Verve Therapeutics

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

August 2023

Forward looking statements

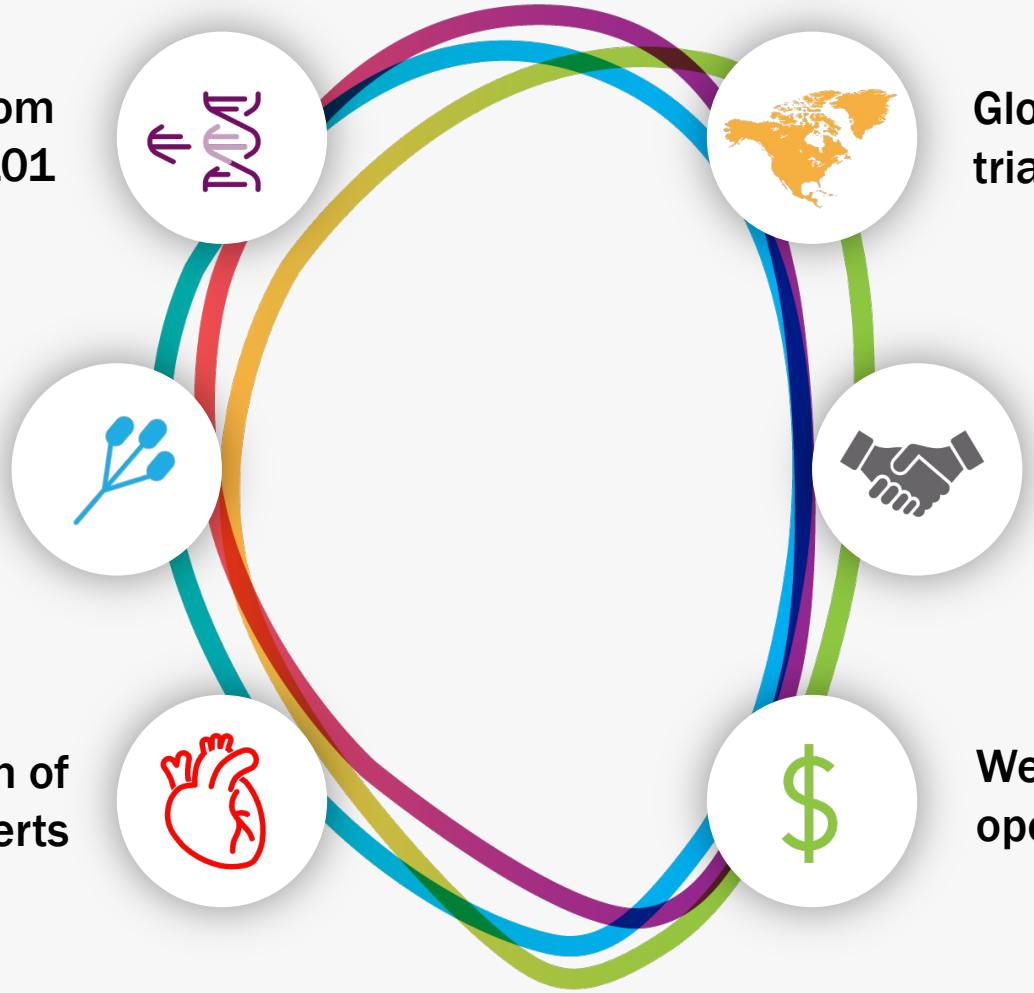
This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the timing and availability of clinical data from the Company's heart-1 clinical trial, the timing of initiation of clinical trials of VERVE-102 and VERVE-201, the Company's research and development plans, the potential advantages and therapeutic potential of the Company’s programs, including VERVE-101, VERVE-102 and VERVE-201, 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.

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

Advanced first CVD base editor from concept to clinic: VERVE-101

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

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



Global Phase 1b heart-1 clinical trial underway in multiple countries

Expanded portfolio through strategic relationships

Well-capitalized with runway to fuel operations into 2026[1]

1. Inclusive of the $60 million in capital received in August 2023 from the collaboration agreement with Eli Lilly and Company.

Atherosclerotic cardiovascular disease (ASCVD): #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

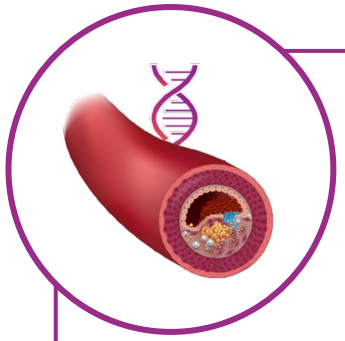
of patients worldwide

~800K heart attacks

per year in the U.S.[2]

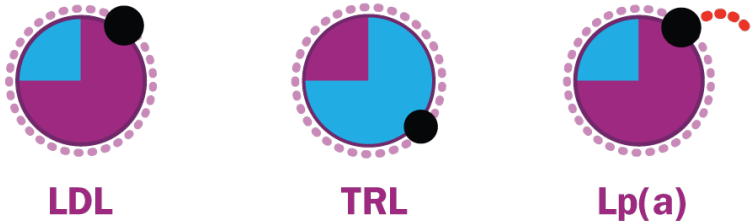
1. Centers for Disease Control and Prevention, National Center for Health Statistics. About Multiple Cause of Death, 1999-2020. CDC WONDER Online Database website. Atlanta, GA: Centers for Disease Control and Prevention; 2022. Accessed February 21, 2022.
2. Tsao CW et al. *Circulation.* 2022;145(8):e153–e639.

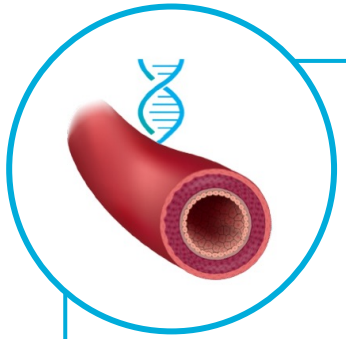
What causes ASCVD and what's a solution?



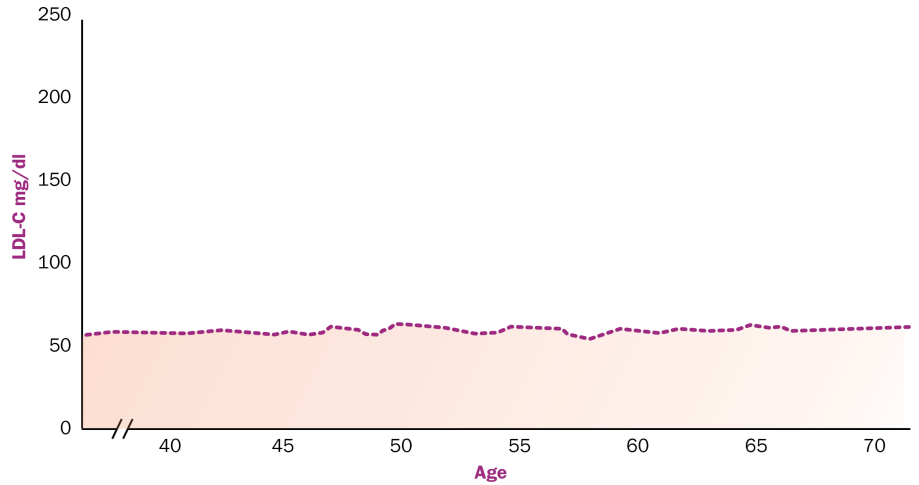
High cumulative life-long exposure to blood cholesterol clogs heart arteries

Cholesterol carried in 3 lipoproteins:





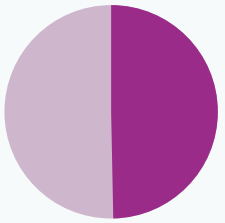
Solution: keep blood cholesterol as low as possible for as long as possible



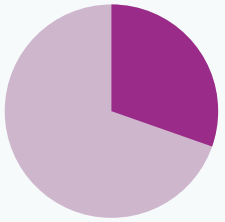
There are 3 pills & 3 injections available now to lower cholesterol. What's the unmet need?

ASCVD

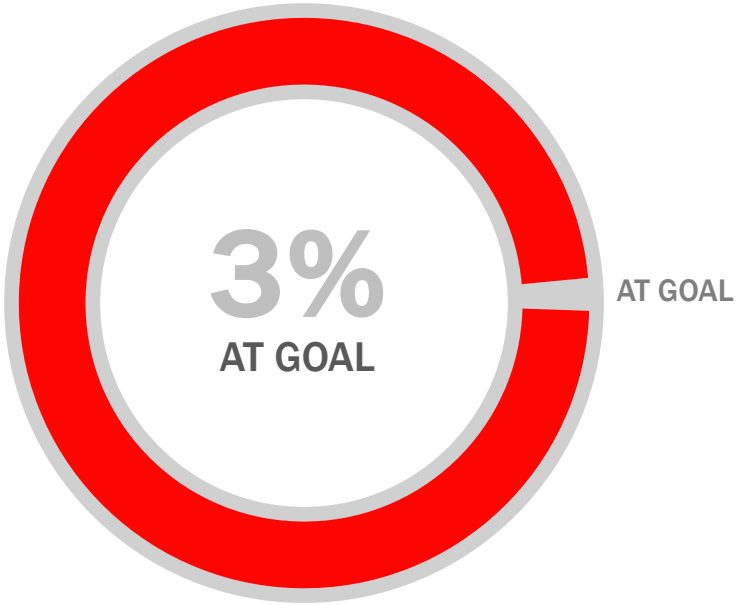
Only 50% ASCVD patients in U.S. on statin[1]



Only 27% ASCVD patients in U.S. at LDL-C goal[2]



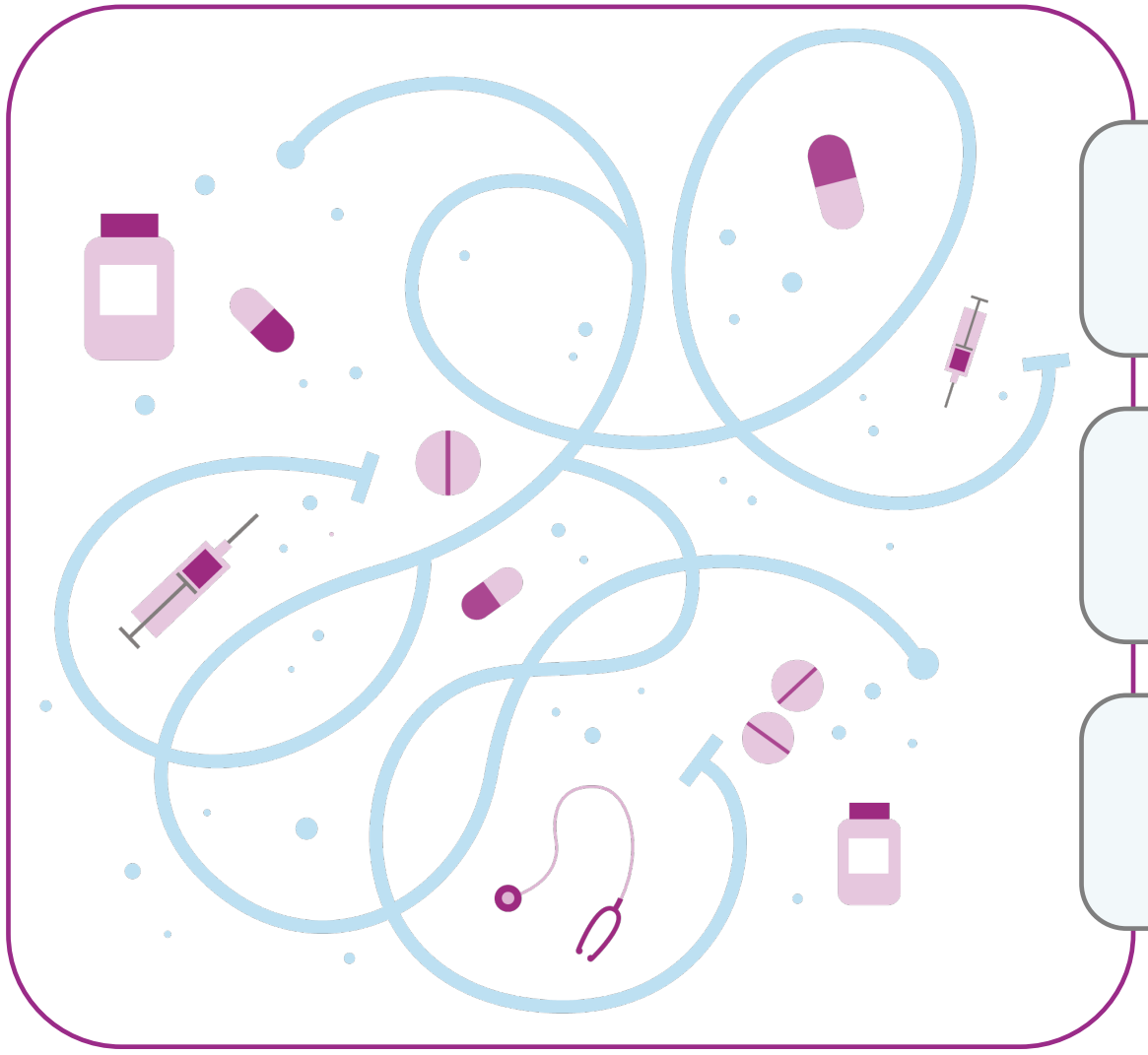
HeFH



In a global registry of Heterozygous Familial Hypercholesterolemia (HeFH) patients, 3% attain LDL-C < 1.8 mmol/L[3]

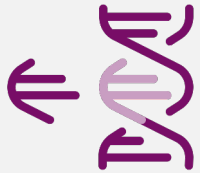
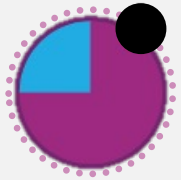
1. Nelson AJ et al., *J Am Coll Card.* 2022;79(18):1802–13.
2. Gu J et al., *Am J Prev Cardiol.* 2022;10:100336.
3. EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). *Lancet.* 2021;398(10312):1713-1725.

Chronic care model to treat chronic disease is broken



- Daily pills or intermittent injections
- Administered often over decades
- Heavy treatment burden on patients, providers, and healthcare system

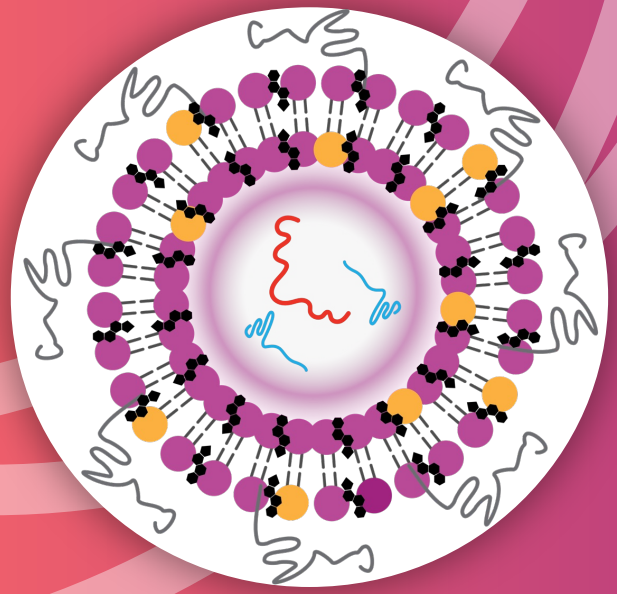
Familial hypercholesterolemia (FH): a genetic subtype of ASCVD, sky-high LDL cholesterol from birth leading to ASCVD at young ages

					
Heterozygous FH (HeFH)	***LDLR*** **mutation in single copy**	**>190 mg/dl**	**30-60 years**	**>95% patients worldwide not at LDL-C goal**	**~3M patients in US/Europe**
Homozygous FH (HoFH)	***LDLR*** **mutation in both gene copies**	**>400 mg/dl**	**Childhood**	**Despite 4 or 5 meds, almost all not at LDL-C goal**	**~3,000 patients in US/Europe**

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

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, Beam
PCSK9 (VERVE-102)	Heterozygous familial hypercholesterolemia / ASCVD	Base Editor				verve, Beam
ANGPTL3 (VERVE-201)	Homozygous familial hypercholesterolemia / Refractory Hypercholesterolemia	Base Editor				verve, Beam
LPA	ASCVD patients with high blood Lp(a)	Novel Editor				verve, Lilly
Undisclosed	Undisclosed ASCVD	Base Editor				verve, Beam
Undisclosed	Undisclosed liver disease	Novel Editor				verve, VERTEX



VERVE-101 targeting PCSK9:

Initial Phase 1b clinical trial results expected in 4Q23

VERVE-101: adenine base editor mRNA + gRNA packaged in an LNP; edit designed to turn off *PCSK9*

DRUG SUBSTANCES

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

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

+

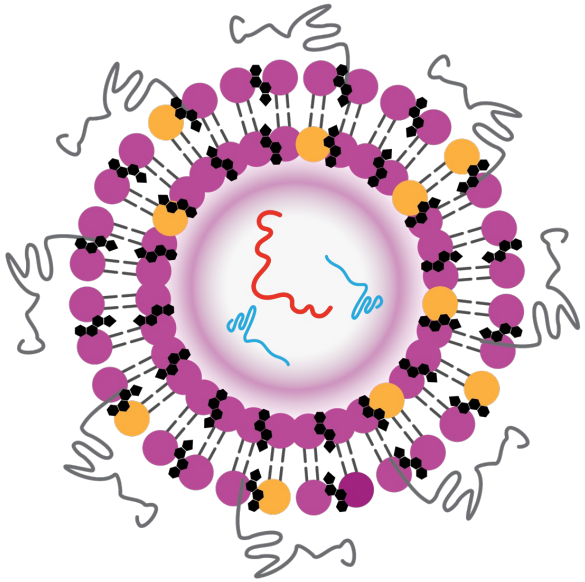
DELIVERY VEHICLE

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

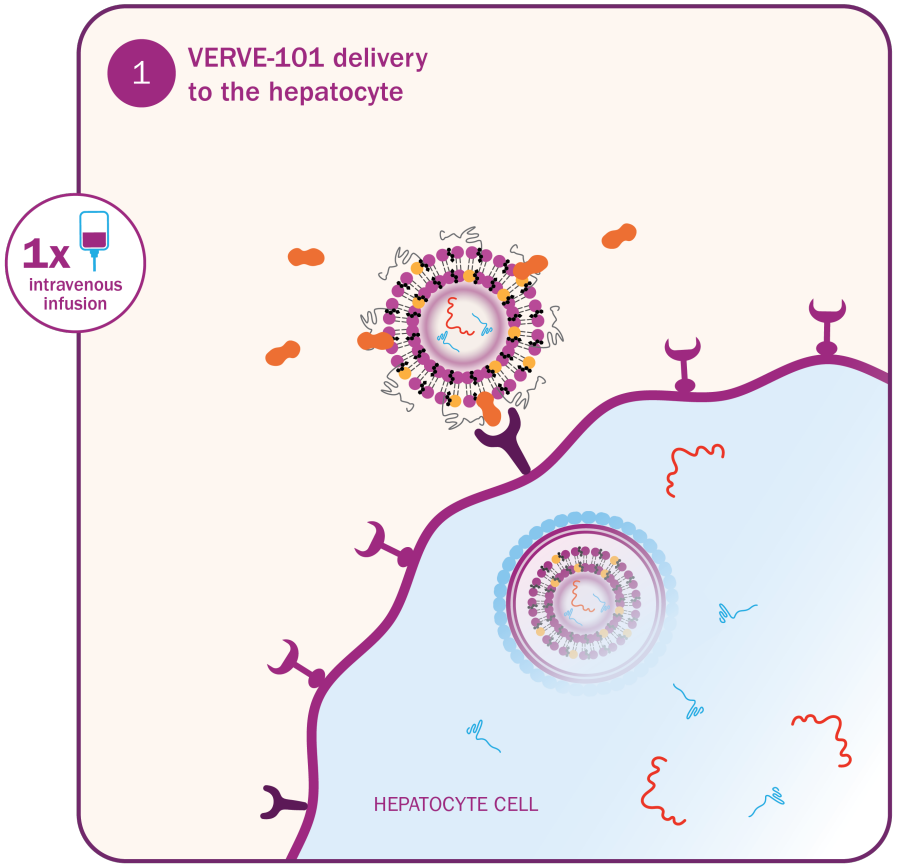
- Ionizable amino lipid (Acuitas)
- DSPC
- Cholesterol
- PEG

=

VERVE-101

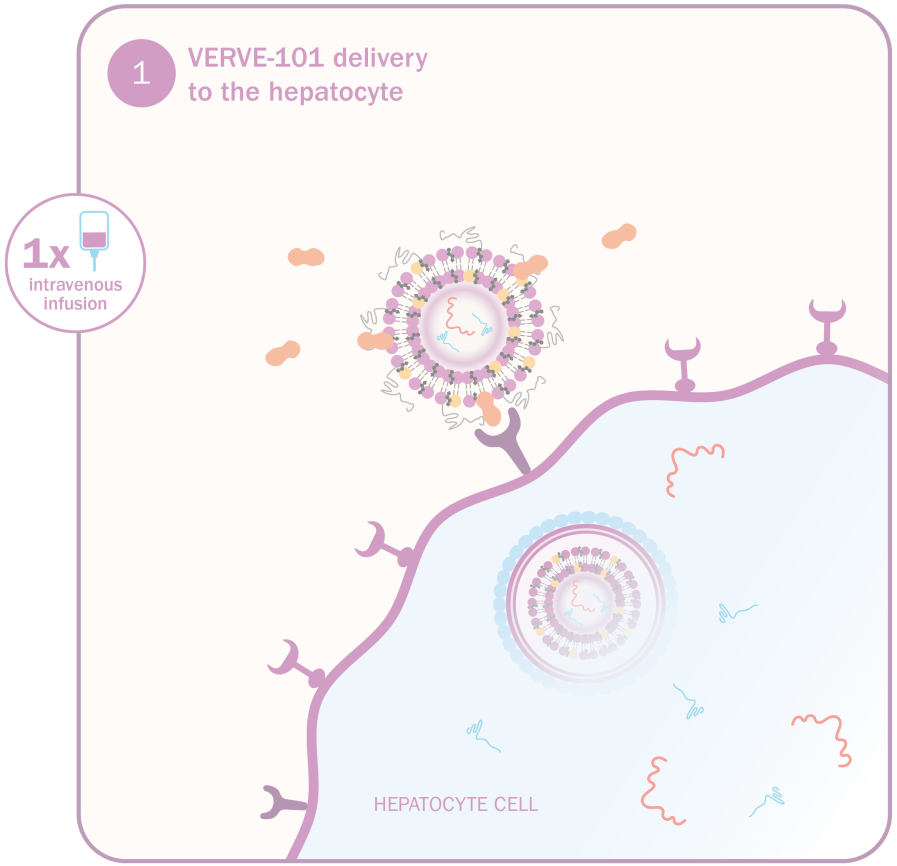


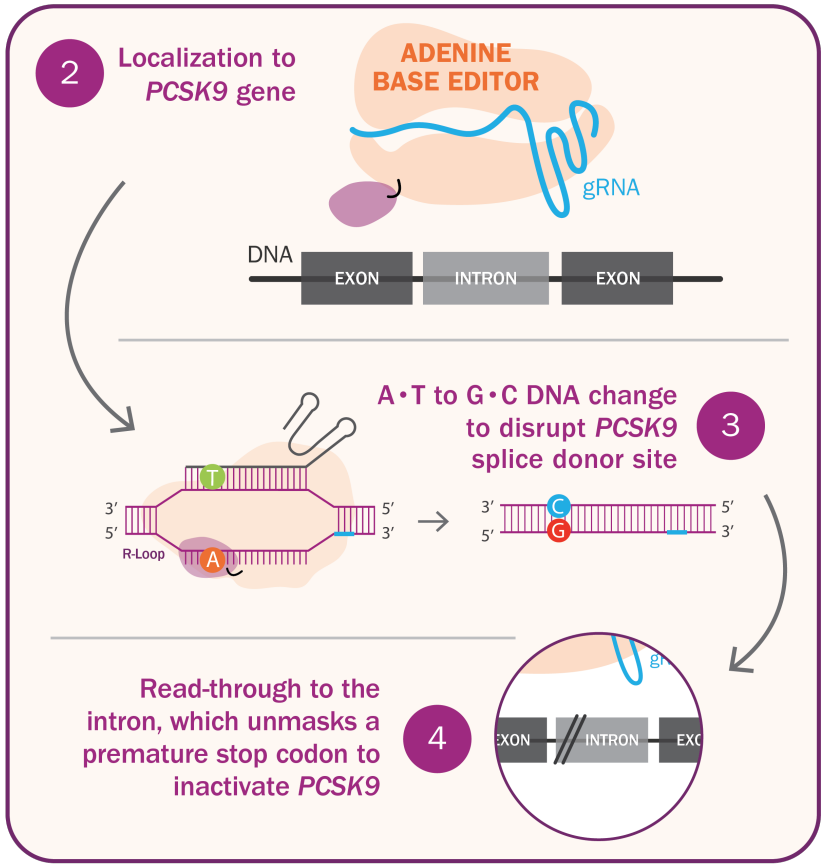
VERVE-101: base editing medicine designed to inactivate hepatic *PCSK9* and lower LDL-C



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

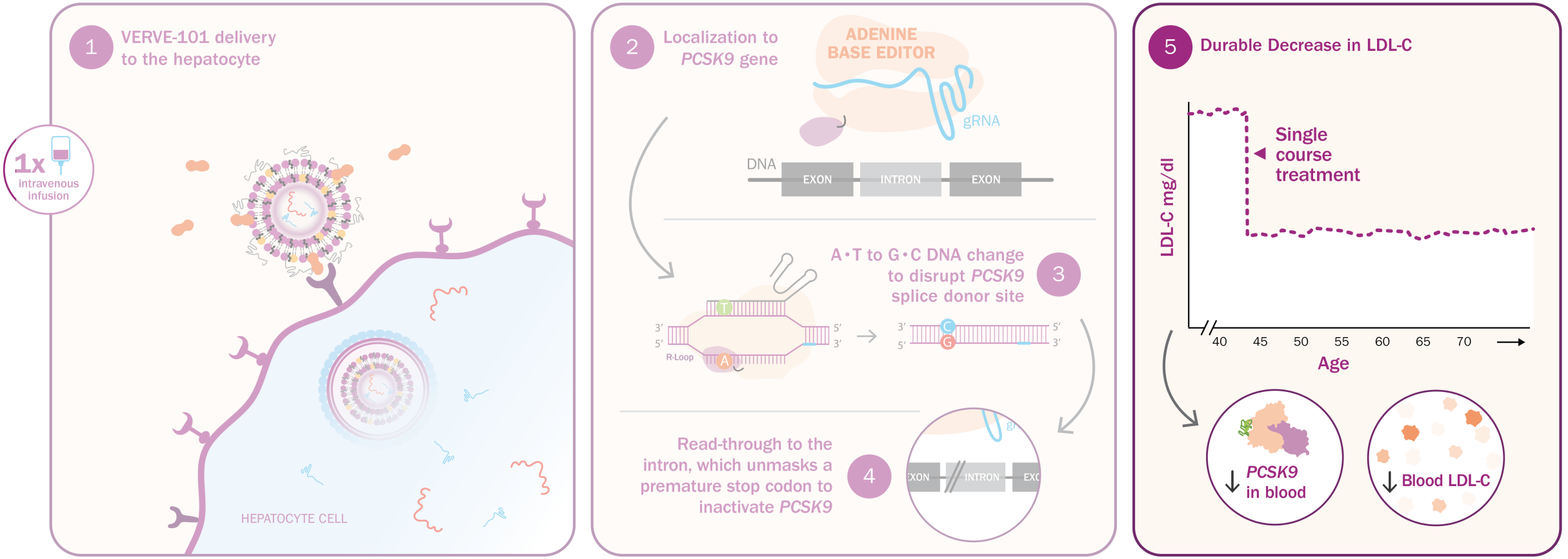
VERVE-101: base editing medicine designed to inactivate hepatic *PCSK9* and lower LDL-C





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

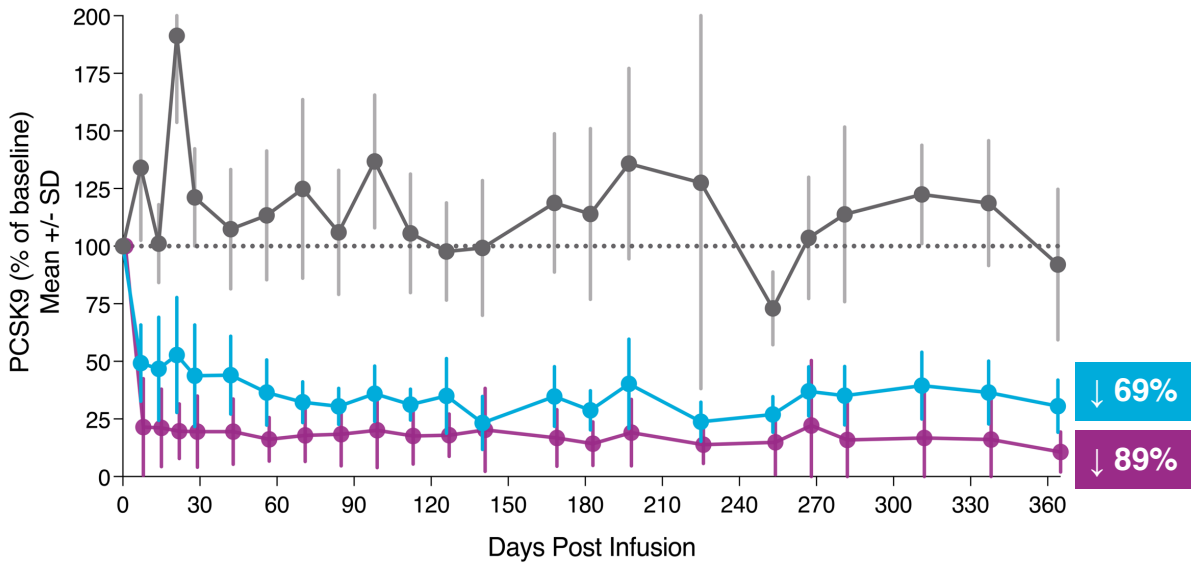
VERVE-101: base editing medicine designed to inactivate hepatic *PCSK9* and lower LDL-C



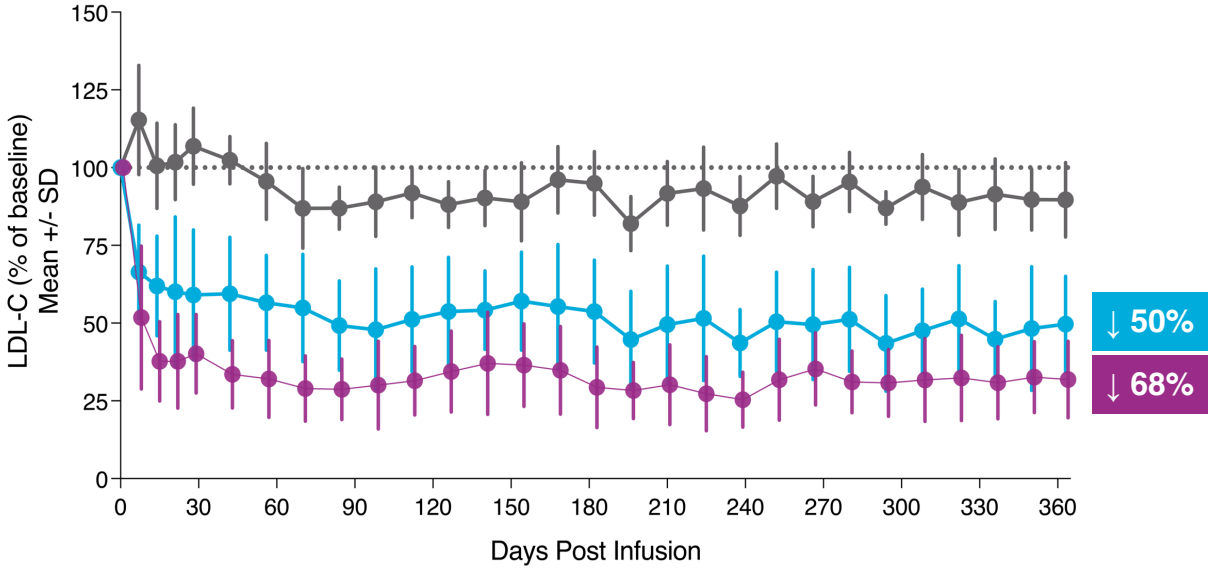
Lipid nanoparticle · Ionizable amino lipid · DSPC · LDL receptor (LDLR) · apoE · mRNA · gRNA · PEG Lipid · Cholesterol

In non-human primates (NHPs), single infusion of VERVE-101 durably lowers blood PCSK9 and LDL-C

Reductions in blood PCSK9 level



Reductions in blood LDL-C level



Vehicle control (N = 10) VERVE-101 0.75 mg/kg (N = 4) VERVE-101 1.5 mg/kg (N = 22)

Initial safety and efficacy data from single ascending dose portion of Phase 1b heart-1 clinical trial expected in 4Q23

heart-1

SINGLE ASCENDING DOSE

Starting dose ····· Low dose ····· Intermediate dose ····· High dose

3-6 participants per group with staggering and sentinel dosing

GLOBAL REGULATORY STRATEGY

- Regulatory clearances in New Zealand and the U.K.

Working to resolve Investigational New Drug (IND) application hold in the U.S.

STUDY ENROLLMENT

- Recruitment ongoing in New Zealand and the U.K.

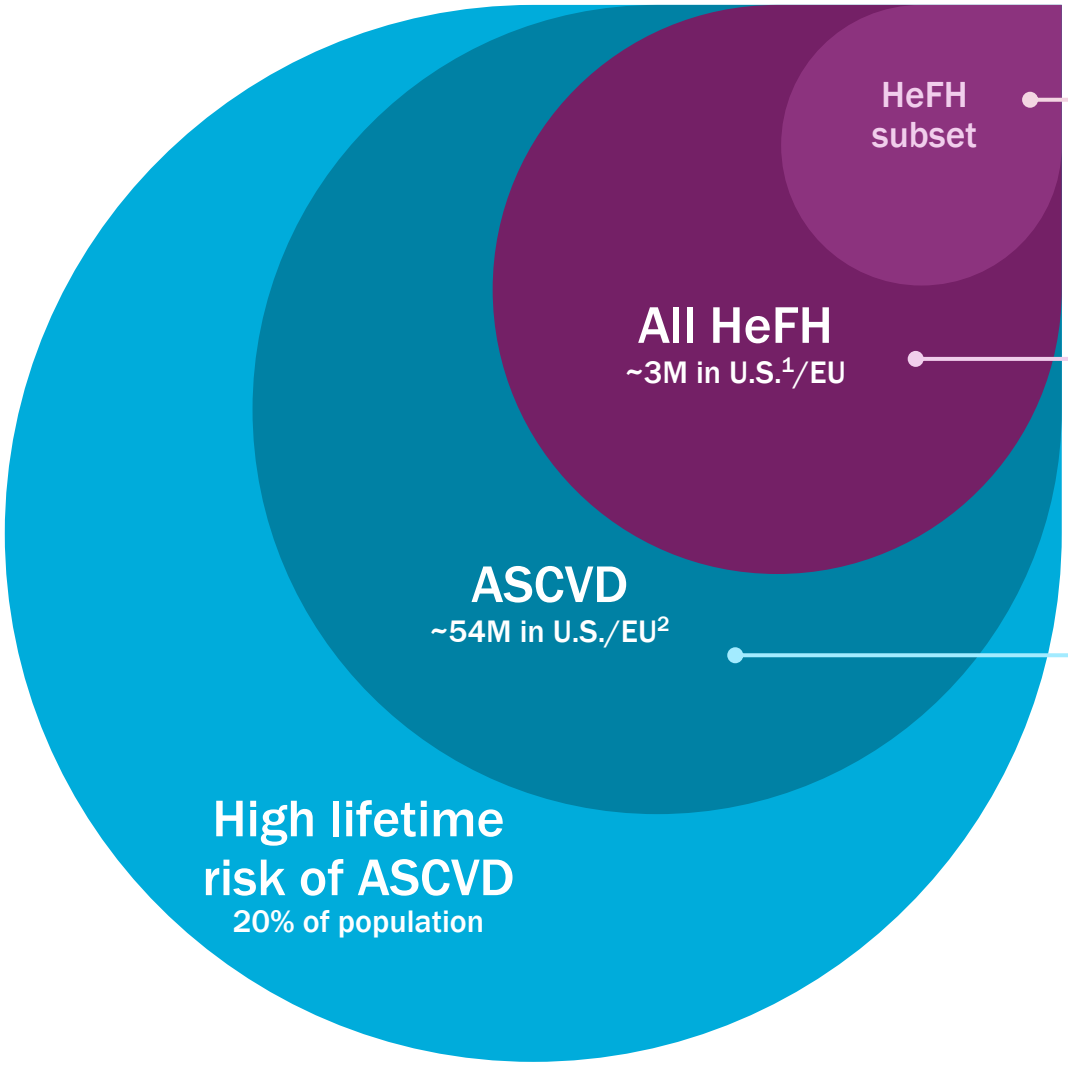
Enrolling high risk HeFH patients with established ASCVD and LDL not at goal

INITIAL DATA IN 4Q23

- Data from dose escalation portion of the study

Safety parameters, blood PCSK9, and blood LDL-C

Stepwise clinical development strategy for VERVE-101 starting with HeFH and potential to expand to broader populations with ASCVD



- Phase 1b proof-of-concept in high-risk HeFH

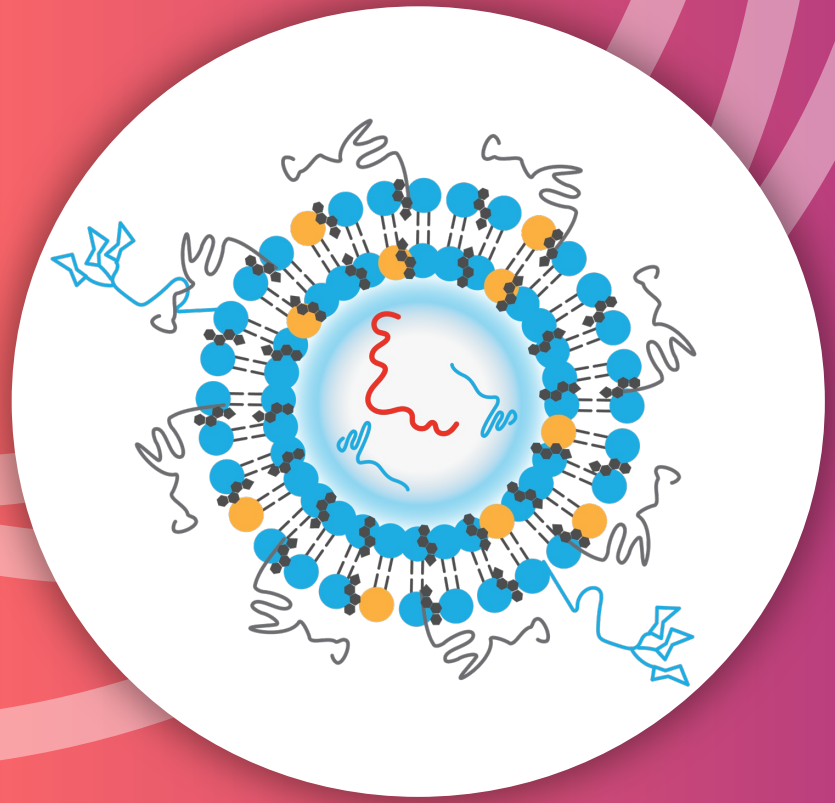
- Phase 2 in all HeFH
- Pivotal Phase 3 in all HeFH (LDL-C endpoint)

- Pivotal Phase 3 in ASCVD (LDL-C endpoint)
- Cardiovascular outcome study in ASCVD

Lowering LDL-C by targeting PCSK9 remains a large unmet need

Clinical development strategy subject to alignment with regulators

1. Tsao CW et al., Heart Disease and Stroke Statistics – 2022 Update: A Report from the American Heart Association. *Circulation.* 2022;145(8):e153–e639.
2. Gu J et al., *Am J Prev Cardiol.* 2022;10:100336.



VERVE-102 targeting PCSK9:

Phase 1b clinical trial initiation expected in 1H24

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

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

+

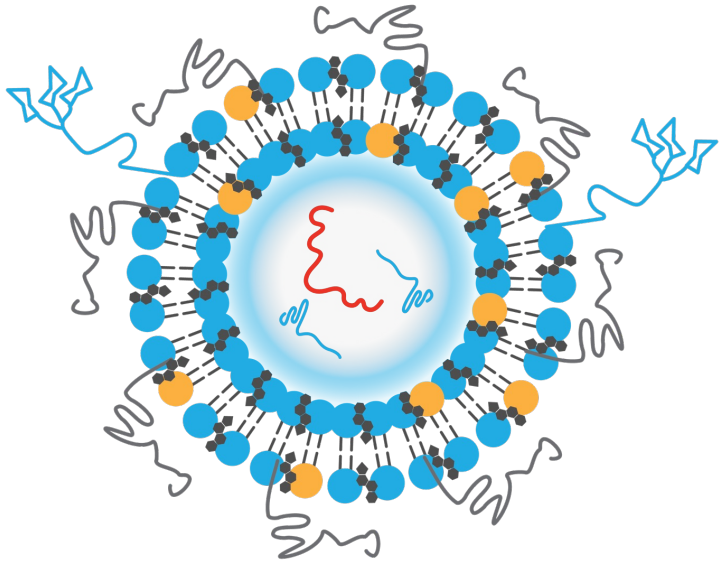
DELIVERY VEHICLE

LNP for delivery to liver cell includes 5 components

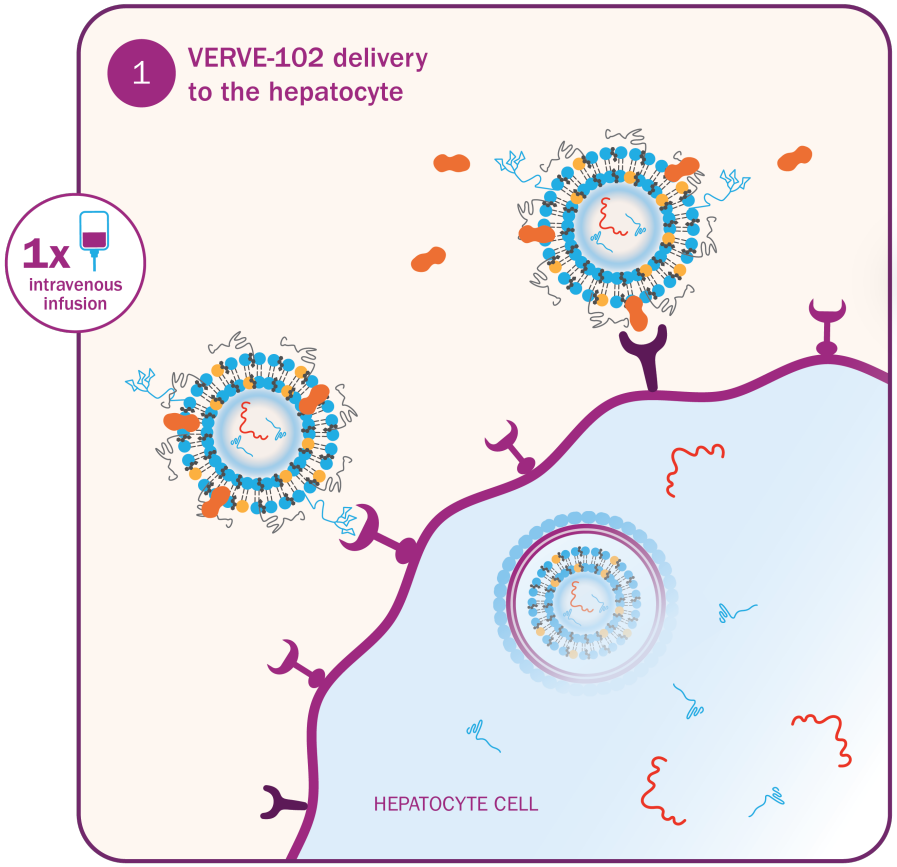
- Ionizable amino lipid (Novartis)
- DSPC
- Cholesterol
- GalNAc
- PEG

=

VERVE-102



VERVE-102: GalNAc-LNP accesses liver cells through either of two liver-abundant receptors, potential for greater potency and tissue specificity

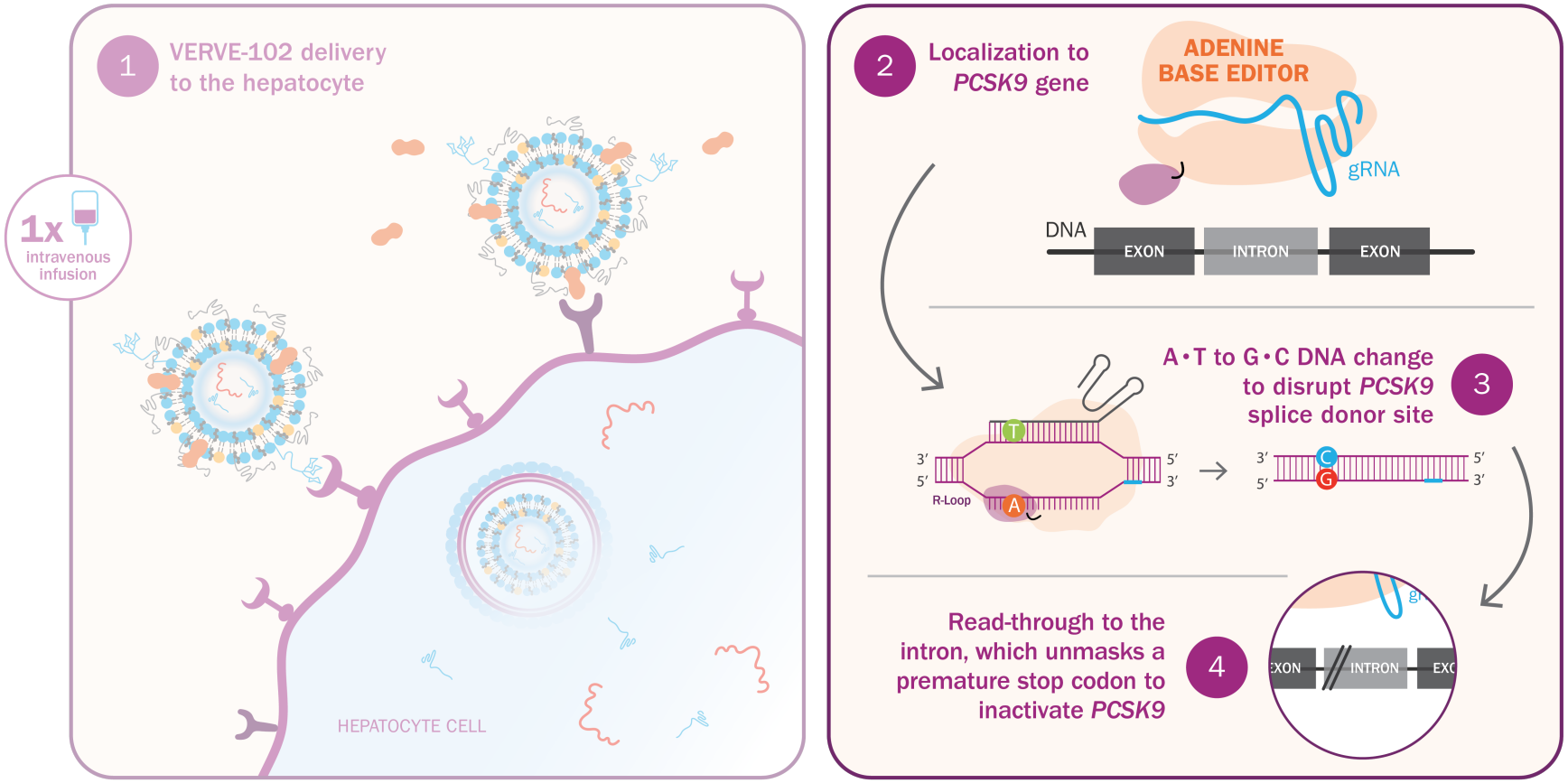


GalNAc-LNP enables delivery into hepatocyte via either of two receptors:

LDLR or **ASGPR**

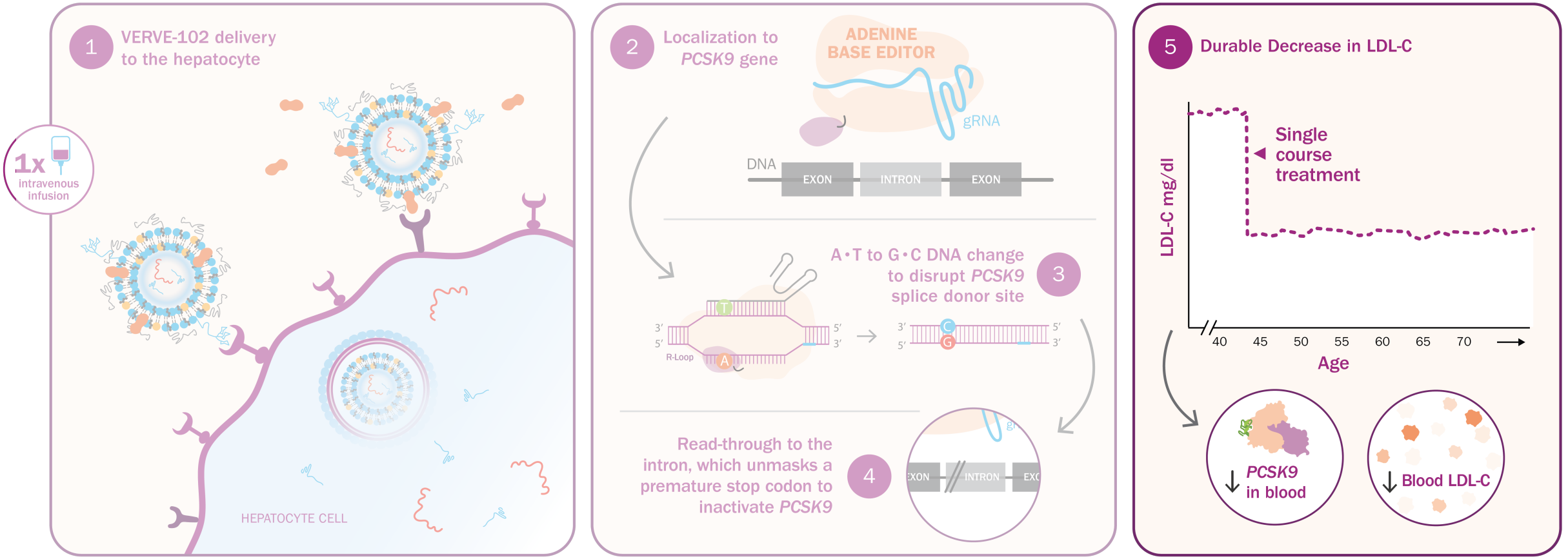
Lipid nanoparticle
Ionizable amino lipid
DSPC
Asialoglycoprotein receptor (ASGPR)
LDL receptor (LDLR)
GalNAc
apoE
mRNA
gRNA
PEG Lipid
Cholesterol

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

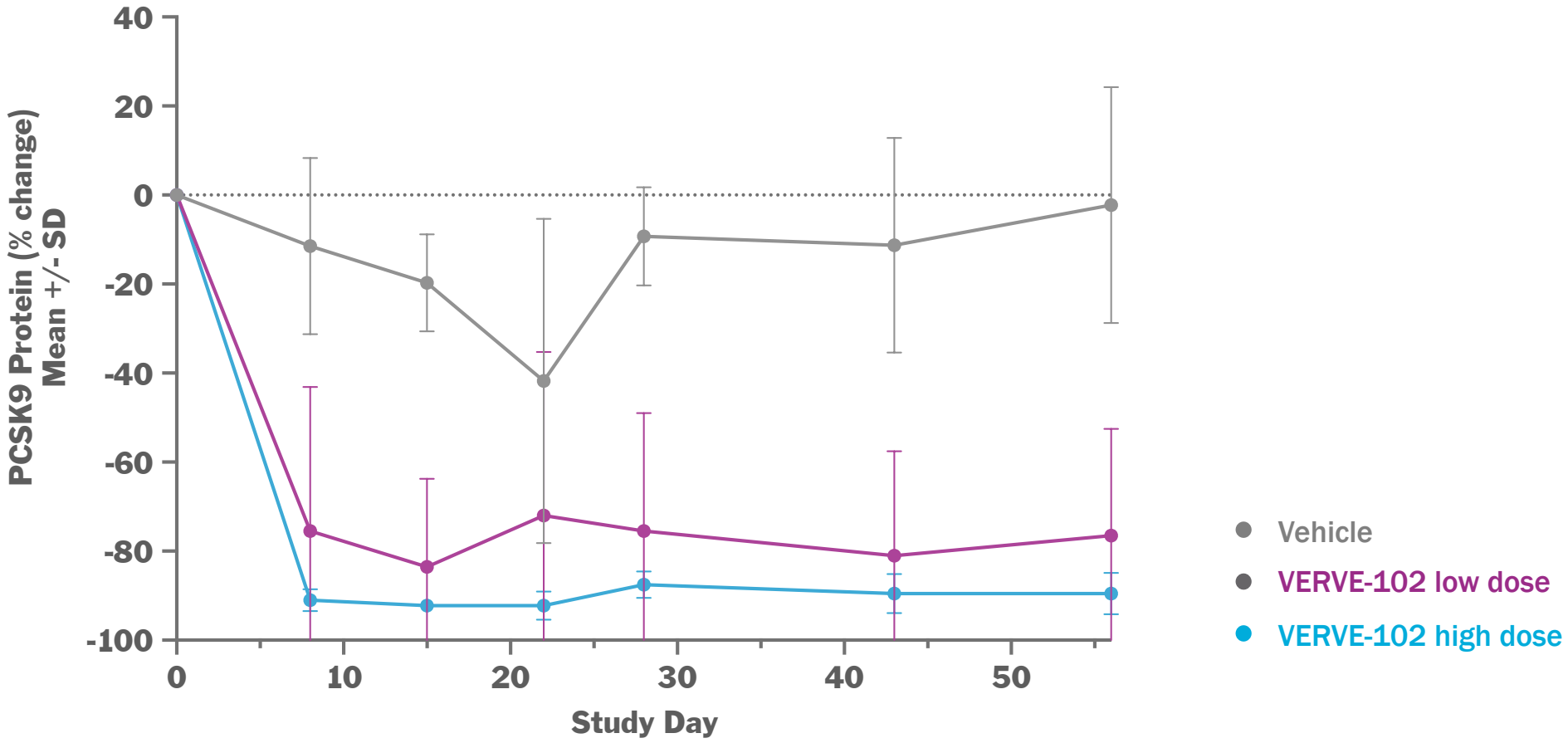
VERVE-102: base editing medicine designed to inactivate hepatic *PCSK9* and lower LDL-C



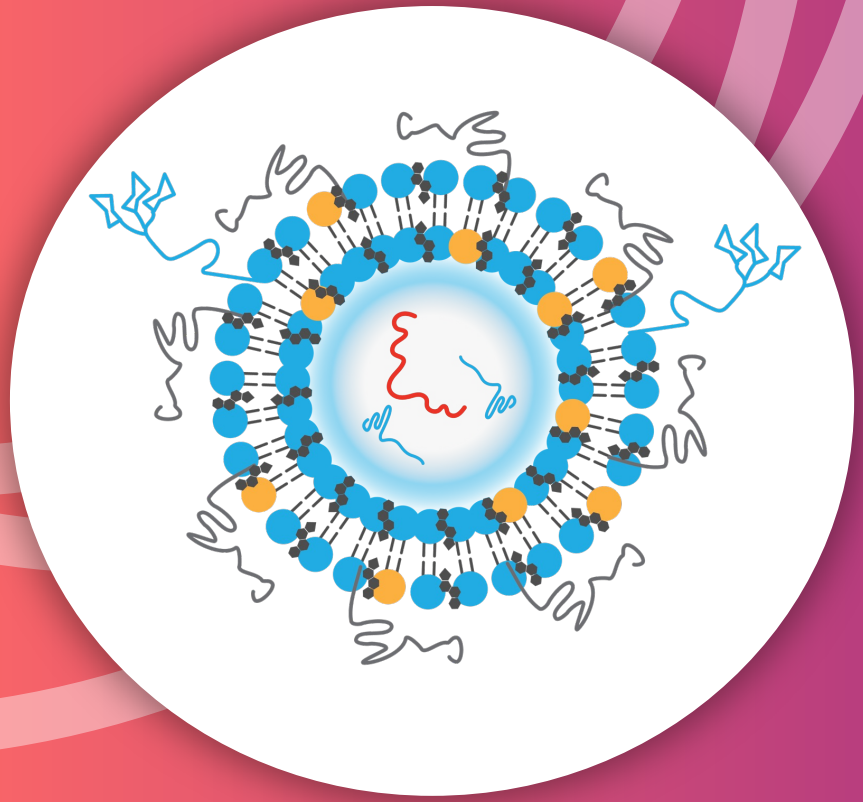
Lipid nanoparticle · Ionizable amino lipid · DSPC · Asialoglycoprotein receptor (ASGPR) · LDL receptor (LDLR) · GalNAc · apoE · mRNA · gRNA · PEG Lipid · Cholesterol

VERVE-102: targets *PCSK9* but using GalNAc-LNP delivery system

Reductions in *PCSK9* protein in wild-type NHPs



Development of VERVE-102: maximize the opportunity to bring the best PCSK9 product forward for patients



VERVE-201 targeting ANGPTL3:

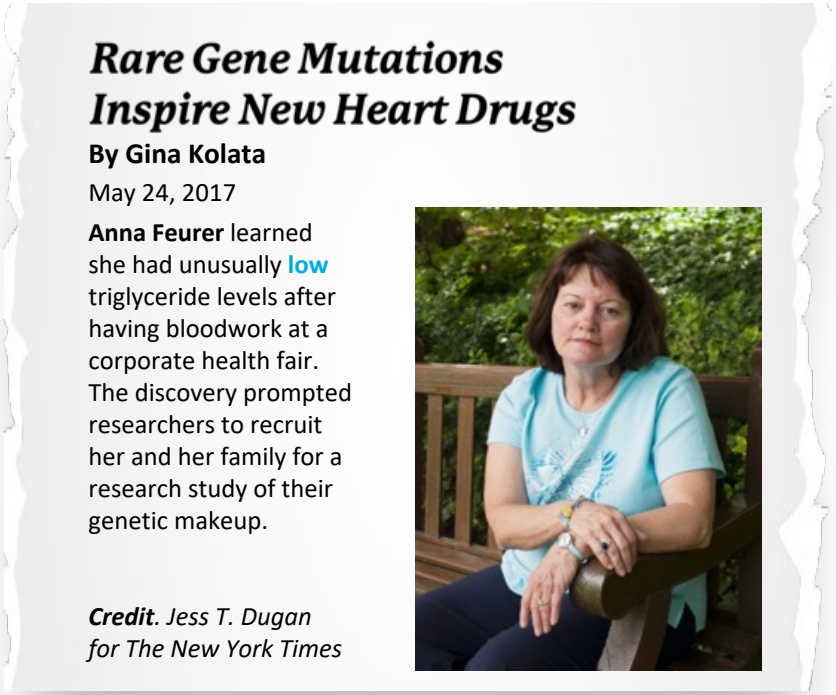
Phase 1b clinical trial initiation expected in 2H24

Inactivation of ANGPTL3 is a compelling target to lower LDL-C: validated by human genetics of ANGPTL3 deficiency

Lower LDL-C, TRL, and ASCVD

Heterozygous deficiency: lower lipids in population, resistant to ASCVD

Homozygous deficiency[1]: 'Human knockout'
LDL-C: 37 mg/dL
TRL: 19 mg/dL



Rare Gene Mutations Inspire New Heart Drugs

By Gina Kolata

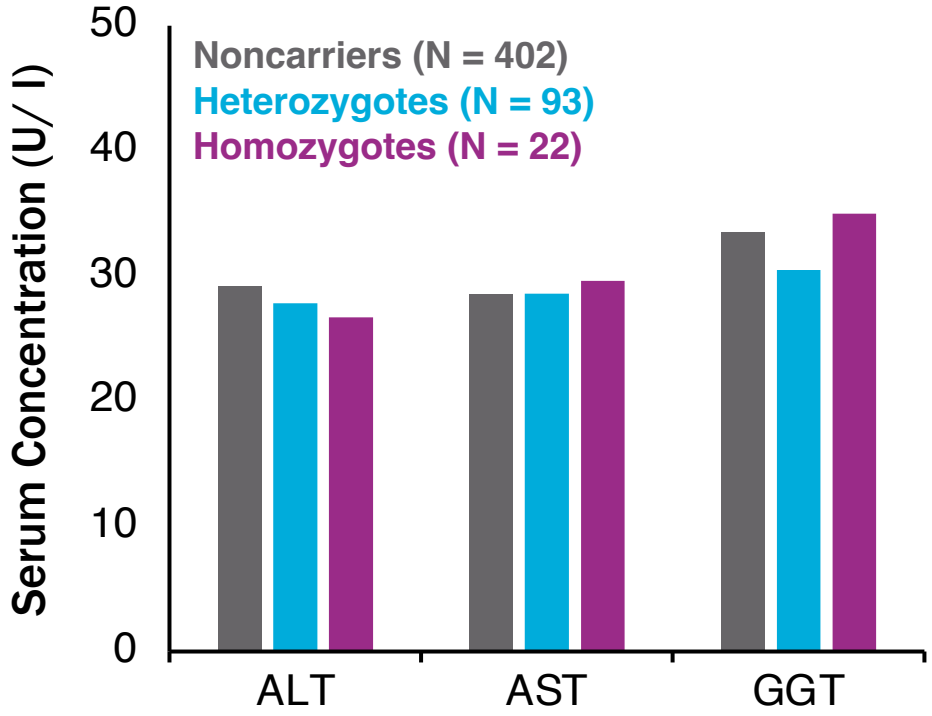
May 24, 2017

Anna Feurer learned she had unusually low triglyceride levels after having bloodwork at a corporate health fair. The discovery prompted researchers to recruit her and her family for a research study of their genetic makeup.

***Credit**. Jess T. Dugan for The New York Times*

No adverse effects

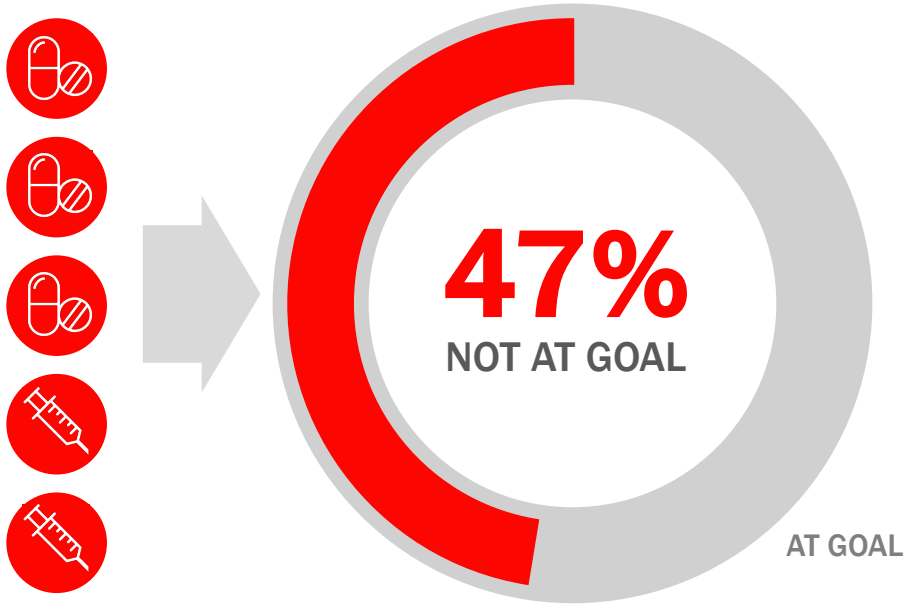
No increase in markers of liver injury or prevalence of liver steatosis in heterozygous or homozygous deficiency[2]



1. Musunuru K et al. *N Engl J Med*. 2010;363(23):2220-7.
2. Minicocci I et al. *J Lipid Res*. 2013;54(12):3481-90.

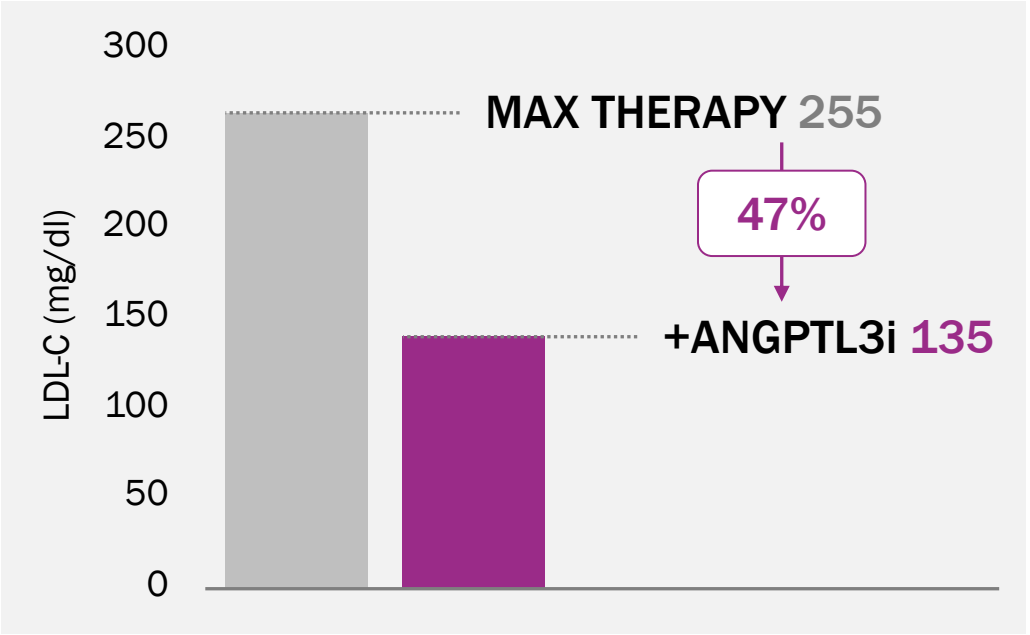
HoFH: severe orphan disease where medicine targeting ANGPTL3 approved to lower LDL-C

Unmet Medical Need



In a global registry of HoFH patients,
47% did not attain LDL-C goal
even on 5 lipid-lowering therapies[1]

Clinical Validation of ANGPTL3 Mechanism



Registration trial of evinacumab (Evkeeza, n=65)
in HoFH patients
on maximum lipid-lowering therapy
ANGPTL3 inhibition ↓ LDL-C by 47%[2]

1. Tromp TR et al. *Lancet*. 2022;399(10326):719-728.
2. Raal FJ et al. *N Engl J Med*. 2020;383(8):711-720.

VERVE-201: adenine base editor mRNA + gRNA packaged in a GalNAc-LNP; edit designed to turn off *ANGPTL3*

DRUG SUBSTANCES

RNA components encode base editor and a guide targeting *ANGPTL3* gene

- mRNA for adenine base editor
- gRNA localizes editor to *ANGPTL3* gene

+

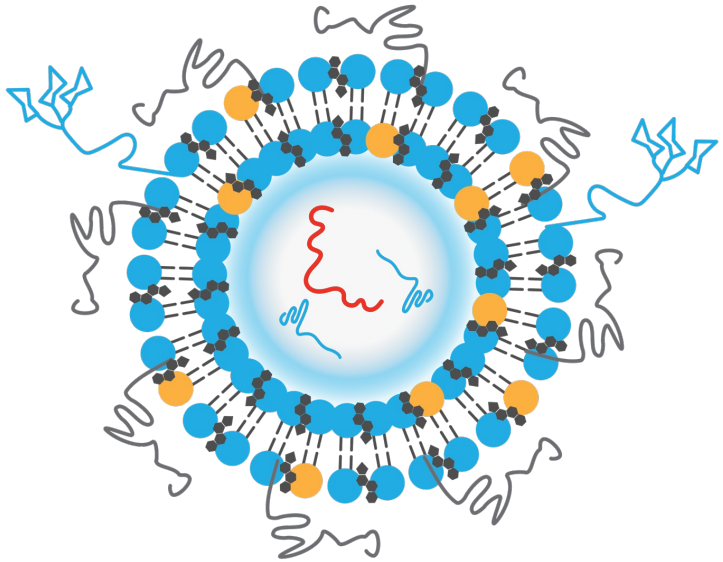
DELIVERY VEHICLE

Lipid nanoparticle for delivery to liver cell includes 5 components

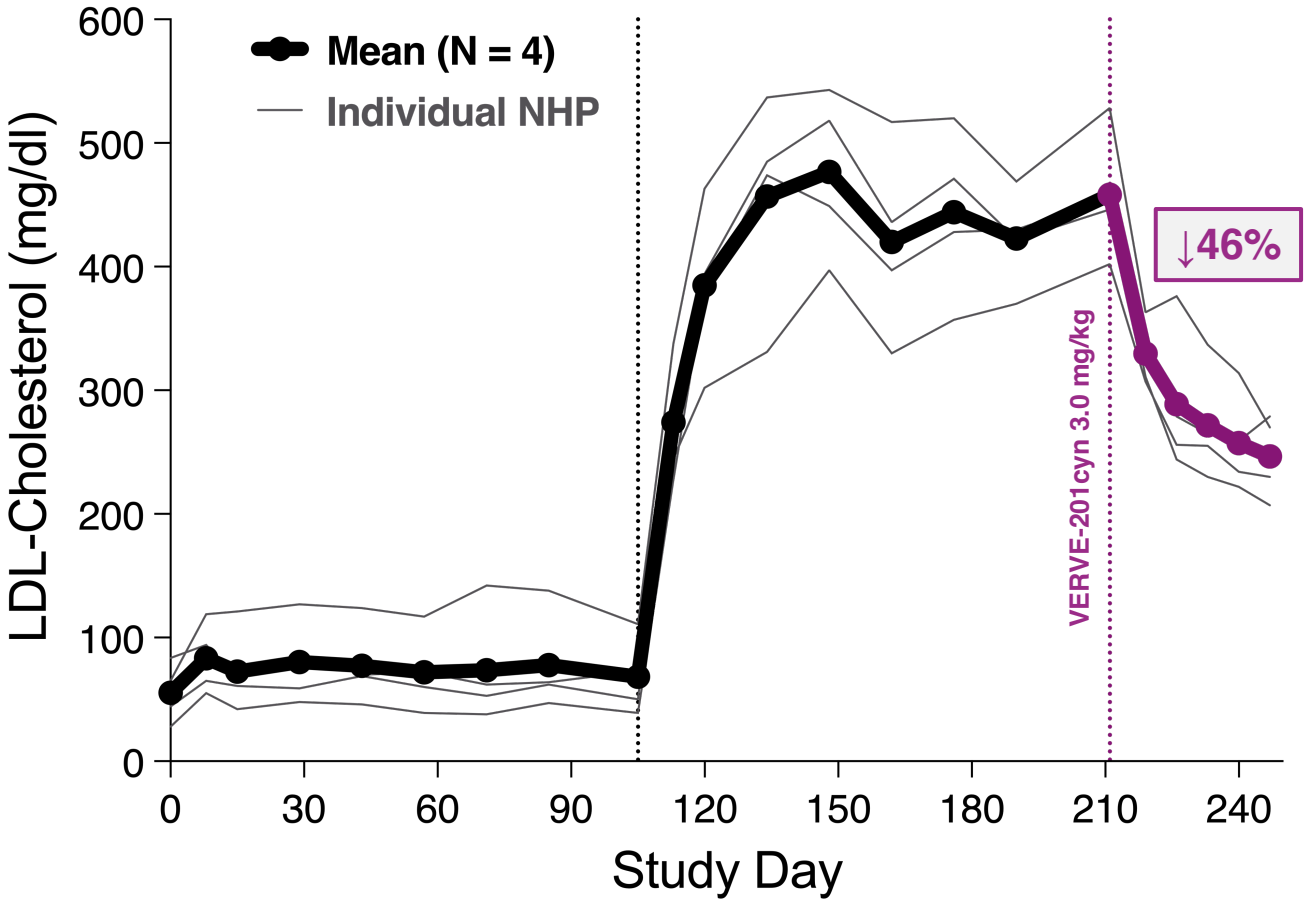
- Ionizable amino lipid (Novartis)
- DSPC
- Cholesterol
- GalNAc
- PEG

=

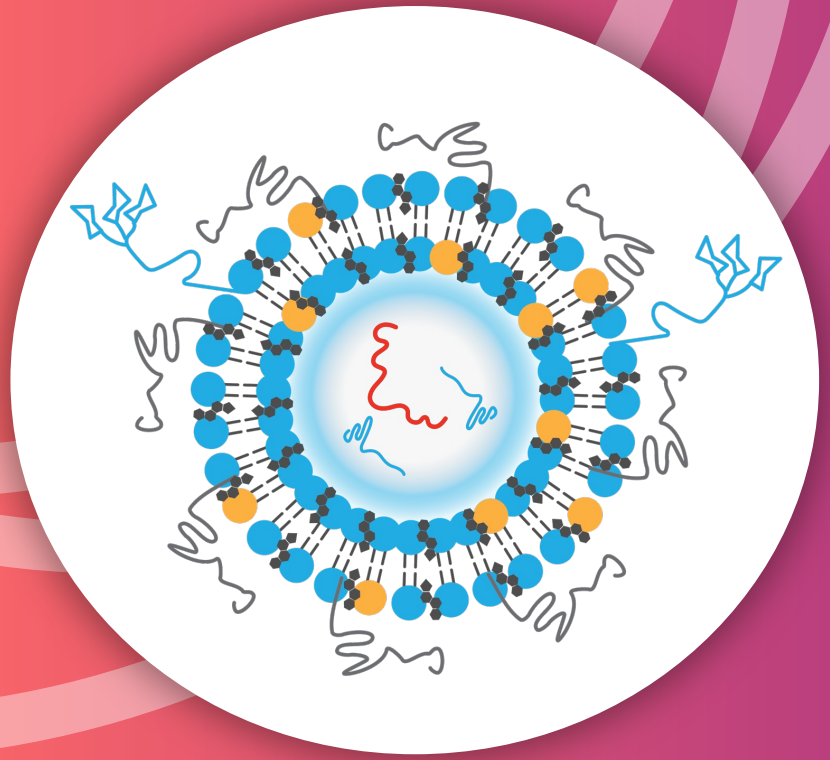
VERVE-201



In LDLR-deficient NHPs treated with VERVE-201cyn, 46% mean decrease in LDL-C observed

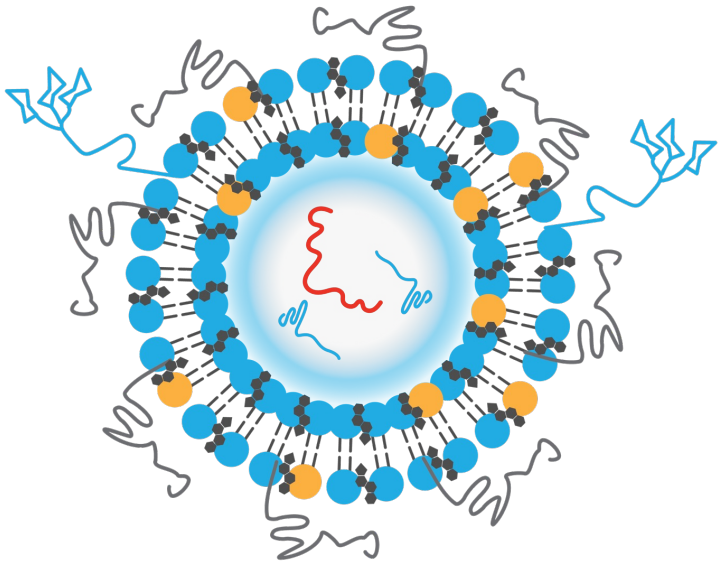


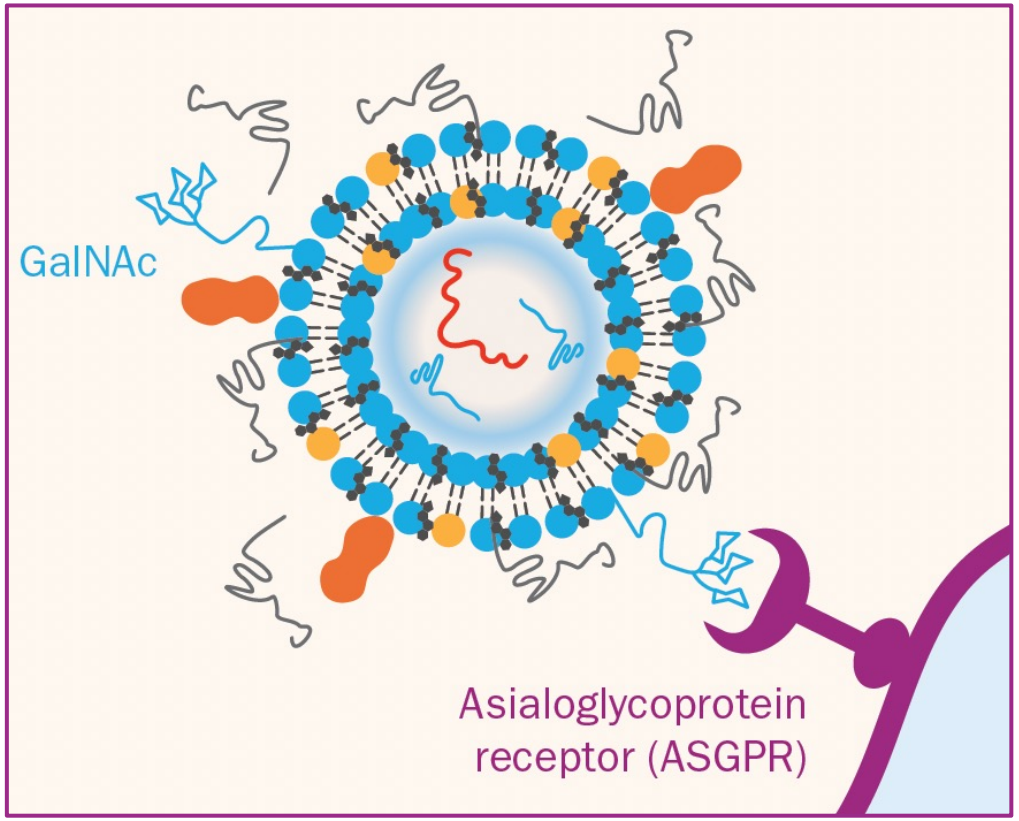
- Treated 4 NHPs with VERVE-201cyn at a dose of 3.0 mg/kg.
- At time of necropsy 5 weeks following dosing:
  - 60% mean *ANGPTL3* liver editing
  - 84% mean reduction from baseline in blood ANGPTL3
- Mean LDL-C decreased from 458 to 247 mg/dL
- VERVE-201cyn in NHPs:
  - 46% decrease in LDL-C
  - 54% decrease in TG



Internally-developed, novel liver delivery platform: GalNAc-LNP

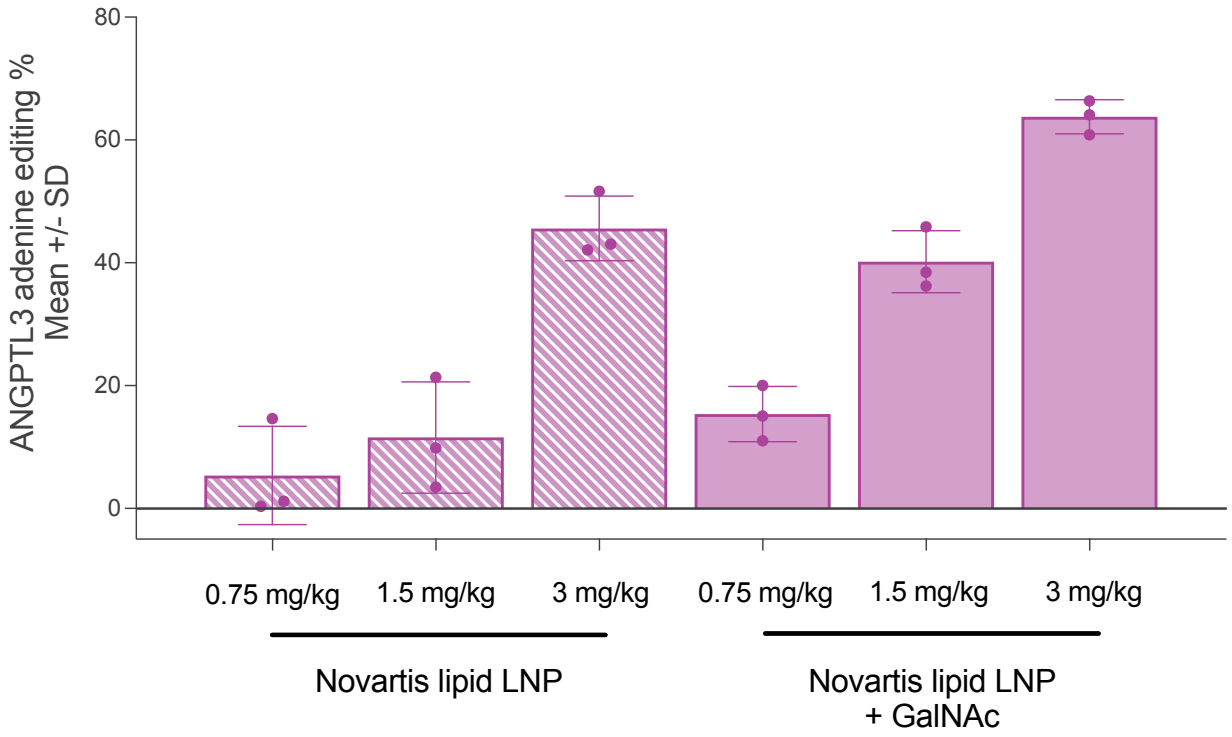
Proprietary GalNAc-LNP technology: potential best-in-class for delivery of genetic medicines to liver



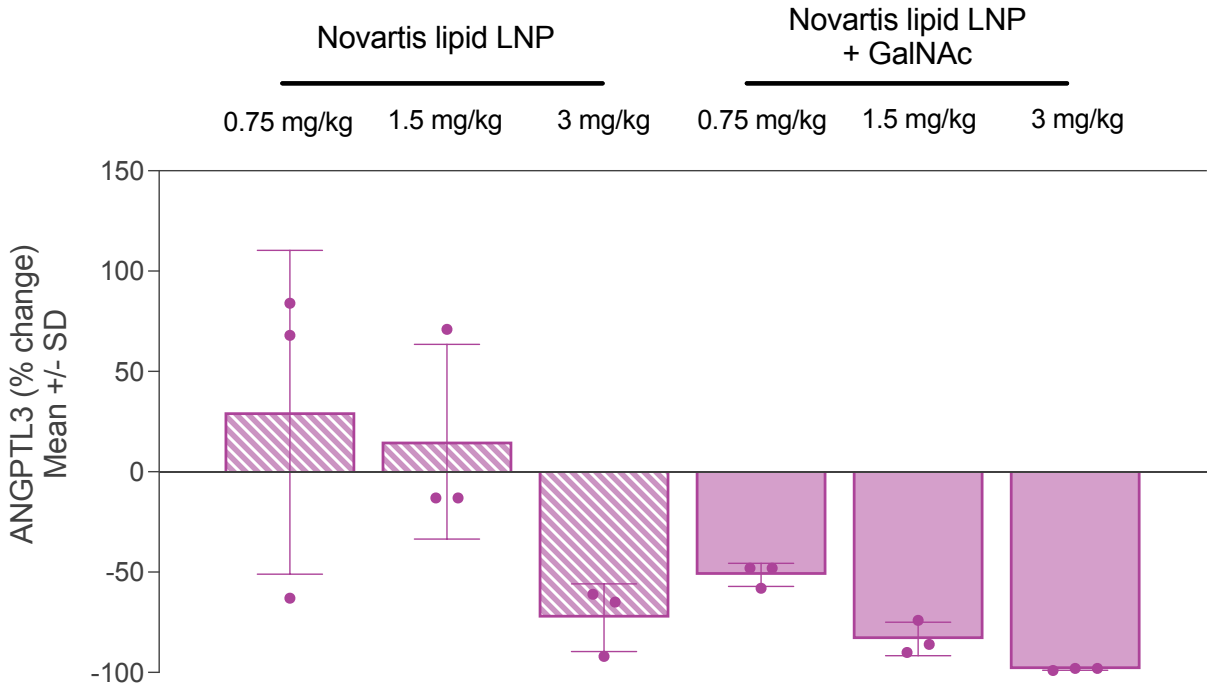


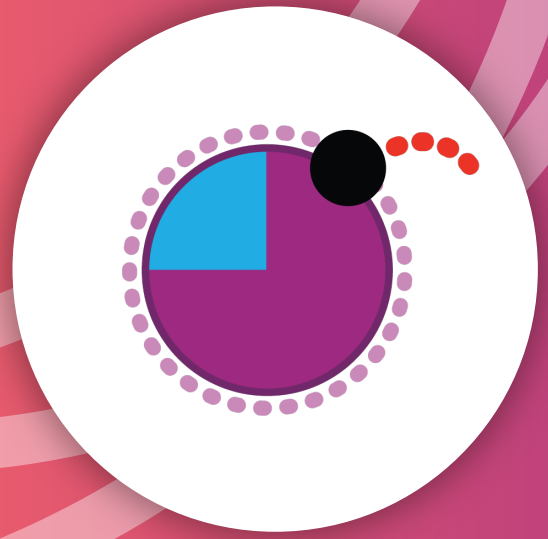
Addition of GalNAc to Novartis lipid LNPs enhances potency of liver editing in wild-type NHPs

ANGPTL3 liver editing



ANGPTL3 protein reduction in blood



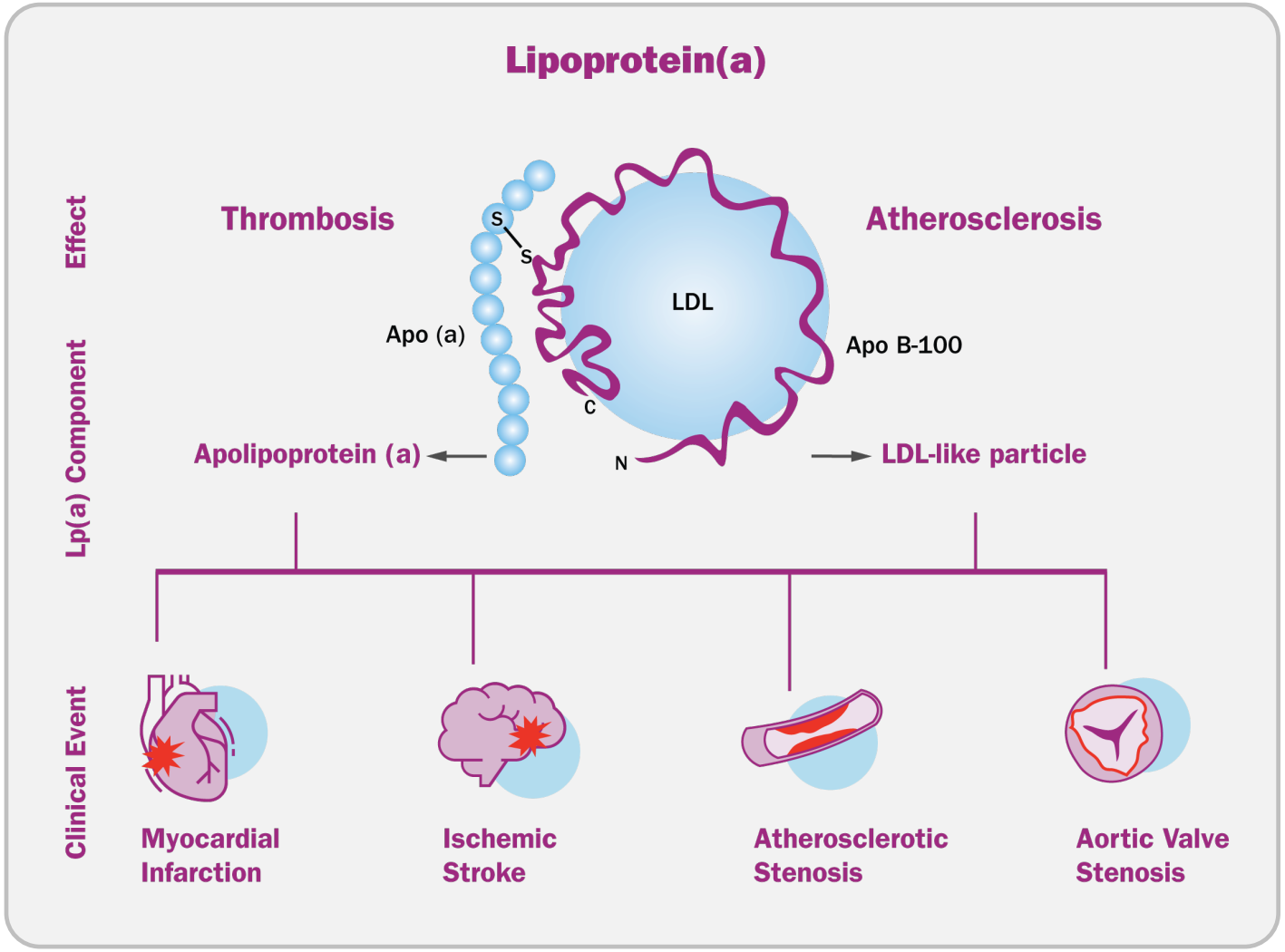


Targeting third pillar of lipoprotein risk: Discovery efforts on Lp(a)

New collaboration: Verve and Lilly

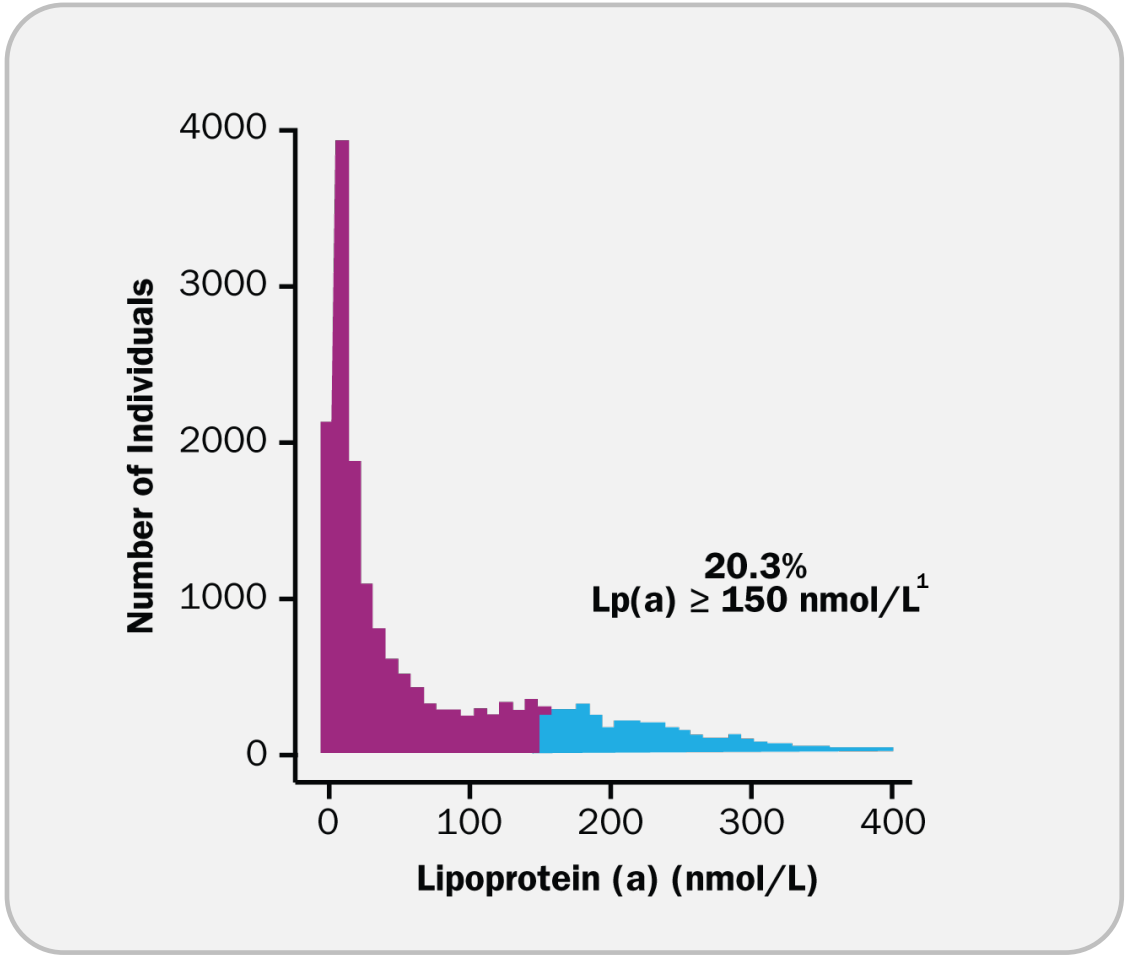
- In June 2023, **Verve announced a global collaboration with Lilly** to advance our *in vivo* gene editing program targeting Lp(a) for the treatment of ASCVD
- In August 2023, **Verve received $60 million in combined upfront payment and equity investment,** which extends our expected operating runway into 2026
- **Lilly will fund research program costs** through Phase 1 clinical trials
- **Verve is eligible to receive up to $465 million** in research, development, and commercial milestones, as well as tiered royalties on global net sales
- **Verve has opt-in rights to co-fund and share in potential margins** of products resulting from the collaboration

High blood levels of lipoprotein(a) contribute to risk for ASCVD



- Liver-derived, circulates in blood
- Associated with higher risk for ASCVD endpoints including myocardial infarction and ischemic stroke

High Lp(a) is large addressable market, distinct ASCVD subset from patients with high LDL-C



- 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 high LDL-C; correlation coefficient between blood LDL-C and Lp(a) is low (r^2=0.01)[2]

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.

Why once-and-done gene editing medicine for Lp(a)?

Humans with genetic Lp(a) deficiency:

- resistant to heart attack & stroke[1]
- no signal for adverse events

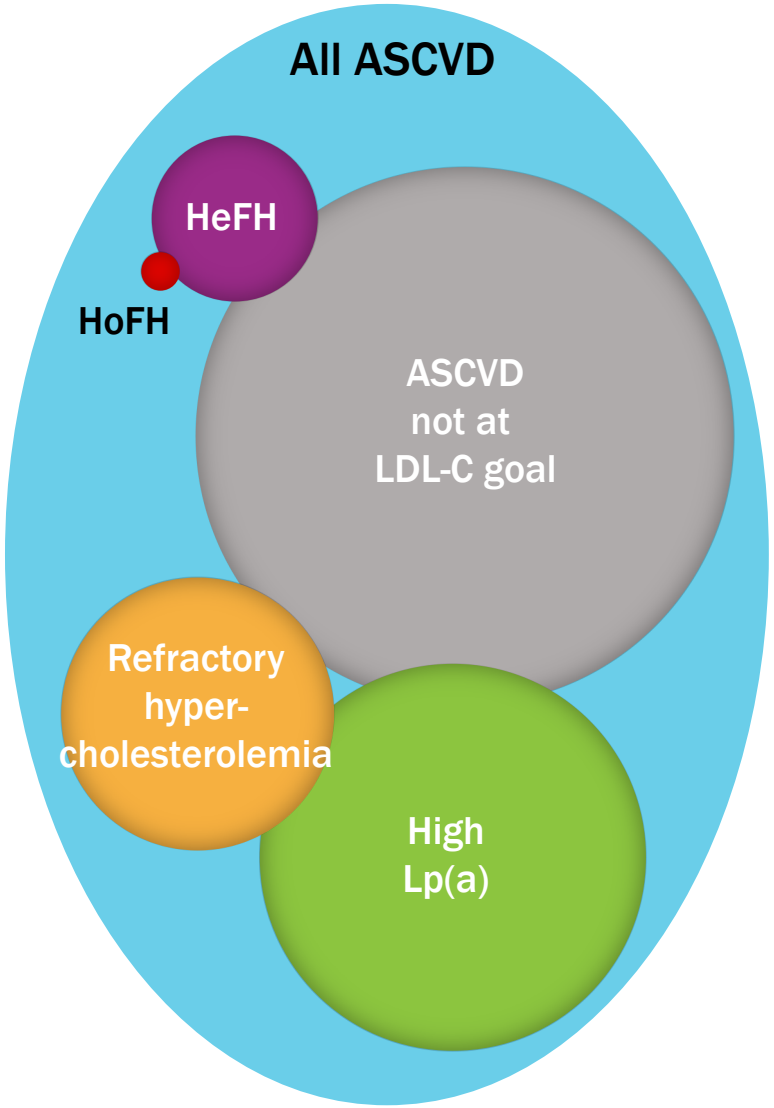
Blood level almost entirely determined by inheritance

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. Emdin CA et al. *J Am Coll Cardiol*. 2016;68(25):2761-2772.

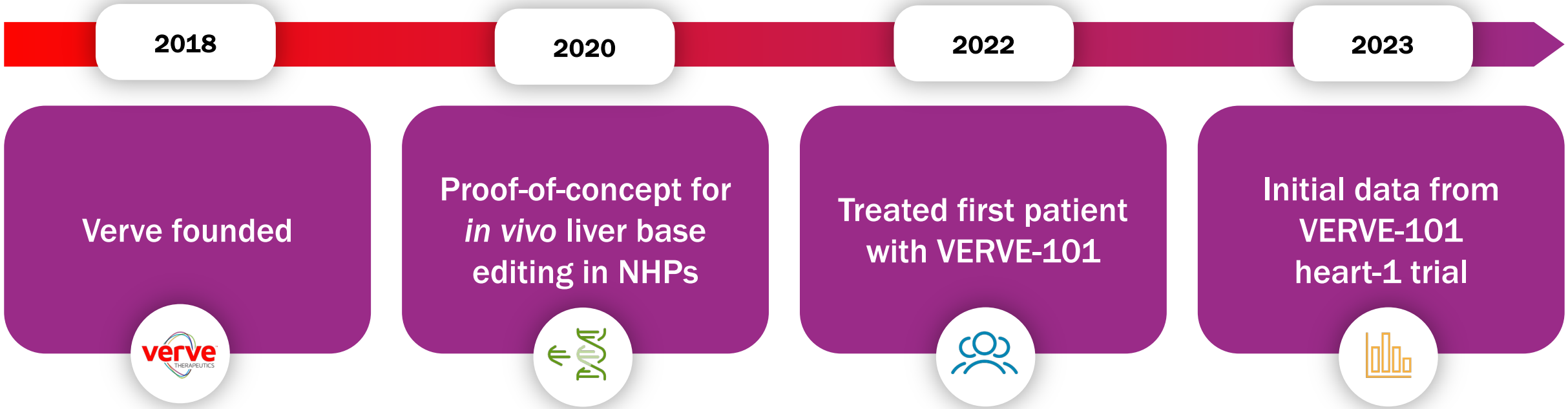
Verve's pipeline of gene editing programs address distinct ASCVD subsets



	POPULATION	PROGRAM
All ASCVD	~ 54M in US/EU	
HeFH	~ 3M in US/EU	VERVE-101 or VERVE-102 (PCSK9)
ASCVD not at LDL-C goal on statin[1,2]	~ 21M in US/EU	VERVE-101 or VERVE-102 (PCSK9)
HoFH	~ 2,800 in US/EU	VERVE-201 (ANGPTL3)
Refractory Hypercholesterolemia[3] (ASCVD not at LDL-C goal on statin + PCSK9i)	~ 7M in US/EU (~13% ASCVD)	VERVE-201 (ANGPTL3)
Elevated Lp(a)	~ 11M in US/EU (~20% ASCVD)	Lp(a) program

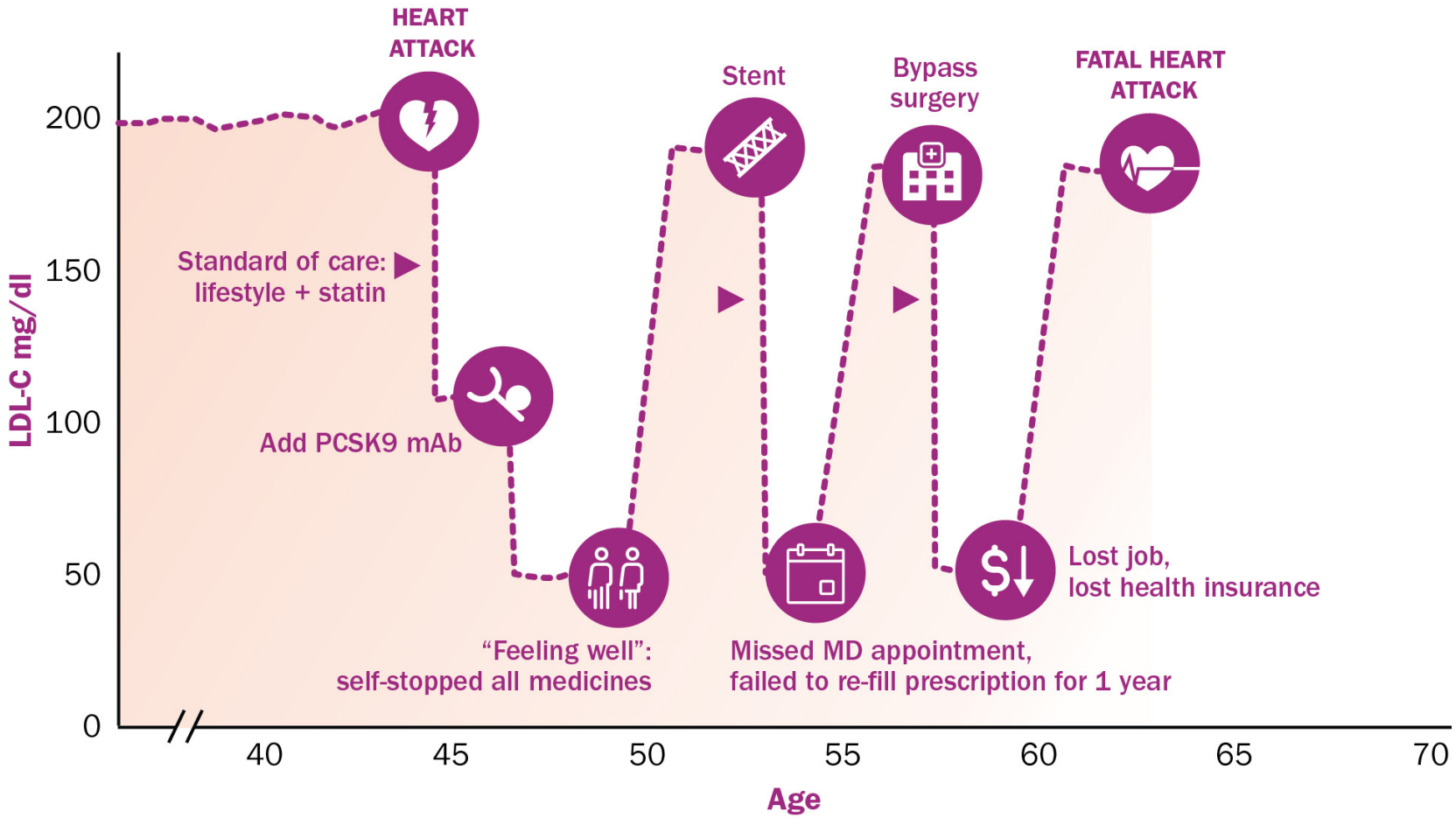
1. Gu J et al., *American Journal of Preventive Cardiology* 10, 100336 (2022). 2. Ray KK et al., *European Journal of Preventive Cardiology*, 2021, 1279–1289. 3. O'Donoghue ML et al. *Circulation*. 2022;146(15):1109-1119.

Focused on our mission: transform the treatment of cardiovascular disease from chronic management to once-and-done gene editing medicines



Focused
Well-capitalized to continue to execute

Current care model for chronic disease: poor control of LDL-C



Can we fundamentally change the way chronic disease is treated?