



# Corporate Presentation

January 2024

# Forward-Looking Statements

This presentation contains statements about our future expectations, plans and prospects that constitute forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including risks relating to: both our and our collaborators' ability to successfully research, obtain regulatory approvals for, develop and commercialize products based upon our technologies; our ability to obtain and maintain proprietary protection for our technologies and product candidates; our reliance on third parties to manufacture our preclinical and clinical drug supplies; competitive pressures; our ability to obtain and maintain strategic collaborations; compliance with our in-license agreements; our ability to successfully execute on, and receive favorable results from, our proprietary drug development efforts; market acceptance of our drug candidates; retaining members of our senior management; and our ability to raise additional funds to finance our operations.



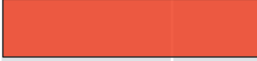
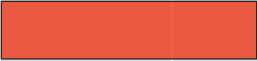
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For more information regarding risks and uncertainties that could affect the results of our operations or financial condition review our filings with the Securities and Exchange Commission (in particular, our most recent Annual Report on Form 10-K and any subsequently filed Quarterly Reports on Form 10-Q).

# Investment Highlights

- **Developing novel therapeutics for metabolic and endocrine diseases**
  - Multiple clinical programs demonstrate best-in-class efficacy data
- **Metabolic Disease Programs**
  - VK2809: Novel, selective thyroid receptor- $\beta$  agonist for NASH and lipid disorders
    - Phase 2b VOYAGE trial successfully achieved primary endpoint; histology data expected 1H24
  - VK2735: Novel GLP-1/GIP dual agonist for obesity
    - Phase 2 VENTURE obesity study ongoing, fully enrolled; data expected 1H24
  - VK2735 Oral: GLP-1/GIP dual agonist for metabolic disorders
    - Phase 1 study ongoing; data expected 1Q24
- **Rare Disease Program**
  - VK0214: Novel, selective thyroid receptor- $\beta$  agonist for X-ALD
    - Phase 1b ongoing

# Pipeline Overview

Development Programs	Indication	Stage of Development				Status
		Preclin	Phase 1	Phase 2	Phase 3	
VK2809 (TR $\beta$ agonist)	<i>NASH</i>					Phase 2b VOYAGE trial ongoing
VK2735 (Dual GLP-1/GIP agonist)	<i>Obesity</i>					Phase 2 VENTURE study ongoing
VK2735 Oral (Dual GLP-1/GIP agonist)	<i>Metabolic disorders</i>					Phase 1 ongoing
VK0214 (TR $\beta$ agonist)	<i>X-ALD</i>					Phase 1b ongoing

## Potential data events expected over next six months

- o VK2809: VOYAGE Phase 2b biopsy results in NASH
- o VK2735: VENTURE Phase 2 obesity data
- o VK2735 Oral: Phase 1 data in healthy subjects
- o VK0214: Topline data, Phase 1b study in X-linked adrenoleukodystrophy



VK2809: Selective Thyroid Receptor- $\beta$  Agonist

NASH

# Metabolic Disease Program: Selective Thyroid- $\beta$ Agonists

- **Proprietary platform for small molecule thyroid hormone mimetics**
  - Highly tissue and receptor selective
  - Produce potent lipid reductions in animals and humans
  - Unique chemical scaffolds, expected wider safety window vs. other approaches
- **Biological profiles suggest potential benefit in multiple indications**
  - Large markets: NASH, hypercholesterolemia, dyslipidemia
  - Rare diseases: X-linked adrenoleukodystrophy (X-ALD), other
- **Lead program VK2809**
  - Oral formulation
  - Shown to be safe and well-tolerated in 8 completed clinical studies
  - Phase 2b VOYAGE trial ongoing

# Thyroid Hormone Receptor Overview

Nuclear hormone receptors: 2 main types

## Thyroid hormone receptor beta (TR $\beta$ )

Liver

### Positive effects

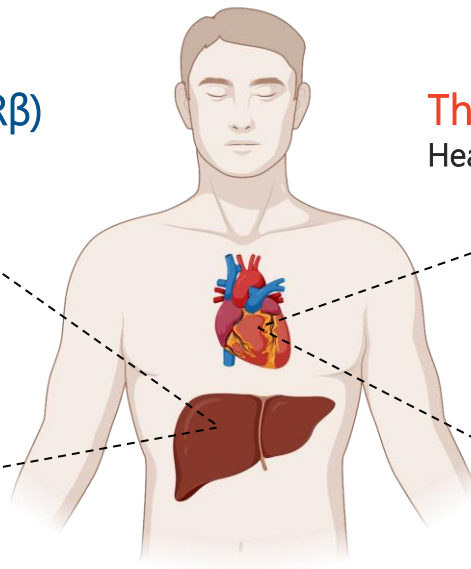
- Regulates lipid metabolism
- Reduces LDL-C, triglycerides, atherogenic proteins
- Improves metabolic control

## Thyroid hormone receptor alpha (TR $\alpha$ )

Heart, skeletal muscle

### Negative effects

- Proarrhythmic potential
- Elevates heart rate
- Bone/cartilage effects



Therapeutic goal, lipid setting: Beta receptor selectivity, minimize alpha effects

# Thyroid Receptor $\beta$ Agonists for NAFLD and NASH



- $\beta$ -Receptor: Key role in lipid metabolism; systemic and liver-specific effects
- Receptor localized to liver, limited ex-hepatic expression
- In vivo evidence suggests  $\beta$ -activation provides anti-fibrotic benefits
- Clinical data indicate correlation between reduced liver fat, improvement in NAS

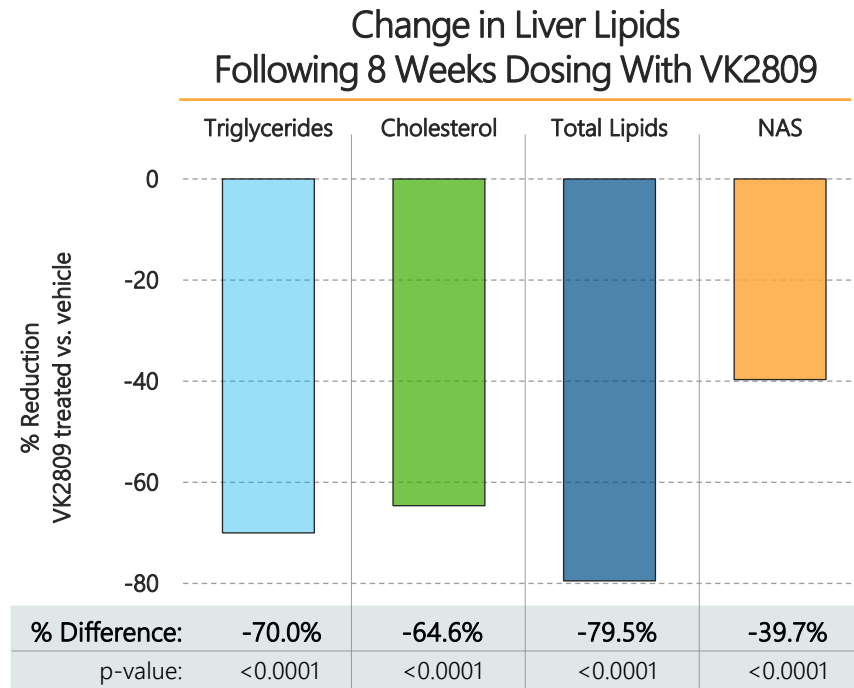
**An agent that reduces liver fat, improves systemic lipids, and antagonizes fibrotic signaling could provide multi-pronged benefits in NASH**





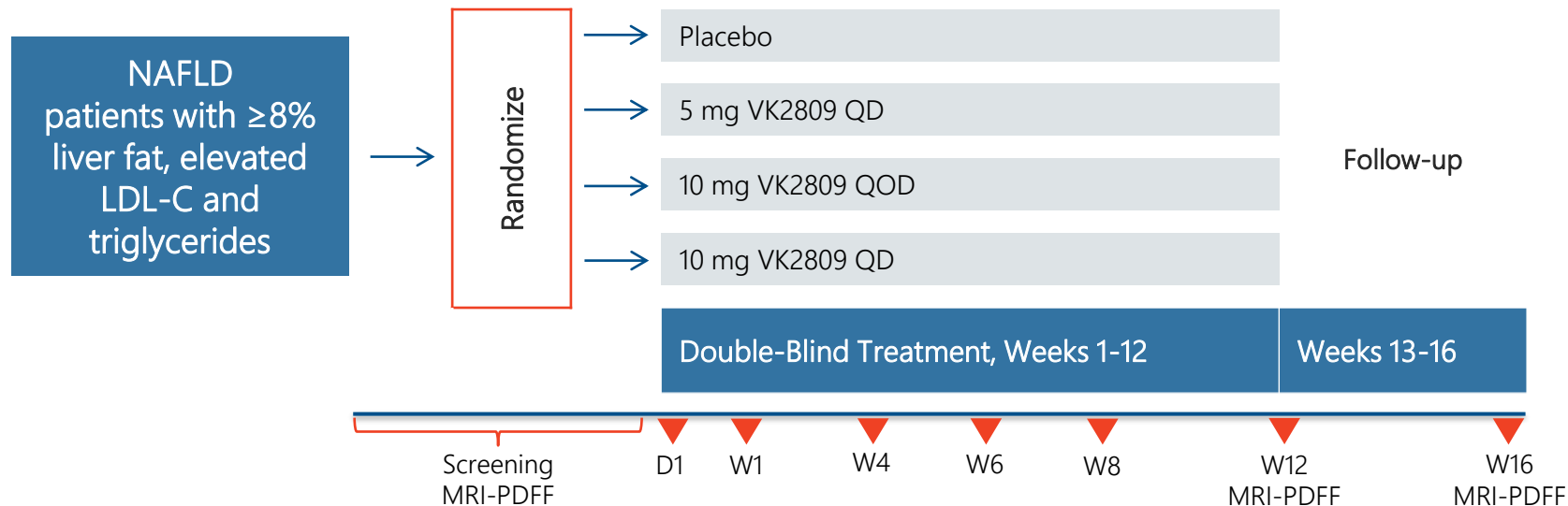
# VK2809 Significantly Reduces Steatosis in Diet-Induced NASH

- Evaluation in biopsy-confirmed diet-induced NASH model
  - Rodent model designed to reflect progression of disease in humans
  - Animals biopsied pre-study; only those with NASH *and* fibrosis selected
  - VK2809 dosed once-daily for 8 weeks



Treatment with VK2809 significantly improves lipids, steatosis, NAS at 8 weeks;  
well-tolerated with no evidence of toxicity

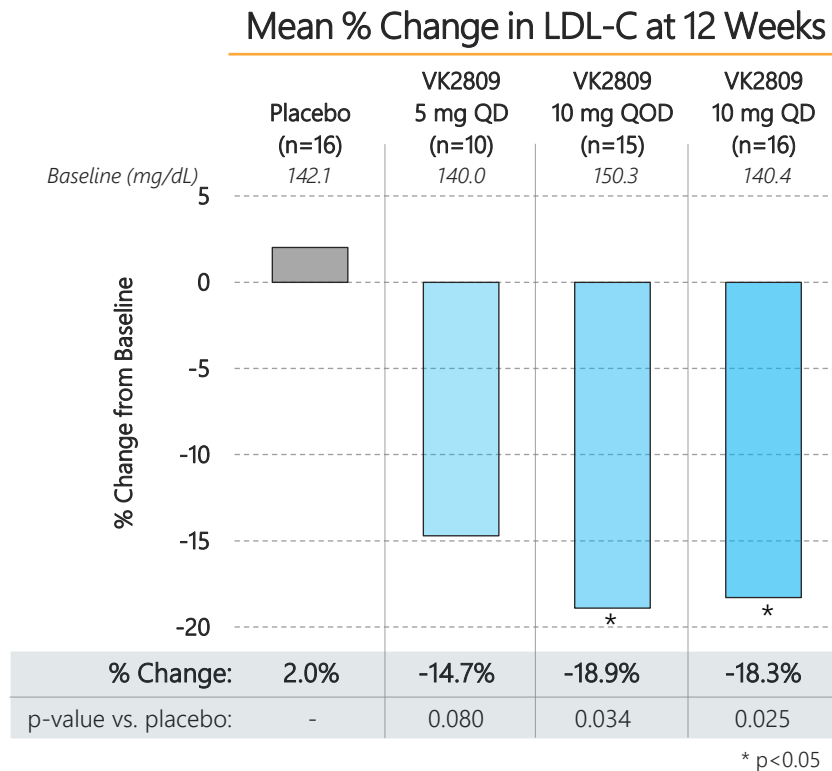
# VK2809-201: Phase 2a Study Design



- Multi-arm, dose-ranging, 12 week Phase 2a trial
  - **Primary endpoint:** Change in LDL-C vs. placebo
  - **Secondary endpoint:** Change in liver fat by MRI-PDFF
  - **Exploratory endpoints:** Changes in atherogenic proteins

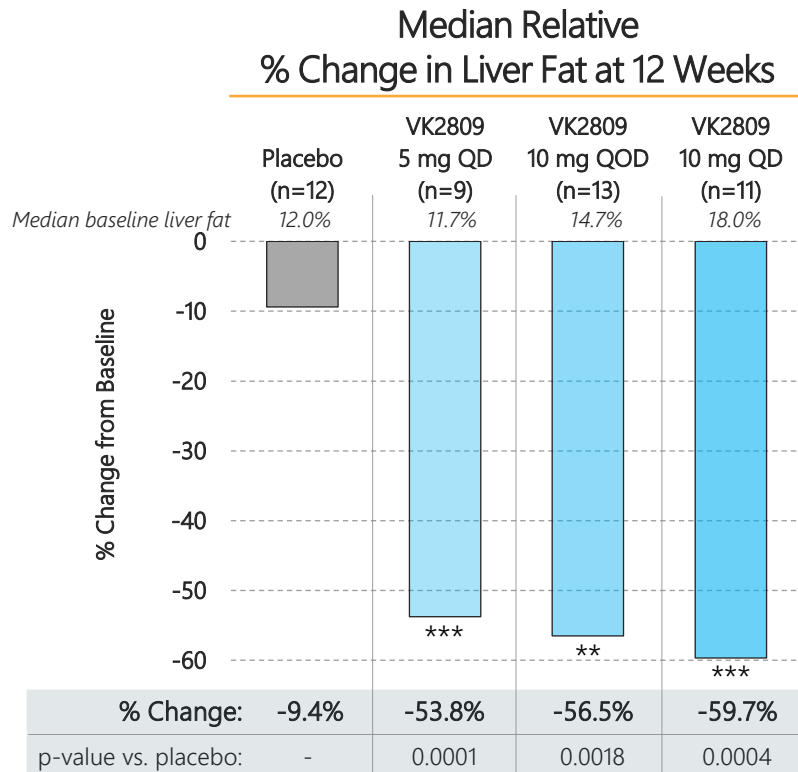
# VK2809 Significantly Reduced LDL-C at 12 Weeks

- Statistically significant reductions in all VK2809 cohorts vs. baseline
- Placebo-adjusted change from baseline
  - 5 mg QD: -23.7 mg/dL
  - 10 mg QOD: -27.1 mg/dL
  - 10 mg QD: -28.3 mg/dL



# VK2809 Produced Significant Relative Reductions in Liver Fat

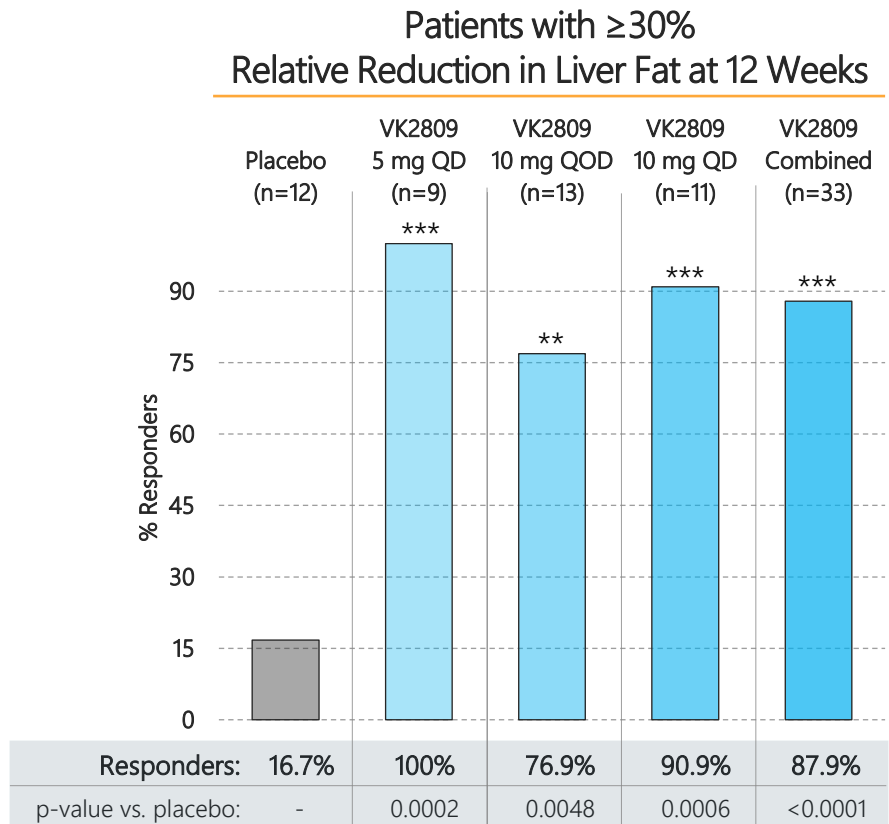
- Significant relative reductions from baseline in liver fat by MRI-PDFF
- Maximal reductions at Week 12
  - 5 mg QD: 78%
  - 10 mg QOD: 72%
  - 10 mg QD: 76%



\*p<0.05; \*\*p<0.01; \*\*\*p<0.001

# VK2809 Cohorts Demonstrated High Relative Response Rates

- Up to 100% of VK2809 patients experienced response, as defined by  $\geq 30\%$  decrease in liver fat at Week 12
- Combined VK2809 cohorts demonstrated 88% response rate
- 70% of all patients receiving VK2809 demonstrated liver fat reductions  $\geq 50\%$
- Reduction in liver fat correlated with improved odds of long-term histology benefit<sup>1</sup>



\*\*p<0.01; \*\*\*p<0.001

# VK2809-201: Encouraging Safety Profile Through 12 Weeks

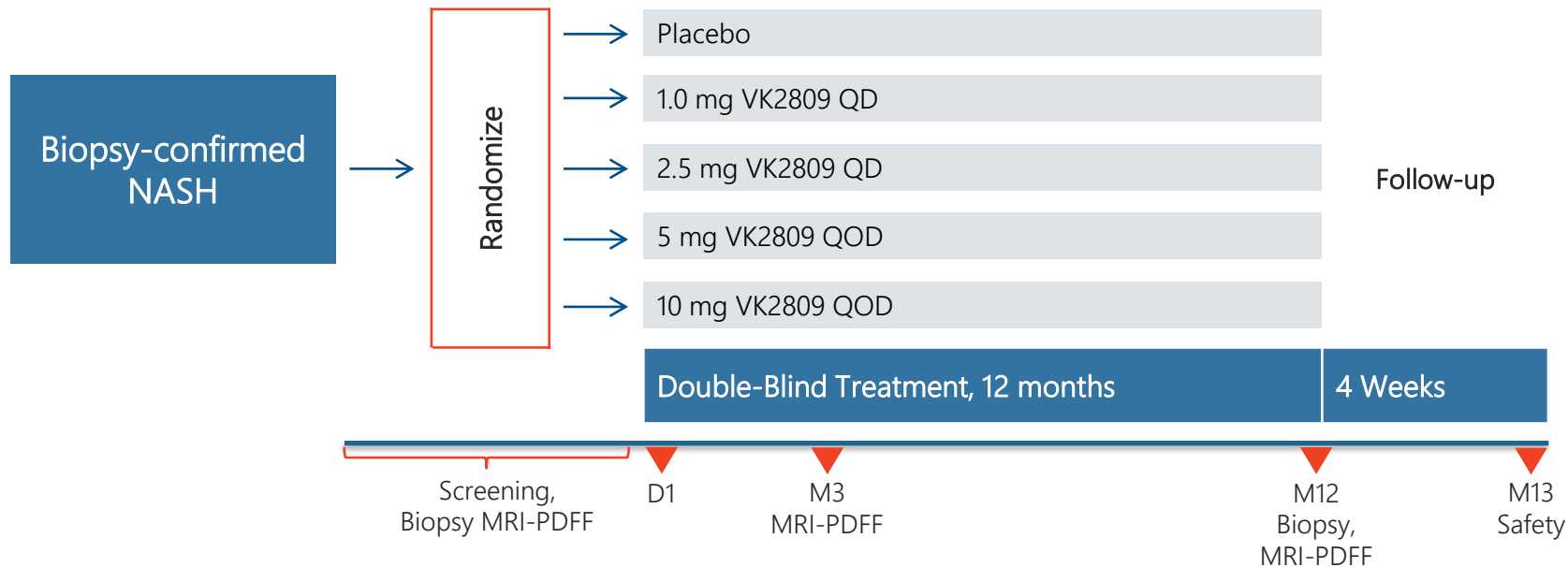
- |   |   |
|---|---|
| • No SAEs observed  | No SAEs reported in completed clinical studies to date  |
| • Mean ALT, AST levels in VK2809-treated subjects reduced relative to placebo at Week 12                  | Patients with elevated baseline ALT demonstrated greater improvement relative to placebo at Weeks 12 and 16                 |
| • No other liver function tests significantly different from placebo                                      | Direct bilirubin, indirect bilirubin, alkaline phosphatase, INR   |
| • No clinically meaningful changes in other key markers among VK2809-treated patients relative to placebo | Thyroid hormones (fT4, tT3, TSH); Cardiovascular markers (troponin, CK-MB, NT proBNP); Vital signs (BP, heart rate, weight) |
| • Excellent tolerability  | GI and nausea events numerically lower vs. placebo  |



VK2809: Phase 2b VOYAGE Study



# VOYAGE Study: 12-Month Phase 2b Study of VK2809

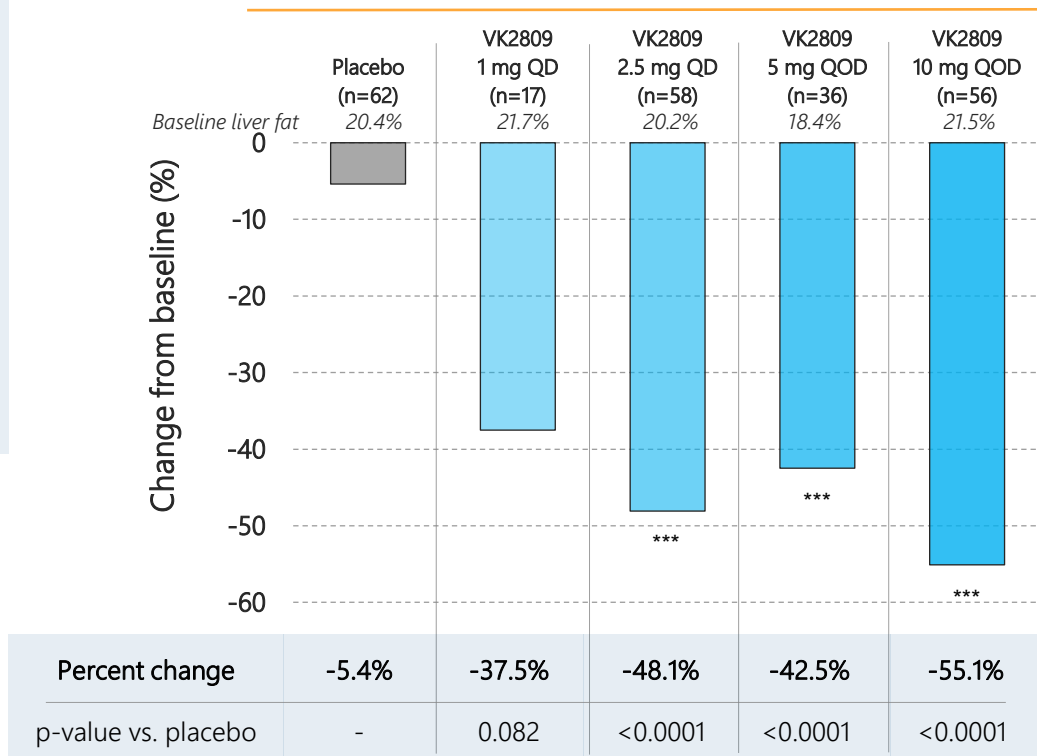


- Multi-arm, dose-ranging, 12-month Phase 2 trial
  - **Primary endpoint:** Change in MRI-PDFF vs. placebo at 3 months
  - **Secondary endpoint:** Change in histology at 12 months (NAS, fibrosis markers, etc.)

# VOYAGE Study Achieves Primary Endpoint

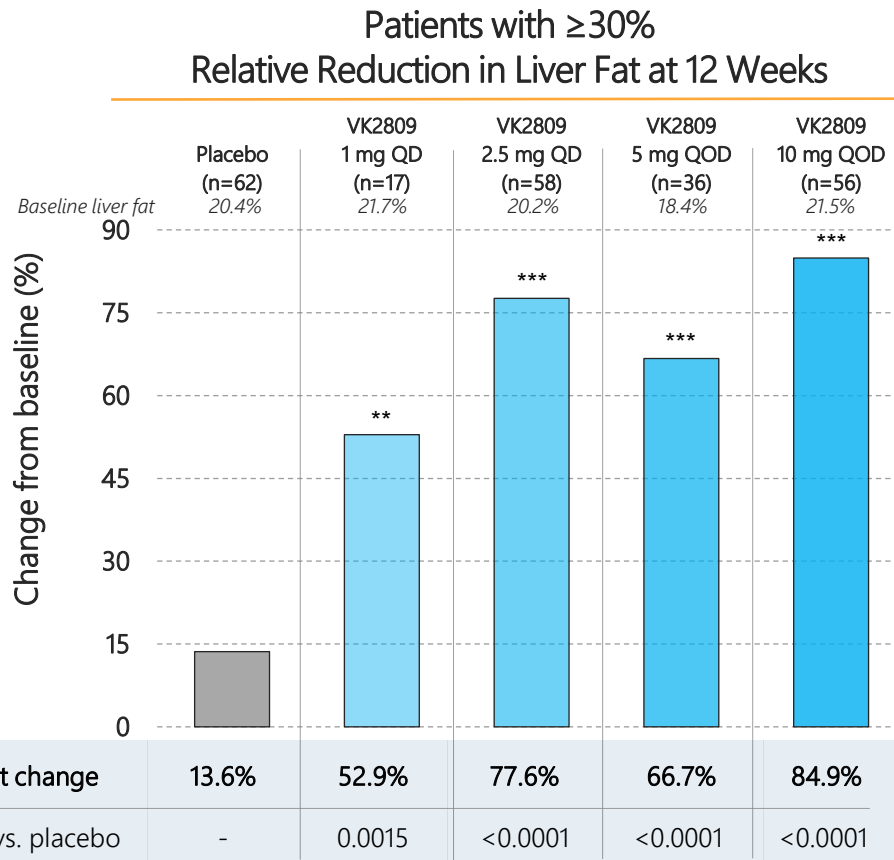
- Significant liver fat reduction observed at 12 weeks
- Up to 55% median reduction
- Overall liver fat effect similar to 12 week NAFLD study

Median Relative % Change in Liver Fat at 12 Weeks



# VK2809 Cohorts Demonstrate High Response Rates

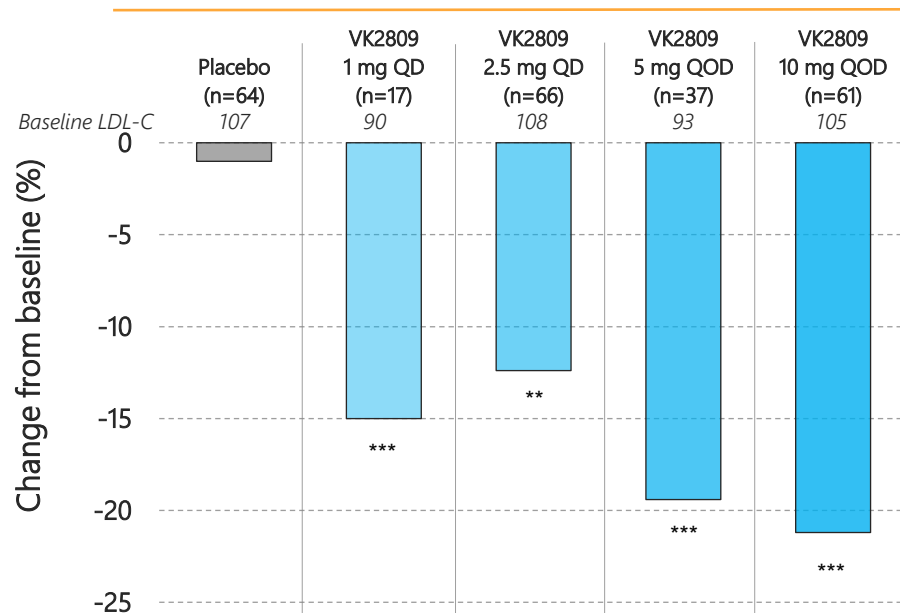
- Up to 85% of VK2809 patients experienced response, as defined by  $\geq 30\%$  decrease in liver fat at Week 12
- Combined VK2809 cohorts demonstrated 75% response rate
- Reduction in liver fat correlated with improved odds of long-term histology benefit<sup>1</sup>



# VOYAGE Study Results: Significant LDL-C Reduction

- Significant reductions in LDL-C observed at 12 weeks
- All cohorts demonstrated reductions
- Magnitude of effect similar to 12 week NAFLD study

Mean Relative % Change in LDL-C at 12 Weeks



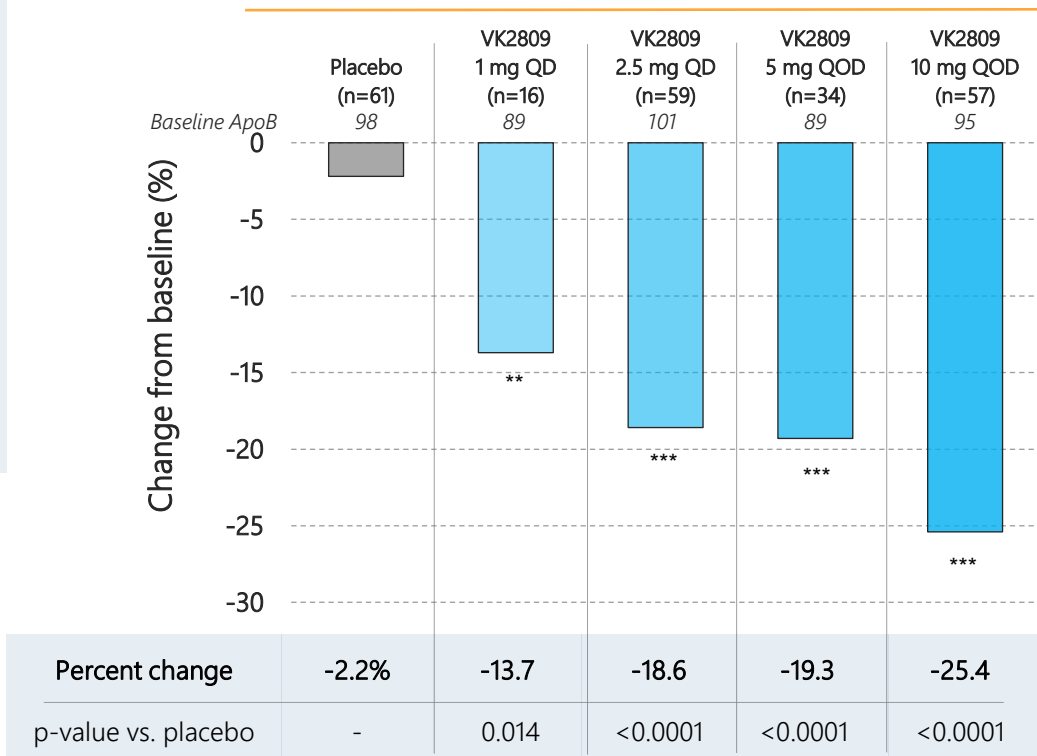
Percent change	-1.0%	-15.0%	-12.4%	-19.4%	-21.2%
p-value vs. placebo	-	0.019	0.0026	<0.0001	<0.0001

\*p<0.05; \*\*p<0.01; \*\*\*p<0.001

# VOYAGE Study Results: Significant ApoB Reduction

- Significant reductions in ApoB observed at 12 weeks
- All cohorts demonstrated reductions
- Significant reductions also observed for triglycerides, Lp(a), Apo CIII

Mean Relative % Change in ApoB at 12 Weeks



\*p<0.05; \*\*p<0.01; \*\*\*p<0.001

# VK2809 Demonstrates Consistent Safety, Tolerability Profile

Most common AEs to date Number of subjects reporting (%)	Placebo (n=65)	VK2809 1 mg QD (n=17)	VK2809 2.5 mg QD (n=66)	VK2809 5.0 mg QOD (n=37)	VK2809 10.0 mg QOD (n=61)	VK2809 Combined (n=181)
Treatment emergent adverse events, TEAEs	47 (72.3%)	14 (82.4%)	52 (78.8%)	29 (78.4%)	54 (88.5%)	149 (82.3%)
Drug-related TEAEs	22 (33.8%)	7 (41.2%)	13 (19.7%)	9 (24.3%)	23 (37.7%)	52 (28.7%)
TEAEs leading to discontinuation	5 (7.7%)	2 (11.8%)	1 (1.5%)	1 (2.7%)	5 (8.2%)	9 (5.0%)
Drug-related GI adverse events	12 (18.5%)	4 (23.5%)	3 (4.5%)	1 (2.7%)	7 (11.5%)	15 (8.3%)
Nausea	5 (7.7%)	2 (11.8%)	2 (3.0%)	1 (2.7%)	3 (4.9%)	8 (4.4%)
Diarrhea	2 (3.1%)	3 (17.6%)	2 (3.0%)	1 (2.7%)	3 (4.9%)	9 (5.0%)

Notes: Study safety population, defined as all patients who were randomized and received at least one dose of study drug. 1) Data as of March 13, 2023. 2) Deemed by investigator as possibly, probably, or definitely related to study drug.

- Majority of reported AEs (94%) mild or moderate
- Discontinuations due to AEs well balanced between placebo, treatment groups
- GI-related AEs similar to placebo

# VK2809 VOYAGE Topline Takeaways

- Achieves primary endpoint demonstrating robust reduction in liver fat
- Up to 85% of patients achieve  $\geq 30\%$  liver fat reduction
- Significant reductions in plasma lipids LDL-C, triglycerides, Lp(a), ApoB, ApoC-III
- Excellent tolerability, rate of GI-related side effects similar to placebo
- Promising safety, 94% of AEs mild to moderate
- 52-Week biopsy results expected 1H24

# VK2809 Competitive Advantages

- Currently >40 NASH programs in Phase 2 or Phase 3 development
- What differentiates VK2809 from the crowd?

- Orally available

Preferred route of administration for chronic therapy

- Liver-targeted

Reduces risk of undesired effects in other tissues

- Potently reduces liver fat

Weight loss and reduced liver fat correlate with NASH resolution, improved fibrosis markers

- Reduces systemic lipids, may improve overall metabolic profile

Bodes well for potential long-term CV benefit  
No elevations in other lipids that may require polypharmacy

- Well tolerated

No GI impact, no pruritis or other tolerability issues to date





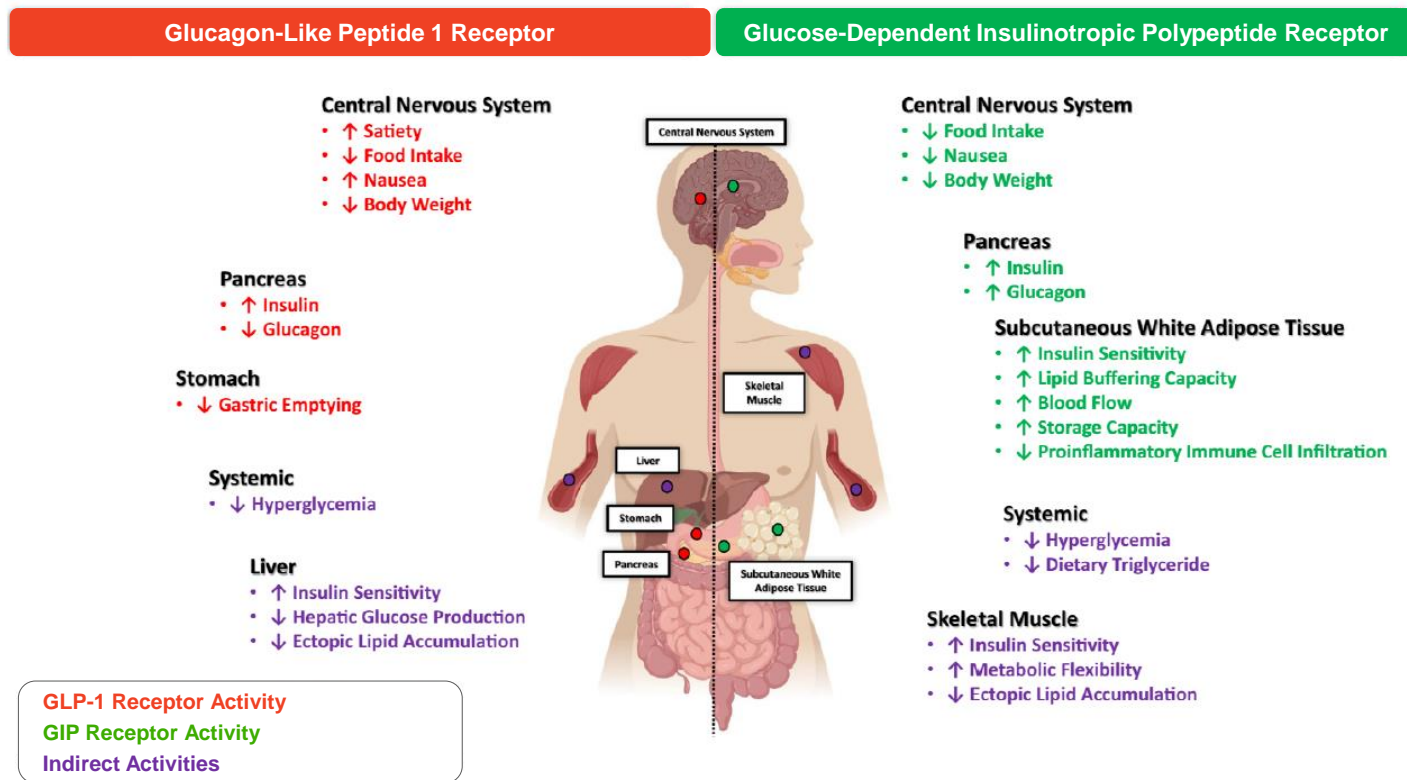
VK2735: Dual GLP-1/GIP Receptor Agonist

Metabolic Disorders

# GLP-1/GIP Dual Agonists for Metabolic Disorders

- Peptides secreted by intestines after meals
- Complementary tissue distribution and activities
- Stimulate insulin production, induce satiety
- Therapeutic benefits in obesity, NASH, diabetes

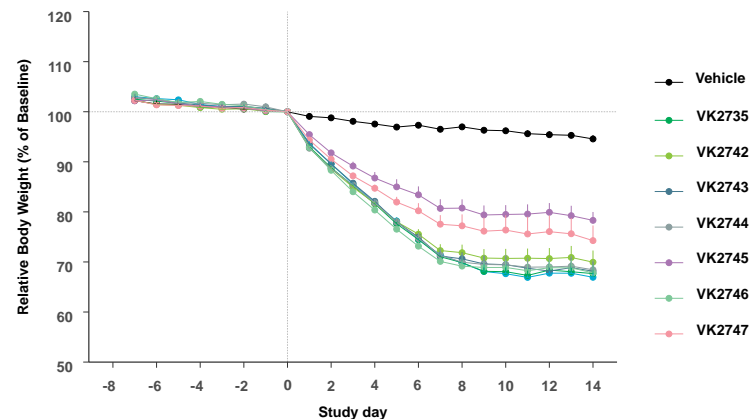
## GLP-1/GIP Receptor Co-Activation and Downstream Effects



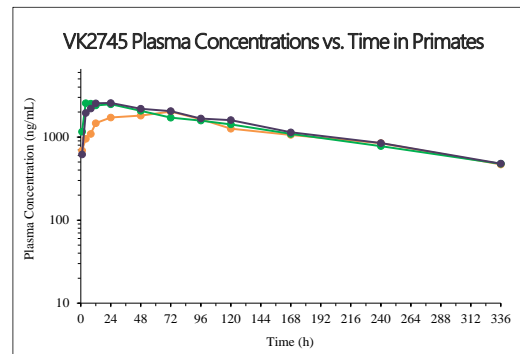
# Novel Peptide-Based Dual Agonists

- Potent binding (<500nM) observed at human GLP-1 and GIP receptors
- Variable GIP activity
- Robust weight loss observed in rodent models
- Predictable PK;  $T_{1/2}$  2 – 7 days in primates; variable exposures
- VK2735 selected for further development

Relative Weight Change at 14 Days in Rodent Model of Obesity

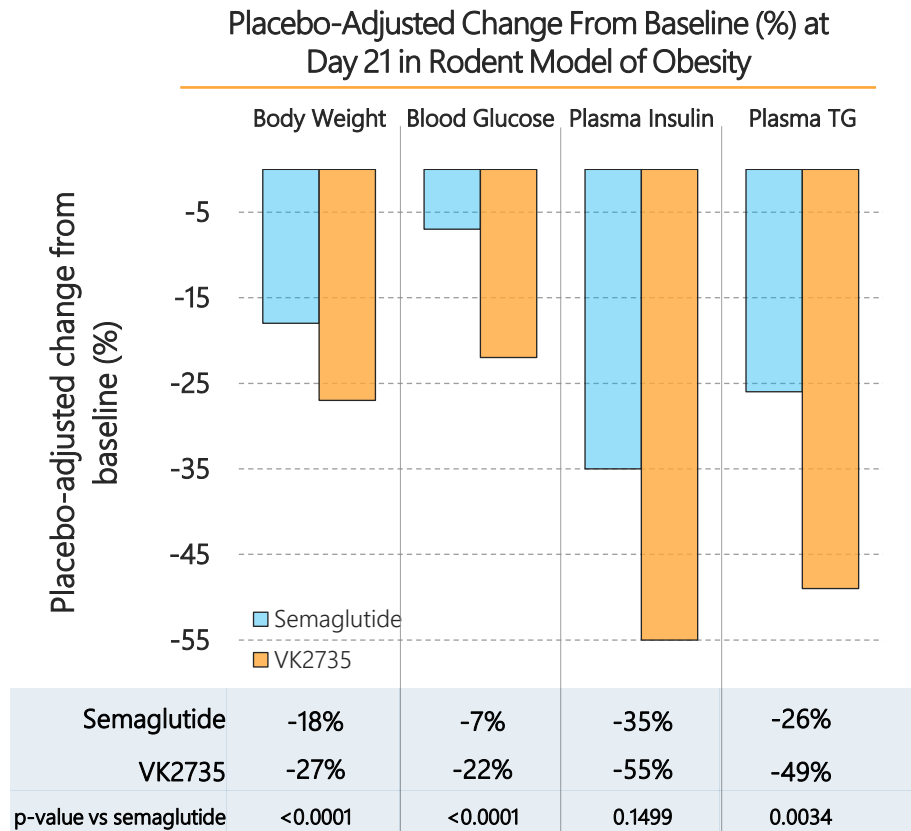


Representative PK profile:  
Generally well-behaved with extended  $T_{1/2}$



# VK2735 Metabolic Effects Exceed GLP-1 Mono-Agonist Effects

- GLP-1 receptor activity similar to known agonist semaglutide (<300nM)
- VK2735 demonstrates broad improvements vs. GLP-1 mono-agonism at same dose level
- Robust reduction in all relevant metabolic markers
- Data support additive benefit of GLP-agonist activity on top of GLP-1 activation



# VK2735 Phase 1 Clinical Study Design

- Randomized, placebo-controlled, stacked SAD/MAD study design
- MAD: Weekly doses for 28 days
- Primary objectives: Safety, tolerability
- Exploratory: Body weight, glucose, liver fat

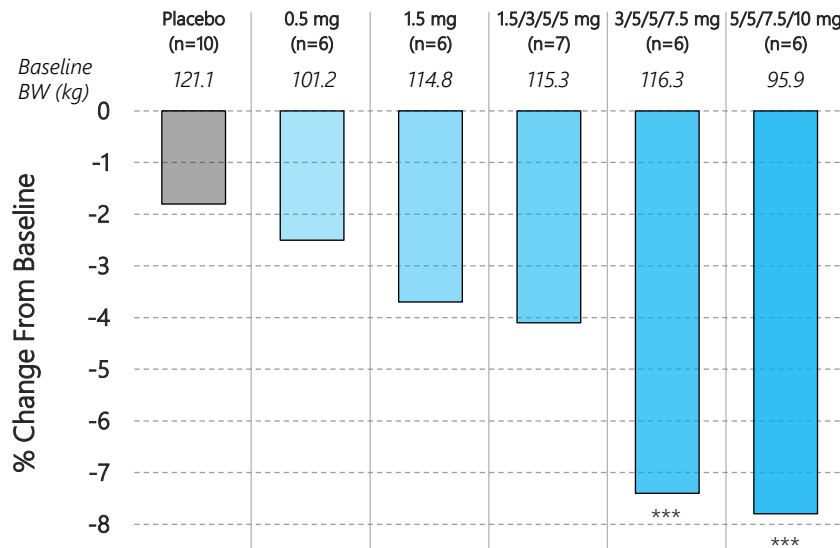
# VK2735 Phase 1 SAD Results

- All planned SAD cohorts were completed
  - 0.25 mg, 0.5 mg, 1.0 mg, 2.5 mg, 5.0 mg, 7.5 mg
- PK profile:  $T_{1/2}$  170 – 250 hours, amenable to weekly dosing
- $T_{max}$  75 to 90 hours implies gradual onset of exposure
- Clinical observations
  - No SAEs reported
  - Nausea reported, increasing with increased dose; expected on-mechanism effect
- No vomiting reported until top dose (7.5 mg); appears to be dose-limiting in SAD setting

# VK2735 Phase 1 MAD Results: Weight Change After 28 Days

- Reduction in body weight observed in all VK2735 dosing cohorts
- Dose dependent effect observed across VK2735 cohorts
- Significant reduction vs. placebo observed at higher VK2735 doses

Mean % Change in Body Weight at Day 29

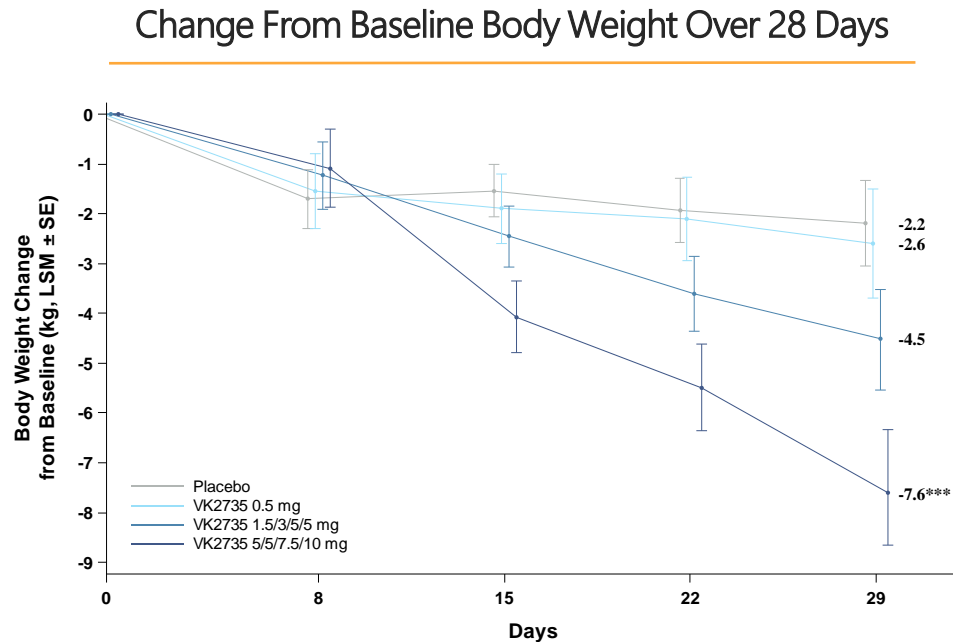


% Change in BW:	-1.8%	-2.5%	-3.7%	-4.1%	-7.4%	-7.8%
Placebo-adjusted:	-	-0.7%	-1.9%	-2.3%	-5.6%	-6.0%
p-value vs placebo	-	0.64	0.17	0.09	0.0003	0.0002

Notes: Baseline BMI  $\geq 30$  in all MAD subjects. \*\*\* $p < 0.001$

# VK2735 Phase 1 Results: Rapid, Progressive Weight Loss Observed

- Progressive weight loss observed in all VK2735 dosing cohorts
- Dose dependent effects observed
- No evidence of plateau in this dosing window



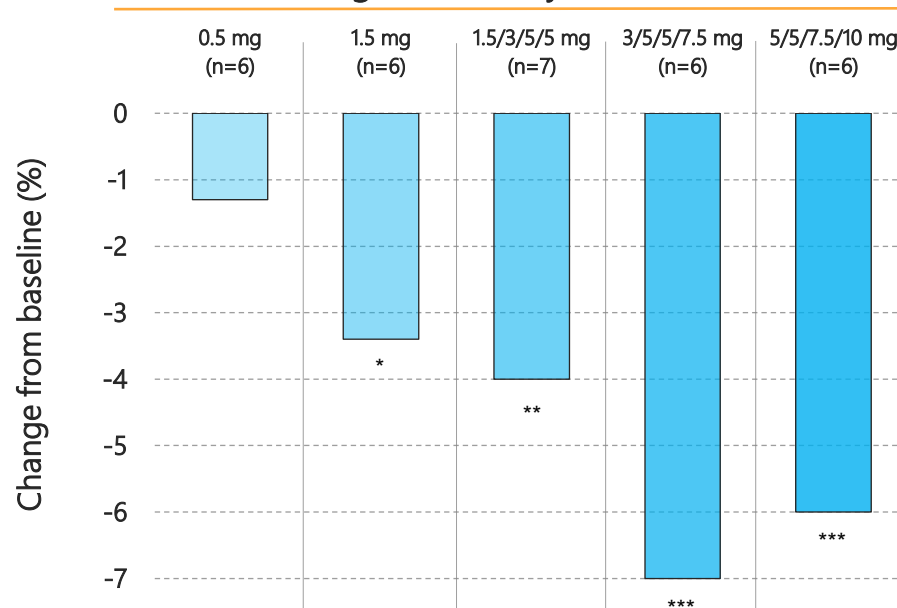
Notes: Baseline BMI  $\geq 30$  in all MAD subjects. \*\*\* $p < 0.001$   
Lowest, middle, and highest dose cohorts displayed.



# VK2735 Phase 1 Results: Robust Weight Loss Maintained At 43 Days

- 21 days after last VK2735 dose
- Differences relative to placebo improve compared to Day 29 timepoint
- Suggests durable benefit following brief exposures

Placebo-Adjusted Change From Baseline Body Weight in Healthy Volunteers



Placebo-adjusted % change in BW	-1.3%	-3.4%	-4.0%	-7.0%	-6.0%
p-value vs. placebo	0.34	0.015	0.004	<0.0001	0.0002

Notes: All subjects in MAD study were required to have baseline BMI  $\geq 30$ .  
\* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$

# VK2735 Phase 1 MAD Study: GI Tolerability Summary

Most common AEs to date Number of subjects reporting (%)	Placebo (n=10)	0.5 mg (n=6)	1.5 mg (n=6)	1.5/3/5/5 mg (n=7)	3/5/5/7.5 mg (n=6)	5/5/7.5/10 mg (n=6)
GERD	0 (0%)	0 (0%)	0 (0%)	3 (43%)	2 (33%)	1 (17%)
Nausea	5 (50%)	2 (33%)	4 (67%)	5 (71%)	5 (83%)	2 (33%)
Vomiting	1 (10%)	2 (33%)	0 (0%)	2 (29%)	1 (17%)	1 (17%)
Abdominal pain	1 (10%)	0 (0%)	1 (17%)	3 (43%)	4 (67%)	2 (33%)
Diarrhea	3 (30%)	1 (17%)	1 (17%)	2 (29%)	0 (0%)	0 (0%)
Constipation	0 (0%)	1 (17%)	1 (17%)	2 (29%)	1 (17%)	0 (0%)

GERD: Gastroesophageal reflux disease.

- Majority of all reported AEs (98%) mild or moderate
- Mechanism-based mild (89%) to moderate (11%) nausea observed
- No discontinuations related to GI adverse events

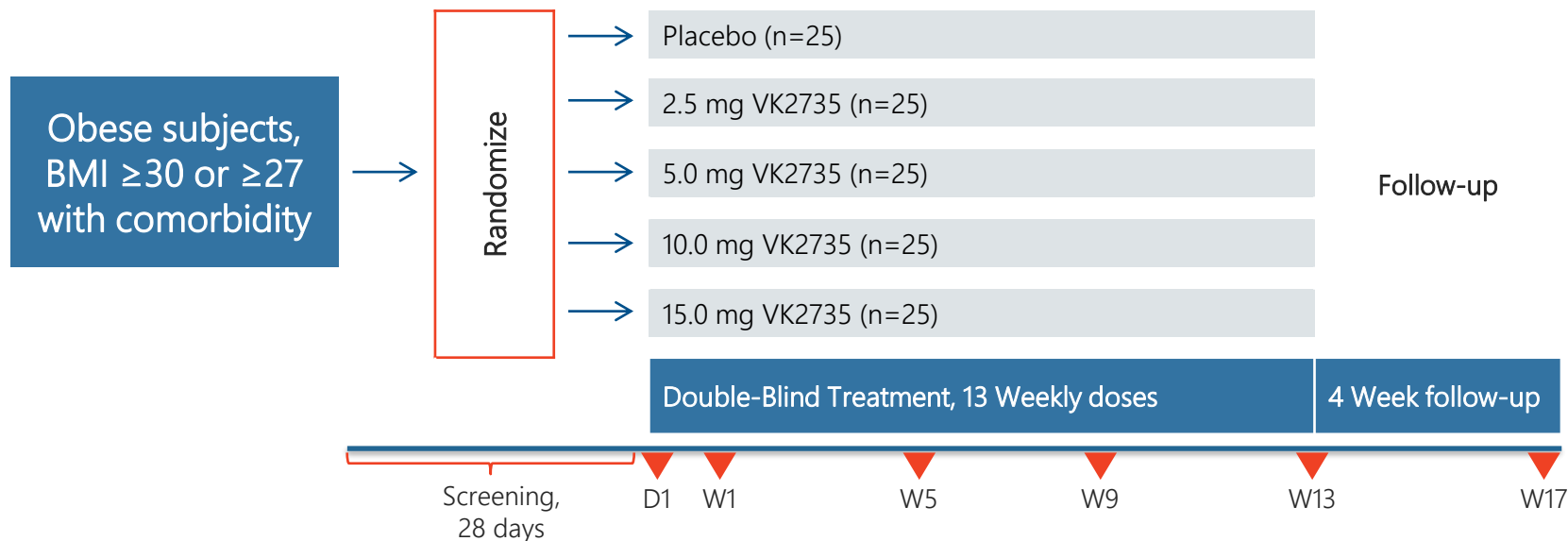
# VK2735-101 Safety Summary, MAD Cohorts

- Overall AEs: 83% mild, 15% moderate, 2% severe (anorexia, headache)
- 2 SAEs reported
  - Acute, complicated choledocholithiasis requiring surgery – gallbladder removal
  - Infectious mononucleosis
- No consistent dose relationship observed for GI AEs
  - Nausea overall 50% pbo vs. 58% Tx
  - Vomiting overall 10% pbo vs. 19% Tx
  - Diarrhea overall 30% pbo vs. 13% Tx

# VK2735 Phase 1 Study Takeaways

- Encouraging early profile observed in healthy subjects with BMI  $\geq 30$
- Dose-dependent improvement in weight loss of up to 7.8% (6.0% placebo-adjusted) reported after 28 days
- Durable weight loss maintained 21 days after last dose
- PK data suggest excellent exposures from weekly dosing regimen
- Promising safety and tolerability, 98% of AEs mild to moderate
- Expected observation of mild to moderate nausea appears manageable

# VK2735 VENTURE Phase 2a Obesity Study Design



- Multicenter, parallel cohort, 13 week trial in obese subjects
  - 3 week titration blocks applied at doses  $\geq 5$  mg
- Primary endpoint: Percent change in body weight at Week 13 vs. placebo

# VK2735 Next Steps

- Phase 2 VENTURE Study in obesity underway, data expected 1H24
- Novel oral tablet formulation demonstrates promising exposures in vivo
- Phase 1 study with oral formulation underway, data expected 1Q24



VK0214: Selective Thyroid Receptor- $\beta$  Agonist

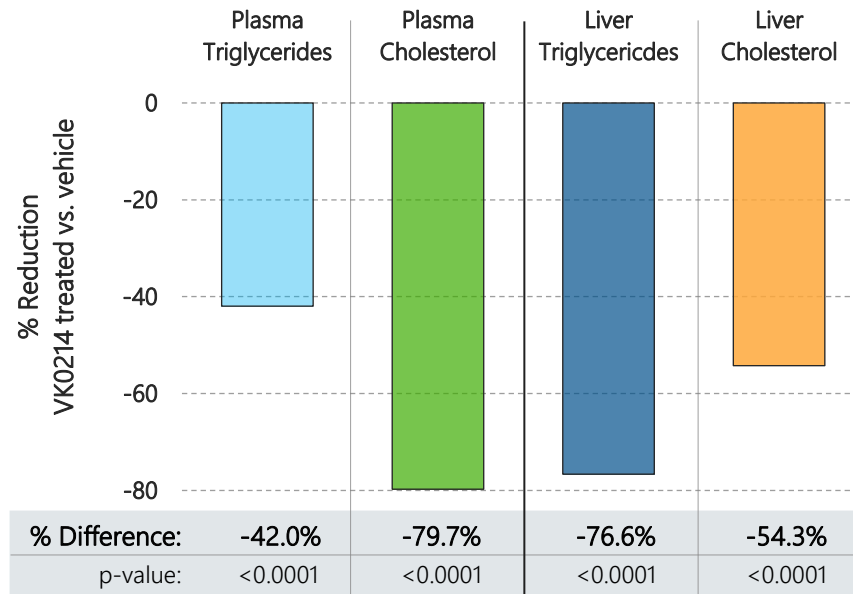
X-Linked Adrenoleukodystrophy

# VK0214: Summary Profile

## VK0214

- Potent small molecule thyroid receptor agonist
- 8 nM Ki at TR $\beta$  receptor
- >20:1 selective for  $\beta$ : $\alpha$
- Oral formulation, once-daily dosing
- Robust lipid lowering effects in multiple models

Change in Lipids Following 12 Weeks of Dosing With VK0214; Rodent NASH model



Demonstrates in vitro and vivo efficacy comparable to VK2809



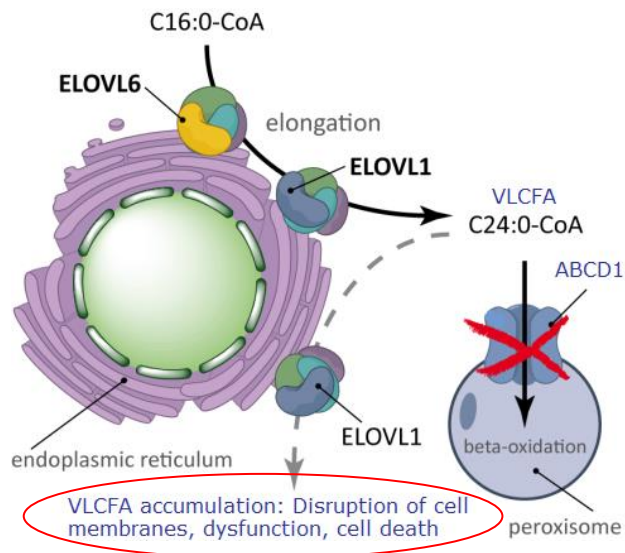
# VK0214 for X-ALD

- **X-Linked adrenoleukodystrophy (X-ALD)**
  - Orphan neurodegenerative disorder
  - X-linked: Carried by females, primarily manifesting in males
- **Most severe form: Cerebral ALD**
  - Rapidly progressive inflammatory demyelination; disruption of BBB
  - Affects ~35% before age 12 (CCALD), ~20% between age 20 – 35 (CALD)
  - Deterioration in speech, cognition; vegetative state within 3-5 years
- **Most common form: Adrenomyeloneuropathy (AMN)**
  - Affects spinal cord, motor neurons
  - Affects nearly all adult patients; considered “default” manifestation of ALD
  - Progressive motor impairment; wheelchair confinement, leg paralysis common

# TR $\beta$ and X-Linked Adrenoleukodystrophy

Caused by mutation in gene for the ATP-Binding Cassette transporter D1 (ABCD1)

- Peroxisomal transporter of very long chain fatty acids (VLCFA)



**ABCD1:** Normal function to transport VLCFA into peroxisome for degradation

**X-ALD: Defective ABCD1** leads to accumulation of VLCFA in tissues

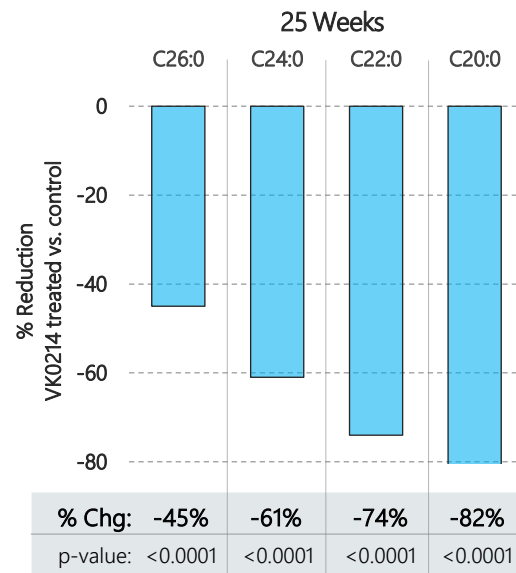
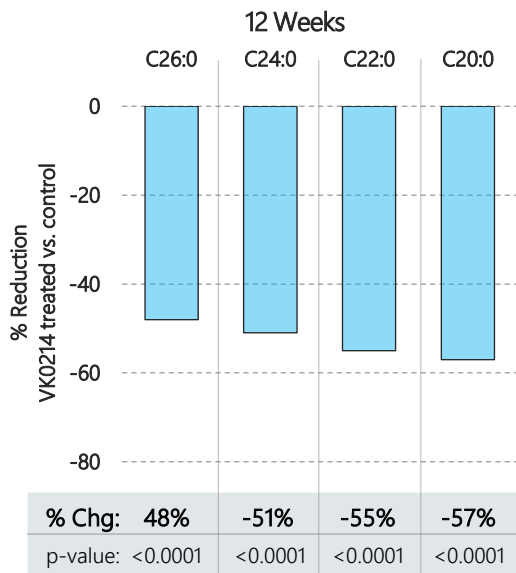
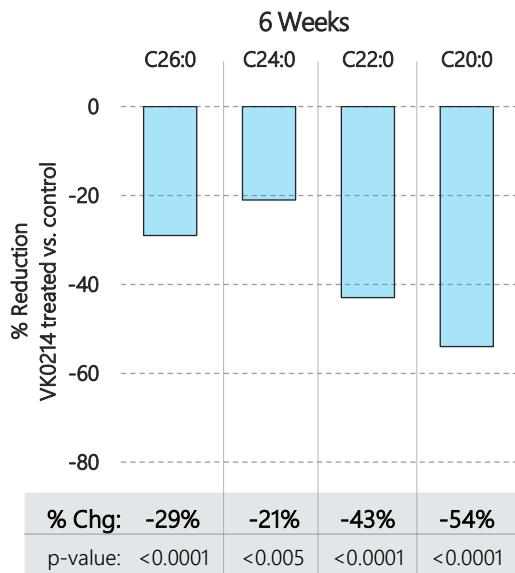
**High VLCFA levels disrupt** cell membranes; inflammatory demyelination in brain tissue; motor neuron deterioration

**TR $\beta$  Agonists:** Stimulate expression of compensatory transporters ABCD2, 3; may mitigate VLCFA elevation

# VK0214: *In Vivo* Proof-of-Concept Data, ABCD1 KO Mouse

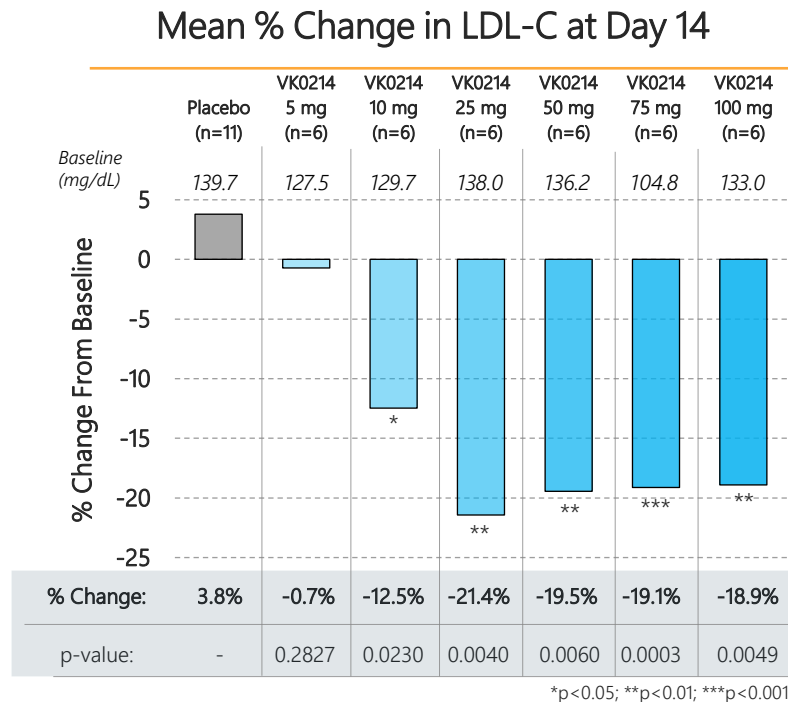
- ABCD1 Knockout model: Mimics biochemical features of human X-ALD
- VK0214: Durable and progressive reductions in plasma VLCFAs
  - Tissue effects suggest encouraging CNS activity following long-term exposure

## Reductions in Plasma VLCFA-LPC, ABCD1 Knockout Model



# VK0214 Phase 1 Results: LDL-C Reduction Observed After 14 Days

- Reduction in LDL-C similar to observations with VK2809
- Initial effect observed @ ~10 mg
- Data to date indicate a ~20% reduction from baseline

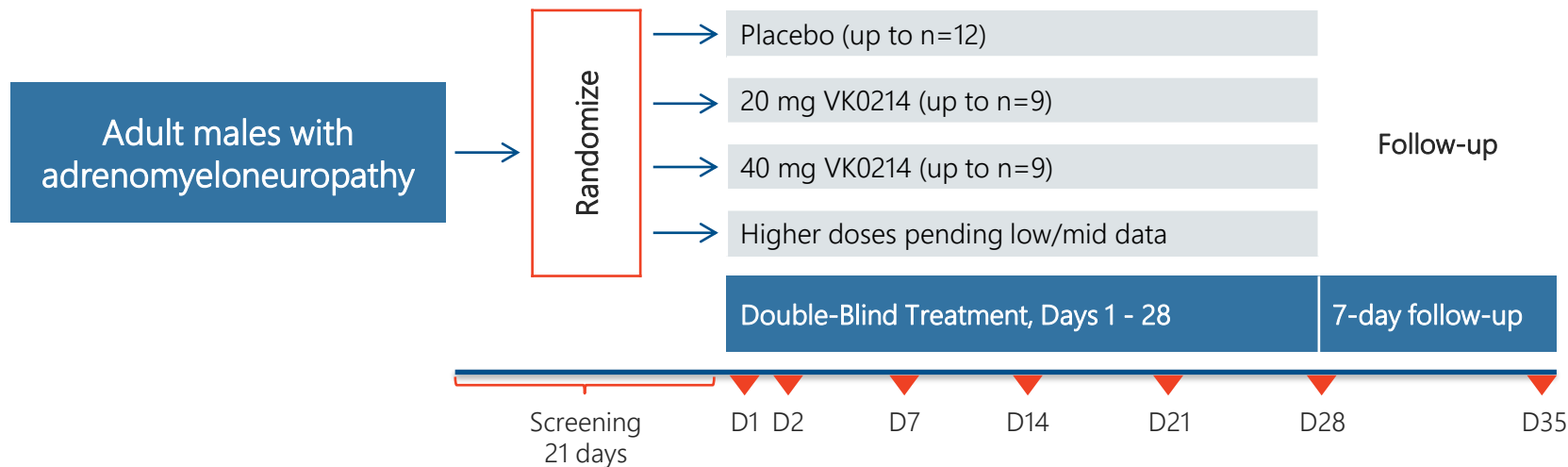


Magnitude of LDL-C reductions are consistent with TR $\beta$  agonist mechanism

# Takeaways From VK0214 Phase 1 SAD/MAD Study

- Encouraging overall safety and tolerability, no SAEs observed
- No meaningful impact to vital signs, cardiovascular parameters, thyroid axis
- Attractive PK profile; predictable exposures with once-daily dosing
- Preliminary lipid data suggest similar efficacy to VK2809
- Results support further study in adrenomyeloneuropathy (AMN) patients

# VK0214 Phase 1b Study in Adrenomyeloneuropathy



- Multicenter, parallel cohort, 28-day Phase 1b trial in adrenomyeloneuropathy
  - Higher doses may be explored pending review of initial cohorts
- Safety, tolerability, change in VLCFAs in male patients with AMN

# Upcoming Data Events

- Phase 2b VOYAGE biopsy results expected in 1H24
- Obesity: Phase 2 VENTURE study results expected in 1H24
- Oral VK2735 Phase 1 results expected 1Q24

# Financial Summary

- Capital structure and summary financials

Capital Structure <sup>1</sup>	In '000s
Shares outstanding	100,029
Options, RSUs	8,283
Total shares, options, RSUs, warrants	108,312

Financials	Sep 30, 2023 (\$'000s)
Cash burn YTD	\$62,673
Cash and ST Investments	\$376,241
Notes: 1) As of September 30, 2023	



# Investment Highlights

- **Developing novel therapeutics for metabolic and endocrine diseases**
  - Multiple clinical programs demonstrate best-in-class efficacy data
- **Metabolic Disease Programs**
  - VK2809: Novel, selective thyroid receptor- $\beta$  agonist for NASH and lipid disorders
    - Phase 2b VOYAGE trial successfully achieved primary endpoint; histology data expected 1H24
  - VK2735: Novel GLP-1/GIP dual agonist for obesity
    - Phase 2 VENTURE obesity study ongoing, fully enrolled; data expected 1H24
  - VK2735 Oral: GLP-1/GIP dual agonist for metabolic disorders
    - Phase 1 study ongoing; data expected 1Q24
- **Rare Disease Program**
  - VK0214: Novel, selective thyroid receptor- $\beta$  agonist for X-ALD
    - Phase 1b ongoing



# Corporate Presentation

January 2024