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

Interim Results from heart-1 Trial of VERVE-101

November 12, 2023

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 safety, tolerability and potential benefits of VERVE-101; the company’s timing and ability to enroll patients in its ongoing heart-1 trial; the expected timing of initiating the expansion cohort of VERVE-101, the receipt of regulatory clearances and timing of initiating the clinical trial of VERVE-102 and Phase 2 clinical trial for the company’s PCSK9 program; 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.

Today's agenda

Topic	Speaker
Introduction and Welcoming Remarks	Sekar Kathiresan, M.D.
Heterozygous Familial Hypercholesterolemia (HeFH) Overview and Unmet Need	Deepak Bhatt, M.D., M.P.H.
Verve's Mission and Vision	Sekar Kathiresan, M.D.
VERVE-101 Overview and Interim Data from the Phase 1b Heart-1 Clinical Trial	Andrew Bellinger, M.D., Ph.D.
Recent Updates, Verve Pipeline Progress and Closing Remarks	Sekar Kathiresan, M.D.
Q & A Session	Sekar Kathiresan, M.D. Andrew Bellinger, M.D., Ph.D. Fred Fiedorek, M.D. Allison Dorval

SPEAKERS

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

Deepak Bhatt, M.D., M.P.H.
Director of Mount Sinai Fuster Heart Hospital,
Dr. Valentin Fuster Professor of
Cardiovascular Medicine,
Icahn School of Medicine

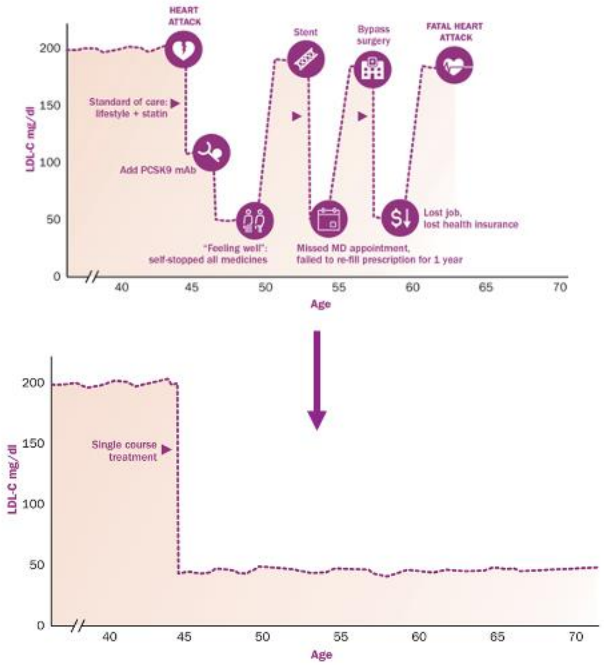
Andrew Bellinger, M.D., Ph.D.
Chief Scientific Officer,
Verve Therapeutics

Fred Fiedorek, M.D.
Chief Medical Officer,
Verve Therapeutics

Allison Dorval
Chief Financial Officer,
Verve Therapeutics

Verve is focused and well-positioned to realize its vision of developing single-course gene editing medicines to treat atherosclerotic cardiovascular disease (ASCVD)

- Human proof of concept for *in vivo* base editing technology
- Three product candidates against highly validated ASCVD targets
- Emerging regulatory path in U.S. with FDA IND clearance for VERVE-101
- New partner in Eli Lilly with shared vision, CV development expertise, and commercialization strength
- Well-capitalized with $485M in cash and runway into 2026[1]

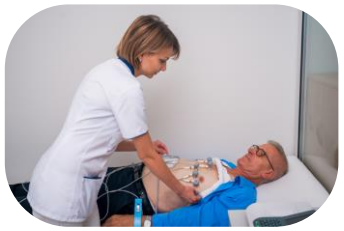


1. As of September 30, 2023

Disease Indication and Unmet Need

Deepak L. Bhatt, MD, MPH, FACC, FAHA, FESC, MSCAI

Unmet need: ASCVD is #1 cause of death worldwide despite available treatments



One person

dies every 34 seconds

from cardiovascular disease in the U.S.[1]

100s of millions

of patients worldwide

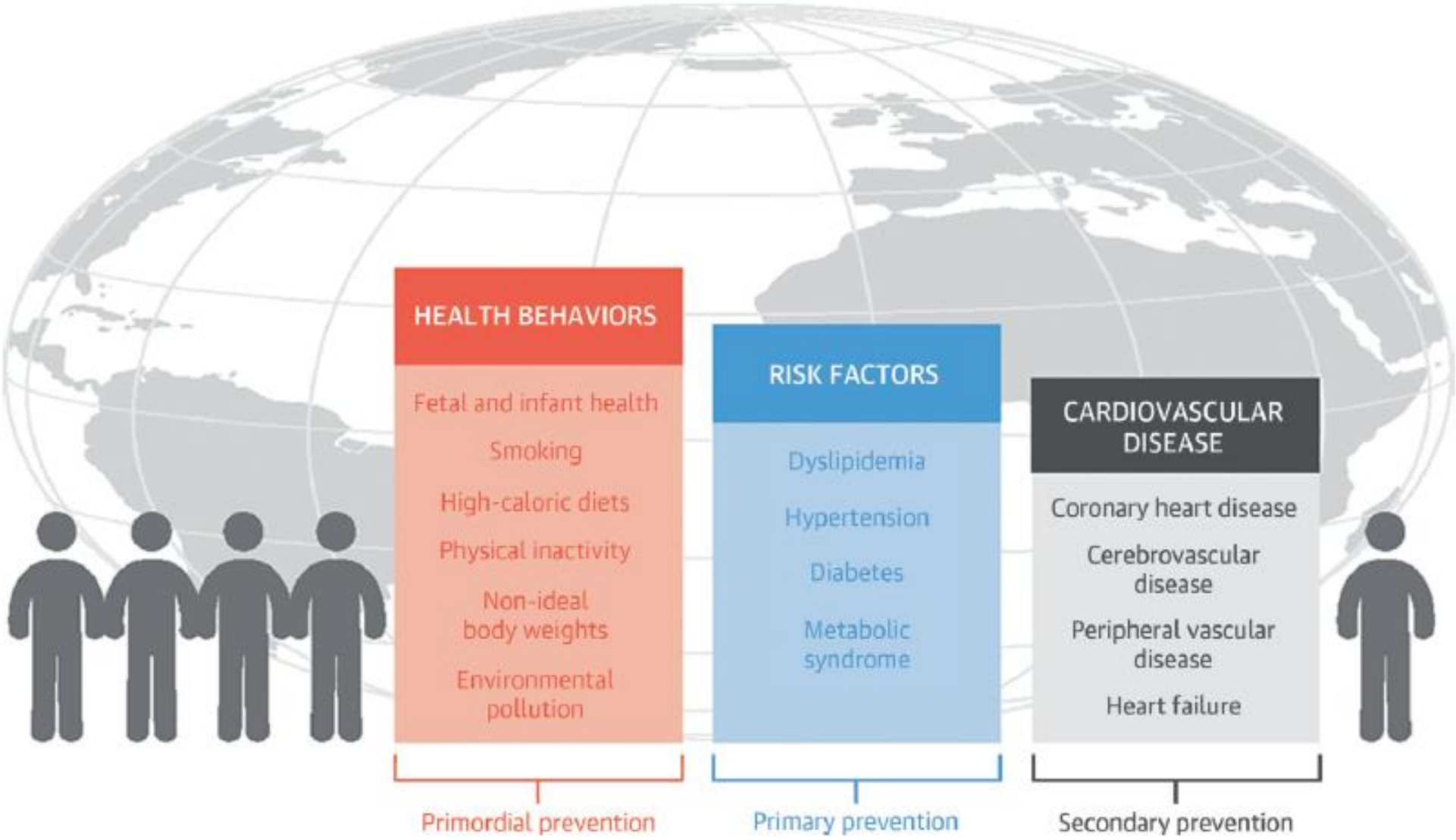
~800K heart attacks

per year in the U.S.[2]

1. Centers for Disease Control and Prevention, National Center for Health Statistics. About Multiple Cause of Death, 1999-2020. CDC WONDER Online Database website. Atlanta, GA: Centers for Disease Control and Prevention; 2022. Accessed February 21, 2022.

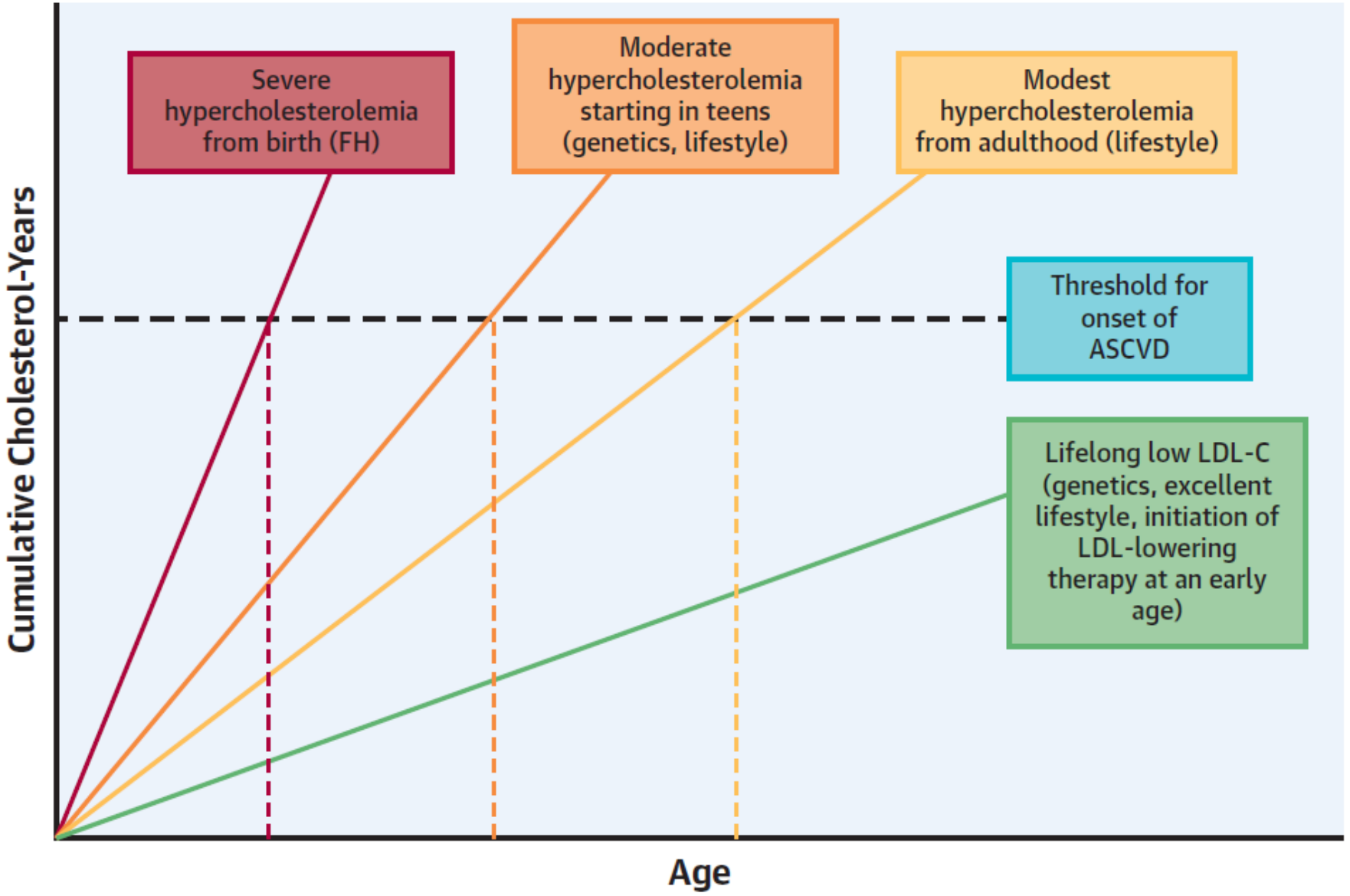
2. Tsao CW et al. *Circulation.* 2022;145(8):e153–e639.

Primordial, Primary, Secondary Prevention



Vaduganathan M, Venkataramini AS, Bhatt DL. *J Am Coll Cardiol*. 2015;66:1535-1537.

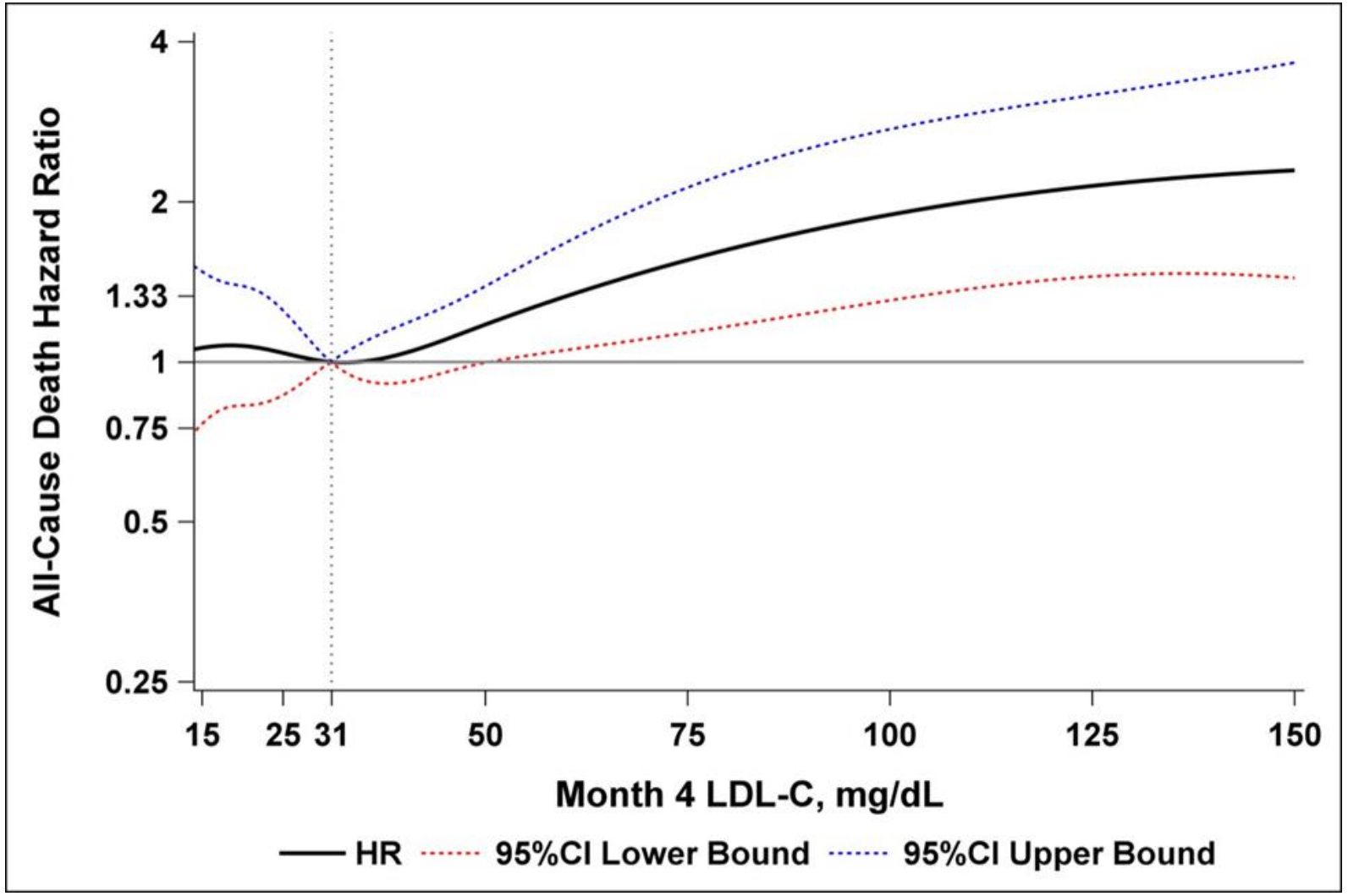
“Cholesterol-Years” for CV Risk Prediction and Treatment



LDL-C, low-density lipoprotein cholesterol

Shapiro MD, Bhatt DL. *J Am Coll Cardiol*. 2020;76:1517-1520.

All-Cause Death by Baseline LDL-C

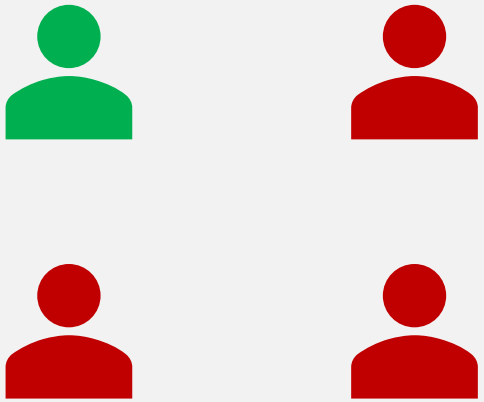


CI, confidence interval

Steg PG, Szarek M, Bhatt DL, Bittner VA, Brégeault MF, Dalby AJ, Diaz R, et al. *Circulation* 2019;140:103-112.

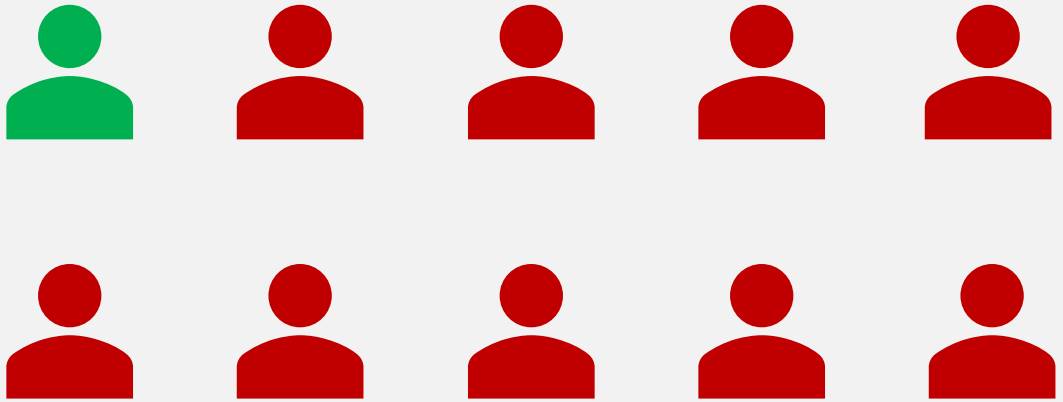
Achievement of Guideline-Directed Targets for LDL-C Among US Adults with CAD

ACC/AHA Guideline Target: ≤ 70 mg/dL



Almost 3 in 4 participants did not meet ACC/AHA guideline target

ESC Guideline Target: ≤ 55 mg/dL



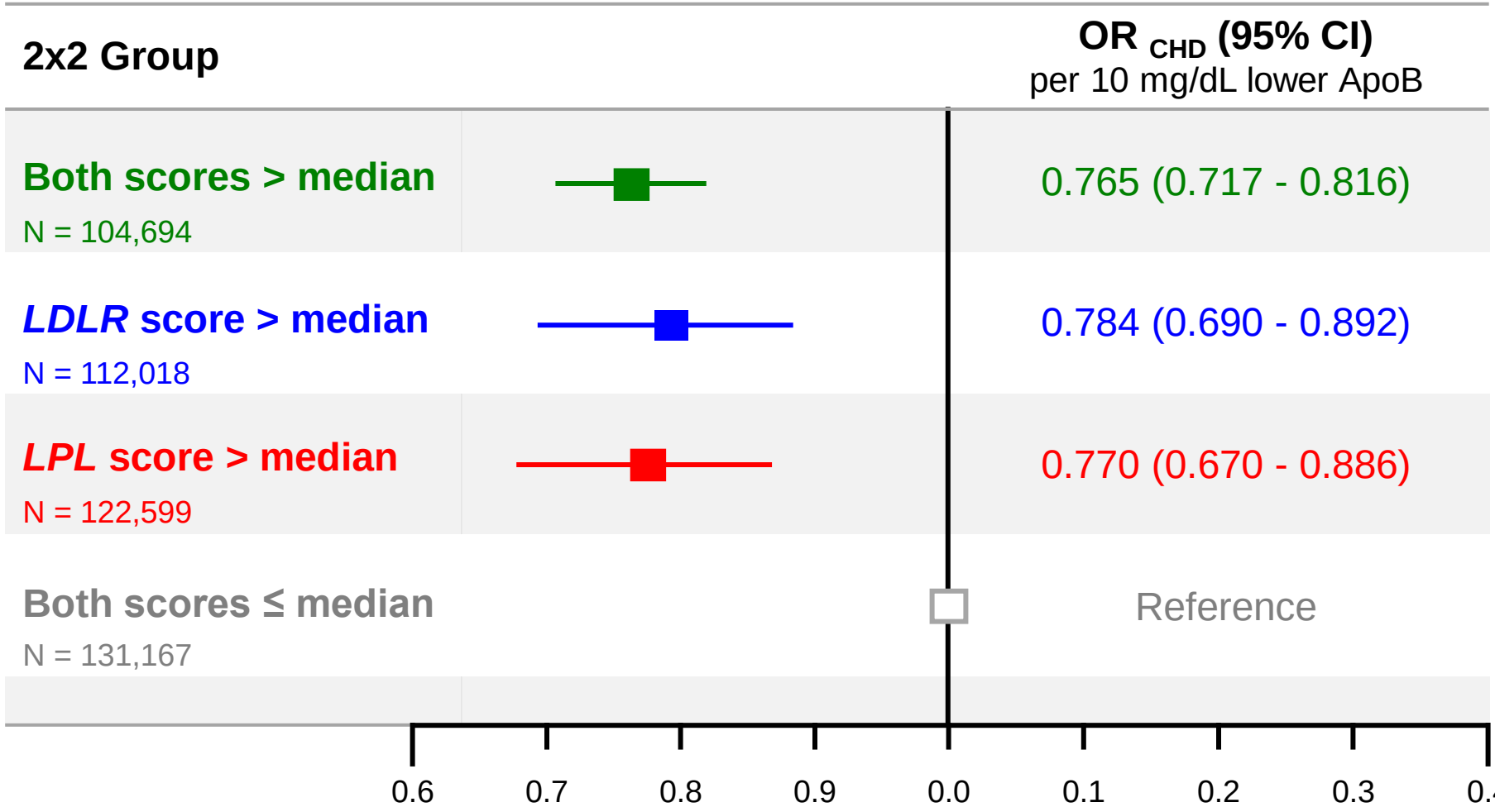
9 in 10 did not meet ESC guideline target

- **73.5%** (95% CI, 68.2%-78.8%) of participants had an LDL-C level greater than or equal to 70 mg/dL
- **88.1%** (95% CI, 83.6%-92.6%) had an LDL-C level greater than or equal to 55 mg/dL

CAD, coronary artery disease; ACC/AHA, American College of Cardiology/American Heart Association; ESC, European Society of Cardiology

Aggarwal R, Chiu N, Libby P, Boden WE, Bhatt DL. *JAMA.* 2023;330:80-82.

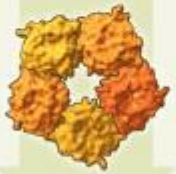
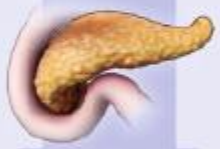
LDL-C Variants and CHD Risk



CHD, coronary heart disease; OR, odds ratio

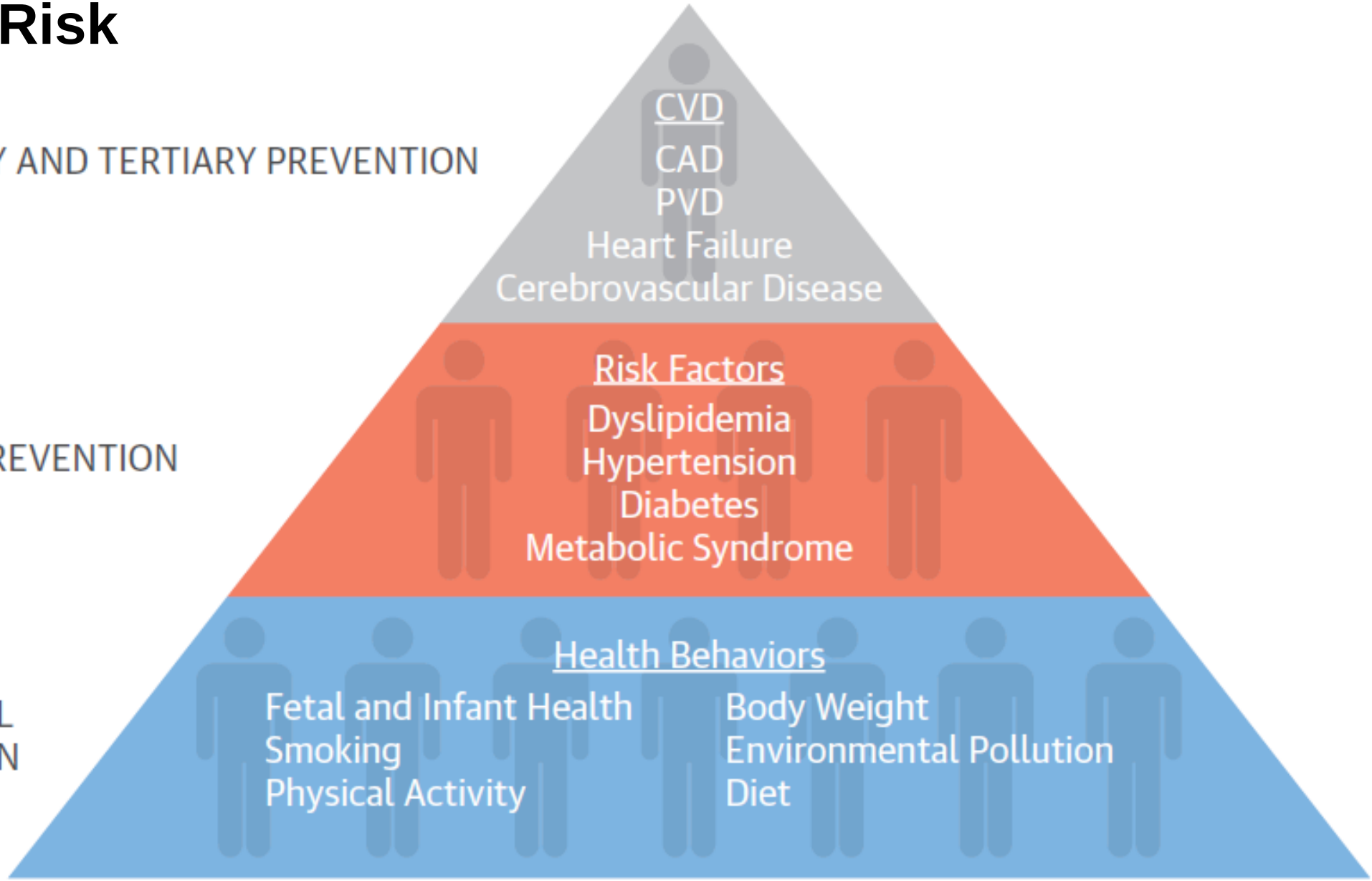
Ference BA, Kastelein JJP, Ray KK, et al., Bhatt DL, Sabatine MS, Catapano AL. Association of Triglyceride-Lowering LPL Variants and LDL-C-Lowering LDLR Variants With Risk of Coronary Heart Disease. *JAMA*. 2019;321(4):364-373.

Redefining Residual Risk in the Current Era

Biological Issue	Residual Cholesterol Risk	Residual Inflammatory Risk	Residual Thrombotic Risk	Residual Triglyceride Risk	Residual Lp(a) Risk	Residual Diabetes Risk
						
Critical Biomarker	LDL-C ≥100 mg/dL	hsCRP ≥2mg/L	No simple biomarker	TG ≥150mg/dL	Lp(a) ≥50mg/dL	HbA1c Fasting glucose
Potential Intervention	Targeted LDL/Apo B Reduction	Targeted Inflammation Reduction	Targeted Antithrombotic Reduction	Targeted Triglyceride Reduction	Targeted Lp(a) Reduction	SGLT2 Inhibitors GLP-1 Agonists
Randomized Trial Evidence	IMPROVE-IT FOURIER SPIRE ODYSSEY	CANTOS COLCOT *LoDoCo2* *OASIS-9*	PEGASUS COMPASS THEMIS	REDUCE-IT *PROMINENT*	Planned	EMPA-REG CANVAS DECLARE CREDENCE LEADER SUSTAIN-6 REWIND

Lawler PR, Bhatt DL, Godoy LC, Lüscher TF, Bonow RO, Verma S, Ridker PM. *Eur Heart J*. 2021;42:113-131.

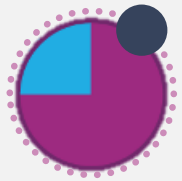
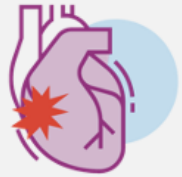
Pyramid of Risk



PVD, peripheral vascular disease

Hong KN, Fuster V, Rosenson RS, Rosendorff C, Bhatt DL. *J Am Coll Cardiol.* 2017;70:2171-2185.

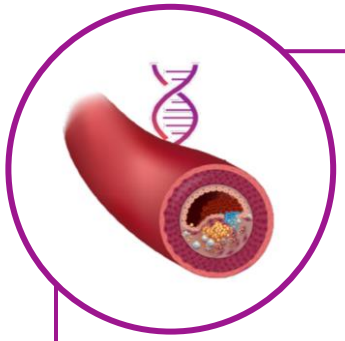
Heterozygous Familial Hypercholesterolemia (HeFH): a serious, inherited subtype of ASCVD with high LDL-C from birth & heart attack at early ages

American Heart Association Diagnostic Criteria				
High LDL-C + Family history (of high LDL-C or premature ASCVD)	Monogenic or polygenic	≥190 mg/dl	30-60 years	>3M adults in US/Europe >20M adults globally

Adapted from Family Heart Foundation; https://familyheart.org/familial hypercholesterolemia/homozygous-familial-hypercholesterolemia.

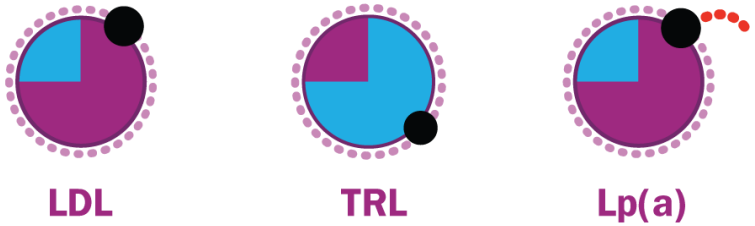
Verve’s mission and vision

What causes ASCVD?

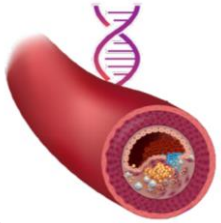


High cumulative life-long exposure to blood cholesterol clogs heart arteries

Cholesterol carried in 3 lipoproteins:



What causes ASCVD and what's a solution?



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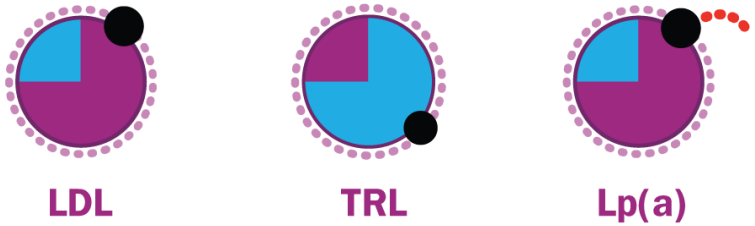
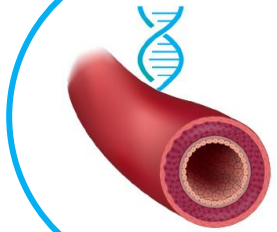
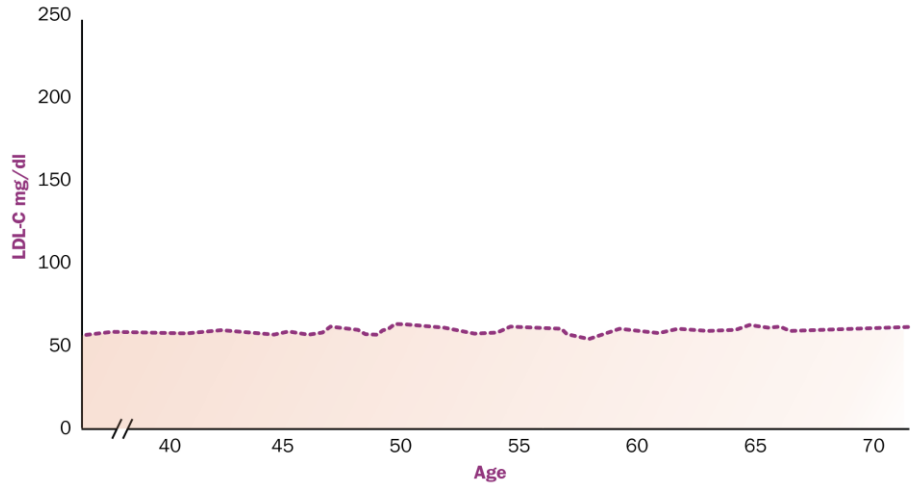




Solution: keep blood cholesterol as low as possible for as long as possible



There are people who have *PCSK9* gene naturally switched off, leading to lifelong low LDL-C and resistance to ASCVD

~50 mg/dl lower LDL cholesterol in blood

~50% lower risk for ASCVD

Healthy

What if we developed a medicine that mimicked resistance mutations?

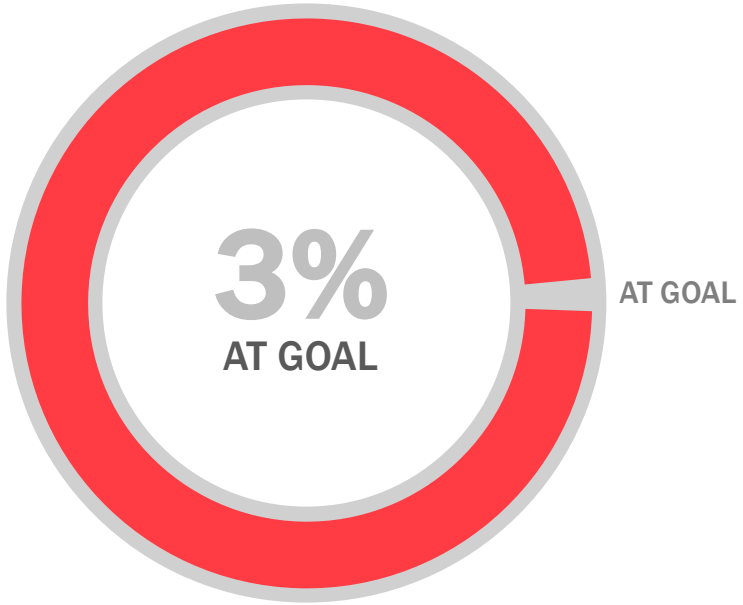
~50 mg/dl lower
LDL cholesterol in blood

~50% lower risk
for ASCVD

Healthy

There are a number of pills & injections available now to lower LDL cholesterol. What's the unmet need?

Heterozygous Familial Hypercholesterolemia



In a global registry of HeFH patients, 3% attain LDL-C < 70 mg/dl[1]

1. EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). *Lancet*. 2021;398(10312):1713-1725.

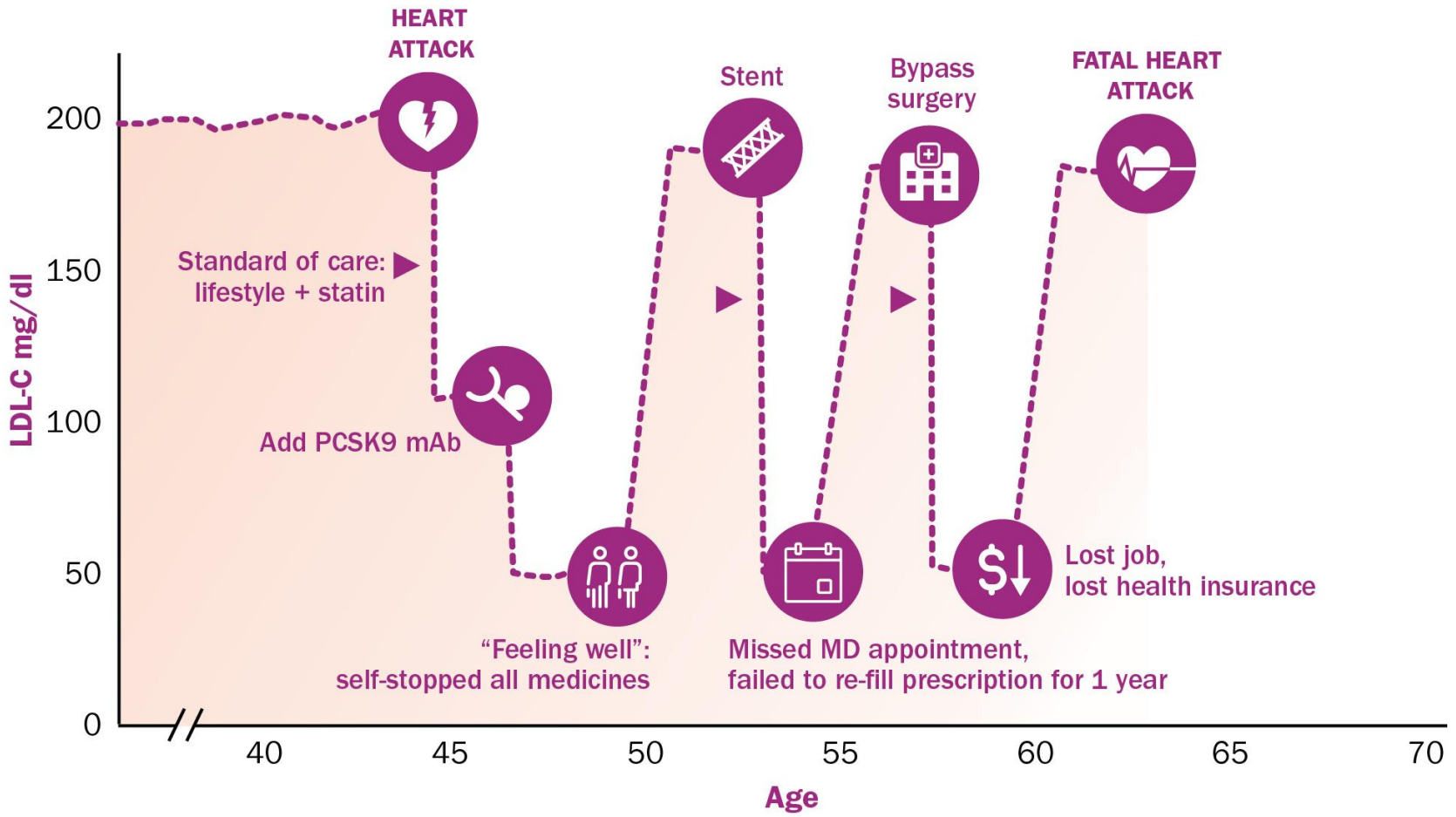
Chronic care model to treat HeFH and ASCVD seems broken

Daily pills or intermittent injections

Administered often over decades

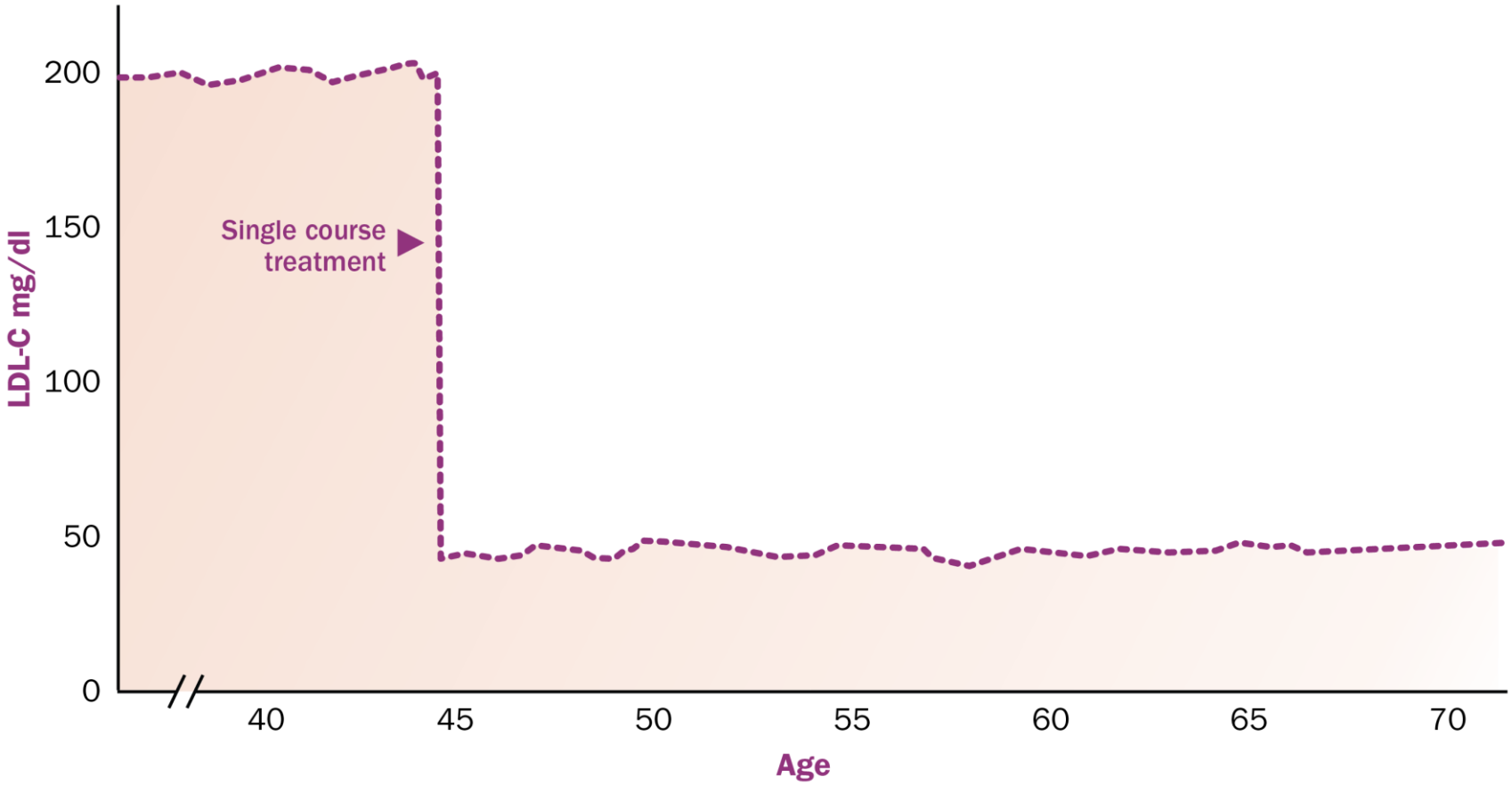
Heavy treatment burden on patients, providers, and healthcare system

What does the chronic care model mean for a patient with HeFH?

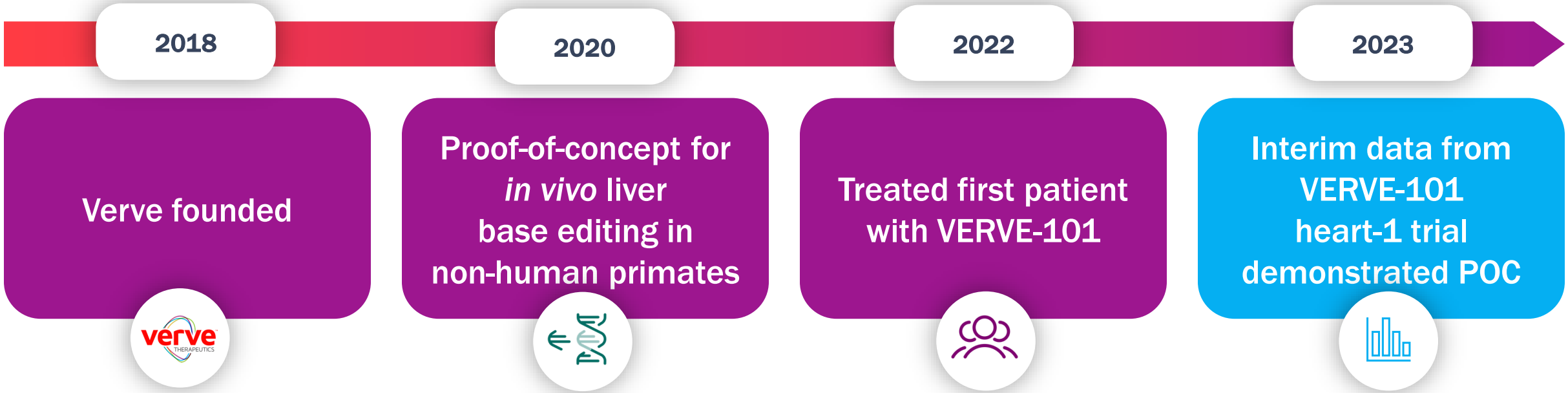


Illustrative graphic depicts the journey of a hypothetical patient with familial hypercholesterolemia who began standard-of-care treatment after suffering a heart attack at age 44

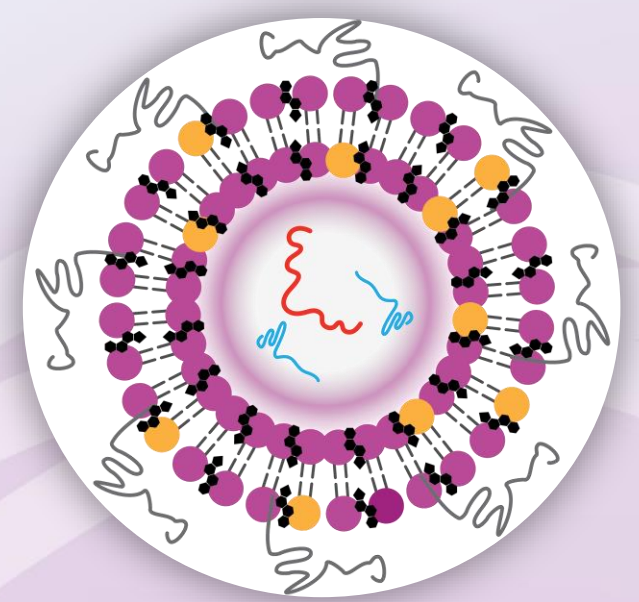
Verve's vision: transform management of HeFH and ASCVD from chronic care to single-course treatments



Significant milestone: interim data has demonstrated proof-of-concept in humans for *in vivo* liver base editing



VERVE-101 preclinical data



VERVE-101: novel base editing medicine designed to inactivate hepatic *PCSK9* and lower LDL-C with a single DNA base pair change

DRUG SUBSTANCES

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

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

+

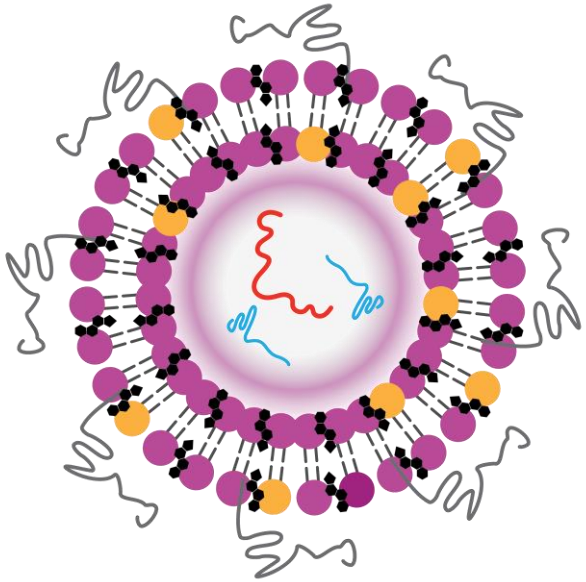
DELIVERY VEHICLE

Lipid nanoparticle (LNP) for delivery to liver cell includes 4 components

- Ionizable amino lipid (Acuitas)
- DSPC
- Cholesterol
- PEG

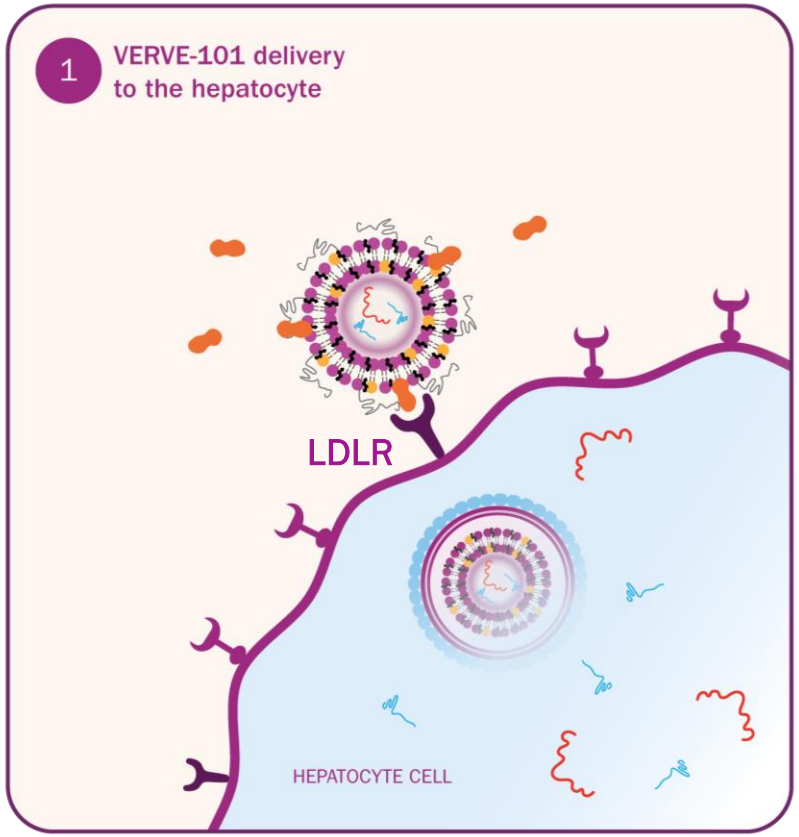
=

VERVE-101



DSPC, distearoyl-sn-glycerol-3-phosphocholine; gRNA, guide RNA; LDL-C, low-density lipoprotein cholesterol; LNP, lipid nanoparticle; mRNA, messenger RNA; PCSK9, proprotein convertase subtilisin/kexin type 9; RNA, ribonucleic acid

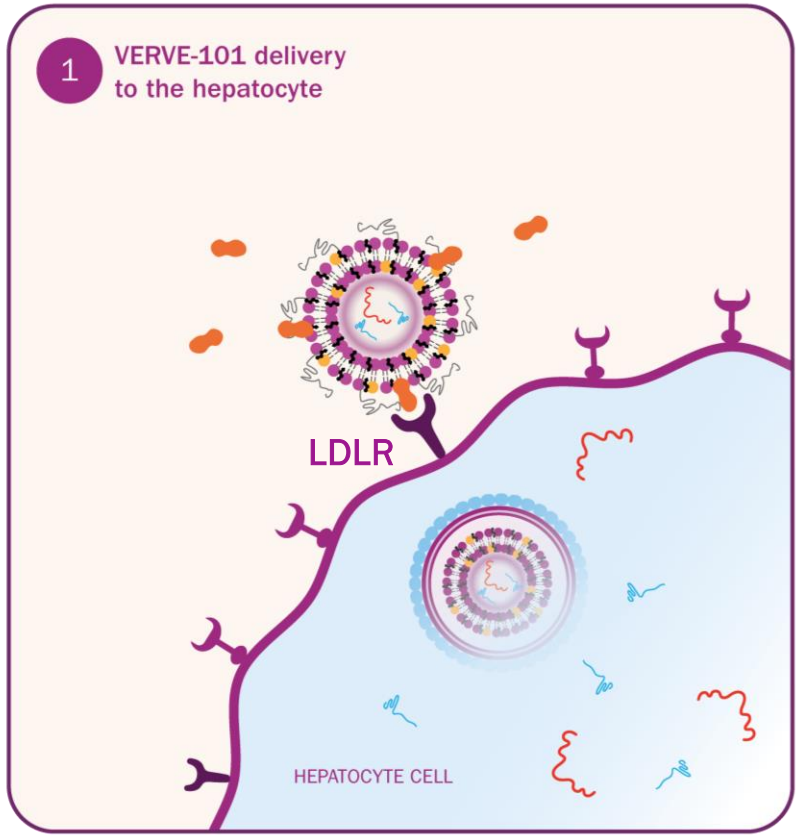
Mechanism of action:
1. Delivery by single intravenous infusion into blood, lipid nanoparticles taken up from blood by hepatocytes through LDL receptor

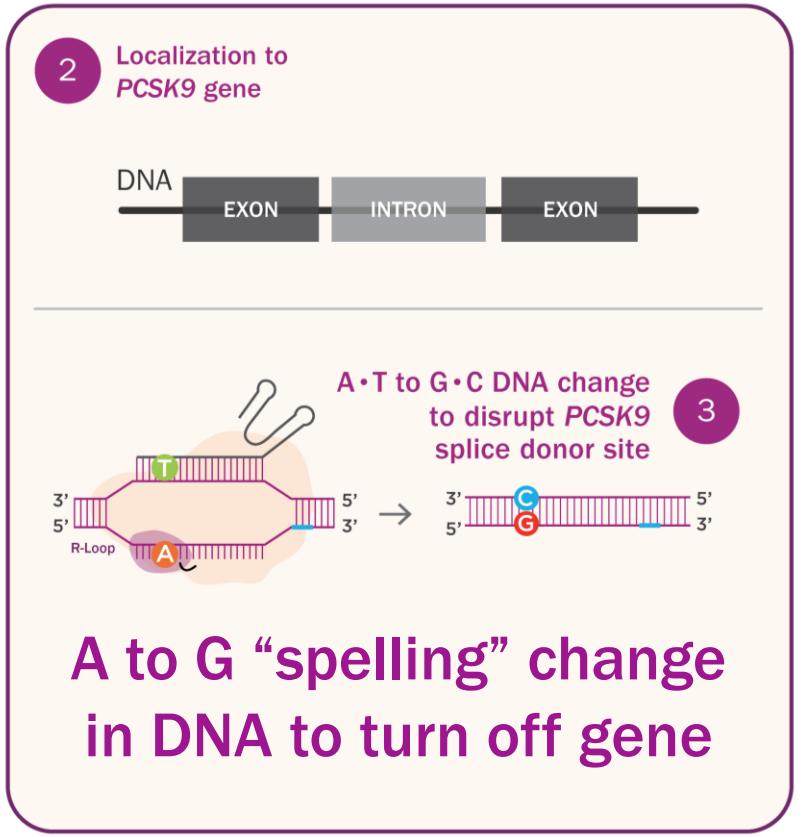


Lipid nanoparticle | Ionizable amino lipid | DSPC | LDL receptor (LDLR) | apoE | mRNA | gRNA | PEG Lipid | Cholesterol

DSPC, distearoyl-sn-glycerol-3-phosphocholine; gRNA, guide RNA; LDL-C, low-density lipoprotein cholesterol; LNP, lipid nanoparticle; mRNA, messenger RNA; PCSK9, proprotein convertase subtilisin/kexin type 9; RNA, ribonucleic acid

Mechanism of action:
2. Localization of base editor to *PCSK9* gene sequence
3. Single spelling change “A to G” to turn off gene, without DNA cutting





DSPC, distearoyl-sn-glycerol-3-phosphocholine; gRNA, guide RNA; LDL-C, low-density lipoprotein cholesterol; LNP, lipid nanoparticle; mRNA, messenger RNA; PCSK9, proprotein convertase subtilisin/kexin type 9; RNA, ribonucleic acid

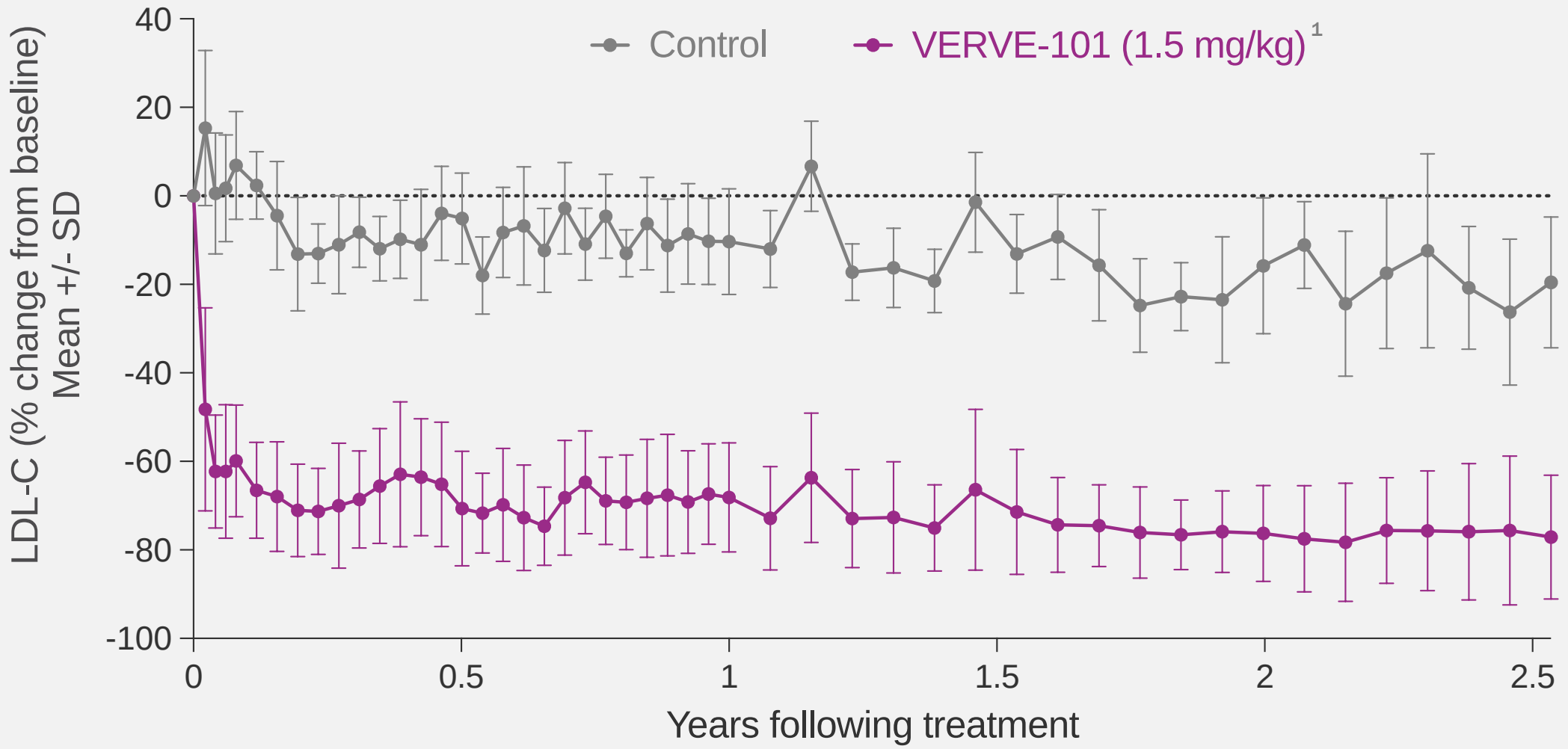
Extensive preclinical evaluation of VERVE-101 in non-human primates & human cells

1. Durability

2. Liver-specific biodistribution

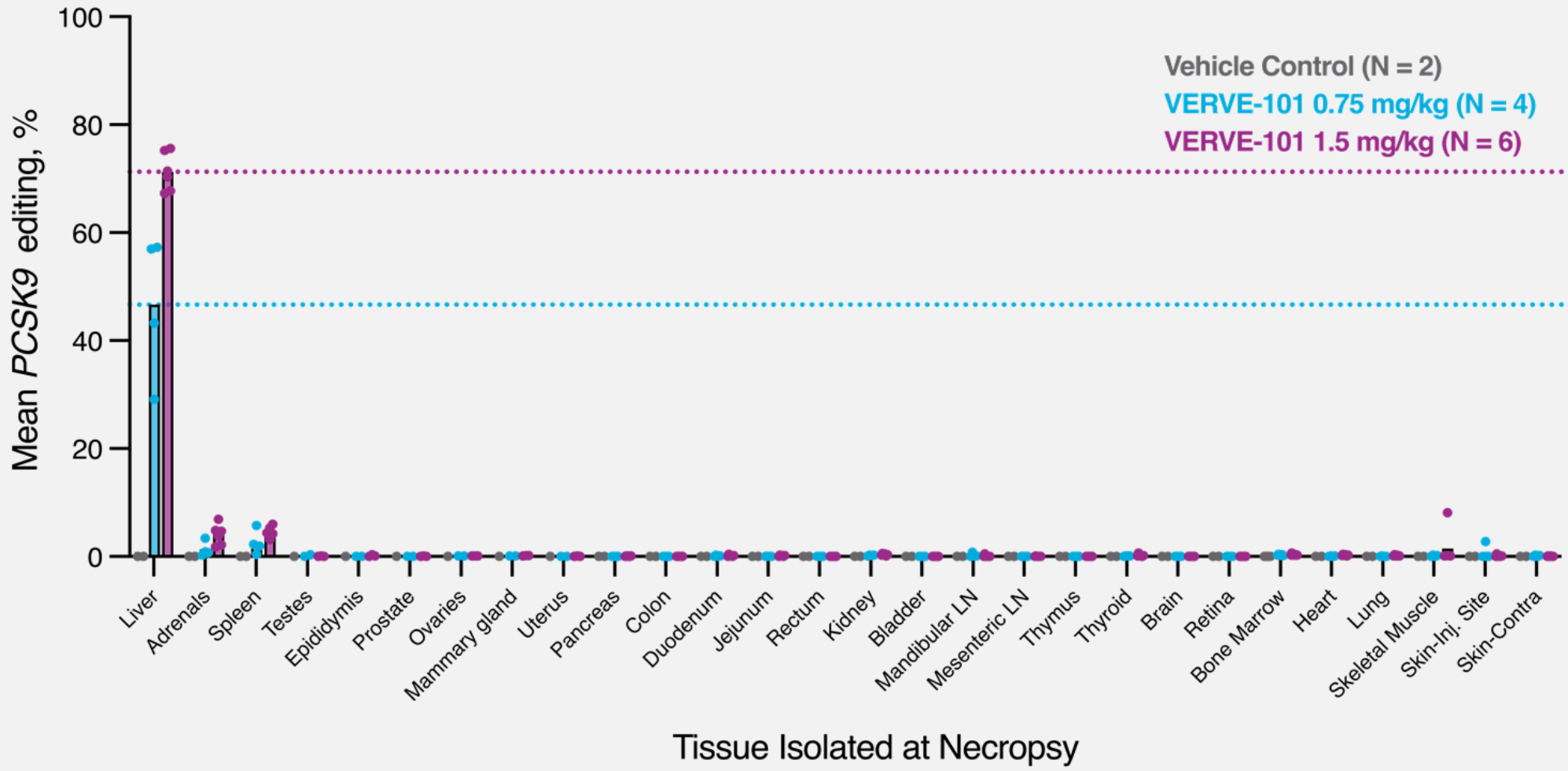
3. Absence of detectable off-target editing

Durability out to 2.5 years observed after a single dose of VERVE-101 in non-human primates

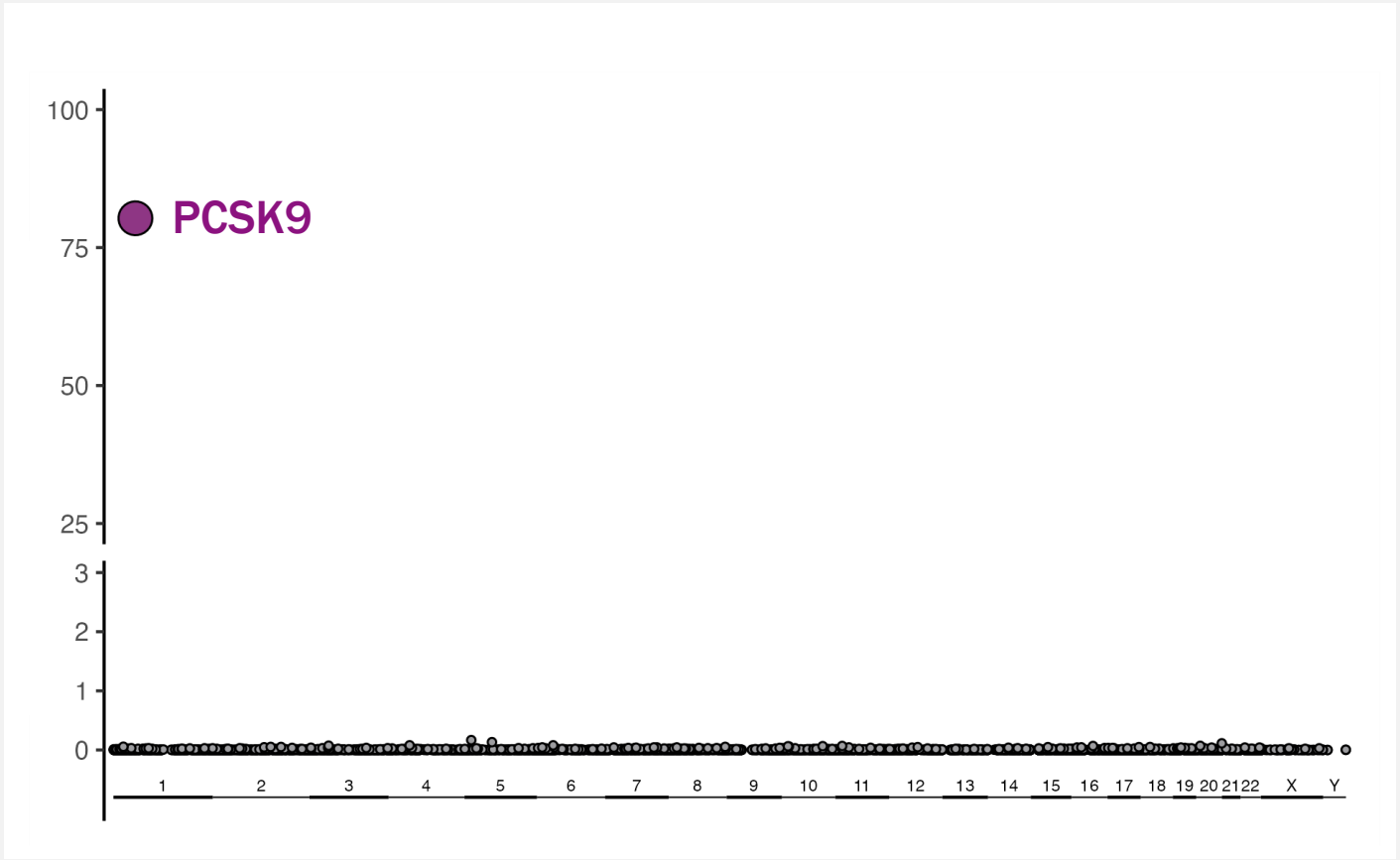


1. Data represents mean +/- SD for cohorts which included N=10 in control and N=22 in VERVE-101 at the earliest time points and N=7 and N=16, respectively, at the last time point

Liver-specific biodistribution in non-human primates treated with VERVE-101



In human liver cells treated with VERVE-101, no evidence for off-target editing

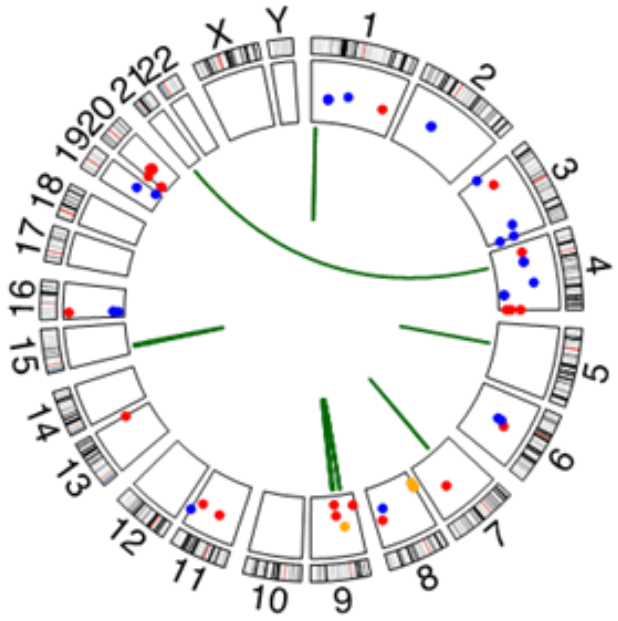


- Donor primary human hepatocytes treated with saturating dose of VERVE-101 LNPs
- ‘Manhattan-style’ plot of ~6000 candidate sites
- No candidate sites show statistically significant net editing

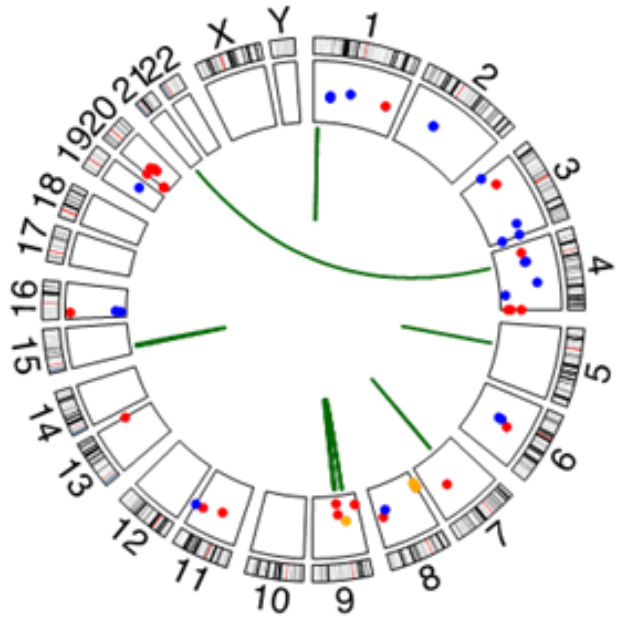
No chromosomal translocations or structural variants identified following treatment of primary human liver cells with VERVE-101

Primary liver cell
Lot 1

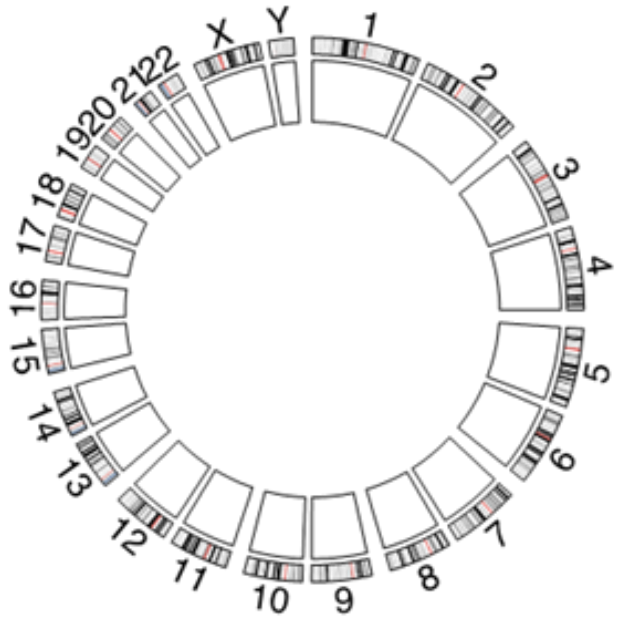
untreated



VERVE-101



VERVE-101 - untreated



● insertion ● duplication ● deletion ● inversion — translocation

Interim results from the heart-1 clinical trial of VERVE-101

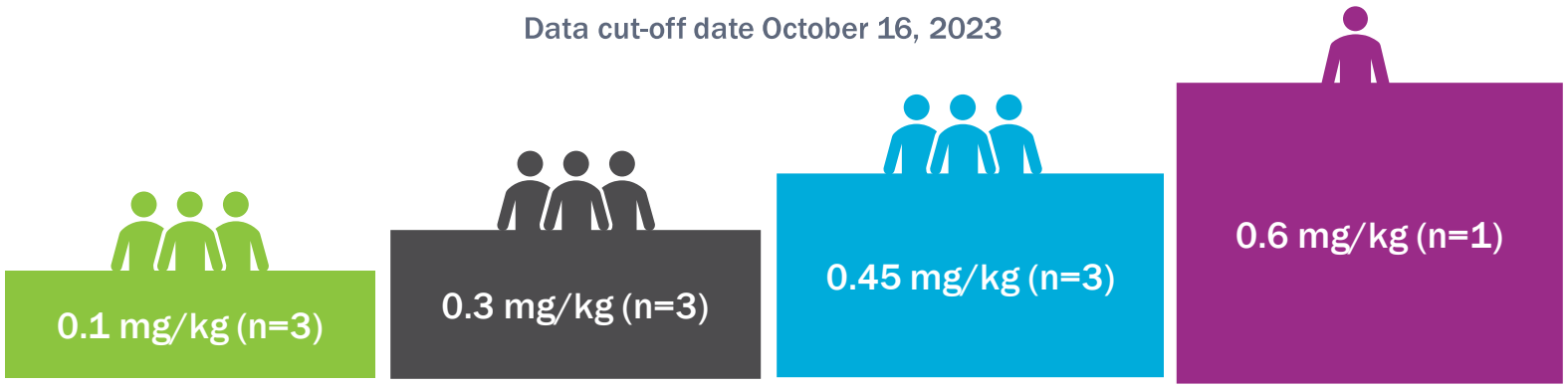
heart-1 is a first-in-human Phase 1b trial designed to evaluate the safety and tolerability of VERVE-101

heart-1

Open-label, single ascending dose design with flexible, adaptive dose levels and n=3 to 6 per cohort

Interim update:
10 participants treated across 4 dose cohorts[1]

Data cut-off date October 16, 2023



Clinical trial registration: NCT05398029; 1. 10 participants included in the safety analysis, but only 9 participants included in the pharmacodynamic analyses as the 10th participant had not reached the 28-day follow-up as of the data cut-off date. Single participant dosed at 0.6 mg/kg prior to initiation of 0.45 mg/kg cohort.

FDA draft guidance on human genome editing products: study population

Subjects with severe or advanced disease may be more willing to accept the risks of an investigational human GE product. However, these subjects may be predisposed to experiencing more AEs or be receiving concomitant treatments, which could make the safety or effectiveness data difficult to interpret. Therefore, in some instances, subjects with less advanced or more moderate disease may be appropriate for inclusion in first-in-human clinical studies.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/human-gene-therapy-products-incorporating-human-genome-editing

heart-1 is a first-in-human Phase 1b trial designed to evaluate the safety and tolerability of VERVE-101

heart-1

Open-label, single ascending dose design

n=3 to 6 per cohort

Interim update:
10 participants treated across 4 dose cohorts[1]

Data cut-off date October 16, 2023

STUDY POPULATION SUMMARY

- Males and females[2] (age 18 to 75)
- HeFH
- Established ASCVD
- Uncontrolled LDL-C[3]
- On maximally-tolerated oral lipid-lowering therapy[4]

DRUG ADMINISTRATION

- Pre-medication with dexamethasone and antihistamines
- VERVE-101 delivered as single infusion via a peripheral IV[5]

TRIAL ENDPOINTS

- Primary: Safety and tolerability
- Additional endpoints:
  - Pharmacokinetics of VERVE-101
  - Blood PCSK9 and LDL-C levels, quantified as percent change from baseline, time averaged from day 28 onward
- Study duration 1y and long-term follow-up required by FDA for another 14y

Clinical trial registration: NCT05398029

1. 10 participants included in the safety analysis, but only 9 participants included in the pharmacodynamic analyses as the 10th participant had not reached the 28-day follow-up as of the data cut-off date; 2. Women of childbearing potential are excluded from the study; 3. LDL-C threshold for inclusion value varies by country-specific protocol; 4. maximum tolerated statin and/or ezetimibe (statin intolerant allowed) 5. dosing based on weight for participants ≤ 100 kg; participants > 100 kg are dosed on an assumed 100 kg weight; single participant dosed at 0.6 mg/kg prior to initiation of 0.45 mg/kg cohort.

verve THERAPEUTICS

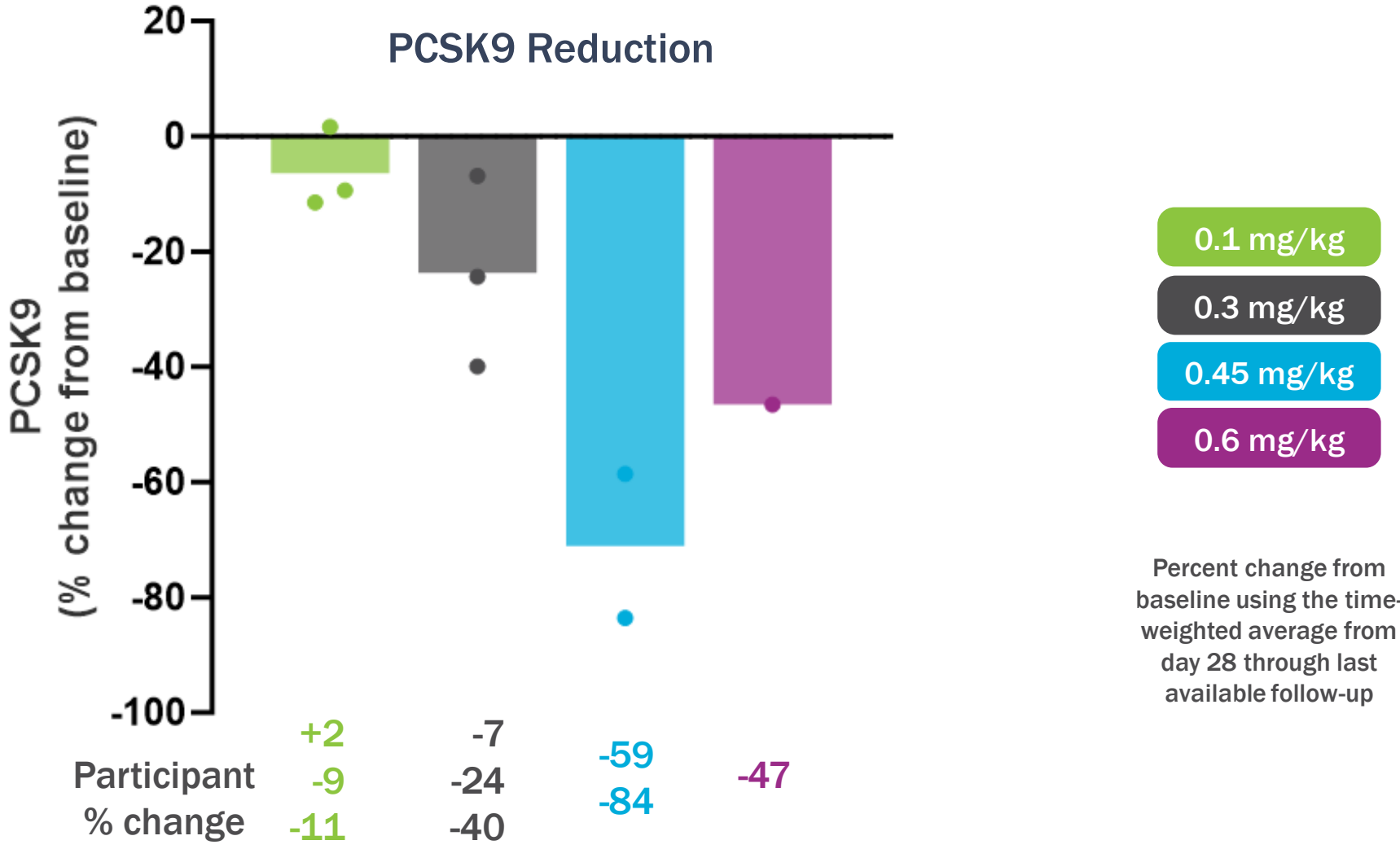
Participants enrolled to date have severe, advanced ASCVD and high risk for cardiovascular events (near-term and lifetime)

Characteristic	Total (n=10)
Mean age, years (min, max)	54 (29, 69)
Sex, male, n	8
Mean screening LDL-C, mg/dL (min, max)	193 (107, 373)
Mutation in *LDLR* detected, n[1]	9
Cardiovascular Risk Profile	
Prior coronary revascularization, n	9
Prior coronary artery bypass grafting, n	3
≥ 1 prior percutaneous coronary intervention, n	7
≥ 1 prior myocardial infarction, n	4
Prior cardiac arrest, n	1
Concomitant and Prior Lipid-Lowering Therapy	
On statin therapy, n	8
Prior use of PCSK9-targeted therapy, n	2

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned

1. One participant diagnosed based on clinical criteria

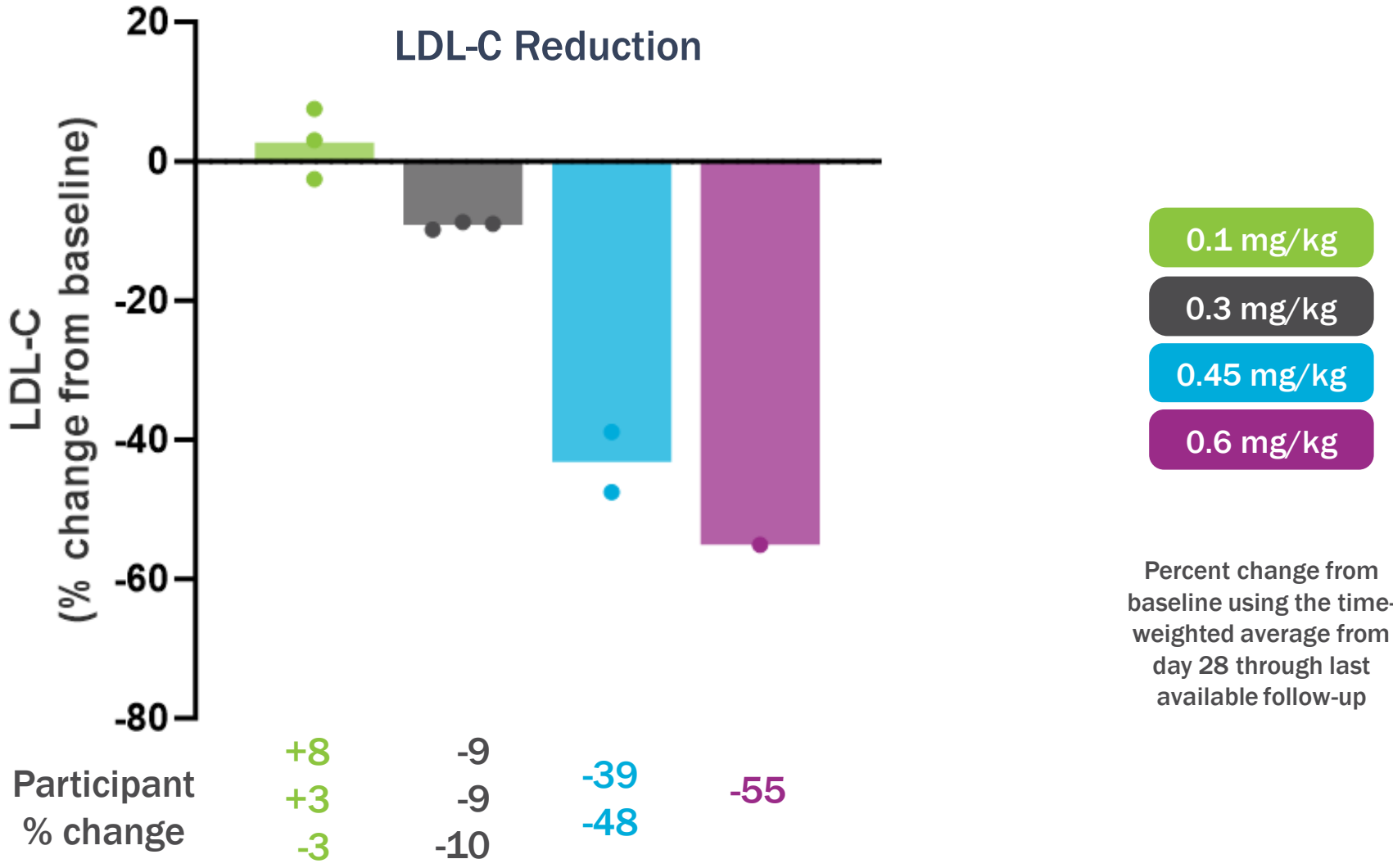
Reductions in blood PCSK9 protein level of 47%, 59% and 84% observed in the two higher dose cohorts following VERVE-101 administration



As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned

Day 28 value was used for time-weighted average in participants where day 28 was latest timepoint. One participant who has not reached day 28 excluded from analysis. Observations in 2 participants in 0.1 mg/kg cohort censored from analysis after changes in lipid lowering treatment (both >90 days after VERVE-101 infusion).

Reductions in blood LDL-C of 39%, 48% and 55% observed in the two higher dose cohorts following VERVE-101 administration



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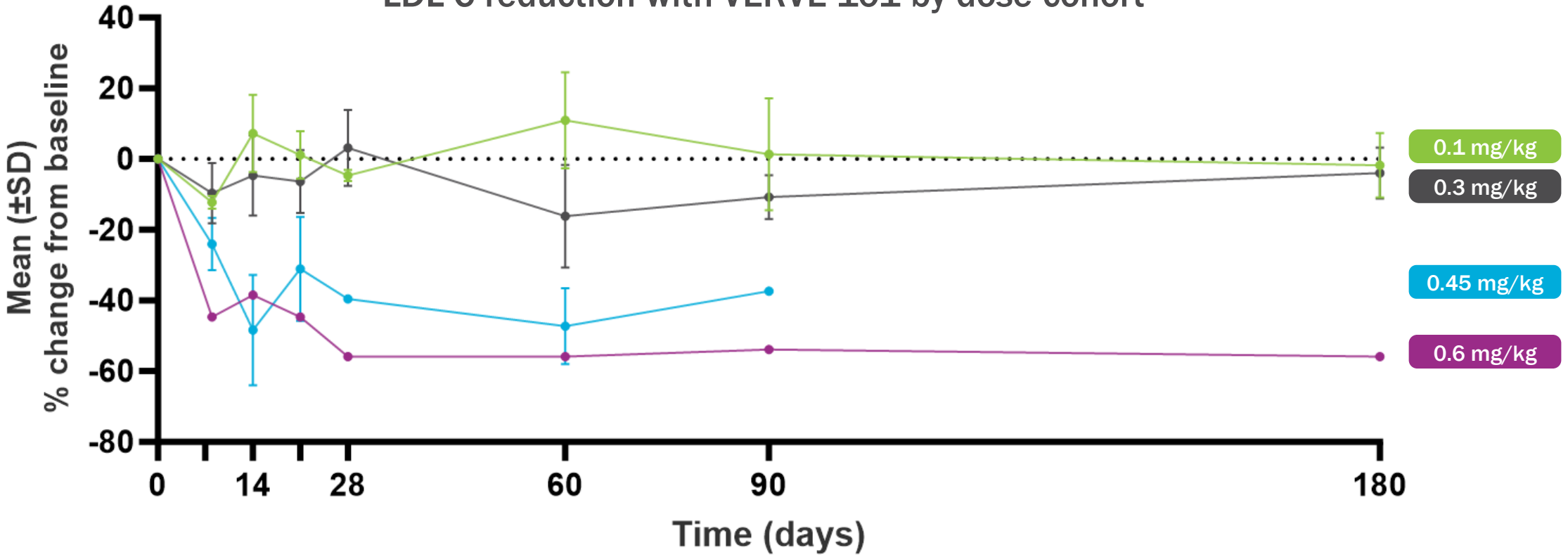
Day 28 value was used for time-weighted average in participants where day 28 was latest timepoint. One participant who has not reached day 28 excluded from analysis. Observations in 2 participants in 0.1 mg/kg cohort censored from analysis after changes in lipid lowering treatment (both >90 days after VERVE-101 infusion).

Durable 55% reduction in LDL-C extending up to 180 days in the single participant in the highest dose cohort

LDL-C reduction with VERVE-101 by dose cohort



Participants, n							
0.1 mg/kg	3	3	3	3	3	3	3
0.3 mg/kg	3	3	3	3	2	2	2
0.45 mg/kg	2	2	2	2	2	1	0
0.6 mg/kg	1	1	1	1	1	1	1

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned
SD, standard deviation

Interim safety summary: observed adverse events (AEs) consistent with a severe, advanced ASCVD patient population

Number of participants experiencing:	0.1 mg/kg (n=3)	0.3 mg/kg (n=3)	0.45 mg/kg (n=3)	0.6 mg/kg (n=1)	Total (n=10)
AE occurring in more than 1 participant	2	0	3	1	6
Infusion-related reaction, n	0	0	3	1	4
Upper respiratory infection and COVID-19, n	2	0	0	1	3
Any serious AE	0	1	1	0	2
Cardiovascular events, n	0	1	1	0	2
Non-cardiovascular events, n	0	0	0	0	0
Any treatment-related AE grade 3 or higher	0	0	1	1	2
Cardiovascular events, n	0	0	1[a]	0	1
Increased liver transaminases, n	0	0	0	1[b]	1

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned
a. Myocardial infarction assessed as potentially related to treatment; b. transient, asymptomatic increase in liver transaminases with bilirubin levels below the upper limit of normal

Adverse events occurring in more than 1 participant

Number of participants experiencing:	0.1 mg/kg (n=3)	0.3 mg/kg (n=3)	0.45 mg/kg (n=3)	0.6 mg/kg (n=1)	Total (n=10)
AE occurring in more than 1 participant	2	0	3	1	6
Infusion-related reaction, n	0	0	3	1	4
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Any serious AE	0	1	1	0	2
Cardiovascular events, n	0	1	1	0	2
Non-cardiovascular events, n	0	0	0	0	0
Any treatment-related AE grade 3 or higher	0	0	1	1	2
Cardiovascular events, n	0	0	1[a]	0	1
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As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned

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Any serious adverse event

Number of participants experiencing:	0.1 mg/kg (n=3)	0.3 mg/kg (n=3)	0.45 mg/kg (n=3)	0.6 mg/kg (n=1)	Total (n=10)
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As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned

a. Myocardial infarction assessed as potentially related to treatment; b. transient, asymptomatic increase in liver transaminases with bilirubin levels below the upper limit of normal

Any treatment-related adverse event, grade 3 or higher

Number of participants experiencing:	0.1 mg/kg (n=3)	0.3 mg/kg (n=3)	0.45 mg/kg (n=3)	0.6 mg/kg (n=1)	Total (n=10)
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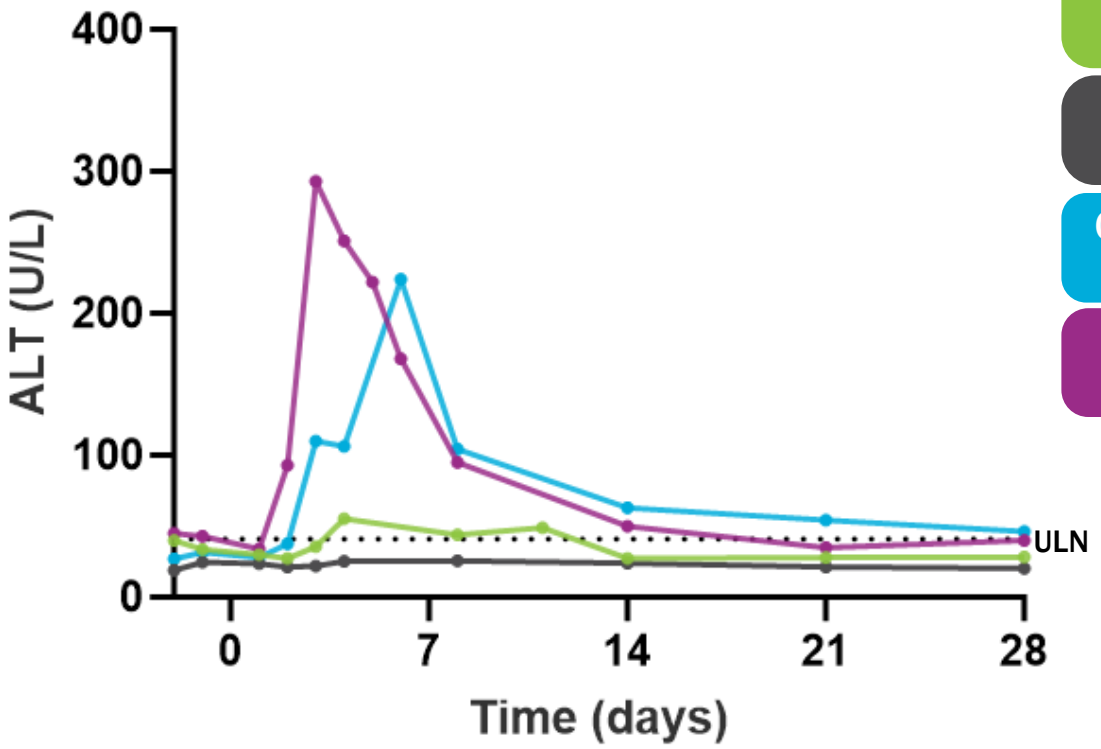
As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned

a. Myocardial infarction assessed as potentially related to treatment; b. transient, asymptomatic increase in liver transaminases with bilirubin levels below the upper limit of normal

Transient, reversible increases in ALT observed at higher doses with mean bilirubin levels below the upper limit of normal

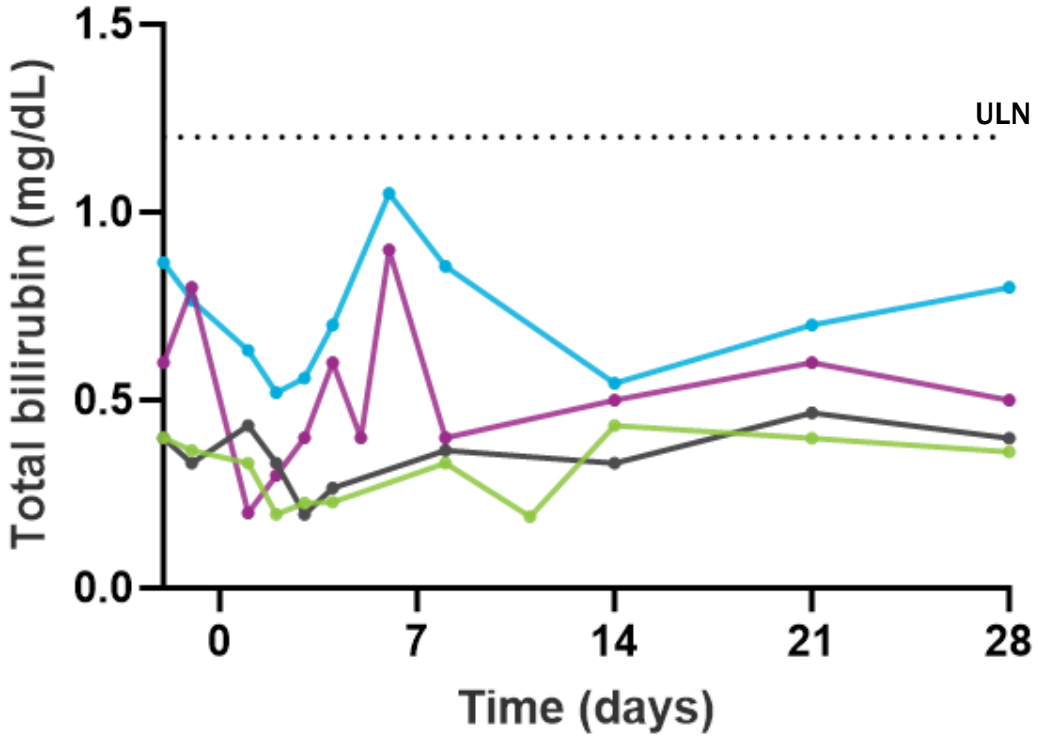


0.1 mg/kg (n=3)

0.3 mg/kg (n=3)

0.45 mg/kg (n=3)

0.6 mg/kg (n=1)



Lines indicate cohort mean values

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned; values for one patient in 0.45 mg/kg cohort are a mix of central and local laboratory values due to a period of hospitalization; ULNs are from central laboratory; ULN on ALT graph is value for males of 41 U/L, female ULN is 33 U/L
ALT, alanine aminotransferase; U, units; ULN, upper limit of normal

Observed serious adverse events consistent with a severe, advanced ASCVD patient population

Cardiovascular SAEs occurred in 2 participants

(3 events in total, of which 2 were determined to be unrelated)

- Fatal cardiac arrest about 5 weeks after infusion (DOSE 0.3 MG/KG)
  - Ischemic cardiomyopathy at baseline & prior cardiac arrest
  - On autopsy, severe underlying CAD; no evidence of pulmonary embolism, myocardial inflammation, or coronary thrombus
  - Investigators & DSMB determined as unrelated to study treatment
- MI and non-sustained ventricular tachycardia (NSVT) (DOSE 0.45 MG/KG)
  - Unstable chest pain symptoms (unreported to investigators) prior to treatment with VERVE-101
  - MI occurred day after infusion
  - On coronary angiography, critical left-main equivalent CAD (in-stent restenosis lesions involving both LAD and LCx arteries)
  - NSVT occurred >4 weeks after infusion
  - Investigators & DSMB determined MI as potentially related to treatment due to proximity to dosing; NSVT determined to be unrelated

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned
SAE, serious adverse event,; CAD, coronary artery disease; MI, myocardial infarction

Observed serious adverse events consistent with a severe, advanced ASCVD patient population

Cardiovascular SAEs occurred in 2 participants

(3 events in total, of which 2 were determined to be unrelated)

- Fatal cardiac arrest about 5 weeks after infusion (DOSE 0.3 MG/KG)
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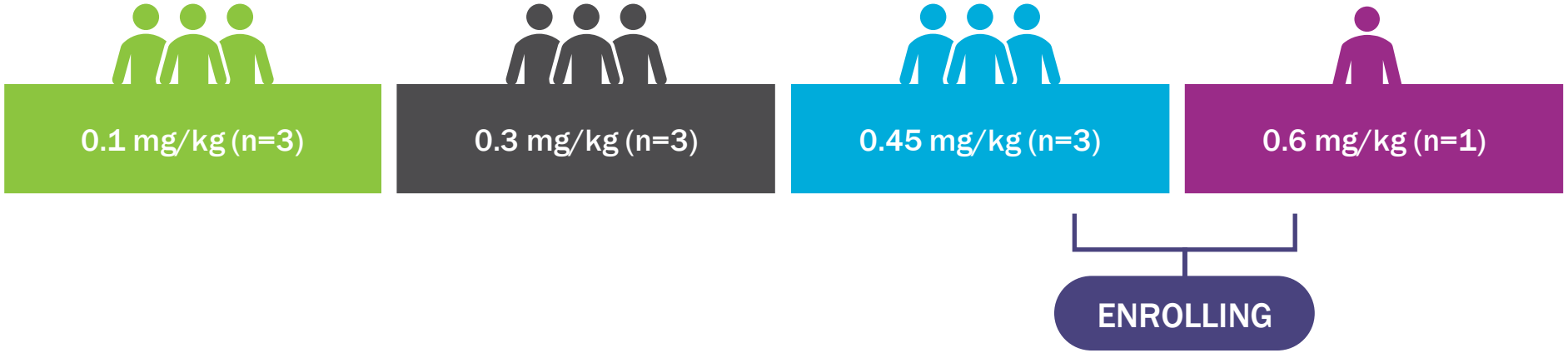
  - NSVT occurred >4 weeks after infusion
  - Investigators & DSMB determined MI as potentially related to treatment due to proximity to dosing; NSVT determined to be unrelated

Independent data and safety monitoring board (DSMB) agreed that SAEs were consistent with a severe, advanced ASCVD patient population and recommended continuing dosing

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned
SAE, serious adverse event,; CAD, coronary artery disease; MI, myocardial infarction

Next steps in the heart-1 trial of VERVE-101



- Enrolling in 0.45 & 0.6 mg/kg cohorts to complete dose escalation phase
- Plan to enroll an expansion cohort in 2024
- For PCSK9 program, plan to initiate a randomized and placebo-controlled phase 2 trial in 2025

Conclusions: initial results of heart-1 trial demonstrated first proof-of-concept for *in vivo* DNA base editing in humans

1. Dose-dependent reductions in blood PCSK9 protein & LDL-C levels following VERVE-101 infusion
2. LDL-C reductions of 39%, 48%, & 55% among participants in the two highest dose cohorts
3. Durability extending to 6 months in the single participant in the highest dose cohort
4. Safety profile supports continued development of VERVE-101

As of October 16, 2023. Data are from an ongoing study with an open database and have not been fully cleaned

heart-1

Thank you to the patients and families, investigators and study staff, our partners, and the independent DSMB for their participation in the heart-1 trial.

Dr. Patrick Gladding
NZCR
Auckland NZ

Dr. Rohit Katial
NZCR
Auckland NZ

Dr. Jorg Taubel
Richmond Pharmacology
London UK

Dr. Tom Ashdown
Richmond Pharmacology
London UK

Dr. Russell Scott
NZCR
Christchurch NZ

Dr. Jane Kerr
NZCR
Christchurch NZ

Dr. Jai Cegla
Imperial College NHS

Dr. Steve Humphries
UCL, UK

Dr. Mahmoud Barbir
Royal Brompton and Harefield

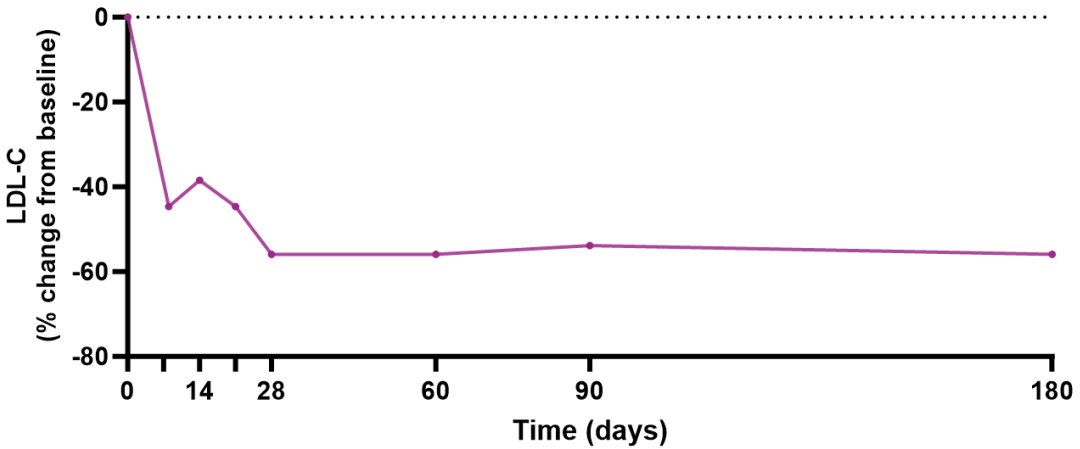
Emma Neves
Royal Brompton and Harefield

Dr. Riyaz Patel
UCL & Barts Health NHS Trust

verve THERAPEUTICS

Where could VERVE-101 fit into the LDL-C treatment landscape?

In patients who require deep LDL-C lowering over decades, single-course gene editing medicines may emerge as an option to overcome limitations of the chronic care model



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ASCVD, atherosclerotic cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; kg, kilogram; LDL-C, low-density lipoprotein cholesterol; mg, milligram

Recent updates

U.S. FDA cleared investigational new drug application (IND) for VERVE-101 in patients with HeFH

Received FDA clearance to initiate heart-1 trial in U.S.

Plan to activate U.S. sites for VERVE-101 development

Plan to incorporate learnings from FDA interaction to impact future pipeline (VERVE-102, VERVE-201)

FDA reviewed our complete response which included:

- Comprehensive experiments to address preclinical requests
- heart-1 clinical trial dataset

First IND for *in vivo* base editing

Verve gains Eli Lilly as collaborator for *PCSK9* and *ANGPTL3* programs, replacing Beam

Lilly has purchased rights to opt-in for PCSK9 and ANGPTL3 programs from Beam in a transaction with total potential deal value of $600M

Lilly's opt-in rights: 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; ex-U.S. is retained by Verve; Verve retains control of development; Verve books revenues

Lilly brings know-how in cardiometabolic space, considerable resources, expertise in late-stage drug development and commercialization for CV indications

Shared vision around application of gene editing to treat HeFH & ASCVD

As part of diligence, Verve provided to Lilly heart-1 clinical trial data as well as preclinical data for its related CV programs

Advancing a pipeline of single-course *in vivo* gene editing programs

TARGET	INDICATION	TECHNOLOGY	DEVELOPMENT STATUS			RIGHTS
			Research	IND-enabling	Clinical	
PCSK9 (VERVE-101)	Heterozygous familial hypercholesterolemia / ASCVD	Base Editor				verve, Lilly
PCSK9 (VERVE-102)	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

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

+

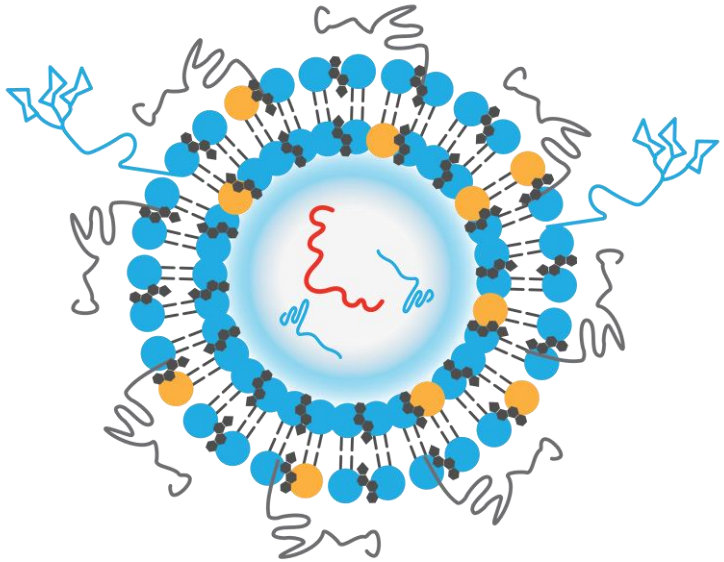
DELIVERY VEHICLE

LNP for delivery to liver cell includes 5 components

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

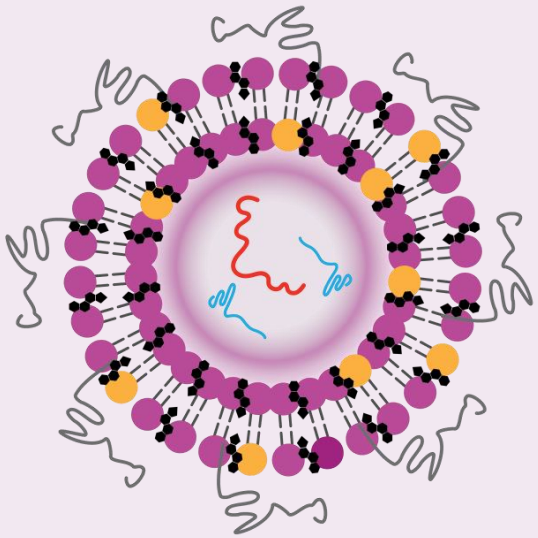
=

VERVE-102



VERVE-102 is differentiated from VERVE-101

VERVE-101

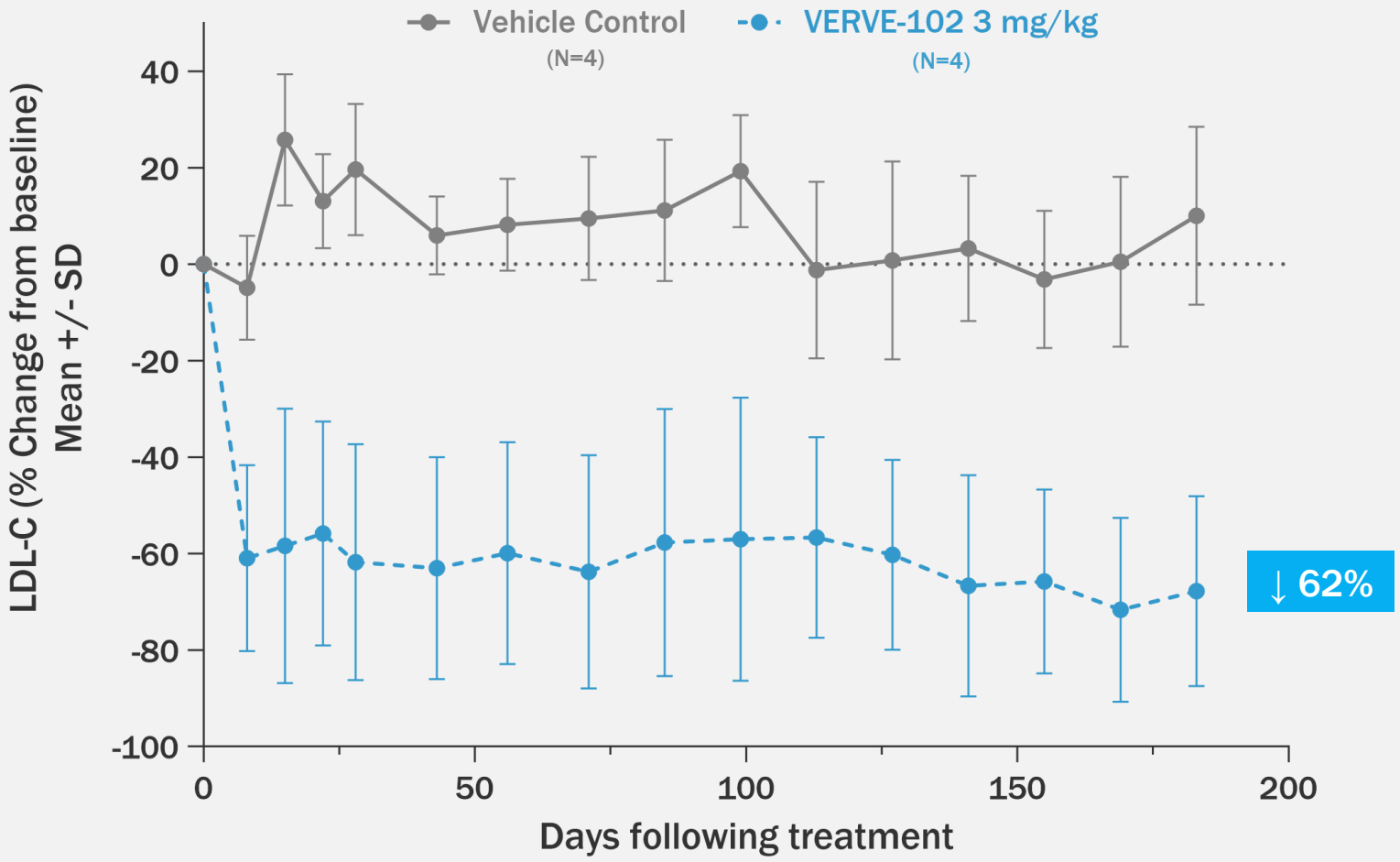


VERVE-102

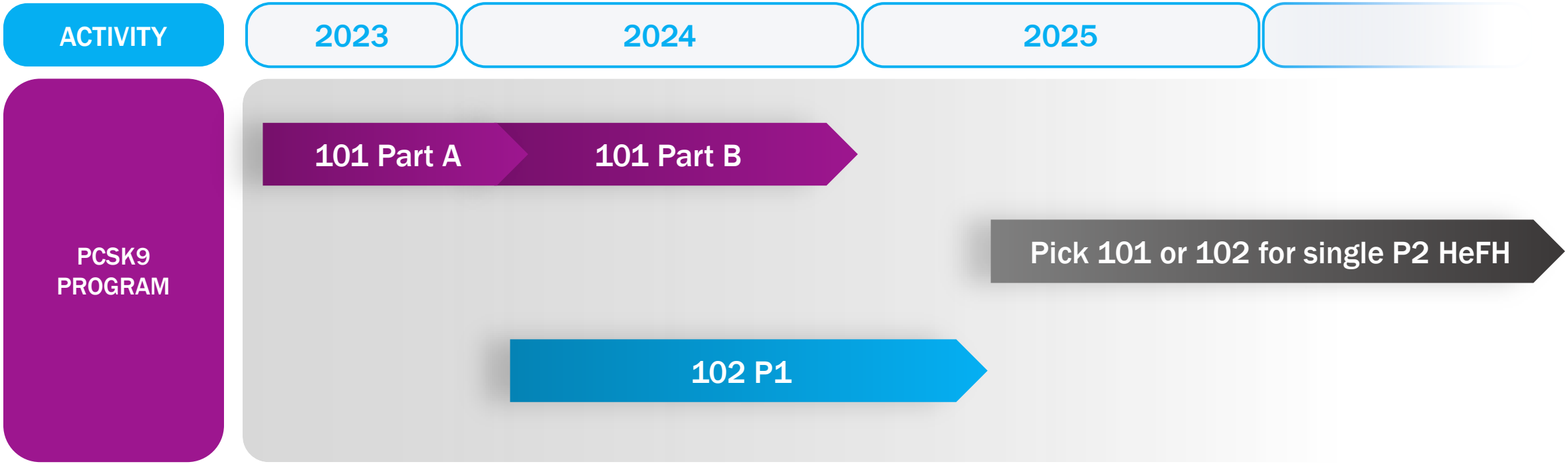
- Different ionizable lipid, licensed from Novartis
- Addition of GalNAc targeting ligand - allowing for entry into hepatocytes by any of two receptors (LDLR or ASGPR)
- These differences may lead to improvements in potency and/or tissue specificity

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

Durable LDL-C reduction to 6 months in non-human primates

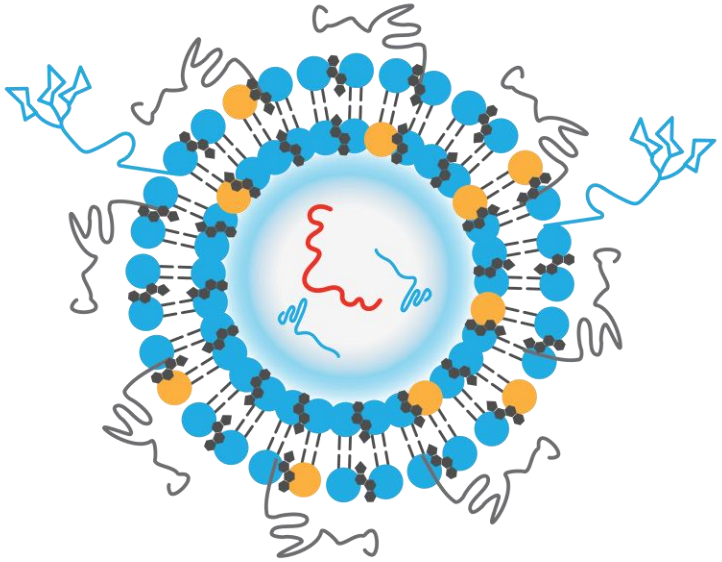


Simultaneous development of VERVE-101 and VERVE-102, followed by selection of one product candidate to take to Phase 2



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

VERVE-201

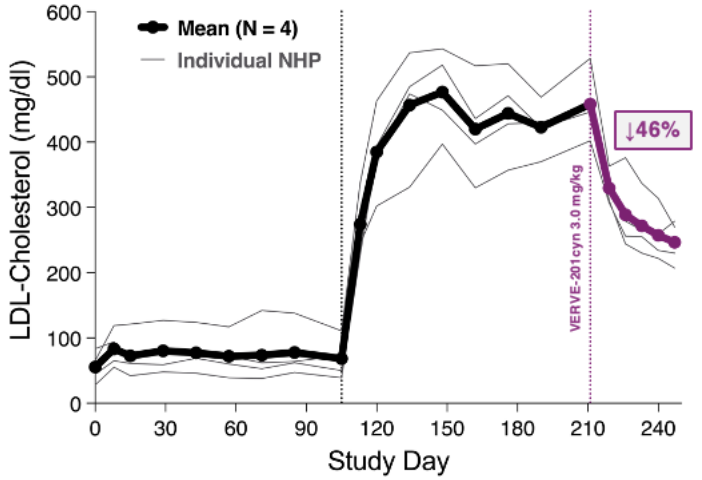


mRNA for adenine base editor

gRNA localizes editor to *ANGPTL3* gene

GalNAc-LNP

PRE-CLINICAL DATA



LDL-C lowering in NHP model of homozygous familial hypercholesterolemia (HoFH)

Clinical Trial Initiation in 2H 2024

What does 2024 and 2025 hold for Verve?

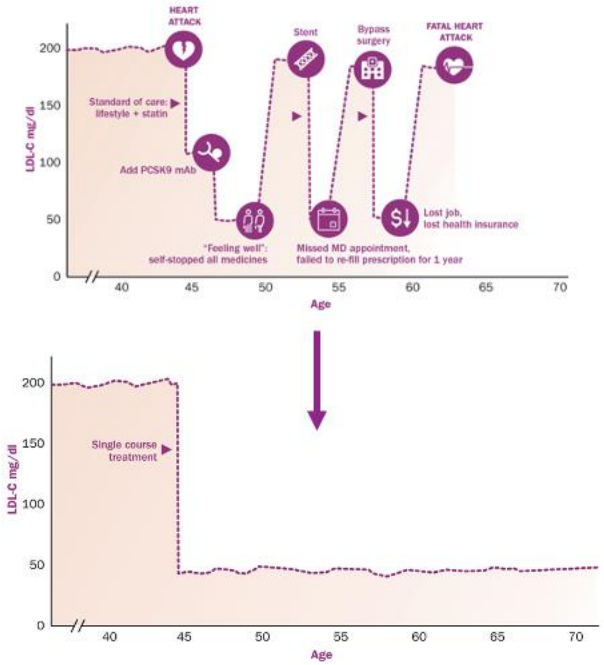
	Anticipated milestones 2024	Anticipated milestones 2025
PCSK9 PROGRAM	**VERVE 101** Complete enrollment in two high dose cohorts (Part A) Enroll in expansion cohort (Part B) Identify doses for potential Phase 2 **VERVE 102[1]** Initiate Phase 1 1H 2024, enroll dose escalation phase	**VERVE 101** **VERVE 102** Clinical data for VERVE-102 Select VERVE-101 or -102 and initiate a randomized, controlled Phase 2 for PCSK9 program
ANGPTL3 PROGRAM	**VERVE 201[1]** Initiate clinical trial in 2H 2024	

Rest of pipeline: Progress pre-clinical collaboration programs with Lilly (*LPA*) and Vertex (undisclosed liver-disease target)

1. Subject to regulatory clearance

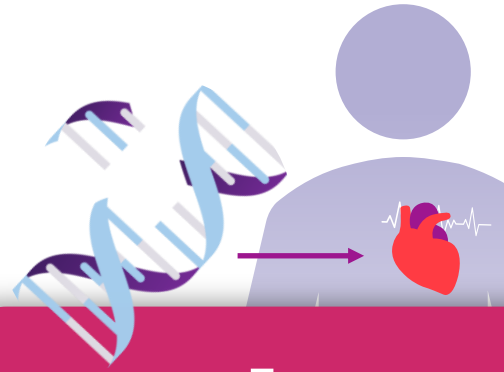
Verve is focused and well-positioned to realize its vision of developing single-course gene editing medicines to treat ASCVD

- Human proof of concept for *in vivo* base editing technology
- Three product candidates against highly validated ASCVD targets
- Emerging regulatory path in U.S. with FDA IND clearance for VERVE-101
- New partner in Eli Lilly with shared vision, CV development expertise, and commercialization strength
- Well-capitalized with $485M in cash and runway into 2026[1]

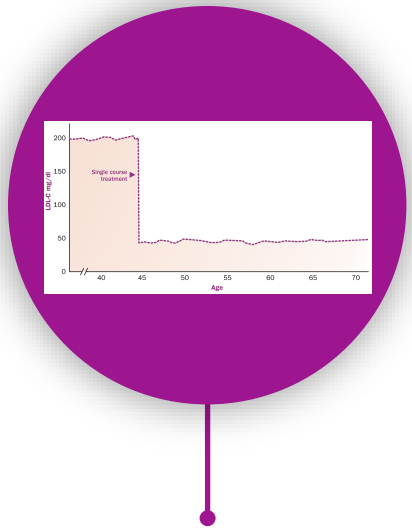


1. As of September 30, 2023

Next 5 years: executing on our vision



From concept
to proof-of-concept in humans
for a first-in-class
base editing treatment



2018 The First 5 Years **2023** The Next 5 Years **2028**

Q&A