UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 28, 2022

89bio, Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-39122	36-4946844
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

142 Sansome Street, Second Floor
San Francisco, CA 94104
(Address of principal executive offices, including zip code)

(415) 432-9270
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	ETNB	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01   Other Events.

On June 28, 2022, 89bio, Inc. (the "Company") issued a press release announcing positive initial data from its Phase 2 trial (ENTRIGUE) of pegozafermin (previously BIO89-100) in patients with severe hypertriglyceridemia (SHTG). The Company will host a conference call today, Tuesday, June 28, 2022 at 4:30 pm, Eastern Time, to discuss the data results.

A copy of the press release and the presentation which will be referenced during the conference call are filed as Exhibit 99.1 and Exhibit 99.2, respectively, to this Current Report on Form 8-K and are incorporated by reference herein.

Item 9.01   Financial Statements and Exhibits

(d) *Exhibits*.

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press Release, dated June 28, 2022
99.2	Slide Presentation, dated June 28, 2022
104	The cover page from the Company's Current Report on Form 8-K formatted in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

89bio, Inc.

Date: June 28, 2022

By: /s/ Rohan Palekar

Rohan Palekar
Chief Executive Officer

Exhibit 99.1

89bio Reports Positive Topline Results from ENTRIGUE Phase 2 Trial of Pegozafermin in Patients with Severe Hypertriglyceridemia (SHTG)

- Trial met primary endpoint demonstrating statistically significant and clinically meaningful reductions across all doses (63% at the 27mg QW dose; p<0.001) in triglycerides (TG) from baseline; results were consistent in patients on or not on background therapy -

- Observed significant and potent reductions in atherogenic lipids (non-HDL-C and apo B), liver fat, and improvements in liver enzymes and glycemic control markers -

- ENTRIGUE results support 89bio's transition to a late-stage development company; Phase 3 expected to initiate in first half of 2023 -

- Conference call and webcast today at 1:30 p.m. PST/4:30 p.m. EST -

SAN FRANCISCO, June 28, 2022 (GLOBE NEWSWIRE) - 89bio, Inc. (Nasdaq: ETNB), today announced positive topline results from ENTRIGUE, the Phase 2 proof-of-concept study evaluating pegozafermin for the treatment of severe hypertriglyceridemia (SHTG). Treatment with pegozafermin resulted in clinically meaningful and significant reductions in triglycerides (TG) from baseline across all doses (with a 63% reduction in the highest dosing group; p<0.001) and various subgroups, statistically significant improvements in key markers of cardiovascular risk (non-HDL-C and apo B), reductions in liver fat, and improvements in glycemic control markers.

"There is a critical need for SHTG treatment options that not only reduce triglycerides but also address broader cardiometabolic risks including hepatic steatosis and improve insulin sensitivity" said Deepak L. Bhatt, MD, MPH, Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital Heart & Vascular Center, Professor of Medicine, Harvard Medical School. "Treatment with pegozafermin demonstrated impressive triglyceride reduction coupled with meaningful reductions in non-HDL-C and improvements in cardiometabolic parameters. Taken together, pegozafermin's profile in ENTRIGUE shows great potential to uniquely address the key needs for patients with SHTG."

Results showed statistically significant reductions in median TGs from baseline across all dose groups treated with pegozafermin, compared to placebo after 8 weeks. Additionally, results were consistent in patients not on background therapy or on background therapy (consistent results on statins or statin combos, prescription fish oils, and fibrates) and across various subgroups, including those with the greatest disease burden, such as Type 2 diabetes and baseline TG levels ≥750 mg/dL.

Median Percent Change in Triglycerides from Baseline at Week 8

Dosing group	Median TG reduction
Placebo (n=18)	-12%
9mg QW (n=16)	-57%***
18mg QW (n=17)	-56%***
27mg QW (n=18)	-63%***
36mg Q2W (n=16)	-36%*

* p<0.05; *** p<0.001 versus placebo based on Wilcoxon Rank-Sum Test

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Median Percent Change in Triglycerides from Baseline at Week 8

Dosing group	Patients on background therapy[1]	Patients not on background therapy
Placebo	-18%	5%
9mg QW	-59%	-50%
18mg QW	-56%	-59%
27mg QW	-68%	-62%
36mg Q2W	-45%	-21%

1. Background therapy defined as concomitant lipid modifying therapy

Patients on background therapy: placebo (n=11), 9mg QW (n=8), 18mg QW (n=9), 27mg QW (n=10), 36mg Q2W (n=8)

Patients not on background therapy: placebo (n=6), 9mg QW (n=8), 18mg QW (n=8), 27mg QW (n=6), 36mg Q2W (n=8)

Responder analysis on primary endpoint of TG reduction demonstrated:

- A significantly higher proportion of patients reached the initial treatment goal of reducing TG <500 mg/dL on pooled pegozafermin vs. placebo (80% vs. 29%; p<0.001).

- Treatment with 27mg QW resulted in a significantly higher proportion of patients achieving TG normalization (<150 mg/dL) vs. placebo (31% vs. 0%; p<0.05) and

- Greater proportion of patients achieved significant TG reduction of ≥ 50% from baseline vs. placebo (75% vs. 6%; p<0.001).

Pegozafermin treatment also resulted in significant improvements compared to placebo (mean percent change from baseline) and clinically meaningful changes on an absolute basis in non-HDL-C and apo B that are key markers of cardiovascular risk (absolute change from baseline of 55 mg/dL and 22 mg/dL in non-HDL-C and apo B respectively with 27mg QW dose). Patients treated across all doses with pegozafermin also demonstrated an improvement in HDL-C and no change in LDL-C vs. placebo.

Mean Percent Change in non-HDL-C and apo B from Baseline at Week 8

Dosing group	non-HDL-C	apo B
Placebo	-3%	-1%
9mg QW	-14%	-11%
18mg QW	-22%**	-14%*
27mg QW	-29%***	-18%**
36mg Q2W	-9%	-1%

* p<0.05; ** p<0.01; *** p<0.001 versus placebo based on MMRM analysis

Pegozafermin treatment resulted in a mean relative reduction in liver fat from baseline at week 8 across all dose groups versus placebo in the substudy of patients with magnetic resonance imaging – proton density fat factor (MRI-PDFF) and the results are summarized in the table below.

Mean Relative Reduction in Liver Fat vs. Baseline at Week 8 in Substudy

Dosing group	MRI-PDFF
Placebo (n=6)	-5%
9mg QW (n=3)	-55%*
18mg QW (n=5)	-38%
27mg QW (n=7)	-44%
36mg Q2W (n=2)	-37%

* p<0.05 versus placebo based on ANCOVA analysis

- A significant proportion of patients responded to therapy with up to 88% and 41% of treated patients vs. 0% of placebo patients achieving a ≥30% or a ≥50% reduction in liver fat versus baseline, respectively.

- Results also demonstrated a significant reduction in liver enzymes and an improvement in glycemic control markers in pegozafermin treated patients.

Pegozafermin continues to be generally well tolerated with a favorable safety profile across doses consistent with prior studies. In ENTRIGUE, the most commonly reported treatment-related adverse events were nausea, diarrhea, and injection site reactions, all which were classified as mild or moderate. No tremors or transaminase elevation adverse events were observed. There were no drug-related serious adverse events and two Grade 2 treatment-related discontinuations.

ENTRIGUE is a randomized, double-blind, placebo-controlled trial that enrolled a total of 85 SHTG patients either on stable background therapy (55% - statin/statin combos, and/or prescription fish oil, and/or fibrates) or not on any background therapy treated weekly or every two-weeks with pegozafermin. The trial enrolled an advanced population with high risk of cardiovascular disease as evidenced by mean baseline values of treated patients with TGs of 733 mg/dL, non-HDL-C of 211 mg/dL, 43.5% with HbA1c ≥6.5%, and liver fat content of 20.1%.

Hank Mansbach, Chief Medical Officer of 89bio, commented, "We are extremely pleased by the robust and consistent results observed across multiple measures and patient subgroups in this study. These results add to the body of evidence demonstrating pegozafermin's unique and differentiated profile based on broad metabolic effects and a favorable safety/tolerability profile. These positive data support the advancement into a Phase 3 trial in SHTG based on regulatory precedent, which we plan to initiate in the first half of 2023. These results also build confidence in our ongoing Phase 2b ENLIVEN trial in NASH with data expected in the first quarter of 2023."

Rohan Palekar, Chief Executive Officer of 89bio, added, "SHTG remains a significant market opportunity with a large patient population who are underserved with the existing therapeutic options. In market research, physicians have indicated a strong preference for a drug that could address the metabolic co-morbidities, especially the liver fat benefit seen in a majority of these patients. We believe the results from ENTRIGUE position pegozafermin as potentially the first FGF21 analog to market and to become an important metabolic drug for treatment of cardio-metabolic and liver disease."

Today's Conference Call Information

89bio will host a conference call and webcast at 1:30 p.m. PST / 4:30 p.m. EST today, June 28, 2022. Analysts and investors can participate in the conference call by dialing (1-877-704-4453) or domestic callers and +1 (1-201-389-0920) for international callers, using the conference ID 13730718. The webcast can be accessed live here and on the Events & Presentations page in the Investors section of the 89bio website, www.89bio.com. The webcast will be archived on the company's website for at least 30 days after the conference call.

About pegozafermin

Pegozafermin is a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (FGF21) being developed for the treatment of non-alcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). FGF21 is an endogenous hormone that modulates important drivers of NASH including glycemic control, steatosis, inflammation and fibrosis. Pegozafermin was specifically engineered using a unique glycoPEGylated technology to extend the half-life while maintaining potency. Recent Phase 1b/2a data with pegozafermin in biopsy-confirmed NASH patients demonstrated clinically meaningful changes on histology endpoints and non-invasive measures of total liver health, in patients with NASH as well as many of the underlying metabolic comorbidities commonly associated with NASH. Pegozafermin is currently being evaluated in the Phase 2b ENLIVEN trial in NASH.

About 89bio

89bio is a clinical-stage biopharmaceutical company dedicated to the development and commercialization of innovative therapies for the treatment of liver and cardiometabolic diseases. The company is focused on rapidly advancing its lead candidate, pegozafermin, through clinical development for the treatment of non-alcoholic steatohepatitis (NASH) and severe hypertriglyceridemia (SHTG). The company is headquartered in San Francisco with operations in Herzliya, Israel. For more information, visit www.89bio.com or follow the company on LinkedIn.

Forward-looking Statements

Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws, including, but not limited to, the therapeutic potential and clinical benefits of pegozafermin for the treatment of SHTG, the efficacy and safety of pegozafermin, pegozafermin's potential as a compelling treatment option for SHTG, the expected timing of the initiation of the Phase 3 trial in SHTG, the expected timing of data from the ongoing Phase 2b ENLIVEN trial in NASH and the relationship between the results from the positive data from Phase 2 ENTRIGUE trial and results of future or ongoing clinical studies, including the ongoing Phase 2b ENLIVEN trial in NASH. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "develop," "plan" or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward looking statements. While 89bio believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to us on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in 89bio's filings with the SEC), many of which are beyond 89bio's control and subject to change. Actual results could be materially different. Risks and uncertainties include: positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; and other risks and uncertainties identified in 89bio's Annual Report on Form 10-K for the year ended December 31, 2021, its Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 and other subsequent disclosure documents filed with the SEC. 89bio claims the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. 89bio expressly disclaims any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.
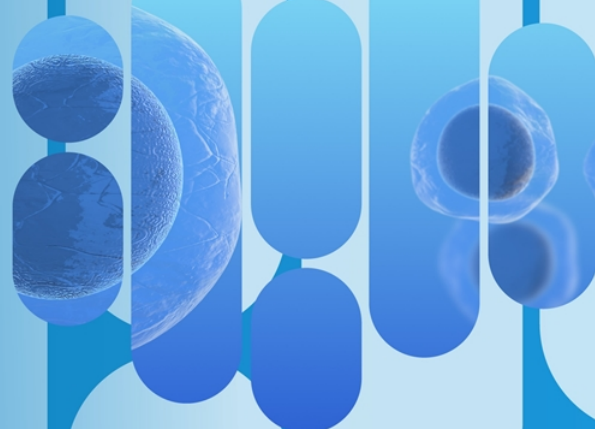
Investor Contact:
Ryan Martins
Chief Financial Officer
investors@89bio.com

Exhibit 99.

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Powerful Science
Meaningful Medicines
Changing Lives

Pegozafermin Phase 2 (ENTRIGUE) Topline Results in Severe Hypertriglyceridemia (SHTG)

Nasdaq: ETNB

Disclaimer

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2

Pegozafermin – Potential Important New Cardio-Metabolic Drug

ENTRIGUE results demonstrate compelling and differentiated profile in SHTG

- Significant impact on triglycerides, liver fat, and associated metabolic co-morbidities
- Favorable safety and tolerability profile
- Exceeds target product profile defined by literature, KOLs & treating physicians

SHTG represents a large potential opportunity given pegozafermin's profile

- High unmet needs for better therapeutic options to address broader metabolic comorbidities
- Approved therapies are sub-optimal resulting in large uncontrolled or untreated population

Results support advancing to Phase 3 – potential first FGF21 analog to market

- Potentially quicker and efficient regulatory path to approval in SHTG
- Phase 3 initiation expected in 1H23; topline results ~ 2 years from study start

ENTRIGUE results increase confidence in overall pegozafermin program - NASH ENLIVEN topline now expected in 1Q23

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SHTG is a Serious Disease in Need of Better Treatment Options

Patients with SHTG have multiple co-morbidities and significant health risks

- Increased Cardiovascular (CV) Risk
  - Increased risk of CV disease, heart failure and ischemic stroke
  - Increased mortality in patients with CHD
- Increased risk of Acute Pancreatitis
- Increased prevalence of Diabetes

> *"Most patients with severe hypertriglyceridemia have multiple ASCVD risk factors and are at enhanced risk of developing atherosclerotic disease. This risk is conveyed by atherogenic VLDL plus other factors, such as obesity, metabolic syndrome, and hyperglycemia" [2018 AHA/ACC Guideline For Cholesterol Management]*

Average patient in ENTRIGUE study was estimated to have a 23% risk of Major Cardiovascular Events (MACE) over 10 years *(per ACC ASCVD risk estimator)*

- Average patient: no prior CV event, 54 years old, male, white, BP 131/81, total cholesterol 240, HDL 28, LDL 89, diabetic, non-smoker, taking anti-hypertensive medication, no statins or aspirin. Individual risks may vary.

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ASCVD = Atherosclerotic cardiovascular disease

SHTG is a Large Underserved Market

High Prevalence Disease: ~4M patients in the United States

Existing therapies have limitations

- Fish Oils: Minimal to moderate TG reduction, LDL elevations (some), no liver benefits
- Fibrates: Moderate TG reduction, major increase in LDL, myopathies
- Statins (not approved for SHTG): Moderate TG reduction with high intensity regimen, other lipid benefits, potential liver and muscle toxicity

~50%* of diagnosed/treated patients are uncontrolled representing ~ 750,000 to 1,000,000 patients

Market needs a therapy that offers:

- More effective triglyceride reduction
- Improvement in other lipids that impact CV risk
- Improvement in liver fat and no worsening of liver function
- Improvement in glycemic control measures

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* 50% is based on registrational trials of Vascepa and Epanova (4mg/day) approved in SHTG

Proposed Mechanisms of Action for Pegozafermin in SHTG

- **Adipose tissue**
  - Decrease lipogenesis and release of FFA
  - Improve insulin resistance
  - Increase TG uptake
  - Increase adiponectin

- **Liver**
  - Increase β-oxidation
  - Decrease de novo lipogenesis
  - Decrease FFA / TG

- **Muscle**
  - Increase FFA oxidation
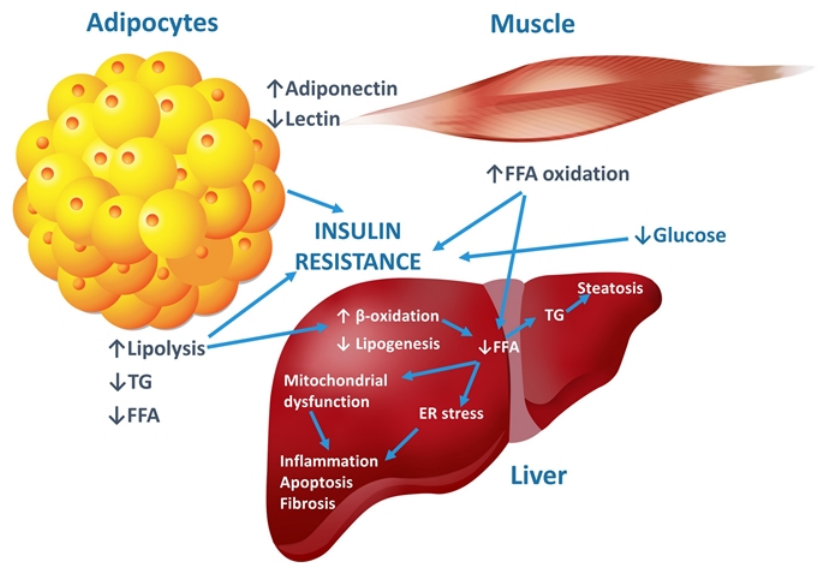
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ENTRIGUE Data

ENTRIGUE – Phase 2 SHTG Trial Design

8 Weeks

		PLACEBO	(n=18)
SCREENING	RANDOMIZATION	9mg QW Pegozafermin	(n=16)
		18mg QW Pegozafermin	(n=17)
		27mg QW Pegozafermin	(n=18)
		36mg Q2W Pegozafermin	(n=16)

SAFETY FOLLOW-UP

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)

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KEY INCLUSION CRITERIA

- TG ≥500 mg/dL and ≤2,000 mg/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

Baseline Characteristics
Represents an Advanced Population at High Risk for CV Disease

Parameter Mean or %	Placebo (n=18)	PGZ Pooled (n=67)	PGZ 9mg QW (n=16)	PGZ 18mg QW (n=17)	PGZ 27mg QW (n=18)	PGZ 36mg Q2W (n=16)	Total (n=85)
Age (years)	57.5	52.7	54.6	49.2	53.9	53.1	**53.7**
Male (%)	66.7	77.6	68.8	82.4	72.2	87.5	**75.3**
Body Weight (kg)	98	99	100	97	99	99	**99**
Type 2 Diabetes (%)	61.1	47.8	56.3	35.3	55.6	43.8	**50.6**
TG (mg/dL)	720	736	722	709	680	840	**733**
Non-HDL-C (mg/dL)	220	209	216	203	203	215	**211**
HDL-C (mg/dL)	28	28	31	27	31	25	**28**
LDL-C (mg/dL)	88	89	92	88	97	80	**89**
Apo-B (mg/dL)	116	115	120	115	119	106	**115**
HbA1c ≥6.5% (%)	38.9	44.8	56.3	35.3	50.0	37.5	**43.5**
ALT (U/L)	29.1	33.9	36.3	36.9	33.0	29.2	**32.8**
Liver Fat Content (%) (n=24)	16.5 [n=6]	21.3 [n=18]	19.8 [n=3]	18.0 [n=5]	22.4 [n=7]	25.5 [n=3]	**20.1** [n=24]

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Baseline Characteristics: Approximately 50% on Background Therapy
Represents Real World Setting

	Placebo (n=18)	PGZ Pooled (n=67)	PGZ 9mg QW (n=16)	PGZ 18mg QW (n=17)	PGZ 27mg QW (n=18)	PGZ 36mg Q2W (n=16)	Total (n=85)
Any background therapy	61%	54%	50%	53%	61%	50%	**55%**
Statins/statin combo	50%	43%	38%	53%	39%	44%	**45%**
Prescription fish oil	11%	15%	6%	12%	22%	19%	**14%**
Fibrates	17%	5%	0	0	17%	0	**7%**
Other	6%	13%	13%	18%	11%	13%	**12%**

Patients may be on > 1 lipid-modifying therapy

Background therapy defined as concomitant lipid-modifying therapy

Other includes bempedoic acid, ezetimibe alone and ezetimibe as ingredient in combination

Pegozafermin Significantly Reduces Triglycerides across All Dose Groups
Primary Endpoint
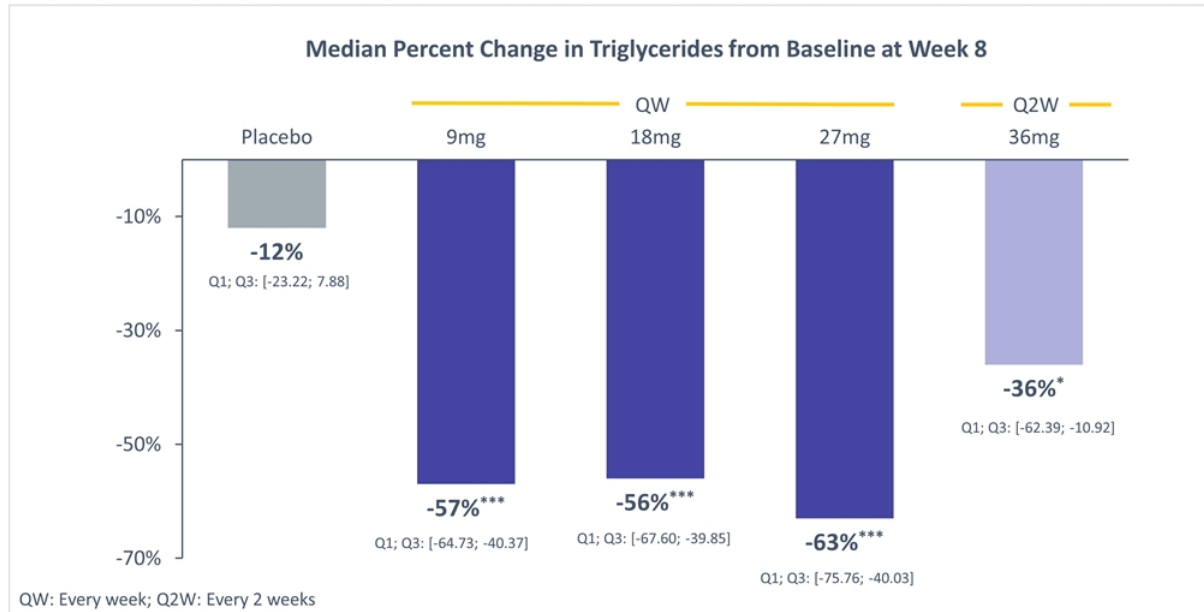
Median Percent Change in Triglycerides from Baseline at Week 8

	QW	QW	QW	Q2W
Placebo	9mg	18mg	27mg	36mg
-12%	**-57%***	**-56%***	**-63%***	**-36%***
Q1; Q3: [-23.22; 7.88]	Q1; Q3: [-64.73; -40.37]	Q1; Q3: [-67.60; -39.85]	Q1; Q3: [-75.76; -40.03]	Q1; Q3: [-62.39; -10.92]

QW: Every week; Q2W: Every 2 weeks

Pegozafermin Shows Significant Decrease in Triglycerides on Top of Background Therapy

Median Percent Change in Triglycerides from Baseline at Week 8
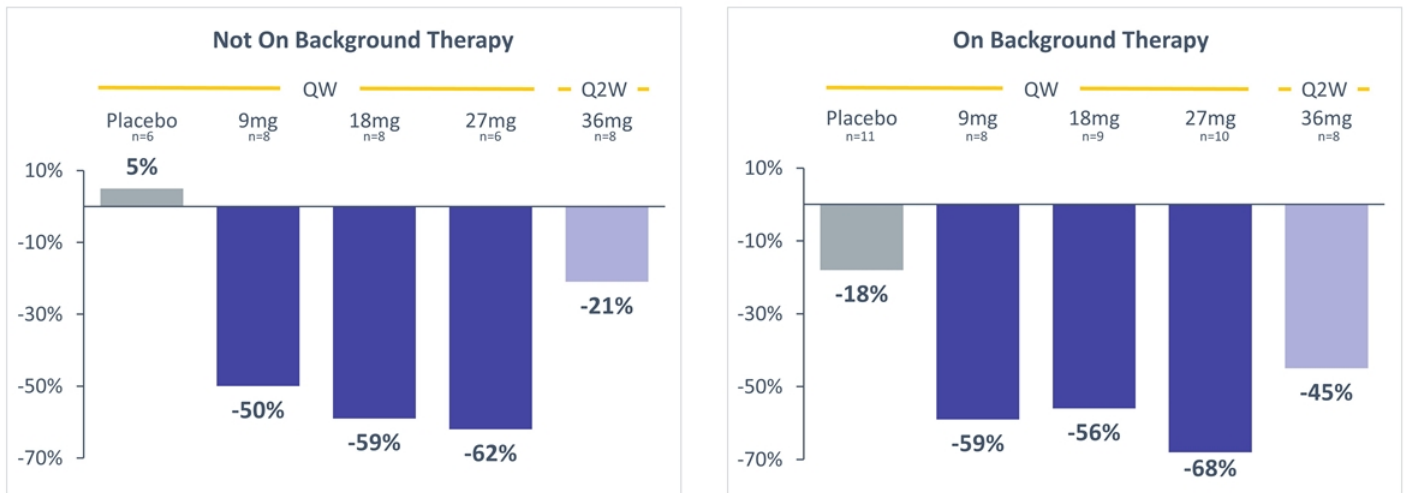
Results are consistent with data from patients on background therapy of statins or statin combos, prescription fish oils, and fibrates

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

Pegozafermin Shows Consistent and Significant Benefit in Triglyceride Reduction across All Key Subgroups

Median Percent Change in Triglycerides from Baseline at Week 8

N=(placebo, PGZ pooled)	Placebo	PGZ pooled
Baseline TG ≥750 mg/dL		
Yes (n=4,23)	-20%	-63%
No (n=13,42)	0%	-52%
Type 2 Diabetes		
Yes (n=10,31)	-17%	-62%
No (n=7,34)	-8%	-51%
Region		
US (n=13,43)	-8%	-58%
EU (n=4,22)	-23%	-57%

Similar trends were observed in subgroup analyses based on other baseline characteristics

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Pegozafermin Shows Significant Decrease in Triglycerides at Different Threshold Levels

A. Responders (< 500 mg/dL)
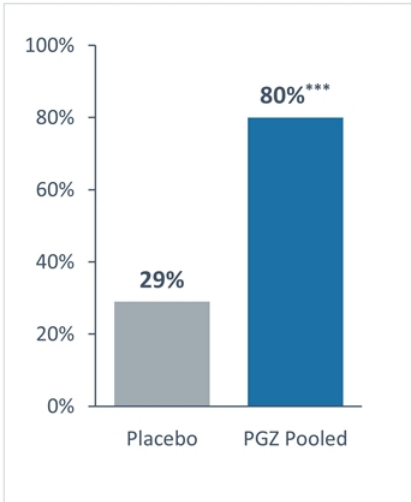
B. TG Normalization (<150mg/dL, <200mg/dL)
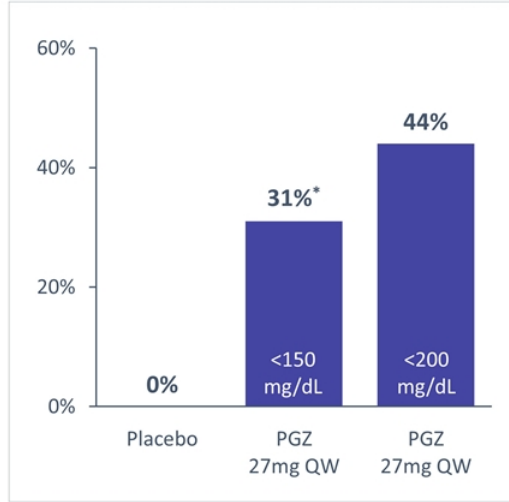
C. TG Reduction ≥50% from baseline
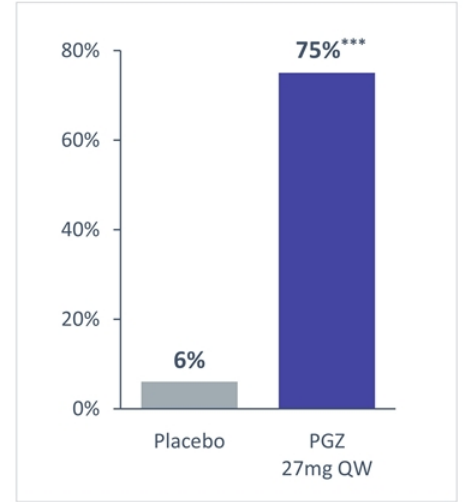
Analysis via unstratified Chi-square test comparing the individual PGZ groups vs placebo. * p<0.05; ** p<0.01; *** p<0.001 versus placebo
TG Responders defined as patients who achieve TG <500 mg/dL
Full Analysis Set

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

Mean Percent Change from Baseline at Week 8
Non-HDL-C
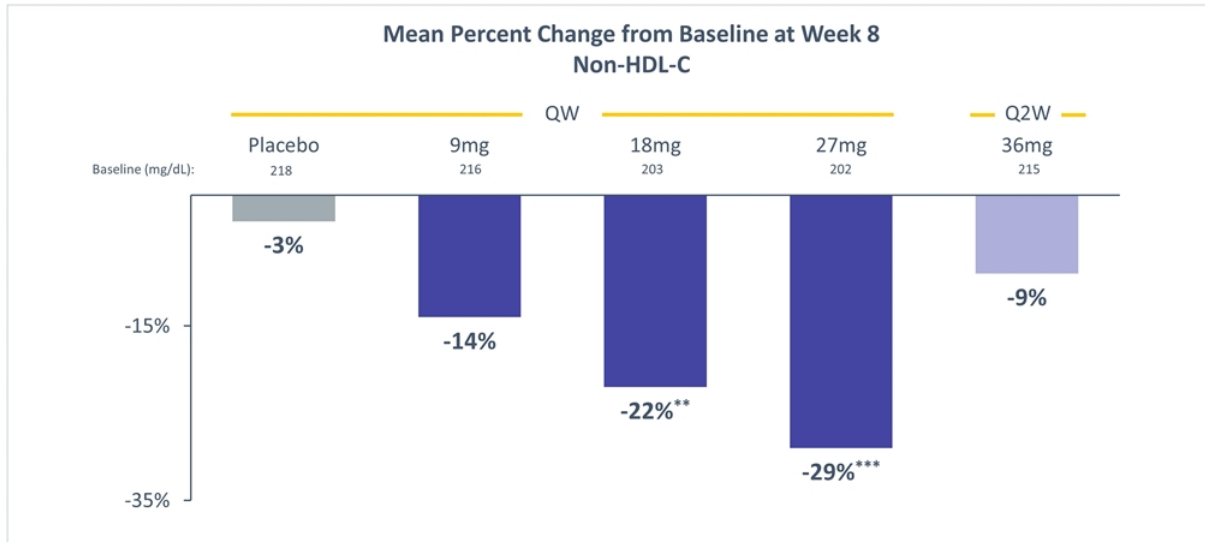
Non-HDL-C measures the cholesterol in atherogenic particles including LDL-C, IDL-C, and VLDL-C and is considered a better measure of CV risk in hypertriglyceridemia [‡]

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Pegozafermin Demonstrated Reduction in Absolute Non-HDL-C
Absolute Non-HDL-C Reduction is Associated with MACE Improvement

Mean Absolute Change from Baseline at Week 8 Non-HDL-C

	QW			Q2W
Placebo	9mg	18mg	27mg	36mg
Baseline (mg/dL): 218	216	203	202	215

Placebo: -14.0
9mg: -41.0
18mg: -54.0
27mg: -55.0
36mg: -27.0

Mean percent change in HDL-C up to 29%

Non-HDL-C reduction of 55 mg/dL is associated with a 25-30% reduction in MI or CV death

Figure adapted from: The HPS3/TIMI55–REVEAL Collaborative Group, NEJM 2017; 377: 1217-27
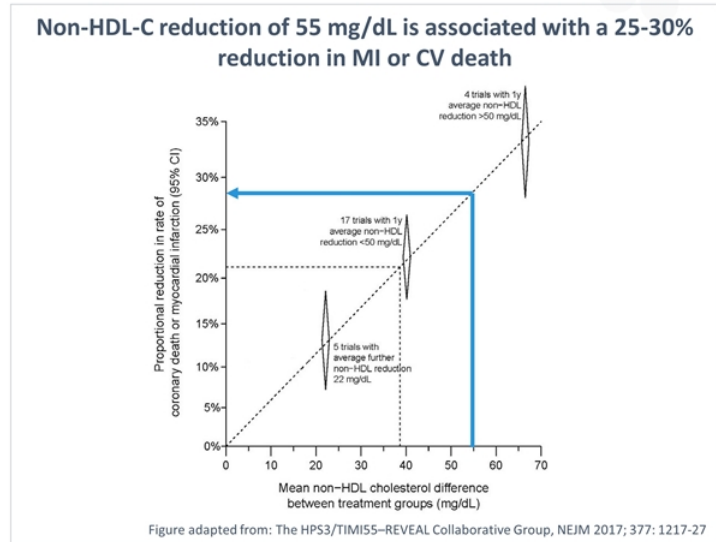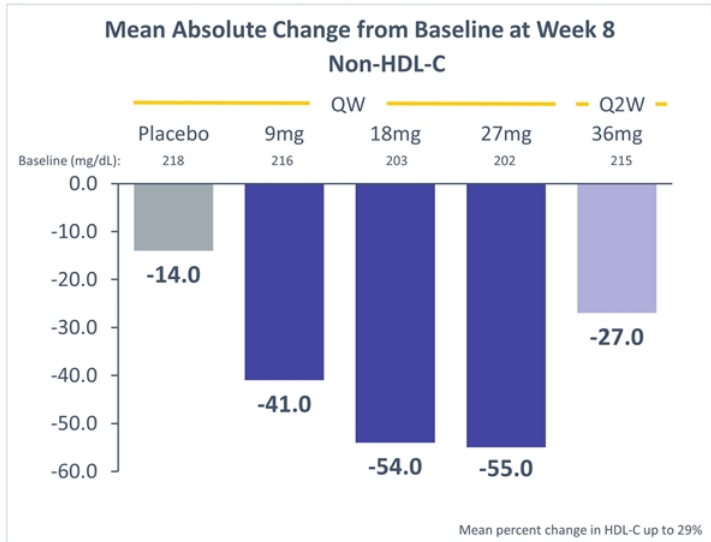
Non-HDL-C reduction of 55 mg/dL is associated with a 25-30% reduction in MI or CV death[†]

Full Analysis Set; * p<0.05; ** p<0.01; *** p<0.001 versus placebo based on MMRM analysis
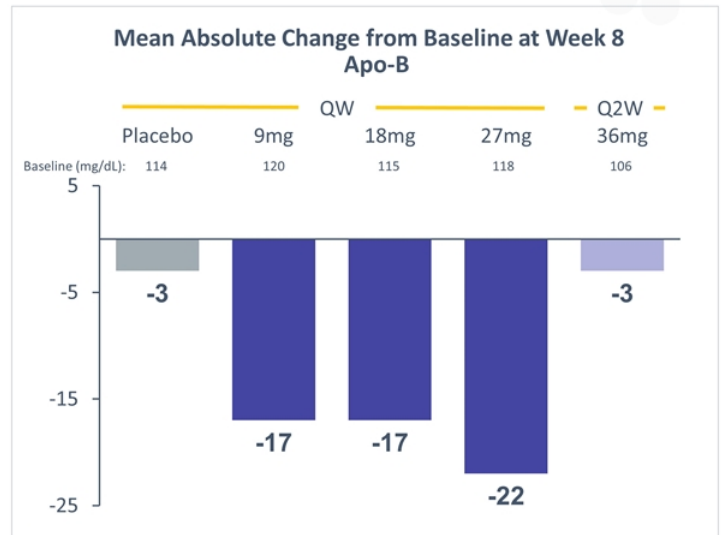[†] The HSP3/TIM55-REVEAL Collaboration Group. NEJM, 2017.

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Pegozafermin Demonstrated Clinically Meaningful Improvements in Apo-B – Key Marker of CV Risk

Mean Percent Change from Baseline at Week 8
Apo-B

	QW			Q2W
Placebo	9mg	18mg	27mg	36mg
Baseline (mg/dL): 114	120	115	118	106

- Placebo: -1%
- 9mg: -11%
- 18mg: -14%*
- 27mg: -18%**
- 36mg: -1%

Mean Absolute Change from Baseline at Week 8
Apo-B

	QW			Q2W
Placebo	9mg	18mg	27mg	36mg
Baseline (mg/dL): 114	120	115	118	106

- Placebo: -3
- 9mg: -17
- 18mg: -17
- 27mg: -22
- 36mg: -3
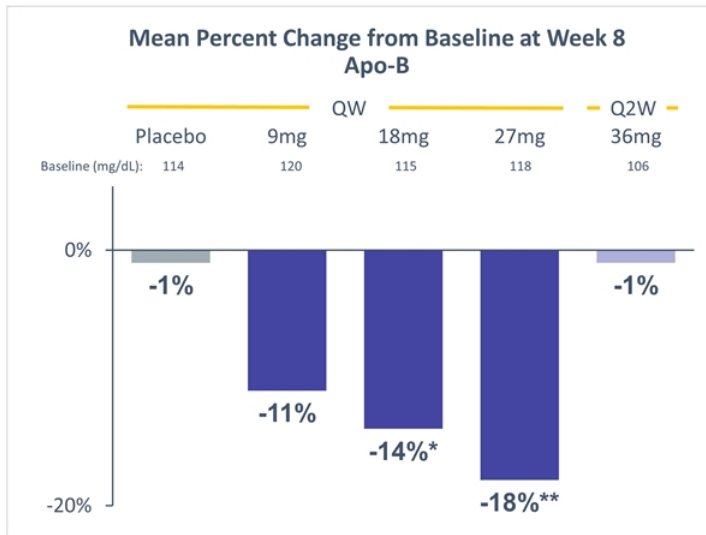
Apo-B is a critical structural protein in atherogenic lipoproteins including LDL-C and is a direct measure of number of atherogenic lipoprotein particles. Apo-B has been proposed as a more accurate indicator of CV risk than LDL-C.[1]

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p value vs placebo based on MMRM analysis
Full Analysis Set; * $p<0.05$; ** $p<0.01$; *** $p<0.001$ versus placebo
[1]Behbodikhah J, Metabolites 2021; Ference B, *JAMA* 2019.

Pegozafermin Demonstrated Significant Reduction in Liver Fat
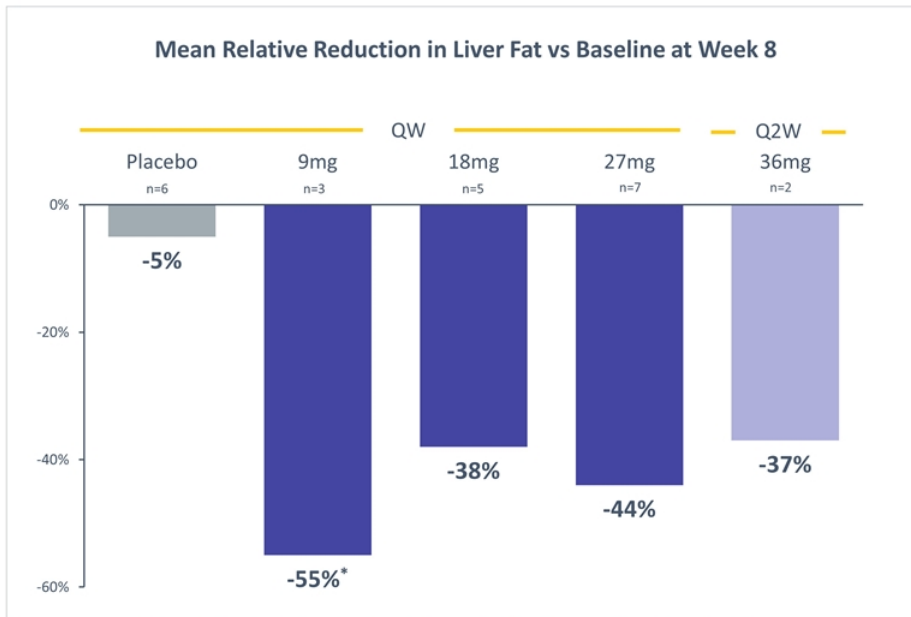## *Liver Fat Is an Important Potentiator of CV Risk*

Mean Relative Reduction in Liver Fat vs Baseline at Week 8

	QW			Q2W
Placebo n=6	9mg n=3	18mg n=5	27mg n=7	36mg n=2
-5%	-55%*	-38%	-44%	-37%

Post-hoc analysis of patients with follow-up MRI-PDFF ≤21 days from date of last dose in 27mg QW cohort (n=5) demonstrated a 63% mean relative reduction from baseline.
*p <0.05 versus placebo
MRI Analysis Set; p value vs placebo based on ANCOVA analysis

HIGH RESPONDER RATES

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

- **≥ 50% Reduction in liver fat: 41%** *vs 0% in placebo*

- **Normalized liver fat: 24%** *vs 0% in placebo*

Pegozafermin (n=17) and Placebo (n=6)
Post-hoc analysis of patients with follow-up MRI-PDFF ≤21 days from date of last dose (n=14) resulted in 29% of patient with normalized liver fat and 100% and 50% of patients with mean relative reductions of ≥30% and ≥50% from baseline, respectively.
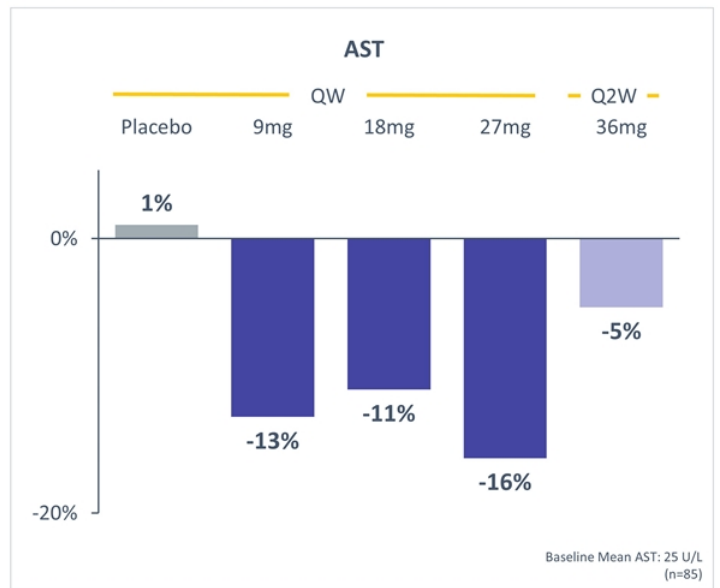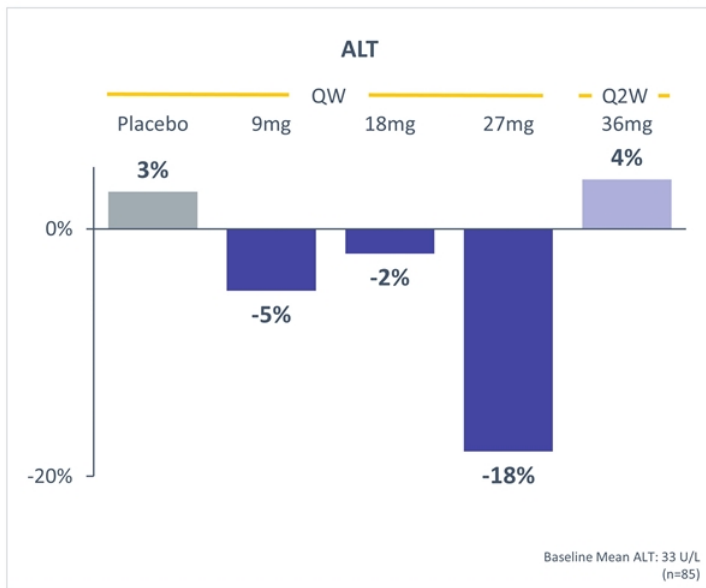
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Pegozafermin Improved Liver Function Despite Normal Levels at Baseline

Mean Percent Change from Baseline at Week 8

Pegozafermin Demonstrated Improvement on HbA1c that May Increase with Longer Treatment

Absolute Change in HbA1c at Week 8 in ENTRIGUE

Total Patient Population

Placebo n=17: -0.1
27mg n=16: -0.3

Mean absolute change

Patients with Baseline HbA1c ≥ 6.5%

Placebo n=6: -0.2
27mg n=9: -0.4

HbA1c: Mean Baseline 27 mg QW: 7.48%; Week 8: 7.08%
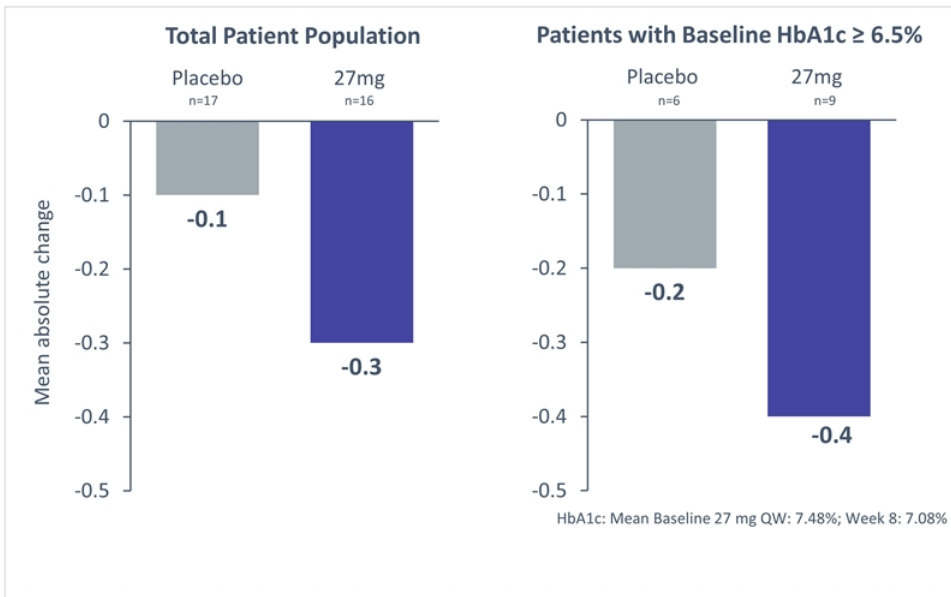
Absolute change in HbA1c in 20-week NASH study

Patients with Baseline HbA1c ≥ 6.5%

Week 12: -0.5*
Week 20: -0.9**

Study BIO89-100-002; Cohort 7: n=10 at PGZ 27 mg QW
HbA1c: Baseline: 7.3%; Week 20: 6.4%
Patients with baseline HbA1c ≥ 6.5% were on an average of 2 anti-diabetic medications.
*p<0.05; **p<0.01; ***p<0.001. p value for change from baseline based on MMRM analysis

89bio   Full analysis set; MMRM analysis

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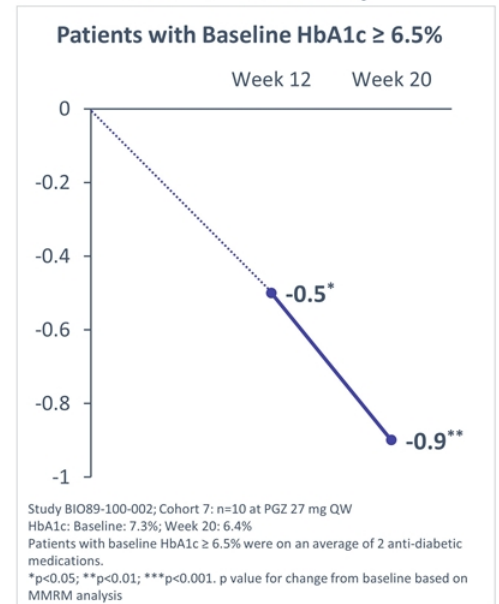
Pegozafermin Was Well Tolerated Across Doses
Safety profile consistent with prior studies

Low Incidence of Treatment-Related AEs in ≥ 7.5% of Pooled Pegozafermin Group

Preferred Term	Placebo (n=18)	PGZ Pooled (n=67)	PGZ 9mg QW (n=12)	PGZ 18mg QW (n=21)	PGZ 27mg QW (n=18)	PGZ 36mg Q2W (n=16)
Nausea	0	10%	0%	5%	22%	13%
Diarrhea	0	9%	17%	5%	17%	13%
Injection site reaction	0	9%	8%	10%	6%	13%

All AEs were Grade 1 or 2; No Grade 3 or higher TEAEs reported. No tremor or transaminase elevation AEs reported.

	Placebo (n=18)	PGZ Pooled (n=67)	PGZ 9mg QW (n=12)	PGZ 18mg QW (n=21)	PGZ 27mg QW (n=18)	PGZ 36mg Q2W (n=16)
Serious adverse event (unrelated)	0	1*	0	0	1	0
Treatment emergent discontinuations (related/unrelated)	0	2^/2	0	0	2^/2	0

*Unrelated SAE of Grade 2 hypertension; patient withdrew
^Grade 2 abdominal cramps (1) and Grade 2 nausea/vomiting (1)

89bio   Safety Analysis Set; patients reported on as treated basis

Pegozafermin – Unique and Differentiated Profile in SHTG

Efficacy

- Significant reduction in triglycerides across all dose groups – up to 63% (27 mg QW)
    - Results consistent in patients with or without background therapy
    - Result consistent across various subgroups (high/low baseline TGs, Type 2 diabetes status)
    - Significant TG normalization rates
- Significant reduction in liver fat and improvements in liver enzymes and glycemic control markers
- Potent reduction in atherogenic lipids (Non HDL-C) and apolipoproteins (Apo B)

Safety/Tolerability

- Well tolerated at all doses with low incidence of treatment related adverse events (all Grade 1 or 2)

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Proposed Clinical Development

Regulatory

- Seek full approval using endpoint of triglyceride lowering (based on FDA precedent)
- Propose study duration and study size based on prior precedents for approved drugs
- Discuss safety database requirements for approval
- End of Phase 2 meeting planned for 2H22

Clinical Development

- Conduct single pivotal Phase 3 trial in SHTG
  - Trial initiation expected in 1H23; Topline results expected in 1H25
- Consider additional studies to meet safety database requirements per FDA discussions
  - Potential trial(s) in other hypertriglyceridemia patient populations
  - Leverage safety data from NASH studies

89bio   Phase 3 program is subject to regulatory review/feedback

Proposed Phase 3 SHTG Trial Design
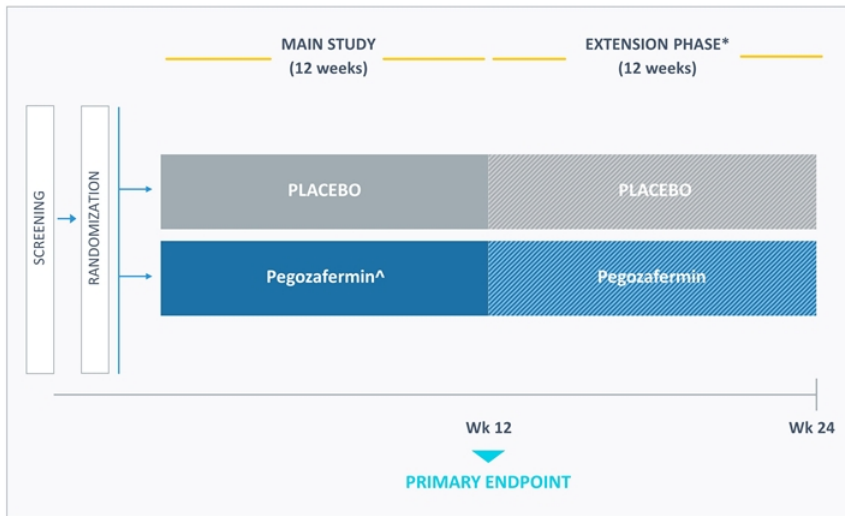
KEY INCLUSION CRITERIA

- TG ≥500 mg/dL
- Background therapy of statins and/or prescription fish oil and/or fibrates OR not on any background therapy

KEY ENDPOINTS

- Reduction in TG from baseline (primary)
- Liver fat (MRI-PDFF)
- Other lipids and metabolic markers

SAMPLE SIZE

- Approximately 300 patients
- >90% power for primary endpoint

^Dose(s) to be decided

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* Extension phase duration expected to be between 12 and 36 weeks
Phase 3 program is subject to regulatory review/feedback

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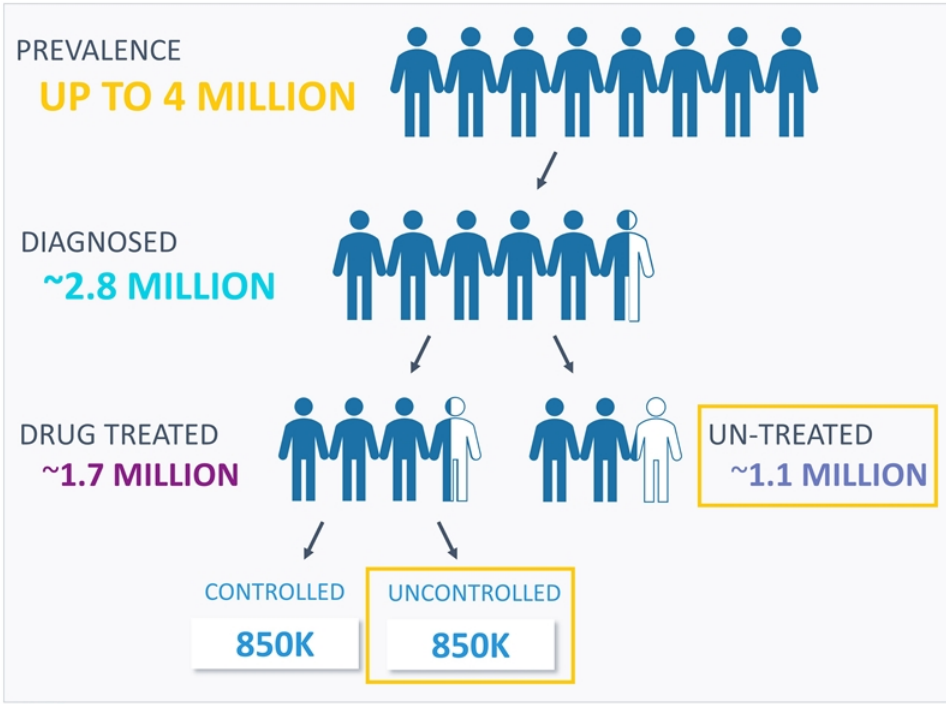## Deepak L. Bhatt, MD, MPH, FACC, FAHA, FSCAI, FESC

- Dr. Deepak L. Bhatt is Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Health and Professor of Medicine at Harvard Medical School.

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SHTG Represents a
Significant Opportunity for
Pegozafermin

SHTG Represents a Large Population with High Unmet Needs

PREVALENCE
UP TO 4 MILLION

DIAGNOSED
~2.8 MILLION

DRUG TREATED
~1.7 MILLION

UN-TREATED
~1.1 MILLION

CONTROLLED
850K

UNCONTROLLED
850K

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 TARGET

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Pegozafermin has Differentiated Profile Compared with Other TG-Lowering Drugs

	IN DEVELOPMENT		APPROVED			
	Pegozafermin Potential	**APOC3**	**Fibrates**	**Prescription Fish Oils**		**Statins**
				Vascepa	**Lovaza**	
Triglyceride reduction	✓✓✓	✓✓✓	✓✓	✓	✓✓	✓✓
Liver fat reduction	✓	—	Worsens liver fat	—	—	—
Insulin sensitizing	✓	—	—	—	—	—
Cholesterol lowering	✓ (non-HDL-C)	✓ (non-HDL-C)	Worsens LDL-C	—	Worsens LDL-C	✓
Apo-B lowering	✓	✓	—	✓	—	—
ALT lowering	✓	Transaminase elevations observed	Monitor ALT	—	May require ALT monitoring	Monitor ALT

For triglyceride reduction: ✓✓✓ = ≥ 60%, ✓✓ = 31%-59%, ✓ = ≤ 30%

— No effect/Not reported

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Pegozafermin Profile Represents Substantial Potential in SHTG *(Quantitative Market Research Results)*

Product profile testing

Profile tested: 30% TG reduction plus 1 metabolic benefit (lower than ENTRIGUE data); audience: 150 physicians in 2020

MARKET SHARE: 50%

Conjoint analysis

Profile tested: ENTRIGUE data; audience: 199 physicians in 2022

MARKET SHARE[*]	ALL PATIENTS	PATIENTS WITH FATTY LIVER
1st line	**35%**	**43%**
2nd line	**66%**	**76%**

Analyst consensus estimate of ~$1.0B in peak sales in the US if approved

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Corporate Highlights

Pegozafermin – potential important new cardio-metabolic drug; balanced effect on multiple key endpoints

- Impacts a broad spectrum of cardio and metabolic endpoints
- Robust data in 2 indications with a favorable safety and tolerability profile
- Potential first-to-market FGF21 analog

Severe Hypertriglyceridemia (SHTG) – Ph. 3 initiation planned in 1H23

- Highly differentiated based on Phase 2 success across multiple endpoints
- Significant opportunity given large, under-served market with limited competition
- Established regulatory pathway allows efficient clinical development

Nonalcoholic Steatohepatitis (NASH) – Ph. 2b enrollment completion in 3Q22; data expected 1Q23

- FGF21 offers greatest promise in this category – addresses multiple facets of the disease
- Pegozafermin has demonstrated compelling results in clinic

Strong cash position with experienced team

- $126.1 million cash* as of March 31, 2022; cash runway expected to extend into 2H23
- Track record of developing and commercializing successful drugs and business development at other companies

89bio   * Includes cash and cash equivalents, restricted cash, and short-term available-for-sale securities

# Plan To Advance Pegozafermin in Clinical Development

| Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
SHTG	Phase 3 trial - Planning				End of Ph. 2 Meeting – 2H22 Phase 3 trial Initiation – 1H23
NASH	Phase 2b trial			ENliven	Complete Enrollment – 3Q22 Topline Data – 1Q23

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Appendix

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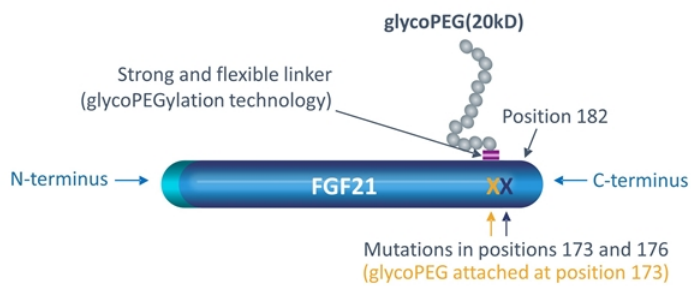

* Composition of matter through 2038
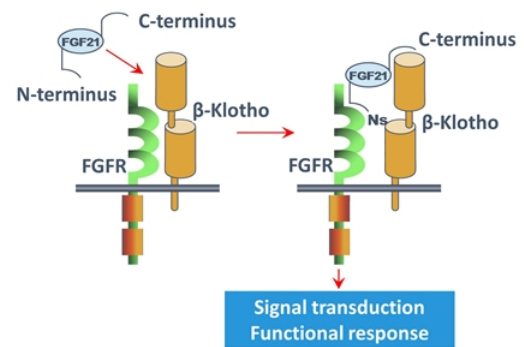
- Proprietary glycoPEGylation technology with site-specific mutations
- Increases half-life of native FGF21 (< 2 hours) to 55-100 hours based on single ascending dose study
- Low nanomolar potency against FGF receptors 1c, 2c, 3c, similar to native FGF21
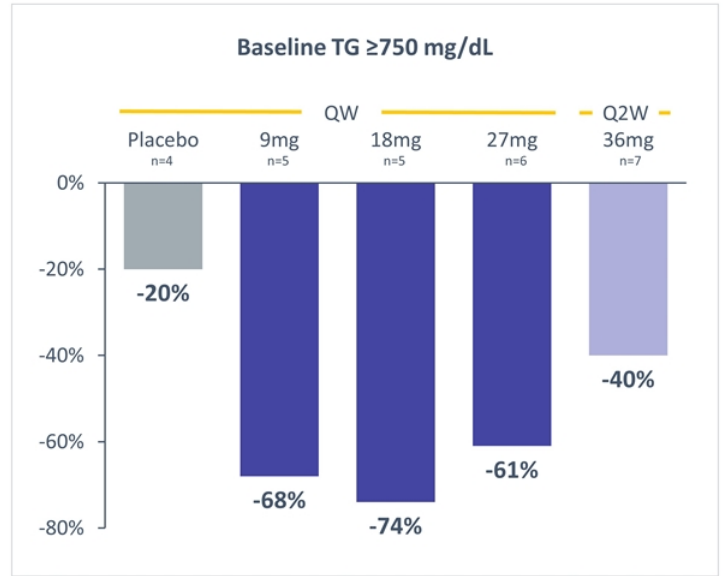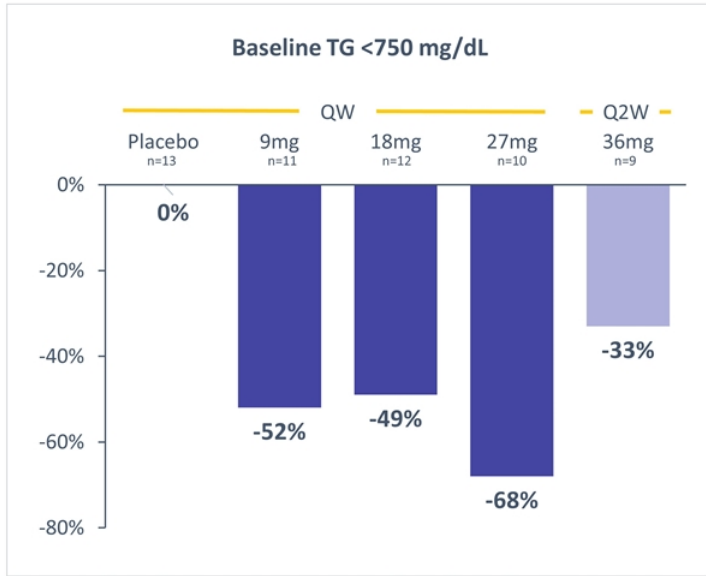- Composition of Matter Patent expiring in 2038

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Pegozafermin Significantly Reduces Triglycerides across All Dose Groups

Median Change in Absolute Triglyceride Levels from Baseline at Week 8
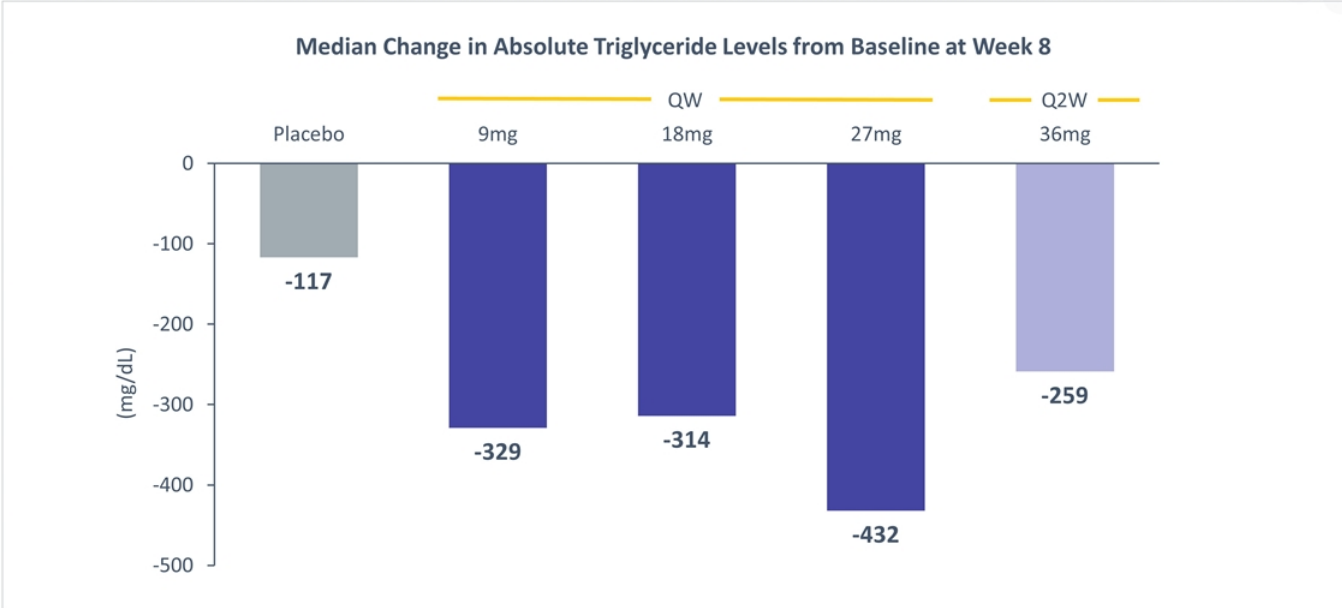
Pegozafermin Demonstrated Significant Decrease in Triglycerides Regardless of Baseline TG Level Category

Median Percent Change in Triglycerides from Baseline at Week 8

Baseline TG <750 mg/dL

	Placebo (n=13)	9mg (n=11)	18mg (n=12)	27mg (n=10)	36mg (n=9)
	0%	-52%	-49%	-68%	-33%

Baseline TG ≥750 mg/dL

	Placebo (n=4)	9mg (n=5)	18mg (n=5)	27mg (n=6)	36mg (n=7)
	-20%	-68%	-74%	-61%	-40%

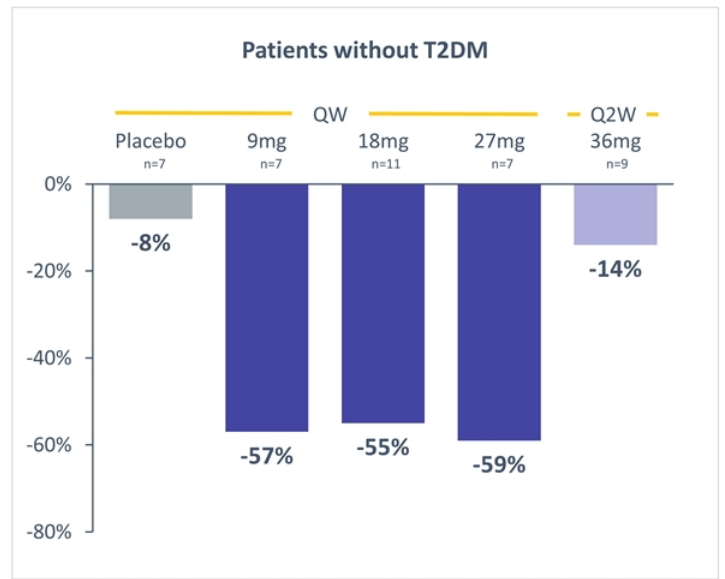# Pegozafermin Demonstrated Significant Decrease in Triglycerides Regardless of Diabetes Status

Median Percent Change in Triglycerides from Baseline at Week 8
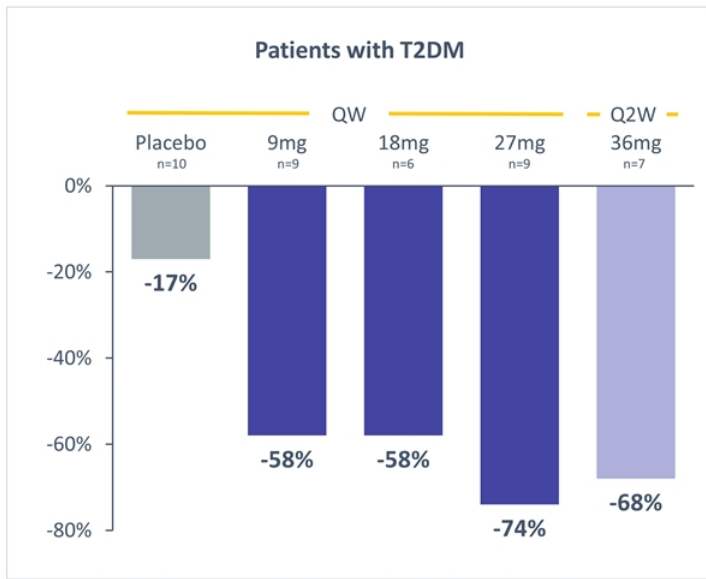
Patients with T2DM

	QW			Q2W
Placebo n=10	9mg n=9	18mg n=6	27mg n=9	36mg n=7
-17%	-58%	-58%	-74%	-68%

Patients without T2DM

	QW			Q2W
Placebo n=7	9mg n=7	18mg n=11	27mg n=7	36mg n=9
-8%	-57%	-55%	-59%	-14%

Pegozafermin Demonstrated Clinically Meaningful Improvements in HDL-C

Mean Percent Change from Baseline at Week 8
HDL-C

	QW			Q2W
Placebo	9mg	18mg	27mg	36mg
Baseline (mg/dL): 29	31	27	31	25

- Placebo: 10%
- 9mg: 19%
- 18mg: 21%
- 27mg: 42%**
- 36mg: 17%

Mean Absolute Change from Baseline at Week 8
HDL-C

	QW			Q2W
Placebo	9mg	18mg	27mg	36mg
Baseline (mg/dL): 29	31	27	31	25

- Placebo: 2
- 9mg: 5
- 18mg: 6
- 27mg: 12
- 36mg: 3
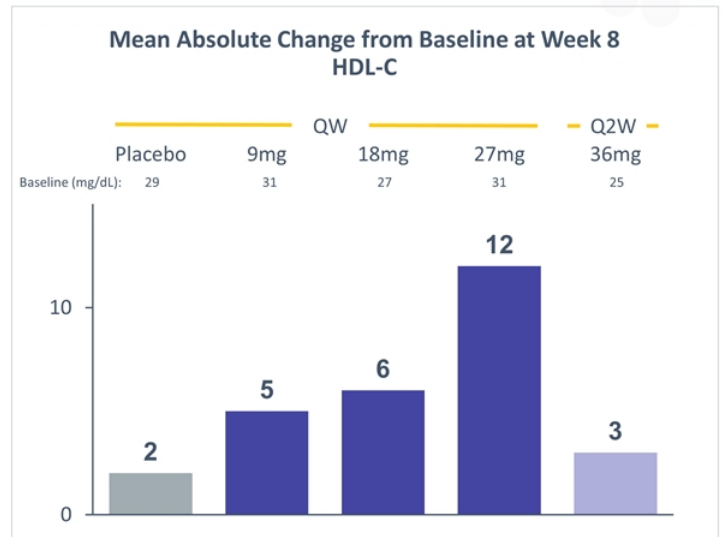
LDL-C mean % change from baseline similar between placebo and pegozafermin

Pegozafermin Shows Significant Decrease in Triglycerides on Top of Statins, Prescription Fish Oils and Fibrates

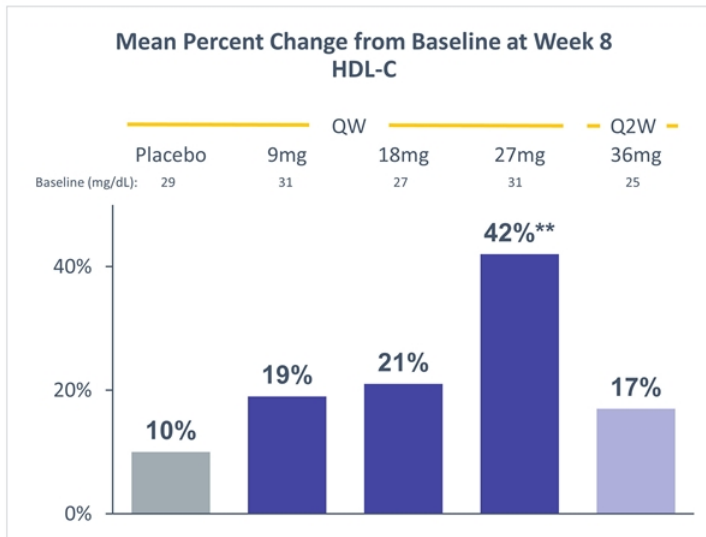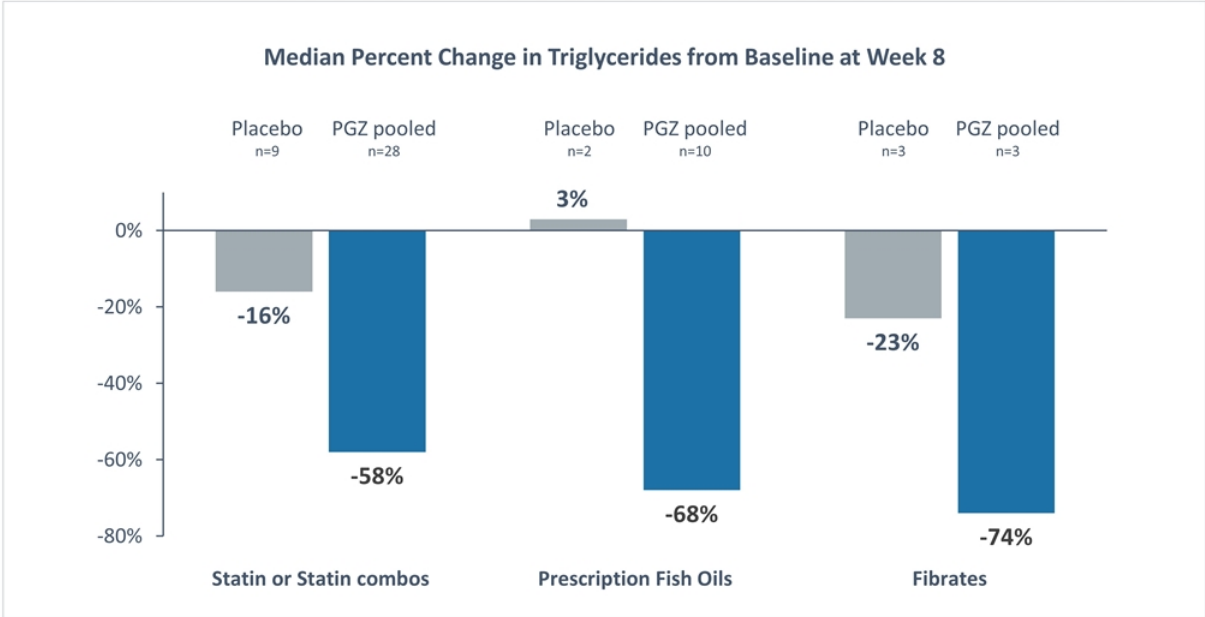**Median Percent Change in Triglycerides from Baseline at Week 8**

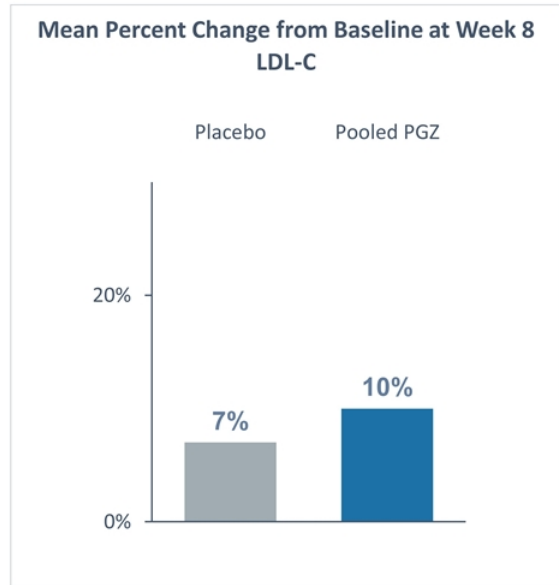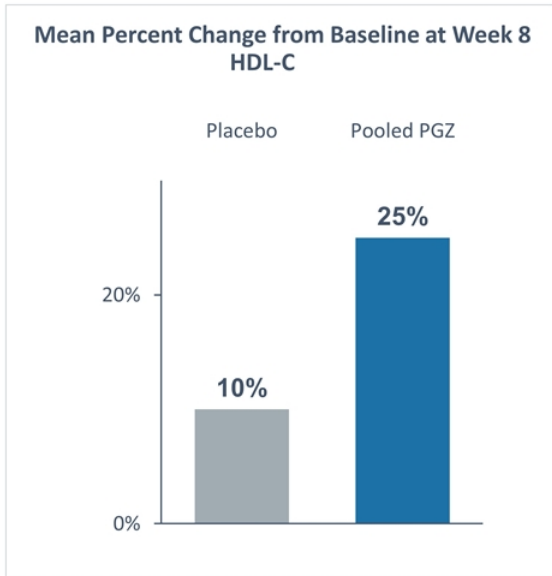# Pegozafermin Demonstrated Clinically Meaningful Improvements in HDL-C and No Change in LDL-C vs. Placebo

Mean Percent Change from Baseline at Week 8 HDL-C

Placebo   Pooled PGZ

25%

20%

10%

0%

Mean Percent Change from Baseline at Week 8 LDL-C
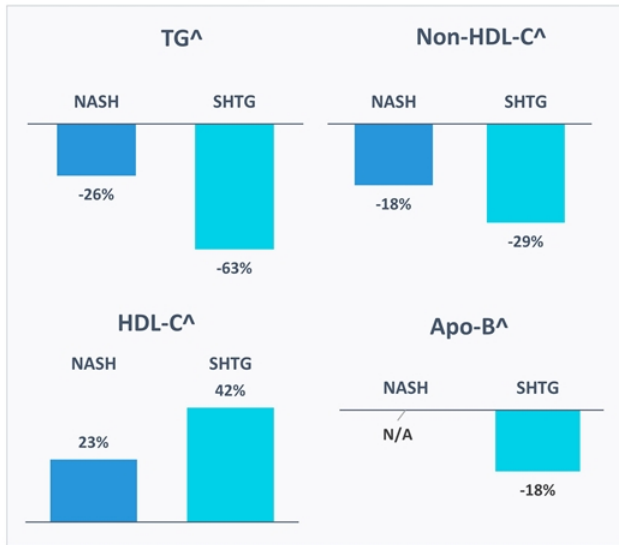
Placebo   Pooled PGZ

20%

10%

7%

0%

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

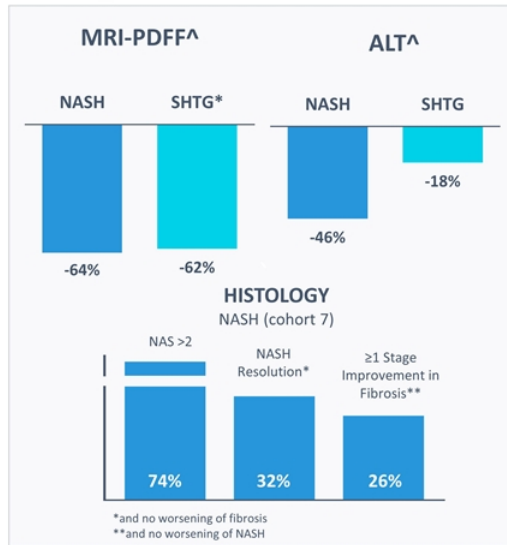Existing therapies for SHTG increase LDL-C up to 45%

Pegozafermin 27mg QW Showed Consistent and Robust Effects in Two Indications *(SHTG Patients at 8 weeks and NASH Patients at 20 weeks)*
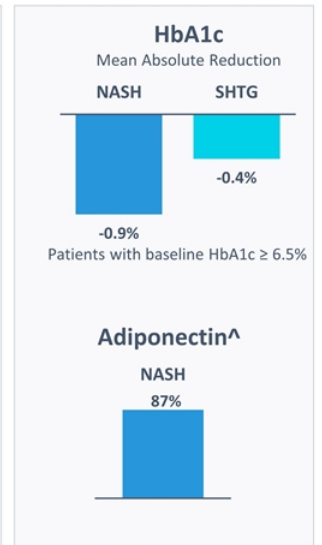
DYSLIPIDEMA

TG^
NASH	SHTG
-26%	-63%

Non-HDL-C^
NASH	SHTG
-18%	-29%

HDL-C^
NASH	SHTG
23%	42%

Apo-B^
NASH	SHTG
N/A	-18%

LIVER HEALTH

MRI-PDFF^
NASH	SHTG*
-64%	-62%

ALT^
NASH	SHTG
-46%	-18%

HISTOLOGY
NASH (cohort 7)

NAS >2	NASH Resolution*	≥1 Stage Improvement in Fibrosis**
74%	32%	26%

*and no worsening of fibrosis
**and no worsening of NASH

INSULIN RESISTANCE

HbA1c
Mean Absolute Reduction
NASH	SHTG
-0.9%	-0.4%

Patients with baseline HbA1c ≥ 6.5%

Adiponectin^
NASH
87%

^Mean change from baseline; TG data for SHTG is presented as median
*Post-hoc analysis of patients with follow-up MRI-PDFF ≤21 days from date of last dose (n=20). Analysis of all patients with follow-up MRI-PDFF (n=23) shows pooled PGZ demonstrated -43% relative reduction from baseline.
SHTG results represents data at 8 weeks from BIO89-100-221 Phase 2 study.
NASH results represents cohort 7 data at 20 weeks from Phase 1b/2a BIO89-100-002 study.

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Target Product Profile Criteria for a New Therapy
(Physician and KOL Research Completed by 89bio Before ENTRIGUE Data Readout)
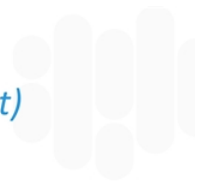
Triglyceride efficacy

- 30% as add-on therapy (50% is upside case)
- 30% achieve TG <500 mg (50% is upside case)

Cardiometabolic benefits offer added value

- **Liver Fat reduction:**
  - 40% reduction from baseline
- **HbA1c:**
  - 0.5% to 0.8% reduction in patients with T2DM
- **Lipid changes:**
  - Non-HDL-C reduced by 25%
  - LDL and HDL not changed (improvements is upside case)

Pegozafermin Profile in ENTRIGUE Significantly Exceeded Target Levels

Extensive Market Research Supports Pegozafermin Promise in SHTG

KOL Experts & Physicians – Market Dynamics

- Lack of good treatment options in 2nd and 3rd line setting – highest unmet need
- Triglyceride management is critical given CV and acute pancreatitis risk; however, often overlooked given limitations of current therapies

KOL Experts & Physicians – Pegozafermin profile is unique and compelling

- Target patient
  - Patient with uncontrolled TGs despite drug therapy or past episode of acute pancreatitis
  - Patient with history of cardiovascular risk factors
  - Patients with background metabolic syndrome symptoms
- Ideal profile – reduces TG to <500 mg/dL and reduces liver fat
  - Glycemic control and other lipid benefits are additive
- Pegozafermin data exceeds threshold for adoption: 30% reduction in triglycerides
  - >50% reduction in triglycerides viewed as "excellent"
  - Metabolic benefits make it a preferred option for patients with Fatty Liver Disease and T2DM
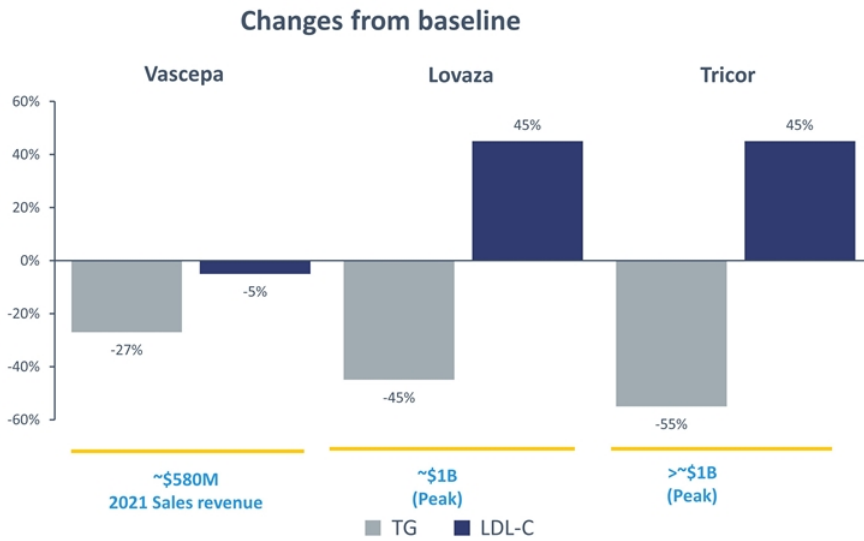
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Payers – Managed Care Directors and PBMs

- Pegozafermin has potential to gain broad coverage based on approved indication; market is not actively managed
- Data supportive of premium pricing in 2nd line setting (threshold – 30% reduction in TG)
- We believe that majority of plans would place pegozafermin on tier with a patient co-pay ≤$60/month

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Current Therapies Have Had Commercial Success Despite Less than Ideal Profiles

Changes from baseline

Lipitor decreases TG by 39% (low dose) and 52% (high dose). Level of sales for hypertriglyceridemia are unknown.

SAFETY / TOLERABILITY

FISH OILS		FIBRATES
Vascepa (EPA)	Lovaza (EPA+DHA)	Tricor
May prolong bleeding time		Myopathy, Creatinine increases, DDI

89bio   * Conclusions on this slide are not based on head-to-head results

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