



Transforming the Care of Cardiovascular Disease Through Single-course Gene Editing Medicines

INITIAL DATA FROM HEART-2 CLINICAL TRIAL OF VERVE-102

APRIL 14, 2025

Today's agenda

Opening remarks and overview of PCSK9 program



Sekar Kathiresan, M.D.
Co-Founder and Chief
Executive Officer

Initial results from Heart-2 clinical trial of VERVE-102



Scott Vafai, M.D.
Senior Vice President,
Clinical Development

VERVE-102 next steps and closing remarks



Sekar Kathiresan, M.D.
Co-Founder and Chief
Executive Officer

Q&A



Sekar Kathiresan, M.D., Co-Founder and Chief Executive Officer
Allison Dorval, Chief Financial Officer
Scott Vafai, M.D., Senior Vice President, Clinical Development

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Verve's mission:

transform the care of cardiovascular disease
from chronic care to a one-dose future





Atherosclerotic Cardiovascular Disease (ASCVD) & Heterozygous Familial Hypercholesterolemia (HeFH)

ASCVD and HeFH:

highly prevalent diseases with profound need for improved treatments

Atherosclerotic Cardiovascular Disease (ASCVD)

What is ASCVD?

Build-up of cholesterol-driven deposits in artery walls that restricts healthy blood flow and can cause heart disease, stroke, and peripheral vascular disease

Heterozygous Familial Hypercholesterolemia (HeFH)

What is HeFH?

Inherited disease characterized by high levels of LDL-C [LDL-C $\geq$ 190 mg/dL] that frequently results in early-onset ASCVD

ASCVD and HeFH:

with current treatment options, majority of patients are not at LDL-C goal

Atherosclerotic Cardiovascular Disease (ASCVD)

What is ASCVD?

Build-up of cholesterol-driven deposits in artery walls that restricts healthy blood flow and can cause heart disease, stroke, and peripheral vascular disease

>30M

Patients with ASCVD not at LDL-C goal in U.S. + EU^{1,2}

~75%

ASCVD patients are not at LDL-C goal²

ASCVD is the leading cause of death in the world

Heterozygous Familial Hypercholesterolemia (HeFH)

What is HeFH?

Inherited disease characterized by high levels of LDL-C [LDL-C $\geq$ 190 mg/dL] that frequently results in early-onset ASCVD

>3M

Patients with HeFH in U.S. + EU³

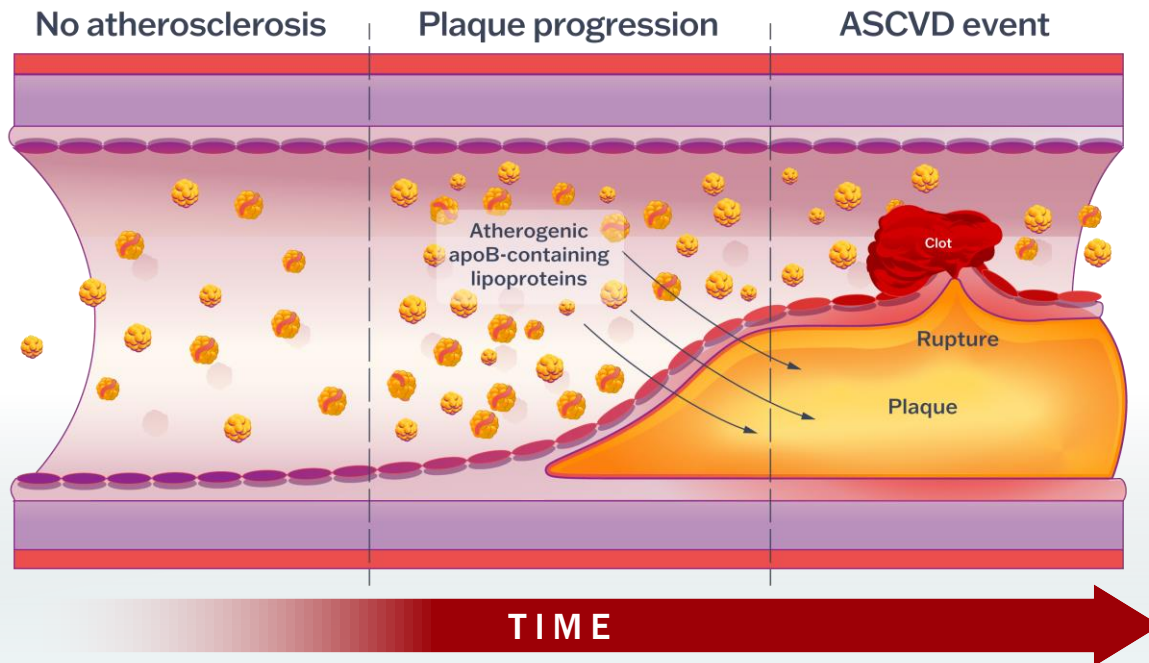
97%

HeFH patients are not at LDL-C goal⁴

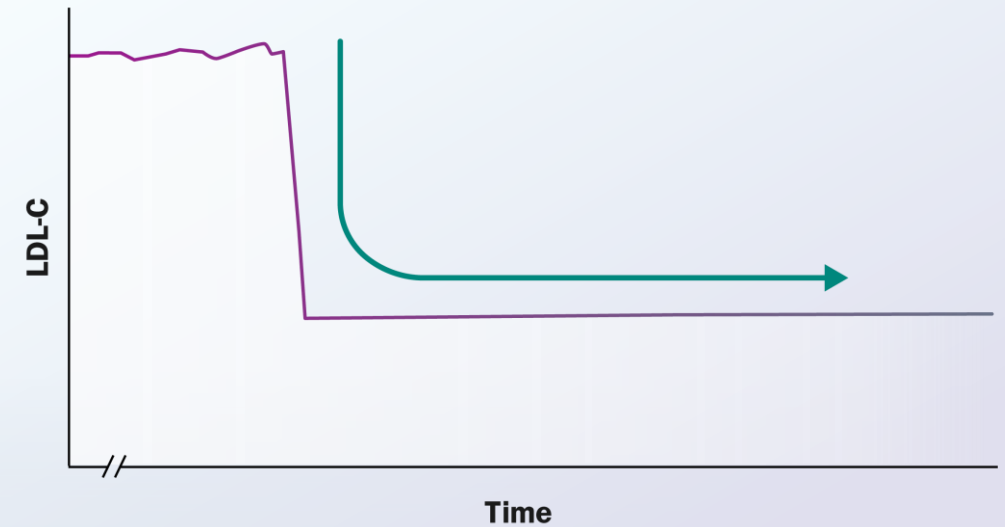
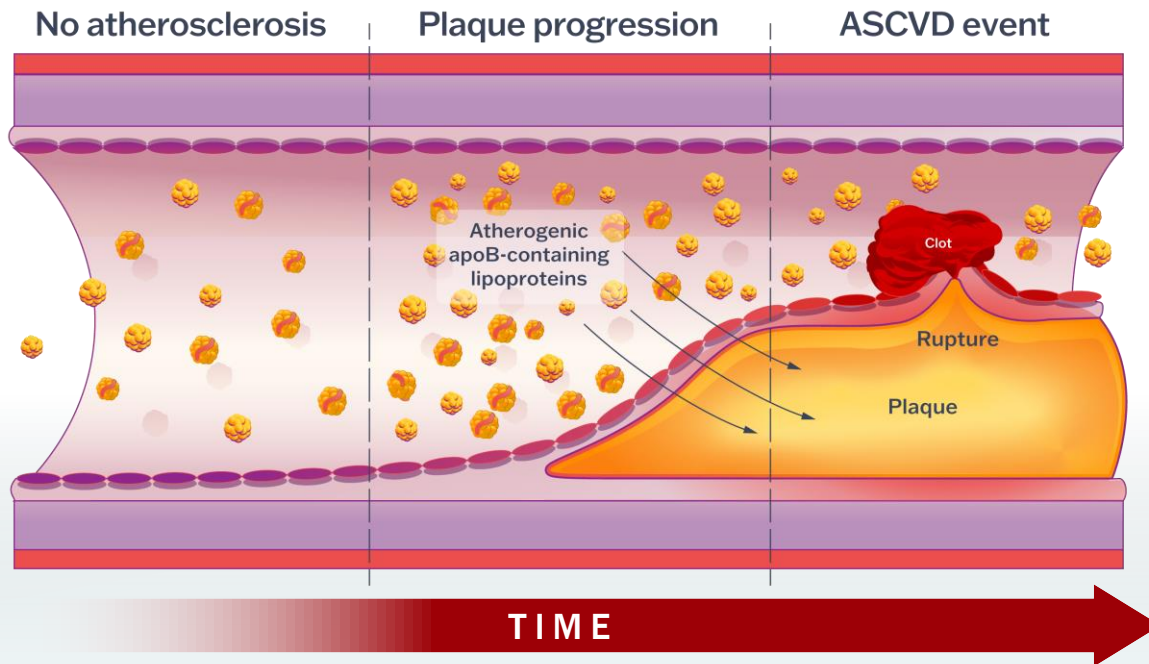
HeFH is the most prevalent genetic disease in humans

ASCVD:

caused by lifelong exposure to blood cholesterol that clogs the arteries



Treatment and prevention of ASCVD: keep blood cholesterol as low as possible for as long as possible



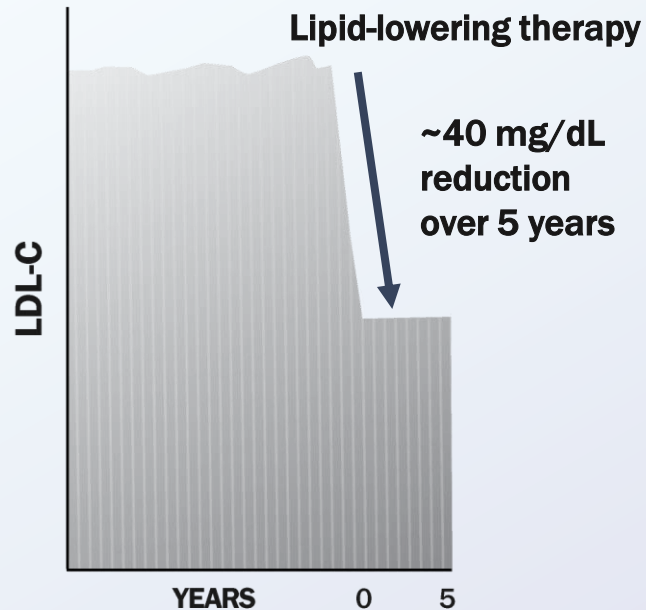


Unmet Need

Significant unmet need: today's chronic care approach leads to transient LDL-C reduction and inadequate efficacy

Today's Approach:

Transient LDL-C Reduction, Inadequate Efficacy



21% Major CVD Event Reduction¹

Learnings from lipid lowering trials:*
5 years of consistent LDL-C lowering
reduces major cardiovascular event risk by 21%

*In 28 trials evaluating efficacy and safety of statin therapy. 1. Cholesterol Treatment Trialists' (CTT) Collaboration. Lancet 2019. LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease

...and frequent discontinuation further limits efficacy

Today's Approach:
Transient LDL-C Reduction, Inadequate Efficacy

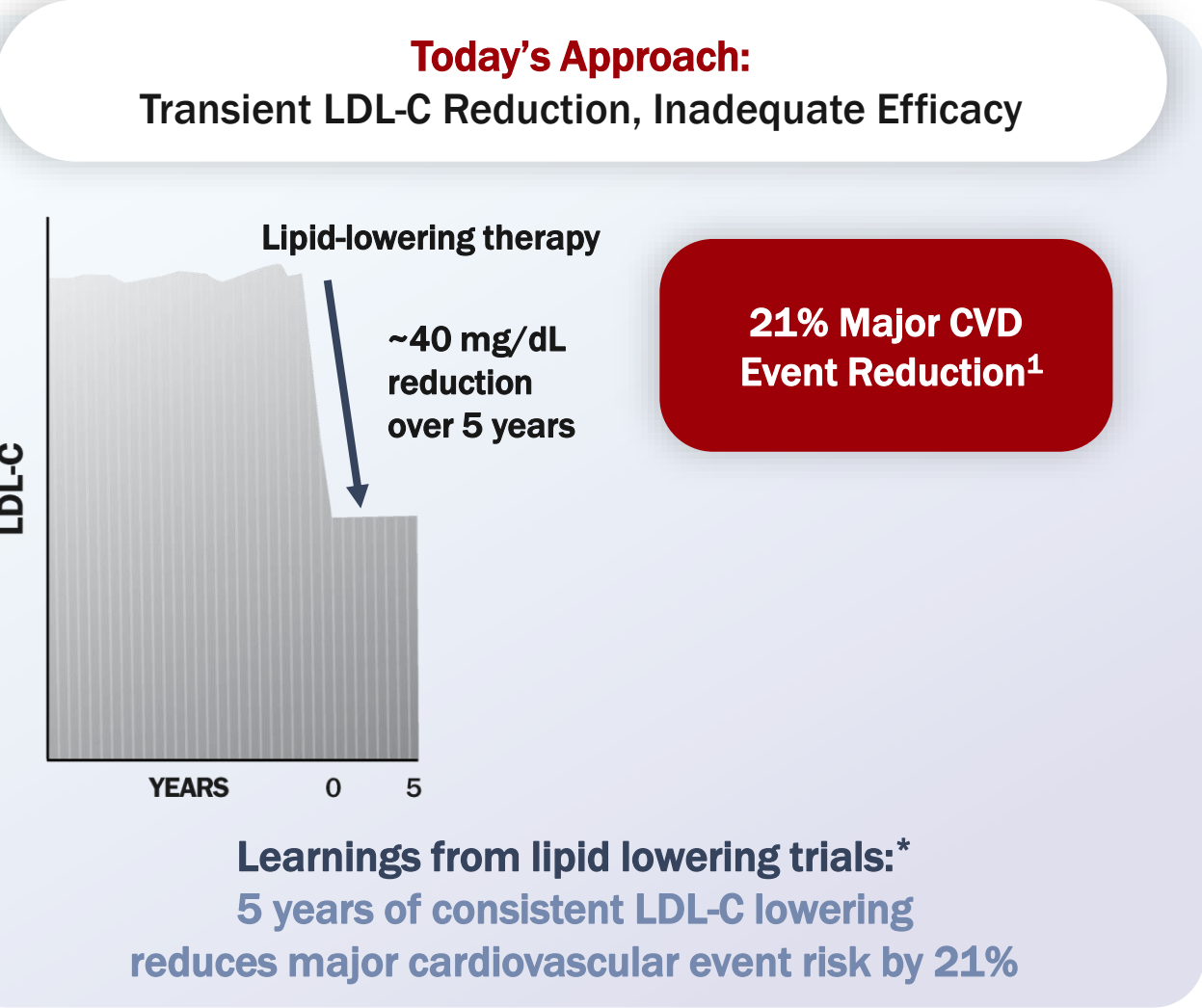
21% Major CVD Event Reduction¹

Learnings from lipid lowering trials:*
5 years of consistent LDL-C lowering
reduces major cardiovascular event risk by 21%

	PCSK9 siRNA	PCSK9 mAb
Dosing	Injection every 6 months	Injection every 2 weeks
1-year Patient Discontinuation Rate ²	~1 in 5	~1 in 2

*In 28 trials evaluating efficacy and safety of statin therapy. 1. Cholesterol Treatment Trialists' (CTT) Collaboration. Lancet 2019. 2. Popadic et al. Journal of Clinical Lipidology 2024. LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease; PCSK9, proprotein convertase subtilisin/kexin type 9; siRNA, small interfering RNA; mAb, monoclonal antibody

...estimated real-world LDL-C reduction of only 23% to 35%



Efficacy is Compromised by Frequent Discontinuation

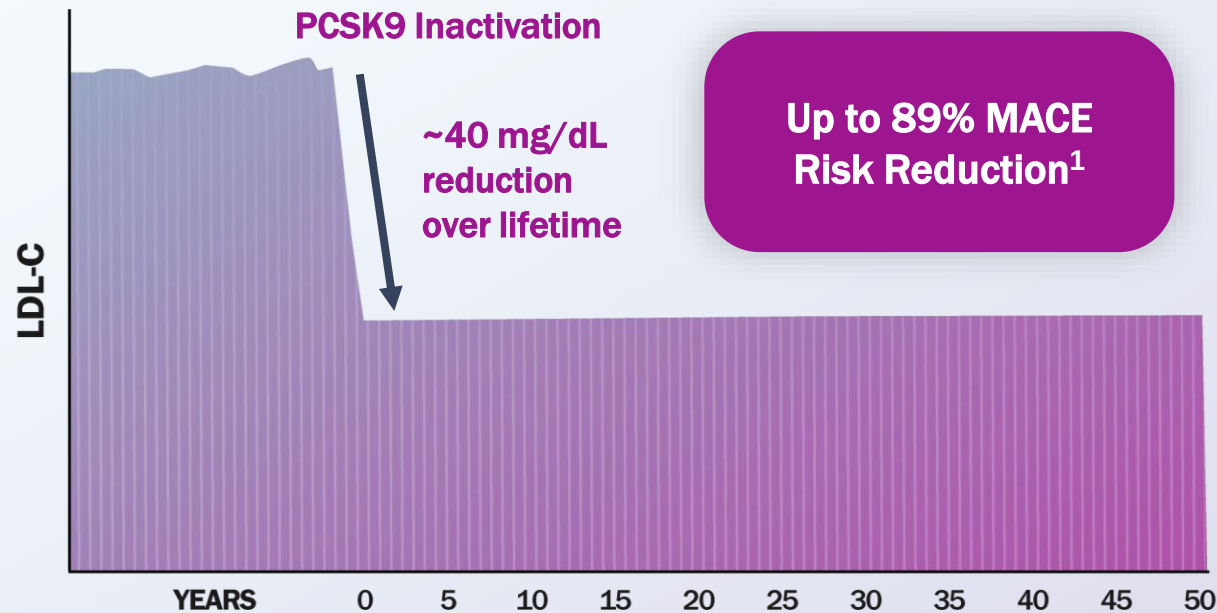
	PCSK9 siRNA	PCSK9 mAb
Dosing	Injection every 6 months	Injection every 2 weeks
1-year Patient Discontinuation Rate ²	~1 in 5	~1 in 2
Estimated Real-world LDL-C Reduction at 1 year ³	- 35%	- 23%

*In 28 trials evaluating efficacy and safety of statin therapy. 1. Cholesterol Treatment Trialists' (CTT) Collaboration. Lancet 2019. 2. Popadic et al. Journal of Clinical Lipidology 2024. 3. Rosenson et al. 2025 ACC. Poster #12209
LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease; PCSK9, proprotein convertase subtilisin/kexin type 9; siRNA, small interfering RNA; mAb, monoclonal antibody

**What is the solution to the
unmet need for improved efficacy?**

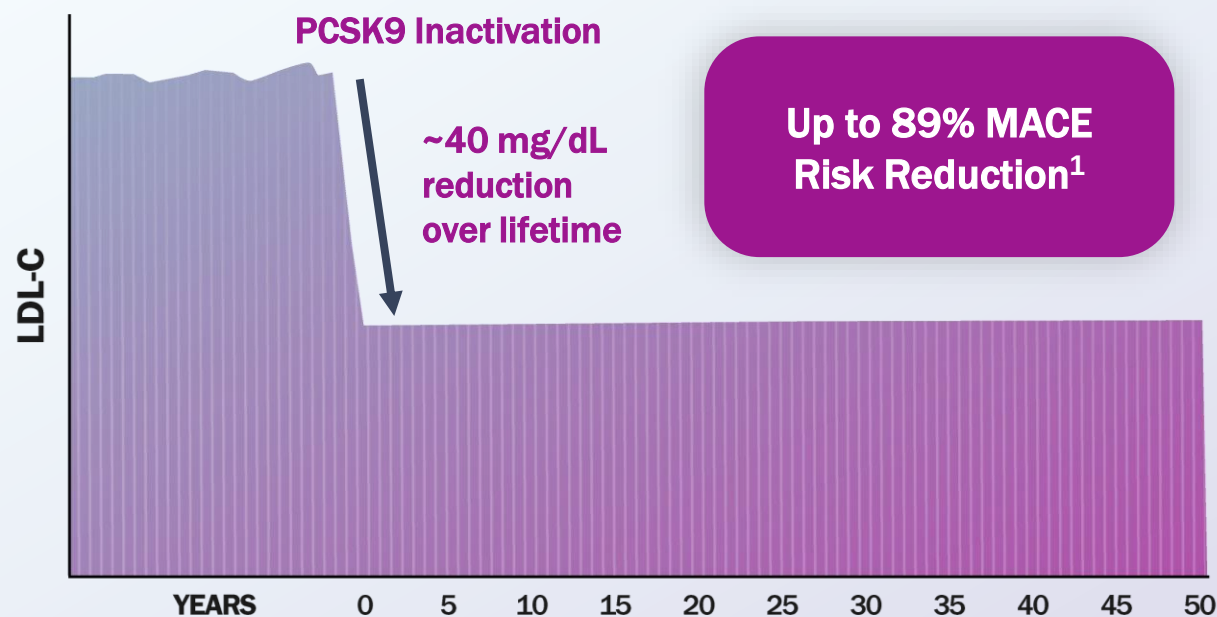


Solution: a treatment approach that can provide **enduring efficacy**;
40 mg/dL reduction over a lifetime = dramatic ASCVD risk reduction



**Lifetime of lowered LDL-C safely reduces
MACE risk by up to 89%**

Solution: a treatment approach that can provide **enduring efficacy**;
40 mg/dL reduction over a lifetime = dramatic ASCVD risk reduction



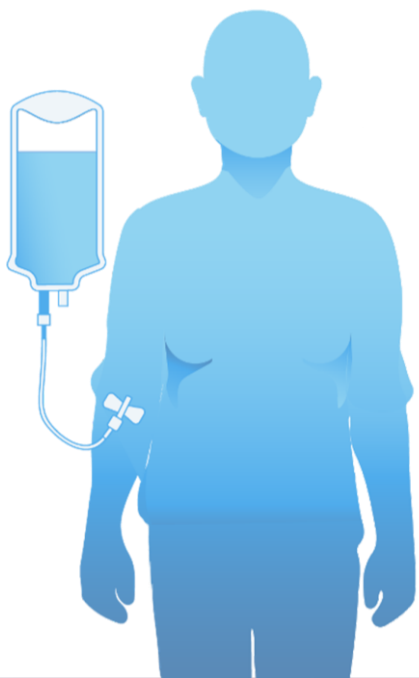
Lifetime of lowered LDL-C safely reduces
MACE risk by up to 89%



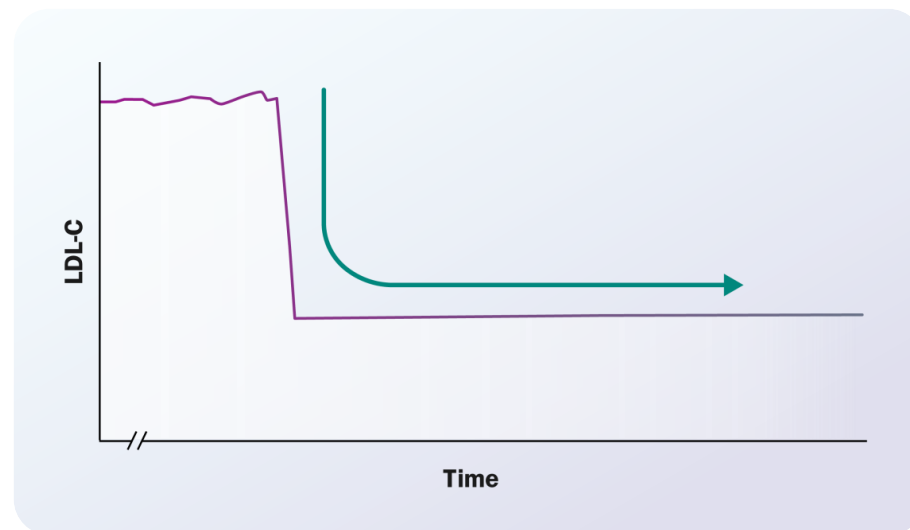
Benefit of LDL-C lowering
accrues over time and
is **maximized when started
early and durably maintained**

Verve's vision: a one dose future to address chronic disease

Single IV Infusion of Verve Product



Lifelong Blood Cholesterol Reduction



VERVE MISSION

Deliver
enduring efficacy
to patients living with
ASCVD

Verve's pipeline addresses the three cholesterol drivers of atherosclerosis — LDL, TRL, and Lp(a) — with a therapeutic target for each (PCSK9, ANGPTL3, LPA)



Today, we focus on the PCSK9 program

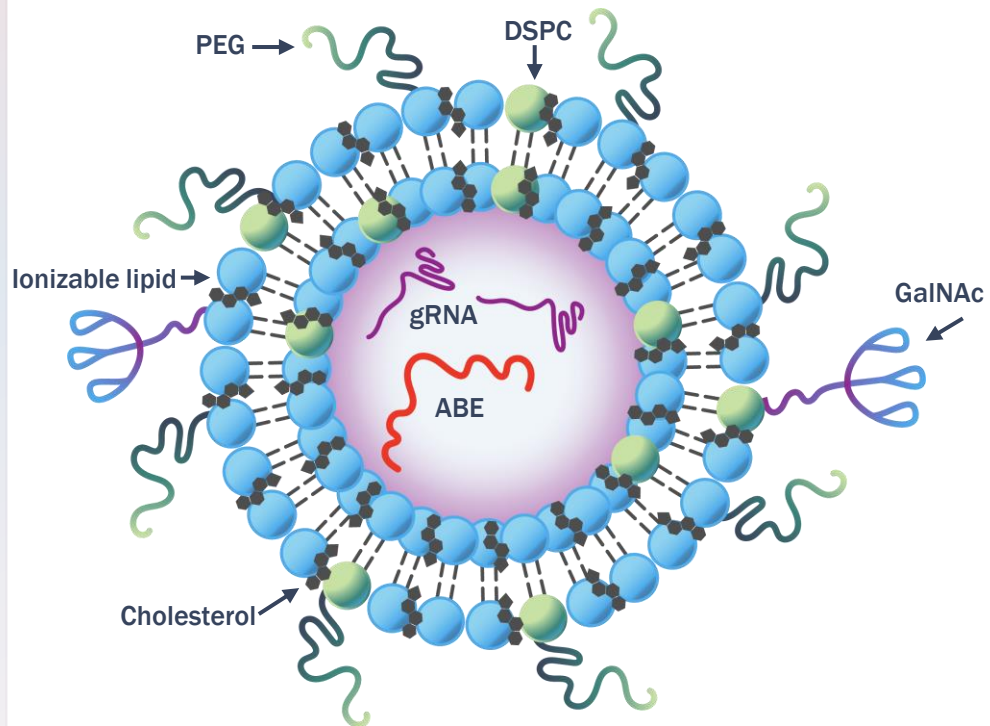


Verve has developed two PCSK9 product candidates:
VERVE-102 has same editing mechanism but improved delivery platform vs. **VERVE-101**

		VERVE-101 (Heart-1 Clinical Trial)	VERVE-102 (Heart-2 Clinical Trial)
TARGET	>	PCSK9 gene	
ADENINE BASE EDITOR (ABE)	>	Same ABE used in both product candidates	
GUIDE RNA (gRNA)	>	Same gRNA targeting <i>PCSK9</i>	
IONIZABLE LIPID	>	ALC-0307	LP000001
PEG LIPID	>	ALC-0159	DMG-PEG ₂₀₀₀
TARGETING LIGAND	>	-	GaINAc

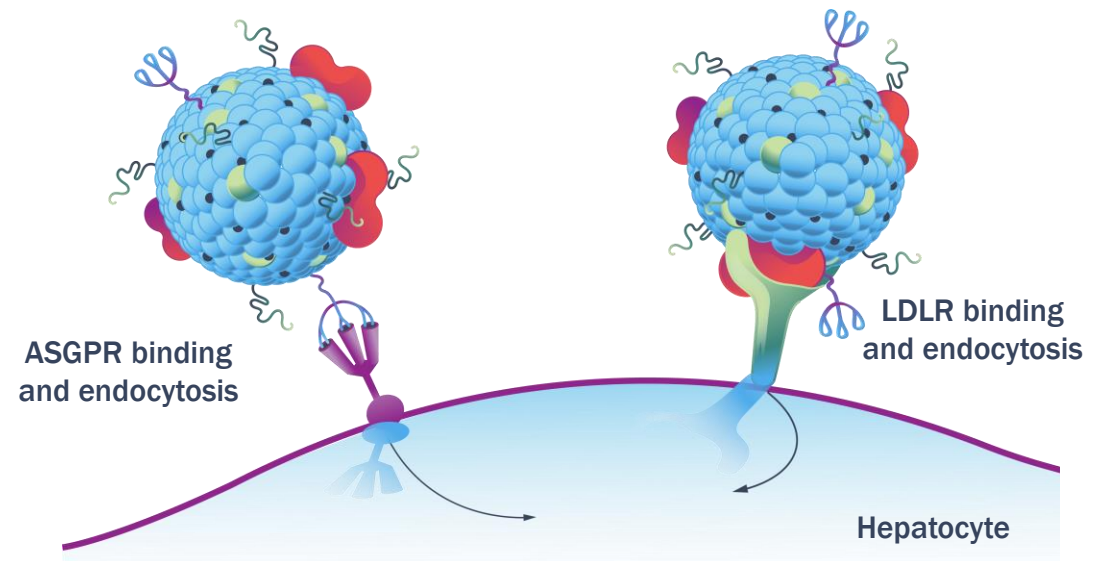
GaINAc-LNP delivery platform: allows LDLR-independent uptake of VERVE-102 into hepatocytes

VERVE-102



Role of the GaINAc Ligand

After IV infusion of the GaINAc-LNP, VERVE-102 enters hepatocytes through LDLR or ASGPR



Key questions for PCSK9 program

Safety

Does novel
GalNAc-LNP in
VERVE-102 allow
for safe delivery of
gene editor to the
liver?



Efficacy

For VERVE-102,
what dose might
drive a potent
LDL-C reduction?



Durability

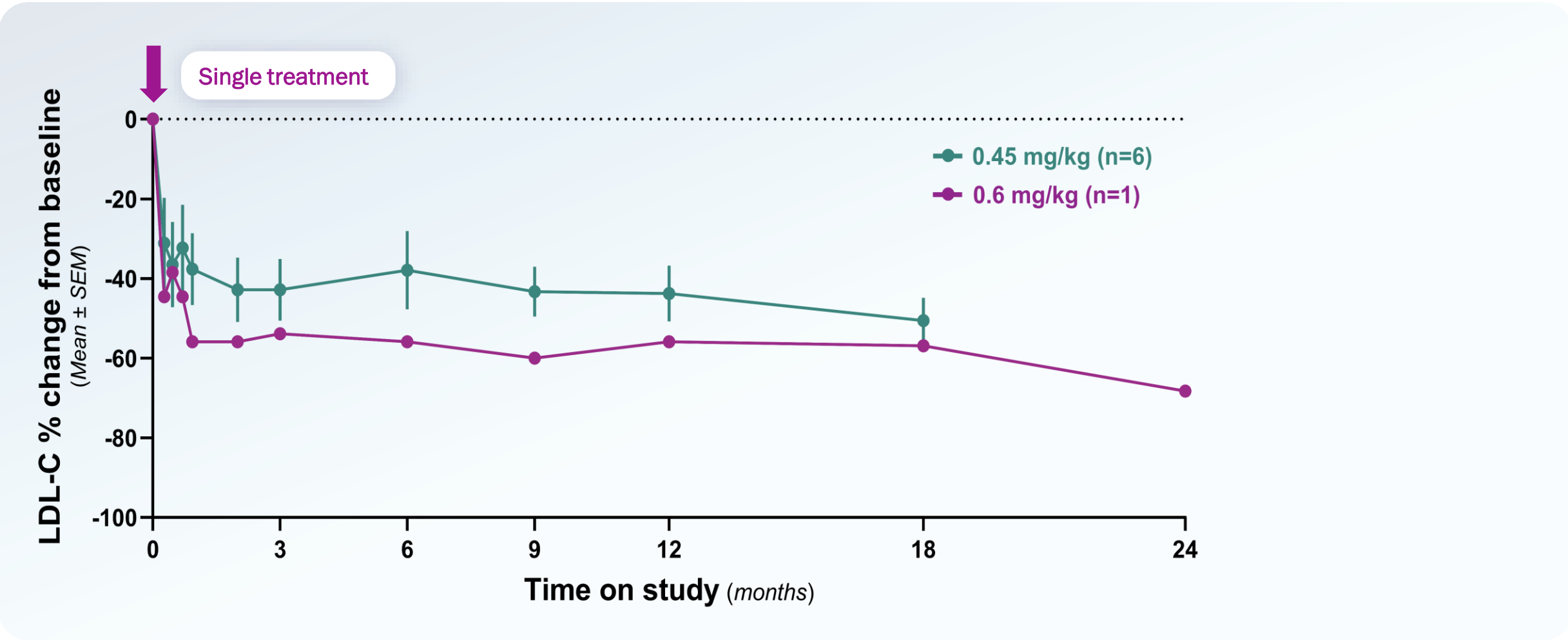
Can potent LDL-C
reduction be
maintained over
time?





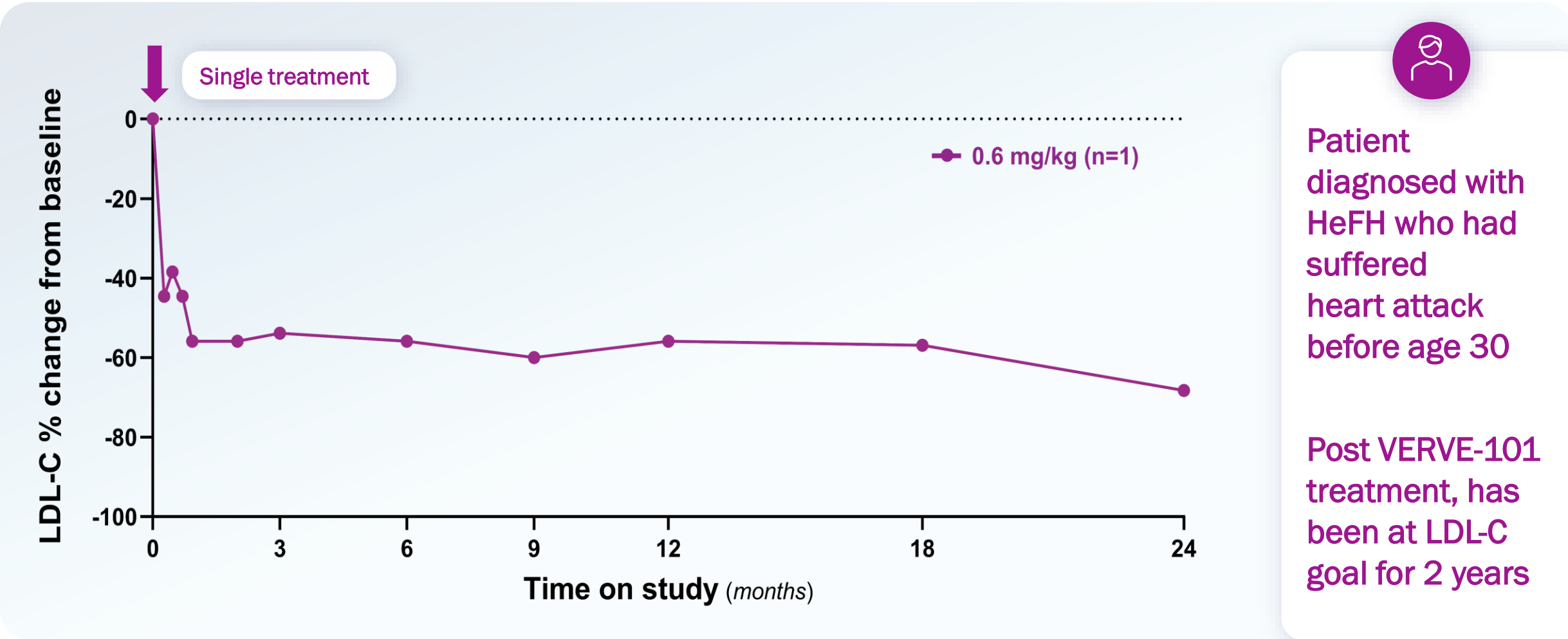
Durability Update for VERVE-101 in Heart-1 Clinical Trial

VERVE-101 data provides proof of concept that base editing mechanism may deliver enduring efficacy: **2 years after treatment, time-averaged LDL-C reduction of 58% for single participant**

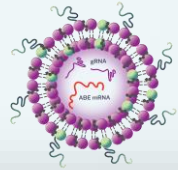


Data from parent Heart-1 study as of February 27, 2025. Data from long-term follow-up study as of March 26, 2025. Data are from ongoing studies with open databases that have not been fully cleaned. Participants in 0.45 mg/kg cohort have variable duration of follow up, with n=2 at 18 months and n=4 at 12 months. Select time points were impacted for two participants in the 0.45 mg/kg cohort due to changes in background lipid-lowering therapy. LDL-C, low-density lipoprotein cholesterol; SEM, standard error of the mean

VERVE-101 data provides proof of concept that base editing mechanism may deliver enduring efficacy: **2 years after treatment, time-averaged LDL-C reduction of 58% for single participant**



LNP-driven, transient laboratory abnormalities (ALT, platelets) with VERVE-101 motivated prioritization of VERVE-102



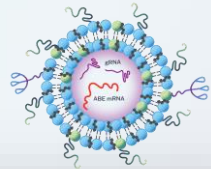
VERVE-101



Transient laboratory abnormalities (ALT, platelets) in clinic



Nonclinical studies conducted in 2024 confirmed LNP as source of laboratory abnormalities



VERVE-102



Nonclinical data indicate that with novel GalNAc-LNP, VERVE-102 is better tolerated at higher doses than VERVE-101

Data demonstrated durability for base editing mechanism; next up: safety and efficacy of VERVE-102

Safety

Does novel
GalNAc-LNP in
VERVE-102 allow
for safe delivery of
gene editor to the
liver?



Efficacy

For VERVE-102,
what dose might
drive a potent
LDL-C reduction?



Durability

VERVE-101 has
demonstrated
durability of base
editing
mechanism out to
24 months





Initial Data from Heart-2 Clinical Trial of VERVE-102

Heart-2: Phase 1b trial designed to evaluate safety and tolerability of VERVE-102



Population: HeFH and/or premature coronary artery disease patients who require additional LDL-C lowering



Intervention:
Single dose administered as a 2- to 4-hour peripheral intravenous infusion¹

Phase 1b
Single ascending dose, n = 3 – 9 per cohort

0.3 mg/kg

0.45 mg/kg

0.6 mg/kg

4th dose level

Phase 2*
Expect first patient dosed H2 2025

Doses selected based on findings from Phase 1

Objectives:

- Primary: Evaluate safety and tolerability
- Secondary: measure changes in blood PCSK9 and LDL-C levels

Initial update: safety and pharmacodynamic data from 14 participants across first three cohorts of Heart-2 trial



Population: HeFH and/or premature coronary artery disease patients who require additional LDL-C lowering



Intervention:
Single dose administered as a 2- to 4-hour peripheral intravenous infusion¹

Phase 1b
Single ascending dose, n = 3 – 9 per cohort

0.3 mg/kg (n=4)

0.45 mg/kg (n=6)

0.6 mg/kg (n=4)

4th dose level

Phase 2*
Expect first patient dosed H2 2025

Doses selected based on findings from Phase 1

Initial data from first 14 participants dosed across first three cohorts with ≥ 28 days of follow up

Objectives:

- Primary: evaluate safety and tolerability
- Secondary: measure changes in blood PCSK9 and LDL-C levels

Baseline characteristics: majority of 14 participants have HeFH; mean baseline LDL-C of 140 mg/dL (3.6 mmol/L)

CHARACTERISTIC	PARTICIPANTS (N=14)
Mean age, years	52
Sex, n	
Male	9
Female	5
Mean weight, kg	79
Mean baseline LDL-C, mg/dL	140
Clinical status, n	
Heterozygous familial hypercholesterolemia (HeFH) only	8
HeFH and premature coronary artery disease	3
Premature coronary artery disease only	3
Pre-existing atherosclerotic cardiovascular disease, n	10
Concomitant statin use, n	
High-intensity	9
Moderate- or low-intensity	3
None	2



Safety

Clinical safety: VERVE-102 was well-tolerated across all dose levels

- No treatment-related SAEs and no DLTs
- No clinically significant laboratory abnormalities
- No cardiovascular events
- Across all 14 participants, there was one infusion-related reaction (IRR)
 - Single Grade 2 IRR in a participant dosed at 0.6 mg/kg (transient symptoms that resolved with acetaminophen)

Clinical safety: majority of adverse events were mild in severity and unrelated to treatment

	0.3 mg/kg (n=4)			0.45 mg/kg (n=6)			0.6 mg/kg (n=4)		
PARTICIPANTS EXPERIENCING:	GR 1	GR 2	GR 3	GR 1	GR 2	GR 3	GR 1	GR 2	GR 3
Any AE	2	1	-	2	-	1*	2	1	-
Any AE related to VERVE-102	1	-	-	-	-	-	1	1	-
Any SAE	-	-	-	-	-	1*	-	-	-
Any SAE related to VERVE-102	-	-	-	-	-	-	-	-	-
AEs OCCURRING IN > 1 PARTICIPANT									
Upper respiratory tract infection	-	-	-	1	-	-	2	-	-
Fatigue	1	-	-	-	-	-	1	-	-
Dizziness	1	-	-	1	-	-	-	-	-

As of March 13, 2025, data cut off date; data are from an ongoing study with an open database and have not been fully cleaned; all AEs are treatment-emergent adverse events.

Participants counted once per row with highest grade AE reported. Treatment-related AEs included Grade 1 dizziness in one participant dosed at 0.3 mg/kg, Grade 1 fatigue and Grade 1 maculopapular rash in one participant dosed at 0.6 mg/kg, and a Grade 2 infusion-related reaction in another participant dosed at 0.6 mg/kg.

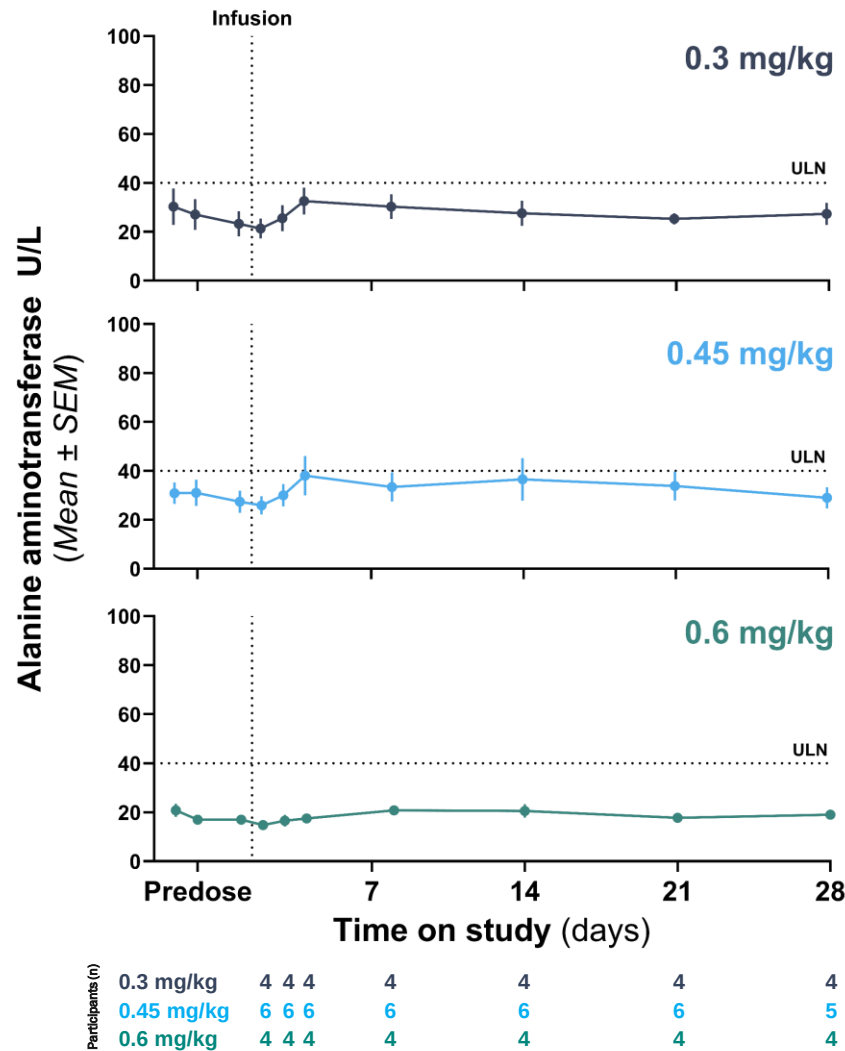
*One unrelated Grade 3 SAE of aspiration pneumonitis occurred more than two weeks after VERVE-102 infusion and resolved in a participant (0.45 mg/kg dose) with a history of gastroesophageal reflux disease and sliding hiatal hernia. AE, adverse event; SAE, serious adverse event

Clinical safety: no serious adverse events related to VERVE-102 treatment were observed

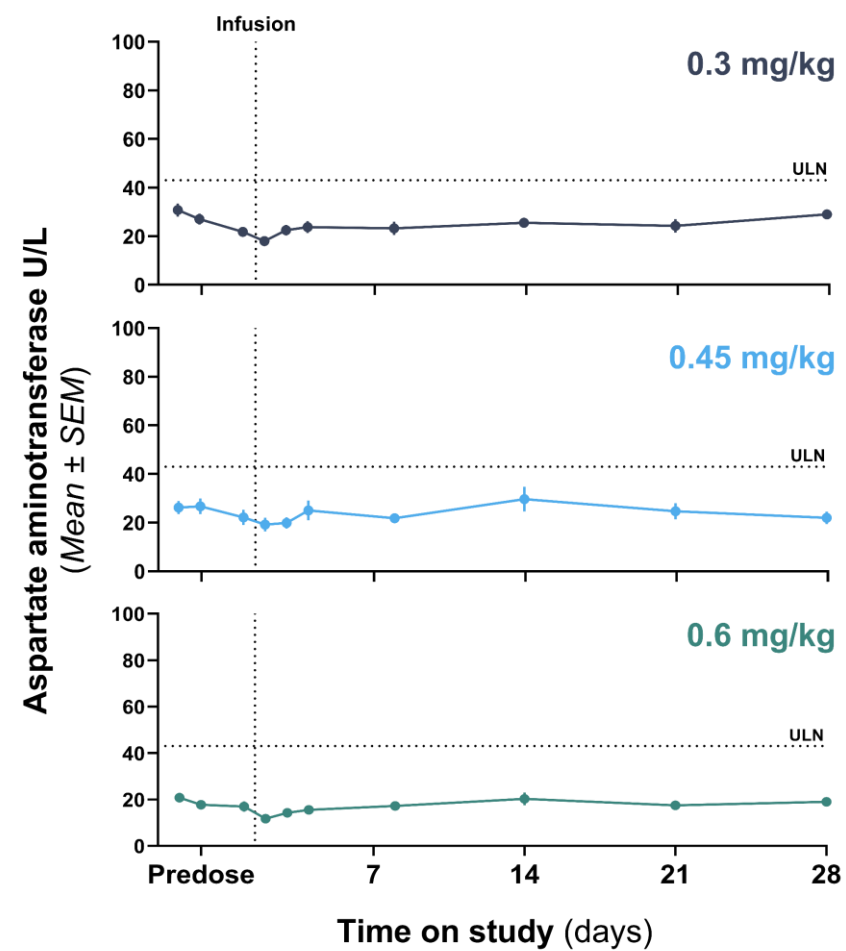
	0.3 mg/kg (n=4)			0.45 mg/kg (n=6)			0.6 mg/kg (n=4)		
PARTICIPANTS EXPERIENCING:	GR 1	GR 2	GR 3	GR 1	GR 2	GR 3	GR 1	GR 2	GR 3
Any AE	2	1	-	2	-	1*	2	1	-
Any AE related to VERVE-102	1	-	-	-	-	-	1	1	-
Any SAE	-	-	-	-	-	1*	-	-	-
Any SAE related to VERVE-102	-	-	-	-	-	-	-	-	-
AEs OCCURRING IN > 1 PARTICIPANT									
Upper respiratory tract infection	-	-	-	1	-	-	2	-	-
Fatigue	1	-	-	-	-	-	1	-	-
Dizziness	1	-	-	1	-	-	-	-	-

As of March 13, 2025, data cut off date; data are from an ongoing study with an open database and have not been fully cleaned; all AEs are treatment-emergent adverse events. Participants counted once per row with highest grade AE reported. Treatment-related AEs included Grade 1 dizziness in one participant dosed at 0.3 mg/kg, Grade 1 fatigue and Grade 1 maculopapular rash in one participant dosed at 0.6 mg/kg, and a Grade 2 infusion-related reaction in another participant dosed at 0.6 mg/kg.
*One unrelated Grade 3 SAE of aspiration pneumonia occurred more than two weeks after VERVE-102 infusion and resolved in a participant (0.45 mg/kg dose) with a history of gastroesophageal reflux disease and sliding hiatal hernia.
AE, adverse event; SAE, serious adverse event

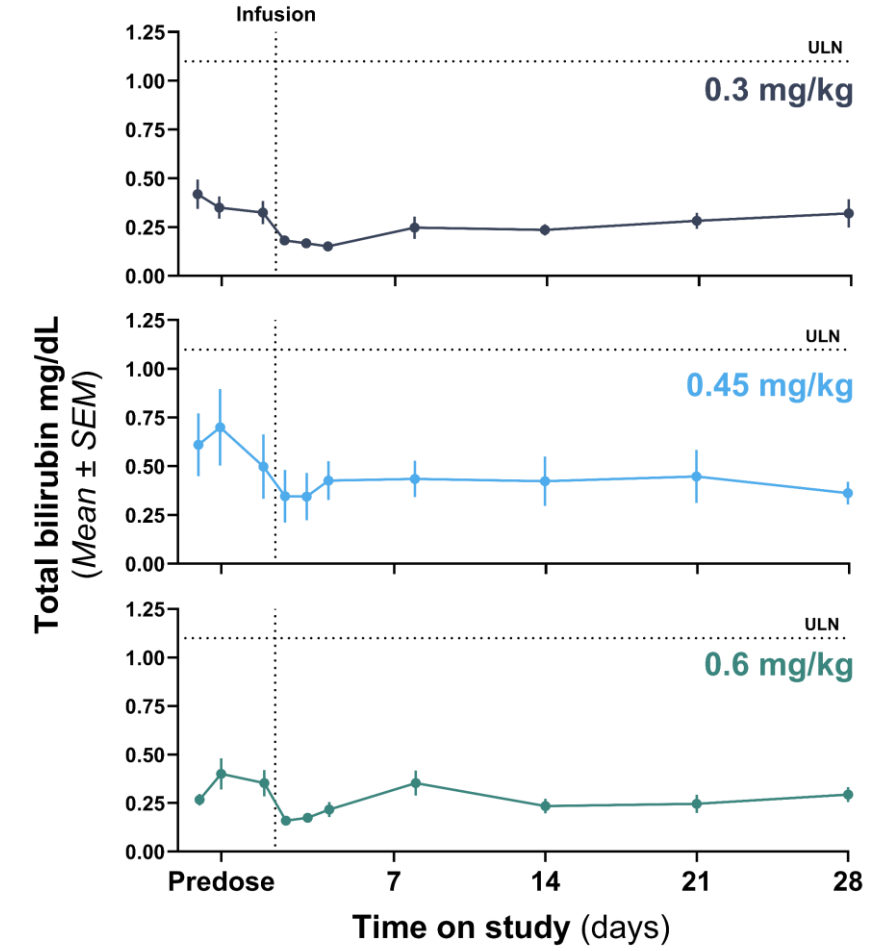
Laboratory assessment: no clinically significant changes in alanine aminotransferase (ALT) at any dose level following VERVE-102 infusion



Laboratory assessment: no clinically significant changes in aspartate aminotransferase (AST) or bilirubin at any dose level following VERVE-102 infusion



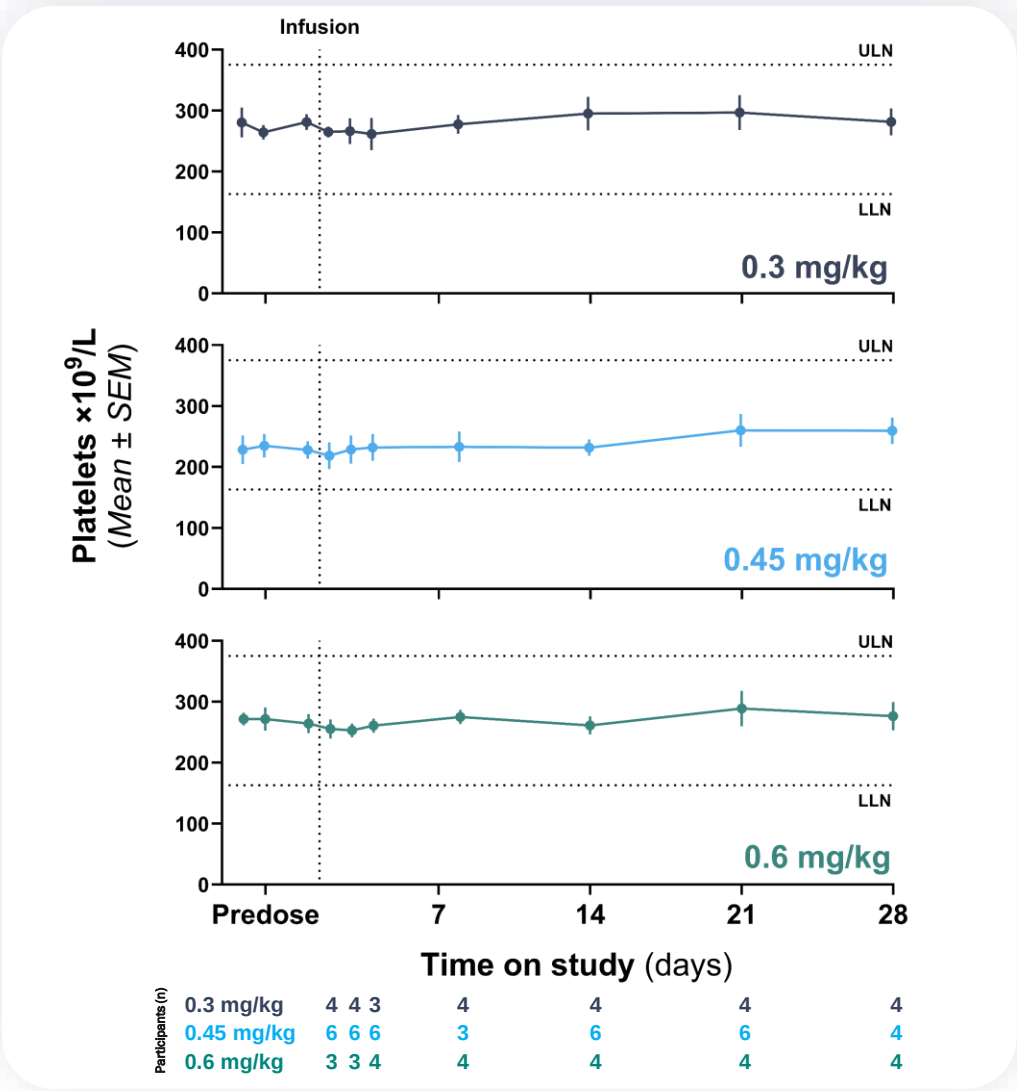
Participants (n)	0.3 mg/kg	4	4	4	4	4	4
0.45 mg/kg	6	6	6	6	6	6	5
0.6 mg/kg	4	4	4	4	4	4	4



Participants (n)	0.3 mg/kg	4	4	4	4	4	4
0.45 mg/kg	6	6	6	6	6	6	5
0.6 mg/kg	4	4	4	4	4	4	4



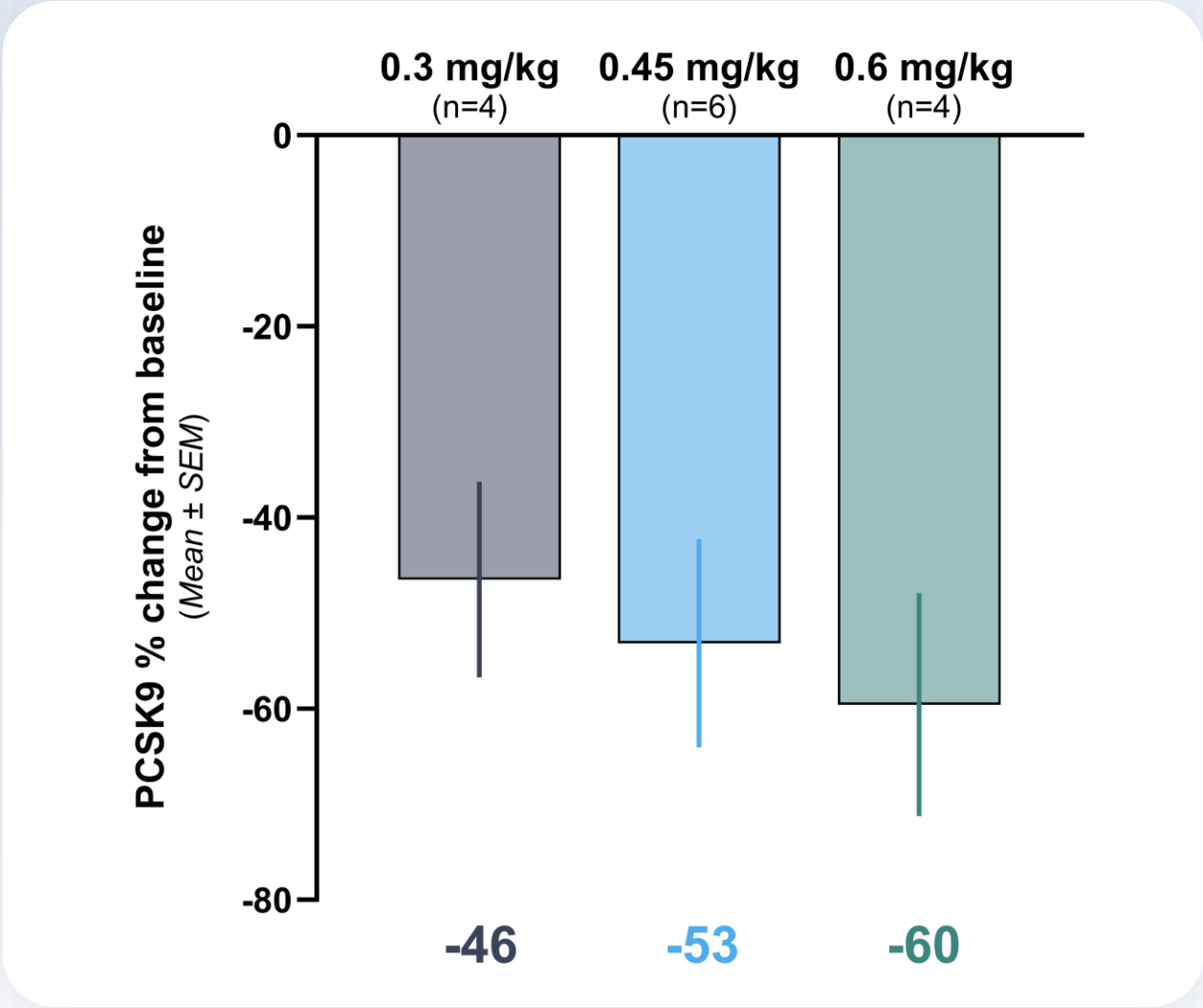
Laboratory assessment: no clinically significant changes in platelets at any dose level following VERVE-102 infusion



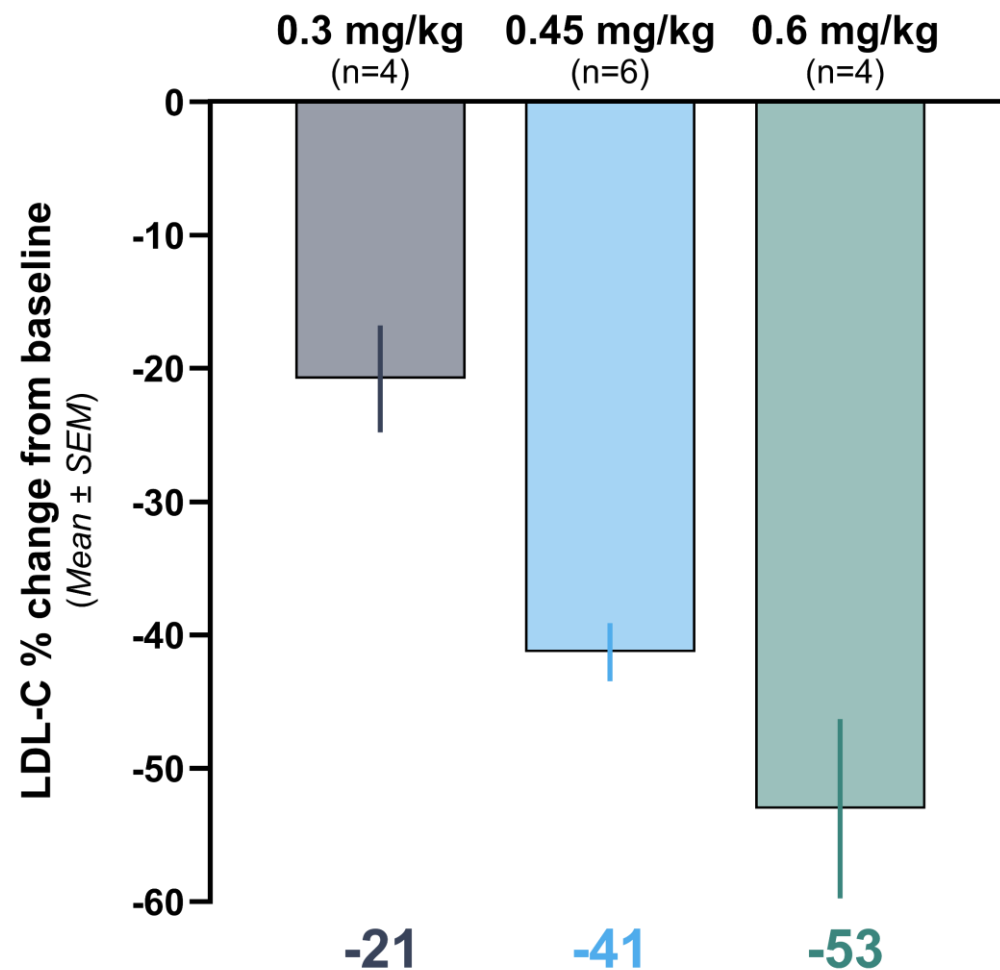


Pharmacodynamics

PCSK9 protein reduction after VERVE-102: dose-dependent reduction;
mean reduction of 60% observed in highest weight-based dose group

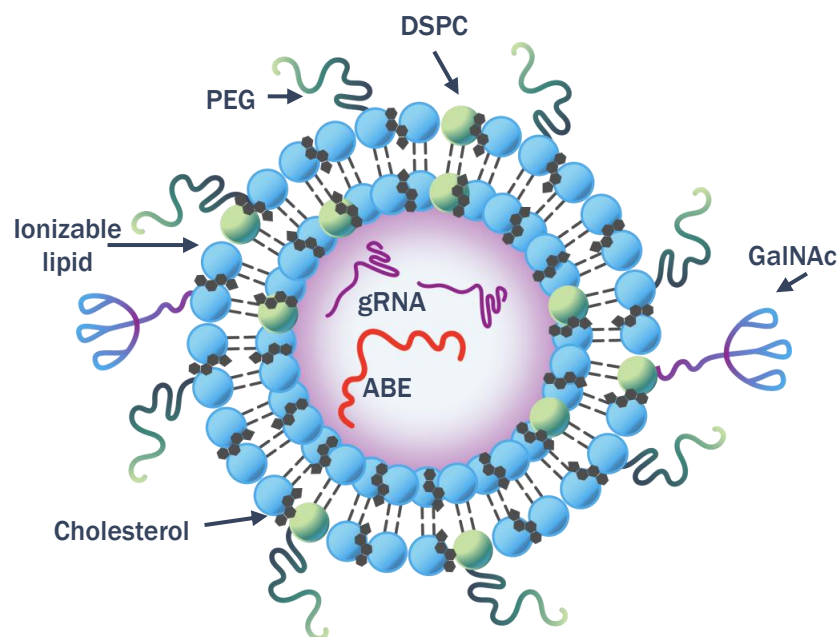


LDL-C reduction after VERVE-102: dose-dependent reduction; mean reduction of 53% observed in highest weight-based dose group



Fixed dose groups: we have evaluated our data by total RNA dose, in line with the field's shift towards fixed doses

VERVE-102



Total RNA Dose

Total RNA dose refers to the total weight (in mg) of the RNA in VERVE-102

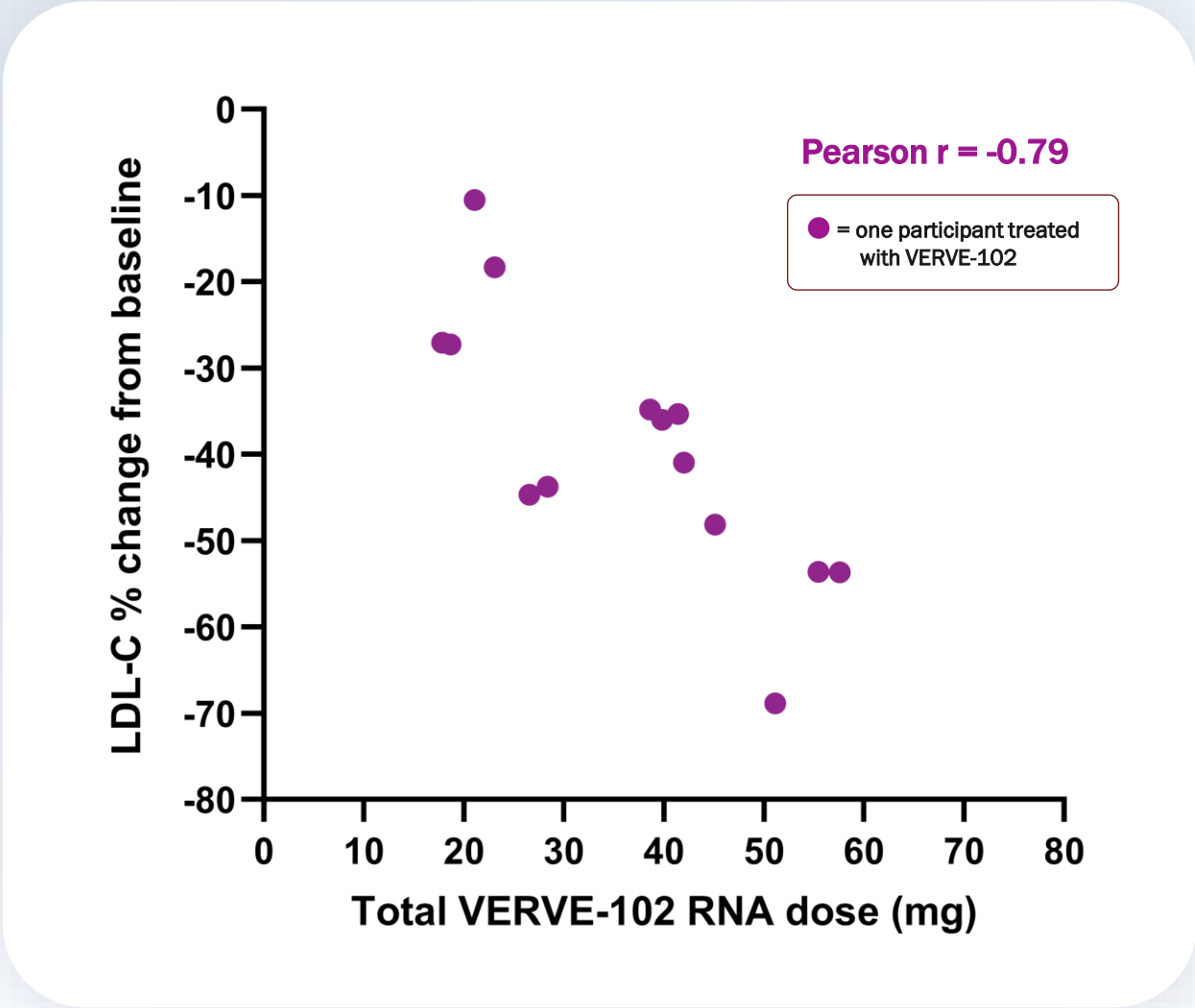
In any given weight-based cohort, there is a range of total RNA doses administered

E.g., at 0.6 mg/kg dose:

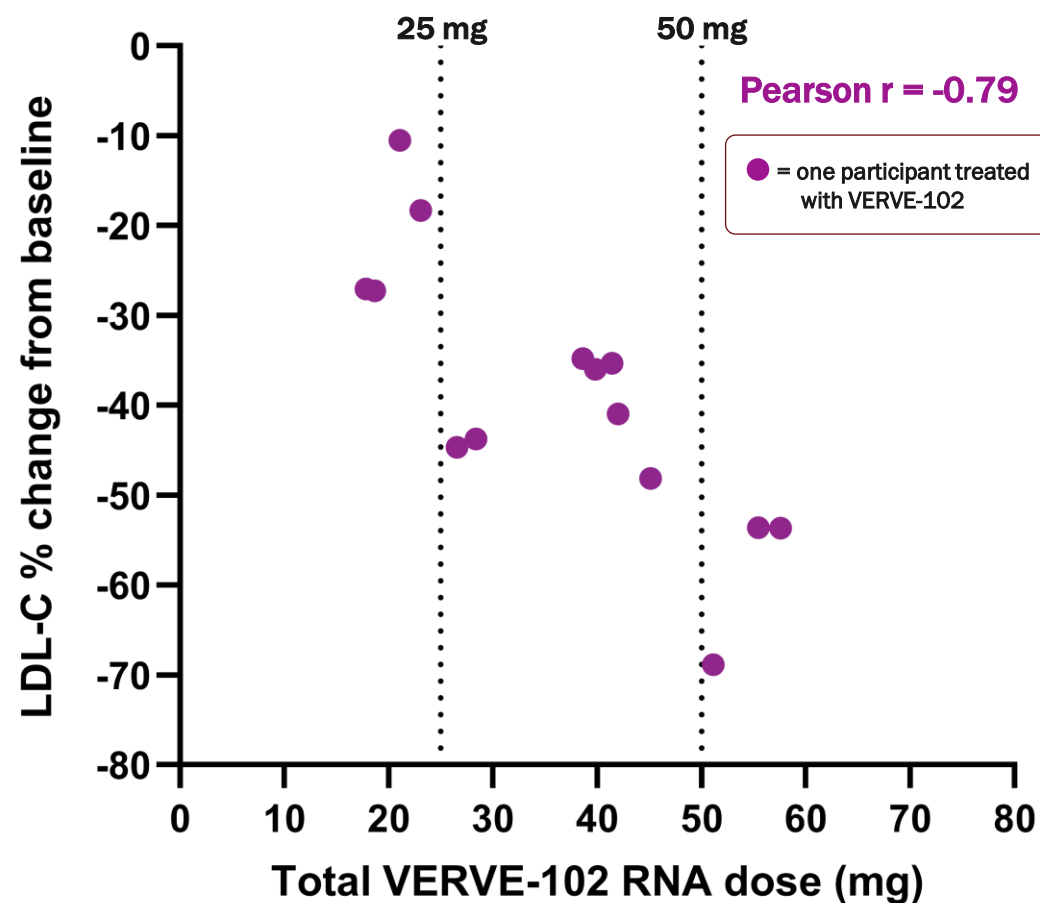
60 kg Person
Receives:
36 mg total RNA

100 kg Person
Receives:
60 mg total RNA

LDL-C by total RNA dose, per participant: across 14 participants, strong dose-dependent response observed with near-linear relationship ($r = -0.79$)



Total RNA dose may be key driver of pharmacodynamics: motivates analysis by ranges of total RNA dose



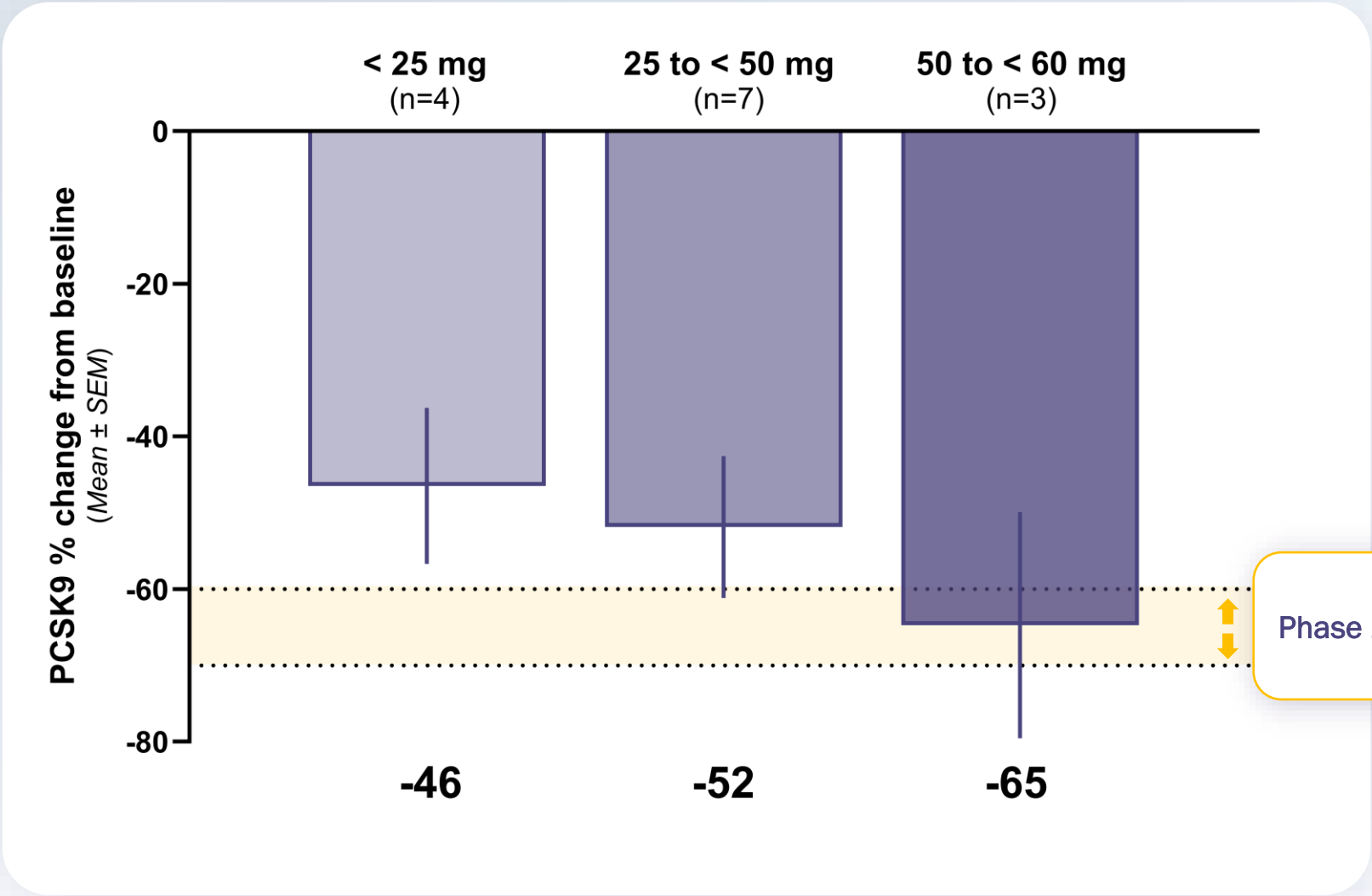
Total RNA Ranges:

< 25 mg

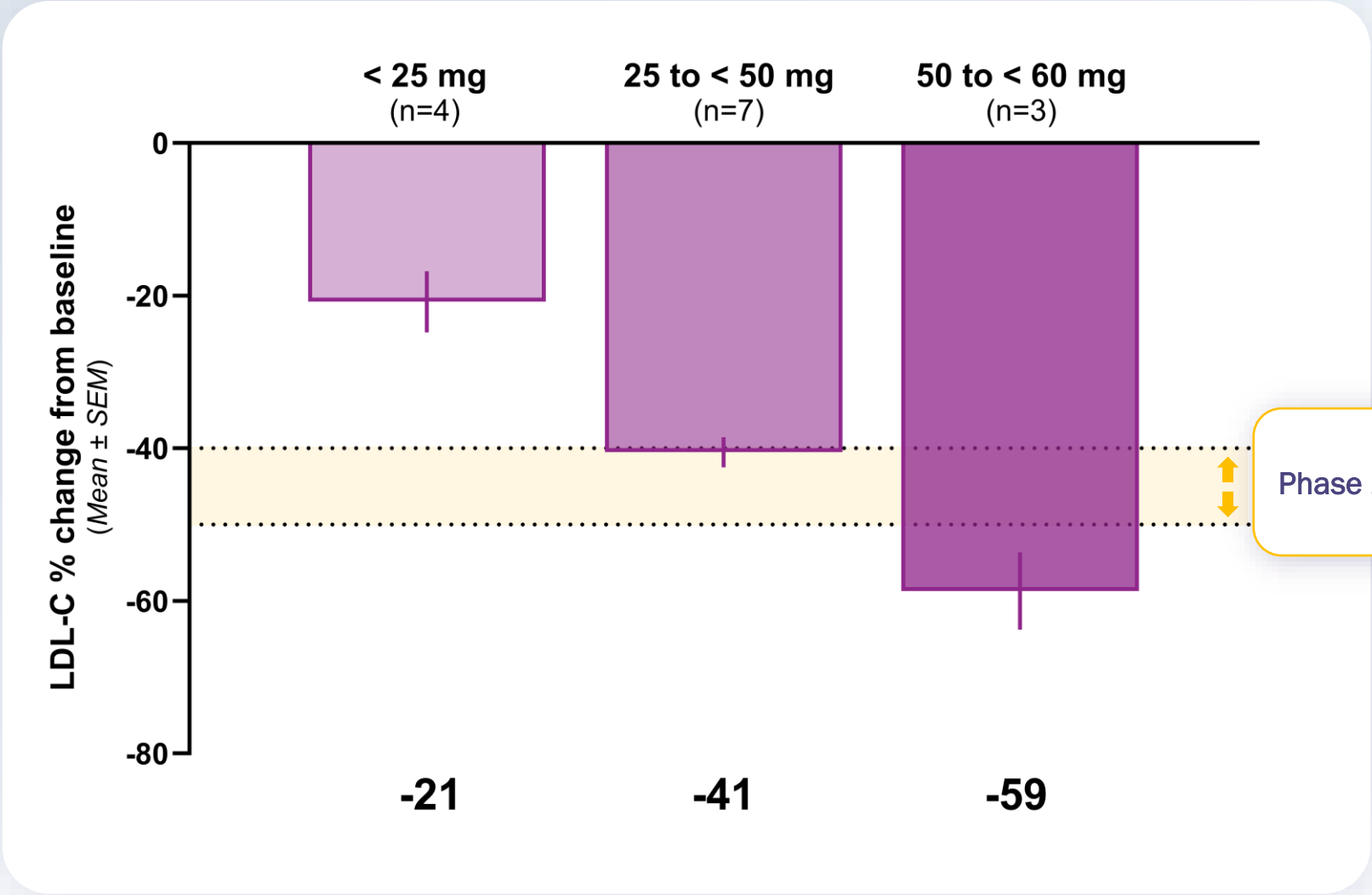
25 – < 50 mg

50 – < 60 mg

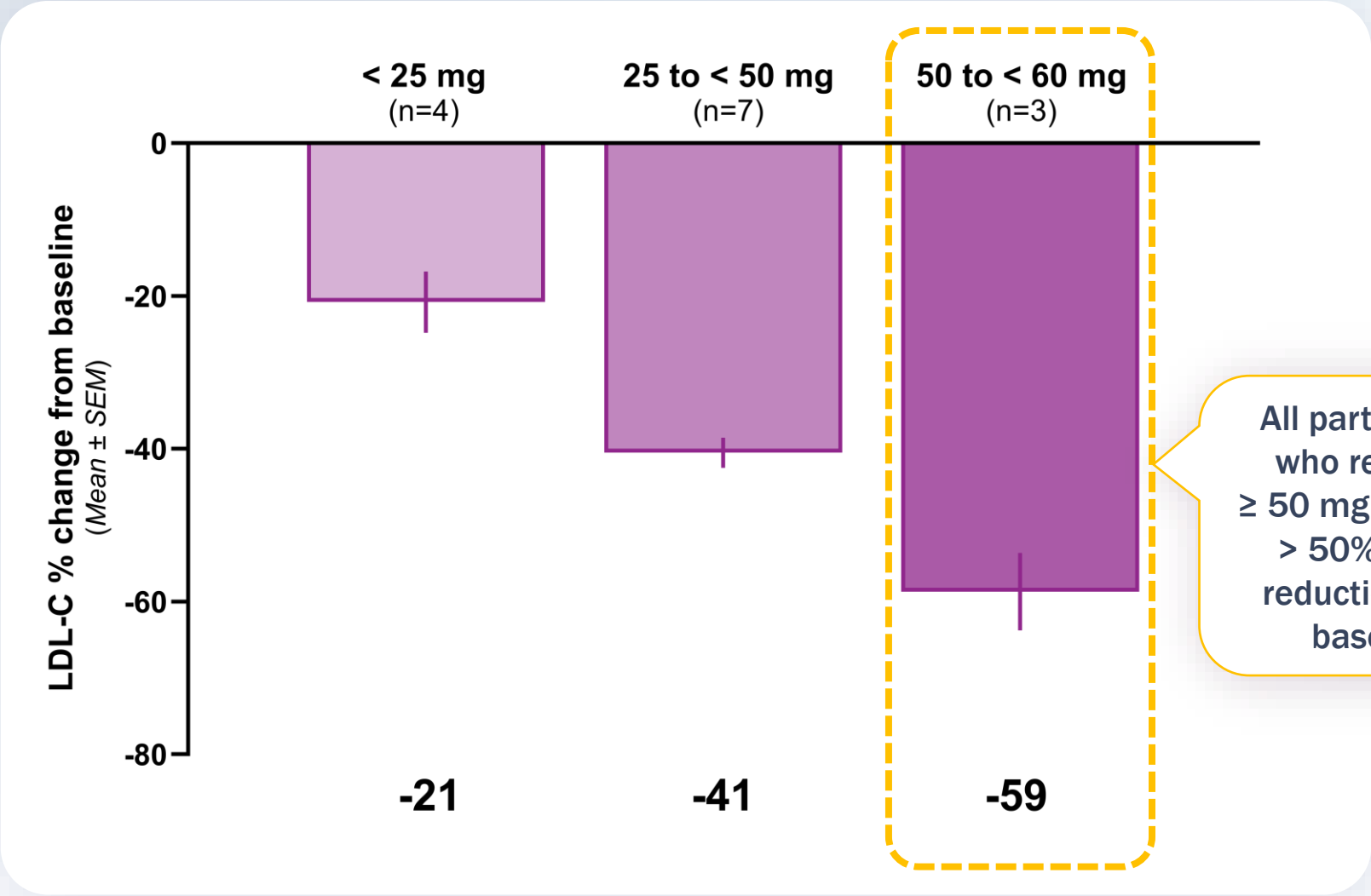
PCSK9: mean reduction of 65% in blood PCSK9 protein observed in highest total RNA dose group of VERVE-102



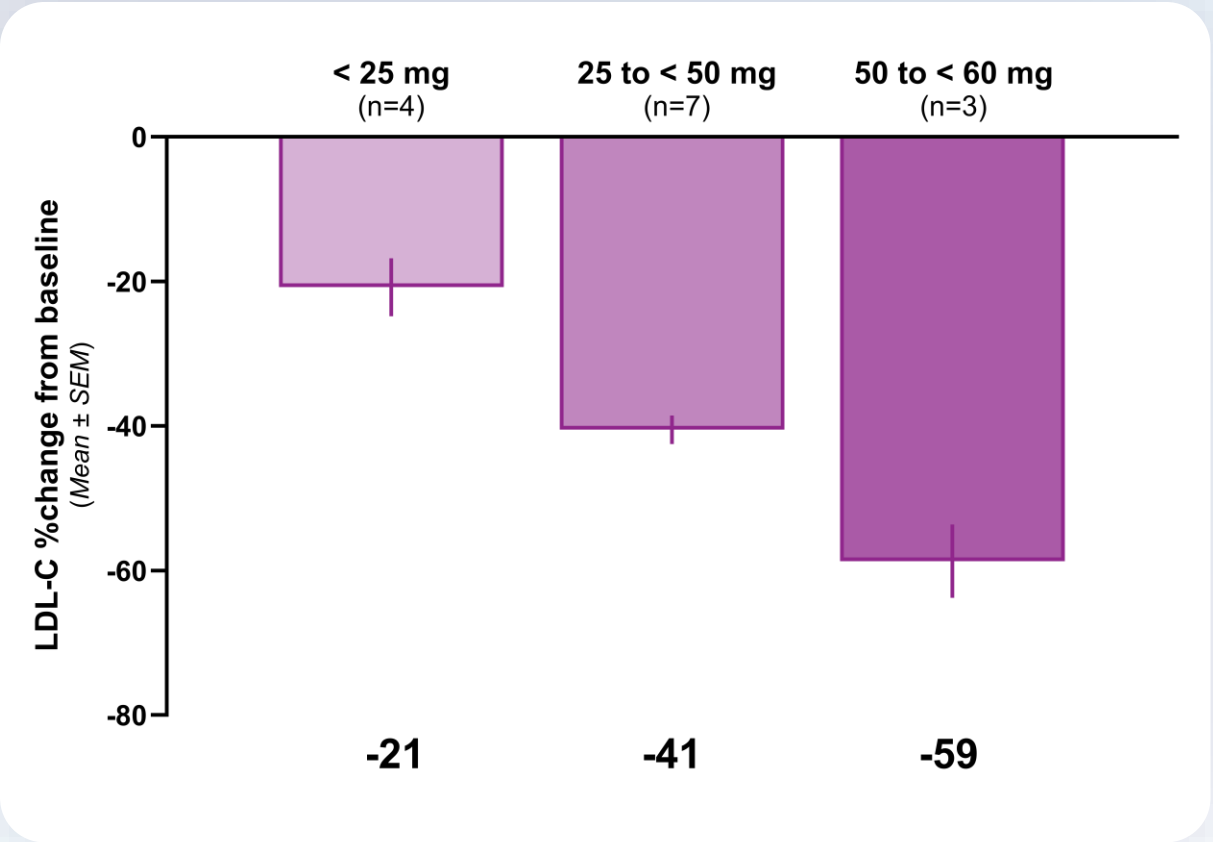
LDL-C: mean reduction of 59% in blood LDL-C observed in highest total RNA dose group of VERVE-102



LDL-C: in highest total RNA dose group of VERVE-102, every participant achieved >50% reduction; maximum LDL-C reduction of 69% in a single participant



LDL-C: mean 55 mg total RNA dose of VERVE-102 translated to mean LDL-C reduction of 59%



VERVE-102 dose range	< 25 mg	25 - < 50 mg	50 - < 60 mg
Participants (n)	4	7	3
Mean total RNA dose	20 mg	37 mg	55 mg
Mean LDL-C % reduction from baseline	-21%	-41%	-59%

Takeaways from the initial data of the Heart-2 clinical trial

VERVE-102 was well-tolerated at all dose levels with proprietary GalNAc-LNP delivery platform

- No treatment-related SAEs
- No clinically significant laboratory abnormalities and no cardiovascular events
- One infusion-related reaction across 14 participants treated

Strong dose-dependent response with total RNA dose identified as a key driver of pharmacodynamics

At total RNA dose ≥ 50 mg, each participant achieved LDL-C reductions from baseline $> 50\%$, with mean LDL-C reduction of 59% and a maximum reduction of 69% in a single participant



Closing Remarks

Initial insights: a one-time infusion of VERVE-102 has the potential to safely and potently reduce LDL-C in patients with HeFH or ASCVD

Safety

Favorable safety for VERVE-102 across first 14 participants; GalNAc-LNP platform potentially best-in-class profile



Efficacy

At ≥ 50 mg RNA dose, mean LDL-C reduction of 59% with maximum reduction of 69% observed in one participant



Durability

VERVE-101 has demonstrated durability of base editing mechanism out to 24 months; VERVE-102 data being collected



Next steps for VERVE-102:

dosing has begun in 4th dose cohort (0.7 mg/kg)

**As of April 7, 2025, Verve has dosed two participants in 4th cohort [0.7 mg/kg]:
Early safety profile at 0.7 mg/kg is in-line with first three cohorts; PD data pending**

Next steps for VERVE-102: expect first patient to be dosed in Phase 2 in H2 2025¹

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**Plan to disclose final data from dose escalation portion of the
Heart-2 clinical trial in H2 2025**

**Anticipate delivery of opt-in package to Lilly in H2 with potential decision by year-end
2025**

Expect first patient to be dosed in Phase 2 trial in H2 2025¹

Beyond the data: VERVE-102 program poised for success

SUCCESS FACTORS FOR VERVE-102

Time to market

Capital

Manufacturing

Commercial

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- 5 CTAs & U.S. IND expand global footprint for Phase 2 onwards
- FDA Fast Track designation received

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- Consistent supply established for Phase 1 and 2 trials; transferring processes to commercial-scale CDMOs
- Low cost of goods expected given precedent for analogous at-scale RNA / LNP products

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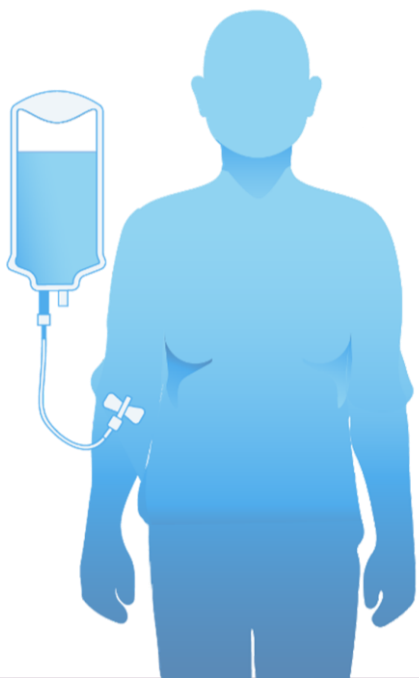
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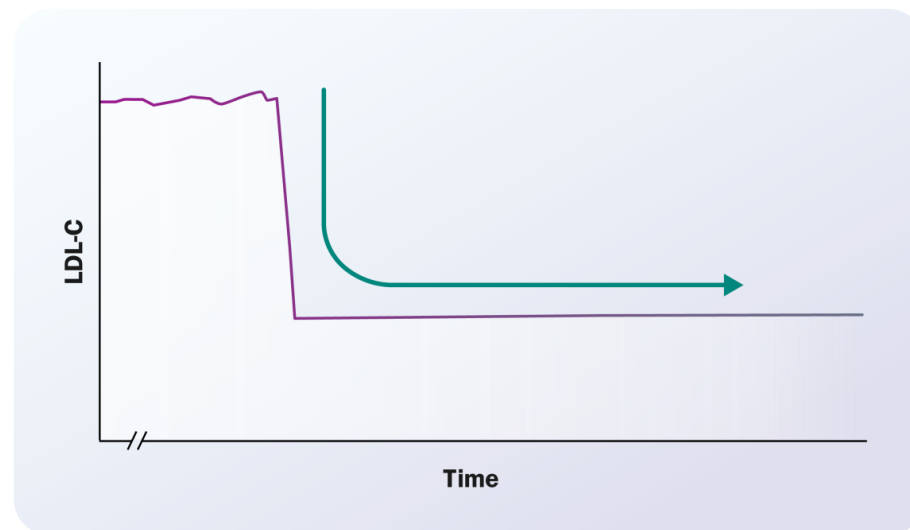
- WW PCSK9 market of ~\$4B; growing at ~40% year-over-year
- Strong enthusiasm for VERVE-102 amongst surveyed patients and HCPs^{1,2}

Verve is innovating a one dose future to address chronic disease

Single IV Infusion of Verve Product



Lifelong Blood Cholesterol Reduction



VERVE MISSION

Deliver
enduring efficacy
to patients living with
ASCVD

Q&A