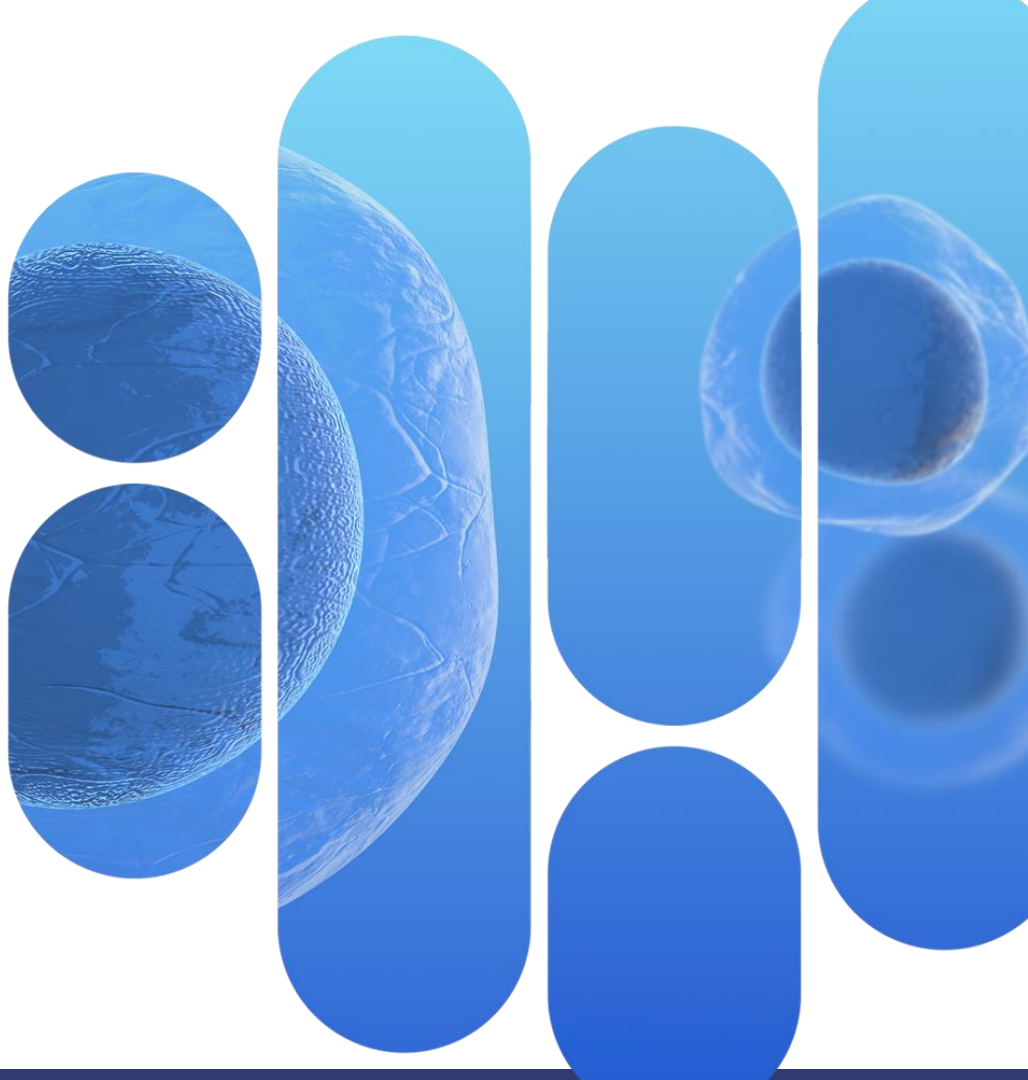




# Developing a Differentiated FGF21 for NASH and SHTG

February 2020



# Disclaimer

## Cautionary Note Regarding Forward-Looking Statements

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, future revenues or performance, financing needs, plans or intentions relating to product candidates, estimates of market size, business trends, the anticipated timing, costs, design and conduct of our planned clinical trials for BIO89-100, our only product candidate, the timing and likelihood of regulatory filings and approvals for BIO89-100, our ability to commercialize BIO89-100, if approved, the pricing and reimbursement of BIO89-100, if approved, the potential to develop future product candidates, our ability to scale up manufacturing, the potential benefits of strategic collaborations and our intent to enter into any strategic arrangements, the timing and likelihood of success, plans and objectives of management for future operations and future results of anticipated product development efforts. 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-Q under the caption “Risk Factors” and elsewhere in such report.

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. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

# 89bio – Investment Highlights

## Significant Commercial Opportunities

- Targeting large and growing unmet need in Non-Alcoholic Steatohepatitis (NASH) and Severe Hypertriglyceridemia (SHTG)

## Potentially Differentiated Asset Targeting Clinically Validated Mechanism in NASH

- FGF21 has the potential to become mainstay of NASH therapy – addresses key liver pathologies and underlying metabolic dysregulation
- BIO89-100 is a glycoPEGylated analog of FGF21 with compelling early human data

## Potentially Differentiated Therapy for SHTG

- Robust reduction in triglyceride levels seen in animal and human studies
- Established development and regulatory path offering a potentially quicker path to market for BIO89-100

## Anticipated Near-term Catalysts

- Two trials with BIO89-100: (i) Ongoing Phase 1b/2a trial in NASH (topline data anticipated in 2H20); (ii) Planned Phase 2 trial in SHTG (topline data anticipated in 1H21)
- Potential to transition to Phase 2b and registrational trials in NASH and SHTG, respectively, by YE21

## Established Manufacturing Expertise; Long IP Protection

- Established manufacturing process in place for near-term clinical supplies
- Issued composition of matter patent expected to expire in 2038

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# OPPORTUNITY IN NASH



# BIO89-100 is A Compelling Drug Candidate in NASH

## NASH IS A SERIOUS LIVER CONDITION

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- Large market size with significant economic burden and no FDA-approved treatment options
- Complicated disease with significant co-morbidities

## FGF21 HAS THE POTENTIAL TO BE MAINSTAY OF THERAPY GIVEN ITS BROAD-BASED EFFECTS

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- Addresses steatosis and fibrosis and underlying metabolic issues

## BIO89-100 HAS THE POTENTIAL TO BE A DIFFERENTIATED FGF21 ANALOG

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- Proprietary glycoPEGylation technology may offer robust biologic effects, favorable tolerability profile and a longer dosing interval

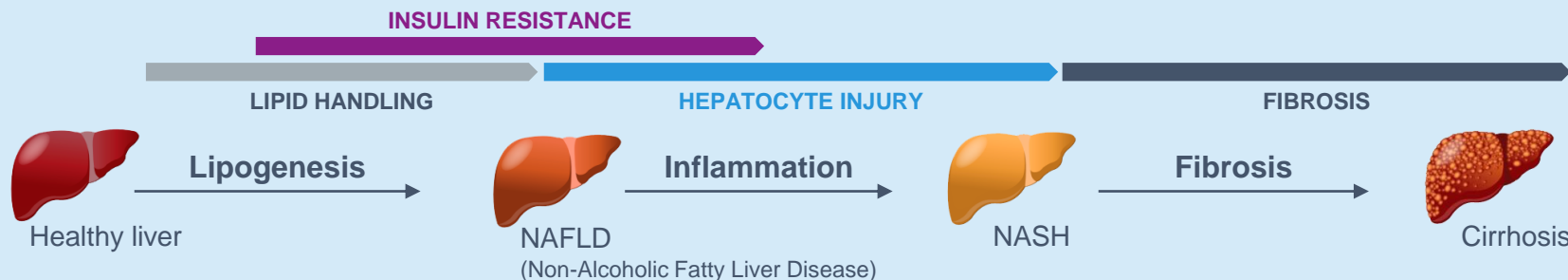
## ROBUST CLINICAL AND PRECLINICAL DATA WITH AN UPCOMING ANTICIPATED EFFICACY READOUT

---

- Phase 1a trial showed favorable tolerability, PK and PD markers building on strong preclinical package
- Phase 1b/2a study in NASH ongoing with topline data expected in 2H20

# NASH is A Serious Liver Condition With No FDA Approved Treatments

Metabolic Dysregulation → Excess Liver Fat Accumulation → Progressive Disease



- **16.5 million** projected to grow to **27 million** by 2030
  - Expected to become the leading cause of liver transplant in 2020
- **Significant economic burden – \$223 billion** expected lifetime economic burden of patients in US (2017)

Co-morbidity	Prevalence in NASH population
Hypertriglyceridemia	83%
Obesity	82%
Hyperlipidemia / Dyslipidemia	72%
Metabolic syndrome	71%
Type 2 diabetes	44%

# NASH Therapeutics - Market Dynamics

## 1 Key Attributes for Successful NASH Therapies

- Robust efficacy with respect to liver pathologies
- Ability to address underlying co-morbidities
- Well tolerated

## 2 Potential for Multiple Winners

- Similarities to multi-billion diabetes and dyslipidemia markets
- Potent injectables have the potential to be a preferred treatment option for some patient populations (e.g. GLP-1 agonists achieved ~\$9 billion in sales in 2018\*)

# FGF21 product candidates have the potential to deliver on key attributes for successful NASH therapies

		FGF21	FXR	THR-β	PPARs*	FGF19	GLP-1
Robust efficacy with respect to liver pathologies	Liver fat reduction	✓	✓	✓		✓	?
	Fibrosis improvement	✓	✓	?	?	✓	
Ability to address underlying co-morbidities	Triglyceride reduction	✓		✓	✓	✓	
	LDL-C improvement	✓	Worsens LDL	✓	✓	Worsens LDL	
	HDL-C improvement	✓			✓		
	Glucose reduction	✓			✓		✓
Well tolerated at effective dose	Limited Side Effects	✓	Pruritis LDL ↑	Drug-drug interaction	Risk of renal toxicity; Hepatitis	LDL ↑	✓ GI effect

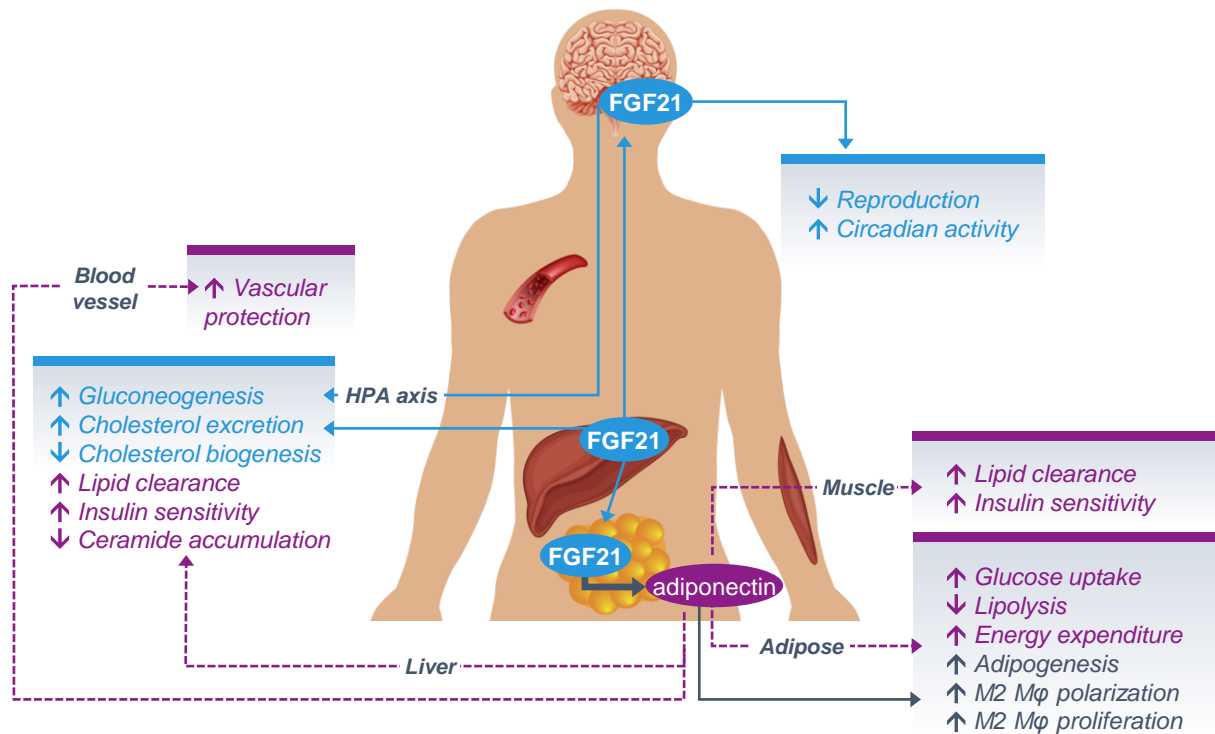
✓ Effective      ? Indeterminate      ✓ Modest Effect      Unknown or Unchanged

\* Based on PPARα/δ and PPARδ candidates in development

NOTE: Table representative of data published and or presented on the mid/late stage clinical programs targeting these mechanisms. Third party company data taken from publications/publicly available presentations.



# FGF21 Has Potential To Be Mainstay of Therapy in NASH

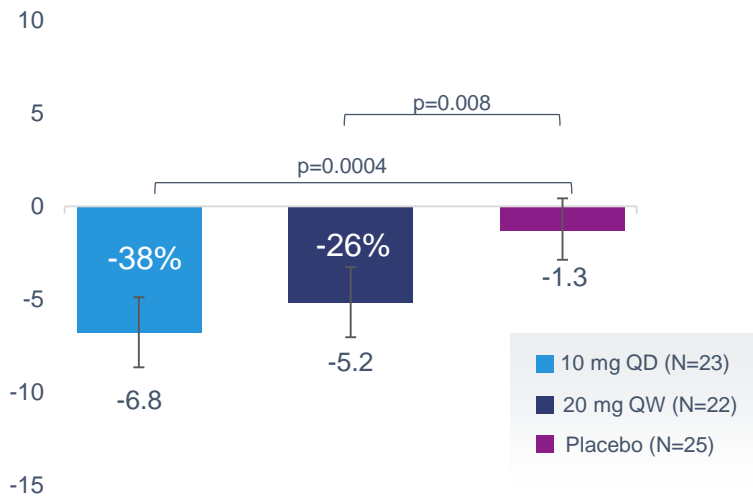


- Endogenous metabolic hormone that regulates energy expenditure and glucose and lipid metabolism
- Activates FGF receptors 1c, 2c, 3c, not believed to activate receptor 4 (leads to increased LDL)
- Signaling requires co-activation of beta-klotho receptor

# FGF21 – Clinically Validated in NASH

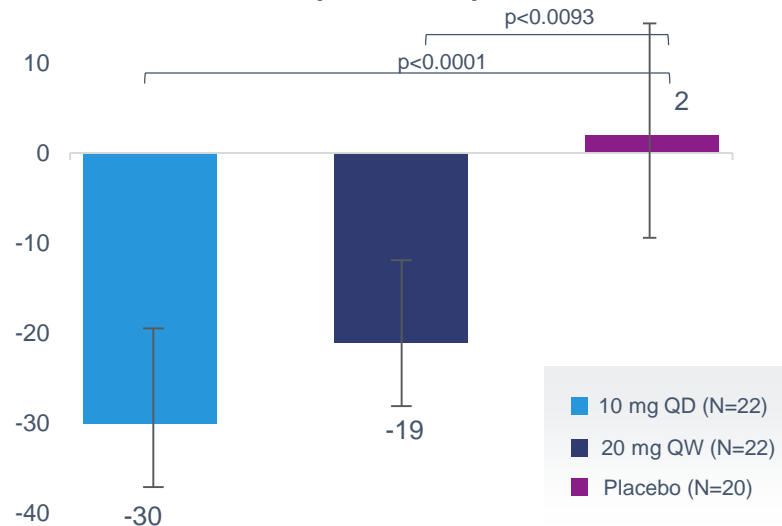
Results from BMS's Phase 2a Study with Pegbelfermin Showed Better Clinical Outcomes with Daily Compared to Weekly Injection

**Absolute Change in % Fat Fraction  
(Week 16)**



Half-life (T1/2) was 19–24 hours

**% Reduction in Serum Pro - C3  
(Week 16)**



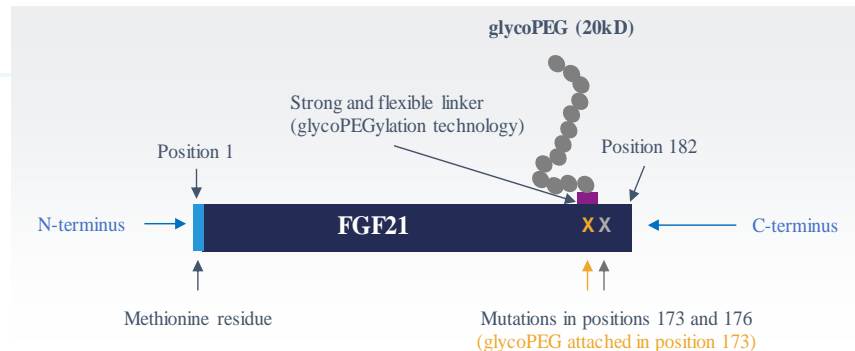
Effect demonstrated also on MRE

*Pegbelfermin was well tolerated; most common adverse events were gastrointestinal AEs*

# BIO89-100 Is A Long Acting glycoPEGylated FGF21 Analog

## TECHNOLOGY TO IMPROVE CLINICAL PROFILE

- Site-specific glycoPEGylation technology designed to prevent degradation, extend half-life, minimize potential for aggregation and retain potency
- Incorporated by Teva for approved product: Lonquex®



## TARGETED MUTATIONS TO KEEP C-TERMINUS INTACT

- Two mutations via substitutions with natural amino acid sequences inserted at positions 173 and 176, near FAP enzyme cleavage site at C-terminus (critical for  $\beta$ -klotho binding)
- Single linear 20 kDa glycoPEG moiety attached at position 173

## LONG HALF-LIFE (55-100 HOURS) MAY SUPPORT WEEKLY OR EVERY 2-WEEK DOSING

- Half-life of 55-100 hours which is significantly longer than Pegbelfermin (19-24 hours)

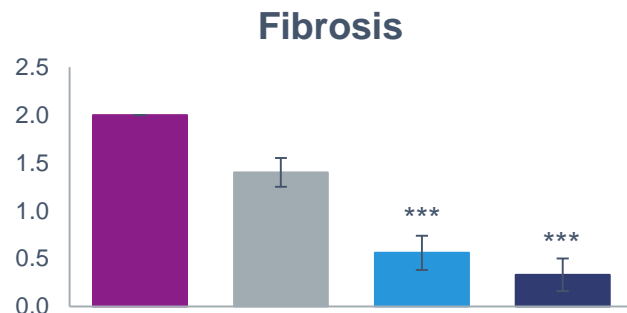
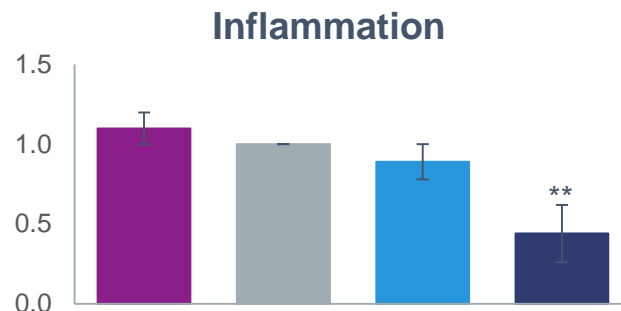
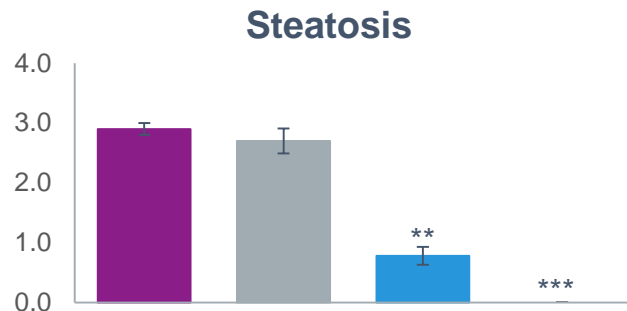
# Strong Preclinical Data with BIO89-100

Preclinical Pharmacology Study with BIO89-100	Reduced Hepatocyte Injury	Reduced Liver Steatosis, Inflammation & Fibrosis	Improved Lipid Handling*	Improved Insulin Sensitivity	Body Weight Reduction
DIN mouse model (10 weeks)	✓	✓	✓	✓	✓
DIN mouse model (19 weeks)	✓	✓	✓	✓	✓
Diabetic obese cynomolgus monkey study (8 weeks; weekly dosing)	✓	Not evaluated	✓	✓	✓
Diabetic obese cynomolgus monkey study (4 weeks; weekly & 2-week dosing)	✓	Not evaluated	✓	✓	✓

✓ Statistically significant benefit observed

\* Improved TG and cholesterol

# Reduction in Steatosis, Inflammation, Fibrosis and NAFLD Activity Score with BIO89-100 in DIN Model



Vehicle

BIO89-100, 0.02 mg/kg

BIO89-100, 0.1 mg/kg

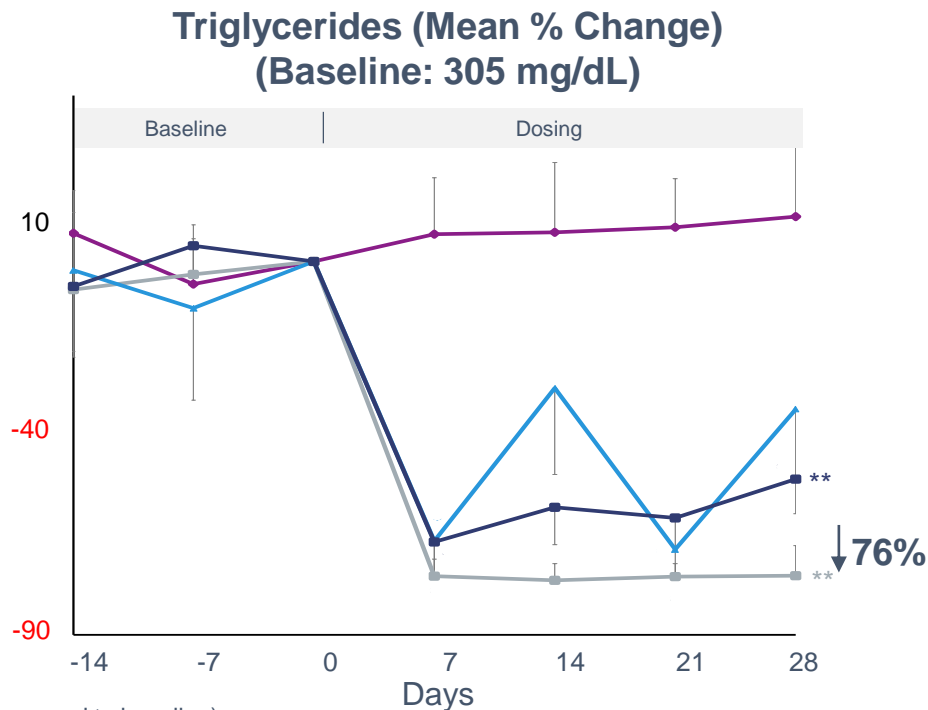
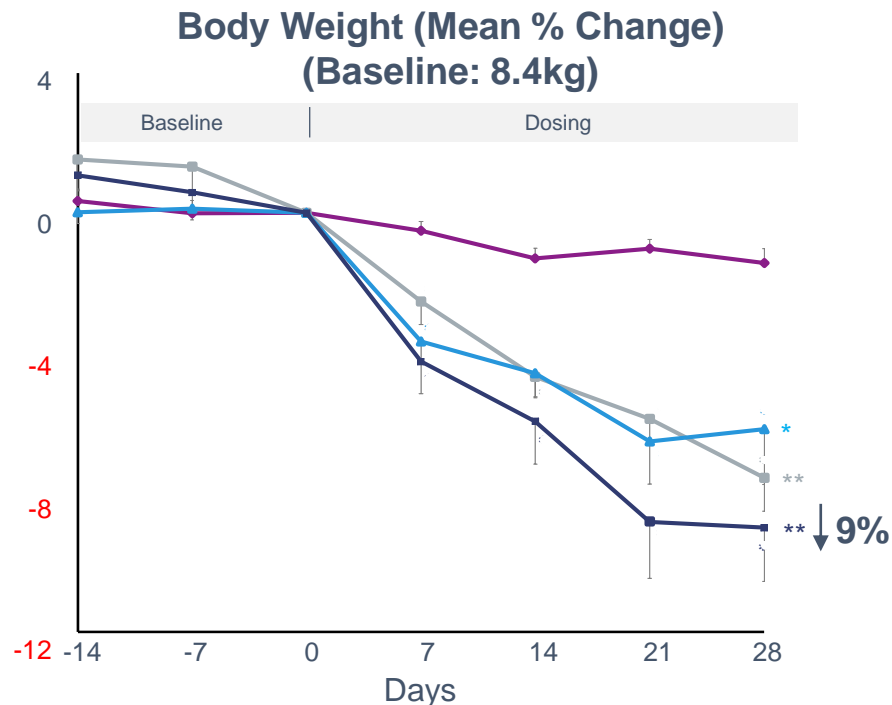
BIO89-100, 0.5 mg/kg

\*p<0.05

\*\*p<0.01

\*\*\*p<0.001

# Significant Reduction in Body Weight and Triglycerides in Diabetic Obese Monkeys With Once Every 2 Weeks Dosing



—●— Vehicle weekly    —●— BIO89-100, 1.0 mg/kg, weekly    —●— BIO89-100, 1.0 mg/kg once every 2 weeks    —●— BIO89-100, 2.0 mg/kg once every 2 weeks

# BIO89-100 Demonstrated a Favorable Clinical Profile in Phase 1a Study

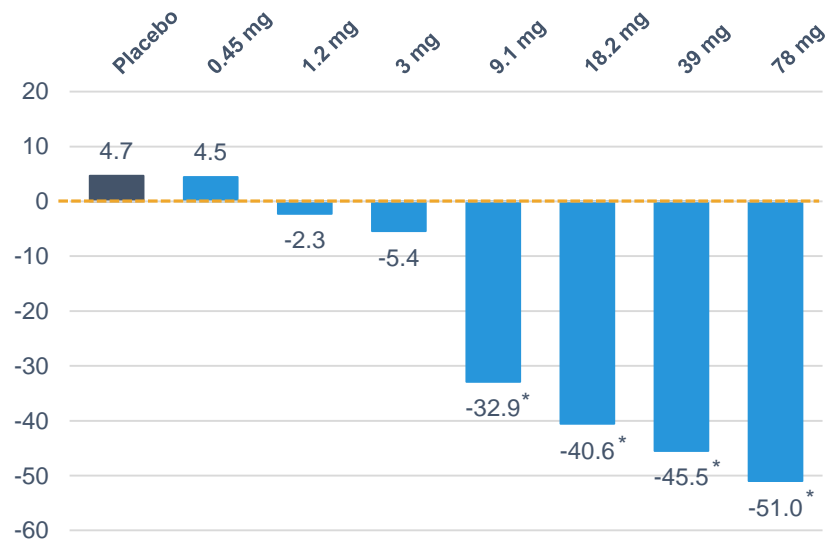
- Well tolerated
  - Most commonly observed treatment related AEs (in  $\geq 2$  subjects) were injection site reaction and headache, all of which were reported as mild
- PK was dose proportional; half-life of 55–100 hours
- Significant improvements in key lipid parameters at 8 and 15 days after single dose (baseline values were in normal range)\*
  - Triglycerides reduction up to 51%
  - LDL-C reduction up to 37%
  - HDL-C increase up to 36%
- Supports weekly and once every 2-week dosing regimen

## **Trial Design:**

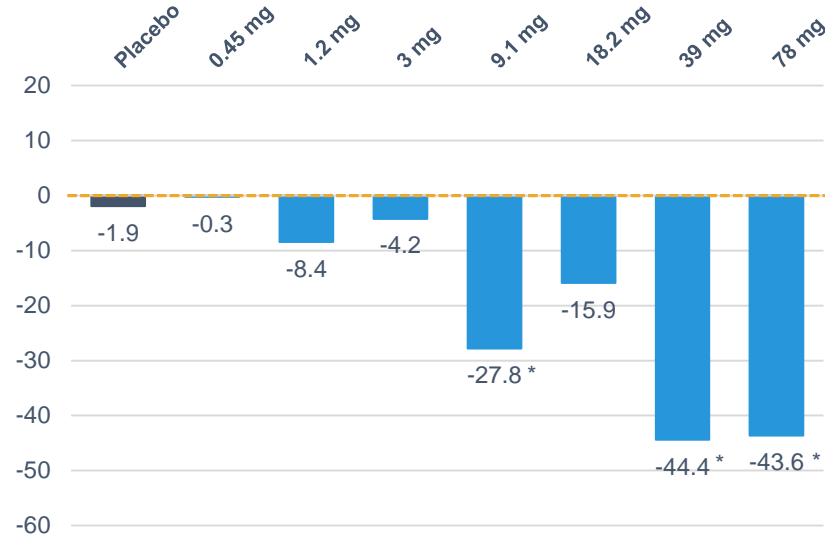
Double-blind,  
placebo-  
controlled Single  
Ascending Dose  
(SAD);  
58 healthy  
volunteers;  
7 dose cohorts

# Robust and Durable Improvement in Triglycerides Following a Single Dose of BIO89-100

Mean Percentage Change at Day 8 from Baseline in Triglycerides (%)



Mean Percentage Change at Day 15 from Baseline in Triglycerides (%)

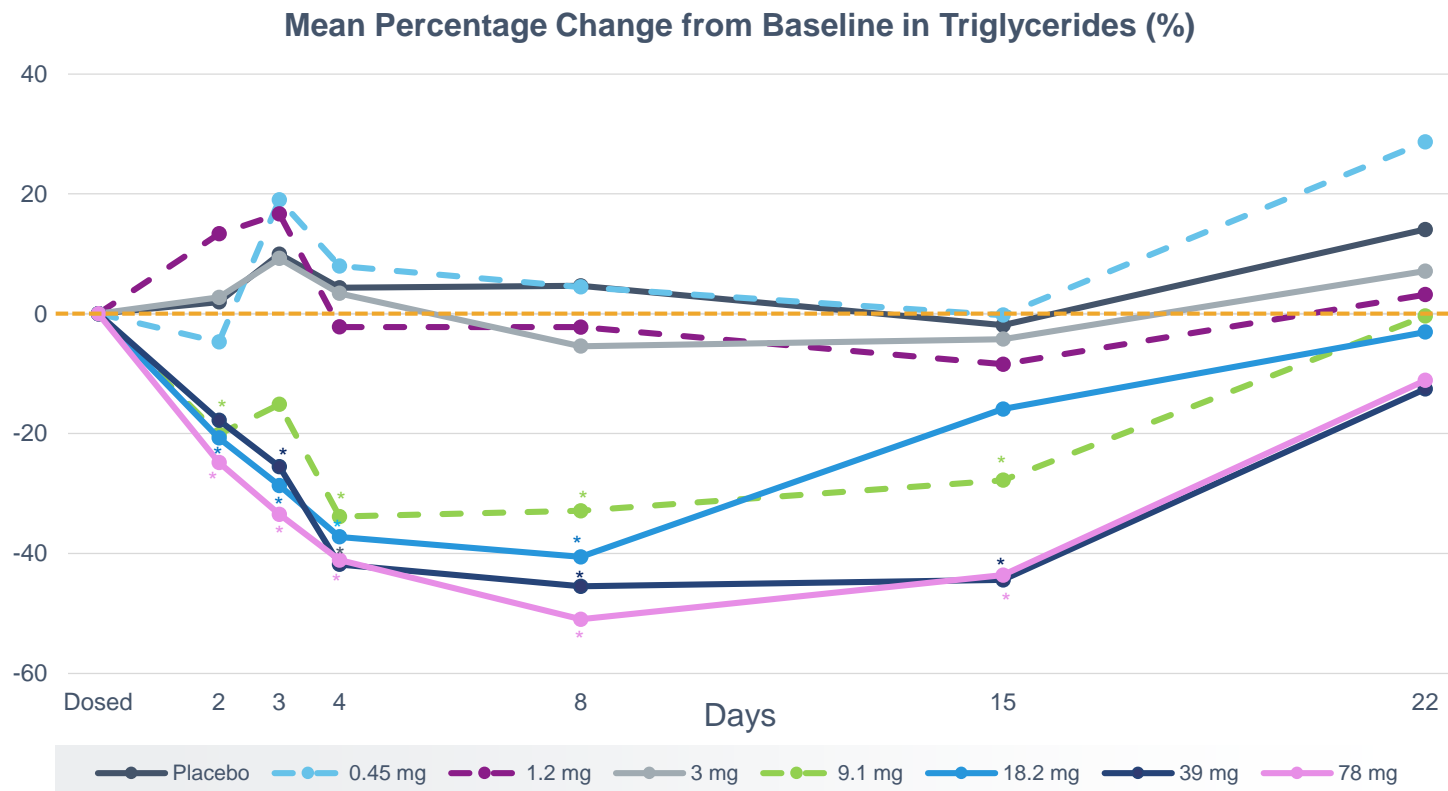


Dose (mg)	Placebo	0.45mg	1.2mg	3mg	9.1mg	18.2mg	39mg	78mg
N	15	6	6	6	7	6	6	6
Baseline	99.3	83.2	76.5	78.2	95.9	84.5	124.5	101.5

\* 95% CI exclude 0% change from baseline



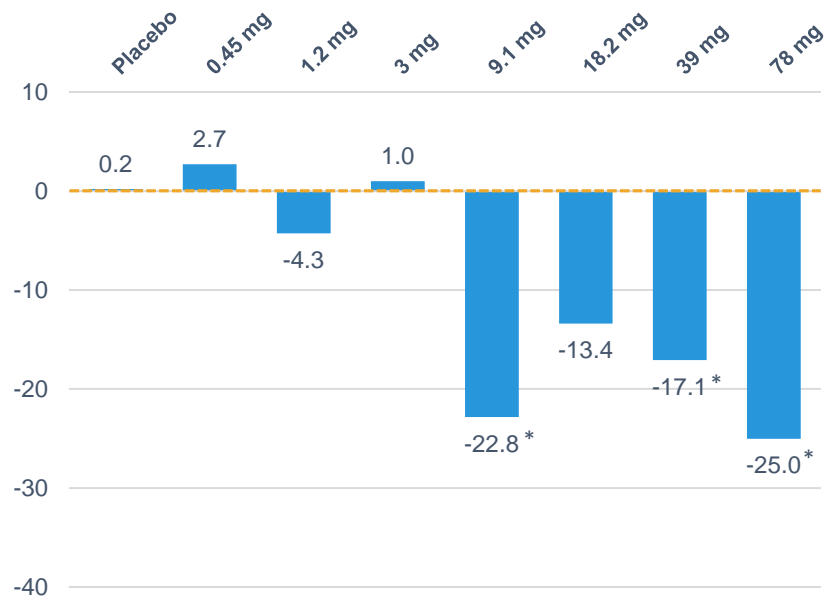
# Rapid and Durable Improvement in Triglycerides Following a Single Dose of BIO89-100



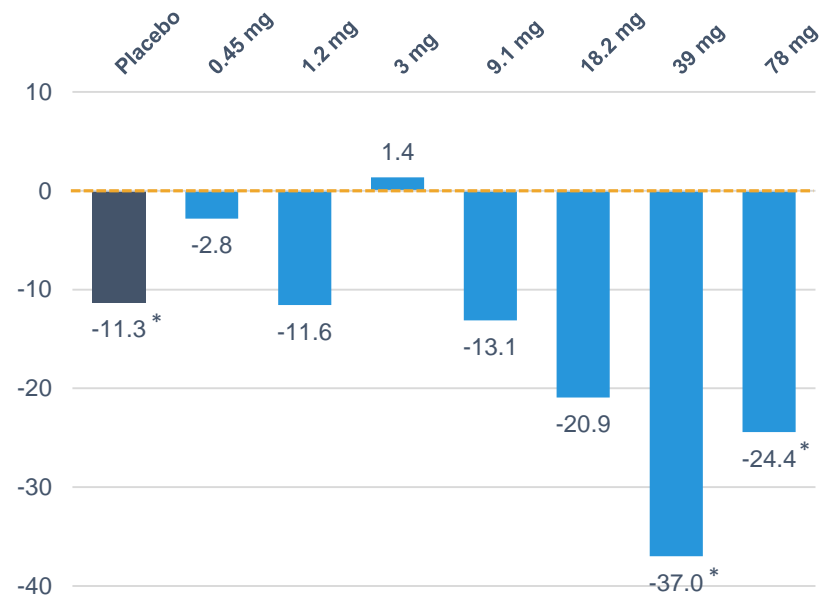
\* 95% CI exclude 0% change from baseline

# Robust and Durable Improvement in LDL Cholesterol Following a Single Dose of BIO89-100

Mean Percentage Change at Day 8 from Baseline in LDL Cholesterol (%)



Mean Percentage Change at Day 15 from Baseline in LDL Cholesterol (%)

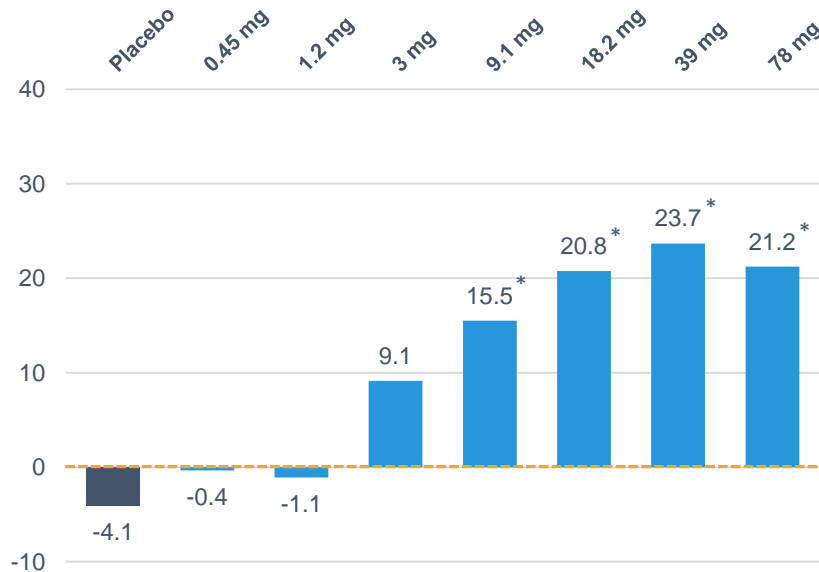


Dose (mg)	Placebo	0.45mg	1.2mg	3mg	9.1mg	18.2mg	39mg	78mg
N	15	6	6	6	7	6	6	6
Baseline	129.6	97.8	122	123.3	120.3	122.8	138.8	130.3

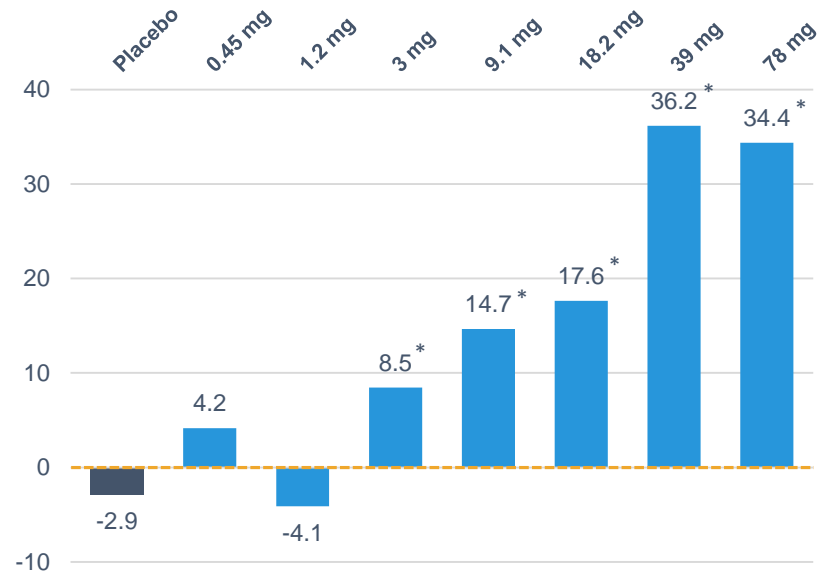
\* 95% CI exclude 0% change from baseline

# Robust and Durable Changes in HDL Cholesterol Following a Single Dose of BIO89-100

Mean Percentage Change at Day 8 from Baseline in HDL Cholesterol (%)



Mean Percentage Change at Day 15 from Baseline in HDL Cholesterol (%)



Dose (mg)	Placebo	0.45 mg	1.2 mg	3 mg	9.1 mg	18.2 mg	39 mg	78 mg
N	15	6	6	6	7	6	6	6
Baseline	50.8	44.5	50	48.5	51	44.8	44.2	42.7

\* 95% CI exclude 0% change from baseline

# Pegbelfermin and AKR-001

## PEGBELFERMIN (BMS)

- Pegylated molecule with moderate half-life of 19-24 hours – dosed daily and weekly
  - Mutations with non-native amino acid substitutions
- Efficacy was lower when dosed weekly versus daily across key lipid measures in Phase 1 and 2a trials

% Change vs. baseline (Day 15)*	Phase 1b study	
	10mg QD	21mg QW
TRIG	-35%	-25%
LDL-C	-25%	-20%
HDL-C	-8%	-9%

- Changes in TG and LDL-C in Phase 2a study in weekly dosing arm were 5% and 1% respectively

## AKR-001 (AKERO)

- Fusion Protein molecule with extended half-life (3–4 days)
- Currently studying a weekly dosing regimen in Phase 2a study in NASH - 28mg, 50mg and 70 mg
- Tolerability issues seen at high doses in Phase 1 study in diabetic patients
  - At 140mg QW (n=9), 4 withdrawals due to GI/ CNS side effects; 4 patients with tremors
- Phase 1 study showed reductions in triglycerides, HDL and other lipids
  - Increase in placebo adjusted LDL at 21mg QW, minor reduction at 70mg QW (MAD study)

# BIO89-100: Phase 1b/2a Study

- Design: Randomized, double-blind, placebo-controlled
- Population: NASH or NAFLD patients with high risk of NASH\*
- Dosing: Weekly or every 2 weeks regimen; six dosing cohorts: 3mg QW to 36mg Q2W
- Duration: 12 weeks
- Size/Power: n=83 patients; powered to show statistical difference on MRI-PDFF
- US Study: Ongoing; Results expected in 2H20

*FDA has concurred with overall trial design including study population, dose selection and study treatment duration*

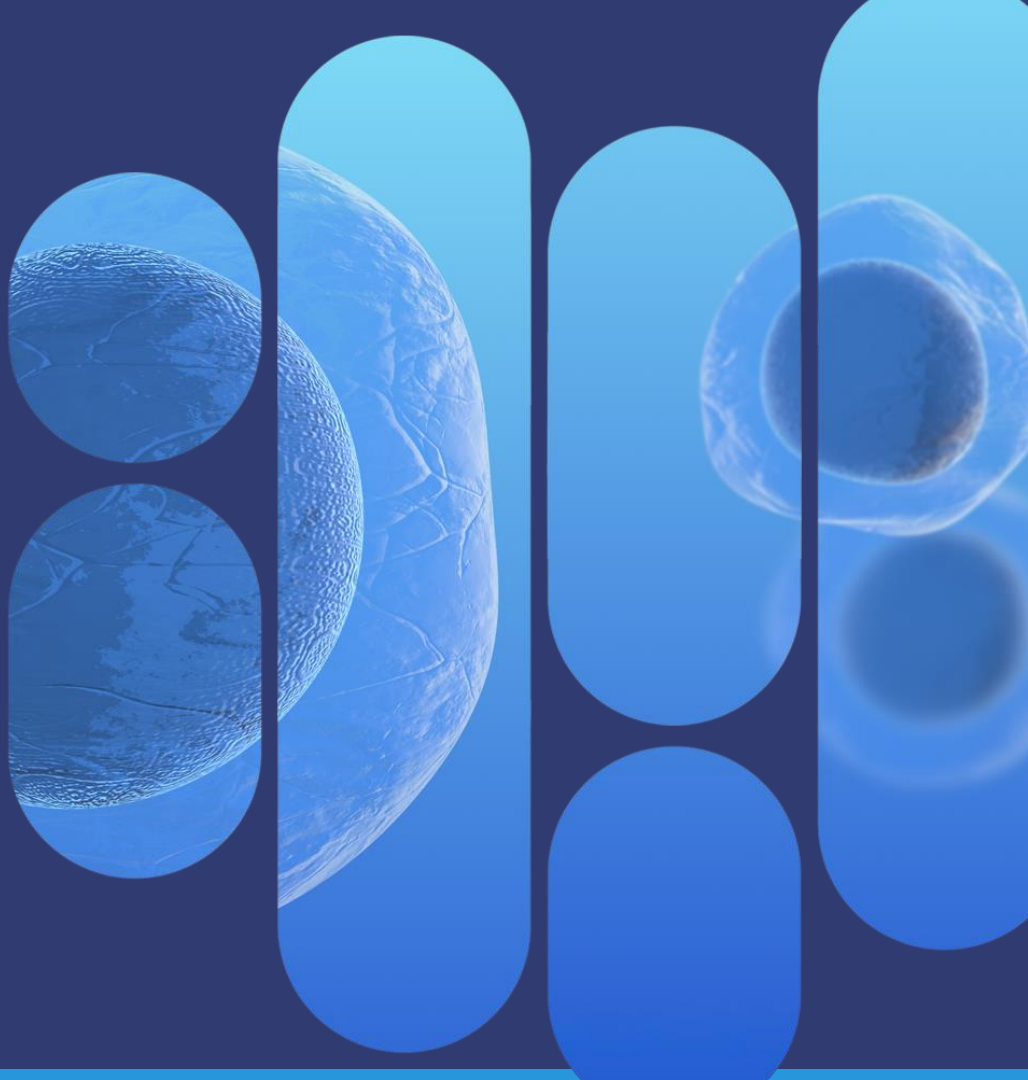
## **Trial Endpoints:**

- **Safety, PK**
- **MRI-PDFF**
- **Serum Lipids**
- **Key NASH biomarkers including:**
  - ALT
  - Pro-C3
  - ELF
  - Inflammatory markers

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# OPPORTUNITY IN SHTG



# BIO89-100: A Compelling Drug Candidate For SHTG

## SIGNIFICANT COMMERCIAL OPPORTUNITY

- Large patient population who are unable to achieve treatment goals with existing therapies
- Increased interest in lowering TGs to reduce residual CV risk

## FGF21 IS A HIGHLY PROMISING MECHANISM OF ACTION FOR TREATMENT OF SHTG

- Removes lipids from circulation, increases lipid catabolism and has the potential to address multiple co-morbidities (dyslipidemia, diabetes)

## BIO89-100 OFFERS A POTENT AND DIFFERENTIATED PROFILE RELATIVE TO EXISTING THERAPIES

- Showed significant reduction in triglycerides in preclinical and clinical studies (up to 78% in monkey study and up to 51% after a single human dose)
- Potential for use as monotherapy or in combination with existing drugs or those in development

## ESTABLISHED REGULATORY PATH; POTENTIAL FOR RELATIVELY SMALLER AND FASTER TRIALS

- Potential to be faster to market than NASH

# SHTG Market Opportunity

## Large Patient Population...

Estimated **up to 4 million** patients in the US with **TG  $\geq$  500 mg/dL**

## ...With Large Unmet Need

**up to 50%\*** of treated patients are **refractory to current standard of care**

**Diagnosis and treatment rates are expected to increase in the future**

### Increasing awareness of the importance of treating elevated TGs

- Residual CV risk despite effective LDL treatments with statins
- Outcome study (REDUCE-IT) demonstrated that reducing TG can significantly lower CV events

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



# SHTG Therapeutics – Key Attributes

## Key Attributes for Successful Therapies

- Robust TG reduction
- Address the multiple co-morbidities patients have (dyslipidemia and insulin resistance)
- Need to have good benefit/risk
- Support compliance with good dosing

# BIO89-100 has the potential to deliver on key attributes for successful SHTG therapy

	FISH OILS			FIBRATES	FGF21 Analogues
	Vascepa (EPA)	Epanova (EPA+DHA)	Lovaza (EPA+DHA)	Tricor	
LDL-C Improvement	■	Worsens LDL	Worsens LDL	Worsens LDL	✓
HDL-C Improvement	■	■	■	■	✓
Effect on other metabolic co-morbidities (liver fat, glycemic control, body weight)	■	■	■	■	✓
Tolerability/ Safety	May prolong bleeding time			Myopathy LDL and LFT increases Drug-drug interactions	✓ GI effect
Dosing convenience	4 capsules / Day with food	2-4 capsules / day	4 capsules / Day with food	1 tablet/day	Infrequent SC injection – compliance benefit

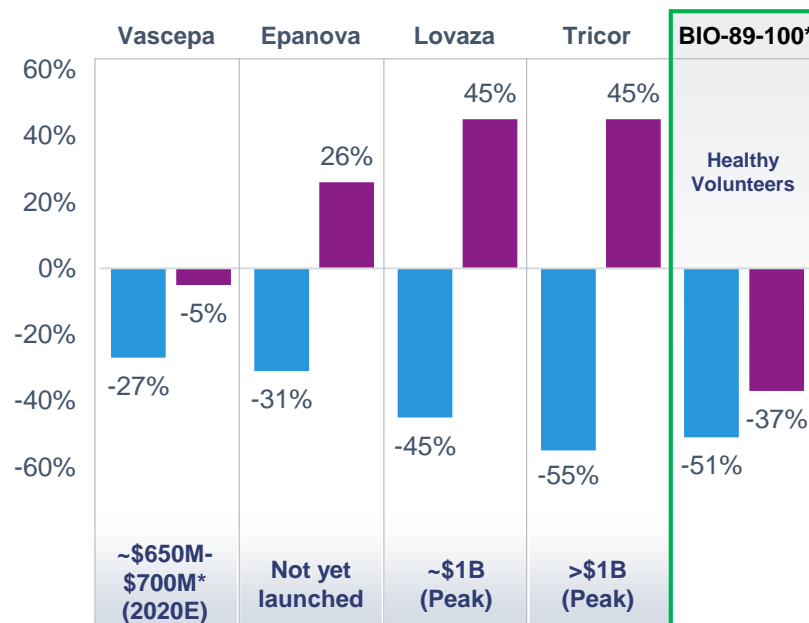
✓ Effective

■ Unchanged or Inconclusive

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## Changes from baseline

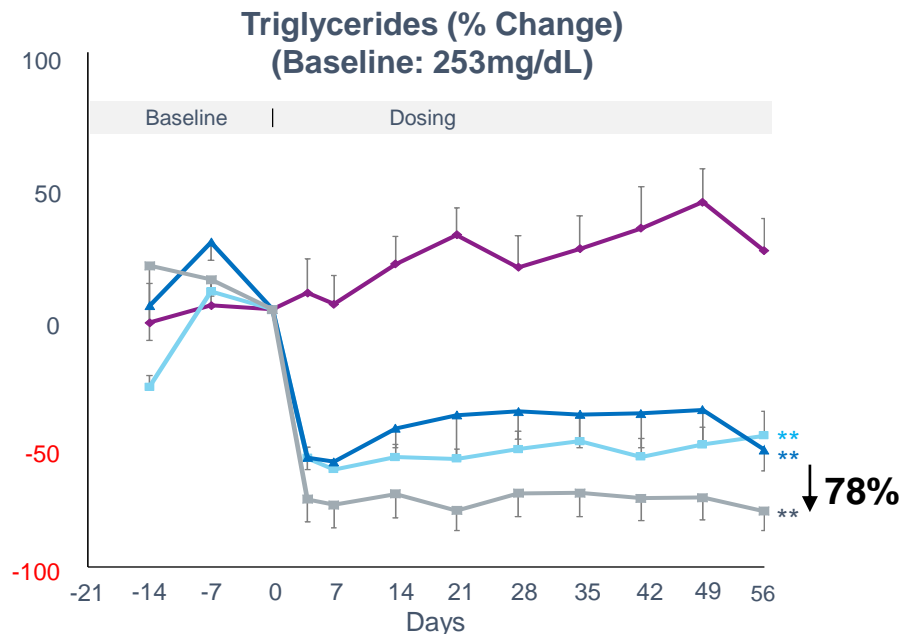


■ TG

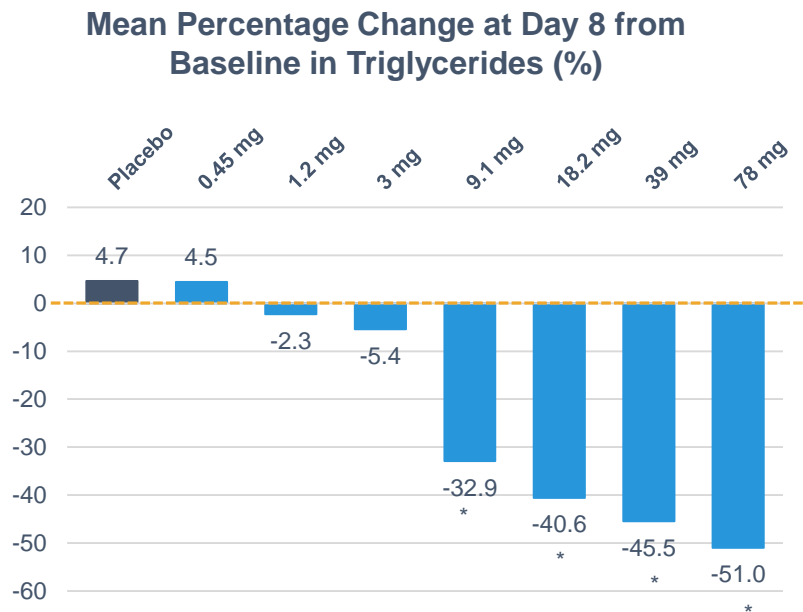
■ LDL-C

\* Maximal data from Phase 1 SAD study

# Potent and Durable Reduction in Triglycerides Observed with BIO89-100



Data from study in obese diabetic monkeys




Data from study in SAD in healthy volunteers

Dose (mg)	Placebo	0.45mg	1.2mg	3mg	9.1mg	18.2mg	39mg	78mg
N	15	6	6	6	7	6	6	6
Baseline	99.3	83.2	76.5	78.2	95.9	84.5	124.5	101.5

# SHTG Clinical and Regulatory Path is Defined and May Represent a Quicker Path to Market

- 1 US approval in SHTG has been granted based on demonstration of TG reduction from baseline; clinical outcome study was not required for certain third-party approvals
- 2 Phase 3 studies for Vascepa and Epanova were single, 12-week trials with 75–100 patients per treatment arm

## BIO89-100 Anticipated Development Plan\*

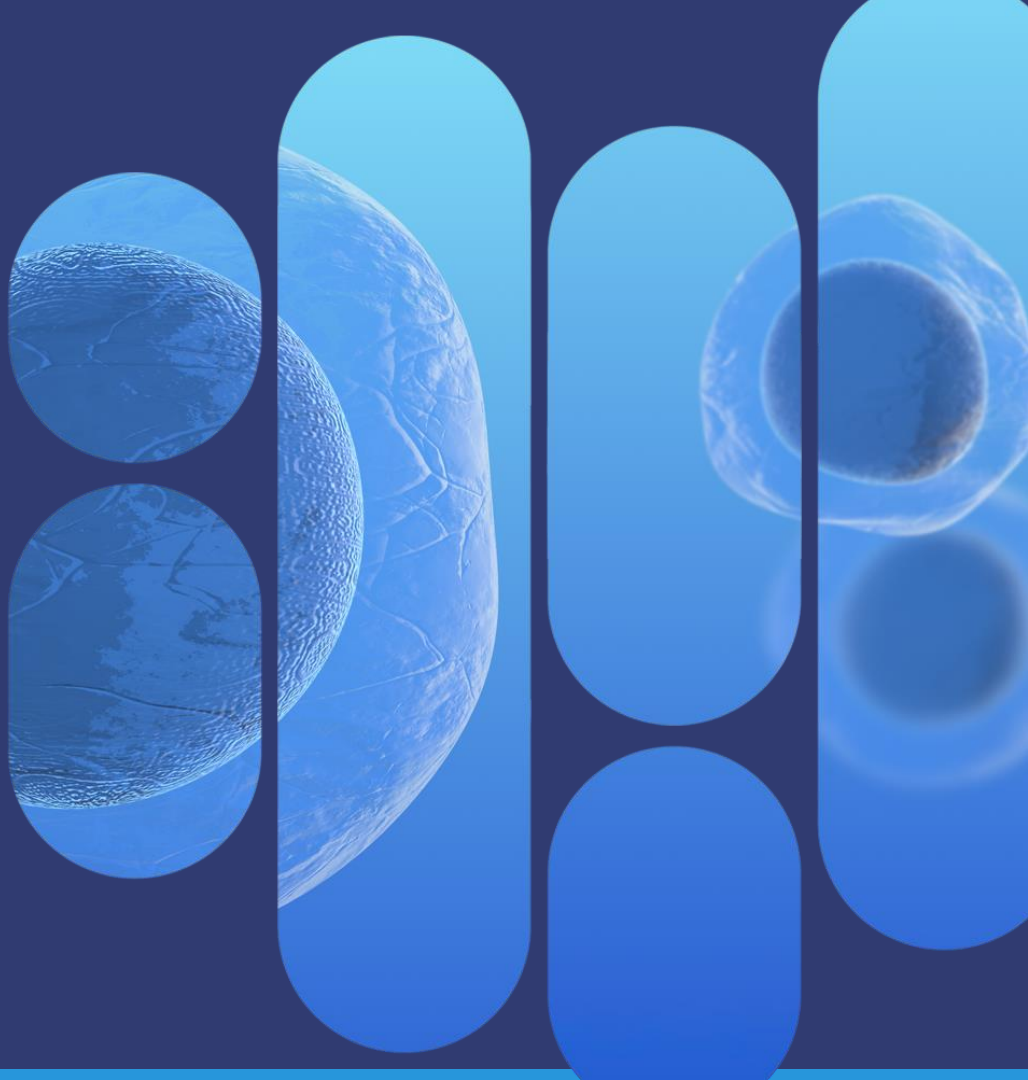
Study	Design	1H20	2H20	1H21
Phase 2 Study	<ul style="list-style-type: none"><li>Adults with TG <math>\geq</math> 500 while on stable dose of statin and/or fish oil; N = 90</li><li>Multiple doses vs placebo</li><li>Primary outcome: Reduction from baseline in TG</li><li>Secondary outcomes: Other lipids, hsCRP, glucose, body weight, safety, PK</li></ul>	 A blue arrow pointing from the 'Start' label in the 1H20 column to the 'Topline Data' label in the 1H21 column, spanning across the 2H20 column.		

*Registrational Trial\* by YE21: Patients with TG  $\geq$  500mg/dL; Endpoint = % reduction of TG from baseline*

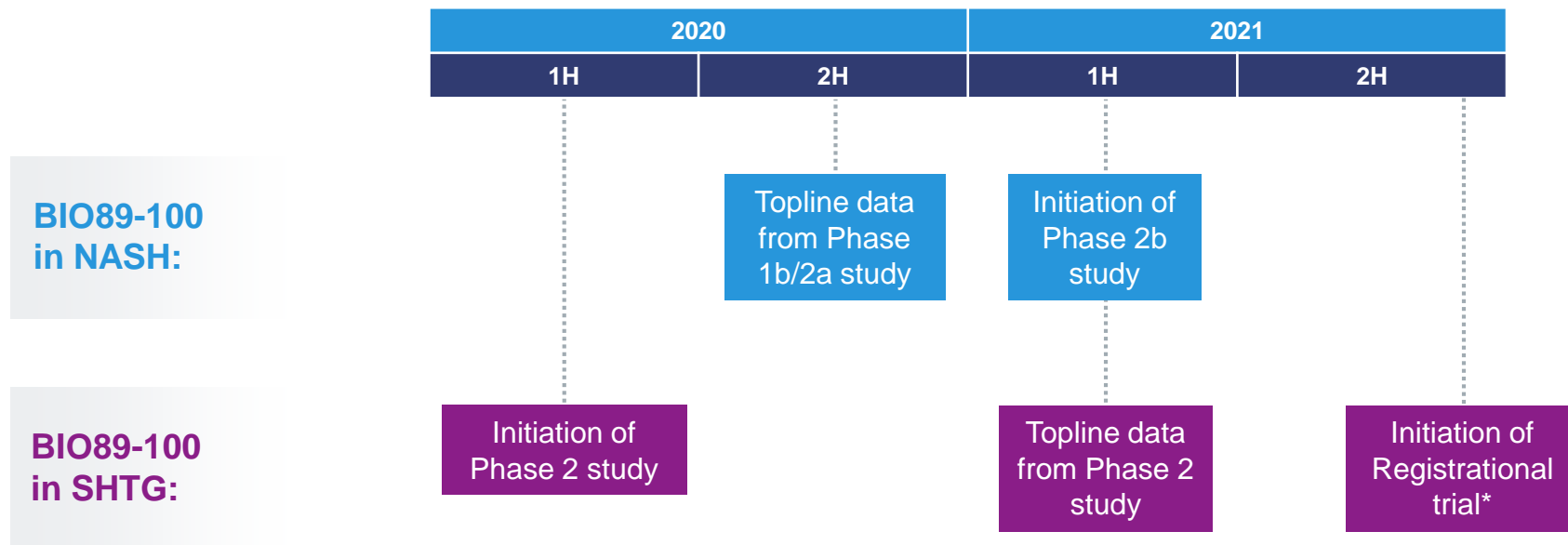
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# SUMMARY



# Recent and Upcoming Anticipated Clinical Milestones



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## Significant Commercial Opportunities

- Targeting large and growing unmet need in Non-Alcoholic Steatohepatitis (NASH) and Severe Hypertriglyceridemia (SHTG)

## Potentially Differentiated Asset Targeting Clinically Validated Mechanism in NASH

- BIO89-100 is a glycoPEGylated analog of FGF21 with compelling early human data
- FGF21 has the potential to become mainstay of NASH therapy – addresses key liver pathologies and underlying metabolic dysregulation

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- Robust reduction in triglyceride levels seen in animal and human studies
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## Anticipated Near-term Catalysts

- Two trials with BIO89-100: (i) Ongoing Phase 1b/2a trial in NASH (topline data anticipated in 2H20); (ii) Planned Phase 2 trial in SHTG (topline data anticipated in 1H21)
- Potential to transition to Phase 2b and registrational trials in NASH and SHTG, respectively, by YE21

## Established Manufacturing Expertise; Long IP Protection

- Established manufacturing process in place for near-term clinical supplies
- Issued composition of matter patent expected to expire in 2038

# Management Team

**Rohan Palekar, CEO**



- CEO, CCO experience
- Avanir, Medivation, J&J
- Commercial, strategy, and R&D experience

**Hank Mansbach, MD  
CMO**



- 20+ years biopharma and R&D leadership in clinical development and medical affairs
- Ultragenyx, Medivation, Valeant, GSK

**Ram Waisbourd  
COO and CBO**



- 20 years of operations, BD, and strategy experience
- VP of strategy and transformation, Teva R&D
- VP of business development, XTL bio

**Ryan Martins, CFO**



- CFO, Strategy/IR, finance, sell-side experience
- Revolution Medicines, Ultragenyx, Chiron, Jefferies, Lazard, Barclays/Lehman Brothers

**Quoc Le-Nguyen  
CTO & Head of Quality**



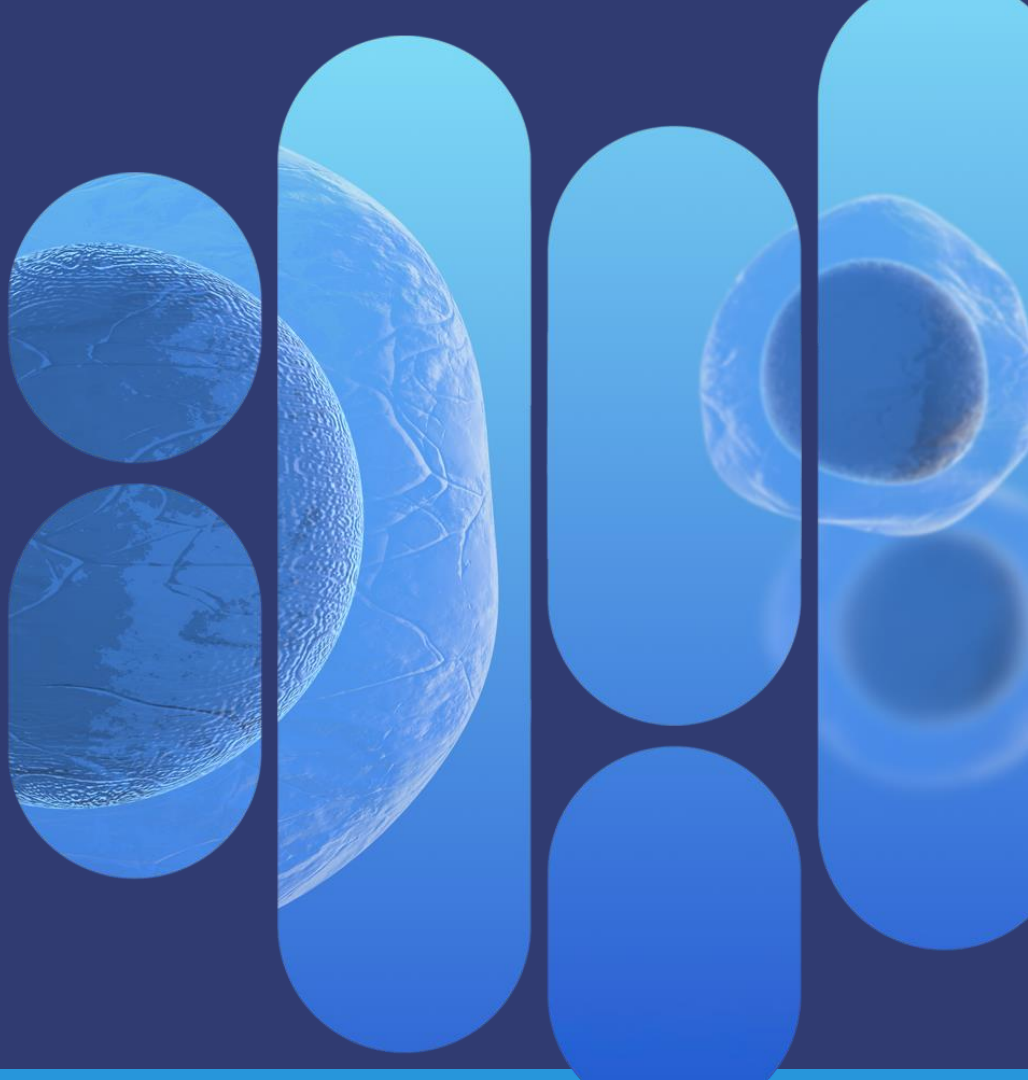
- 20+ years biopharma and leadership in technical operations, product supply, and quality
- Aduro, Bayer, Novartis, Chiron, BioMarin



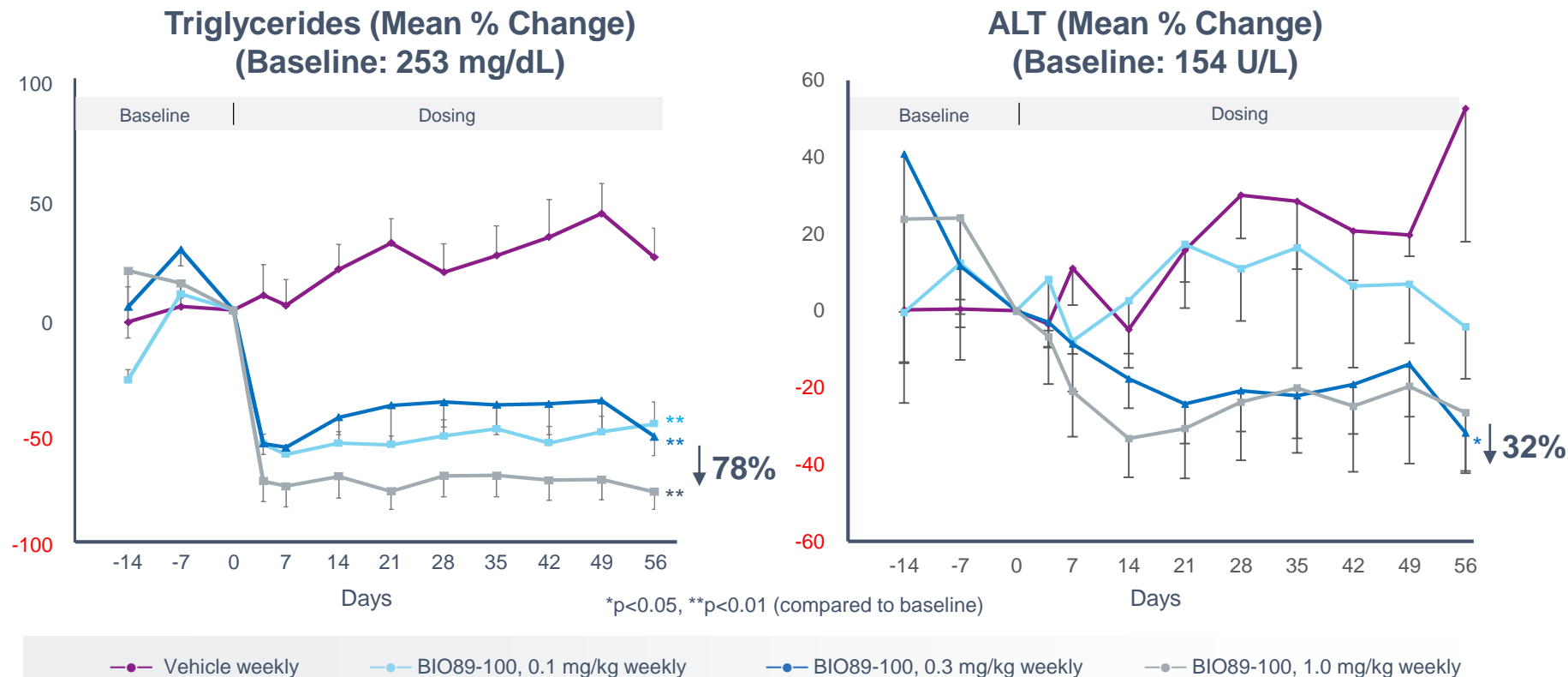
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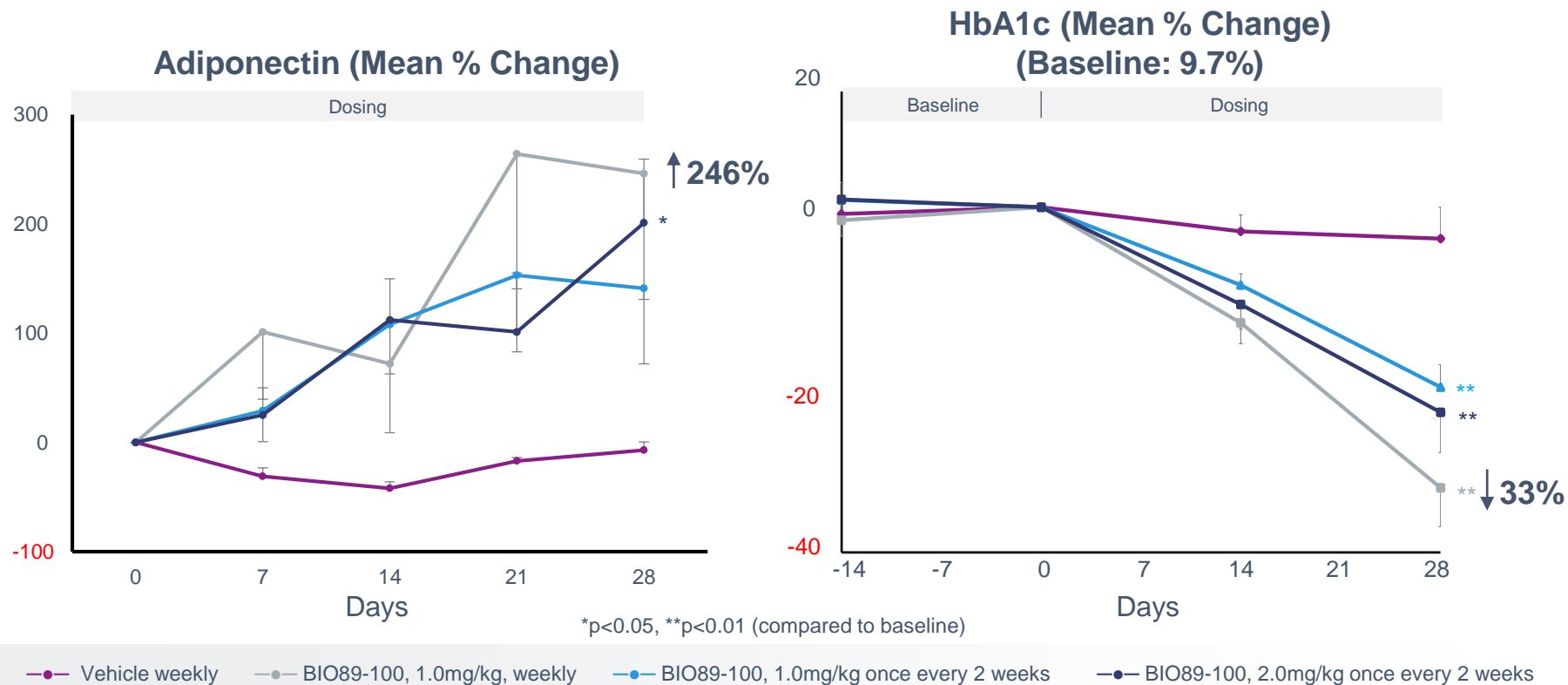
# APPENDIX



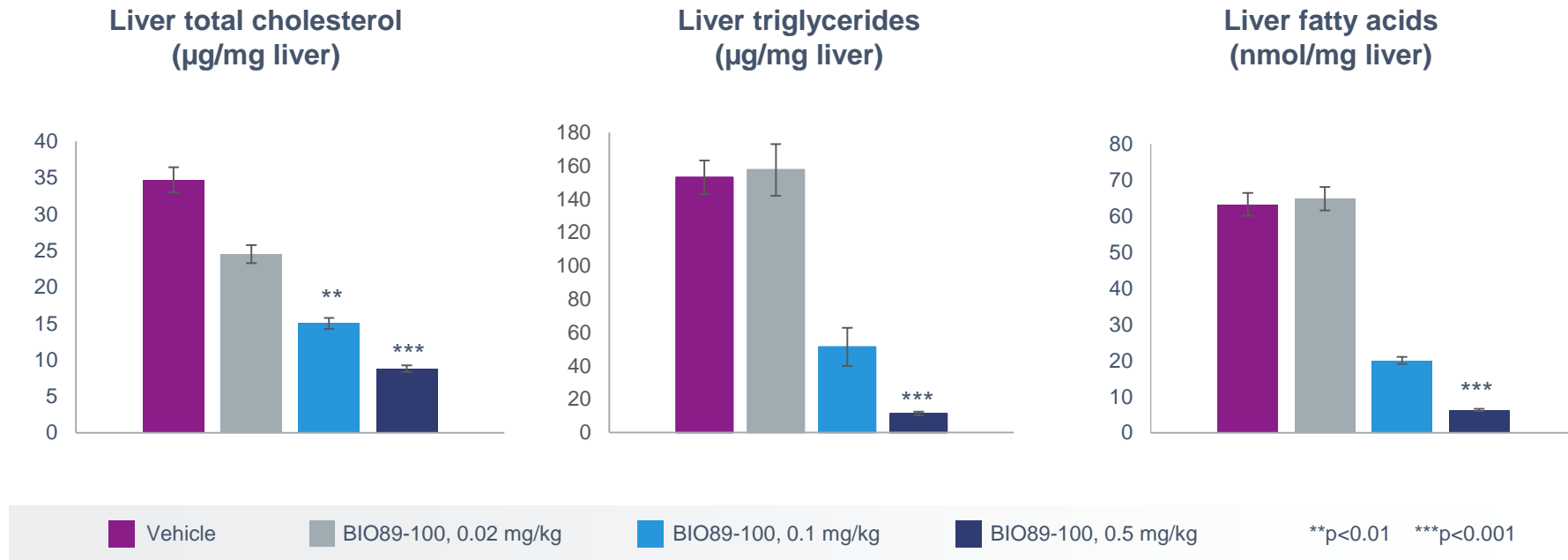
# Significant Reduction in Triglycerides and ALT with BIO89-100 in 8-Week Diabetic Obese Monkey Study



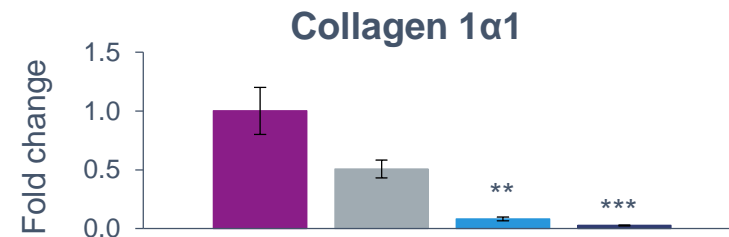
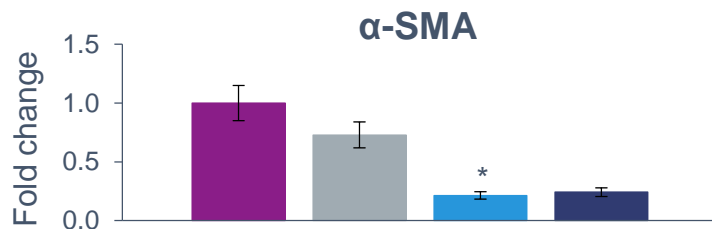
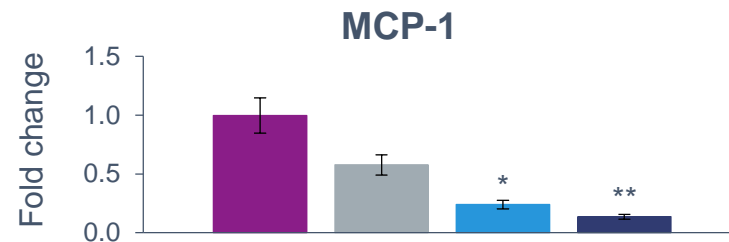
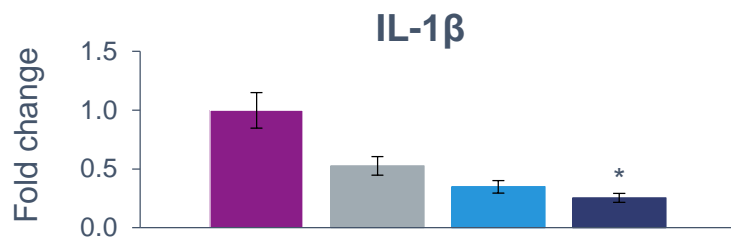
# Significant Changes in Adiponectin and HbA1c in Diabetic Obese Monkeys With Once Every 2 Weeks Dosing



# Reduction in Liver Cholesterol, Triglycerides and Fatty Acids with BIO89-100 in DIN Model



# Improvement in Inflammatory and Fibrotic Markers with BIO89-100 in DIN Model



Vehicle

BIO89-100, 0.02 mg/kg

BIO89-100, 0.1 mg/kg

BIO89-100, 0.5 mg/kg

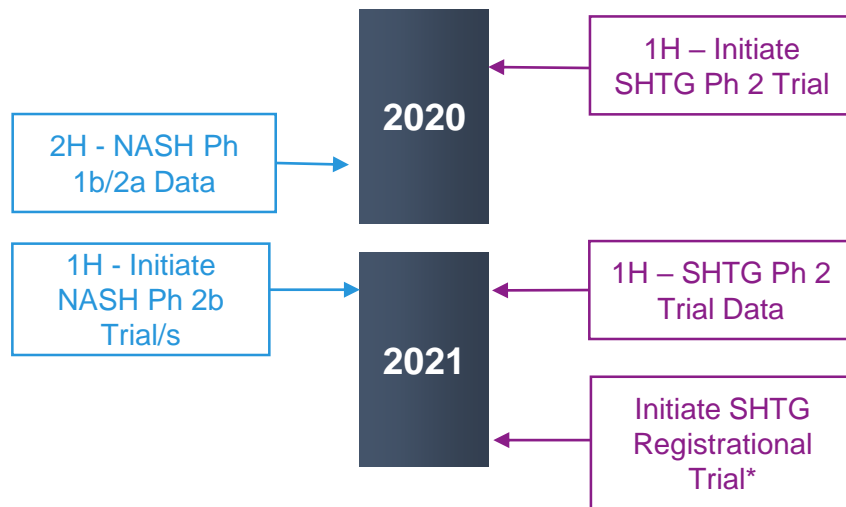
\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

# Significant Progress Since Inception With Multiple Anticipated Near-Term Catalysts

## Achievements Over the Last Year

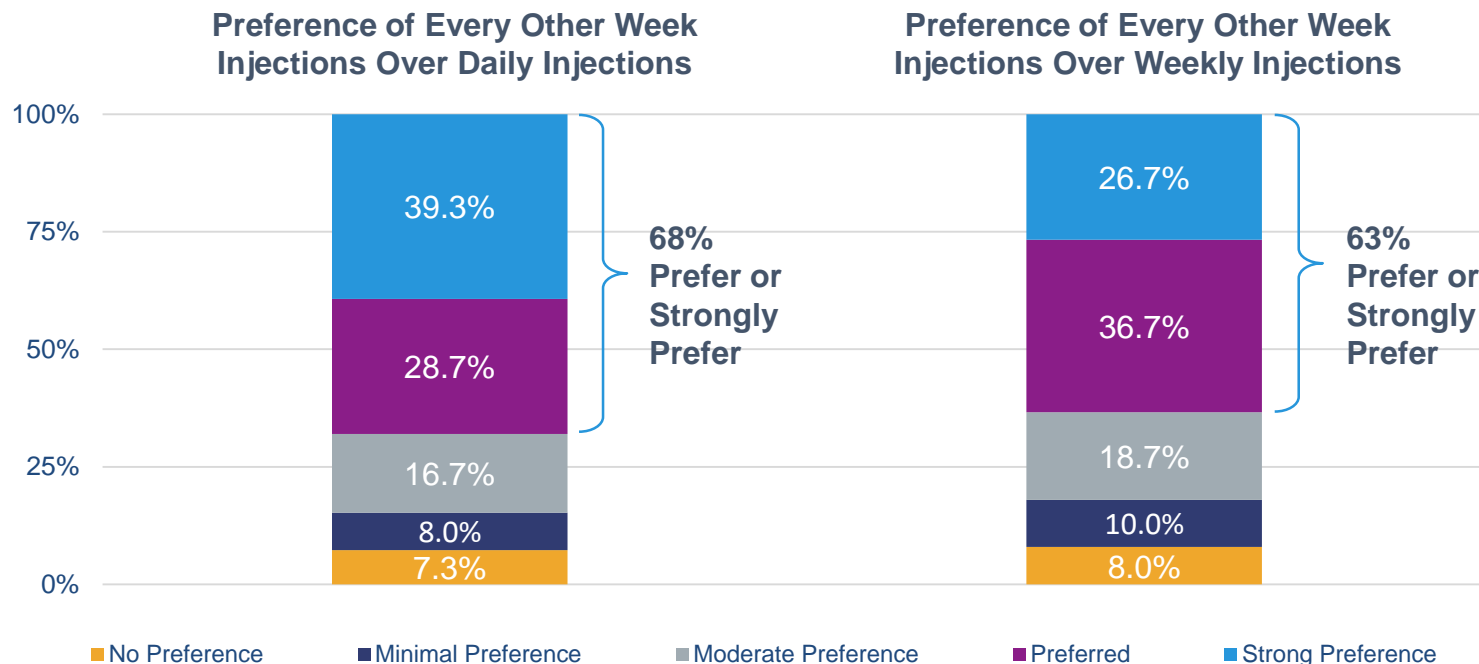
- ✓ Human data – favorable tolerability profile, robust and durable PD effect
- ✓ Toxicology – long term animal safety
- ✓ Developed know-how to manufacture multiple batches using a contract manufacturer
- ✓ New composition of matter IP through 2038
- ✓ Expanded management team to include full C-suite + depth across functions

## Upcoming Anticipated Catalysts



\* Study designs and development plan to be confirmed with regulatory feedback

# Dosing Preference Study: >60% of T2D Patients Prefer or Strongly Prefer Every Other Week Injections



Study conducted in obese Type 2 diabetics (n=150); dosing preferences for treatment of chronic liver condition  
Q's 20 & 22: Please rate your level of preference of "dosing frequency" over "dosing frequency" for long-term use