Disrupting the care of cardiovascular disease with single-course gene editing medicines

July 2022

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 initiation, and timing, of the Company’s planned regulatory submissions, clinical trials, its research and development plans and the potential advantages and therapeutic potential of the Company’s programs. 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 timing of and the Company’s ability to submit applications for, and obtain and maintain regulatory approvals for, its product candidates; continue to advance its product candidates in clinical trials; initiate and enroll 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 and its other product candidates; 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. 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.

Atherosclerotic cardiovascular disease (ASCVD): blood low-density lipoprotein cholesterol (LDL-C) clogging heart arteries

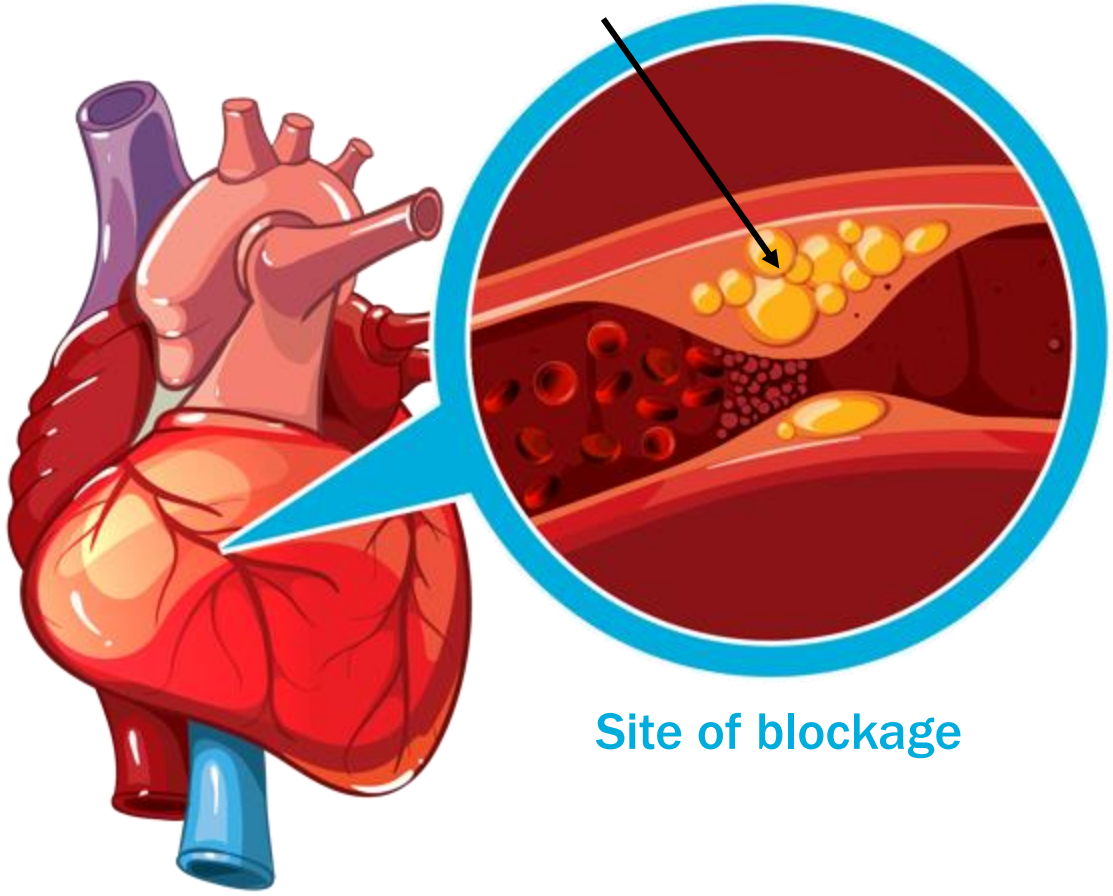
#1 cause of death worldwide

100s of millions of patients worldwide

31M with genetic form of ASCVD:

familial hypercholesterolemia (FH)

- *Heterozygous FH (HeFH; 1 in 250)
- *Homozygous FH (HoFH; 1 in 250,000)



Solution to ASCVD revealed by human genetics and pharmacology: get LDL-C as low as possible for as long as possible

ESC European Society of Cardiology

European Heart Journal (2022) **43**, 249–250
https://doi.org/10.1093/eurheartj/ehab532

Braunwald's Corner

How to live to 100 before developing clinical coronary artery disease: a suggestion

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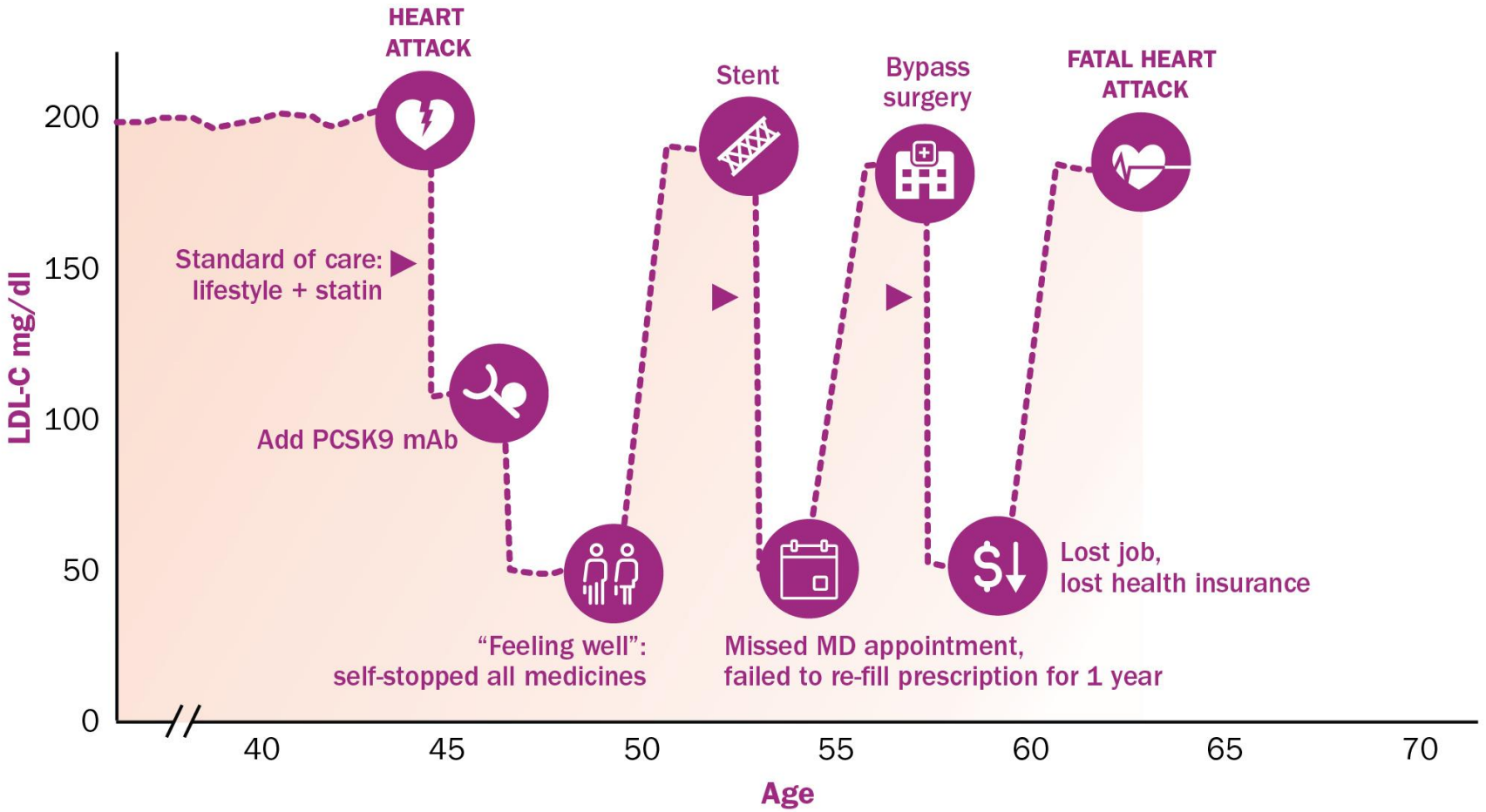
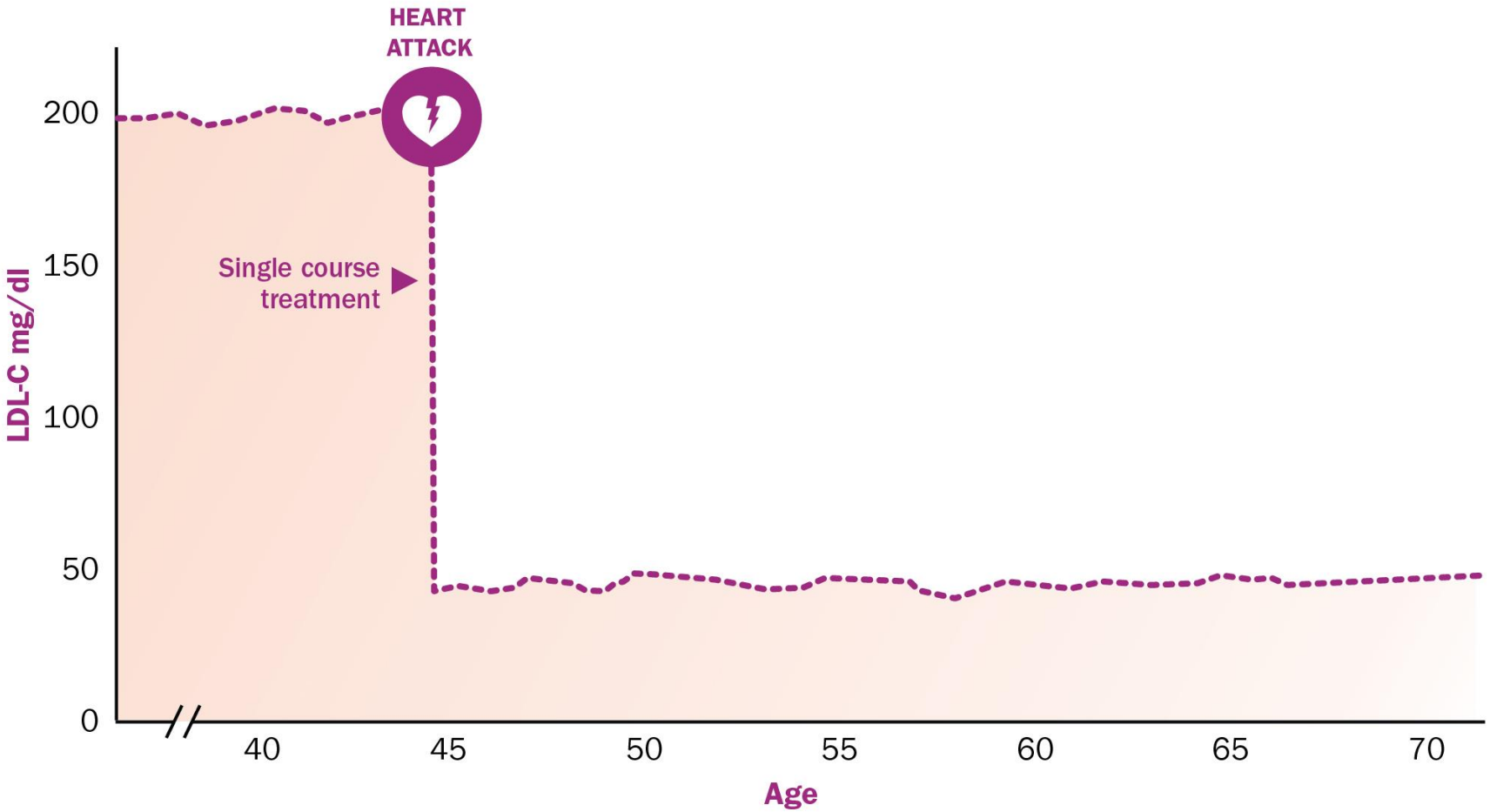
Unmet need: current chronic care model for ASCVD results in poor control of cumulative blood LDL-C exposure



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

Single-course treatment for ASCVD could address key unmet need: getting LDL-C as low as possible for as long as possible



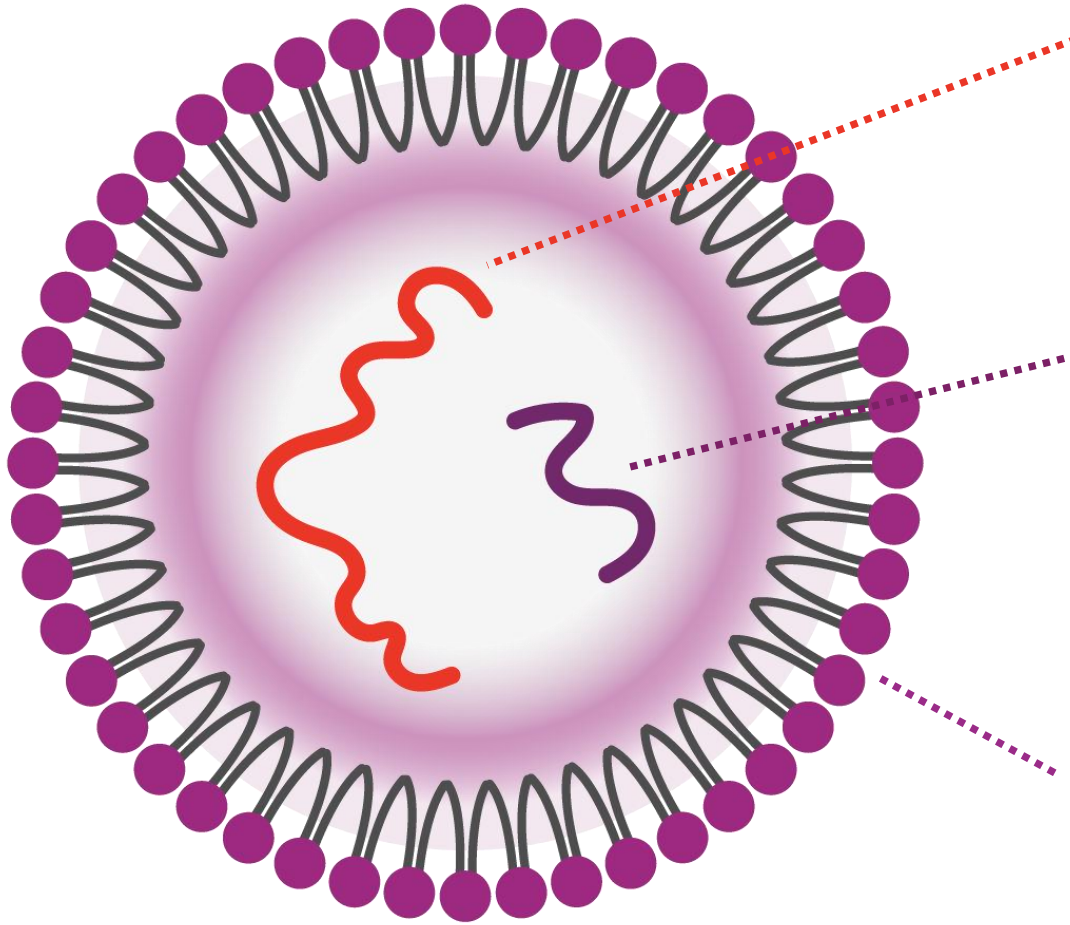
Illustrative graphic depicts the journey of a hypothetical patient with familial hypercholesterolemia who began standard-of-care treatment after suffering a heart attack at age 44

Advancing a pipeline of single-course *in vivo* gene editing programs to safely and durably lower LDL-C and treat ASCVD

PROGRAM	INDICATIONS	DEVELOPMENT STATUS				
		Research/ Lead optimization	IND-Enabling	Phase 1	Phase 2	Phase 3
Low-density lipoprotein cholesterol (LDL-C)						
VERVE-101 PCSK9	Heterozygous familial hypercholesterolemia					
	ASCVD not at LDL-C goal on oral therapy					
LDL-C & Triglyceride-rich lipoprotein (TRL)						
ANGPTL3	Homozygous familial hypercholesterolemia					
	ASCVD not at LDL-C goal on oral + PCSK9i					

VERVE-101: Phase 1b clinical trial initiated

VERVE-101's three components have been designed to maximize on-target and minimize the risk of off-target editing



Adenine base editor (ABE)

- Single base pair change without double stranded breaks
- Delivered as an mRNA

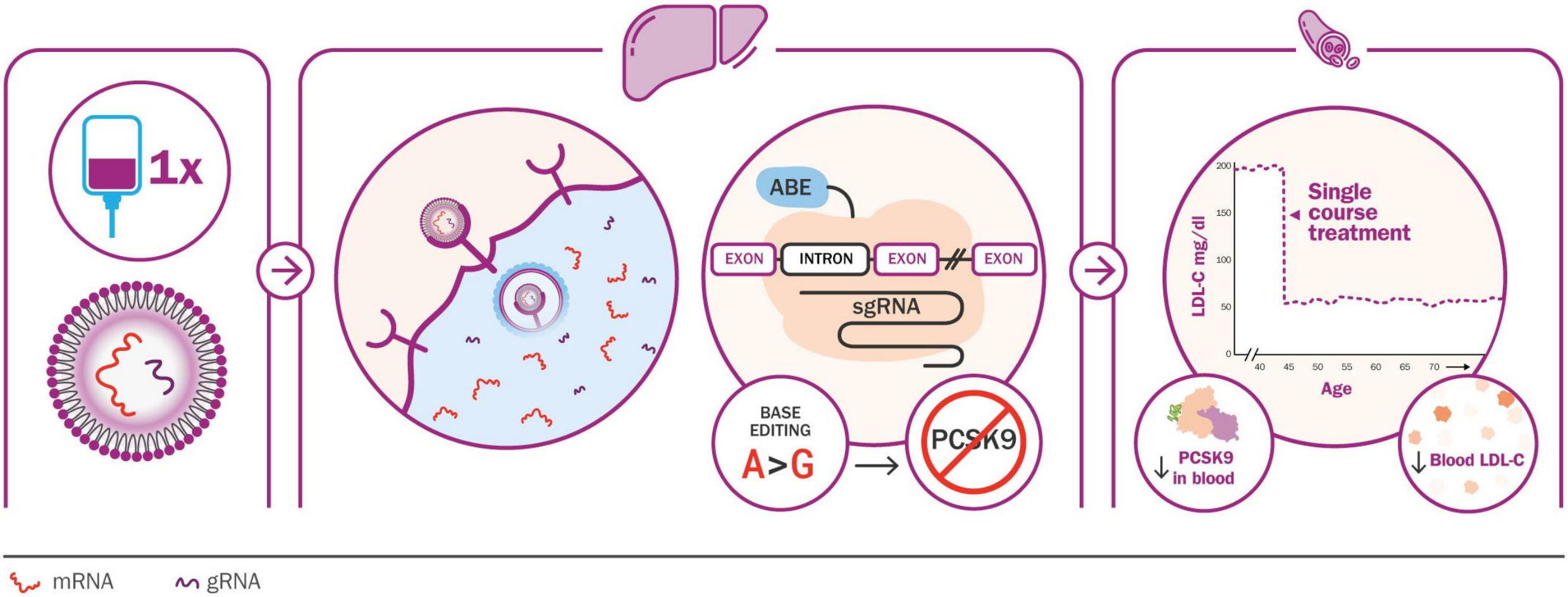
Unique PCSK9 guide RNA (gRNA)

- No 0, 1, or 2 mismatch sites in genome
- Conserved site across human population

Non-viral lipid nanoparticle (LNP) delivery

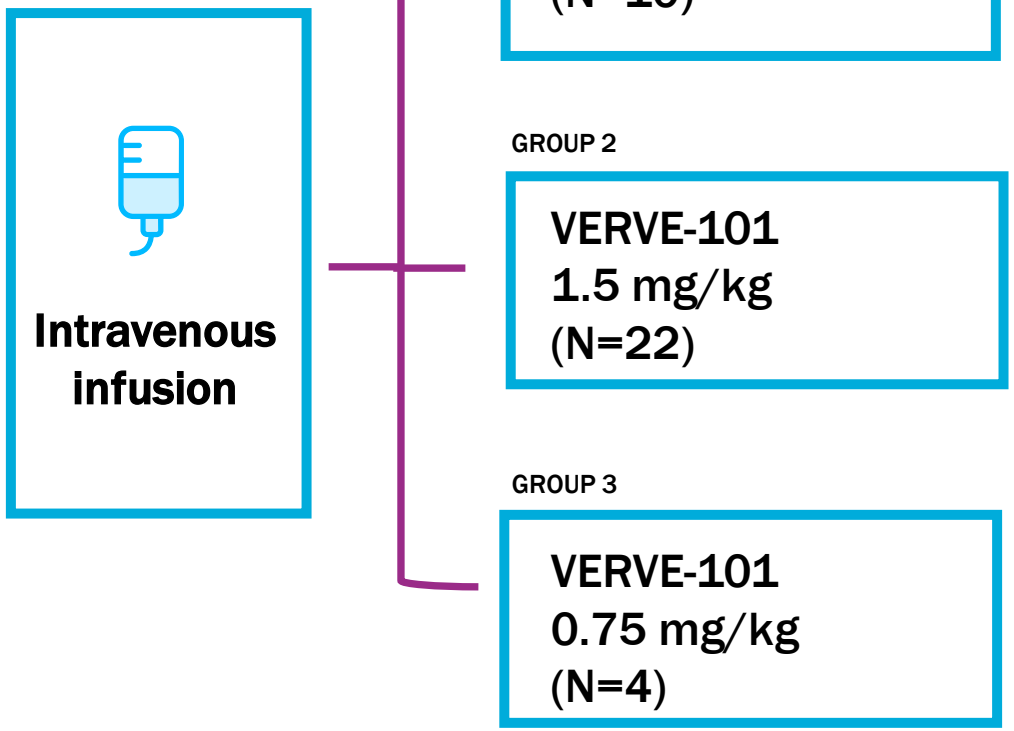
- Delivery predominantly to liver
- Transient exposure < 7 days

Goal: single course gene editing medicines to durably lower LDL-C and treat ASCVD



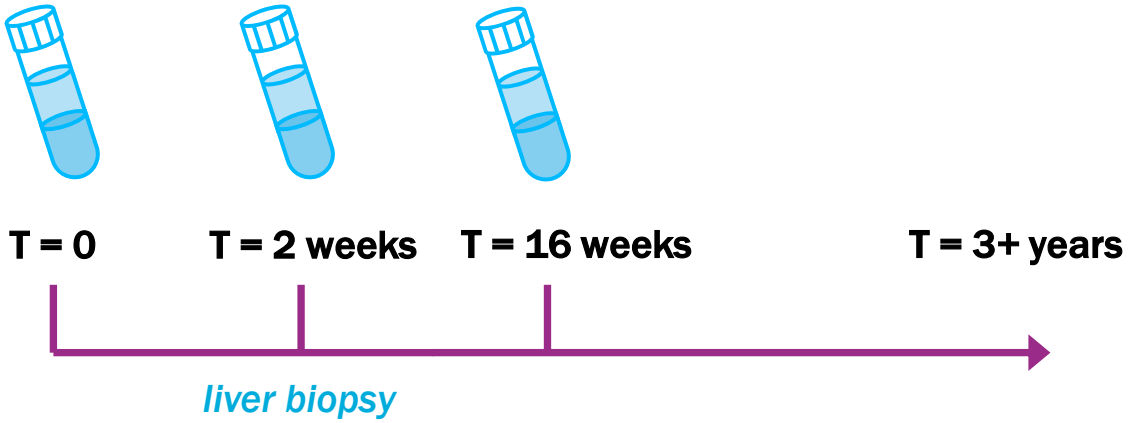
mRNA gRNA

VERVE-101 has been potent, durable, and well tolerated in NHPs



Primary endpoints

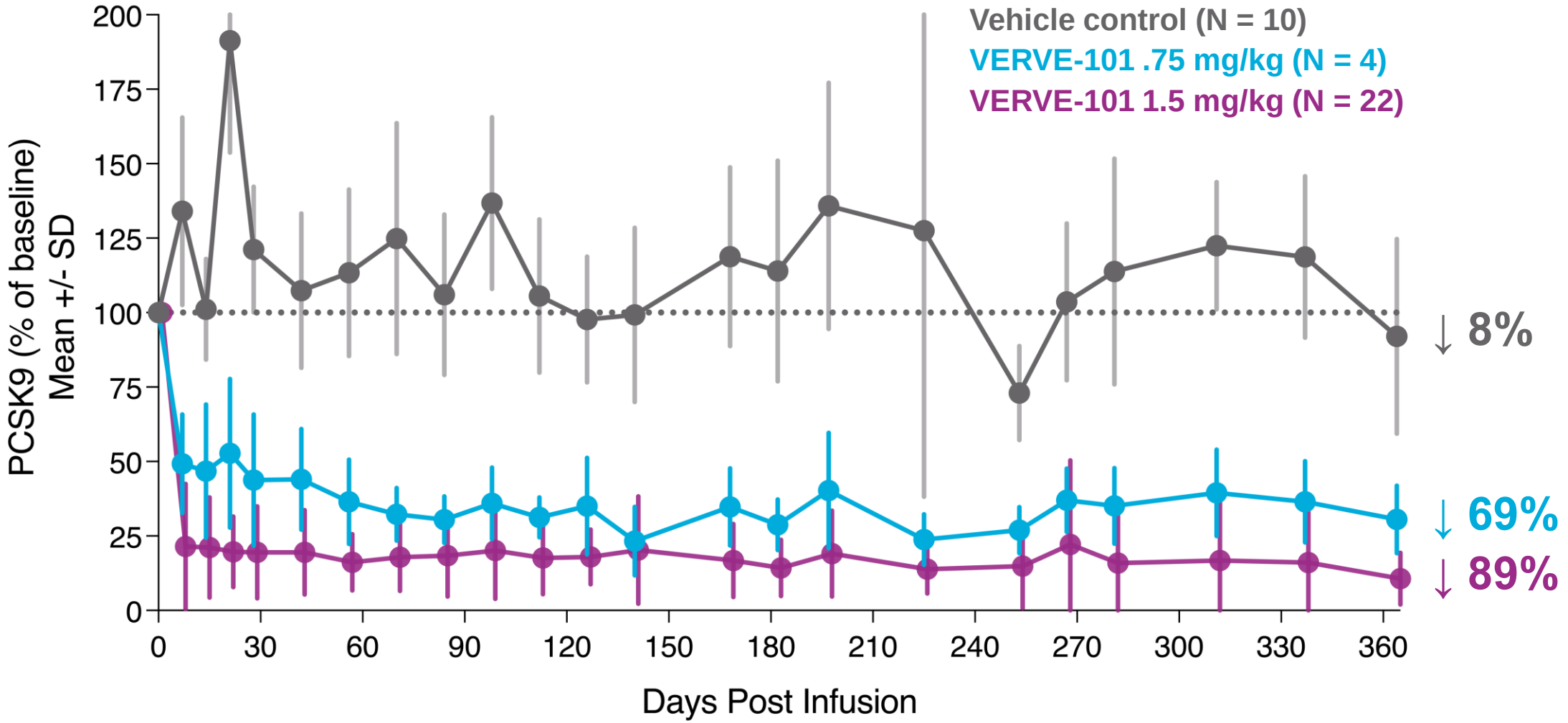
1. Whole liver DNA editing
2. Blood PCSK9 levels
3. Blood LDL-C levels



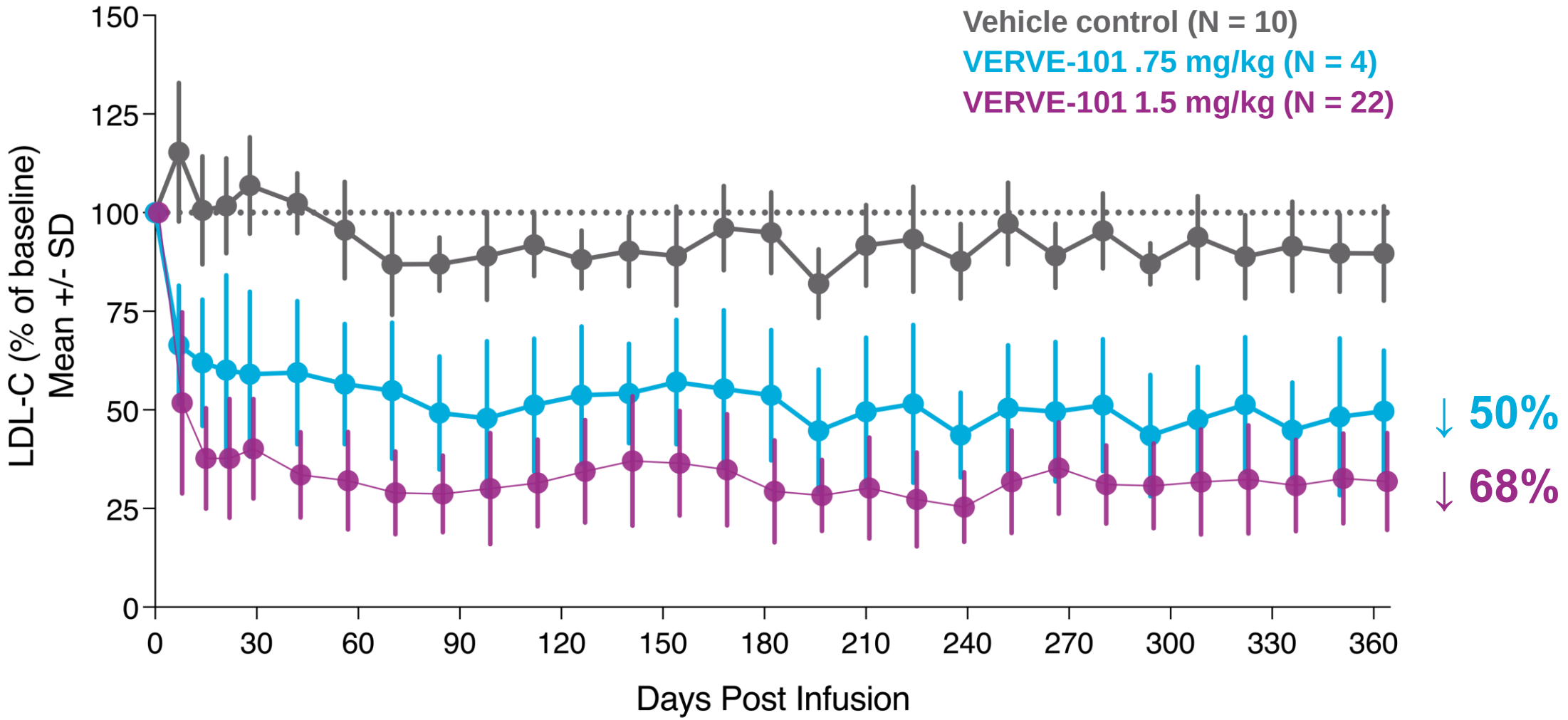
Safety endpoints

1. Liver function testing
2. Glucose homeostasis

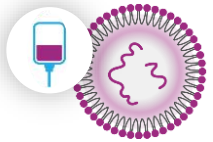
Blood PCSK9 level: 89% reduction observed at one year after one-time intravenous infusion of VERVE-101 in non-human primates (NHPs)



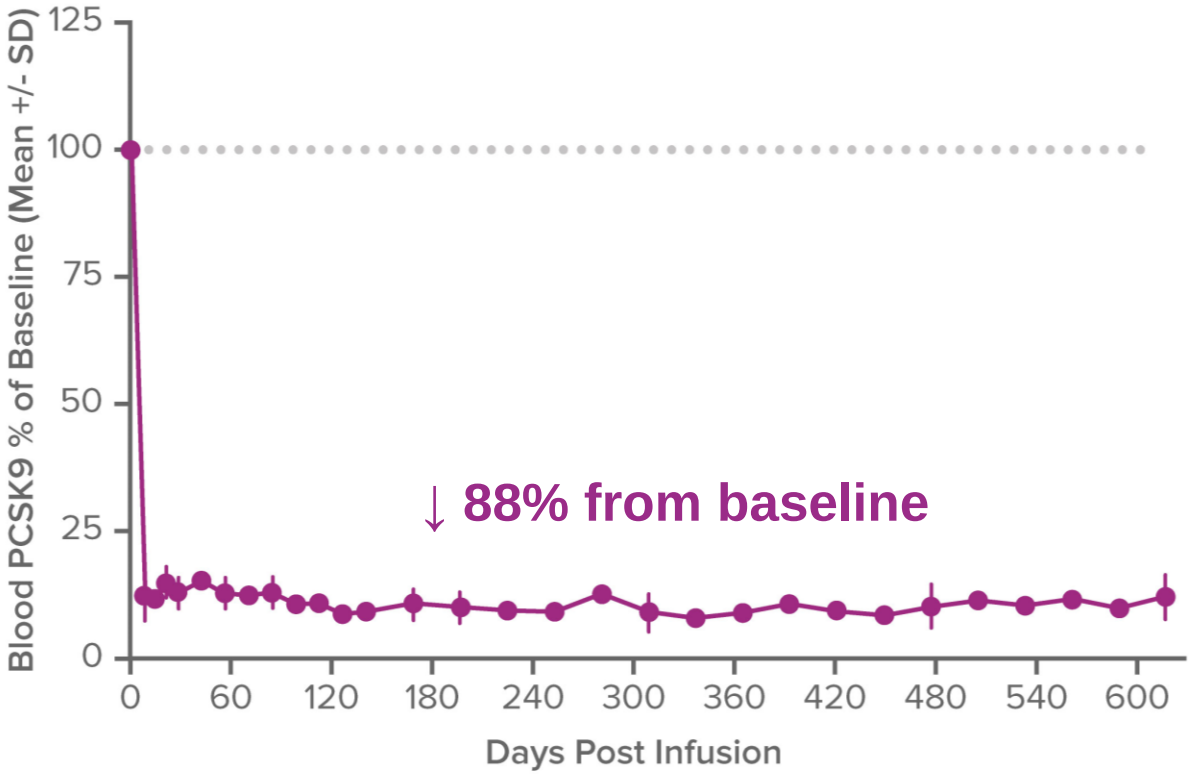
Blood LDL-C level: 68% reduction observed at one year after one-time intravenous infusion of VERVE-101 in NHPs

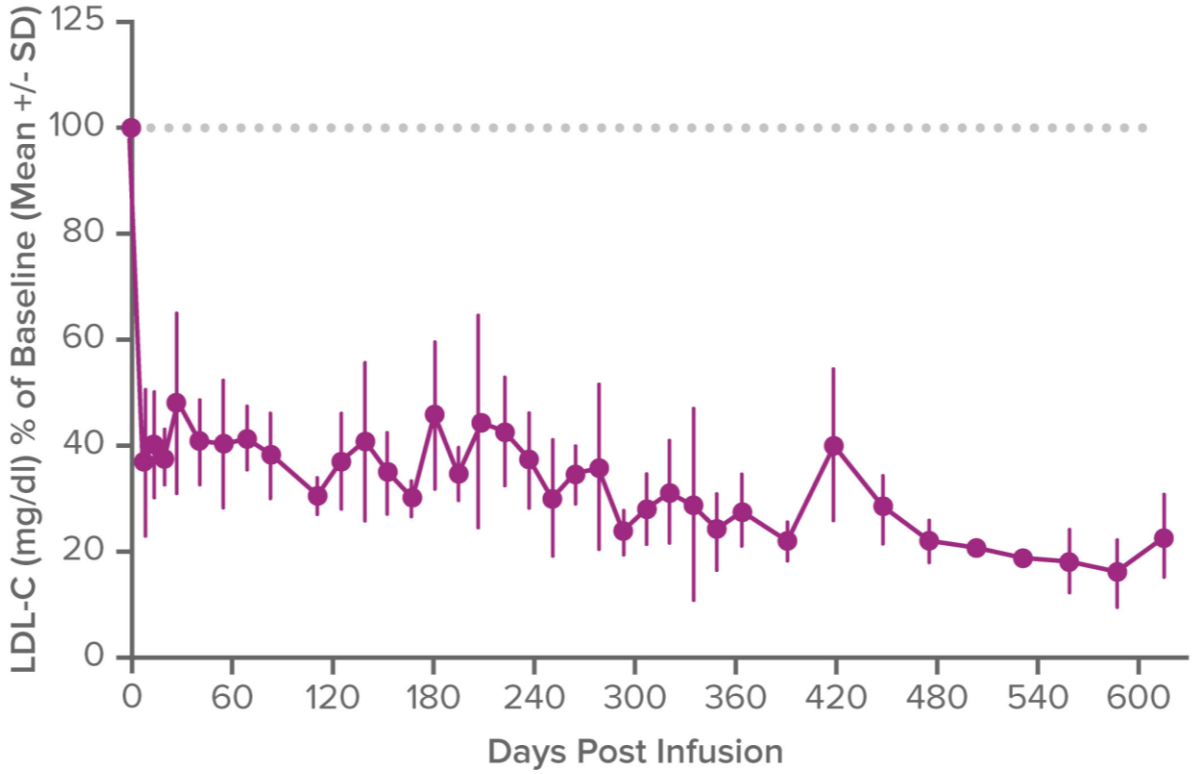


Even longer durability of PCSK9 and LDL-C reductions with precursor formulation, now out to 20 months in NHPs



VERVE-101 Precursor
3.0 mg/kg
N = 4





Multiple orthogonal techniques have been used to nominate ~3000 candidate off-target sites

entire human genome

identification techniques

Experimental: ABE-digenome-seq

Unbiased whole genome sequencing of liver genomic DNA treated with ABE in vitro

Experimental: ONE-Seq

library of ~30,000 barcoded sites with greatest sequence similarity to on-target site treated with ABE in vitro

Bioinformatics:

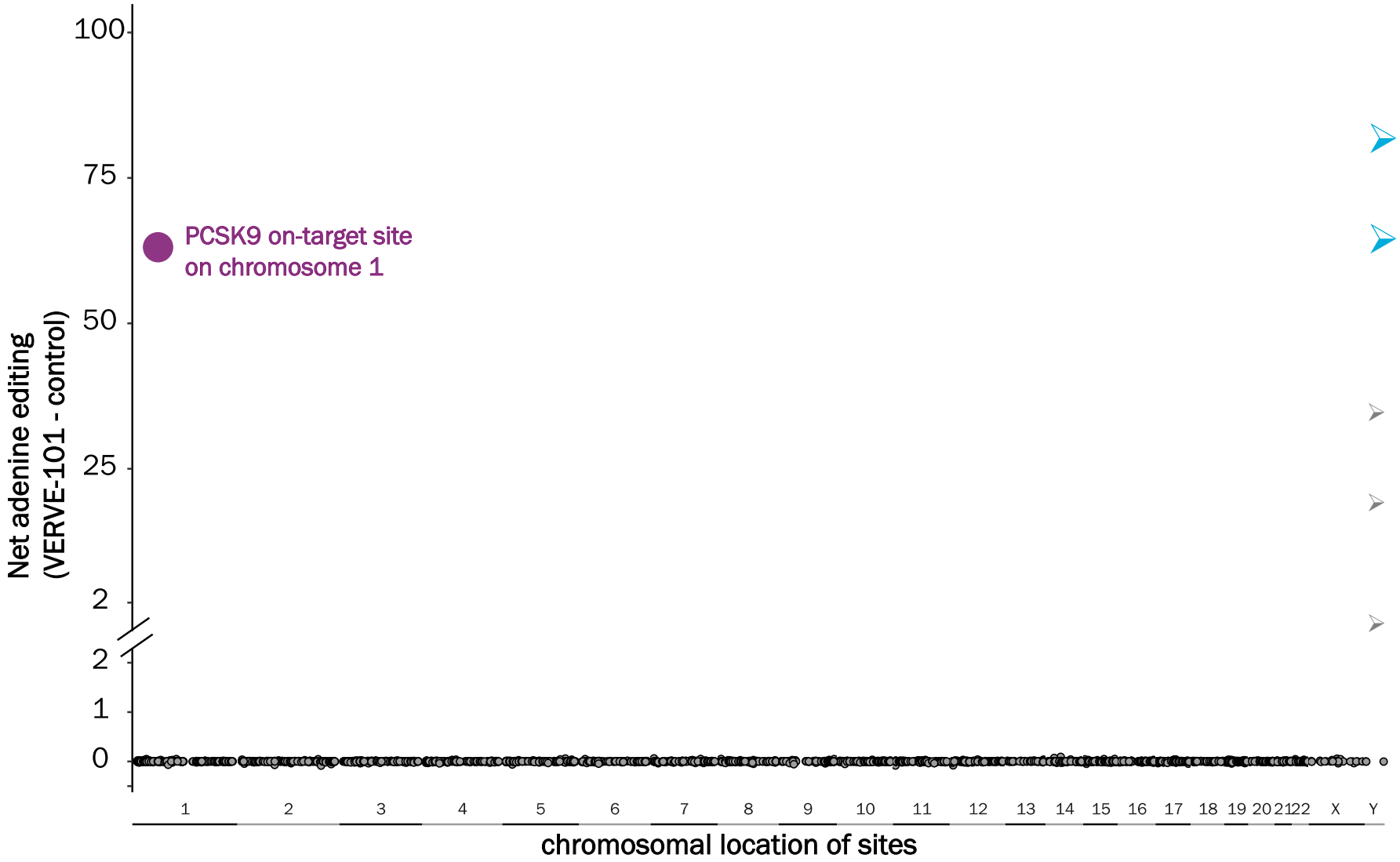
sites of greatest sequence homology

panel of candidates

3166 sites

across the human genome with the greatest experimental or bioinformatic similarity to the on-target site

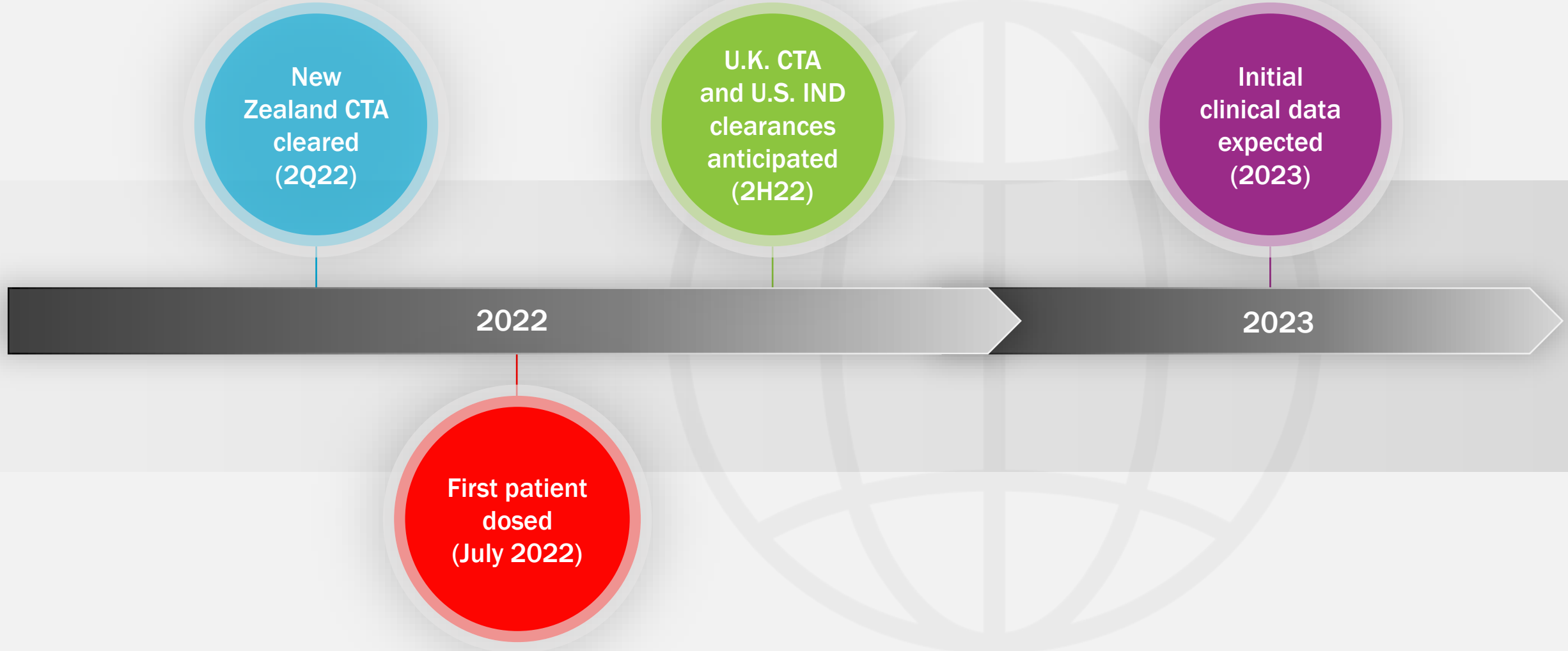
No observed significant off-target editing at ~3000 candidate sites in primary human liver cells treated with VERVE-101



- **Manhattan style plot of ~3000 candidate sites**
- **No candidate sites show statistically significant net editing**

- Y axis indicates net editing (alternate allele frequency in treated primary human hepatocytes - matched untreated controls)
- Logistic regression statistical test is performed at each candidate site comparing alternate read counts in treated cells versus untreated cells
- Sites of somatic variation seen in the untreated primary cells have been removed from the plot for clarity

VERVE-101: first human dosed with an investigational *in vivo* base editing medicine as a potential treatment for HeFH



heart-1 clinical trial: first-in-human Phase 1b clinical trial of VERVE-101

heart-1

~40 patients with HeFH
due to *LDLR* mutation, ASCVD, LDL-C ≥ 100 mg/dl on oral standard of care (SOC) therapy

PART A Single Ascending Dose

- High dose
- Intermediate dose
- Low dose
- Starting dose

3-6 participants per group with staggering and sentinel dosing

PART B Expansion Cohort

12 to 20 *additional* participants get one selected dose

PART C Optional Second Dose Cohort

Second dose offered to a subset of participants in part A who received a lower dose than participants in part B

Study Timing

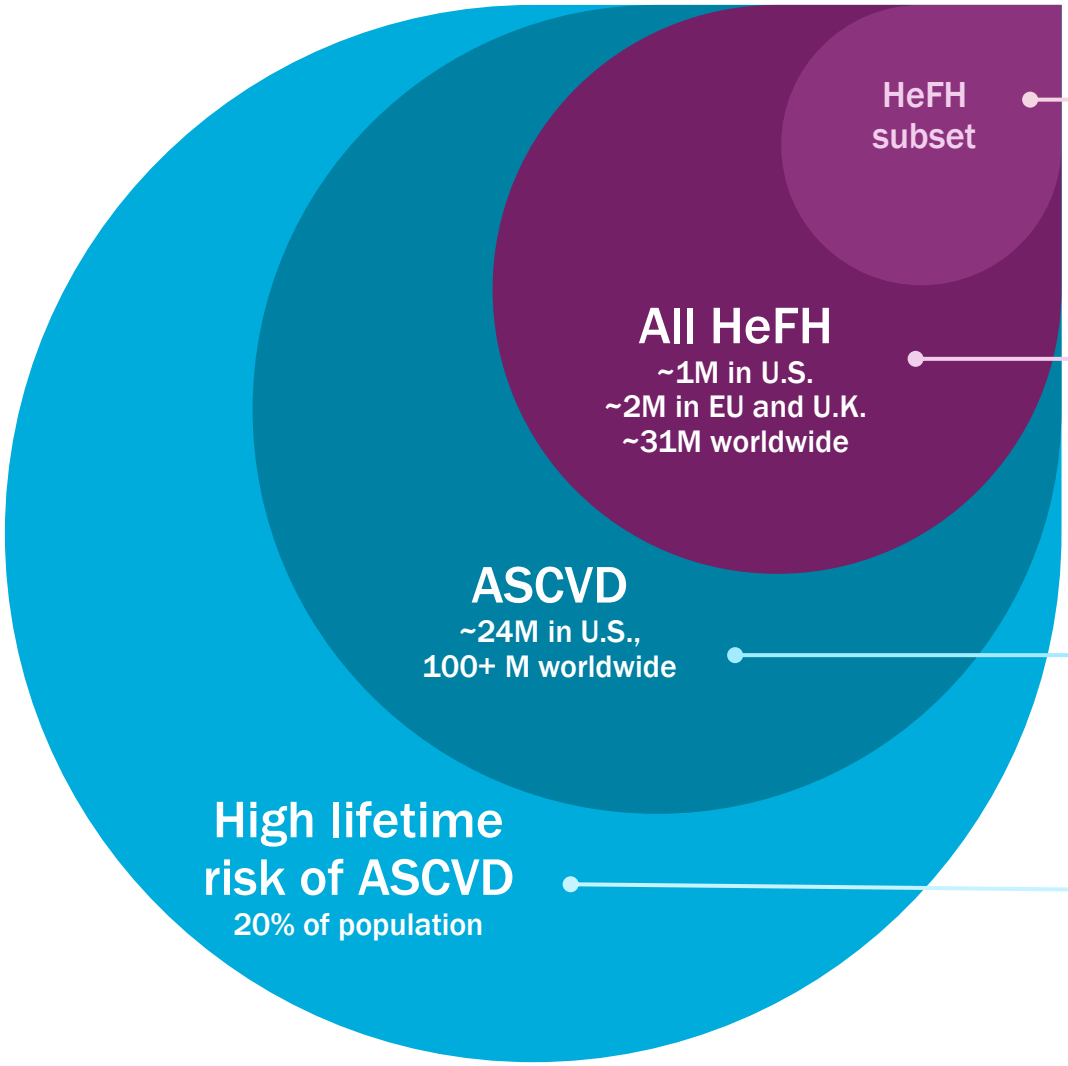
VERVE-101 IV administration

3-months

End of interventional study

Periodic interim analyses of 3-month data expected to enable early readouts of:
Safety and tolerability // Blood PCSK9 reduction // LDL-C, apolipoprotein B (apoB) reduction

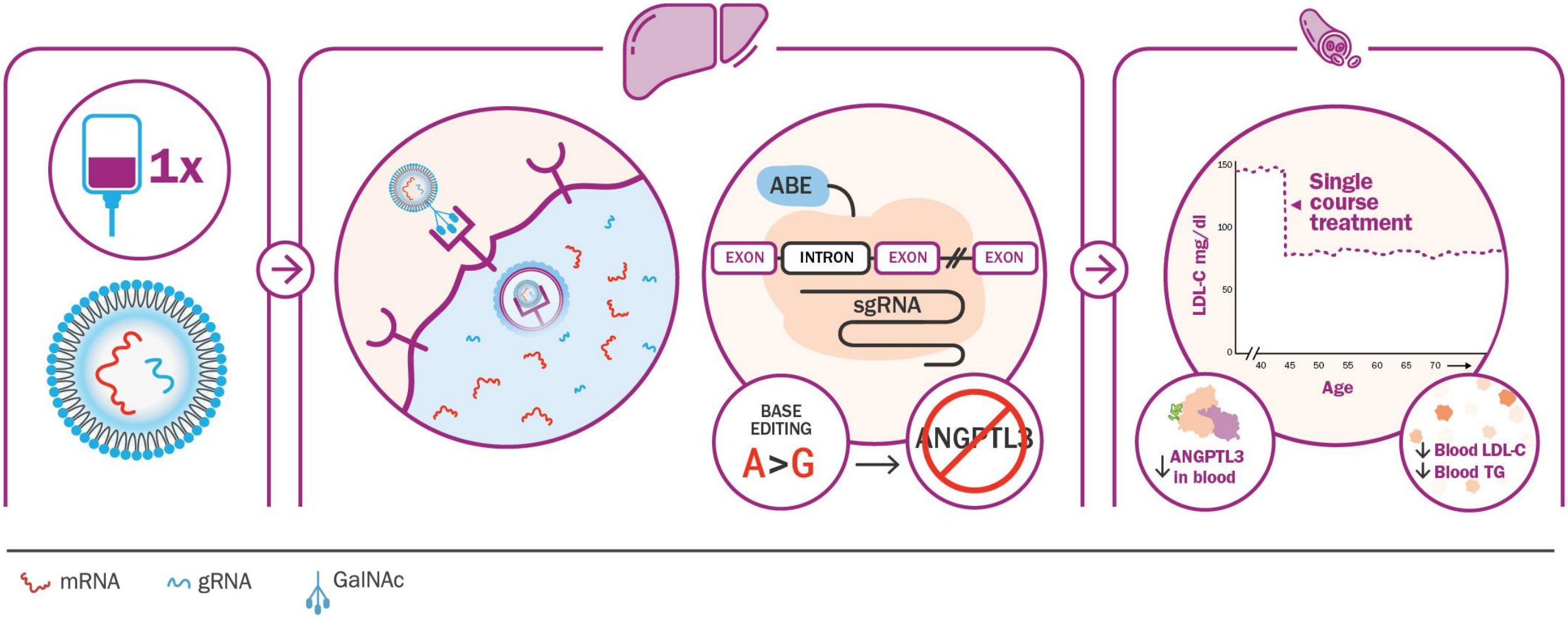
Stepwise clinical development strategy starting with HeFH and potential to expand to broader population with ASCVD



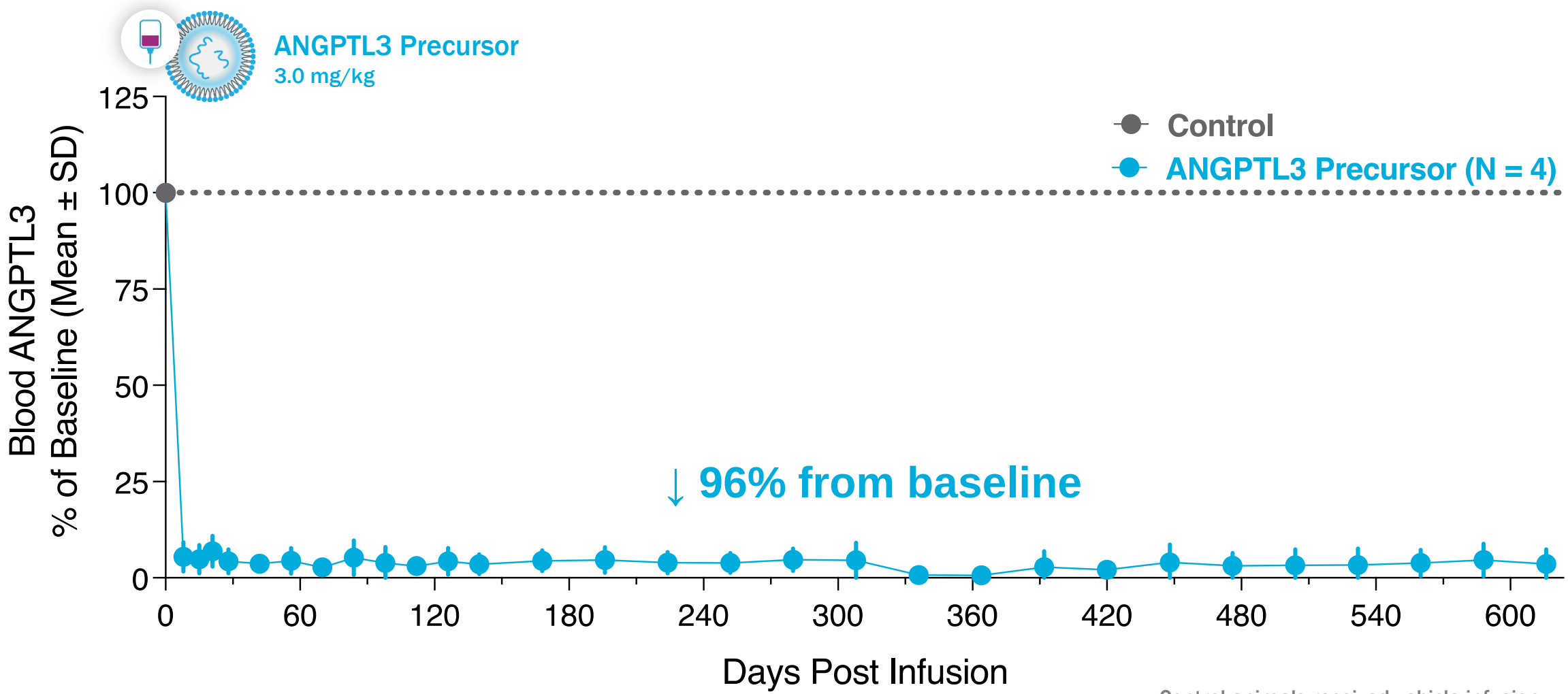
- Phase 1b proof-of-concept in high-risk HeFH
- Phase 2 in all HeFH
- Pivotal Phase 3 in all HeFH
- Pivotal Phase 3 in ASCVD
- Post-approval studies including cardiovascular outcome study in ASCVD

Advancing ANGPTL3 program to IND-enabling studies in 2H 2022

Goal: ANGPTL3 program turns off gene with base editing to lower LDL-C and treat ASCVD



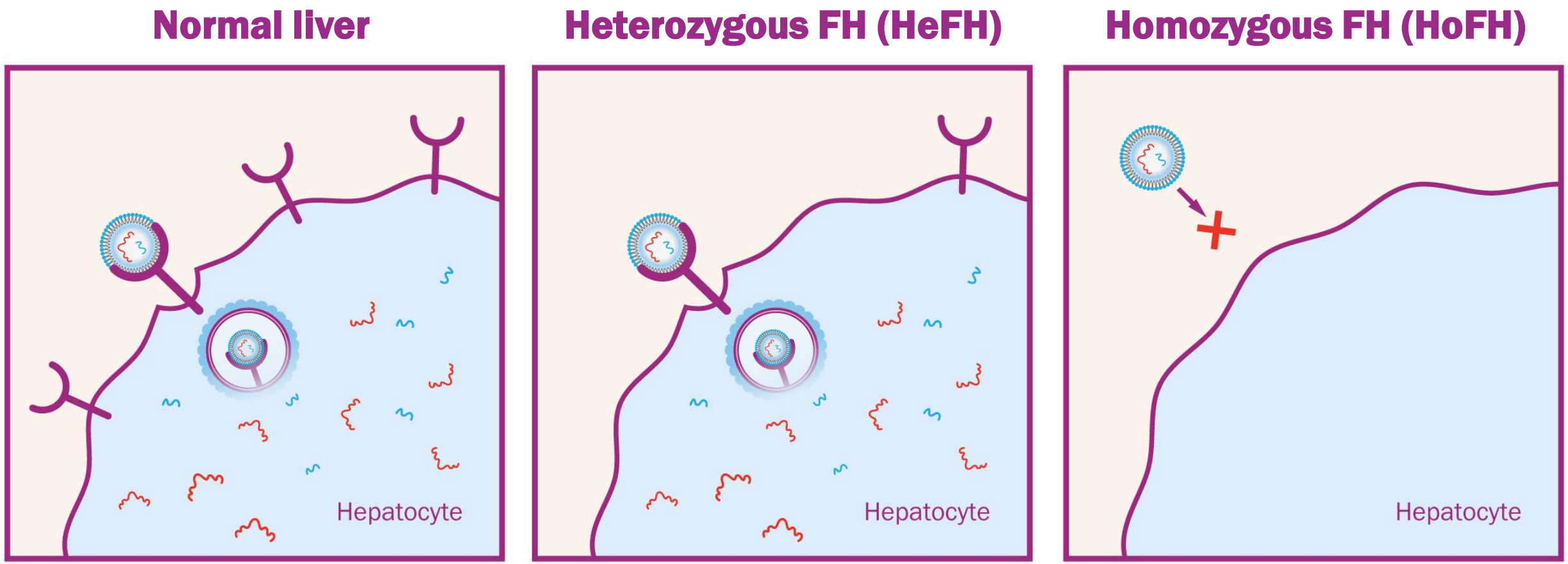
Verve ANGPTL3 precursor administered to NHPs:
616 days following infusion, durable >90% reduction in blood ANGPTL3



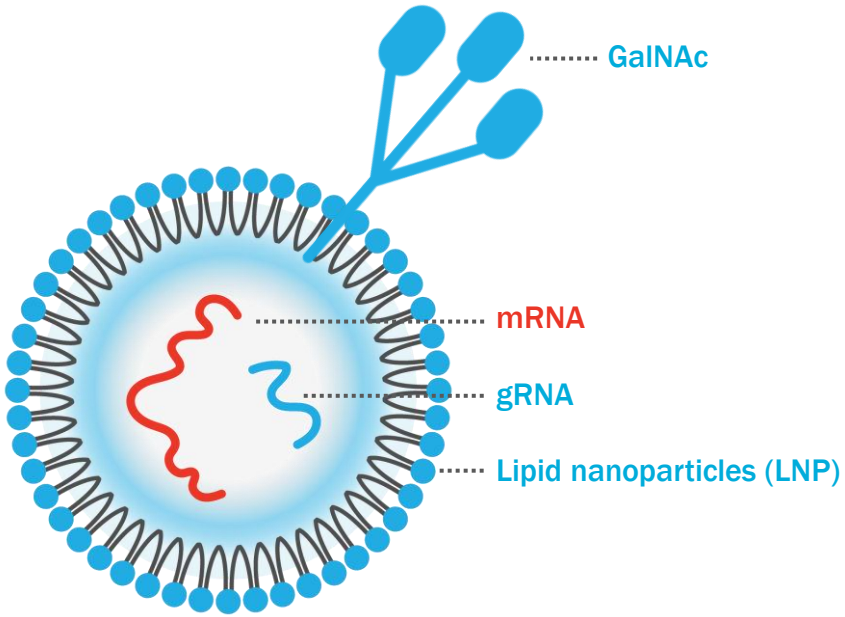
Control animals received vehicle infusion

Novel GalNAc-LNP delivery technology platform

Delivery challenge: HoFH patients completely lack LDL receptor; in this setting, standard LNPs don't work

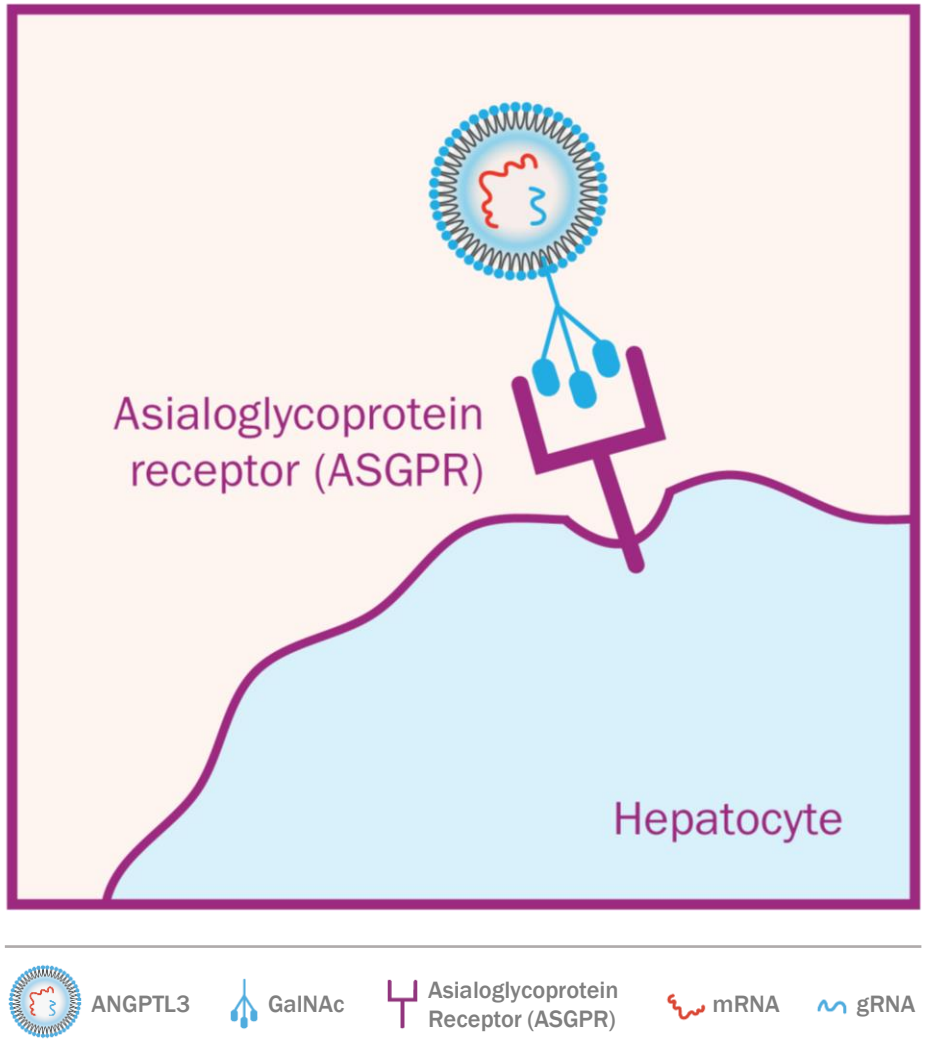


Proprietary GalNAc-LNP technology: potential best-in-class for delivery of genetic medicines to liver



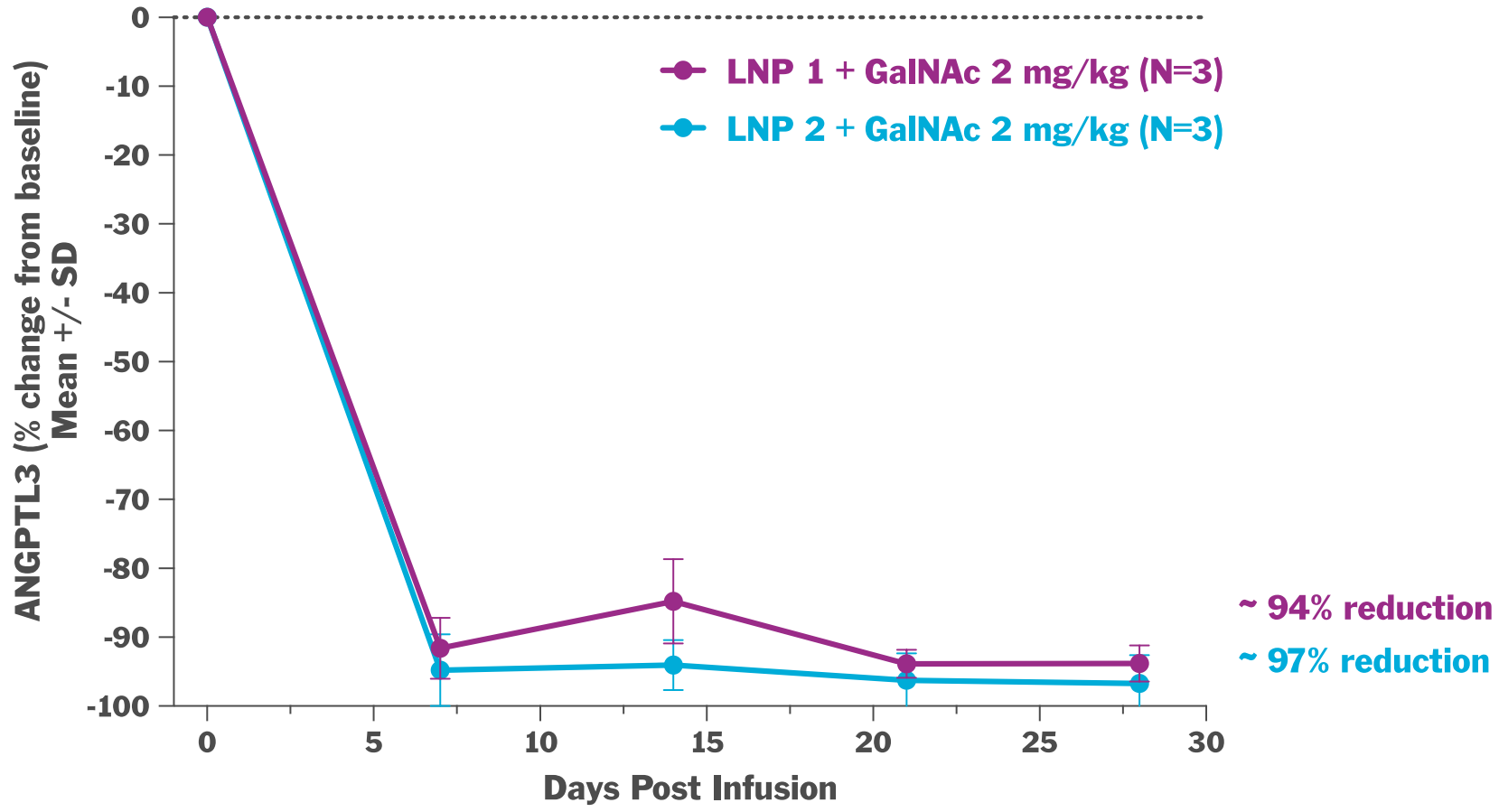
United States Patent
Rajeev et al.

Patent No.: US 11,207,416 B2
Date of Patent: Dec. 28, 2021



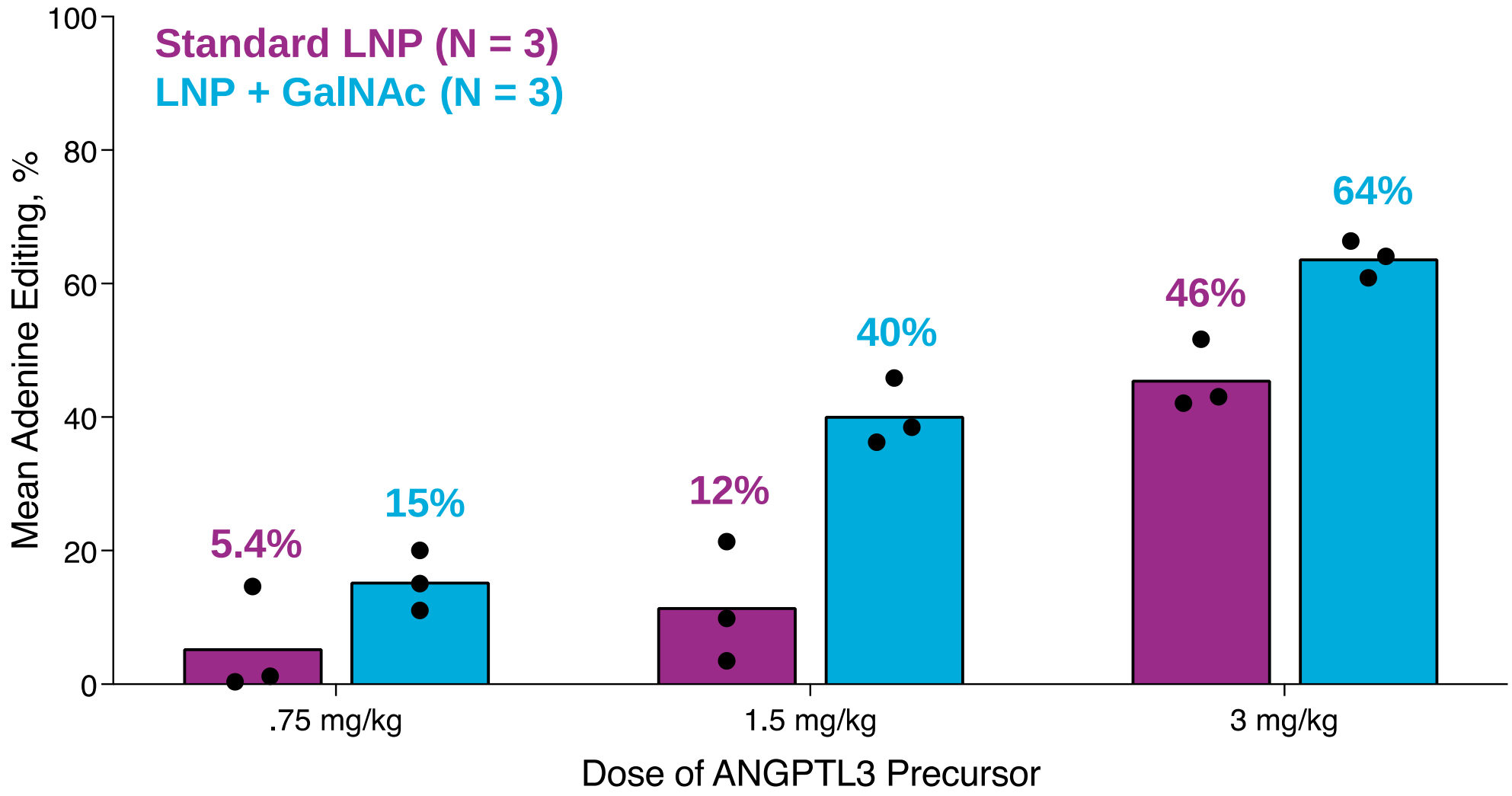
Base editing of ANGPTL3 via GalNAc-LNPs reduced blood ANGPTL3 by 94% - 97% in NHP model of HoFH

GalNAc LNPs (encapsulating ABE-ANGPTL3 base editing payload) dosed to HoFH NHPs that have stable disruption of liver LDLR protein and markedly elevated LDL-C

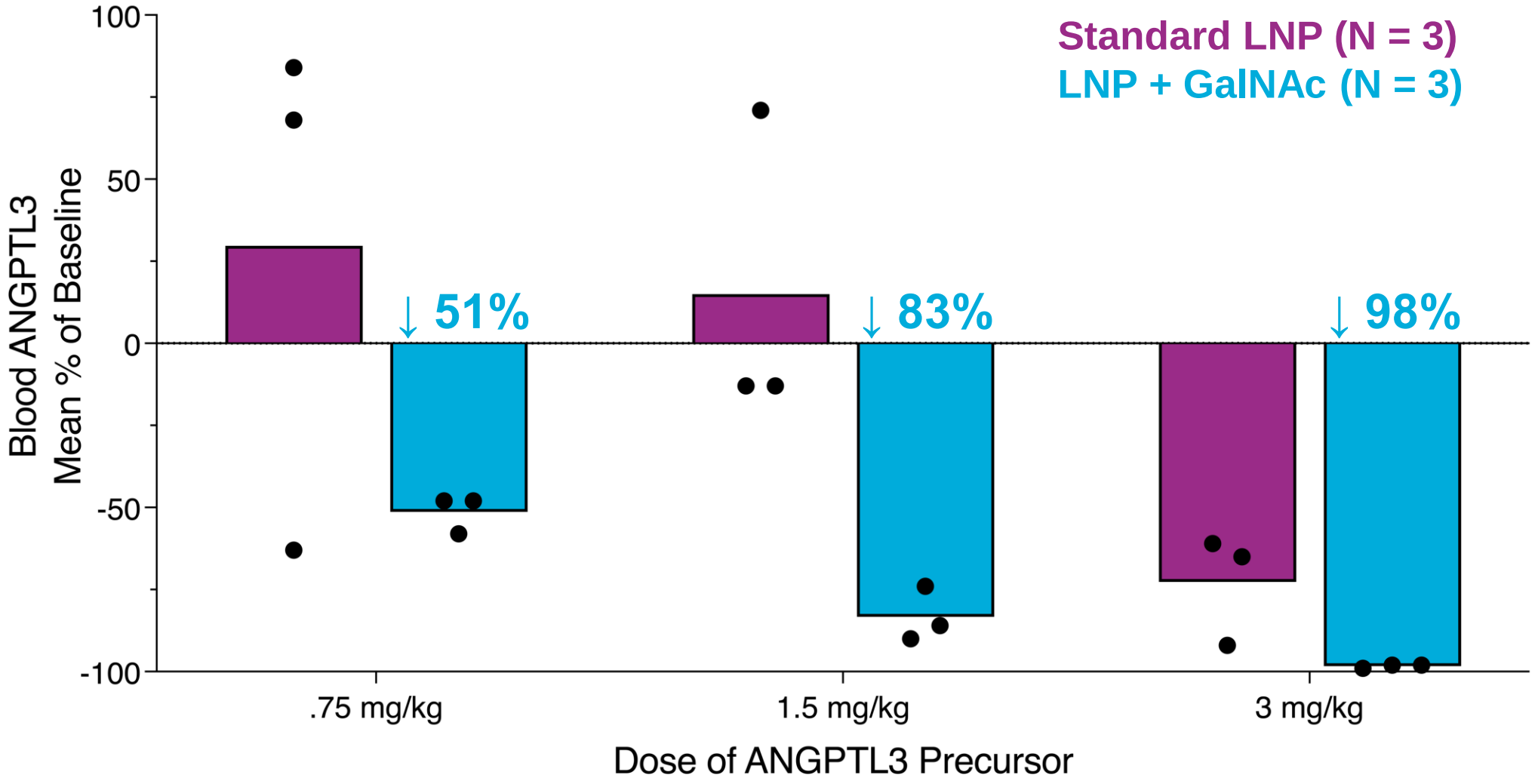


Hypothesis: In wild-type NHPs, GalNAc-LNP is more potent when compared with standard LNP

In wild-type NHPs, GalNAc-LNP led to greater ANGPTL3 editing potency compared with standard LNP



In wild-type NHPs, GalNAc-LNP led to up to 98% reduction in blood ANGPTL3, reflecting improved consistency compared with standard LNP

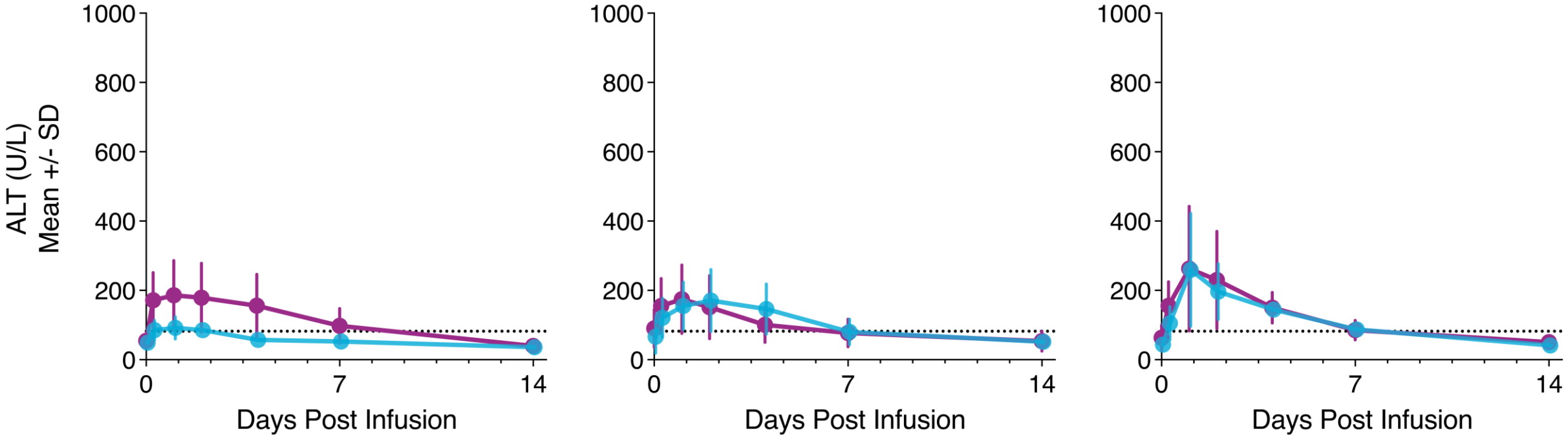


Addition of GalNAc to LNP did not alter safety profile: transient impact on alanine aminotransferase

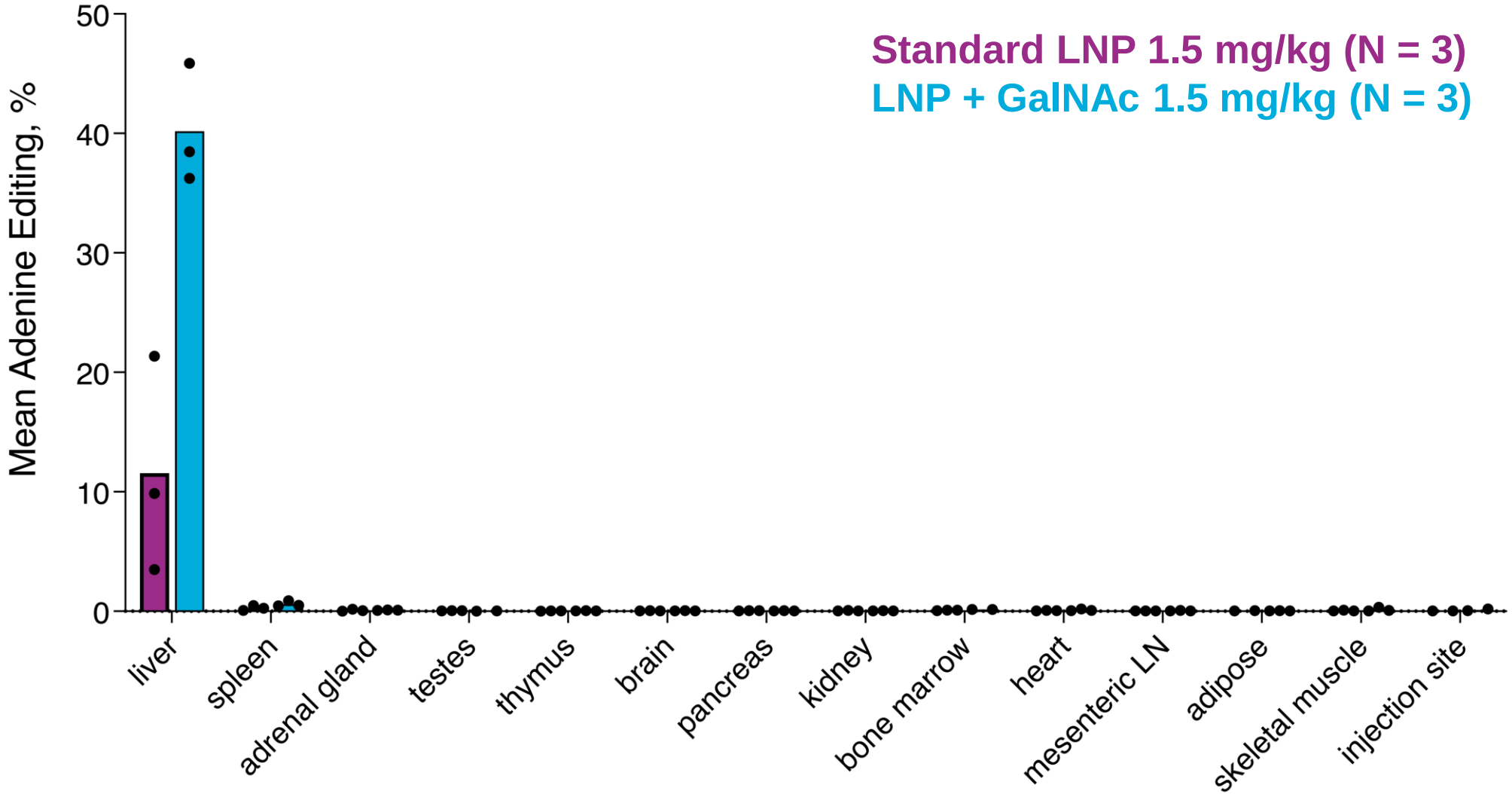
Standard LNP 0.75 mg/kg (N = 3)
LNP + GalNAc 0.75 mg/kg (N = 3)

1.5 mg/kg (N = 3)
1.5 mg/kg (N = 3)

3.0 mg/kg (N = 3)
3.0 mg/kg (N = 3)



Specific delivery to the liver with GalNAc-LNP



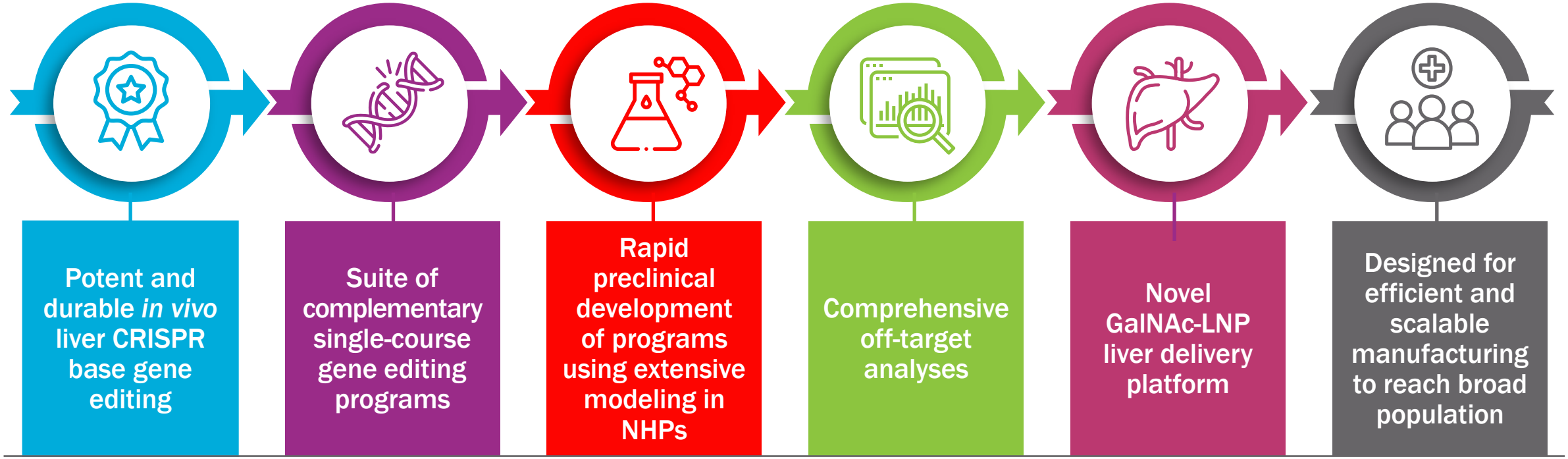
A world-class team to nimbly solve problems

The Boston Globe
TOP PLACES TO WORK 2021
MASSACHUSETTS

BOSTON BUSINESS JOURNAL
BPtW
2021 BEST PLACES TO WORK

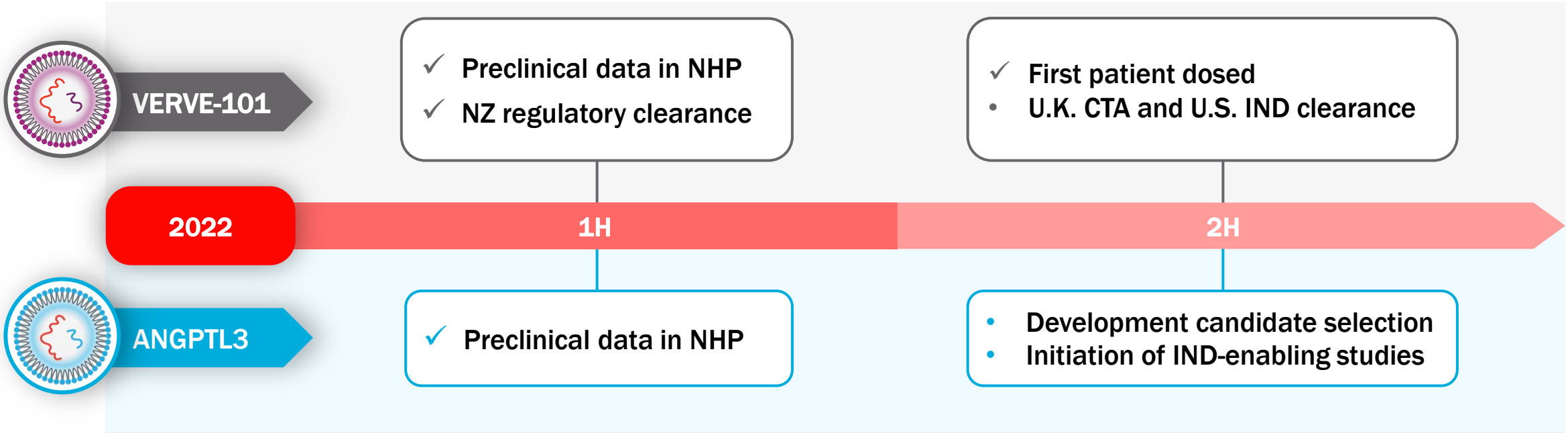
BOSTON BUSINESS JOURNAL
BPtW
2020 BEST PLACES TO WORK

A platform aiming to transform the treatment of cardiovascular disease…



…from chronic management to single-course gene editing medicines

Key milestones



<u>Milestones anticipated over next 6-12 months:</u>

1. U.K. CTA clearance (2H 2022)
2. U.S. IND clearance (2H 2022)
3. Nomination of development candidate for ANGPTL3 program (2H 2022)
4. Initiation of IND-enabling studies for ANGPTL3 program (2H 2022)
5. Interim clinical data for VERVE-101 heart-1 trial (2023)