Verve Therapeutics

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

November 2024

Forward looking statements and disclaimers

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the Company’s ongoing Heart-2 clinical trial and Pulse-1 clinical trial; the timing and availability of data for the Heart-2 trial, PCSK9 program and Pulse-1 trial; expectations for the Company’s Heart-1 clinical trial; the company’s strategic plans and prospects; and the period over which the Company believes that its existing cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the Company’s strategy, future operations, future financial position, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with the Company’s limited operating history; the Company’s ability to timely submit and receive approvals of regulatory applications for its product candidates; advance its product candidates in clinical trials; initiate, enroll and complete its ongoing and future clinical trials on the timeline expected or at all; correctly estimate the potential patient population and/or market for the Company’s product candidates; replicate in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials of VERVE-101, VERVE-102 and VERVE-201; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; and raise the substantial additional capital needed to achieve its business objectives. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company’s actual results to differ from those contained in the forward-looking statements, see the “Risk Factors” section, as well as discussions of potential risks, uncertainties and other important factors, in the Company’s most recent filings with the Securities and Exchange Commission and in other filings that the Company makes with the Securities and Exchange Commission in the future. In addition, the forward-looking statements included in this presentation represent the Company’s views as of the date hereof and should not be relied upon as representing the Company’s views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company’s views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

We are on a mission to protect the world from cardiovascular disease

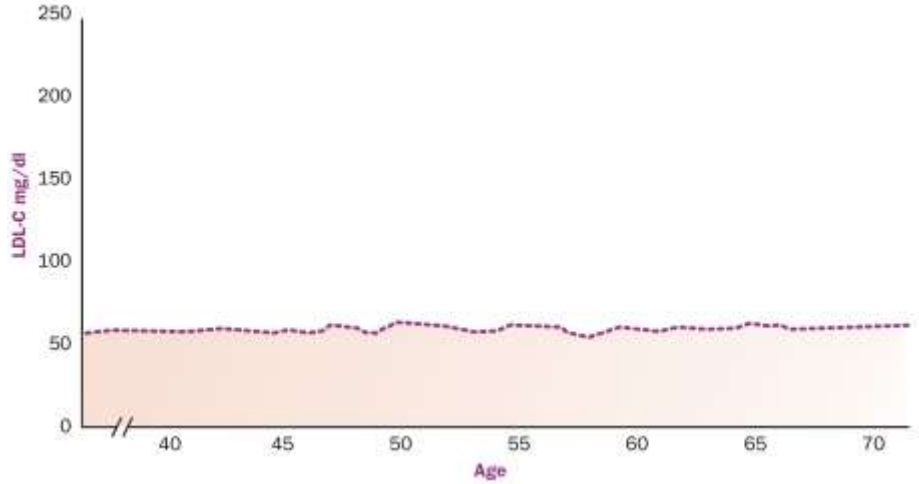
What causes atherosclerotic cardiovascular disease (ASCVD) and what's a solution?

High cumulative lifelong exposure to blood cholesterol clogs heart arteries

Cholesterol carried in 3 lipoproteins:

Cholesterol Triglycerides *Apolipoprotein B* *Apolipoprotein(a)*

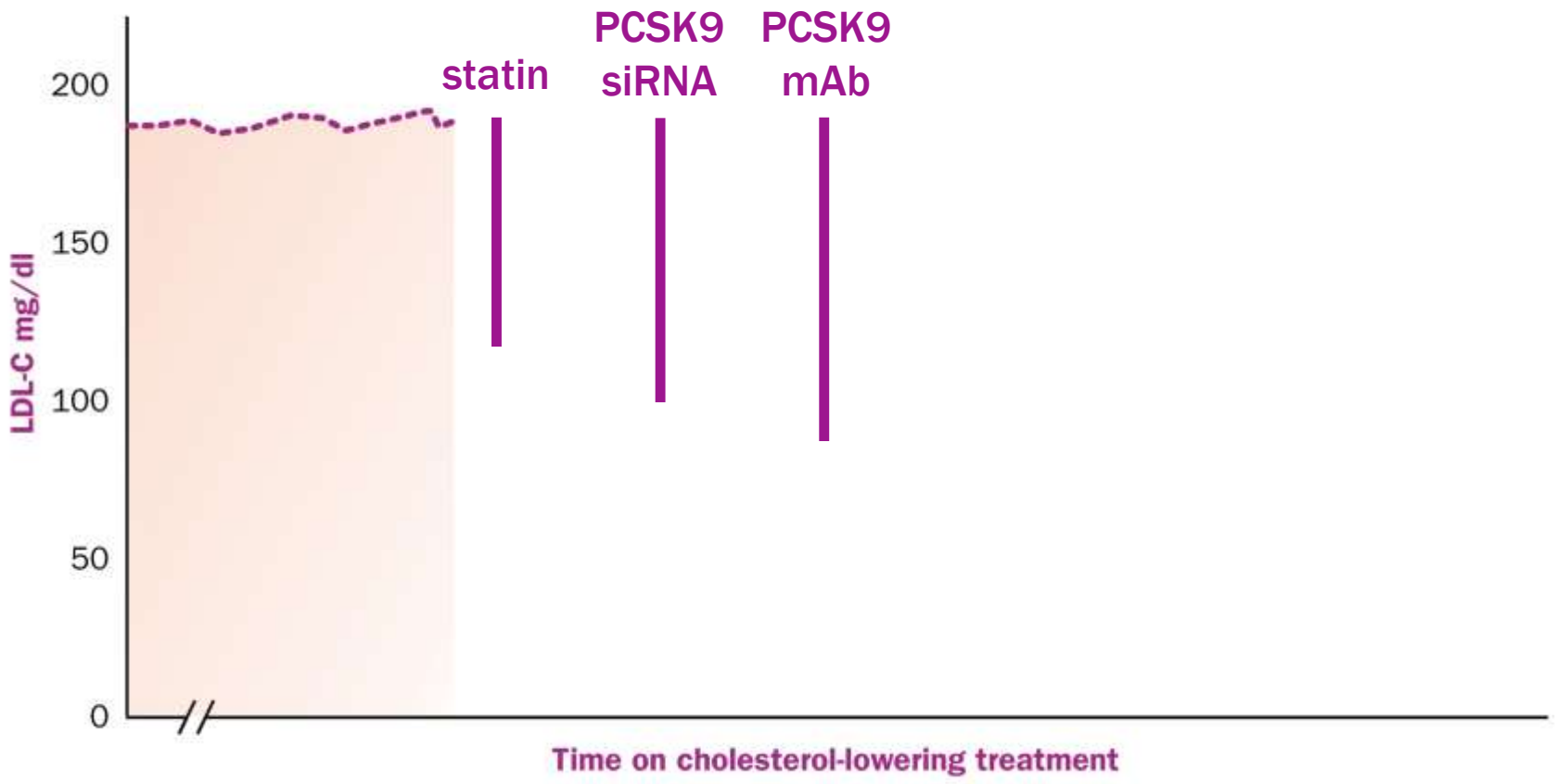
Solution: keep blood cholesterol as low as possible for as long as possible



LDL, low-density lipoprotein; TRL, triglyceride-rich lipoprotein; Lp(a), lipoprotein(a)

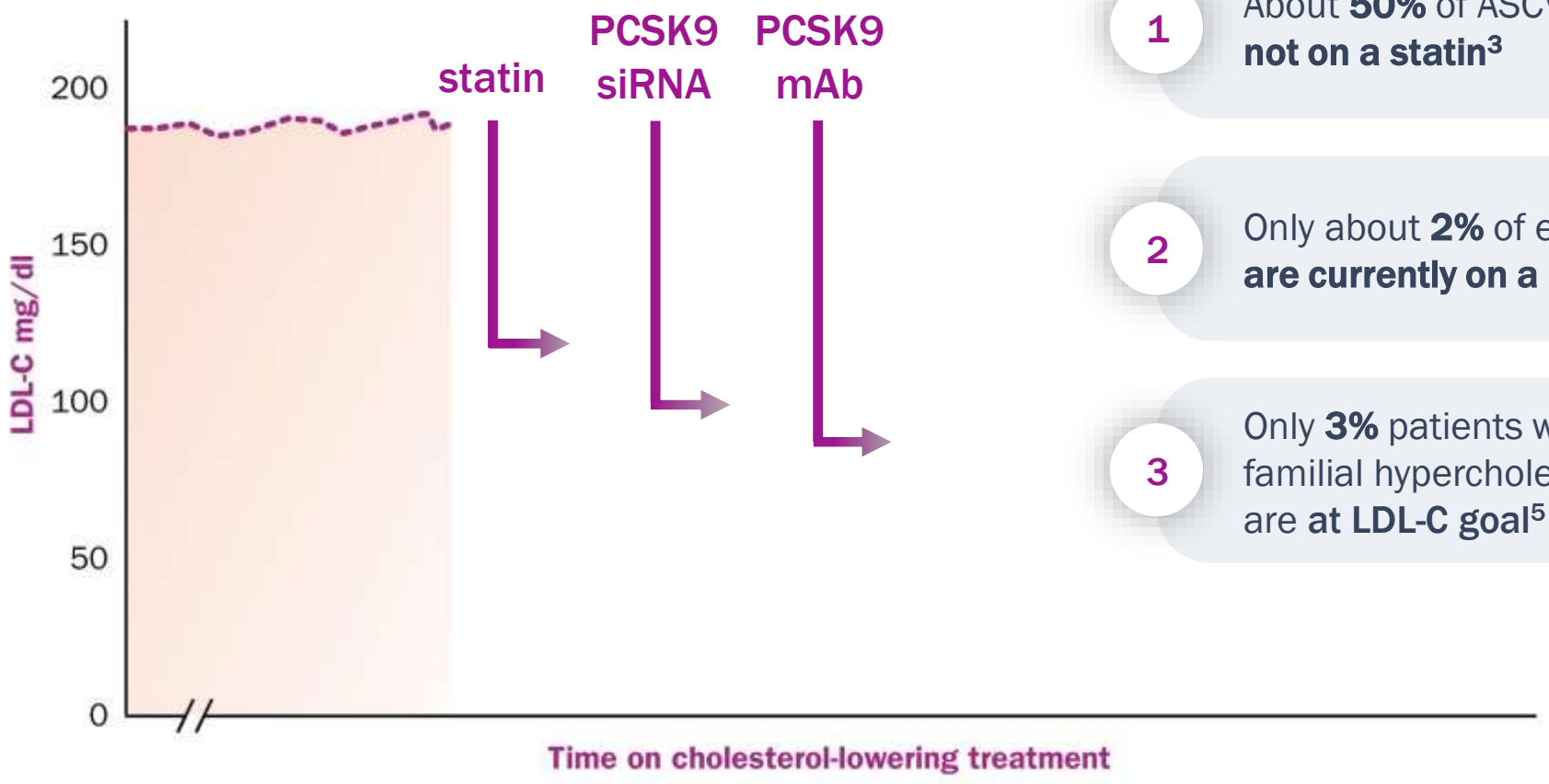
How is ASCVD treated today and is there an unmet need?

Current treatment options lower LDL-C by about 40% to 60% & intended to be taken lifelong



But, up to 50% of patients discontinue CVD medications within 12 months[1,2]

Unmet need: for many, real-world LDL-C lowering is close to zero

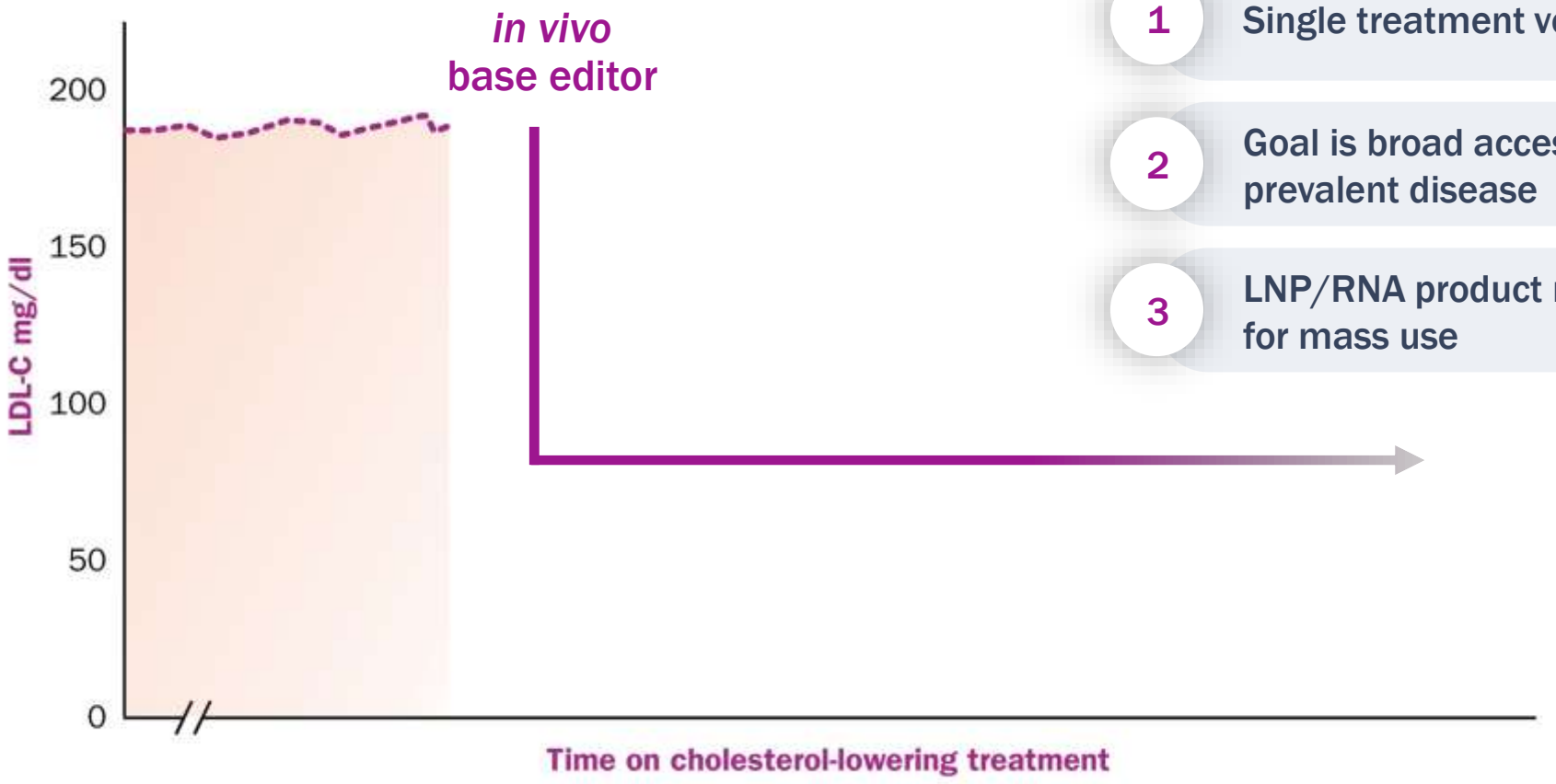


1. About **50%** of ASCVD patients **not on a statin**[3]
2. Only about **2%** of eligible patients **are currently on a PCSK9 agent**[4]
3. Only **3%** patients with heterozygous familial hypercholesterolemia are **at LDL-C goal**[5]

1. Nelson A et al., *Nature Reviews Cardiology* 2024. https://doi.org/10.1038/s41569-023-00972-1; 2. Naderi SH et al., *Am J Med.* 2012;125, 882–887.e1; 3. Nelson AJ et al., *J Am Coll Card.* 2022;79(18):1802–13; 4. Dayoub EJ et al., *J Am Heart Assoc.* 2021 May 4; 10(9): e019331; 5. EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). *Lancet*. 2021;398(10312):1713-1725

How might we address this unmet need?

A new treatment option: one-time procedure, lifelong cholesterol lowering

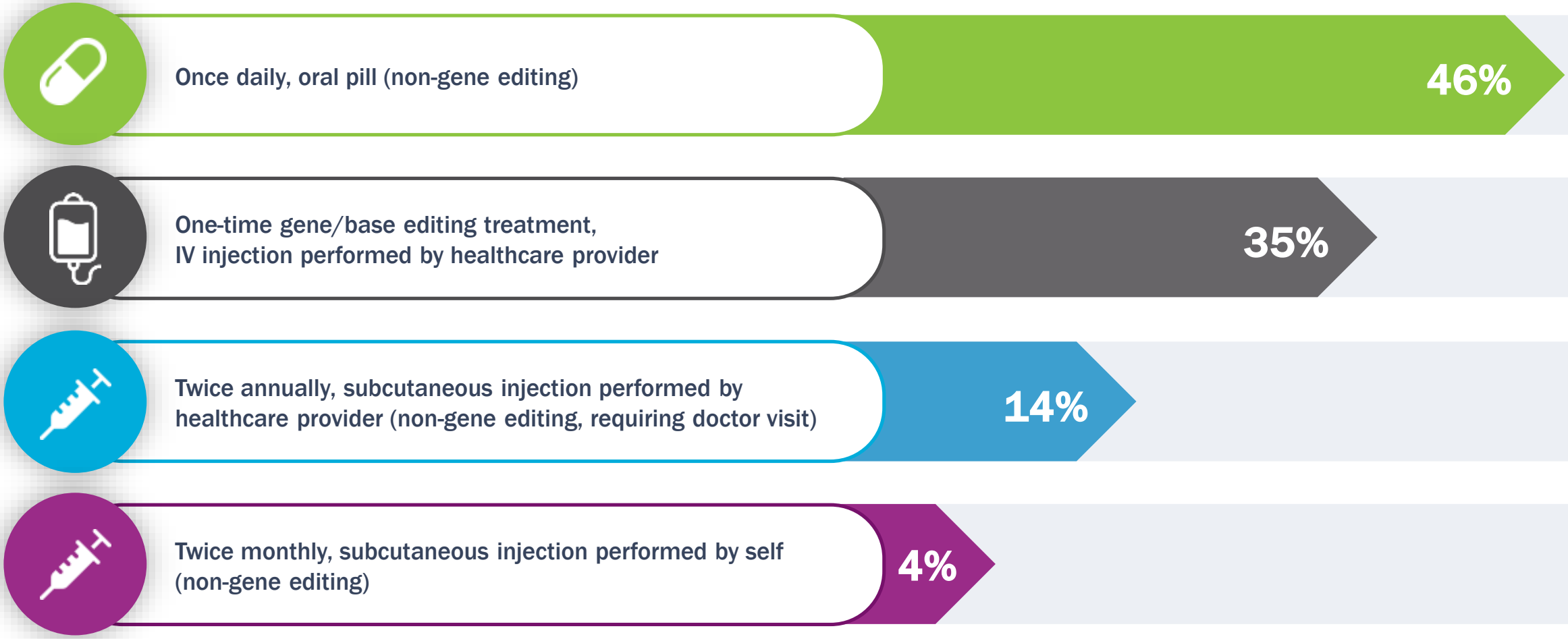


Differentiation:

1. Single treatment versus chronic care
2. Goal is broad access for highly prevalent disease
3. LNP/RNA product now precedented for mass use

Will patients be open to a one-time gene editing procedure as a solution?
Patient preference surveys show remarkable openness

Assuming you will have lifelong therapy in the treatment of high cholesterol and/or cardiovascular disease, please select the therapeutic option that is most appealing to you (N=484)



Source: Patient preferences survey conducted by polling firm Morning Consult; LifeSci Capital

Verve is advancing a pipeline of *in vivo* gene editing programs designed to lower cholesterol lifelong after a single treatment

TARGET	INDICATION	TECHNOLOGY	RESEARCH	IND-ENABLING	CLINICAL	RIGHTS
PCSK9 (VERVE-102)	Heterozygous familial hypercholesterolemia ASCVD	Base Editor (novel GalNAc-LNP)				verve / Lilly
PCSK9 (VERVE-101)[1]	Heterozygous familial hypercholesterolemia ASCVD	Base Editor				verve / Lilly
ANGPTL3 (VERVE-201)	Homozygous familial hypercholesterolemia Refractory hypercholesterolemia	Base Editor (novel GalNAc-LNP)				verve / Lilly
LPA	ASCVD patients with high blood Lp(a)	Novel Editor				verve / Lilly
Undisclosed	Undisclosed ASCVD	Base Editor				verve / Lilly
Undisclosed	Undisclosed liver disease	Novel Editor				verve / VERTEX

1. As of April 2, 2024, Verve has paused enrollment of the Heart-1 Phase 1b trial of VERVE-101 and is prioritizing clinical development of VERVE-102.

Verve's pipeline of gene editing programs designed to address distinct groups of patients with ASCVD

All ASCVD ~ *54M in US/EU*

HeFH

~ 3M in US/EU

PCSK9 PROGRAM

ASCVD not at LDL-C goal on statin[1,2]

~ 21M in US/EU

PCSK9 PROGRAM

HoFH

~ 2,800 in US/EU

ANGPTL3 PROGRAM

Refractory-hypercholesterolemia[3]

(ASCVD not at LDL-C goal on maximum standard of care)

~ 7M in US/EU
(~13% ASCVD)

ANGPTL3 PROGRAM

Elevated Lp(a)

~ 11M in US/EU
(~20% ASCVD)

LPA PROGRAM

1. Gu J et al., *Am J Prev Cardiol.* 2022; 10:100336
2. Ray KK et al., *European Journal of Preventive Cardiology.* 2021; 28(11):1279–1289
3. O'Donoghue ML et al., *Circulation*. 2022; 146(15):1109-1119

HeFH, heterozygous familial hypercholesterolemia; HoFH, homozygous familial hypercholesterolemia; Lp(a), lipoprotein(a)

Transforming the treatment of cardiovascular disease (CVD) from chronic care to once-and-done

Advanced first three ASCVD base editing product candidates from concept to clinic

Developed novel lipid nanoparticle (LNP) liver delivery technology: GalNAc-LNP

Assembled a world-class team of CVD and gene editing experts

Heart-2 Phase 1b trial of VERVE-102 enrolling patients; seven participants dosed as of October 29, 2024 across two cohorts

Established strategic relationships with Eli Lilly & Vertex to support and build pipeline

Well-capitalized with runway through 2026

Verve collaborating with Eli Lilly across multiple programs

Lilly's opt-in rights for PCSK9 and ANGPTL3 programs: in exchange for paying for 33% of worldwide development costs and 50% of U.S. commercialization expenses, Lilly receives right to 50% of U.S. profits Verve retains ex-U.S. rights and remains responsible for development; Verve books revenues

Timing of Lilly's opt-in decision for PCSK9 and ANGPTL3 programs: after the last patient of the Phase 1 study is dosed, Verve will prepare and deliver the final data package to Lilly. Lilly then has a certain amount of time to review the final data package.

Global collaboration with Lilly on Verve's Lp(a) program: Lilly pays 100% of Verve's development costs through Phase 1; Program transfers to Lilly at end of Phase 1 and Verve has ability to opt-in to cost-profit share at end of Phase 1

Shared vision around application of gene editing to treat cardiovascular disease

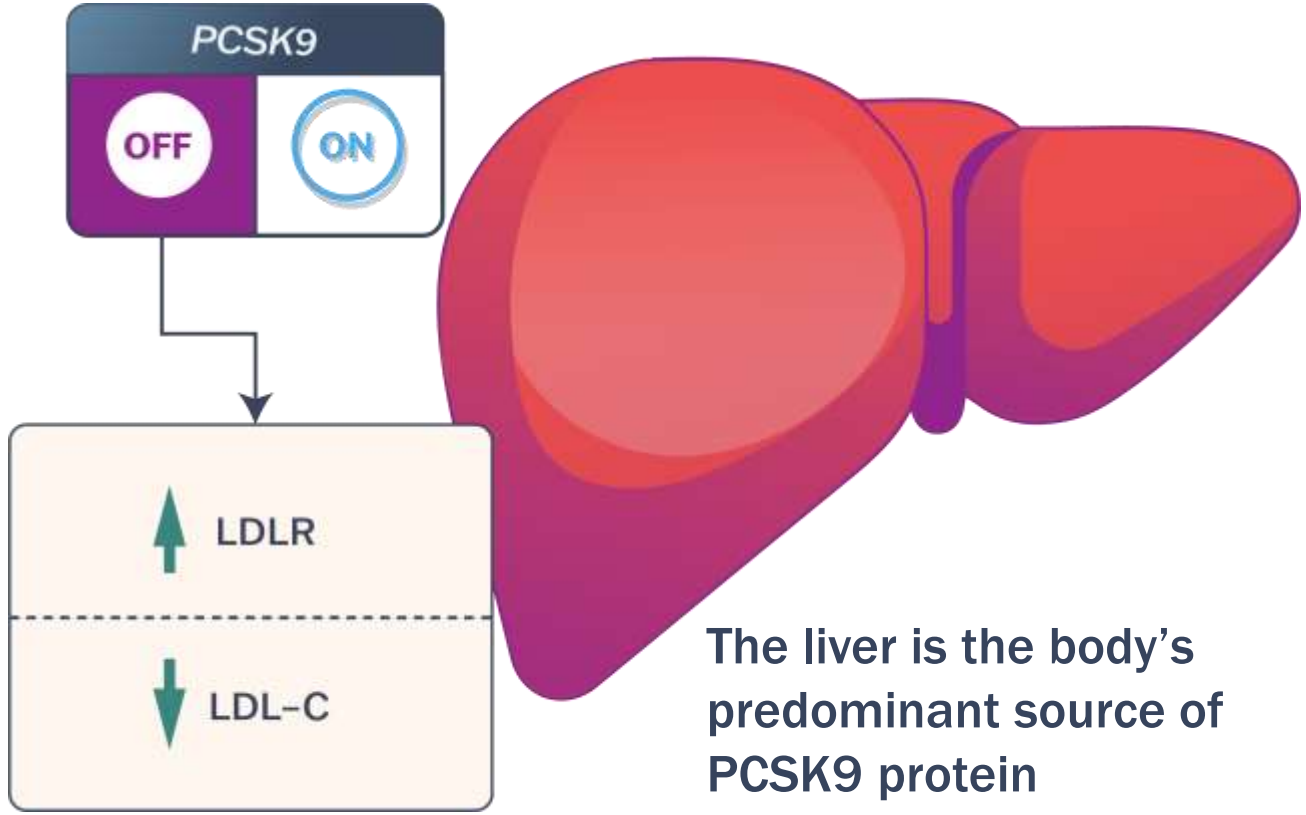
PCSK9 Program

Human genetics suggests turning off the *PCSK9* gene in the liver may enable permanent LDL-C lowering

Naturally occurring gene variants that turn off *PCSK9* result in:

- Lifelong LDL-C lowering
- Protection against ASCVD
- No apparent deleterious effects[1–3]

Pharmacologic validation of target



The liver is the body's predominant source of PCSK9 protein

1. Zhao Z, et al. Am J Hum Genet. 2006;79:514-523; 2. Cohen JC, et al. N Eng J Med. 2006;354:1264-1272; 3. Rao AS, et al. Circ Genom Prec Med. 2018;11(7):e002162.
LDLR, low-density lipoprotein receptor; PCSK9, proprotein convertase subtilisin/kexin type 9

Verve's PCSK9 program has two product candidates: VERVE-101 and VERVE-102

	VERVE-101 (Heart-1 Clinical Trial)	VERVE-102 (Heart-2 Clinical Trial)
TARGET	*PCSK9* gene	
ADENINE BASE EDITOR (ABE)	Same adenine base editor (ABE) used in both product candidates	
GUIDE RNA	Same guide RNA (gRNA) targeting *PCSK9*	
IONIZABLE LIPID	ALC-0307	LP000001
PEG LIPID	ALC-0159	DMG-PEG$_{2000}$
LIVER-TARGETING LIGAND	—	GalNAc

- **Ionizable lipid and PEG-lipid in VERVE-102 have been well-tolerated in >80 patients (third-party clinical trials)**
- **Addition of GalNAc in VERVE-102 allows for LDLR- or ASGPR-mediated uptake into hepatocytes**

ASGPR, asialoglycoprotein receptor; LDLR, low-density lipoprotein receptor

Heart-1 provides human proof of concept for *in vivo* base editing of the *PCSK9* gene with VERVE-101

heart-1

13

patients dosed

Dose-dependent reductions in blood PCSK9 protein & LDL-C

Mean PCSK9 protein reductions of >60% for two higher dose cohorts (0.45 and 0.6 mg/kg)

Mean LDL-C reductions of 42% at 0.45 mg/kg (n=6) and 57% at 0.6 mg/kg (n=1)[1]

Mild-to-moderate infusion reactions and transient, asymptomatic ALT increases

Transient laboratory abnormalities in one patient of ALT increase and grade 3 SAE of drug-induced thrombocytopenia

Cardiovascular events consistent with severe ASCVD population

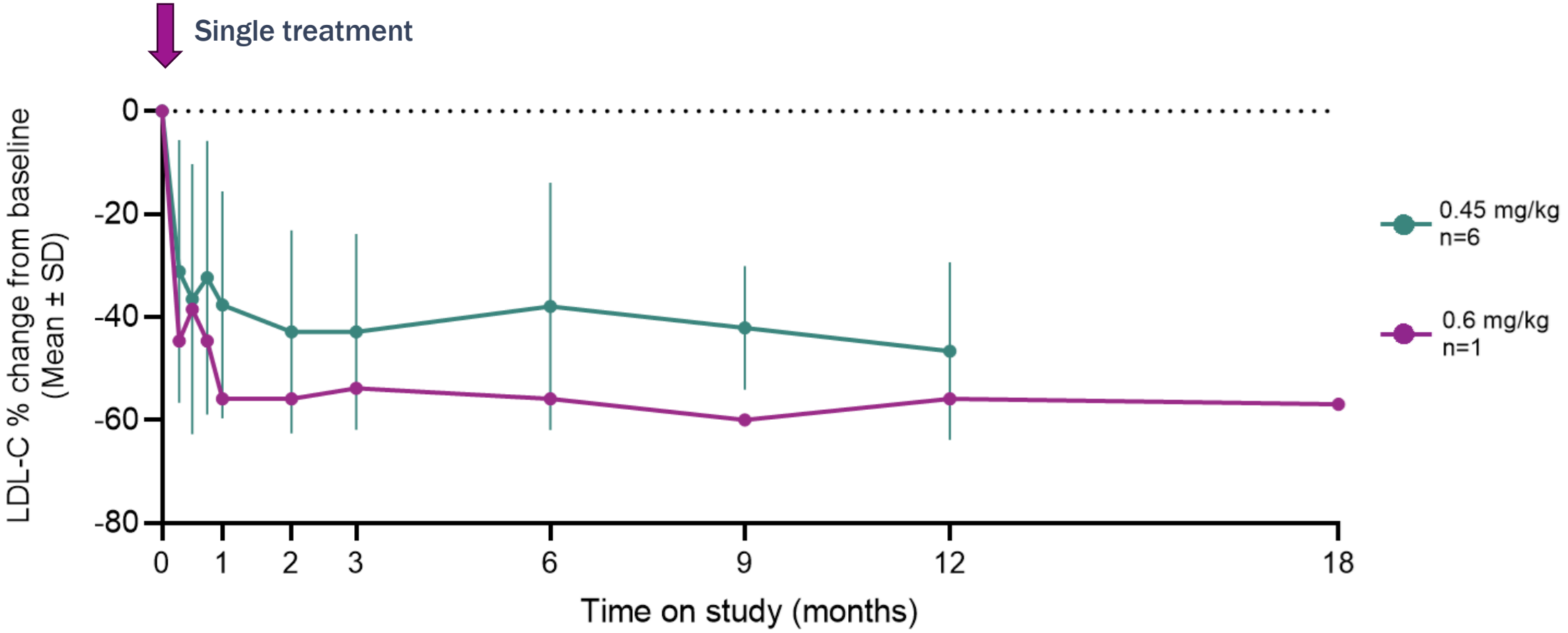
No new treatment-related adverse events occurred more than 2 days after treatment

Preliminary findings from investigation support hypothesis that laboratory abnormalities attributable to LNP; enrollment remains paused during dose escalation portion of Heart-2 trial

As of data cut off date of October 3, 2024. Data are from an ongoing study with an open database and have not been fully cleaned.
1. Means are based on time-averaged reduction in LDL-C and PCSK9 protein from day 28 through last available follow up; observations from one participant dosed at 0.45 mg/kg censored after change in lipid lowering therapy from baseline more than 6 months after VERVE-101 treatment; effective dose for participant at 0.6 mg/kg was ~0.5 mg/kg.; ALT, alanine aminotransferase; SAE, serious adverse event

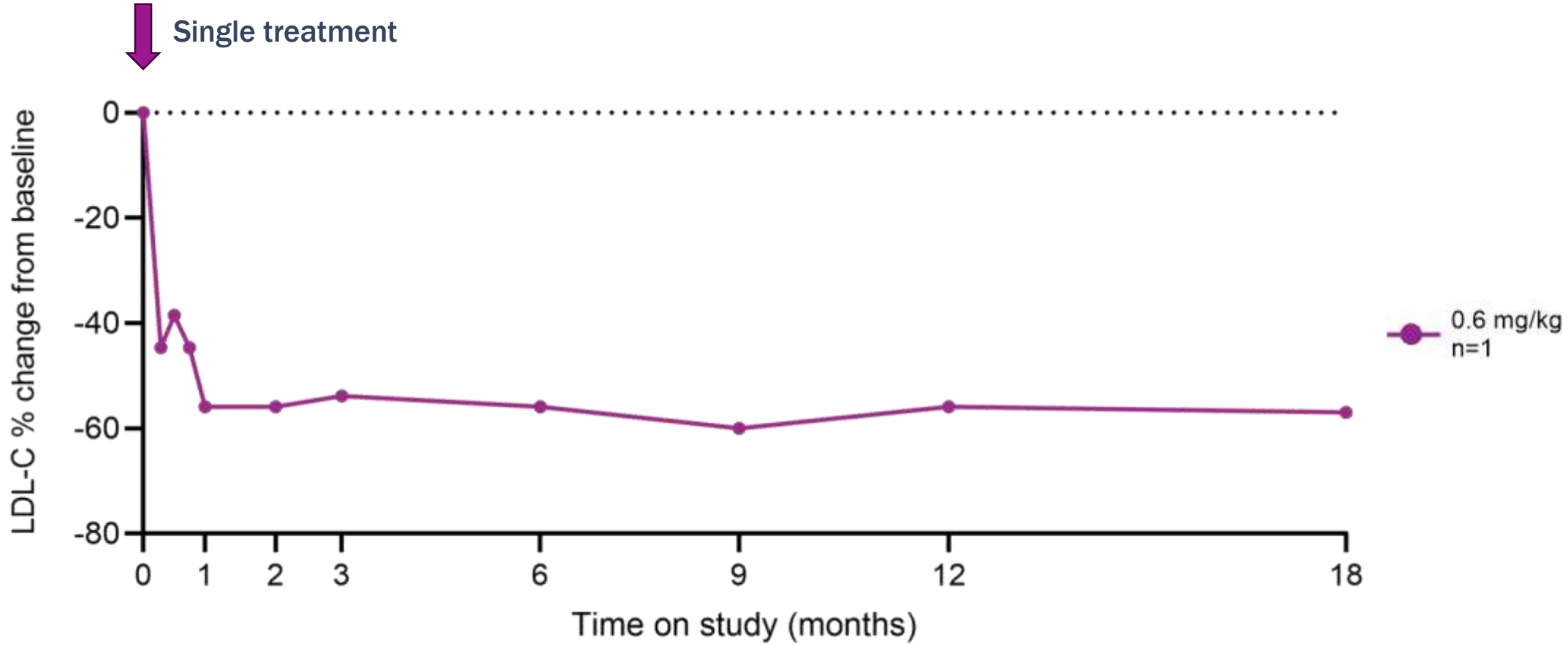
verve THERAPEUTICS

Durability in humans: evidence for sustained LDL-C reduction following single VERVE-101 treatment in two higher dose cohorts



As of October 3, 2024. Data are from an ongoing study with an open database and have not been fully cleaned. Participants in 0.45 mg/kg cohort have variable duration of follow up, with n=6 at 6 months and n=3 at 9 months and 12 months. One of the six 0.45 mg/kg participants intensified statin therapy from baseline more than 6 months after VERVE-101 treatment.
SD, standard deviation

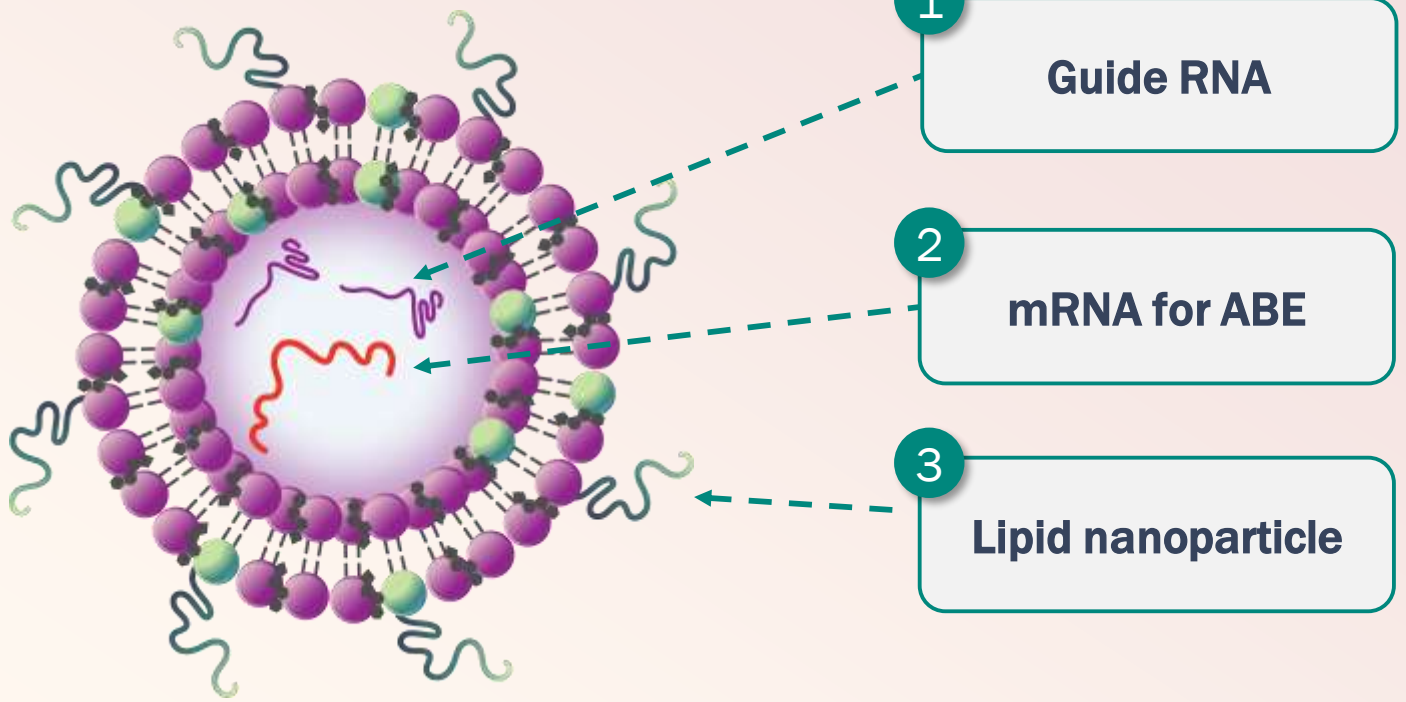
Durability: proof-of-concept for LDL-C lowering extends to 18 months in participant dosed at 0.6 mg/kg



As of October 3, 2024. Data are from an ongoing study with an open database and have not been fully cleaned.

Heart-1 learnings: ABE editor and guide RNA work as designed, LNP suspected to contribute to acute laboratory abnormalities

VERVE-101 Components



1 2

ABE and gRNA edit *PCSK9 in vivo* and durably lower LDL-C

3

LNP suspected cause of laboratory safety findings

ABE, adenine base editor; gRNA, guide RNA; LNP, lipid nanoparticle

Prioritizing the clinical development of VERVE-102

Editor and Guide Work

Heart-1 data for VERVE-101 demonstrate that *in vivo* liver editing for *PCSK9* has the potential to meaningfully and durably reduce LDL-C in HeFH patients

Change LNP Delivery System

VERVE-102 uses a different LNP delivery system with a well tolerated ionizable lipid and a GalNAc liver-targeting ligand

Preliminary findings from nonclinical studies support hypothesis that observed laboratory abnormalities attributable to LNP

Current focus on VERVE-102

Regulatory clearances in Australia, Canada, Israel, New Zealand, and the U.K.

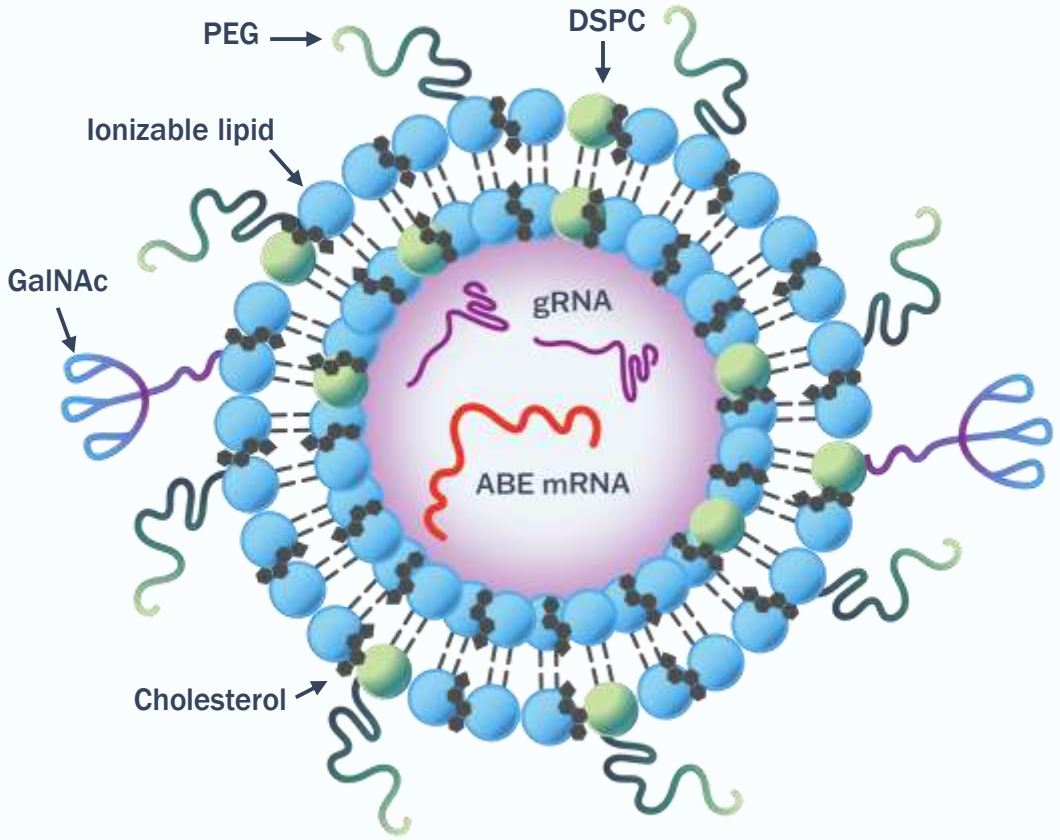
Heart-2 trial currently enrolling patients

Initial Phase 1 data expected in 1H 2025

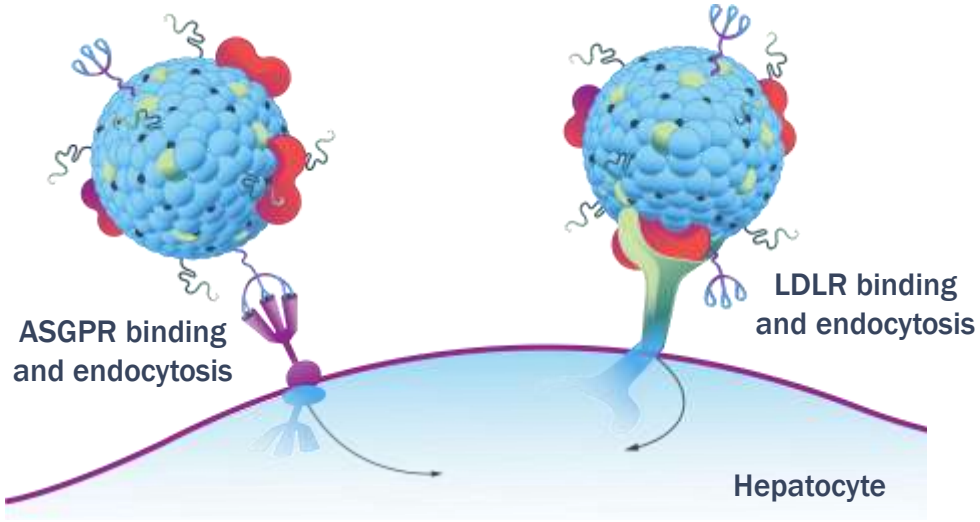
LNP, lipid nanoparticle

VERVE-102 is an investigational *in vivo* base editing medicine that is delivered by a GalNAc-LNP and inactivates *PCSK9*

VERVE-102 LNP



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



The translated adenine base editor (ABE) pairs with the gRNA to target and inactivate *PCSK9* with precise DNA edit

ASGPR, asialoglycoprotein receptor; DSPC, 1,2-distearoyl-sn-glycero-3-phosphocholine; gRNA, guide RNA; LDLR, low-density lipoprotein receptor; mRNA, messenger RNA; PEG, polyethylene glycol

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

heart-2

First-in-human, open-label trial in adults with HeFH and/or premature coronary artery disease (CAD)

Single Ascending Dose

Three to nine participants per cohort receive a single dose; adaptive design

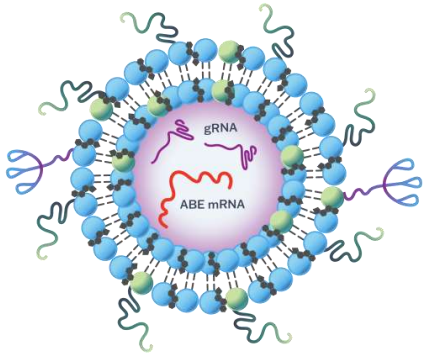
STUDY POPULATION SUMMARY

- Males and females (age 18 to 70)
- HeFH and/or premature CAD
- Require additional LDL-C lowering despite maximally tolerated oral therapies

TRIAL ENDPOINTS

- Primary: Safety and tolerability
- Pharmacokinetics of VERVE-102
- Changes in blood PCSK9 and LDL-C

VERVE-102



First patient dosed in 2Q 2024

Clinical trial registration: NCT06164730
Women of childbearing potential are excluded from the study.

verve THERAPEUTICS

Heart-2 is progressing as planned with initial clinical data expected in 1H2025

As of October 29, 2024

Dosing has been completed in seven participants in the first two dose cohorts, 0.3 mg/kg and 0.45 mg/kg, in the Heart-2 clinical trial.

VERVE-102 has been well-tolerated. No serious adverse events and no clinically significant laboratory abnormalities have been observed.

Following the standard review from the independent data and safety monitoring board (DSMB), the company expects to continue the dose escalation portion of the clinical trial.

ANGPTL3 Program

VERVE-201 targets *ANGPTL3* – a compelling target with human genetics & pharmacology validation to lower LDL-C, via a mechanism additive to PCSK9 inhibition

Humans with ANGPTL3 deficiency:

- ✓ Very low LDL-C
- ✓ Very low triglycerides
- ✓ Healthy

EVKEEZA®

(mAb targeting ANGPTL3)

lowers LDL-C by ~50% in 2 patient populations

1. Homozygous FH (rare, orphan, FDA-approved label indication)
2. Refractory hypercholesterolemia[1] (~7 M people in US/EU)

mAb, monoclonal antibody; 1. Rosenson RS et al., *N Engl J Med*. 2020;383(24):2307-2319

VERVE-201 clinical development planned in two ASCVD indications with unmet medical need: homozygous FH and refractory hypercholesterolemia

Patients with homozygous familial hypercholesterolemia

Rare, orphan disease

LDL-C levels above 500 mg/dL

~2,800 patients in the U.S./EU

Patients with refractory hypercholesterolemia

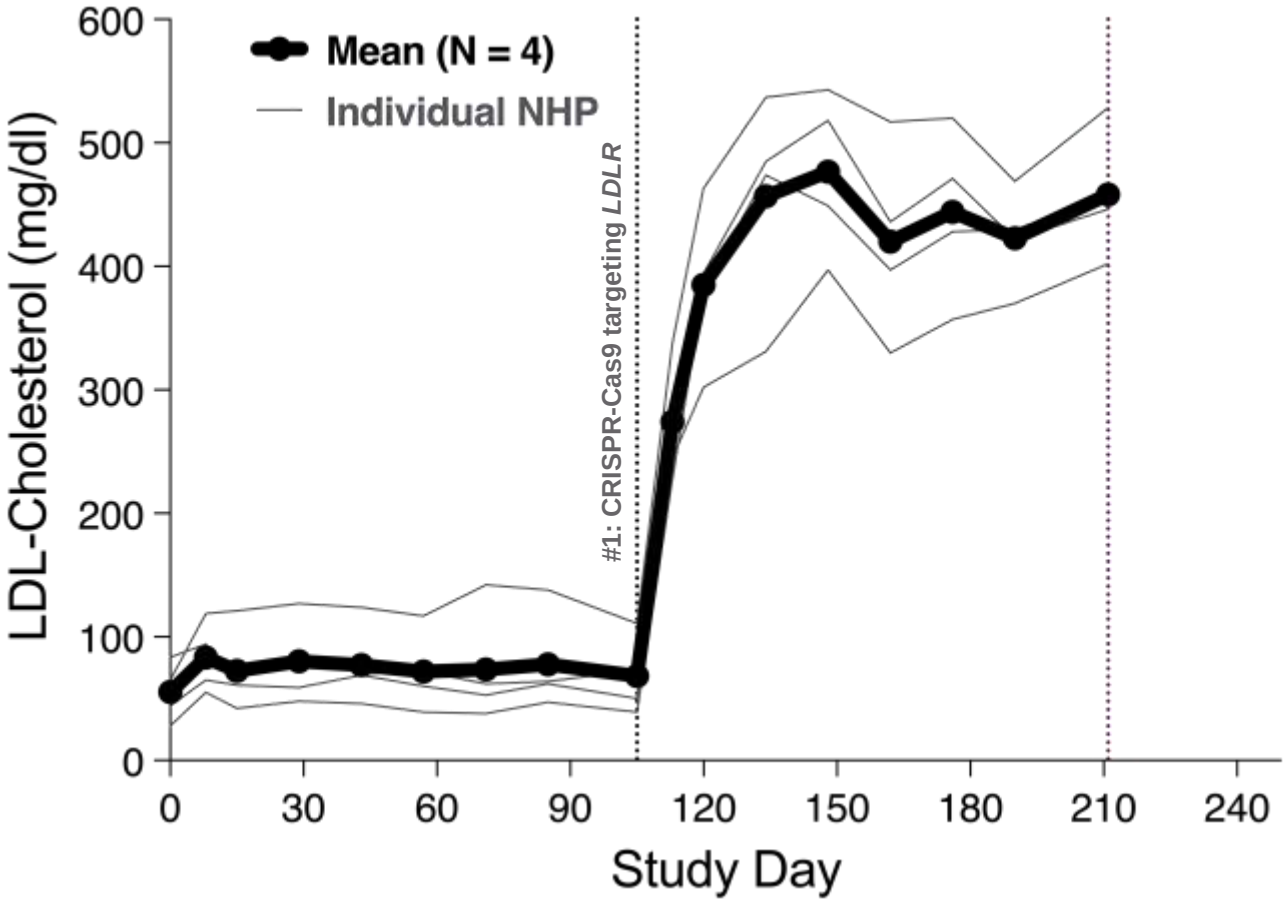
ASCVD not at LDL-C goal on maximally-tolerated standard of care, potentially including PCSK9 inhibitors

~7M patients in the U.S.[1]/EU

ASCVD, atherosclerotic cardiovascular disease; FH, familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol

1. O'Donoghue et al., *Circulation*. 2022;146:1109–1119.

Verve developed a non-human primate model of HoFH (LDLR deficiency in liver) where mean blood LDL-C is 458 mg/dl



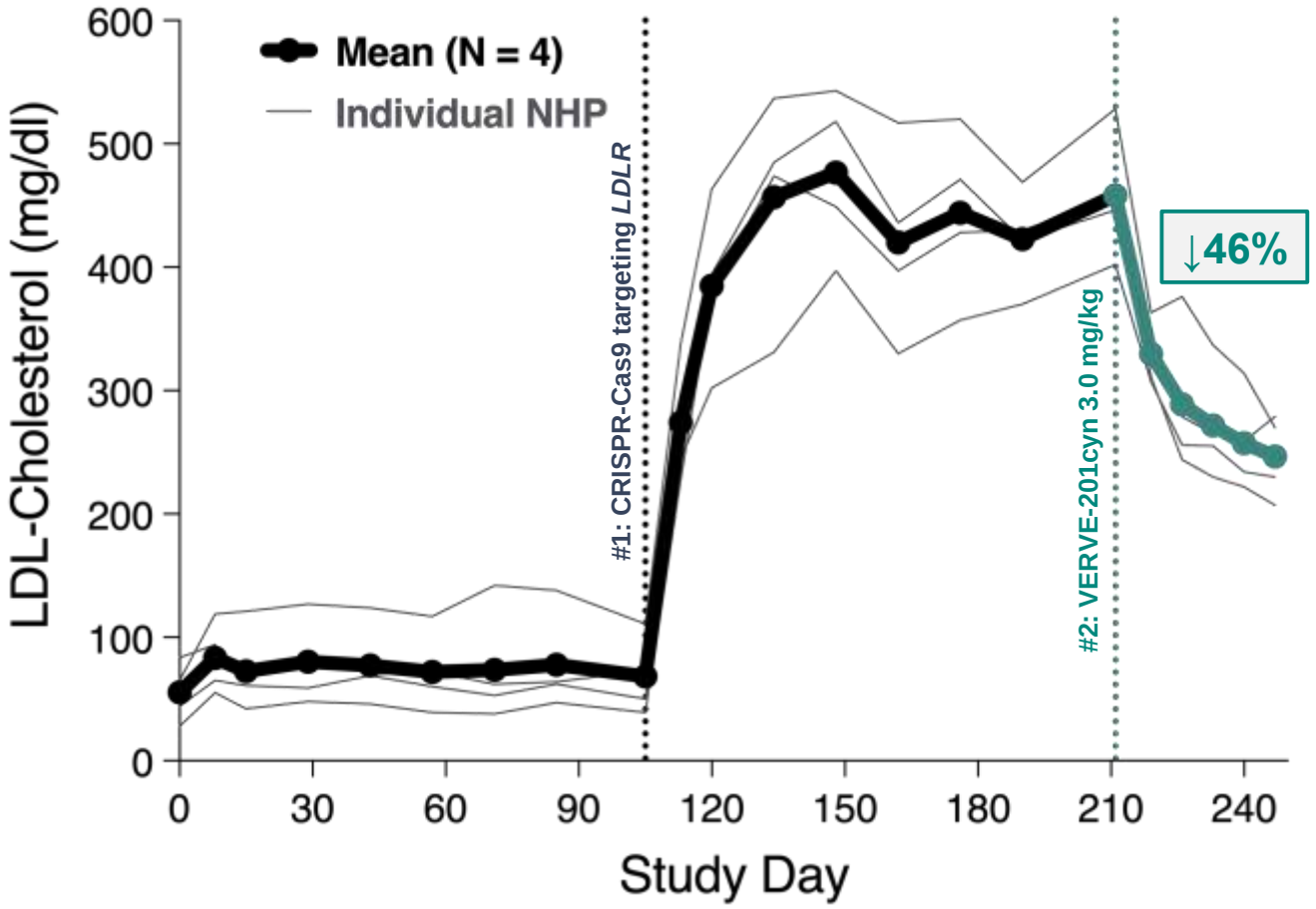
Step #1: Develop LDLR-deficient NHPs

- Created NHP model of LDLR-deficiency by dosing 4 NHPs with CRISPR-Cas9 to inactivate *LDLR* in the liver and increase LDL-C.[1]

LDLR, low-density lipoprotein receptor; NHP, non-human primates; LDL-C, low-density lipoprotein cholesterol

1. Method previously described In Kasiewicz et al. *Nat Comm*, 2023;14(1):2776.

In LDLR-deficient NHPs treated with VERVE-201cyn, 46% mean decrease in LDL-C observed (458 to 247 mg/dl)



Step #1: Develop LDLR-deficient NHPs

- Created NHP model of LDLR-deficiency by dosing 4 NHPs with CRISPR-Cas9 to inactivate *LDLR* in the liver and increase LDL-C.[1]

Step #2: Dose with VERVE-201cyn

- Mean LDL-C decreased from 458 to 247 mg/dl
- VERVE-201cyn in NHPs:
  - 46% decrease in LDL-C
  - 54% decrease in TG

LDLR, low-density lipoprotein receptor; NHP, non-human primates; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides

1. Method previously described In Kasiewicz et al. *Nat Comm*, 2023;14(1):2776.

VERVE-201: base editing medicine designed to inactivate *ANGPTL3*

- VERVE-201 designed to address high unmet need among patients with hypercholesterolemia refractory to standard of care therapies and HoFH
- In non-human primates, VERVE-201cyn achieved potent mean reduction in blood ANGPTL3 protein of >90% durable out to 22 months
- VERVE-201 surrogates were well-tolerated in nonclinical studies, with no evidence of long-term liver toxicity and a reduction in liver triglyceride content observed in NHPs
- GalNAc LNP delivery system enabled potent *ANGPTL3* liver editing in a NHP model of HoFH physiology, achieving a 46% mean reduction in LDL-C from 458 to 257 mg/dL
- VERVE-201 enables precise inactivation of the *ANGPTL3* gene, with no detectable off-target editing in any of ~3,000 candidate sites in primary human hepatocytes

Pulse-1: Phase 1b trial designed to evaluate safety & tolerability of VERVE-201

pulse-1

First-in-human, open-label trial in adults with refractory hypercholesterolemia

Single Ascending Dose

Three to nine participants per cohort receive a single dose; adaptive design

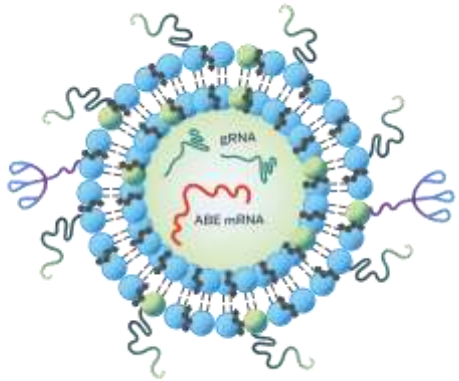
STUDY POPULATION SUMMARY

- Males and females (age 18 to 70)
- Refractory hypercholesterolemia
- Require additional LDL-C lowering despite maximally tolerated standard of care therapies, potentially including PCSK9 inhibitors

TRIAL ENDPOINTS

- Primary: Safety and tolerability
- Pharmacokinetics of VERVE-201
- Changes in blood ANGPTL3 and LDL-C

VERVE-201



First patient dosed in 4Q 2024

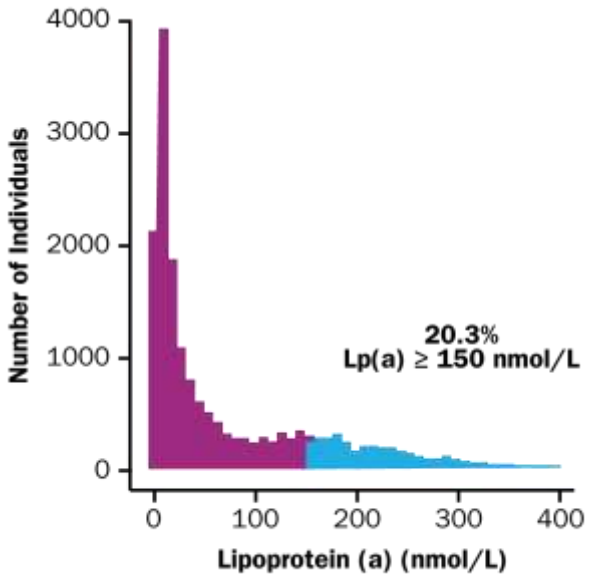
Clinical trial registration: NCT06451770
Women of childbearing potential are excluded from the study.

Lp(a) Program

In collaboration with Lilly, advancing potential gene editing treatment for elevated Lp(a)

Lp(a) market opportunity

- Large addressable market: ~11M in the U.S./EU
- 20% of ASCVD patients with Lp(a) > 150 nmol/L (~ 70 mg/dL)[1]
- Distinct patients from those with elevated LDL-C; correlation coefficient between blood LDL-C and Lp(a) is low (r2=0.01)[2]



Significant potential for once-and-done gene editing medicine

- Humans with genetic Lp(a) deficiency:
  - resistant to heart attack & stroke
  - no signal for adverse events
- Blood level almost entirely determined by inheritance
- Lifestyle factors and statins have minimal to no impact on blood Lp(a)

Research efforts ongoing to develop a bespoke gene editor tailored to target LPA

1. Patel AP et al., *Arterioscler Thromb Vasc Biol*. 2021;41(1):465-474.
2. Welsh P et al., *Eur J Prev Cardiol*. 2022;28(18):1991-2000.

Anticipated 2024 and 2025 milestones for Verve

2024

PCSK9 PROGRAM

- ✓ Dose first patient in Heart-2 trial (VERVE-102)

ANGPTL3 PROGRAM

- ✓ Initiate Phase 1 trial (VERVE-201)

2025

PCSK9 PROGRAM

- Interim Phase 1 data for VERVE-102 (1H 2025)
- Complete enrollment for VERVE-102 trial
- Deliver opt-in package to Lilly
- Initiate randomized, controlled Phase 2 (2H 2025)[1]

ANGPTL3 PROGRAM

- Data update for VERVE-201

WELL-CAPITALIZED WITH CASH RUNWAY THROUGH 2026

1. Subject to regulatory clearance