

# **Corporate Presentation**

February 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.

The forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. While we may elect to update these forward-looking statements in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

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
  - o Multiple clinical programs demonstrate best-in-class efficacy data

#### Metabolic Disease Programs

- o VK2735: GLP-1/GIP dual agonist for obesity
  - VENTURE Phase 2 obesity study successfully achieved primary, secondary endpoints
- o VK2735 Oral: GLP-1/GIP dual agonist for obesity
  - Phase 1 study ongoing; data expected 1Q24
- o VK2809: Selective thyroid receptor-β agonist for NASH/MASH
  - VOYAGE Phase 2b trial successfully achieved primary endpoint; histology data expected 1H24

#### Rare Disease Program

- o VK0214: Selective thyroid receptor-β agonist for X-ALD
  - Phase 1b in patients ongoing; data expected 1H24



### **Pipeline Overview**

Development Programs	Indication	Stage of Development			Status	
		Preclin	Phase 1	Phase 2	Phase 3	
VK2735 (Dual GLP-1/GIP agonist)	Obesity					Phase 2 VENTURE study recently completed
VK2735 Oral (Dual GLP-1/GIP agonist)	Obesity					Phase 1 ongoing
<b>VK2809</b> (TRβ agonist)	NASH					Phase 2b VOYAGE trial ongoing
<b>VK0214</b> (TRβ agonist)	X-ALD					Phase 1b ongoing

#### Potential data events expected over next 6 months

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





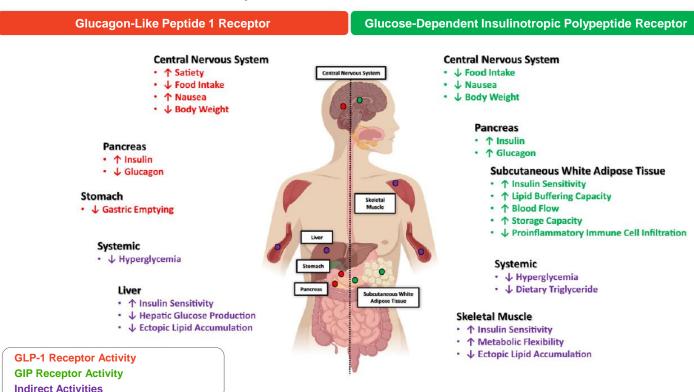
VK2735: Dual GLP-1/GIP Receptor Agonist

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**

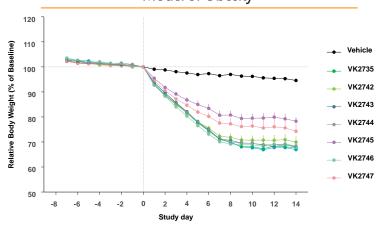




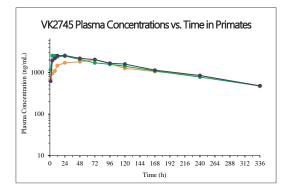
### **Novel Peptide-Based Dual Agonists**

- Potent binding (<500nM) to 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



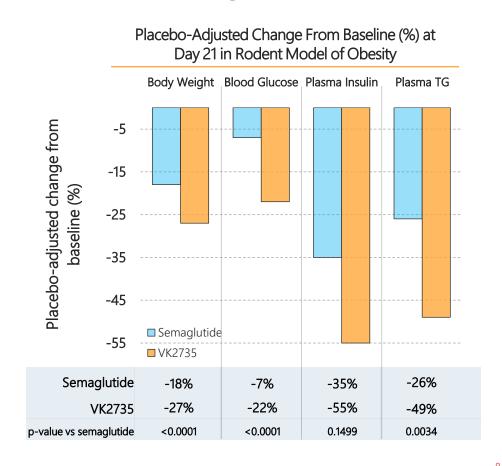
Representative PK profile: Generally wellbehaved with extended T<sub>1/2</sub>





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

- GLP-1 receptor activity similar to known agonist semaglutide (<300nM)</li>
- VK2735 demonstrates broad improvements vs. GLP-1 monoagonism at same dose level
- Robust reduction in all relevant metabolic markers
- Data support additive benefit of GIP-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

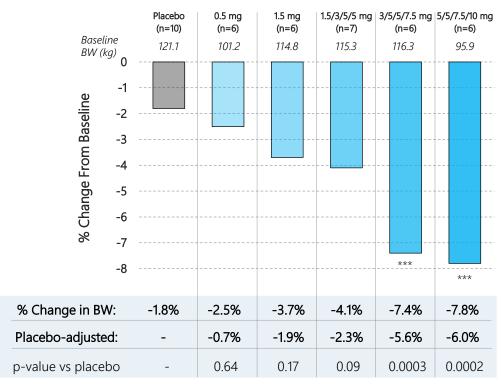
- All planned SAD cohorts were completed
  - o 0.25 mg, 0.5 mg. 1.0 mg, 2.5 mg, 5.0 mg, 7.5 mg
- PK profile:  $T_{1/2}$  170 250 hours, amenable to weekly dosing
- T<sub>max</sub> 75 to 90 hours implies gradual onset of exposure
- Clinical observations
  - No SAEs reported
  - o Nausea reported, increasing 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



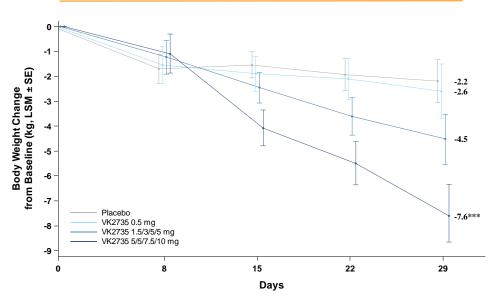
Notes: Baseline BMI ≥30 in all MAD subjects. \*\*\*p<0.001



### 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

#### Change From Baseline Body Weight Over 28 Days



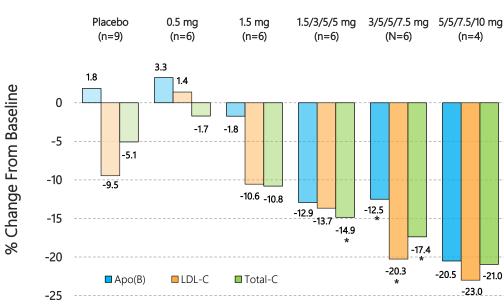
Notes: Baseline BMI ≥30 in all MAD subjects. \*\*\*p<0.001 Lowest, middle, and highest dose cohorts displayed.



### VK2735 Phase 1 Results: Effects on Plasma Lipids

- Reductions in plasma lipids observed after 4 weekly doses
- Dose dependent effects observed across cohorts
- No changes to HDL-C vs. placebo

#### Mean Change in Apo(B), LDL-C, Total-C at Day 29



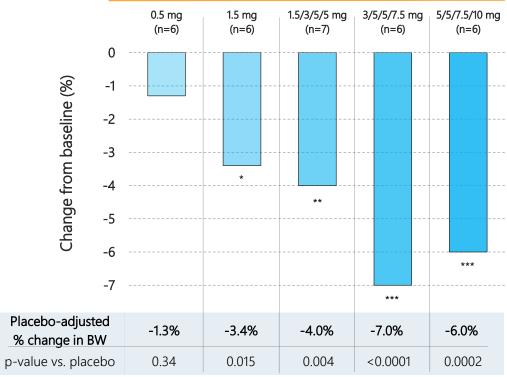
Notes: Baseline BMI ≥30 in all MAD subjects. \*p<0.05.



### 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







Notes: All subjects in MAD study were required to have baseline BMI ≥30.

### 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

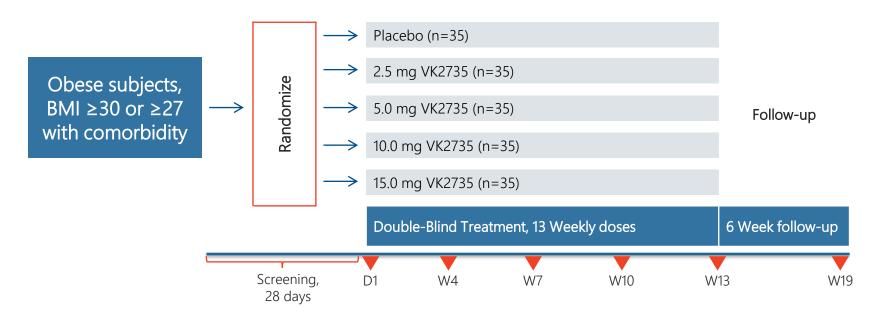


### VK2735 Phase 1 Study Takeaways

- Encouraging early profile observed in healthy subjects with BMI ≥30
- Dose-dependent improvement in weight loss of up to 7.8% (6.0% placeboadjusted) reported after 28 days
- Durable weight loss maintained 21 days after last dose
- Reductions in plasma lipids, liver fat indicate broad metabolic benefits
- PK data suggest excellent exposures from weekly dosing regimen
- Promising safety and tolerability, 98% of AEs mild to moderate



## VK2735 VENTURE Phase 2 Obesity Study Design



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



## VK2735 VENTURE Study Demographics

Mean Baseline Characteristics	Placebo (n=34)	2.5 mg (n=35)	5.0 mg (n=35)	10.0 mg (n=35)	15.0 mg (n=35)
Age	48	50	52	47	51
Sex, M:F (%)	18:82	23:77	34:66	34:66	23:77
White (%)	77	80	89	74	80
Weight (kg)	105	103	98	103	101
BMI (kg/m²)	39	38	36	37	37

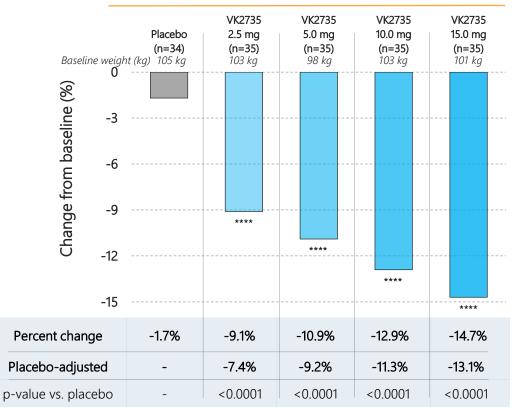
- Well-balanced demographics among cohorts
- Gender breakout generally 2:1 to 3:1 women to men
- BMI, weight consistent across Tx arms



### **VENTURE Study Achieves Primary Endpoint**

- Significant reduction in body weight observed after 13 weeks
- Up to approximately 15% reduction from baseline
- Dose dependent effect observed across cohorts

#### Mean % Change in Body Weight After 13 Weeks

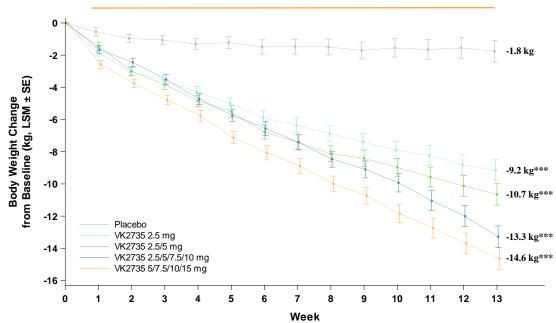




### VENTURE Phase 2 Results: Rapid, Progressive Weight Loss Observed

- Progressive weight loss observed in all VK2735 dosing cohorts
- All doses statistically significant vs. placebo starting in Week 1 and maintained through Week 13
- Dose dependent effects observed
- No evidence of plateau suggests further body weight reduction possible with continued dosing

#### Change From Baseline Body Weight Over 13 Weeks



Notes: \*\*\*p<0.0001. Patients were required to have baseline BMI  $\geq$ 30 kg/m² or BMI $\geq$ 27 kg/m² with at least one weight-related comorbid condition. Patients treated with VK2735 were titrated to final doses as indicated:

2.5 mg cohort = 2.5 x 13 weeks

5 mg cohort = 2.5 mg x 3 wks, 5 mg x 10 wks

10 mg cohort = 2.5 mg x 3 wks, 5 mg x 3 wks, 7.5 mg x 3 wks, 10 mg x 4 wks

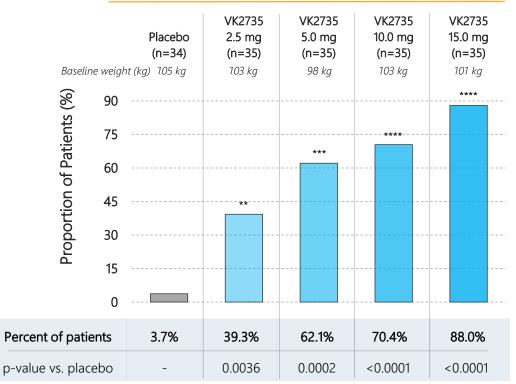
15 mg cohort = 5 mg x 3 wks, 7.5 mg x 3 wks, 10 mg x 3 wks, 15 mg x 4 wks



### **VENTURE Study Achieves Key Secondary Endpoint**

- Up to 88% of patients experienced ≥10% weight loss
- Majority of patients receiving ≥5 mg and greater demonstrated 10% weight loss
- Lowest 2.5 mg dosing cohort showed 10x placebo rate

#### Patients Reporting ≥10% Weight Loss at 13 Weeks



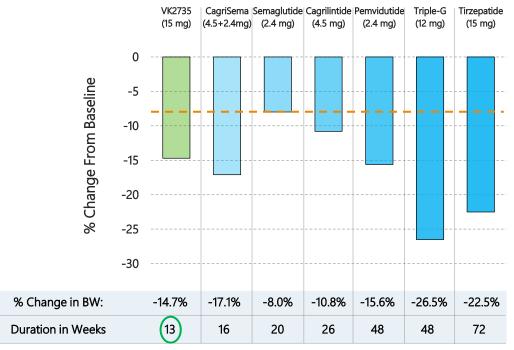




### Comparison With Published Data for Other Weight Loss Agents

- VK2735 weight loss appears competitive with other agents despite shorter trial duration
- Longer-term data will be key for determining maximal efficacy

#### Change in Body Weight Across Competitive Landscape



Notes: Data represent change from baseline. — Indicates approximate tirzepatide 12 week weight loss in Phase 3 Surmount 1 study (~8%).



#### **VENTURE Study Discontinuation Rates Well-Balanced**

Number of subjects reporting (%)	Placebo (n=35)	VK2735 2.5 mg (n=35)	VK2735 5 mg (n=35)	VK2735 10 mg (n=35)	VK2735 15 mg (n=35)	VK2735 Combined (n=140)
Discontinued treatment early	5 (14%)	2 (6%)	4 (11%)	5 (14%)	7 (20%)	18 (13%)
Discontinued study early	2 (6%)	0 (0%)	1 (3%)	2 (6%)	2 (6%)	5 (4%)
Overall TEAEs	24 (69%)	25 (71%)	31 (89%)	30 (86%)	32 (91%)	118 (84%)
Drug related TEAEs	15 (43%)	21 (60%)	27 (77%)	26 (74%)	30 (86%)	104 (74%)
Drug related TEAEs leading to study discontinuation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (3%)	1 (1%)

Notes: Study safety population, defined as all patients who were randomized and received at least one dose of study drug. Data as of February 20, 2024.

- Discontinuations well balanced between placebo, VK2735 treatment groups
- Majority (92%) of drug related TEAEs among VK2735 patients mild or moderate
- One VK2735 treated patient experienced SAE of dehydration



### **VENTURE Phase 2 Study: GI Tolerability Summary**

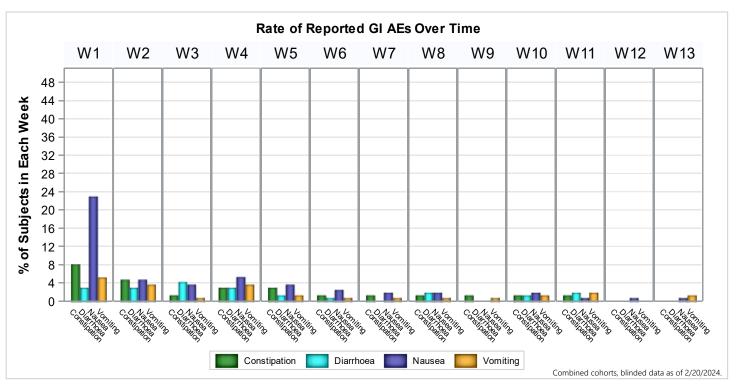
Common GI related TEAEs  Number of subjects reporting (%)	Placebo (n=35)	VK2735 2.5 mg (n=35)	VK2735 5 mg (n=35)	VK2735 10 mg (n=35)	VK2735 15 mg (n=35)	VK2735 Combined (n=140)
GERD	1 (3%)	2 (6%)	5 (14%)	4 (11%)	6 (17%)	17 (12%)
Nausea						
Mild	7 (20%)	6 (17%)	11 (31%)	9 (26%)	15 (43%)	41 (29%)
Moderate	0 (0%)	3 (9%)	5 (14%)	4 (11%)	7 (20%)	19 (14%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Vomiting	0 (0%)	3 (9%)	6 (17%)	6 (17%)	10 (29%)	25 (18%)
Abdominal pain	1 (3%)	1 (3%)	2 (6%)	1 (3%)	2 (6%)	6 (4%)
Diarrhea	3 (9%)	11 (31%)	6 (17%)	7 (20%)	4 (11%)	28 (20%)
Constipation	4 (11%)	7 (20%)	10 (29%)	9 (26%)	10 (29%)	36 (26%)
Decreased appetite	0 (0%)	2 (6%)	5 (14%)	9 (26%)	6 (17%)	22 (16%)

GERD: Gastroesophageal reflux disease.

Majority (95%) GI specific TEAEs among VK2735 patients mild or moderate



### Time Course of GI AEs Through 13 Weeks; Combined Cohorts



- GI AEs most common, expected per GLP-1 mechanism: nausea, vomiting, diarrhea, constipation
- Generally observed early, subside over time

#### **VENTURE Phase 2 Study Takeaways**

- Up to 14.7% weight loss from baseline observed after 13 weeks of VK2735 treatment
- Promising tolerability, 92% of all drug related TEAEs mild to moderate
- Majority of GI-related AEs occur early in treatment, resolve
- Further evaluation of lipids, clinical chemistry to follow when available



### VK2735 Next Steps

- Follow-up VENTURE data expected 2Q24
- Type C meeting with FDA planned for mid-year
- Phase 1 study with oral formulation underway, data expected 1Q24



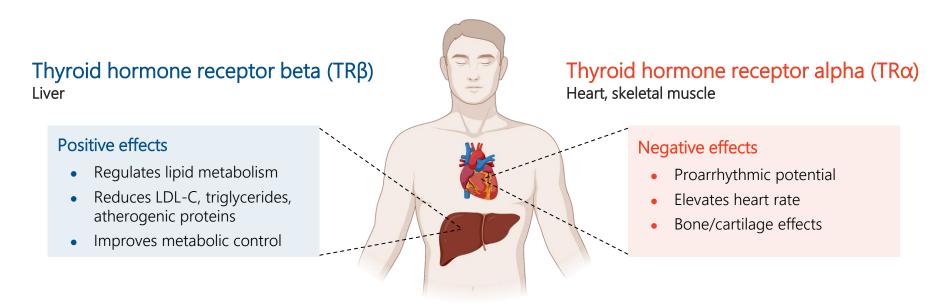


VK2809: Selective Thyroid Receptor-β Agonist

NASH/MASH

### Thyroid Hormone Receptor Overview

Nuclear hormone receptors: 2 main types



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



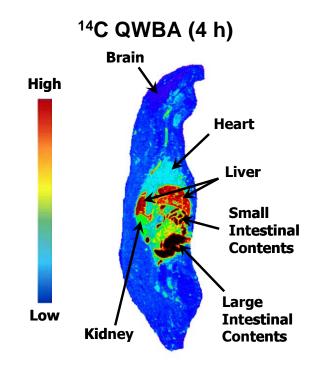
### VK2809: Unique Liver-Targeted Characteristics

VK2809, Novel Prodrug

#### Following oral dosing:

- Cyp3A4-mediated cleavage of prodrug
- 3A4 is primarily expressed in liver
- Results in targeted delivery of drug to liver

VK2809A, Potent TRβ Agonist, 2.2 nM Ki



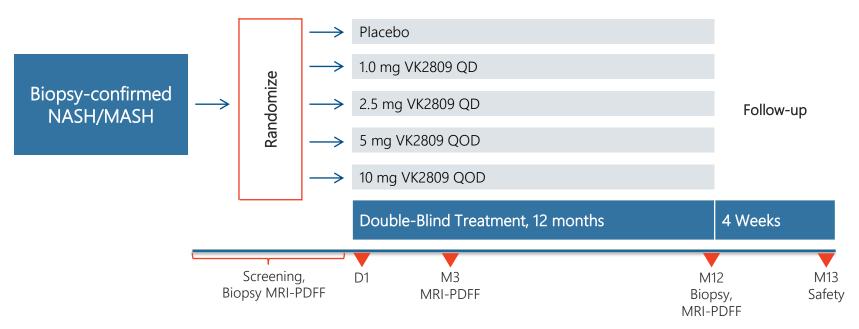
Selective activation, differentiated chemistry lends VK2809 liver selectivity; potentially minimizes risk of systemic effects





VK2809: Phase 2b VOYAGE Study

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



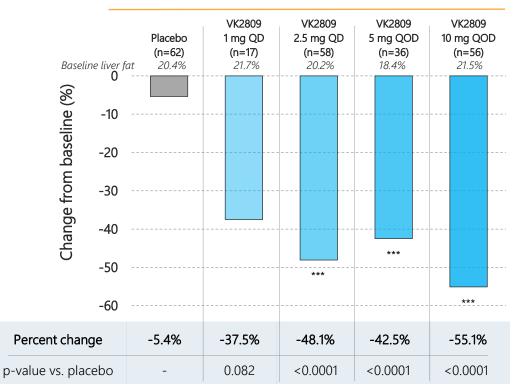
- Multi-arm, dose-ranging, 12-month Phase 2 trial
  - o **Primary endpoint:** Change in MRI-PDFF vs. placebo at 3 months
  - Secondary endpoint: Change in histology at 12 months (NAS, fibrosis markers, etc.)



### **VOYAGE Study Achieves Primary Endpoint**

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

#### Median Relative % Change in Liver Fat at 12 Weeks

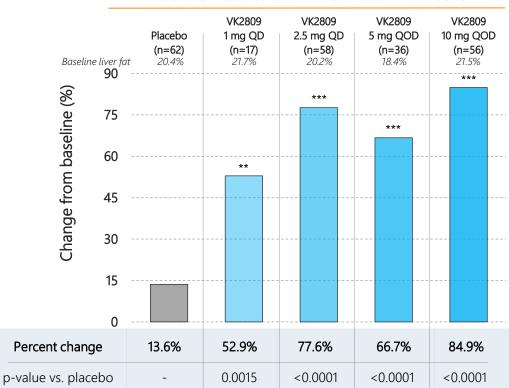




### VK2809 Cohorts Demonstrate High Response Rates

- Up to 85% of VK2809 patients experienced response, as defined by ≥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>

#### Patients with ≥30% Relative Reduction in Liver Fat at 12 Weeks

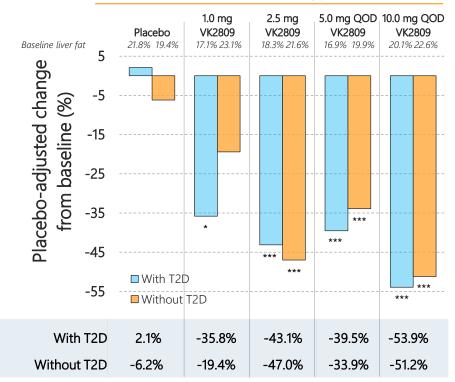


<sup>\*\*</sup>p<0.005; \*\*\*p<0.0001

#### VK2809 Demonstrates Consistent Liver Fat Reduction in T2D

- 44% of VOYAGE patients had type 2 diabetes
- VK2809 demonstrated consistent liver fat reductions across diabetic, non-diabetic subgroups
- Type 2 patients remain highly responsive to targeted TRβ agonism

#### LSM Change From Baseline (%) at Week 12 Among Patients With and Without Type 2 Diabetes

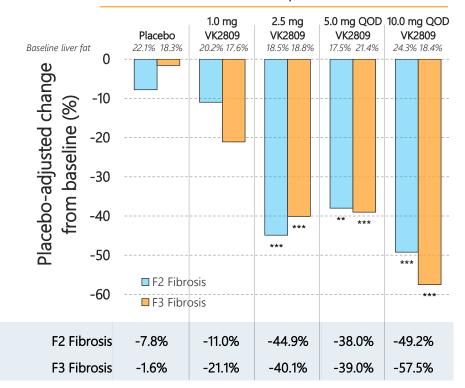




#### VK2809 Demonstrates Consistent Liver Fat Reduction Across F2, F3

- VOYAGE enrolled approximately 75% F2, F3 fibrosis; 25% F1
- VK2809 demonstrated similar efficacy across all fibrosis stages
- Suggests consistent benefit among advanced fibrosis patients with elevated liver fat

#### LSM Change From Baseline (%) at Week 12 Among Patients With F2, F3 Fibrosis





### 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 and Next Steps

- Achieves primary endpoint demonstrating robust reduction in liver fat
- Up to 85% of patients achieve ≥30% liver fat reduction
- Consistent liver fat reduction across T2D, non-T2D, F2, F3 fibrosis
- 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





VK0214: Selective Thyroid Receptor-β Agonist

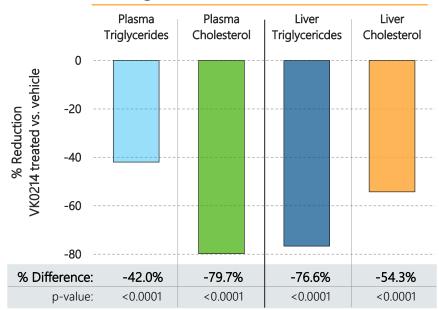
X-Linked Adrenoleukodystrophy

### VK0214: Summary Profile

#### VK0214

- Potent small molecule thyroid receptor agonist
- 8 nM Ki at TRβ 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



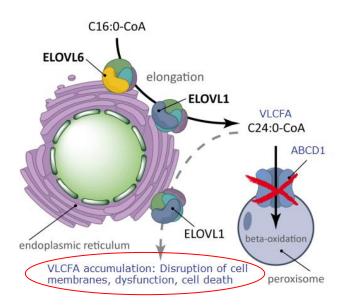
Demonstrates in vitro and vivo efficacy comparable to VK2809



### TRβ 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

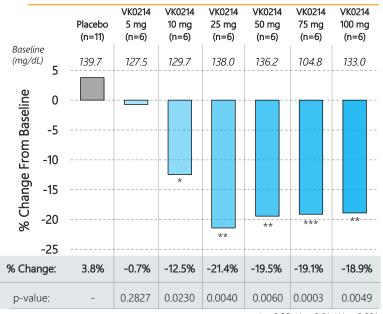
TRβ Agonists: Stimulate expression of compensatory transporters ABCD2, 3; may mitigate VLCFA elevation



#### 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

#### Mean % Change in LDL-C at Day 14

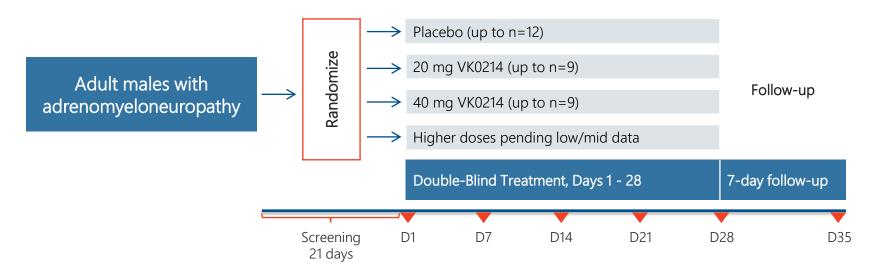


\*p<0.05; \*\*p<0.01; \*\*\*p<0.001

Magnitude of LDL-C reductions are consistent with TRβ agonist mechanism



### 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



## **Financial Summary**

• Capital structure and summary financials

Capital Structure <sup>1</sup>	In '000s
Shares outstanding	100,114
Options, RSUs	8,287
Total shares, options, RSUs	108,401

Financials	Dec 31, 2023 (\$'000s)
Cash burn YTD	\$76,835
Cash and ST Investments	\$362,079
Notes: 1) As of December 3	1, 2023



#### **Investment Highlights**

- Developing novel therapeutics for metabolic and endocrine diseases
  - o Multiple clinical programs demonstrate best-in-class efficacy data

#### Metabolic Disease Programs

- o VK2735: GLP-1/GIP dual agonist for obesity
  - VENTURE Phase 2 obesity study successfully achieved primary, secondary endpoints
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February 2024