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Corporate Presentation

# 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 subsequently filed Quarterly Reports on Form 10-Q).

# Investment Highlights

## Focused on best-in-class drugs for metabolic and endocrine diseases

- Two Phase 2 programs supported by positive clinical data

## Metabolic Disease Program: VK2809, for hypercholesterolemia, NAFLD

- Novel, selective thyroid receptor-β (TRβ) agonist
- Phase 2 trial expected to complete in 2H18

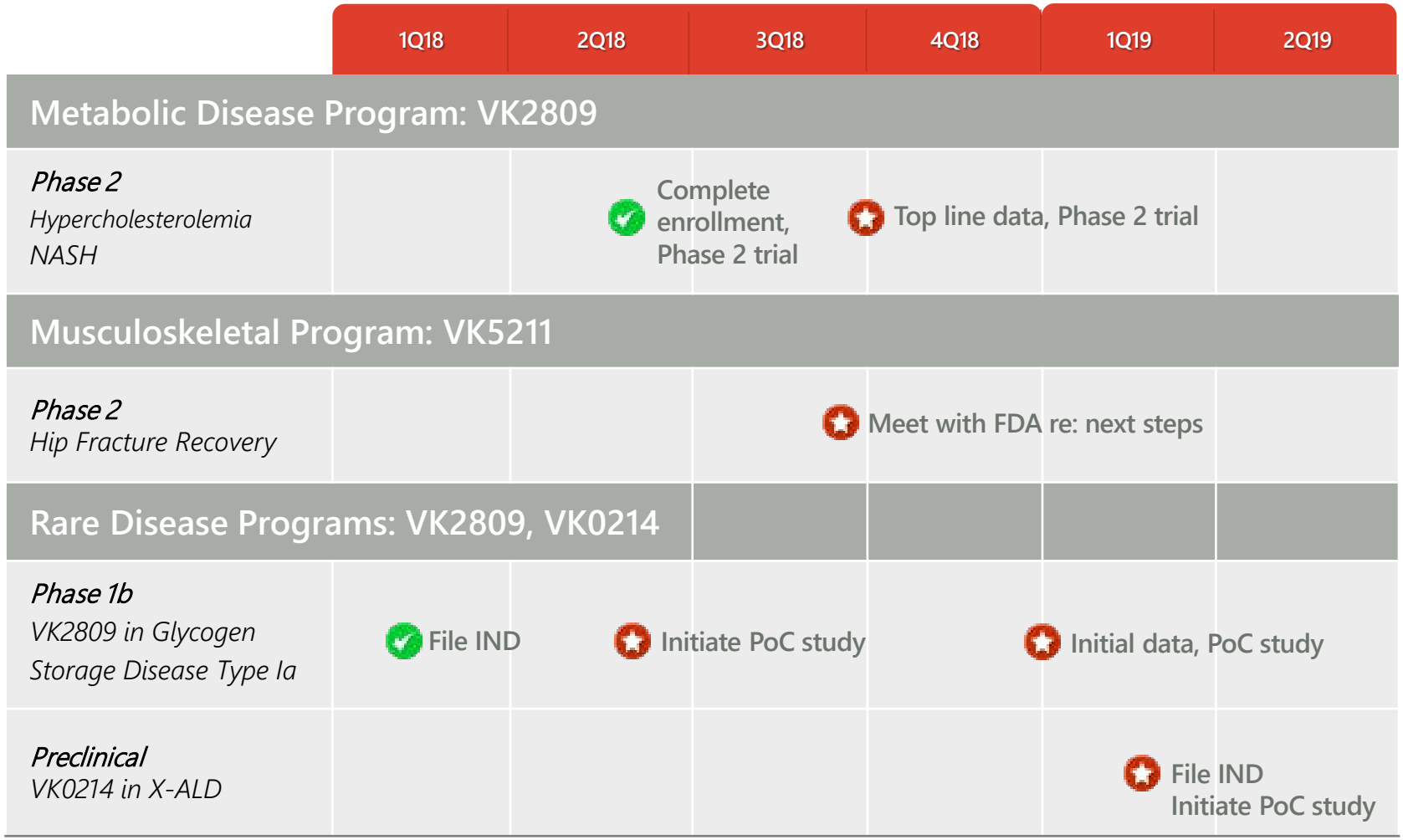
## Musculoskeletal Program: VK5211 for hip fracture recovery

- Non-steroidal selective androgen receptor modulator (SARM)
- Phase 2 results demonstrate significant increases in lean body mass

## Rare Disease Programs: GSD; X-ALD

- VK2809 in GSD Ia:  PoC study expected to begin 1H18
- VK0214 in X-ALD:  Potential IND, PoC study to begin 1H19

# Pipeline Catalysts and News Flow




Key VK2809 clinical data expected to read out in 2018

Denotes expected event.

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# Metabolic Disease Program

## VK2809: Selective Thyroid Receptor-β Agonist

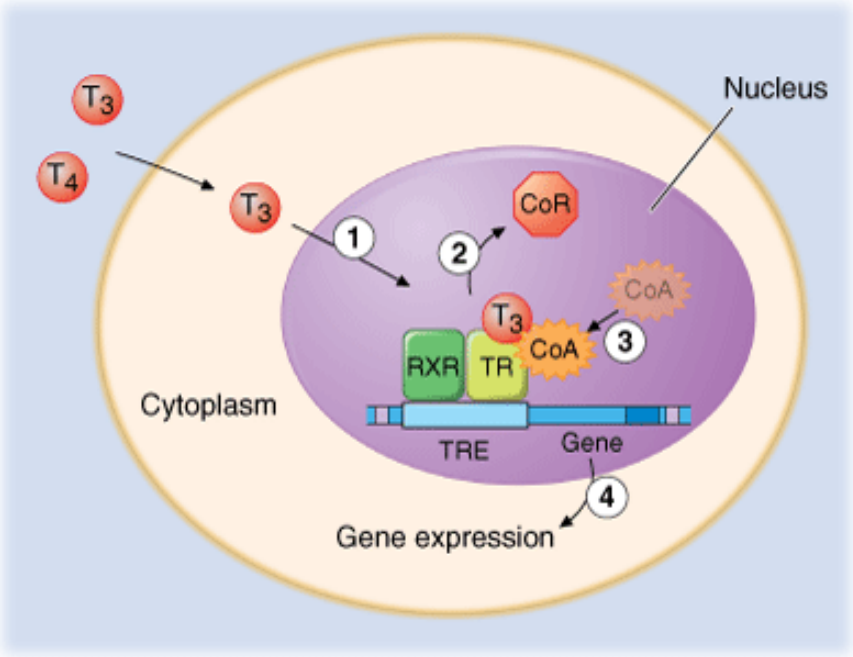
Liver Disorders

# Metabolic Disease Program: Selective Thyroid-β 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**
  - Broad: NASH, hypercholesterolemia, dyslipidemia
  - Rare: Glycogen storage disease, type Ia (GSD Ia)

    X-linked adrenoleukodystrophy (X-ALD)
- **Lead molecules VK2809, VK0214**
  - Oral, once-daily formulations
  - VK2809: Ongoing Phase 2 trial, fatty liver disease and hypercholesterolemia
    - Proof-of-concept study to begin 1H18, GSD Ia
  - VK0214: Preclinical, X-ALD

# Thyroid Receptor Overview




Key steps in receptor activation: Endogenous thyroid hormone T3 crosses mitochondrial membrane (1) binding thyroid receptor TR, dissociating co-repressor CoR (2). Subsequent binding of co-activator CoA (3) results in altered gene expression (4). RXR: retinoid X receptor; TRE: thyroid response element.

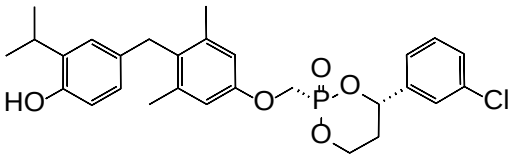
- **Nuclear hormone receptors**
- **Two major subtypes**
  - **Thyroid beta receptor:** Liver, brain; modulates cholesterol, triglyceride levels
  - **Thyroid alpha receptor:** Cardiac tissue, modulates heart rate, contraction

Therapeutic goal, lipid setting: β-receptor selectivity; minimize alpha-effects



Graphic: *Harrison's Principles of Internal Medicine,* 17th Edition, Chapter 335, Fig 335-4, copyright McGraw-Hill, 2008.

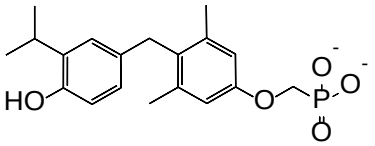
# VK2809: Unique Liver-Targeted Characteristics



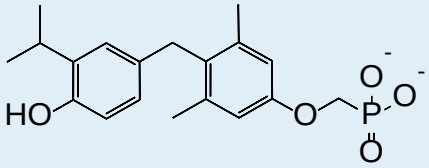
VK2809, Novel Prodrug

Following oral dosing:

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

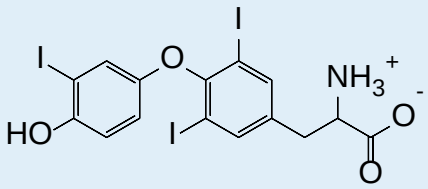


VK2809A, Potent TRβ Agonist, 2.2 nM Ki



VK2809A

- 17:1 selective for β:α
- Highly negatively charged
  - Poor passive diffusion
- Not actively transported
  - Due to altered chemistry
- Targeted hepatic re-uptake
  - Selective liver re-absorption via hepatic OATP1B3 transporter



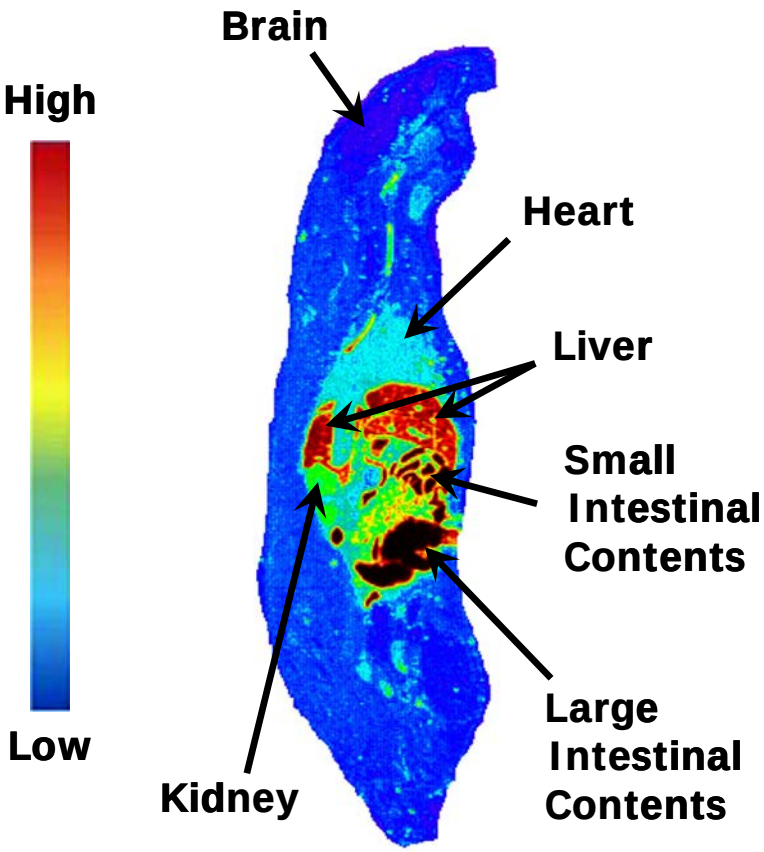
T3 Thyroid Hormone

- 1:2 selective for β:α
- Effectively neutral charge
- Active uptake in multiple tissues via MCT8
- Broad systemic availability
- Impractical for development due to safety

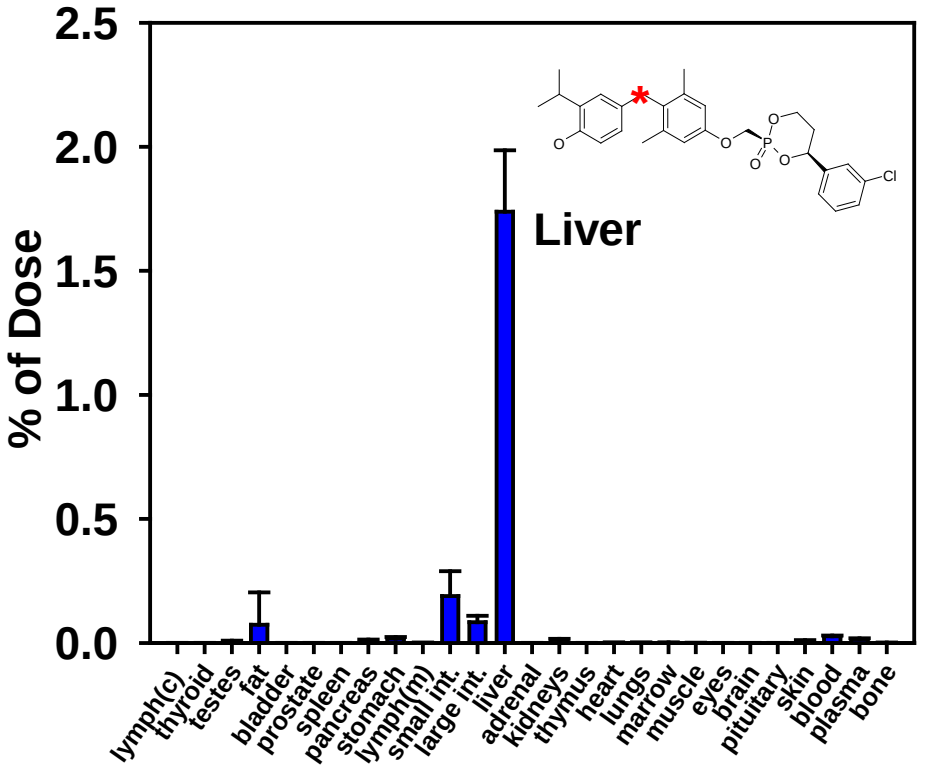
Selective activation, differentiated chemistry lends VK2809 liver selectivity; potentially minimizes risk of systemic effects

# VK2809: Evidence of Liver Selectivity

## $^{14}$C QWBA (4 h)




## $^{14}$C Tissue Distribution (24 h)



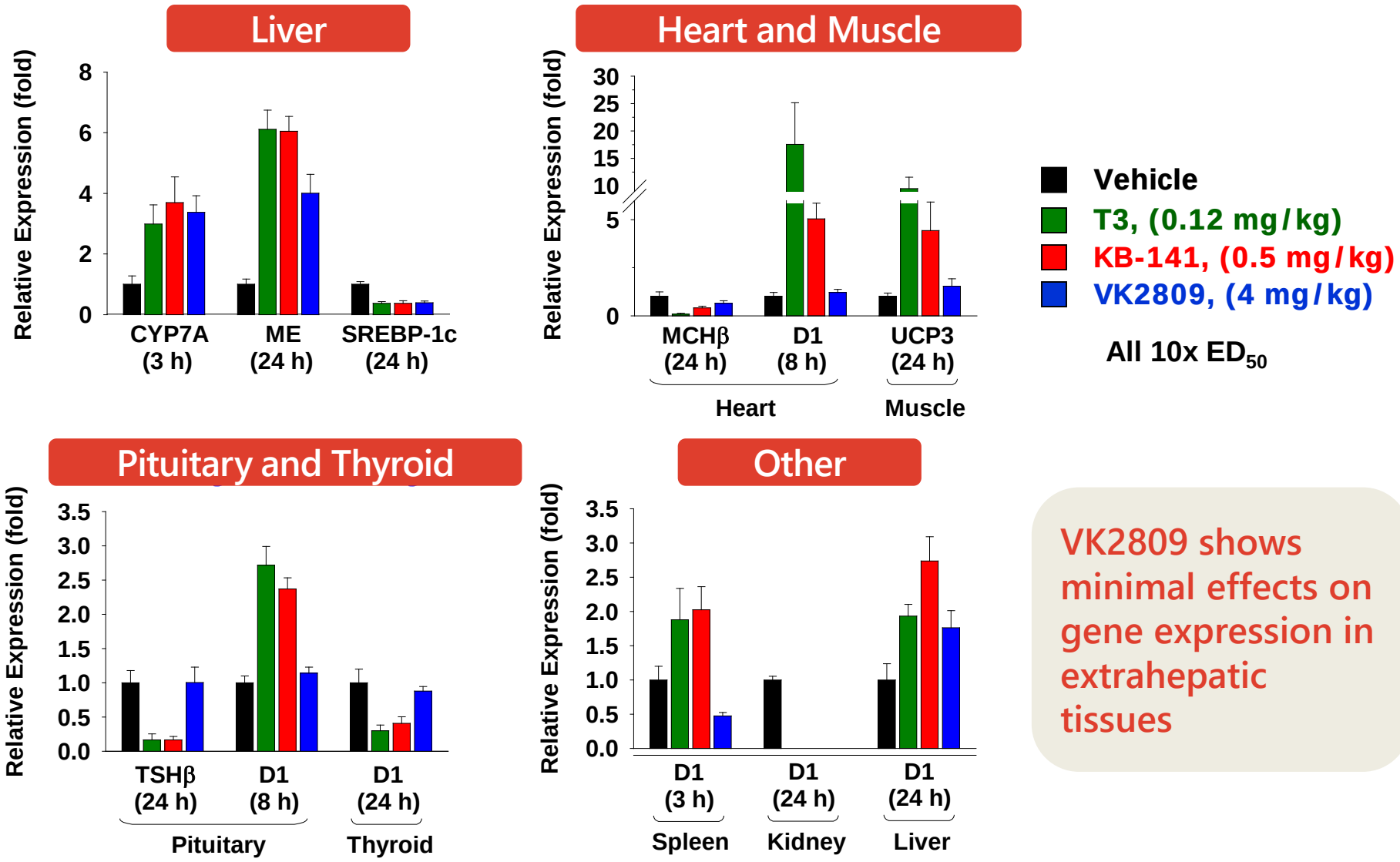

SD rat, 5mg/kg dose; approx. 30x anticipated human doses

Liver selectivity confirmed via radiologic analysis



1) *Drug Metab. Disp.*, 36(11), 2393-2403, (2008).

# VK2809: Liver-Selective Transcriptional Effects




VK2809 shows minimal effects on gene expression in extrahepatic tissues



1) *Proc. Nat. Acad. Sci.*, 104(39), 15490-15495, (2007).

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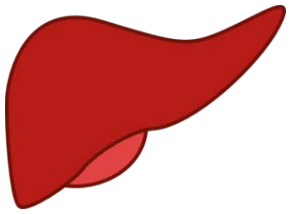
# VK2809: Potential Treatment for NAFLD and NASH

## Development of NASH:



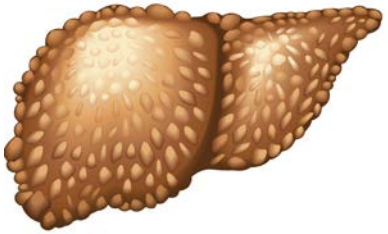
Healthy liver

First Hit: Accumulation of fatty acids, triglycerides

Subsequent: Oxidative stress, inflammatory response

NASH: Steatosis, ballooning, hepatocyte damage

NAFLD Disease Progression



- Cirrhosis
- HCC
- Liver failure

- Growing body of evidence suggests removing lipotoxic fat allows healing
  - Multiple studies indicate liver fat reduction >25% correlates with improved histology
  - Bariatric surgery patients: 70% experience NASH resolution; 66% improve/resolve fibrosis
- Targeted TRβ activation may have broad metabolic benefits in this setting

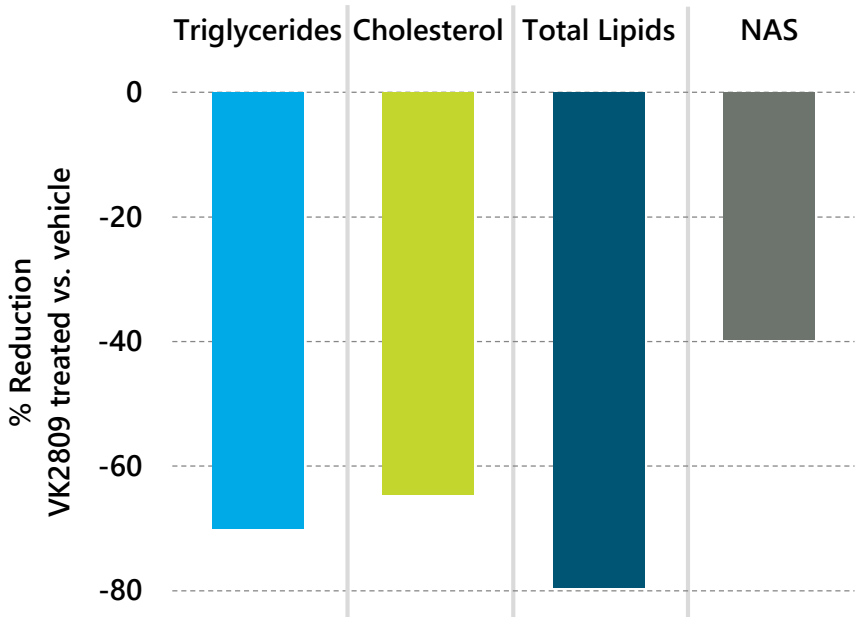


*1) Therap. Adv. Gastro.* 9(5), 692-701, 2016; AASLD 2017, abstracts 182, 612, 2123, 2169. 2) Meta analysis: *Clin. Gastro. Hepatol.* **6** (2008) 1396-1402. See also: Taitano et al. *DDW 2014, Abstract 233.*

# 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

**Change in Liver Lipids Following 8 Weeks Dosing With VK2809**




| | Triglycerides | Cholesterol | Total Lipids | NAS |
|---|---|---|---|---|
| % Difference: | -70.0% | -64.6% | -79.5% | -39.7% |
| p-value: | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

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



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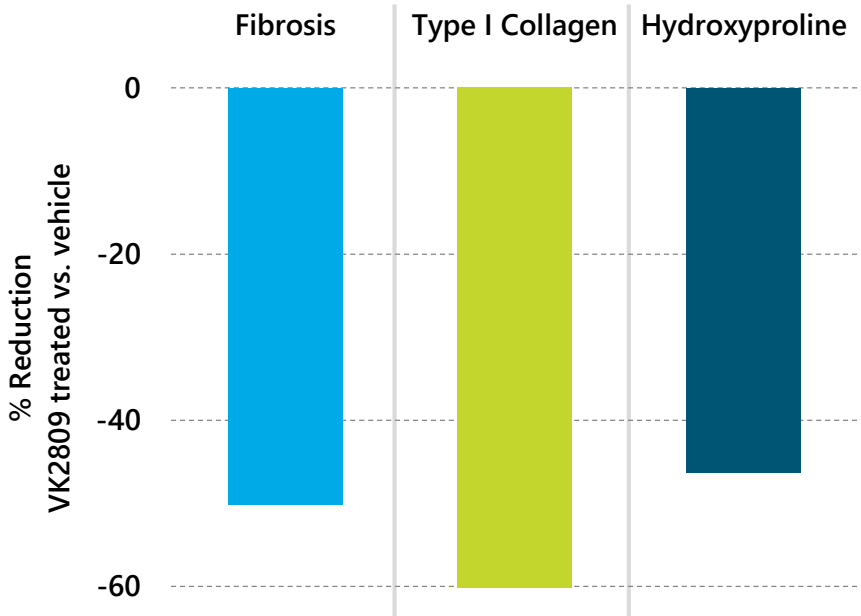
# VK2809 Improves Fibrosis in Diet-Induced NASH Model

- Significant reductions in fibrosis, collagen, hydroxyproline after 8 weeks
- Supports thesis that selective TRβ activation produces broad metabolic benefits
- Gene expression data show improvements in genes related to lipid metabolism, insulin sensitivity, fibrogenic signaling

**Change in Liver Fibrosis Following 8 Weeks Dosing With VK2809**




| | Fibrosis | Type I Collagen | Hydroxyproline |
|---|---|---|---|
| % Difference: | -50.2% | -60.2% | -46.3% |
| p-value: | <0.01 | <0.005 | 0.01 |

VK2809 significantly improved NASH and fibrosis in this model



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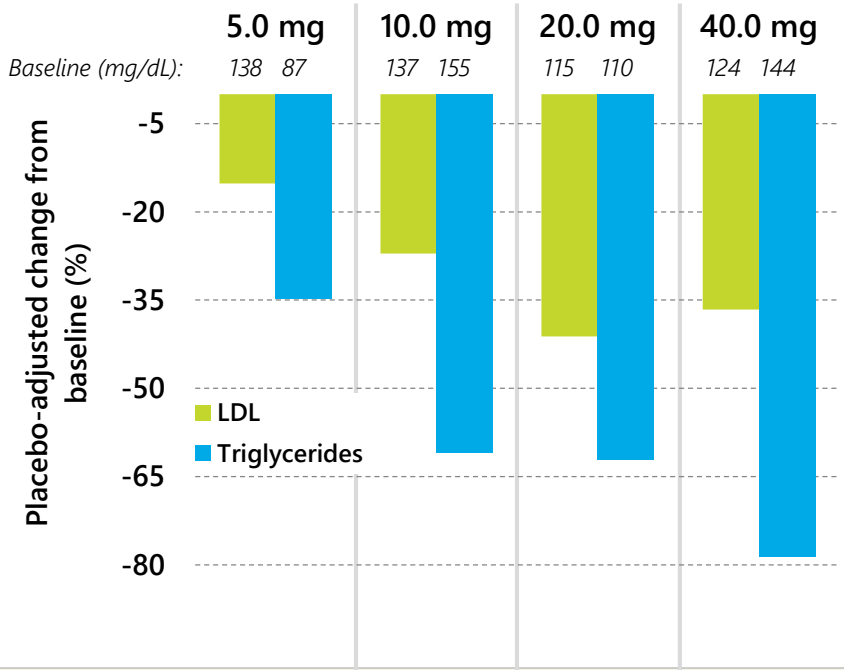
# VK2809 Clinical Highlights: 14-Day Phase 1b Study

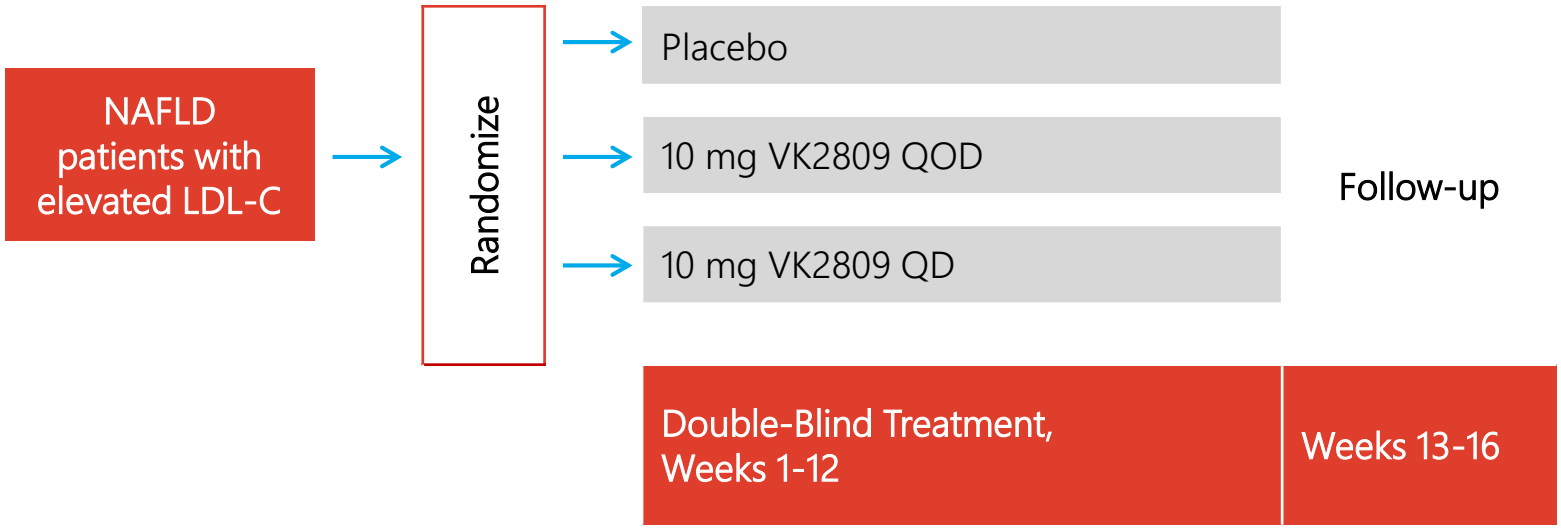
- Placebo-controlled trial (n=56), mild hypercholesterolemia
  - Enrollment criterion: LDL ≥ 100 mg/dL
- Results: clinically, statistically significant reductions in LDL
- Up to 79% reduction in triglycerides
  - Major component of liver fat
- Encouraging safety and tolerability, no SAEs

**Placebo-Adjusted Change From Baseline (%)**




| | 5.0 mg | 10.0 mg | 20.0 mg | 40.0 mg |
|---|---|---|---|---|
| **Placebo-adjusted reduction, LDL:** | -15.2% p=0.026 | -27.1% p=0.0003 | -41.2% p<0.0001 | -36.6% p<0.0001 |
| **Placebo-adjusted reduction, triglycerides:** | -34.8% p=0.052 | -61.0% p=0.0019 | -62.1% p=0.0007 | -78.6% p=0.0001 |

# VK2809: Phase 2 Trial in Fatty Liver, Hypercholesterolemia




## Phase 2 trial, patients with fatty liver disease, hypercholesterolemia

- Multi-arm, dose ranging, ~20 patients per arm
- Primary endpoint: ΔLDL-C
- Exploratory: Changes in liver fat (MRI), inflammatory markers, other
- Topline data expected 2H18

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# Musculoskeletal Program

## VK5211: Selective Androgen Receptor Modulator

Hip Fracture

# Musculoskeletal Program: VK5211 for Hip Fracture

- **Novel Selective Androgen Receptor Modulator (SARM), for hip fracture**
  - VK5211 is a potentially best-in-class small molecule SARM
- **Promising efficacy signals to date**
  - Significant improvements in lean body mass in animals and humans
- **Target indication: Rehabilitation post-hip fracture**
  - Population rapidly loses muscle, bone, function
  - >300,000 patients per year, U.S.; expect continued growth
  - Market opportunity potentially exceeds $1B annually
  - No approved therapies, no known SARMs in development
- **Potential benefits in other fractures, joint replacements, and muscle wasting disorders**

# VK5211: Potential Therapeutic Benefits of SARMs

- ↑ Muscle Mass
- ↑ Muscle Strength

- ↑ Bone Formation
- ↑ Bone Strength
- ↓ Bone Resorption

- ↑ Cognition
- ↑ Libido
- ↑ Energy

Goal: Retain beneficial properties of natural androgens with fewer side effects relative to anabolic steroids



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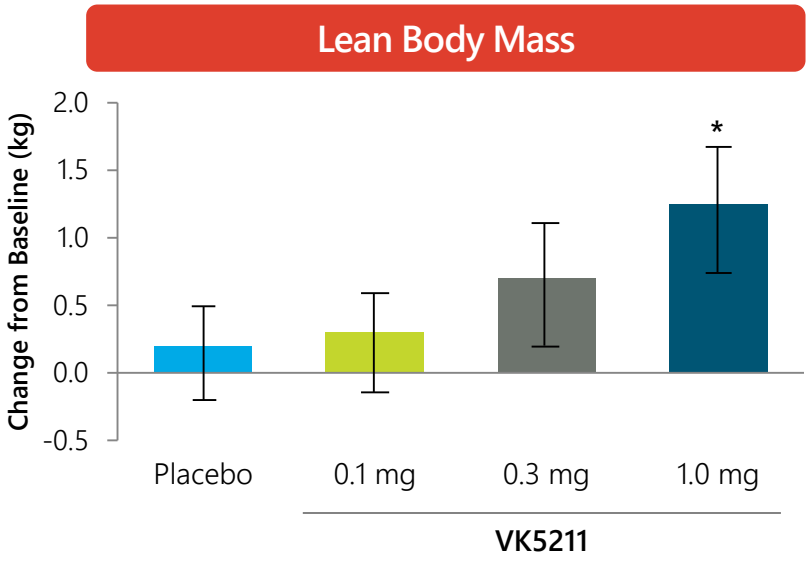
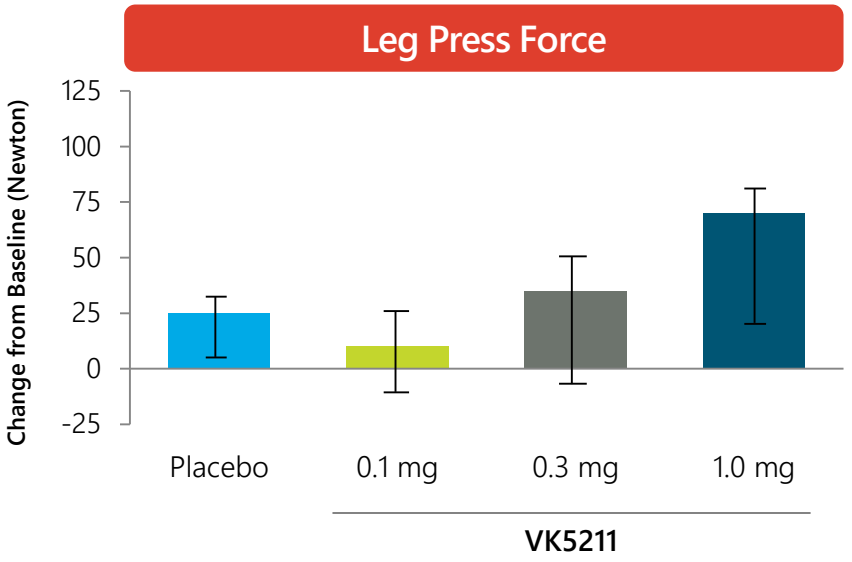
# VK5211: Preclinical and Early Clinical Highlights

- 0.9 nM Ki, AR; Positive effects on muscle and bone in animal models
- Three Phase 1 studies successfully completed[1-3]
  - Multiple ascending dose study: Healthy men (n=76) dosed once-daily for 21 days[2]
  - Statistically significant improvement in LBM after 21 days
  - Encouraging safety and tolerability, no drug-related SAEs



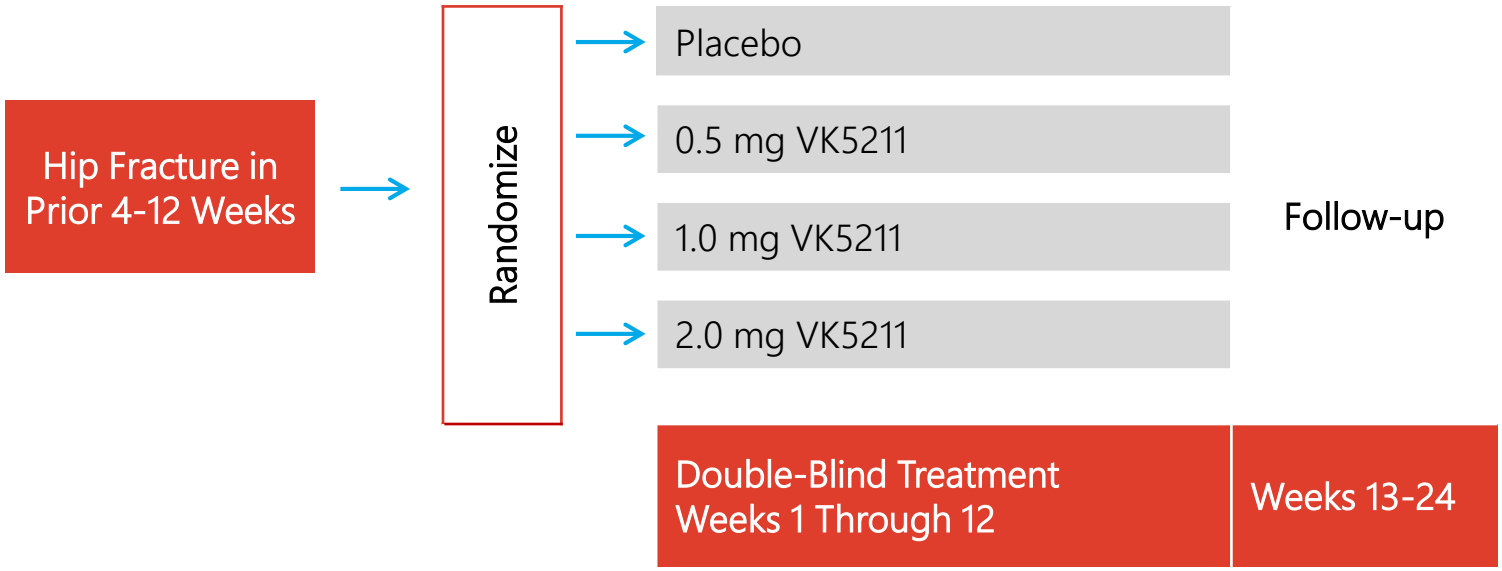




**LS-Mean (SE) Change from Baseline Up to Day 28** ***p = 0.047 vs. Placebo**



*1) Endo J.*, 57 Suppl 2, 2010, abstract P8-2-7. 2) *J. Gerontol. A. Biol. Med. Sci.* 2013, Jan; 68(1):87-95. 3) *5th Fracture Fragility Network Congress*, Poster TP15-10, Sept., 2016.

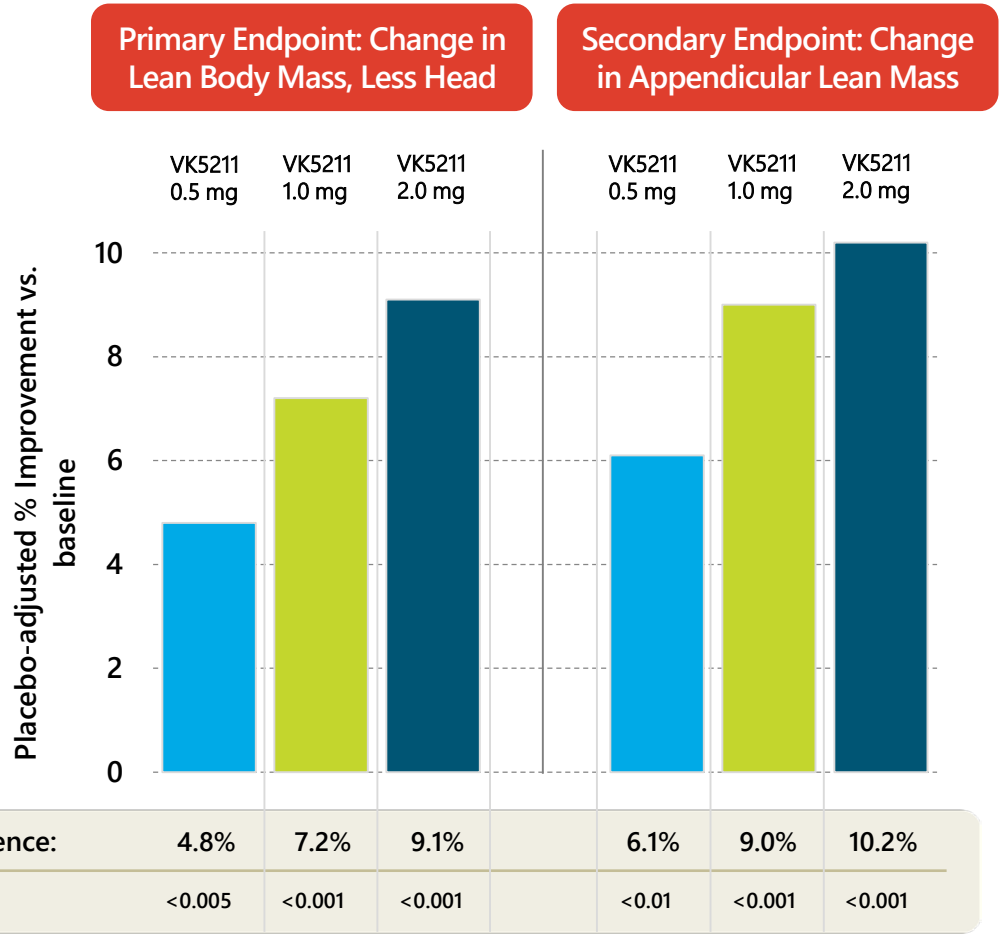
# VK5211: Phase 2 Trial, Hip Fracture




- **12-week Phase 2 trial in 108 patients**
  - Once-daily oral dosing
  - Primary endpoint: Change in lean body mass
  - Secondary and exploratory endpoints: Change in appendicular lean mass, total lean body mass, BMD, functional status, ADL, QOL

# Phase 2 Results Show Significant Increases in Lean Body Mass

- Significant increases in LBM and appendicular lean mass following 12 weeks of daily dosing
- Consistent dose response observed across primary, secondary efficacy measures
- Encouraging safety and tolerability, no drug-related SAEs

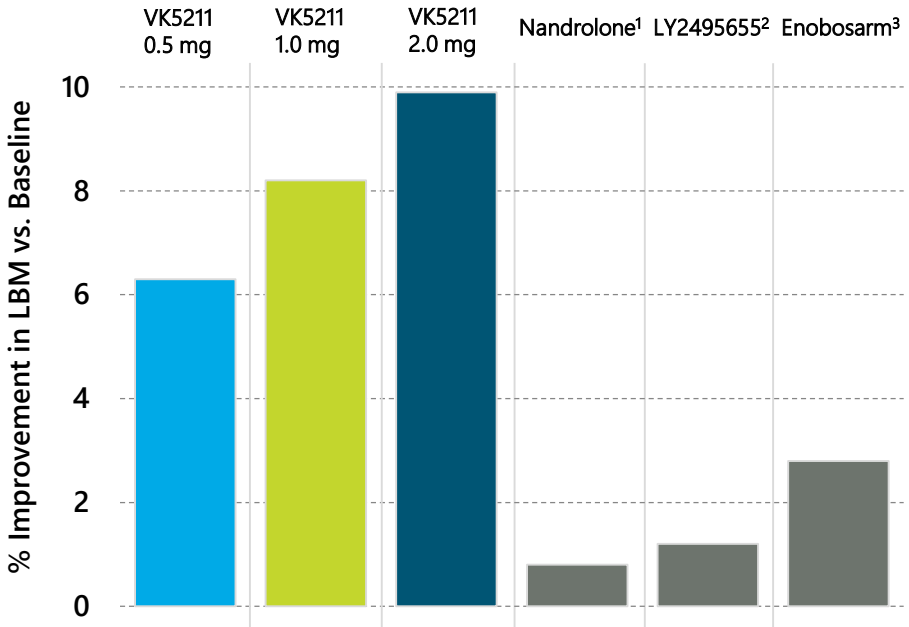



VK5211 produced robust dose-dependent effects on primary and all secondary measures of lean body mass

# VK5211 Demonstrates Potency Advantages to Other Mechanisms

- Significantly greater potency relative to testosterone analogs
- Improved potency on muscle compared with myostatin-targeting approaches
- Competitive effect on total lean body mass relative to other clinical-stage SARMs

## Reported Changes in Total Lean Body Mass in Older Adults




| | VK5211 0.5 mg | VK5211 1.0 mg | VK5211 2.0 mg | Nandrolone[1] | LY2495655[2] | Enobosarm[3] |
|---|---|---|---|---|---|---|
| % Difference: | 6.3% | 8.2% | 9.9% | 0.8% | 1.2% | 2.8% |
| p-value: | <0.005 | <0.001 | <0.001 | <0.05 | 0.02 | <0.001 |

VK5211 in older adults provides increases in lean body mass that compare favorably to other developmental mechanisms



1) Change in LBM at 6 months in hip fracture patients. *Clin. Nutrition*, 2004, 23, 587-596 2) Myostatin antibody. Change in LBM at 12 weeks in older weak fallers. *Lancet Diabet. Endo.* 2015, Dec; 3, 948-957. 3) Change in LBM at 12 weeks in men and women >60 yrs old. *J. Cachexia Sarcop. Muscle*, 2011, 2:153-161.

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# VK5211 Phase 2 Study: Overall Safety and Adverse Events

| | Placebo (n=28) | 0.5 mg (n=29) | 1.0 mg (n=26) | 2.0 mg (n=25) |
|---|---|---|---|---|
| Number reported adverse events | 31 | 21 | 16 | 38 |
| Number (%) of subjects with at least one reported: | | | | |
| Serious TEAE | 4 (14.3) | 2 (6.9) | 3 (11.5) | 5 (20.0) |
| Drug-related TEAE | 3 (10.7) | 3 (10.3) | 2 (7.7) | 6 (24.0) |
| Drug-related serious TEAE | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| TEAEs leading to discontinuation | 3 (10.7) | 1 (3.4) | 1 (3.8) | 3 (12.0) |

- Encouraging safety and tolerability
- Frequency of reported adverse events demonstrates no dose-relationship
- No drug-related treatment-emergent serious adverse events

# VK5211: Next Steps and Future Plans

- Will seek FDA feedback regarding data, registration path
- Explore partnering and licensing opportunities
- Plan for next steps in orthopedic settings with partner

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# Rare Disease Programs

## VK2809, VK0214

Glycogen Storage Disease
X-Linked Adrenoleukodystrophy

# Rare Disease Program: VK2809 for GSD Ia

- Glycogen Storage Disease, Type Ia (GSD Ia)
  - Orphan metabolic disorder; von Gierke's disease
- Characterized by inability to convert glycogen to glucose
  - Patients experience hypertriglyceridemia, with hepatic adenomas in up to 75%
  - May progress to transplant or HCC
- Natural history studies:  Lipid/metabolic control reduces adenoma risk
- High unmet medical need
  - ~2,000 U.S. patients
  - No approved therapy; slow release cornstarch is standard of care



(1) *Orphanet J. Rare Dis.*, **6**:27 (2011). (2) *Genetics Med.* **16**(11): e1 (2014). (3) *Eur. J. Pediatr.* **161**: S65-S69 (2002). (4) *J. Pediatr.* **159**(3): 442-446 (2011).

# TRβ Agonists Uniquely Suited for GSD Ia

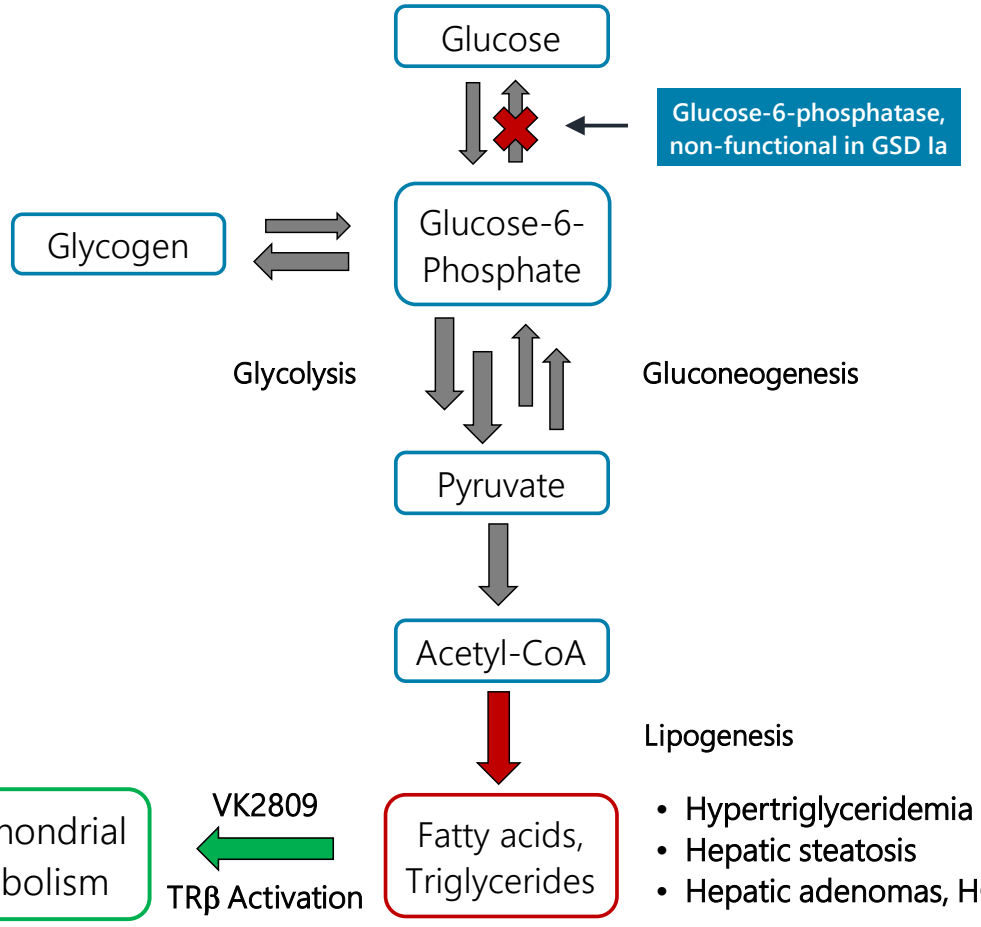
## TRβ modulates triglyceride, cholesterol metabolism

- VK2809 designed to selectively activate hepatic TRβ

VK2809: Stimulates genes important for lipid control

May provide efficient path for lipid metabolism and reduce steatosis, triglyceride burden

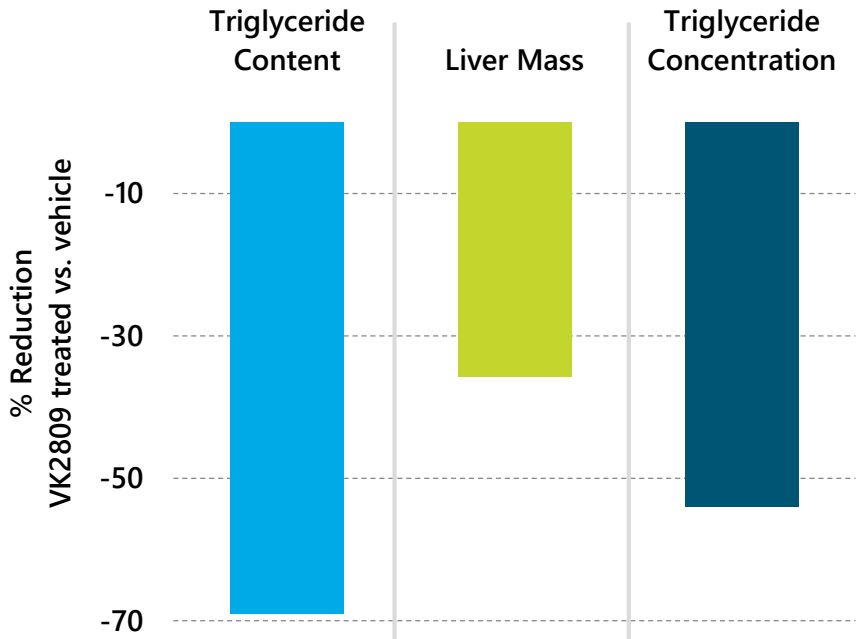
Potentially benefits overall lipid profile, reduce risk of adenomas, potential transformation to HCC



# VK2809 Significantly Reduces Liver Fat in GSD Ia Model

- Glucose-6-phosphatase KO mouse
  - Mimics human enzyme loss; hypertriglyceridemia, steatosis
- VK2809 leads to rapid improvement in hepatic fat content
- Next steps: POC study to begin 1H18

**Change in Liver Lipids Following Dosing With VK2809**




| | Triglyceride Content | Liver Mass | Triglyceride Concentration |
|---|---|---|---|
| % Difference: | -69.0% | -35.7% | -54.0% |
| p-value: | <0.0001 | <0.05 | 0.07 |

Suggests potential to improve liver lipids and metabolic control in patients with GSD Ia and potentially other GSDs



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# Rare Disease Program: VK0214 for X-ALD

- X-Linked adrenoleukodystrophy (X-ALD)
  - Orphan neurodegenerative disorder
  - X-linked: Carried by females, primarily manifesting in males
  - No cure, no approved therapy
- 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; no inflammatory component or brain involvement
  - Affects nearly all adult patients; considered "default" manifestation of ALD
  - Progressive motor impairment; wheelchair confinement, leg paralysis common

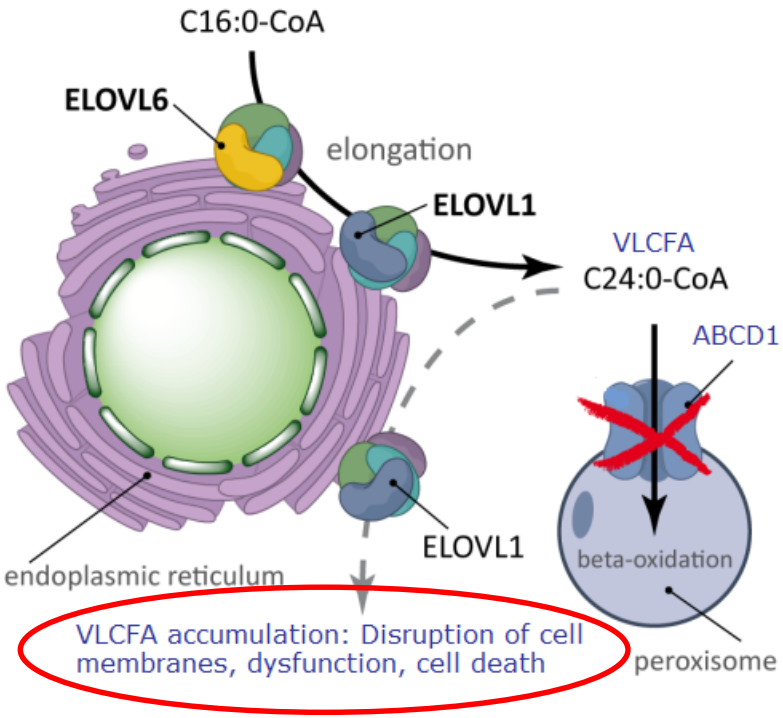


(1) *Biochimie*, **98** (2014) 135-142. (2) *Ann. Neurol.* **49**:512-517 (2001). (3) *Biochim. Biophys. Acta* **1822** (2012) 1465-1474. (4) *Orphanet J. Rare Dis.* **7**:51 (2012). (5) *Brain Pathol.* **20**(4): 845-856 (2010).

# TRβ: 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

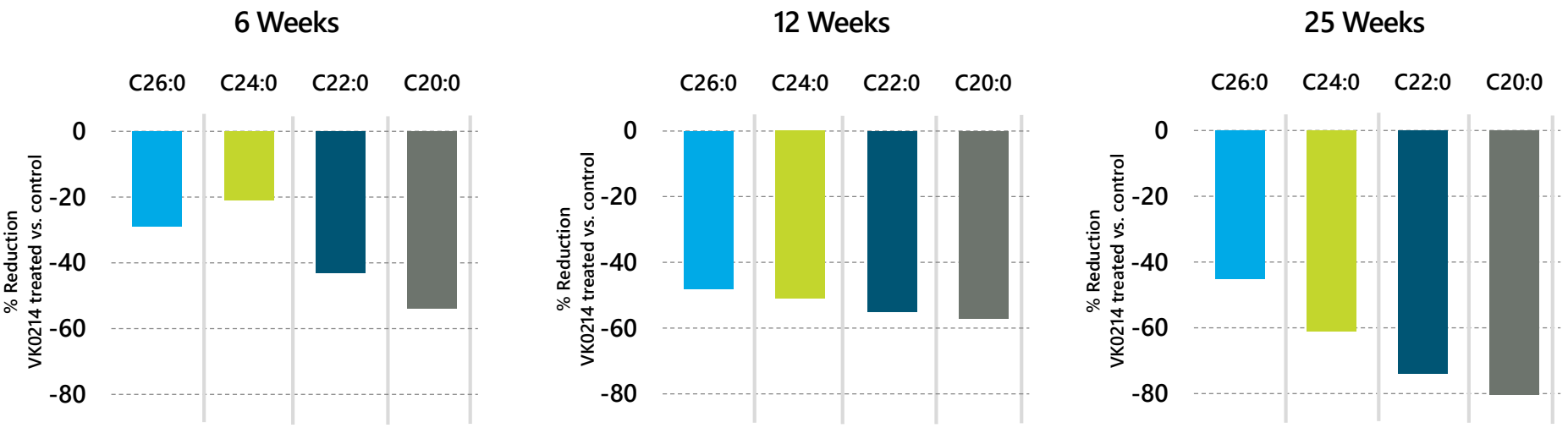


Graphic adapted from http://www.x-ald.nl/origin-and-metabolism-of-vlcfa/.

# 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

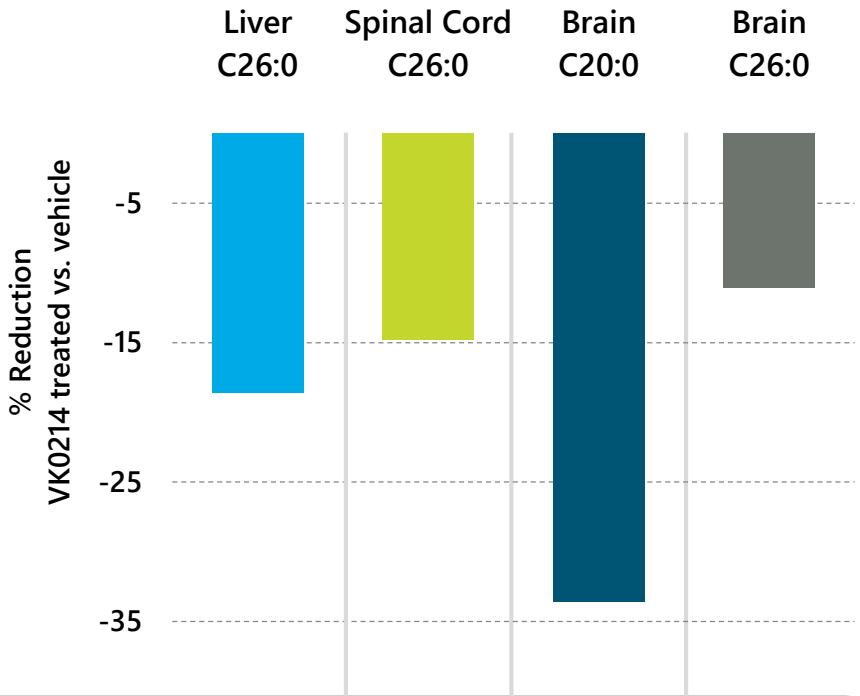



| | C26:0 | C24:0 | C22:0 | C20:0 |
|---|---|---|---|---|
| % Chg: | -29% | -21% | -43% | -54% |
| p-value: | <0.0001 | <0.005 | <0.0001 | <0.0001 |
| % Chg: | -48% | -51% | -55% | -57% |
| p-value: | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| % Chg: | -45% | -61% | -74% | -82% |
| p-value: | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

# VK0214: Reduces VLCFA Levels in Key Tissues

- Significant VLCFA reductions observed in multiple tissues
- Encouraging evidence of CNS activity
- Reductions in multiple VLCFAs consistent with plasma observations
- Suggests potential benefit in both cerebral and AMN forms of X-ALD
- Next steps: IND-filing, PoC study planned 1H19

## Change in Tissue VLCFAs: CNS and Peripheral Tissue




| | Liver C26:0 | Spinal Cord C26:0 | Brain C20:0 | Brain C26:0 |
|---|---|---|---|---|
| % Difference: | -19% | -15% | -34% | -11% |
| p-value: | <0.05 | <0.01 | <0.0001 | 0.07 |

# Financial Summary

- Capital structure and summary financials

| Capital Structure[1] | In '000s |
|---|---|
| Shares outstanding | 50,933 |
| Options, RSUs | 2,104 |
| Warrants | 8,781 |
| Total shares, options, RSUs, warrants | 61,818 |

| Financials[1] | March 31, 2018 ($'000s) |
|---|---|
| Cash, cash equivalents and short-term investments | $77,468 |
| Convertible notes[2] | $3,901 |

Notes: 1) Unaudited as of March 31, 2018. 2) Convertible notes held by Ligand.

# Investment Highlights

- **Focused on best-in-class drugs for metabolic and endocrine diseases**
  - Two Phase 2 programs supported by positive clinical data
- **Metabolic Disease Program: VK2809, for hypercholesterolemia, NAFLD**
  - Novel, selective thyroid receptor-β (TRβ) agonist
  - Phase 2 trial expected to complete in 2H18
- **Musculoskeletal Program: VK5211 for hip fracture recovery**
  - Non-steroidal selective androgen receptor modulator (SARM)
  - Phase 2 results demonstrate significant increases in lean body mass
- **Rare Disease Programs: GSD; X-ALD**
  - VK2809 in GSD Ia:  PoC study expected to begin 1H18
  - VK0214 in X-ALD:  Potential IND, PoC study to begin 1H19

VIKING
THERAPEUTICS

Corporate Presentation