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

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<td>Heterozygous Familial Hypercholesterolemia (HeFH) Overview and Unmet Need</td>
<td>Deepak Bhatt, M.D., M.P.H.</td>
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<td>Sekar Kathiresan, M.D.</td>
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**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. 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

Primordial, Primary, Secondary Prevention

- **HEALTH BEHAVIORS**
  - Fetal and infant health
  - Smoking
  - High-caloric diets
  - Physical inactivity
  - Non-ideal body weights
  - Environmental pollution

- **RISK FACTORS**
  - Dyslipidemia
  - Hypertension
  - Diabetes
  - Metabolic syndrome

- **CARDIOVASCULAR DISEASE**
  - Coronary heart disease
  - Cerebrovascular disease
  - Peripheral vascular disease
  - Heart failure

- **Prevention Levels**
  - Primordial prevention
  - Primary prevention
  - Secondary prevention

“Cholesterol-Years” for CV Risk Prediction and Treatment

- Severe hypercholesterolemia from birth (FH)
- Moderate hypercholesterolemia starting in teens (genetics, lifestyle)
- Modest hypercholesterolemia from adulthood (lifestyle)
- Threshold for onset of ASCVD
- Lifelong low LDL-C (genetics, excellent lifestyle, initiation of LDL-lowering therapy at an early age)
All-Cause Death by Baseline LDL-C

CI, confidence interval
Among US Adults with CAD

Almost 3 in 4 participants did not meet ACC/AHA 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

9 in 10 did not meet ESC guideline target
<table>
<thead>
<tr>
<th>2x2 Group</th>
<th>OR$_{CHD}$ (95% CI) per 10 mg/dL lower ApoB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both scores &gt; median</td>
<td>0.765 (0.717 - 0.816)</td>
</tr>
<tr>
<td>N = 104,694</td>
<td></td>
</tr>
<tr>
<td>LDLR score &gt; median</td>
<td>0.784 (0.690 - 0.892)</td>
</tr>
<tr>
<td>N = 112,018</td>
<td></td>
</tr>
<tr>
<td>LPL score &gt; median</td>
<td>0.770 (0.670 - 0.886)</td>
</tr>
<tr>
<td>N = 122,599</td>
<td></td>
</tr>
<tr>
<td>Both scores ≤ median</td>
<td>Reference</td>
</tr>
<tr>
<td>N = 131,167</td>
<td></td>
</tr>
</tbody>
</table>

CHD, coronary heart disease; OR, odds ratio
### Redefining Residual Risk in the Current Era

<table>
<thead>
<tr>
<th>Biological Issue</th>
<th>Residual Cholesterol Risk</th>
<th>Residual Inflammatory Risk</th>
<th>Residual Thrombotic Risk</th>
<th>Residual Triglyceride Risk</th>
<th>Residual Lp(a) Risk</th>
<th>Residual Diabetes Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical Biomarker</td>
<td>LDL-C ≥100 mg/dL</td>
<td>hsCRP ≥2 mg/L</td>
<td>No simple biomarker</td>
<td>TG ≥150 mg/dL</td>
<td>Lp(a) ≥50 mg/dL</td>
<td>HbA1c Fasting glucose</td>
</tr>
<tr>
<td>Potential Intervention</td>
<td>Targeted LDL/Apo B Reduction</td>
<td>Targeted Inflammation Reduction</td>
<td>Targeted Antithrombotic Reduction</td>
<td>Targeted Triglyceride Reduction</td>
<td>Targeted Lp(a) Reduction</td>
<td>SGLT2 Inhibitors GLP-1 Agonists</td>
</tr>
<tr>
<td>Randomized Trial Evidence</td>
<td>IMPROVE-IT FOURIER SPIRE ODYSSEY</td>
<td>CANTOS COLCOT LooDoCo2 OASIS-9</td>
<td>PEGASUS COMPASS THEMIS</td>
<td>REDUCE-IT PROMINENT</td>
<td>Planned</td>
<td>EMPA-REG CANVAS DECLARE CREDENCE LEADER SUSTAIN-6 REWIND</td>
</tr>
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</table>

Pyramid of Risk

SECONDARY AND TERTIARY PREVENTION
- CVD
- CAD
- PVD
- Heart Failure
- Cerebrovascular Disease

PRIMARY PREVENTION
- Risk Factors
  - Dyslipidemia
  - Hypertension
  - Diabetes
  - Metabolic Syndrome

PRIMORDIAL PREVENTION
- Health Behaviors
  - Fetal and Infant Health
  - Smoking
  - Physical Activity
  - Body Weight
  - Environmental Pollution
  - Diet

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

<table>
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<th>American Heart Association Diagnostic Criteria</th>
<th>Monogenic or polygenic</th>
<th>≥190 mg/dl</th>
<th>30-60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>High LDL-C + Family history (of high LDL-C or premature ASCVD)</td>
<td></td>
<td></td>
<td></td>
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</table>

>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:

- **LDL**
- **TRL**
- **Lp(a)**

Cholesterol carried in 3 lipoproteins:

- **Cholesterol**
- **Triglycerides**
What causes ASCVD and what’s a solution?

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

Cholesterol carried in 3 lipoproteins:
- LDL
- TRL
- Lp(a)

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.
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?

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

---

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

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
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.

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

Data cut-off date October 16, 2023

- 0.1 mg/kg (n=3)
- 0.3 mg/kg (n=3)
- 0.45 mg/kg (n=3)
- 0.6 mg/kg (n=1)

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

<table>
<thead>
<tr>
<th>STUDY POPULATION SUMMARY</th>
<th>DRUG ADMINISTRATION</th>
<th>TRIAL ENDPOINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Males and females² (age 18 to 75)</td>
<td>• Pre-medication with dexamethasone and antihistamines</td>
<td>• Primary: Safety and tolerability</td>
</tr>
<tr>
<td>• HeFH</td>
<td>• VERVE-101 delivered as single infusion via a peripheral IV⁵</td>
<td>• Additional endpoints:</td>
</tr>
<tr>
<td>• Established ASCVD</td>
<td></td>
<td>- Pharmacokinetics of VERVE-101</td>
</tr>
<tr>
<td>• Uncontrolled LDL-C³</td>
<td></td>
<td>- Blood PCSK9 and LDL-C levels, quantified as percent change from baseline, time averaged from day 28 onward</td>
</tr>
<tr>
<td>• On maximally-tolerated oral lipid-lowering therapy⁴</td>
<td></td>
<td>• Study duration 1y and long-term follow-up required by FDA for another 14y</td>
</tr>
</tbody>
</table>

Interim update: 10 participants treated across 4 dose cohorts¹

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (min, max)</td>
<td>54 (29, 69)</td>
</tr>
<tr>
<td>Sex, male, n</td>
<td>8</td>
</tr>
<tr>
<td>Mean screening LDL-C, mg/dL (min, max)</td>
<td>193 (107, 373)</td>
</tr>
<tr>
<td>Mutation in LDLR detected, n&lt;sup&gt;1&lt;/sup&gt;</td>
<td>9</td>
</tr>
</tbody>
</table>

**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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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

Mean (±SD) % change from baseline

Time (days)

0 14 28 60 90 180

0.1 mg/kg 0.3 mg/kg 0.45 mg/kg 0.6 mg/kg

Participants, n

0.1 mg/kg 3 3 3 3 3
0.3 mg/kg 3 3 3 3 2
0.45 mg/kg 2 2 2 2 1
0.6 mg/kg 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

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

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

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<td>1</td>
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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 serious adverse event

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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Cardiovascular events, n</td>
<td>0</td>
<td>0</td>
<td>1(^a)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Increased liver transaminases, n</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1(^b)</td>
<td>1</td>
</tr>
</tbody>
</table>

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

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

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

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)
  - Ischemic cardiomyopathy at baseline & prior cardiac arrest
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- MI and non-sustained ventricular tachycardia (NSVT) (DOSE 0.45 MG/KG)
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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
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
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.
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

<table>
<thead>
<tr>
<th>TARGET</th>
<th>INDICATION</th>
<th>TECHNOLOGY</th>
<th>DEVELOPMENT STATUS</th>
<th>RIGHTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCSK9 (VERVE-101)</td>
<td>Heterozygous familial hypercholesterolemia</td>
<td>Base Editor</td>
<td>IND-enabling</td>
<td>verve, Lilly</td>
</tr>
<tr>
<td>PCSK9 (VERVE-102)</td>
<td>Heterozygous familial hypercholesterolemia</td>
<td>Base Editor</td>
<td>IND-enabling</td>
<td>verve, Lilly</td>
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<tr>
<td>ANGPTL3 (VERVE-201)</td>
<td>Homozygous familial hypercholesterolemia</td>
<td>Base Editor</td>
<td>IND-enabling</td>
<td>verve, Lilly</td>
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<tr>
<td>LPA</td>
<td>ASCVD patients with high blood Lp(a)</td>
<td>Novel Editor</td>
<td>IND-enabling</td>
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<td>Undisclosed</td>
<td>Undisclosed ASCVD</td>
<td>Base Editor</td>
<td>IND-enabling</td>
<td>verve, Lilly</td>
</tr>
<tr>
<td>Undisclosed</td>
<td>Undisclosed liver disease</td>
<td>Novel Editor</td>
<td>IND-enabling</td>
<td>verve, Lilly</td>
</tr>
</tbody>
</table>
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

- 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

- Vehicle Control (N=4)
- VERVE-102 3 mg/kg (N=4)

↓ 62%
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

#### PCSK9 PROGRAM

- Complete enrollment in two high dose cohorts (Part A)
- Enroll in expansion cohort (Part B)
- Identify doses for potential Phase 2

- VERVE 102

#### ANGPTL3 PROGRAM

- Initiate Phase 1 1H 2024, enroll dose escalation phase

- VERVE 201

### Anticipated milestones 2025

#### PCSK9 PROGRAM

- Clinical data for VERVE-102
- Select VERVE-101 or -102 and initiate a randomized, controlled Phase 2 for PCSK9 program

#### Rest of pipeline: Progress pre-clinical collaboration programs

- Subject to regulatory clearance
- Initiate clinical trial in 2H 2024

- VERVE 101

- VERVE 102

**Note:**
- PCSK9 PROGRAM
- ANGPTL3 PROGRAM
- Rest of pipeline: Progress pre-clinical collaboration programs with Lilly (LPA) and Vertex (undisclosed liver-disease target)
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
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