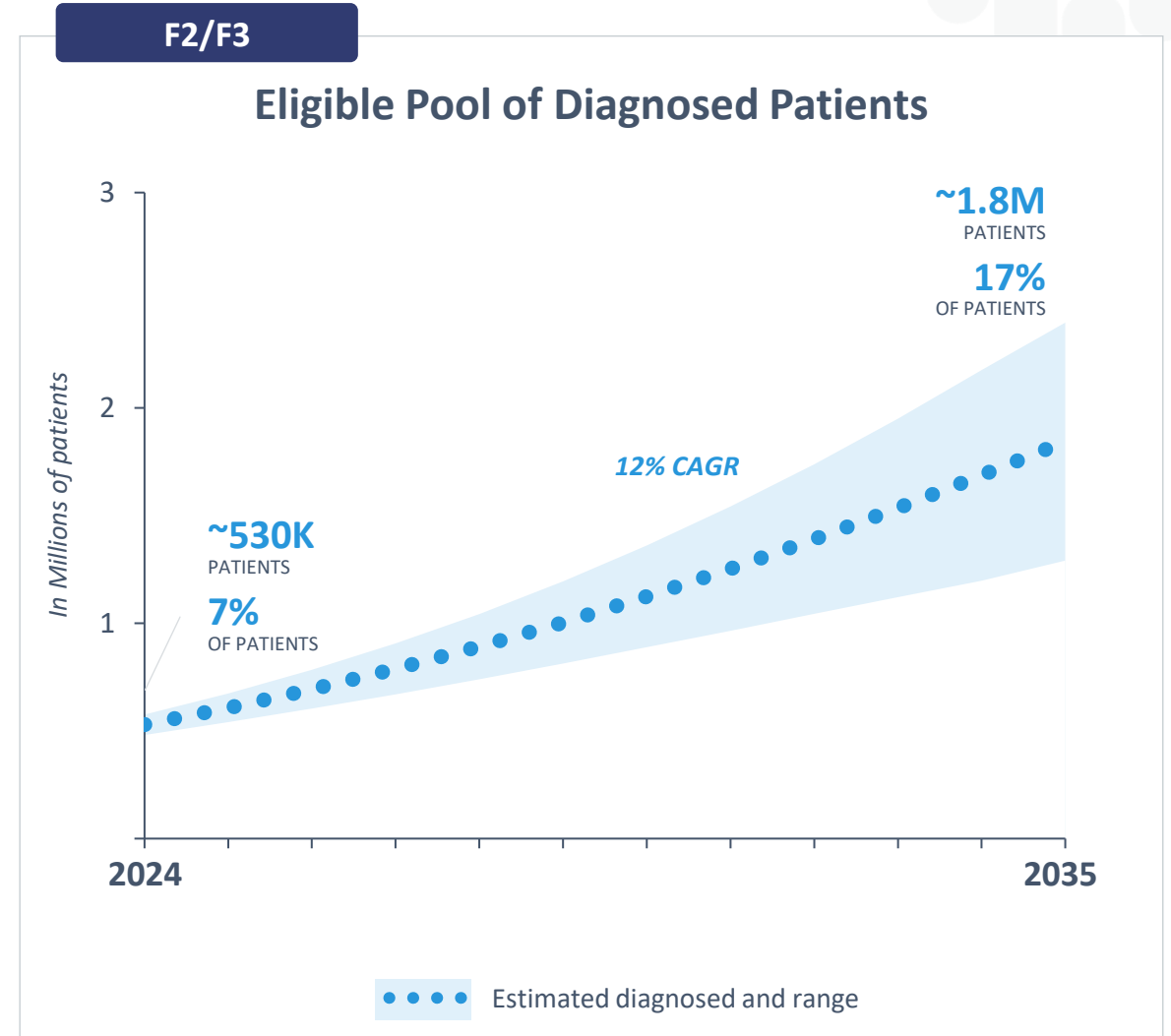
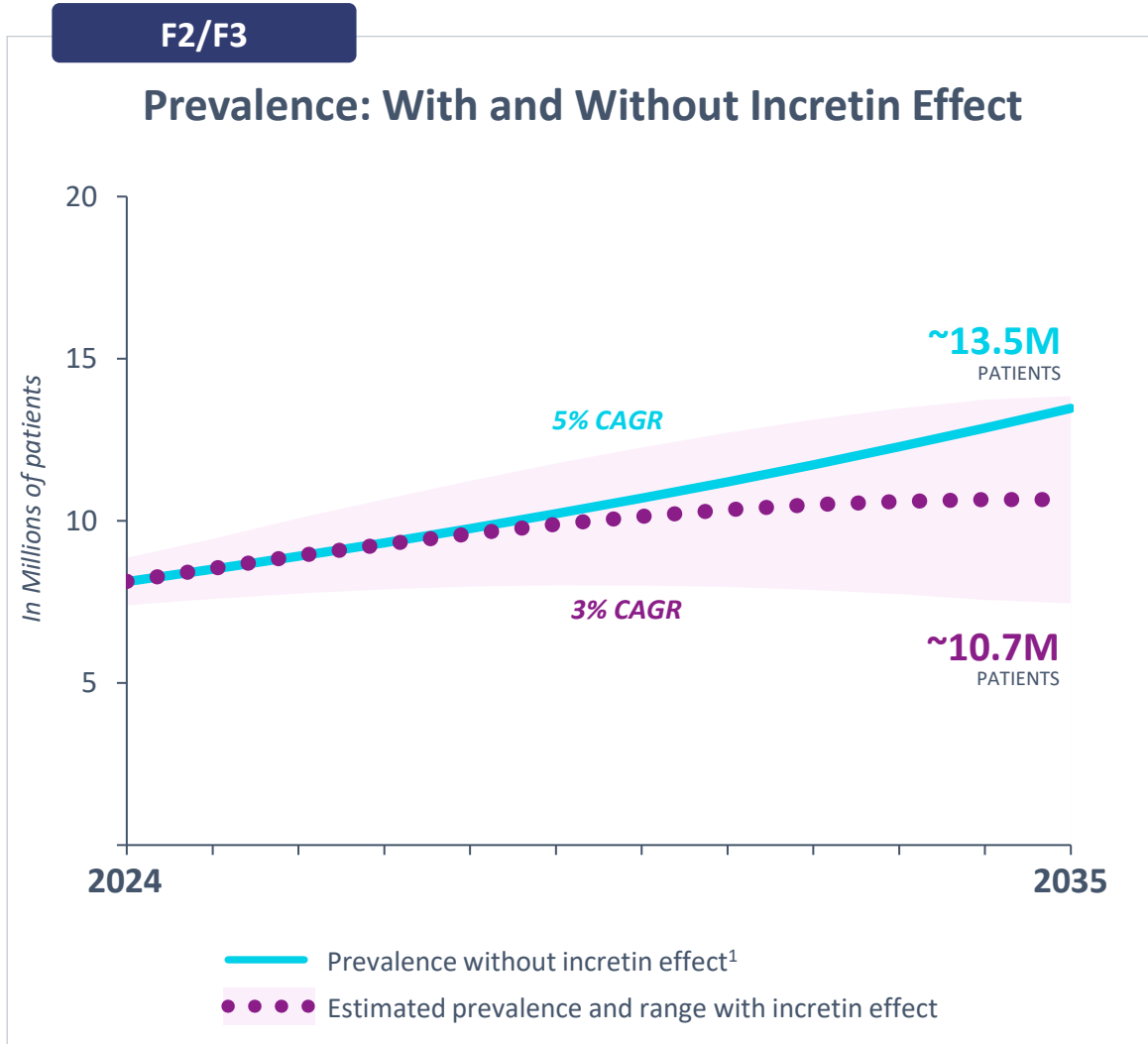
FGF21: PREFERRED CLASS

Direct anti-fibrotic effect and broad metabolic health benefits of FGF21 targeted agents recognized by HCPs

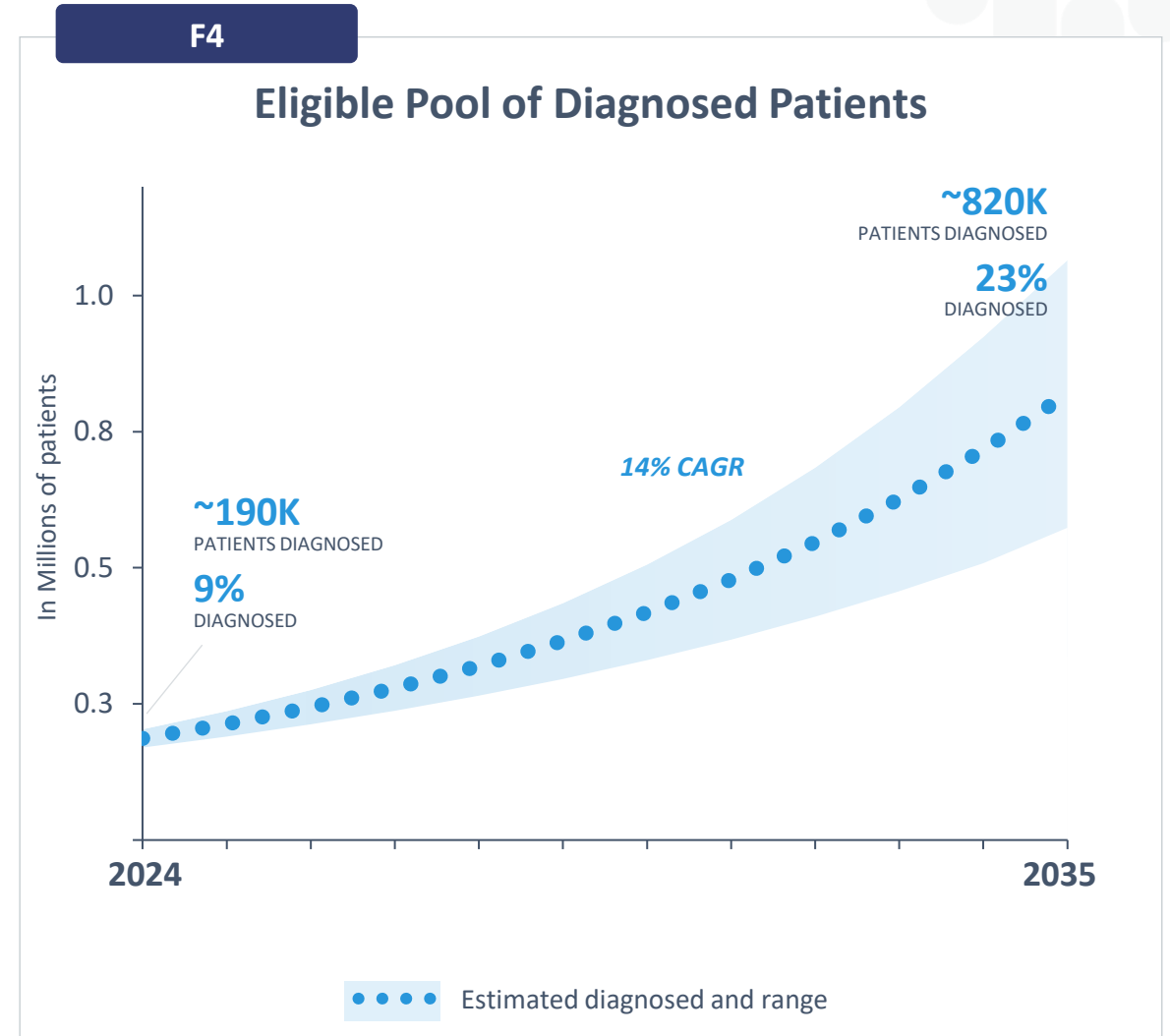
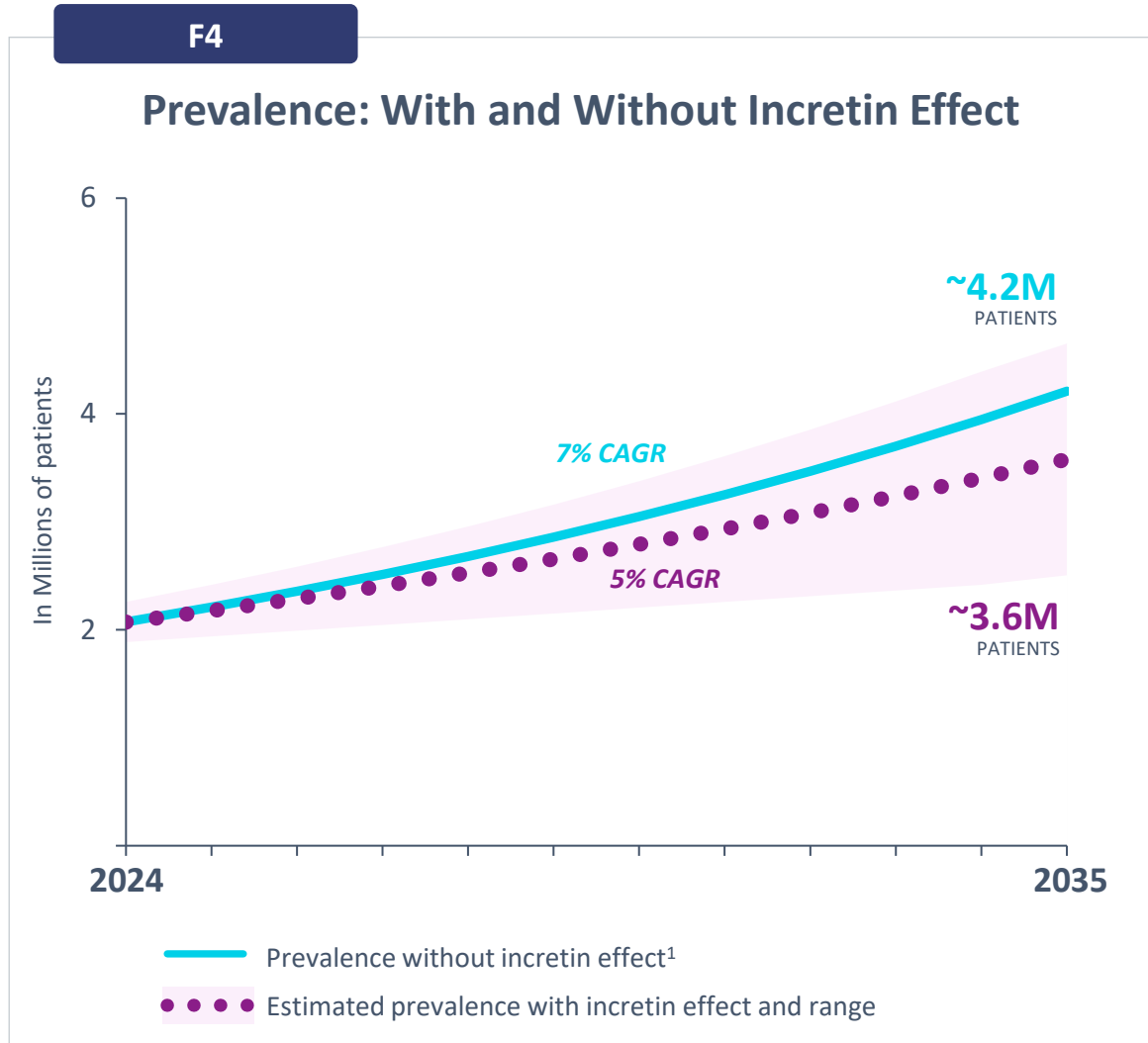
PGZ: MOST FAVORABLE OVERALL PROFILE

Best overall efficacy and tolerability profile, especially fibrosis improvement, with fewer injections

Advanced MASH (F2/F3) Represents a Significant Market



Market Opportunity in Compensated F4 Patients Continues to Grow

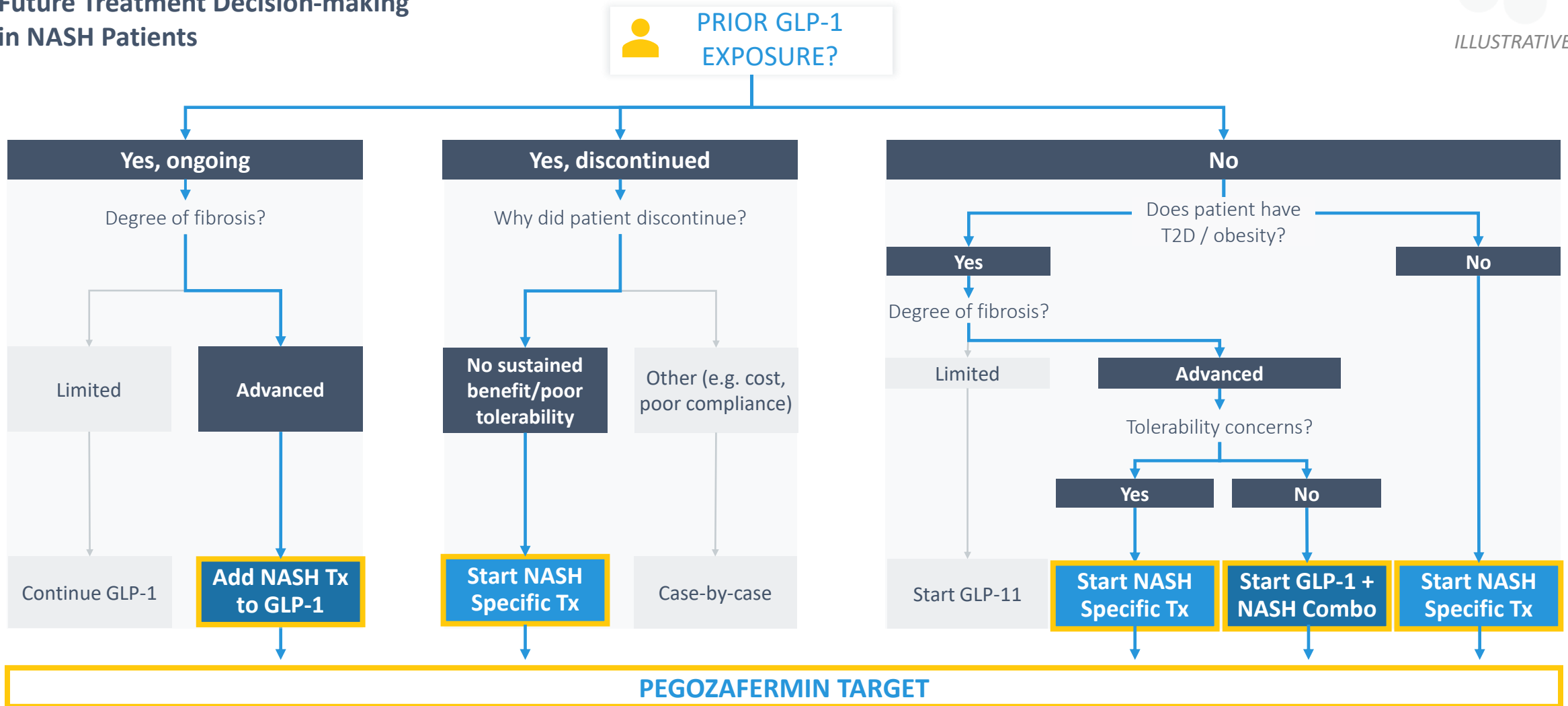


Pegozafermin – Potential Usage in Multiple Settings with GLP-1

Based on Treatment History, Fibrosis Stage and Comorbidities



Future Treatment Decision-making in NASH Patients

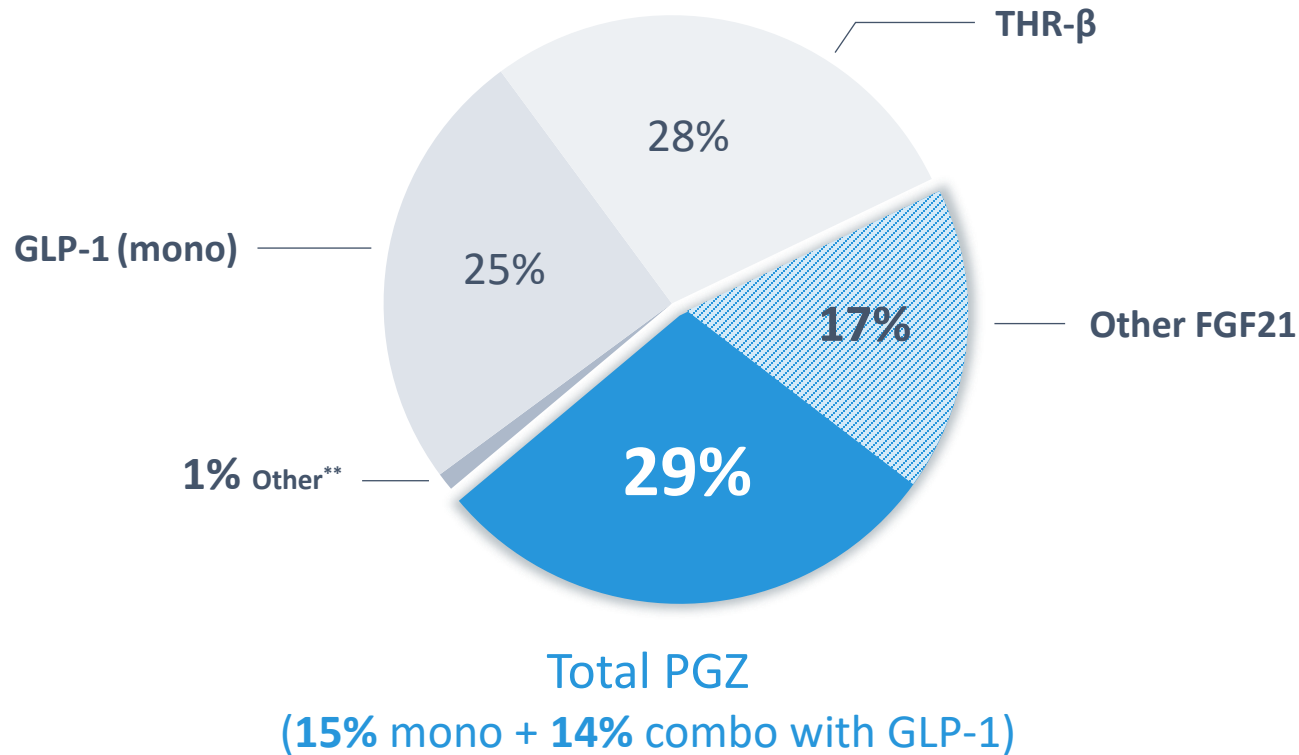


Pegozafermin Expected to Garner Significant Market Share In F3 Patients

F3

EXPECTED PRESCRIBING AMONGST HEP/GI PHYSICIANS

(% treated MASH patients)



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

- PGZ benefit/risk profile and fewer injections make it preferred FGF21
- ~50% of usage in combination with GLP-1

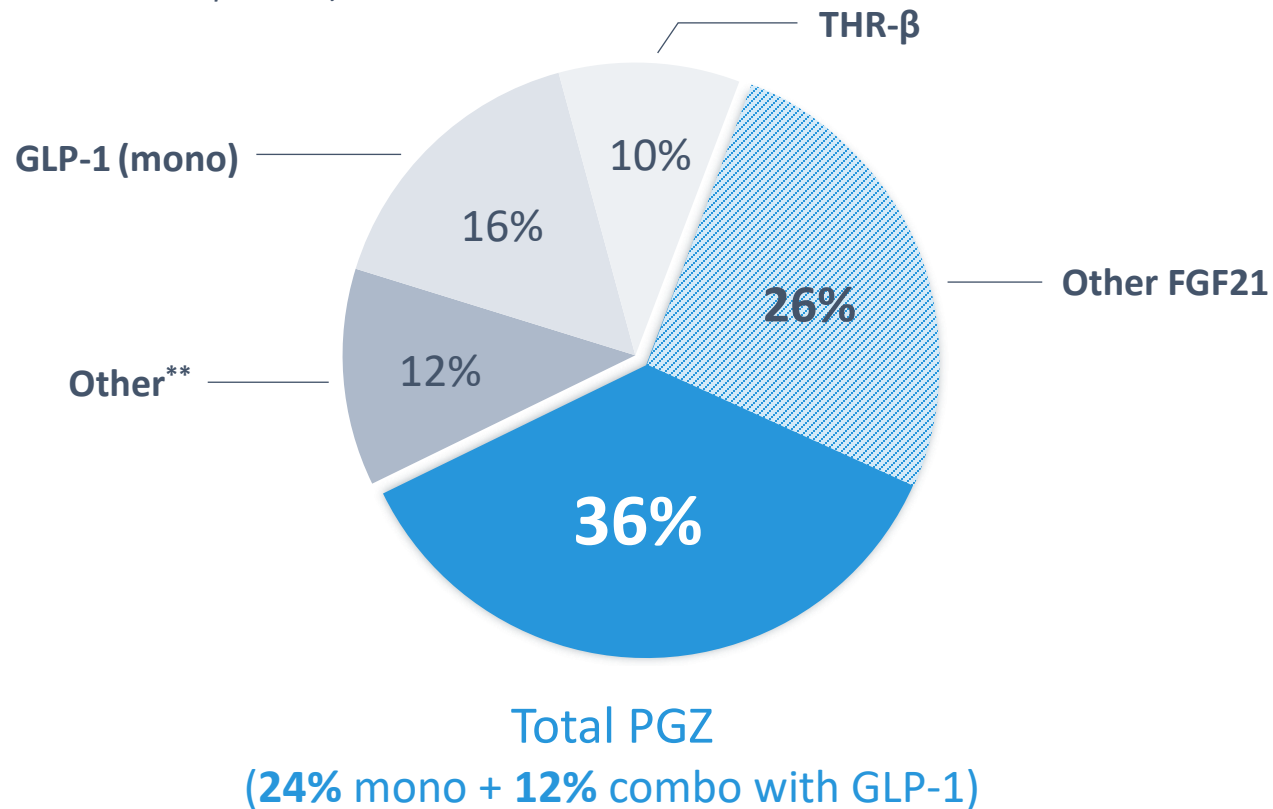
Total GLP-1 usage (combo + mono):
~65%

Pegozafermin Expected to Garner Significant Market Share In Compensated F4 Patients

Compensated F4[^]

EXPECTED PRESCRIBING AMONGST HEP/GI PHYSICIANS

(% treated MASH patients)



FGF21s garner ~60% market share, with ~60% gained by PGZ

- PGZ benefit/risk profile and fewer injections make it preferred FGF21
- 1/3rd of usage in combination with GLP-1

Total GLP-1 usage (combo + mono):
~45%

Pegozafermin is Positioned for Success on Multiple Fronts



EFFICACY DIFFERENTIATION: Reversal of fibrosis and pleiotropic metabolic benefits observed in clinical data



TOLERABILITY AND DOSING: Best-in-class (FGF21) tolerability profile, convenience of every-two-week injections, liquid formulation



LARGE MARKET OPPORTUNITY: Growing market opportunity in F4 MASH and large eligible F2/F3 market despite potential impacts from GLP-1



MULTIPLE SHOTS ON GOAL: Phase 3 trials in F3/F3 and F4 MASH with accelerated approval pathways; Phase 3 trial in SHTG

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Q&A

