Verve Therapeutics

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

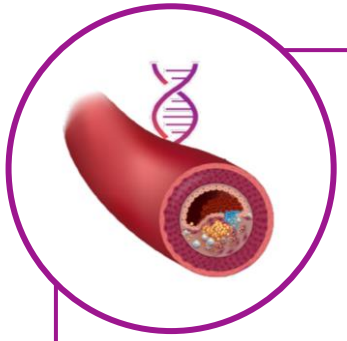
April 2024

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 expectations for the Company’s Heart-1 trial; the timing of initiating the clinical trial of VERVE-102 and Phase 2 clinical trial for the company’s PCSK9 program; the receipt of regulatory clearances and timing of initiating the clinical trial of VERVE-201; the timing and availability of clinical data from the Company’s PCSK9 and ANGPTL3 programs; and the company’s strategic plans and prospects. 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.

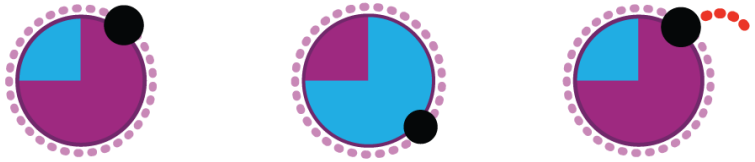
We are on a mission to protect the world from cardiovascular disease

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

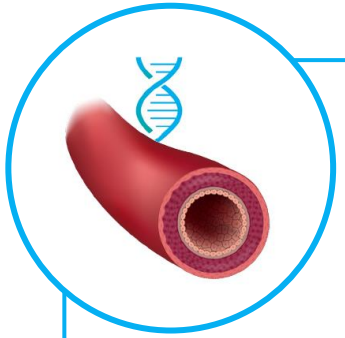


High cumulative life-long exposure to blood cholesterol clogs heart arteries

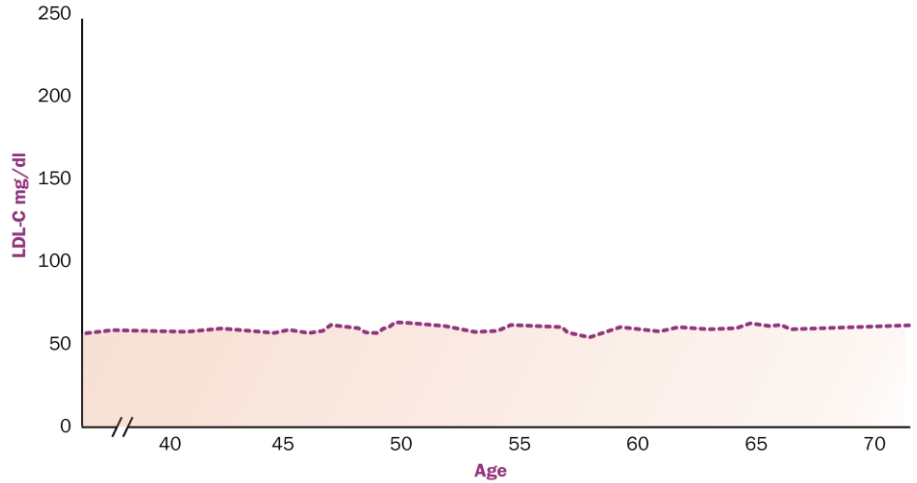
Cholesterol carried in 3 lipoproteins:



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



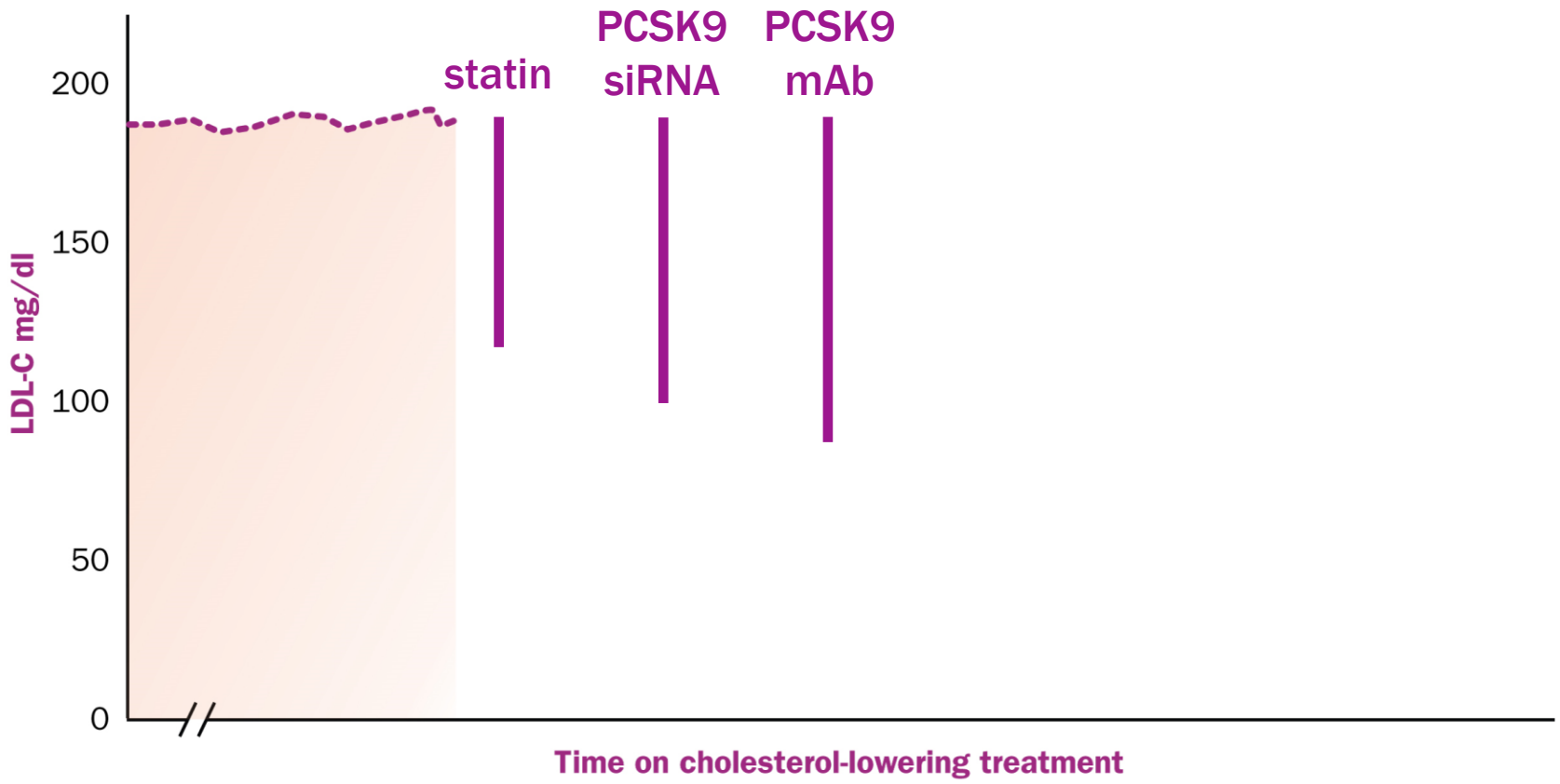
Solution: keep blood cholesterol as low as possible for as long as possible



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

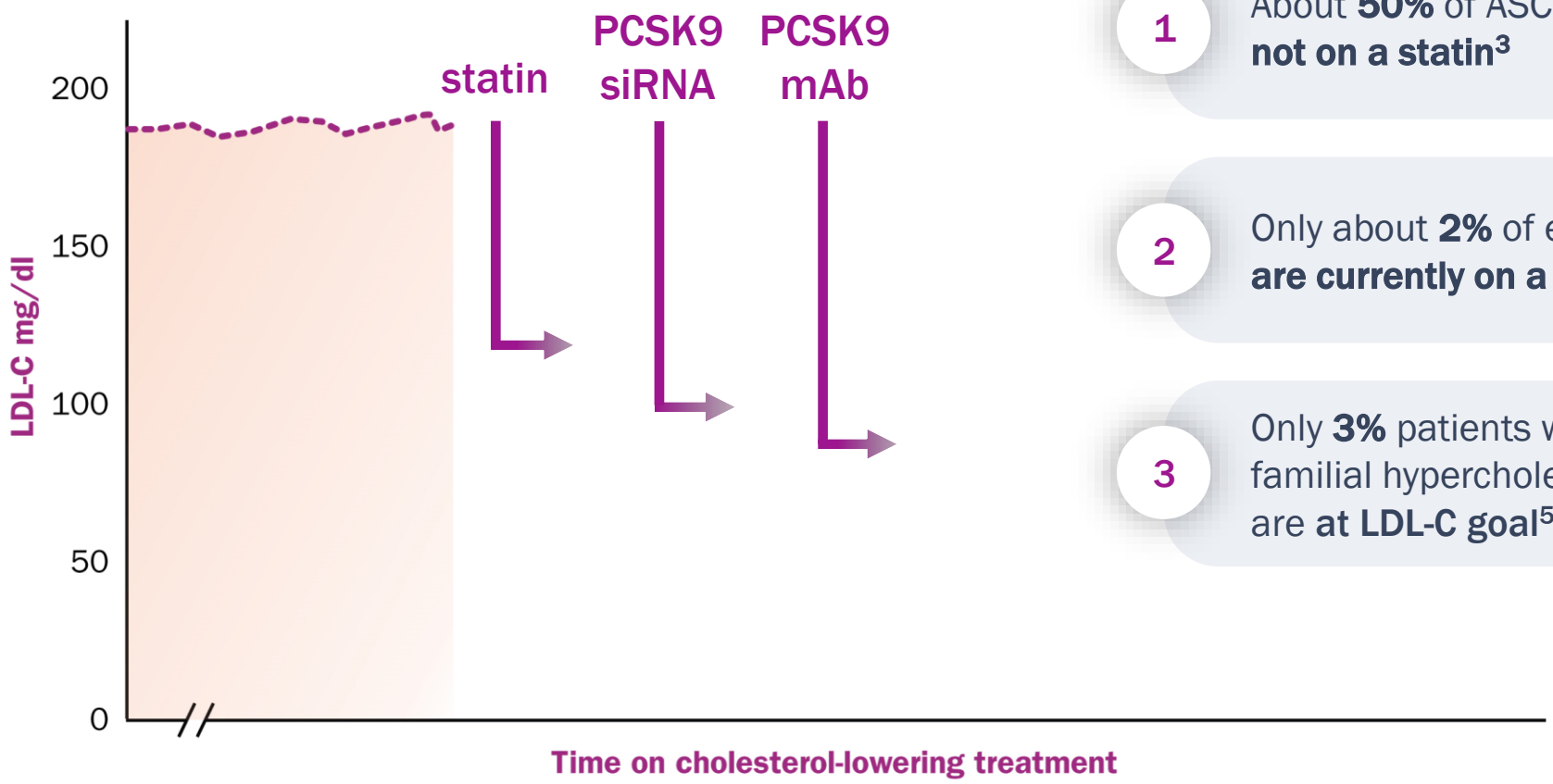
How is ASCVD treated today and is there an unmet need?

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]

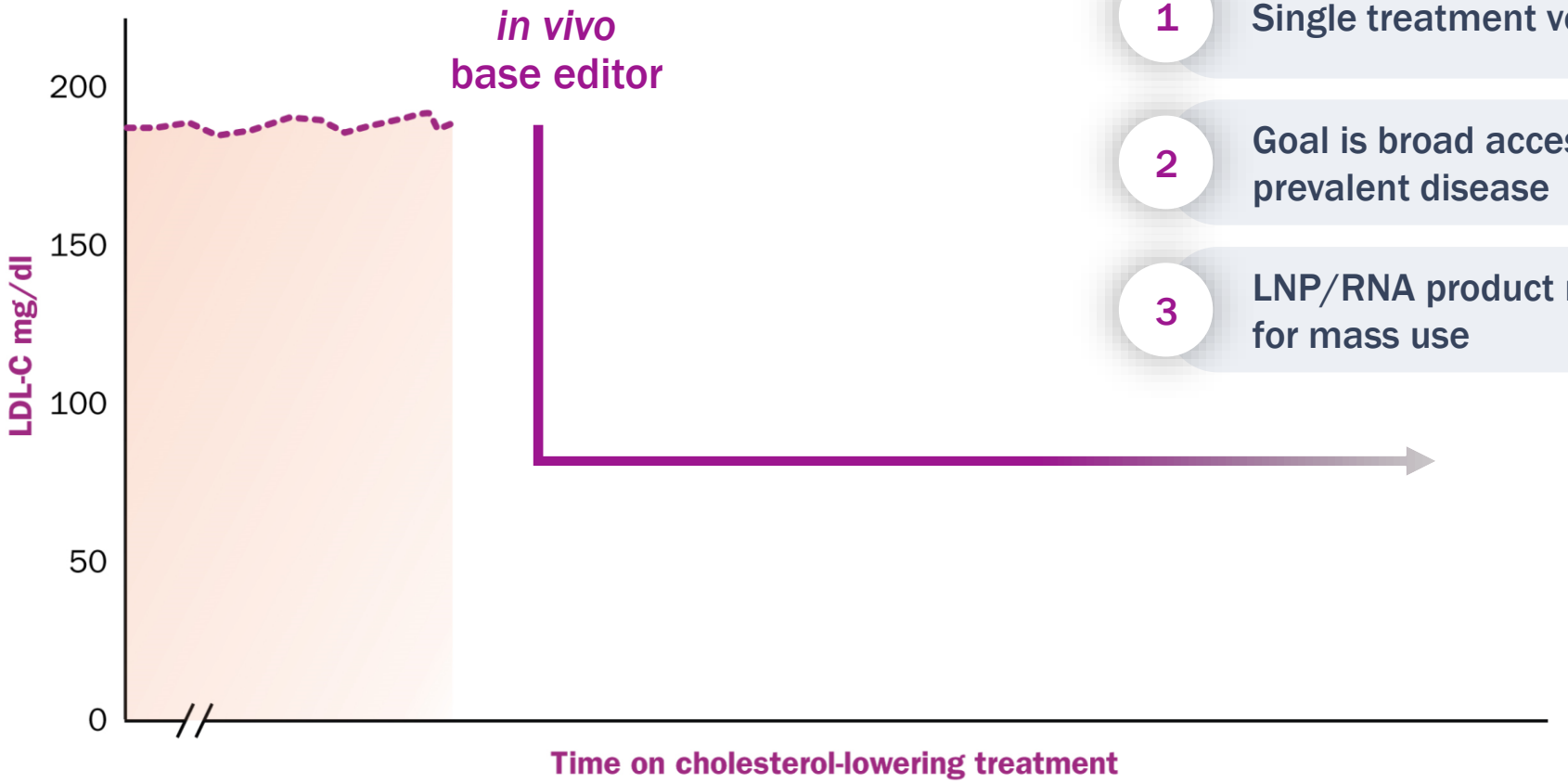
Unmet need: for many, real-world LDL-C lowering is close to zero



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

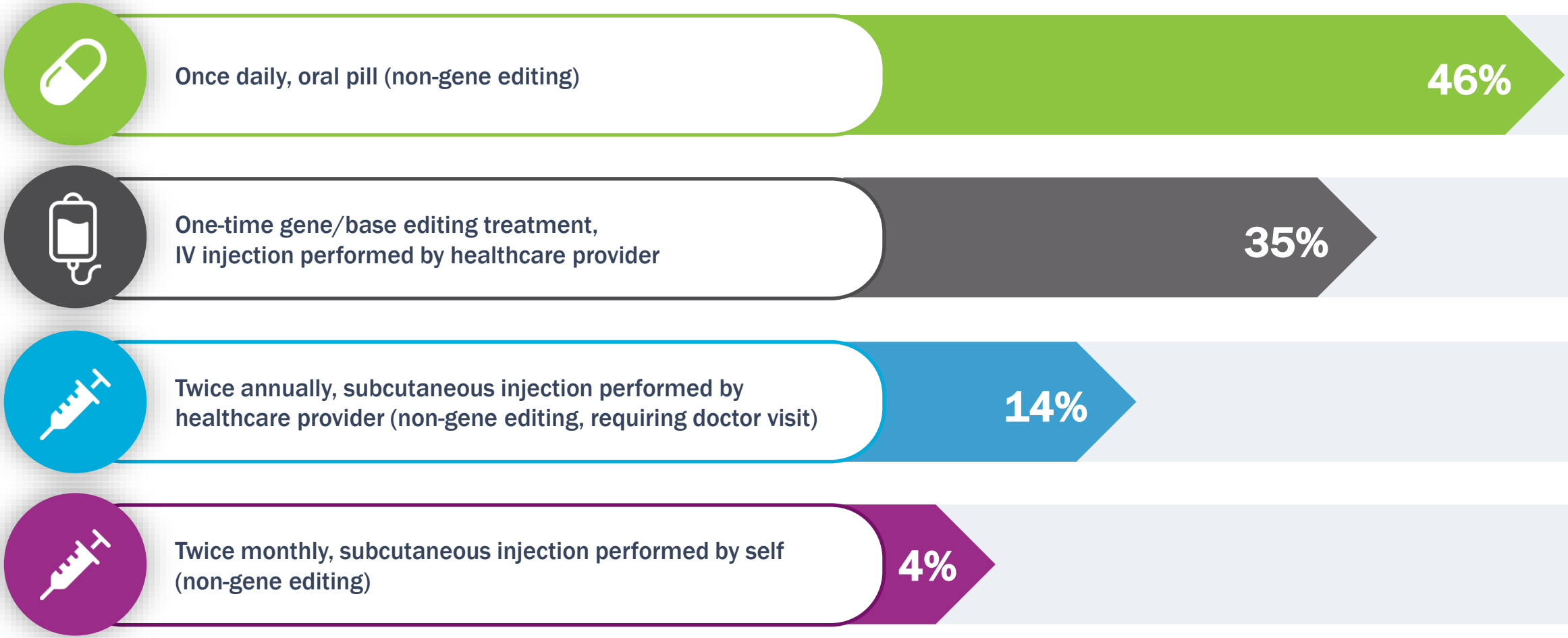


Differentiation:

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)



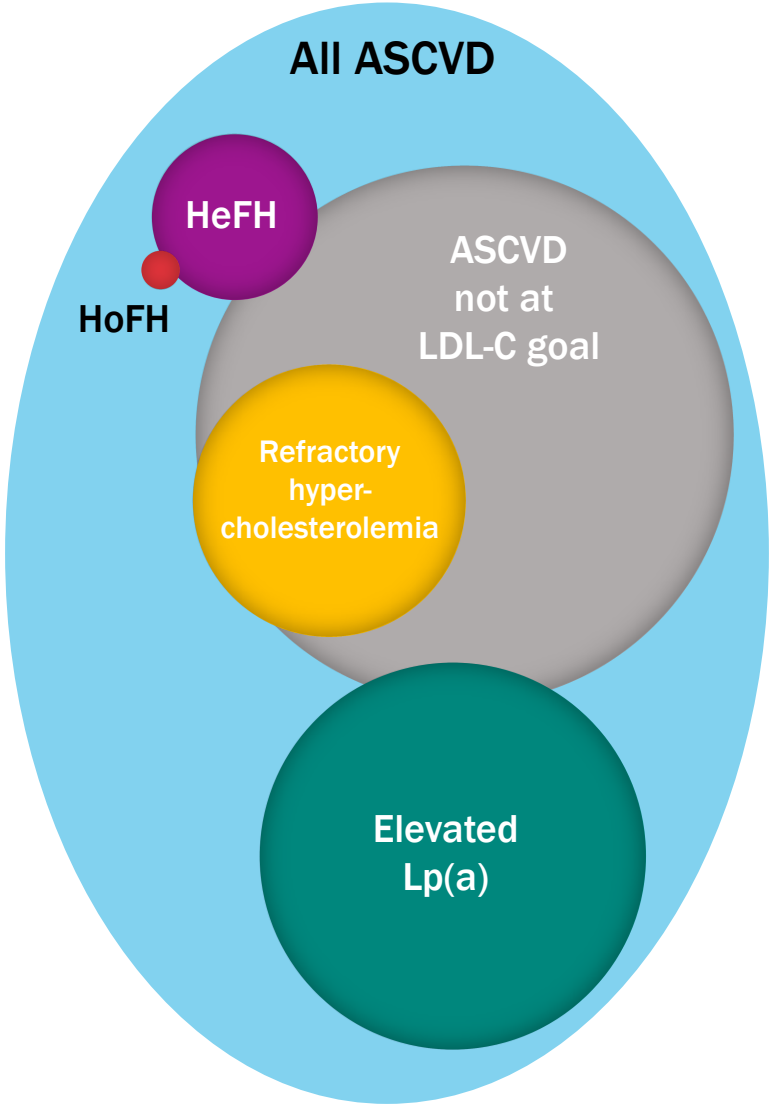
Source: Patient preferences survey conducted by polling firm Morning Consult; LifeSci Capital

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

TARGET	INDICATION	TECHNOLOGY	DEVELOPMENT STATUS			RIGHTS
			Research	IND-enabling	Clinical	
PCSK9 (VERVE-101)	Heterozygous familial hypercholesterolemia / ASCVD	Base Editor				verve, Lilly
PCSK9 (VERVE-102)[1]	Heterozygous familial hypercholesterolemia / ASCVD	Base Editor				verve, Lilly
ANGPTL3 (VERVE-201)	Homozygous familial hypercholesterolemia / Refractory hypercholesterolemia	Base Editor				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 trial and is prioritizing clinical development of VERVE-102.

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



	POPULATION	PROGRAM
All ASCVD	~ 54M in US/EU	
HeFH	~ 3M in US/EU	PCSK9
ASCVD not at LDL-C goal on statin[1,2]	~ 21M in US/EU	PCSK9
HoFH	~ 2,800 in US/EU	ANGPTL3
Refractory hypercholesterolemia[3] (ASCVD not at LDL-C goal on standard of care)	~ 7M in US/EU (~13% ASCVD)	ANGPTL3
Elevated Lp(a)	~ 11M in US/EU (~20% ASCVD)	LPA

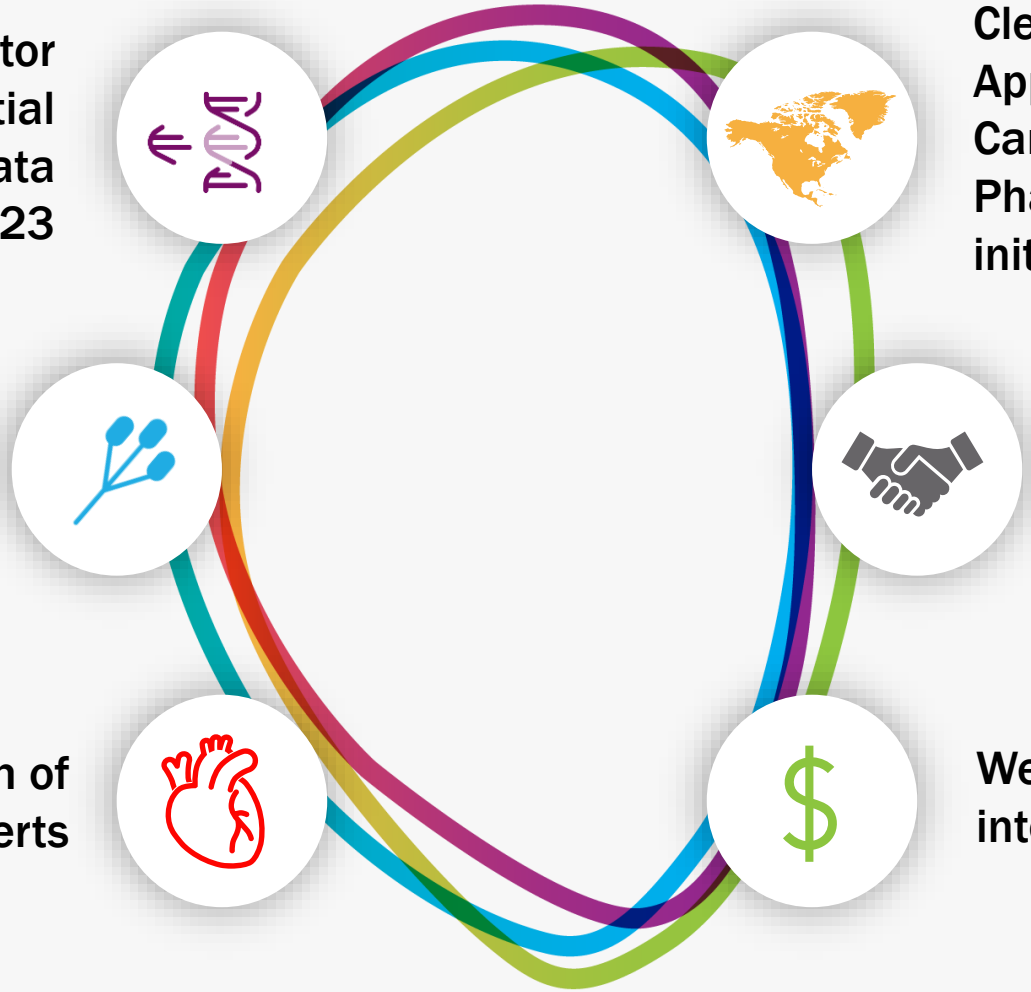
1. Gu J et al., *Am J Prev Cardiol.* 2022; 10:100336
2. Ray KK et al., *European Journal of Preventive Cardiology.* 2021; 28(11):1279–1289
3. O'Donoghue ML et al., *Circulation.* 2022; 146(15):1109-1119

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

Advanced first ASCVD base editor from concept to clinic with initial Heart-1 Phase 1b trial data presented in Nov 2023

Developed novel lipid nanoparticle (LNP) liver delivery technology: GalNAc-LNP; To be tested in the clinic in Heart-2 clinical trial

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



Clearance of Clinical Trial Applications (CTAs) in the U.K. and Canada for VERVE-102; Heart-2 Phase 1b clinical trial expected to initiate in 2Q 2024

Establishing strategic relationships to support and build pipeline

Well-capitalized with runway into late 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

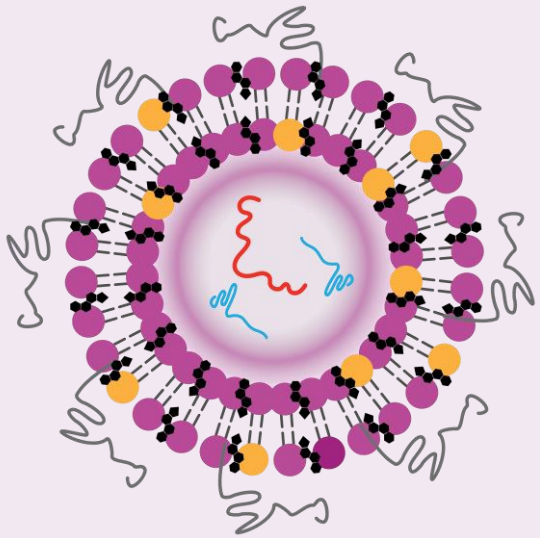
Global collaboration with Lilly on Verve's Lp(a) program: Lilly pays 100% of Verve's development costs through Phase 1; Verve has ability to opt-in to cost-profit share at end of Phase 1

Shared vision around application of gene editing to treat cardiovascular disease

PCSK9 Program

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

VERVE-101



VERVE-102

- Different ionizable lipid that has been used in third-party clinical trials of gene editing product candidates and has been well tolerated in these trials[1]
- Addition of GalNAc targeting ligand - allowing for entry into hepatocytes by any of two receptors (LDLR or ASGPR)

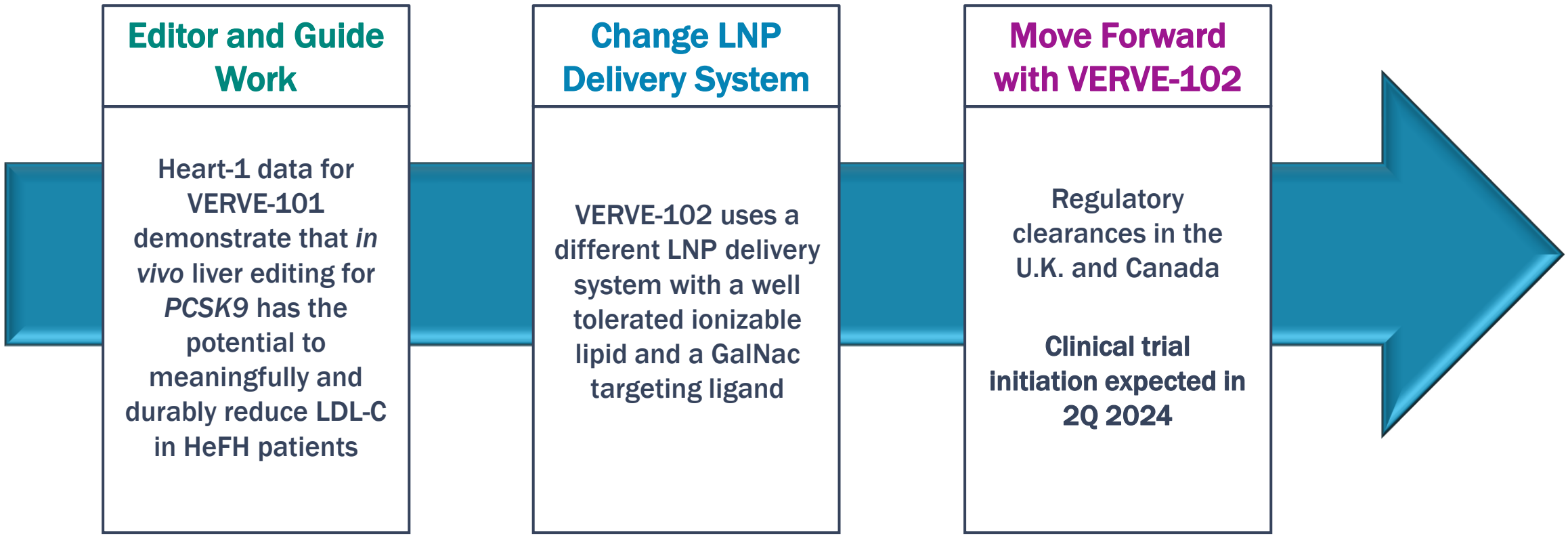
1. Ionizable lipid for VERVE-102 licensed from Novartis.

Update on the Heart-1 Phase 1b clinical trial of VERVE-101: human proof of concept for *in vivo* base editing of the *PCSK9* gene

- 0.45 mg/kg cohort complete (n=6);
  13 participants have now been dosed with VERVE-101
- Participants with follow-up to at least 28 days in the 0.45 mg/kg cohort (n=5) demonstrated a time-averaged LDL-C reduction ranging from 21 – 73%[1]
- In the two patients with the longest follow-up in the 0.45 mg/kg or 0.6 mg/kg cohorts, LDL-C lowering has been durable out to 270 days, with follow-up ongoing
- Sixth participant in the 0.45 mg/kg cohort experienced a Grade 3 drug-induced transient increase in serum ALT as well as a SAE of Grade 3 drug-induced thrombocytopenia
- Paused enrollment in Heart-1; conducting investigation into the laboratory abnormalities in order to define a path forward for VERVE-101

1. As of March 18, 2024.
ALT, alanine aminotransferase; SAE, serious adverse event

For now, prioritizing the clinical development of VERVE-102



LNP, lipid nanoparticle

VERVE-102: adenine base editor mRNA + gRNA packaged in a GalNAc-LNP; edit designed to inactivate *PCSK9*

DRUG SUBSTANCES

RNA components encode base editor and a guide targeting *PCSK9* gene

(same construct as VERVE-101)

- mRNA for adenine base editor
- gRNA localizes editor to *PCSK9* gene

+

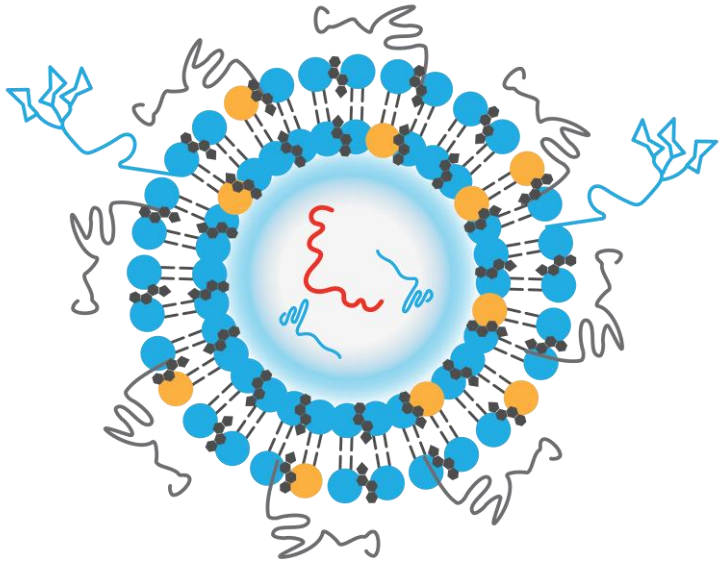
DELIVERY VEHICLE

LNP for delivery to liver cells includes 5 components

- Ionizable amino lipid (Novartis)
- DSPC
- Cholesterol
- GalNAc
- PEG

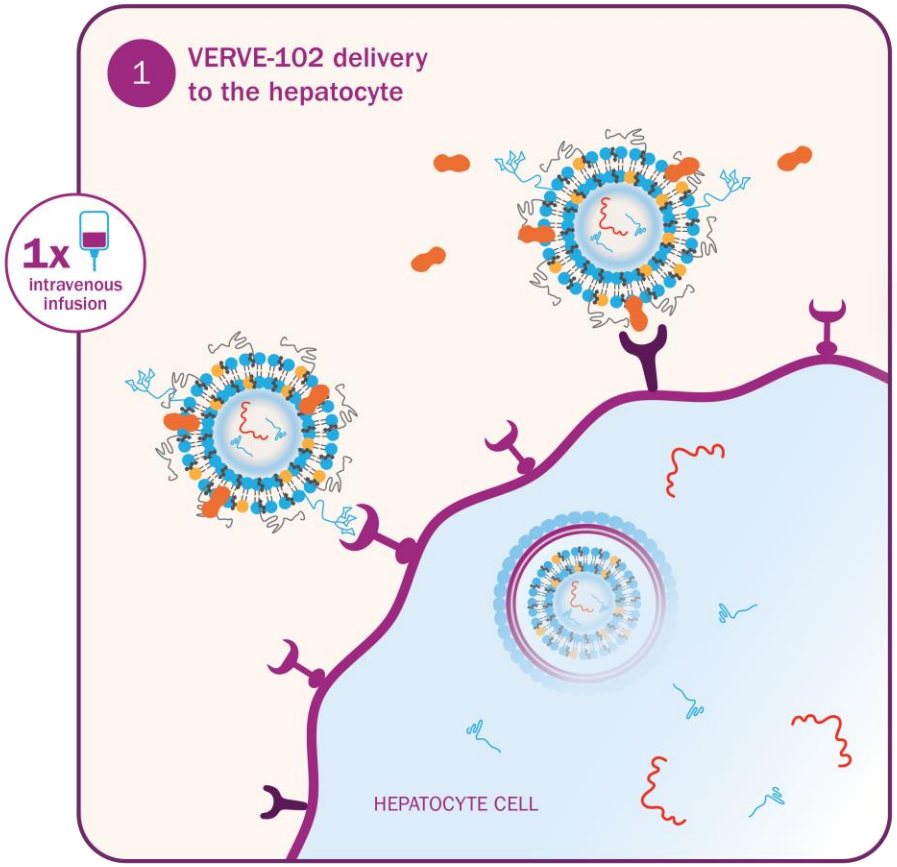
=

VERVE-102



mRNA, messenger RNA; gRNA, guide RNA; GalNAc, N-acetylgalactosamine; LNP, lipid nanoparticle; PCSK9, proprotein convertase subtilisin/kexin type 9; RNA, ribonucleic acid; DSPC, distearoyl-sn-glycerol-3-phosphocholine; PEG, polyethylene glycol

VERVE-102: base editing medicine designed to inactivate hepatic PCSK9 and lower LDL-C

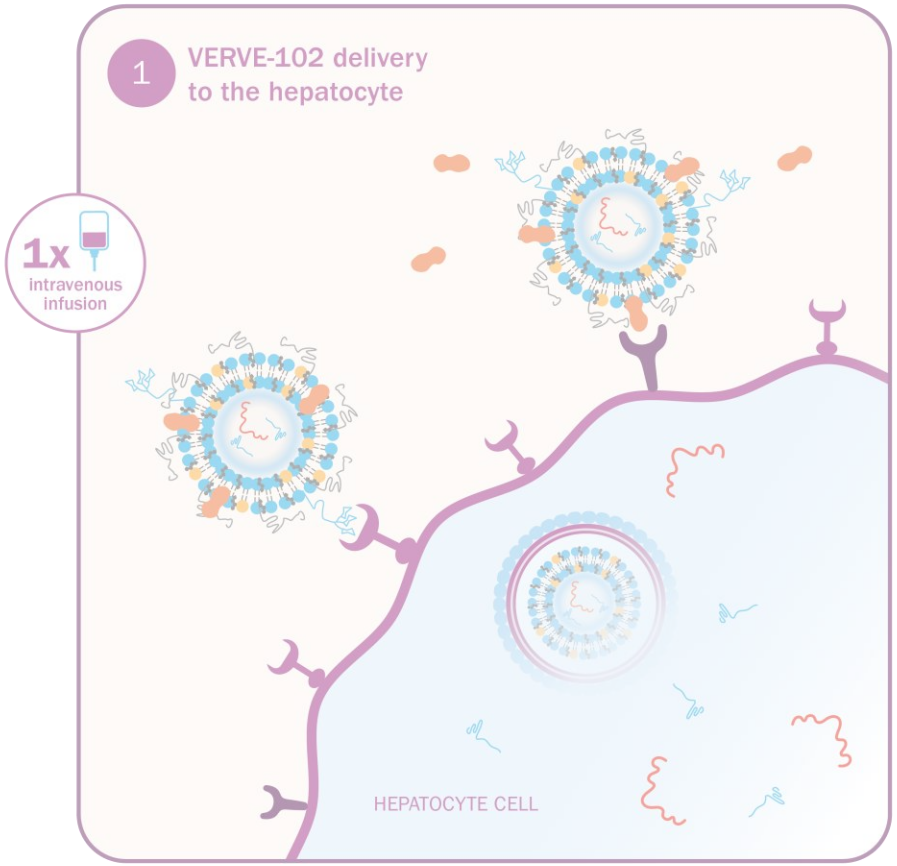


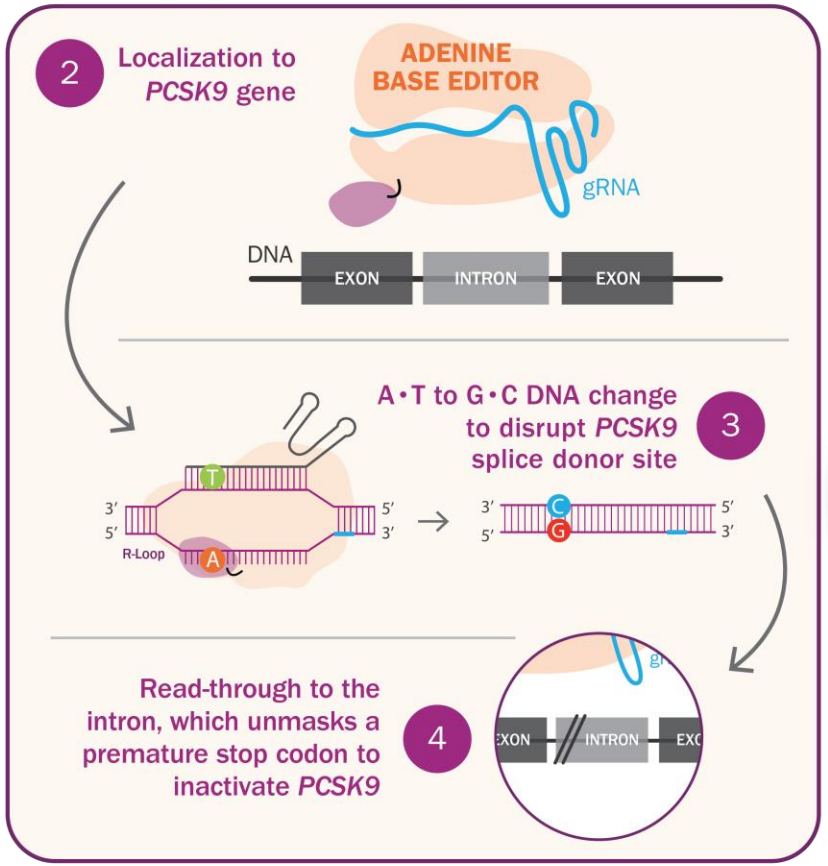
GalNAc lipid nanoparticle:

- **Enables delivery into hepatocyte via either of two receptors: LDLR or ASGPR**
- **Potent editing in target liver tissue with minimal editing elsewhere**
- **No potential for exogenous DNA to integrate into patient DNA (as can occur with viral vectors)**

Lipid nanoparticle | Ionizable amino lipid | DSPC | Asialoglycoprotein receptor (ASGPR) | LDL receptor (LDLR) | GalNAc | apoE | mRNA | gRNA | PEG Lipid | Cholesterol

VERVE-102: base editing medicine designed to inactivate hepatic PCSK9 and lower LDL-C



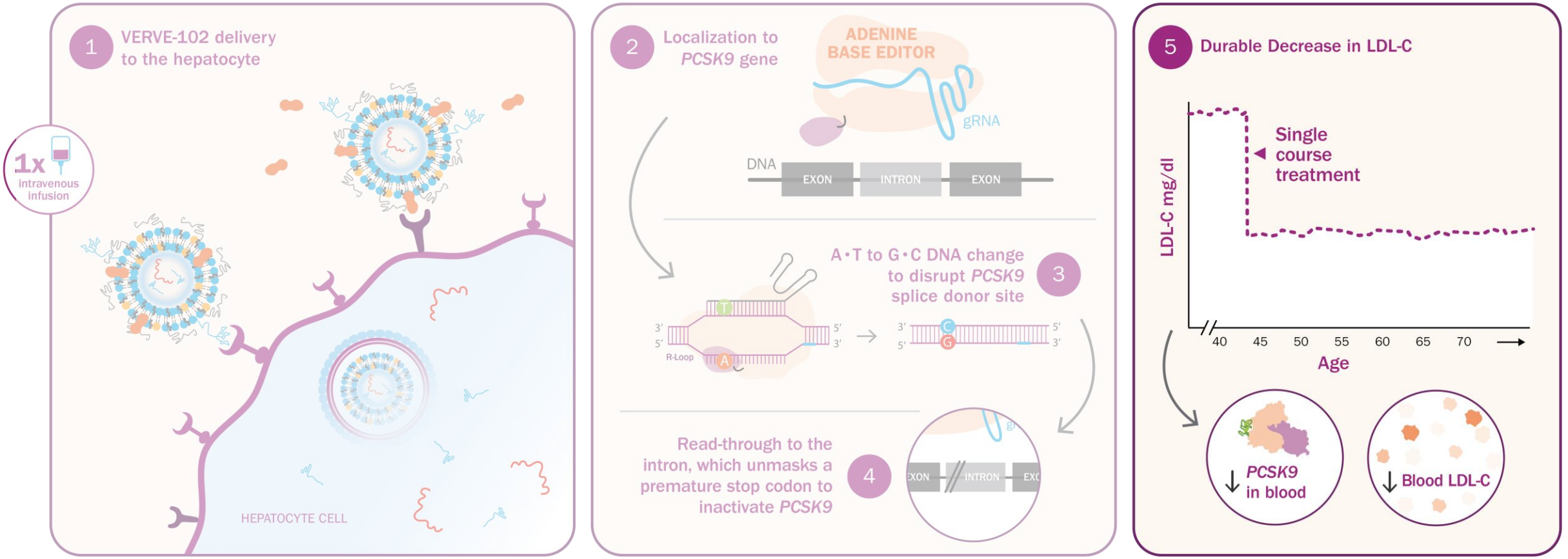


Adenine Base Editor:

- **Precise and predictable DNA change to inactivate gene**
- **No requirement for a double-strand DNA break, as needed for Cas9 nuclease**
- **Elimination from body within days**

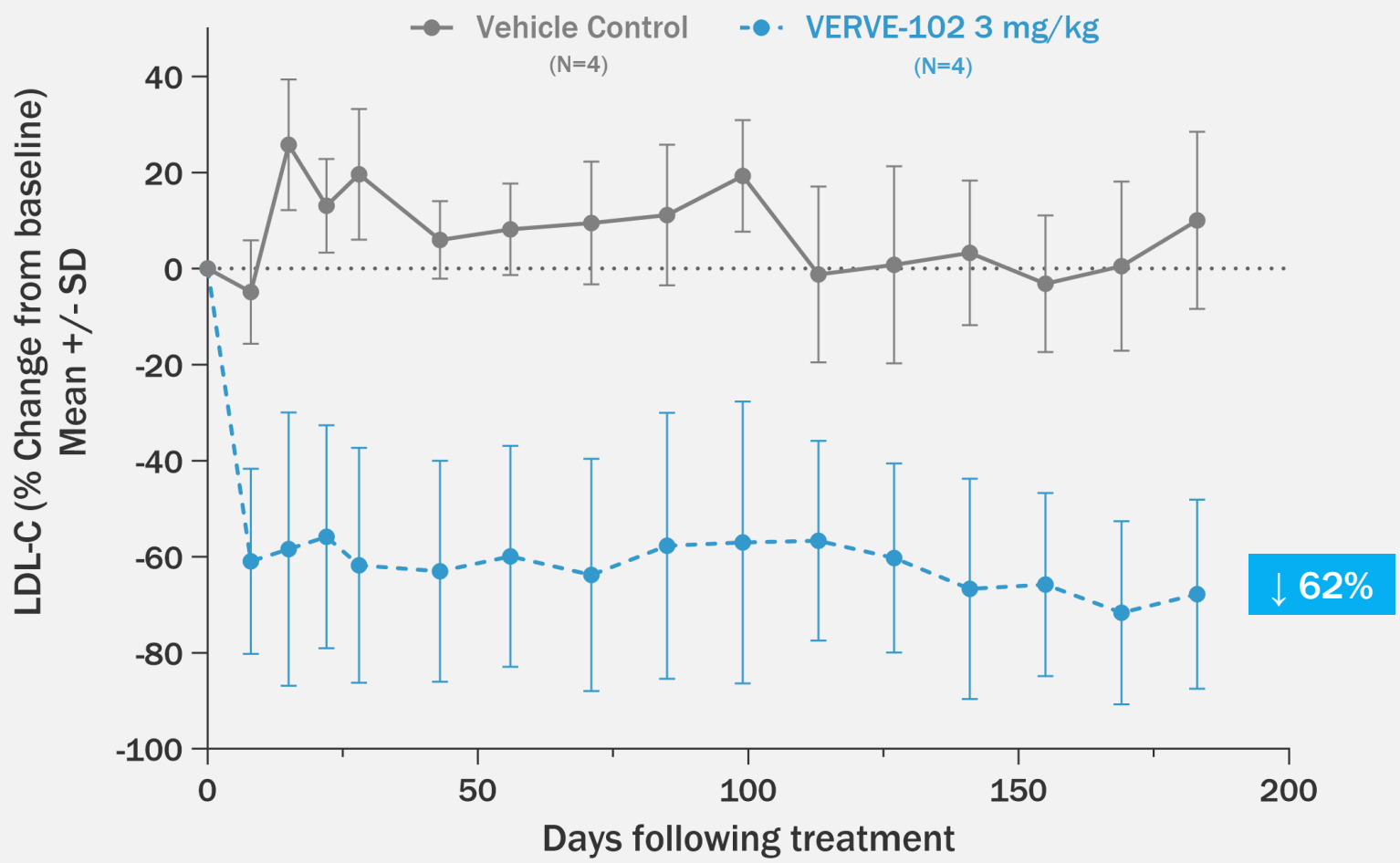
Lipid nanoparticle · Ionizable amino lipid · DSPC · Asialoglycoprotein receptor (ASGPR) · LDL receptor (LDLR) · GalNAc · apoE · mRNA · gRNA · PEG Lipid · Cholesterol

VERVE-102: base editing medicine designed to inactivate hepatic PCSK9 and lower LDL-C



Lipid nanoparticle
Ionizable amino lipid
DSPC
Asialoglycoprotein receptor (ASGPR)
LDL receptor (LDLR)
GalNAc
apoE
mRNA
gRNA
PEG Lipid
Cholesterol

VERVE-102 has demonstrated durable LDL-C reduction in non-human primates out to 6 months



Heart-2 is a Phase 1b trial designed to evaluate the safety, pharmacokinetics and pharmacodynamics of VERVE-102

heart-2

First-in-human, open-label trial in adults with heterozygous familial hypercholesterolemia (HeFH) or premature coronary artery disease (CAD)

PART A Single Ascending Dose

Three to nine participants per cohort receive a single dose

PART B Optional Second Dose Cohort

Eligible participants from Part A who received a low dose may be retreated

STUDY POPULATION SUMMARY

- Males and females (age 18 to 65)
- HeFH 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

CTAs cleared in the U.K. and Canada

Trial initiation expected in 2Q 2024

CTA, clinical trial application; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9

verve THERAPEUTICS

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®

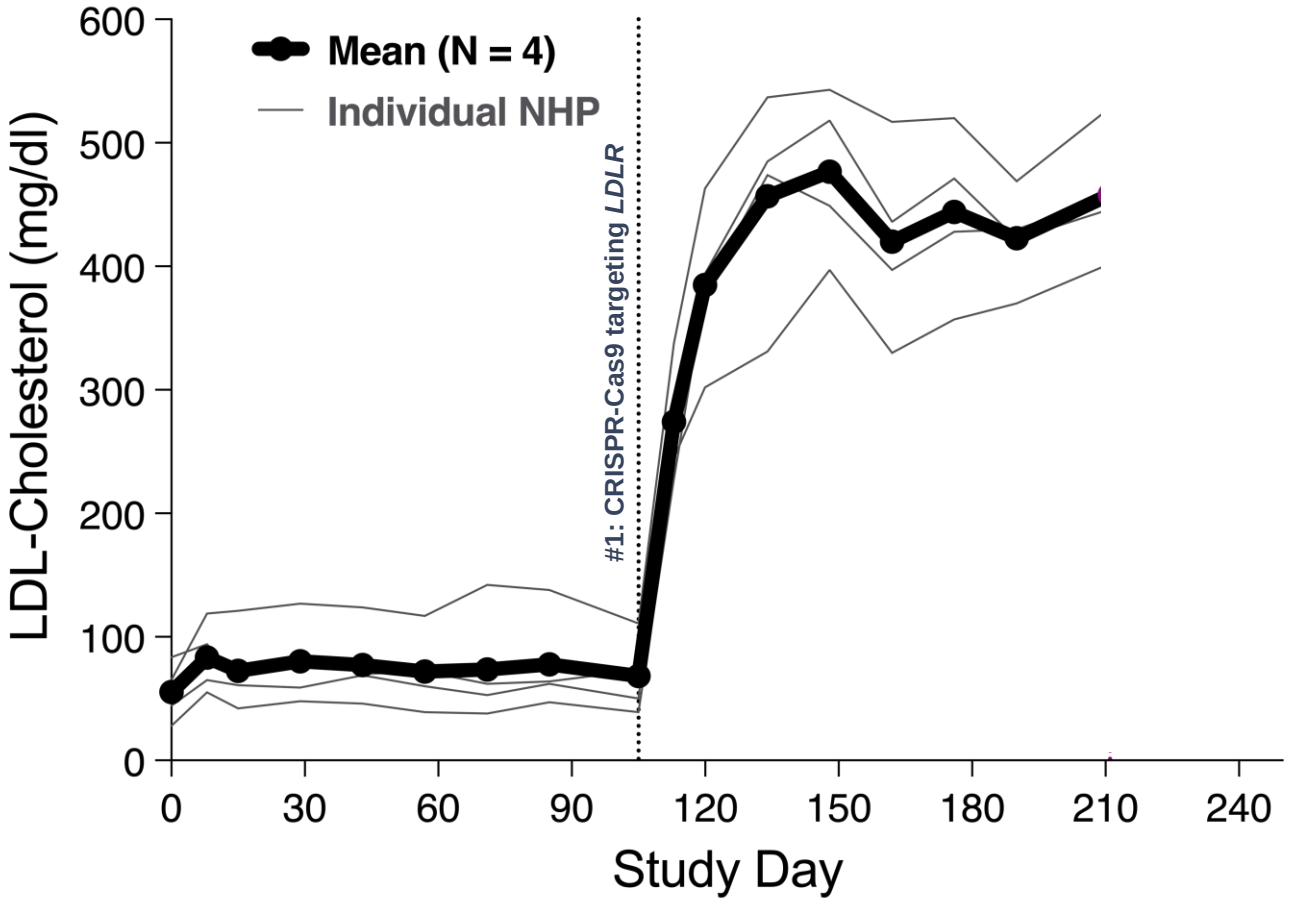
(mAb targeting ANGPTL3)

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)

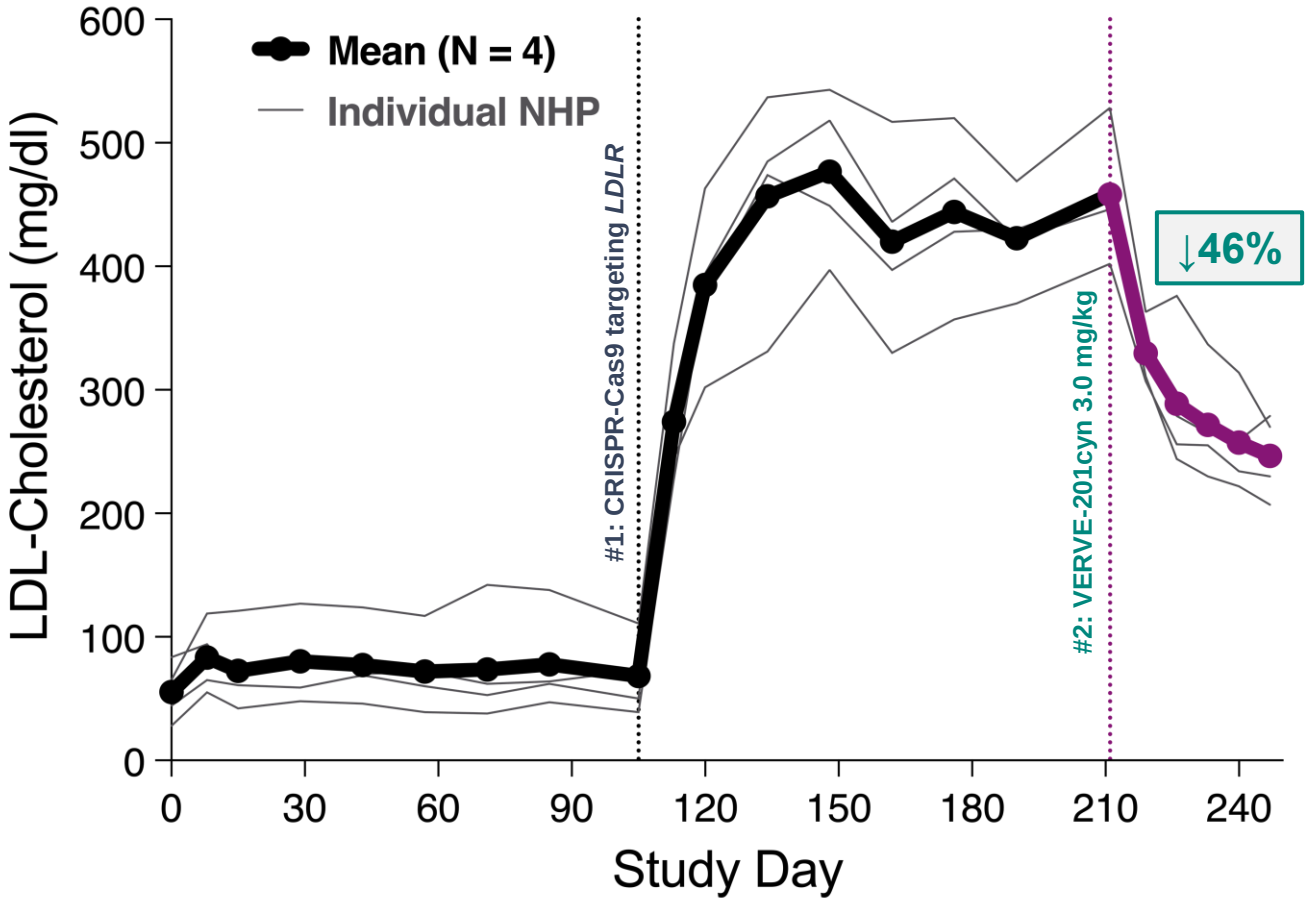
mAb, monoclonal antibody; 1. Rosenson RS et al., *N Engl J Med*. 2020;383(24):2307-2319

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



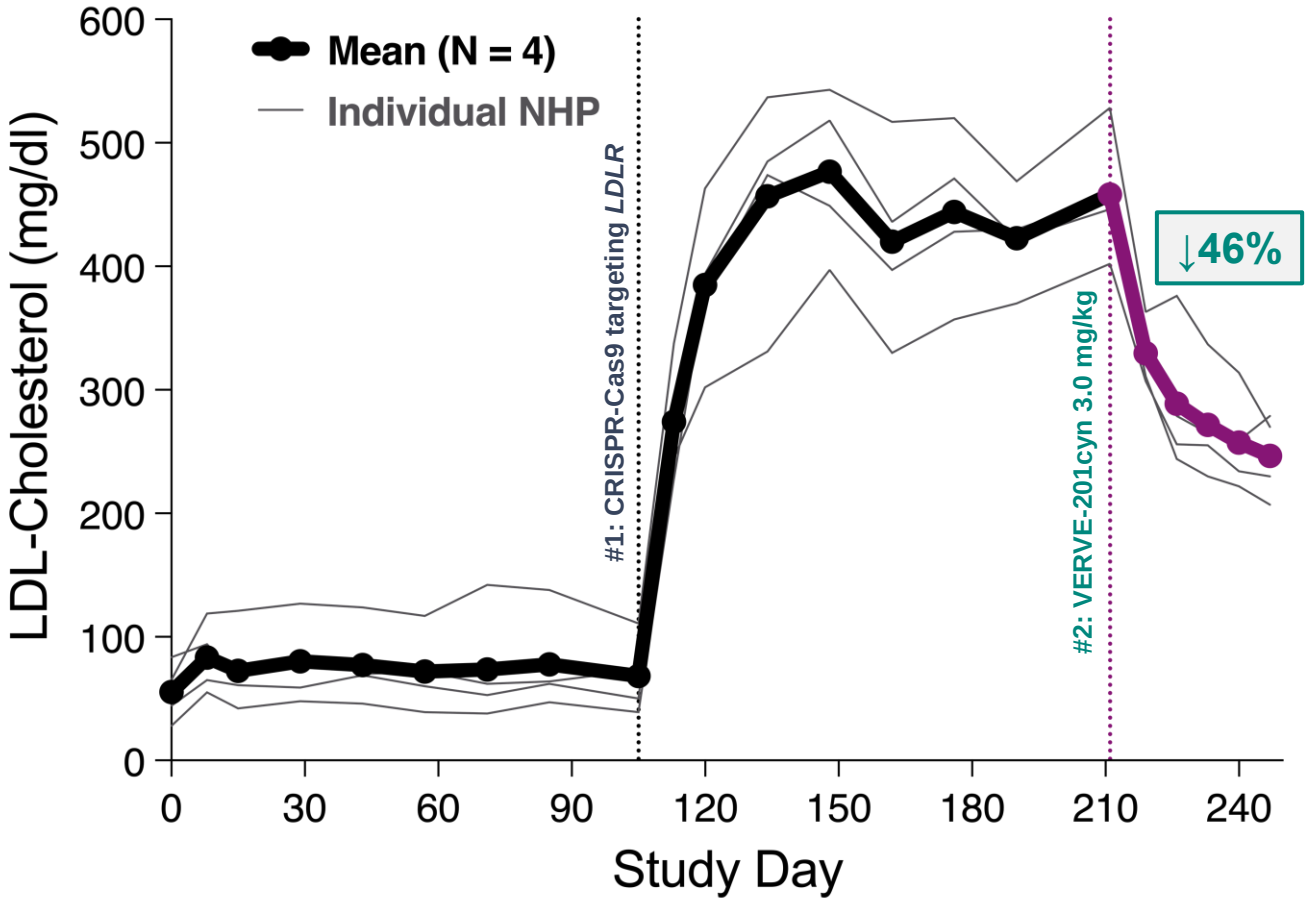
Kasiewicz et al., *Nat Comm* 2023;14(1):2776.

In LDLR-deficient non-human primates treated with VERVE-201cyn targeting ANGPTL3, 46% mean decrease in LDL-C observed (458 to 247 mg/dL)



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

Clinical trial initiation for VERVE-201 planned in 2H 2024



2H 2024

Clinical trial initiation expected in 2H 2024

Subject to regulatory clearance.

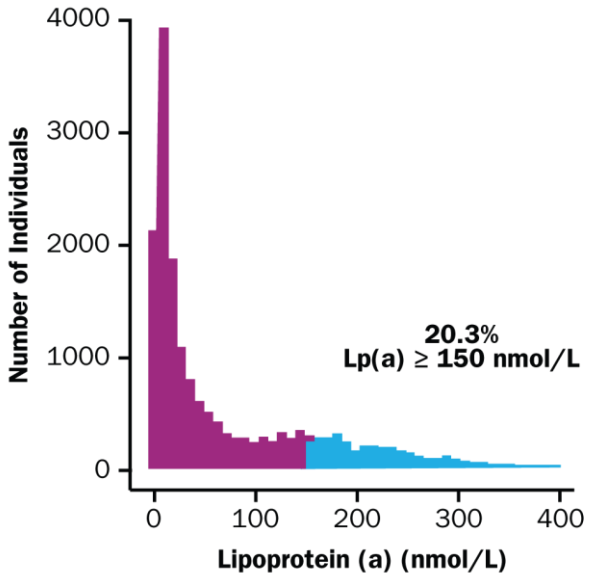
Kasiewicz et al., *Nat Comm* 2023;14(1):2776.

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)[1]

2025

PCSK9 PROGRAM

- Data update for PCSK9 program
- Complete enrollment for VERVE-102 trial
- Select PCSK9 product candidate
- Deliver opt-in package to Lilly
- Initiate randomized, controlled Phase 2

ANGPTL3 PROGRAM

- Data update for VERVE-201

Well-capitalized with runway into late 2026

1. Subject to regulatory clearance.