Zacks Small-Cap Research

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Viking Therapeutics, Inc. (VKTX - Nasdaq)

VKTX: Initiating Coverage of Viking Therapeutics, Inc.; Developing Novel Therapies for Metabolic and Endocrine Disorders

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	11/16/2015
Current Price (11/16/15)	$4.82
Target Price	**$15.00**

INITIATION

We are initiating coverage of Viking Therapeutics, Inc. with a Buy rating and a $15.00 price target.

Viking is a clinical stage biopharmaceutical company developing therapies for the treatment of metabolic and endocrine disorders. The company currently has exclusive worldwide rights to five drug candidates. The company's lead asset, VK5211, is a small molecule drug that recently entered Phase 2 testing for acute rehabilitation following non-elective hip fracture surgery. The company's second clinical program is focused on two lead compounds, VK2809 and VK0214, for the treatment of the orphan disease adrenoleukodystrophy.

Viking completed an IPO in May 2015 and currently has $17.5 million in cash and cash equivalents, which should fund clinical development into 2017.

SUMMARY DATA

52-Week High	**$9.70**
52-Week Low	**$4.71**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**6,013**
Shares Outstanding (mil)	**10**
Market Capitalization ($mil)	**$47**
Short Interest Ratio (days)	**2.09**
Institutional Ownership (%)	**1**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2013 Estimate	**N/A**
P/E using 2014 Estimate	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	0 A	0 A	0 A	0 A	0 A
2015	0 A	0 A	0 A	0 E	0 E
2016					0 E
2017					0 E

Earnings per Share
(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	A	A	A	A	-$5.23 A
2015	-$0.81 A	-$1.07 A	-$0.53 A	-$0.51 E	-$2.82 E
2016					-$0.46 E
2017					-$0.49 E

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WHAT'S NEW

Initiating Coverage

We are initiating coverage of Viking Therapeutics, Inc. (VKTX) with a Buy rating and a $15.00 price target. Viking is a clinical stage biopharmaceutical company focused on developing treatments for metabolic and endocrine related disorders. We believe that Viking's products represent potential best-in-class treatments due to their unique mechanisms of action and strong safety profile in early clinical testing. With a market cap of less than $50 million, we believe the market does not fully appreciate the multiple billion-dollar opportunities Viking is pursuing, thus representing a compelling investment opportunity.

The company's lead asset, VK5211, is an orally available small molecule drug candidate in development for maintenance or improvement of lean body mass (LBM), bone mineral density (BMD), and function in patients recovering from non-elective hip fracture surgery. VK5211 belongs to a class of drugs known as selective androgen receptor modulators (SARMs), which are designed to selectively bind to a subset of receptors that interact with naturally occurring hormones known as androgens. Systemic activation of androgen receptors, with compounds such as testosterone, can stimulate the growth of bone and muscle, but is often accompanied by unwanted side effects such as prostate growth, excessive hair growth, and acne. VK5211 produces the same effect as testosterone in muscle and bone, but without the unwanted side effects, by selectively interacting with androgen receptors in those tissues. VK5211 was previously tested in three Phase 1 studies, with data showing that the drug rapidly stimulated the formation of LBM, which is vitally important for patients who have suffered a hip fracture. Preclinical data in a validated animal model of osteoporosis have also demonstrated a positive effect on BMD and bone formation. A Phase 2 proof-of-concept study has recently been initiated and we expect data from the study in the second half of 2016.

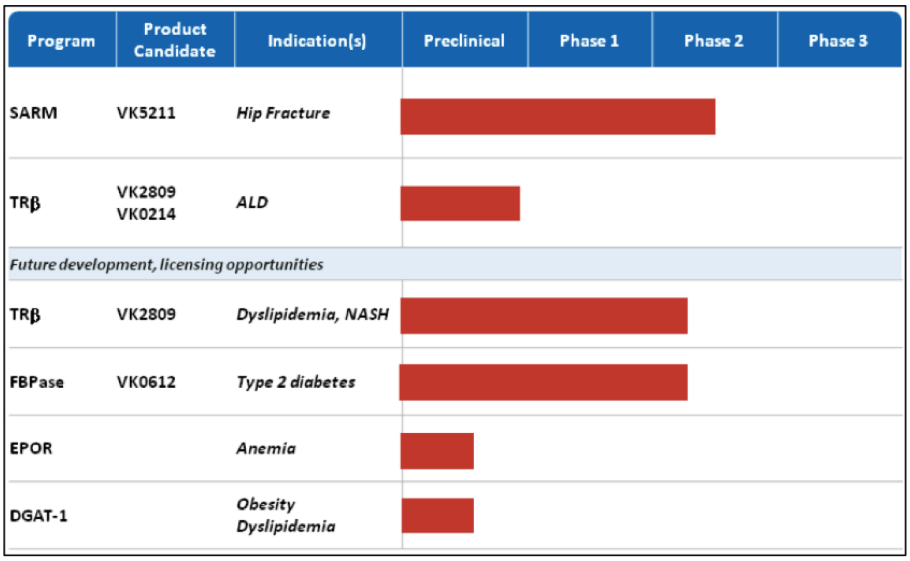
Viking's second clinical program is centered on two orally available small molecule thyroid receptor β (TRβ) agonists, VK2809 and VK0214. The compounds are being developed for the treatment of hypercholesterolemia, fatty liver disease, and adrenoleukodystrophy (ALD). For hypercholesterolemia and fatty liver disease, the company is planning to initiate a Phase 2 clinical trial in late 2015 with VK2809, with the results of that trial dictating future development directions for the compound. Data from this study are expected in the second half of 2016 or first half of 2017. ALD is a rare neurological disorder caused by a mutation in the transporter of very long chain fatty acids (VLCFA), encoded by the adenosine triphosphate binding cassette transporter D1 (*ABCD1*) gene. TRβ agonists have previously been shown to increase expression of a related transporter, encoded by *ABCD2*, which could replace the function of the mutated transporter. The company is currently finishing preclinical work with VK2809 and VK0214 to determine which compound to move into clinical testing for the treatment of ALD. Evaluation of both compounds in an animal model of the disease is expected to commence in the fourth quarter of 2015. If successful, the company expects to begin IND-enabling studies in 2016, potentially initiating a proof-of-concept trial in humans in 2017.

In addition to VK5211 and VK2809/VK0214, the company has three additional programs: VK0612, for the treatment of type 2 diabetes; an erythropoietin receptor agonist program, for the treatment of anemia; and a diacylglycerol acyltransferase-1 inhibitor program, for the treatment of obesity and lipid disorders. Each of those programs will be advanced upon securing additional funding.

The company completed an initial public offering (IPO) in May 2015 where a total of 3,000,000 shares of common stock was sold for $8 per share followed up by a full over-allotment of 450,000 shares sold to the underwriters of the IPO. Total net proceeds to the company were approximately $25.4 million, which should be sufficient to fund operations into 2017. All compounds in the company's pipeline are derived from a Master License Agreement signed with Ligand Pharmaceuticals (LGND), which grants Viking an exclusive, worldwide license to develop and commercialize each of them.

INVESTMENT THESIS

Viking Therapeutics, Inc. is focused on the development of medicines to treat metabolic and endocrine disorders. The company currently has five drug candidates in the pipeline that were in-licensed from Ligand Pharmaceuticals.



Source: Viking Therapeutics, Inc.

VK5211

Hip Fracture

Hip fractures are a serious health threat for elderly individuals. In the U.S., there are over 300,000 hip fractures every year (U.S. Department of Health and Human Services). More than 95% of hip fractures are due to falls (Parkkari *et al*., 1999). The consequences of hip fracture are numerous:

- Up to 30% of those with a hip fracture will die within the next year (Goldacre *et al*., 2002), with some long-term studies indicating excess mortality even 5 years after the incident (Forsén *et al*., 1999).
- Of those who survive, only 50% walk independently again and 20% move to a long-term care facility (Landefeld, 2011).
- Only 50% of patients recover prefracture capability of activities of daily living and only 25% recover full capability of their daily activities (Magaziner *et al*., 1990).

In addition to the physical toll, hip fracture also results in a significant financial burden for patients and the healthcare system. The lifetime attributable cost of hip fracture is estimated to be over $80,000, with almost half of that cost related to nursing facility expenses (Braithwaite *et al*., 2003). The estimated annual cost of hip fractures is estimated to be $10.3 to $15.2 billion in the U.S. (Dy *et al*., 2011).

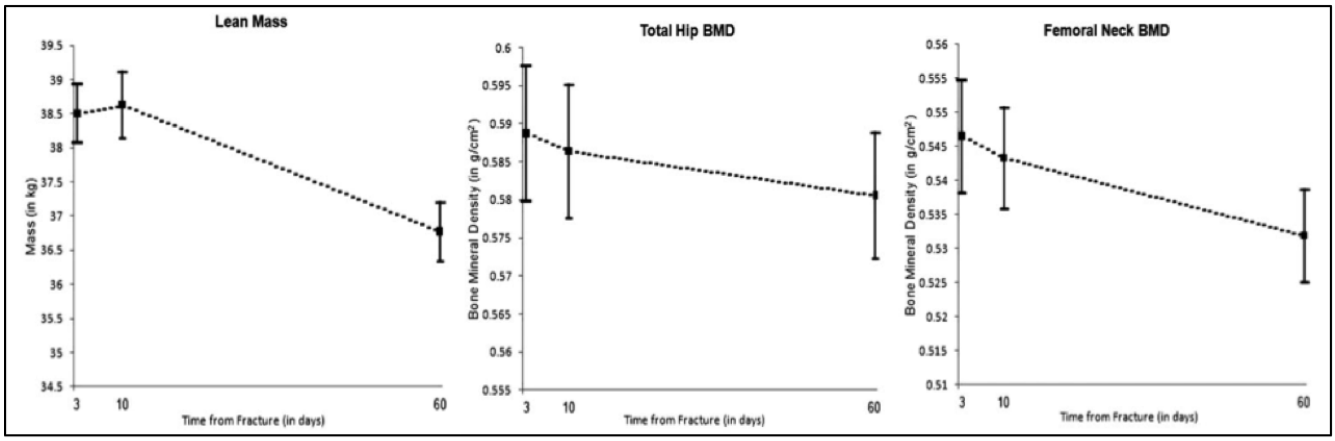
Women experience the majority of hip fractures (80%), with the average age at the time of hip fracture being 80 years and almost all patients being older than 65 (Parker *et al*., 2006). The lifetime risk for hip fracture is 20% for women and 10% for men. Due to the aging population in Western nations, by 2050 it is estimated there will be 500,000 to 1 million hip fractures per year in the U.S. (Brown *et al*., 2012).

Surgery is the most viable treatment option for most patients. Thromboembolic events are a common complication during recovery from a hip fracture, thus patients are typically put on low molecular weight heparin for up to 35 days after the incident. Suffering a hip fracture is a major risk factor for another hip fracture, thus some patients receive bisphosphonate therapy since studies show bisphosphonates reduce the risk of osteoporotic fractures through an increase in hip BMD (Wells *et al*., 2008). However, use of bisphosphonates for more than five years is associated with an increased risk of rare bone fractures (Park-Wyllie *et al*., 2011), thus a lot of doctors are hesitant about

prescribing them to patients recovering from hip fracture.

Changes in Body Composition After Hip Fracture

Hip fracture is associated with a number of morbidities, the majority of which are the result of deleterious changes in body composition following the injury. Body mass consists of three components: lean body mass (LBM), fat body mass (FBM), and bone. Fat mass and lean mass are known to undergo opposite and deleterious changes following hip fracture. In the first year after a hip fracture, fat mass increases by up to 7% (Karlsson *et al*., 1996) while lean mass decreases by up to 11% (Fox *et al*., 2000). This is in comparison to healthy older females who lose approximately 1% of lean mass per year and gain approximately 1.7% in fat mass (Karlsson *et al*., 2000). In addition, bone mineral density (BMD) declines in patients who have suffered hip fracture, which is in part due to a decrease in mobility in these patients. The following figures show that the change in body composition happens very quickly after hip fracture, with a significant decrease in LBM and BMD within two months of the incident.



Source: D'Adamo *et al*., 2014

The ability to slow or prevent the loss of LBM and BMD would likely have a profound impact on patient recovery following hip fracture. A number of studies have examined different therapeutic methods for improving body composition after hip fracture with mixed results:

- Binder *et al*., 2004: This study examined whether extended outpatient rehabilitation that included progressive resistance training improved physical function and reduced disability compared with low-intensity home exercise among physically frail elderly patients with hip fracture. Results showed that resistance training improved measures of physical activity, muscle strength, and walking speed but had no effect on BMD or FBM.

- Eriksen *et al*., 2009: This study examined whether the timing of first infusion of zoledronic acid (Reclast®) affected the antifracture efficacy and mortality benefit of the drug. Dosing the drug within two weeks of hip fracture resulted in an increase in hip BMD, a significant decrease in the risk of subsequent fracture, and a reduction in mortality.

- Boonen *et al*., 2011: This study tested the efficacy of once-yearly zoledronic acid in increasing BMD in men with a recent hip fracture. Results showed that while patients who received zoledronic acid had a significant increase in BMD, there was no difference in the rate of new clinical fractures.

- Orwig *et al*., 2011: This study tested whether a home-based exercise program initiated after usual care would improve the outcome of older patients following hip fracture. Results showed that while there was a small effect size in BMD in the home exercise group, there was no difference in body composition, activities of daily living, or psychosocial functioning.

What the preceding studies and others like them show is that while bisphosphonates have been shown to decrease the risk of hip fracture and to increase BMD (Lyles *et al*., 2007), no treatments are currently available that restore or preserve body composition in patients following hip fracture, thus representing a significant unmet medical need for a growing population of patients.

Selective Androgen Receptor Modulators

Androgens are a group of hormones that regulate the reproductive system as well as maintain homeostasis of the muscular, skeletal, cardiovascular, metabolic, and central nervous systems. The most prominent androgen is testosterone, which is predominantly produced in the testes in men and in the adrenal glands and ovaries in women, although at lower levels than in men. Testosterone stimulates the growth of muscle and bone (anabolic effects) as well as the prostate and sebaceous glands (androgenic effects), and is considered a non-tissue-selective androgen. Androgens act through binding to androgen receptor (AR). AR is a nuclear receptor that is activated by binding to androgenic hormones (testosterone and dihydrotestosterone) in the cytoplasm after which it is translocated to the nucleus where it acts as a DNA binding transcription factor to regulate gene expression (Roy *et al*., 1999).

Amongst other things, androgens inhibit fat accumulation and increase skeletal muscle growth, two properties that make them ideal therapeutic candidates for restoring or preserving body composition following hip fracture. Unfortunately, the use of testosterone therapy has a number of side effects including prostate growth (Meikle *et al*., 1997) and polycythemia (Snyder *et al*., 2000) in men and acne, alopecia, and hirsutism in women (Phillips *et al*., 1997). Thus, what would be most beneficial would be a product that provided the anabolic effects of androgen therapy with limited androgenic effects.

Selective androgen receptor modulators (SARMs), first described in 1998 (Dalton *et al*., 1998; Edwards *et al*., 1998), are compounds designed to act as AR agonists in muscle and bone while being partial agonists in other areas of the body (e.g., prostate). The proposed mechanism for the tissue selectivity of SARMs includes the following factors:

- ✓ SARMs are resistant to metabolism by 5α-reductase and aromatase. The most potent androgen in the prostate is dihydrotestosterone (DHT), which is formed by 5α-reduction of testosterone. 5α-reductase is expressed in high levels in the prostate and low levels in muscle and bone, indicating the significance of DHT in prostate and testosterone in muscle and bone. Conversion of testosterone to estradiol by aromatase, which is ubiquitously expressed in the male reproductive tract, causes prostate growth. Since non-steroidal SARMs are not metabolized by either enzyme, their effects can be directed to AR binding and not to metabolic conversion products.

- ✓ Coregulator function. The function of AR is dependent on a class of proteins known as coregulators, which bind hormone-bound receptors to either enhance (coactivators) or reduce (corepressors) AR transactivation. More than 300 coactivators have been identified (Smith *et al*., 2004). Conformational changes in AR structure upon binding androgens is different from those that occur upon binding SARMs, which can lead to the recruitment of different coregulator complexes (Kazmin *et al*., 2006). Thus, it is proposed that SARM binding to AR could result in the differential recruitment of coactivator complexes in muscle and bone and corepressor complexes in prostate, however at this point it is mostly theoretical.

- ✓ Intracellular signaling cascades. Androgens affect different tissues in different ways through both AR-dependent and AR-independent mechanisms. For example, testosterone signals through inhibition of the p38 MAPK, Notch-1, Notch-2, and Jagged-1 signaling pathways in macrophages but through activation of PI3K-Akt pathways in bone (Guo *et al*., 2004; Kang *et al*., 2004). In addition, the osteo-protective effects of androgens are exerted through non-genomic signaling while development of the sexual organs is imparted through genomic effects (Kousteni *et al*., 2001). Separation of those two effects by SARMs leads to an increase in BMD with no effect on the prostate.

SARMs represent a novel class of compounds that could usher in a new way of treating patients that require anabolic therapy, including those suffering from hip fracture, cancer, osteroporosis, or other muscle wasting diseases.

VK5211

Viking's lead drug candidate is VK5211 is a third-generation non-steroidal SARM that is being developed for maintenance or improvement of LBM, BMD, and function in patients recovering from non-elective hip fracture surgery. VK5211 (then known as LGD-4033) was originally developed by Ligand Pharmaceuticals, Inc. (LGND) and was previously tested in preclinical models and early stage clinical trials. Two Phase 1 clinical trials showed the drug to be safe and well-tolerated at all doses following daily oral administration for up to 21 days. The drug selectively activates AR in muscle and bone, stimulating muscle and bone growth, while avoiding undesirable side

effects, such as unwanted hair growth, acne, or prostate growth. Viking recently reported completion of a third Phase 1 trial in healthy elderly subjects, which confirmed the safety, tolerability, and pharmacokinetic profile observed in younger subjects.

Phase 1 Trial #1: The first Phase 1 trial involving VK5211 was a randomized, double blind, placebo controlled trial in 48 healthy male volunteers and was conducted in 2009. Six cohorts received an escalating single dose of VK5211 ranging from 0.1 mg to 22 mg. The primary objective of the trial was to evaluate the safety and tolerability of VK5211 in healthy male subjects. Secondary objectives included examining the pharmacokinetics (PK) and pharmacodynamics (PD) of single doses of VK5211. The PD results showed dose-related reductions in total testosterone and sex-hormone binding protein, which is consistent with the mechanism of action of SARMs. In addition, a dose-related decrease in fasting serum HDL was observed.

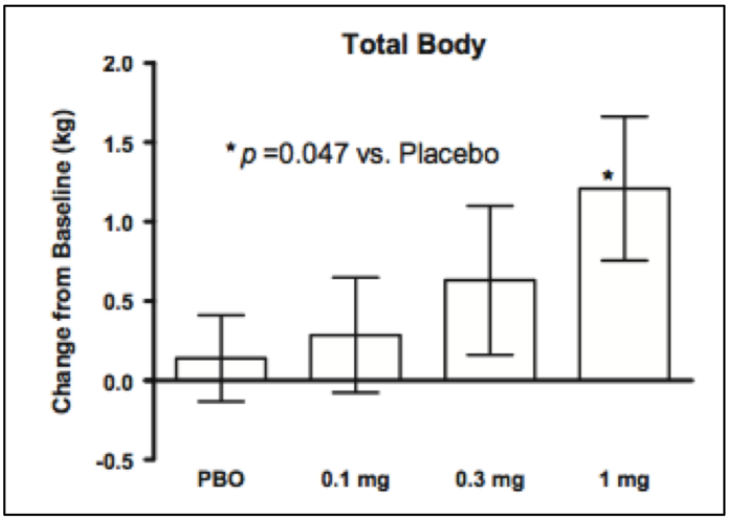
Phase 1 Trial #2: In a subsequent Phase 1 multiple ascending dose clinical trial, which was conducted from 2010-2011, 76 healthy men in three cohorts received daily doses of placebo, 0.1 mg, 0.3 mg, or 1 mg of VK5211 for 21 consecutive days (Basaria *et al*., 2013). The primary objective of this study was to evaluate the safety and tolerability of VK5211 when dosed for 21 days. Secondary objectives included examining PK and PD data following once-daily administration for 21 days. Exploratory objectives included a determination of LBM after once-daily administration of VK5211 for 21 days by dual energy X-ray absorptiometry (DEXA) scan, maximal voluntary strength measured by the one repeat maximum method, and stair climbing power.

- PK: VK5211 displayed a prolonged elimination half-life (24-36 hours) and linear PK. There was a dose proportional increase in drug concentration on days 1 and 21, suggesting that accumulation occurs upon multiple dosing.

- Hormone levels: There was a dose-dependent suppression of total testosterone and sex-hormone binding levels from baseline to day 21. Free testosterone suppression was only noted at the 1.0 mg dose level. Serum leutinizing hormone did not show any meaningful changes from baseline, while follicle-stimulating hormone levels were suppressed only in the 1.0 mg dose group. Following discontinuation of the drug, hormone levels returned to baseline by day 56.

- Plasma Lipids: Total and low density lipoprotein (LDL) cholesterol levels did not change significantly from baseline at any dose. However, high density lipoprotein (HDL) cholesterol levels decreased from baseline at doses ≥ 0.3 mg and at the 1.0 mg dose the average HDL of 49.2 mg/dL decreased by an average of 19.4 mg/dL. After treatment was discontinued, HDL levels returned to baseline. Triglyceride levels decreased for all doses tested. All of these results are consistent with data reported from other SARMs.

- Body Composition and Muscle Performance: There was a dose dependent increase in LBM (*p* for trend = 0.04). The average increase in LBM at the 1.0 mg dose was 1.2 kg (*p* = 0.047 vs. placebo). FBM did not change significantly for any treatment group. For the 1.0 mg dose, the average increase in strength (assessed by leg press) was 68.3 N, however this was not statistically different from the placebo group. Stair-climbing speed and power also showed a trend toward dose-related improvement but these changes were not statistically significant.



Source: Basaria *et al*., 2013

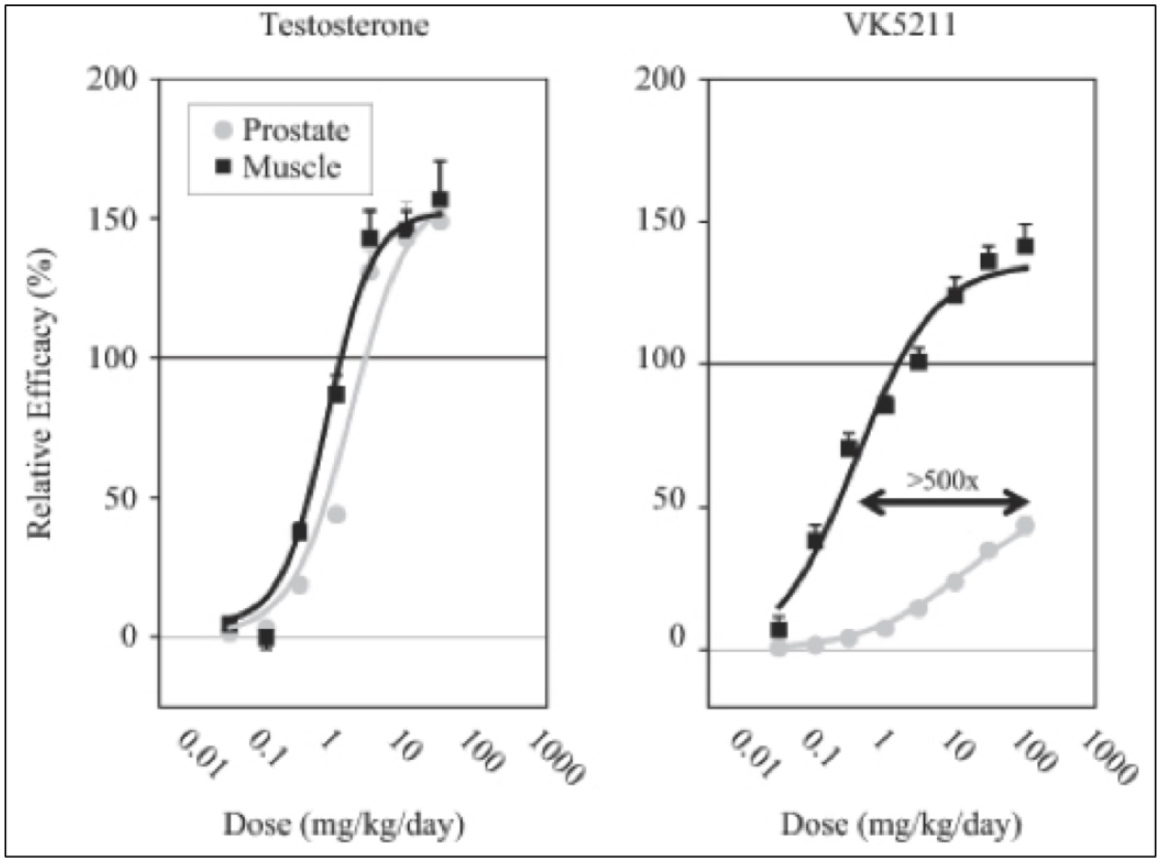
Phase 1 Trial #3: This study was conducted to evaluate the safety, tolerability and pharmacokinetics properties of VK5211 in elderly subjects, which Viking believes is potentially representative of the hip fracture population. The results showed VK5211 to be safe and well tolerated at all doses evaluated. No serious adverse events were observed and all subjects received all scheduled doses. In addition, the observed pharmacokinetic properties were similar to those previously reported in younger male subjects.

Preclinical Data: The binding and transcriptional activity of VK5211 was characterized *in vitro* while the effects on bone, muscle, and off-target tissues were examined *in vivo* (Vajda *et al*., 2009). VK5211 was shown to bind with high affinity and selectivity, as shown in the following table.

Receptor	Receptor Binding K_i (nM)	Transcriptional Activity Efficacy (%)	Transcriptional Activity EC_{50} (nM)
Androgen Receptor	0.9	132	4.4
Mineralocorticoid Receptor	>10,000	1	--
Glucocorticoid Receptor	5,797	1	--
Estrogen Receptor α	nd	1	--
Progesterone Receptor	4,009	1	--

Source: Vajda *et al*., 2009

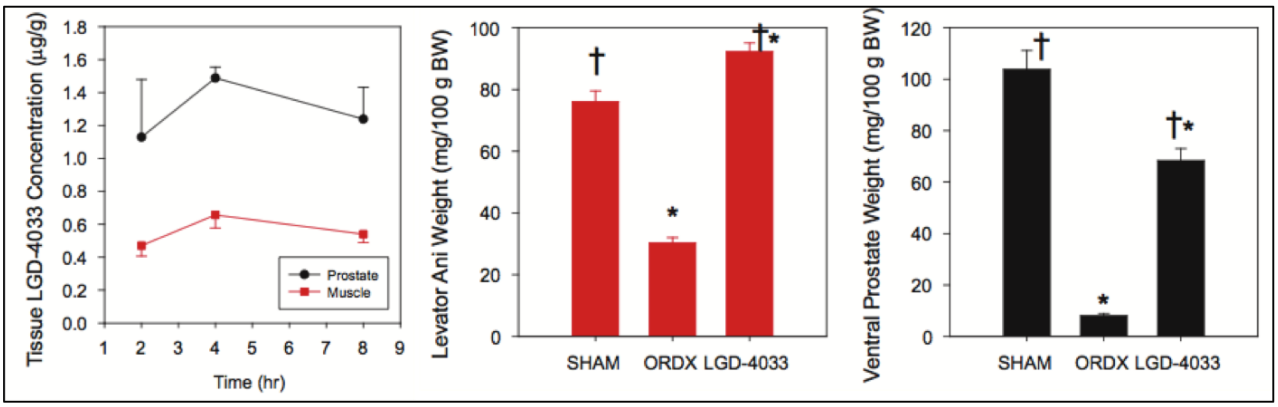
VK5211 tissue selectivity was shown in castrated rats, which were left untreated for 14 days to allow for muscle and prostate atrophy. The rats were then treated with varying concentrations of VK5211 for 14 days. Results in the following graph are shown in relation to castrated (0%) and control rats (100%) and show much higher activity (>500x) of the drug against muscle than prostate. This is in comparison to testosterone, which shows no tissue selectivity.



Source: Viking Therapeutics, Inc.

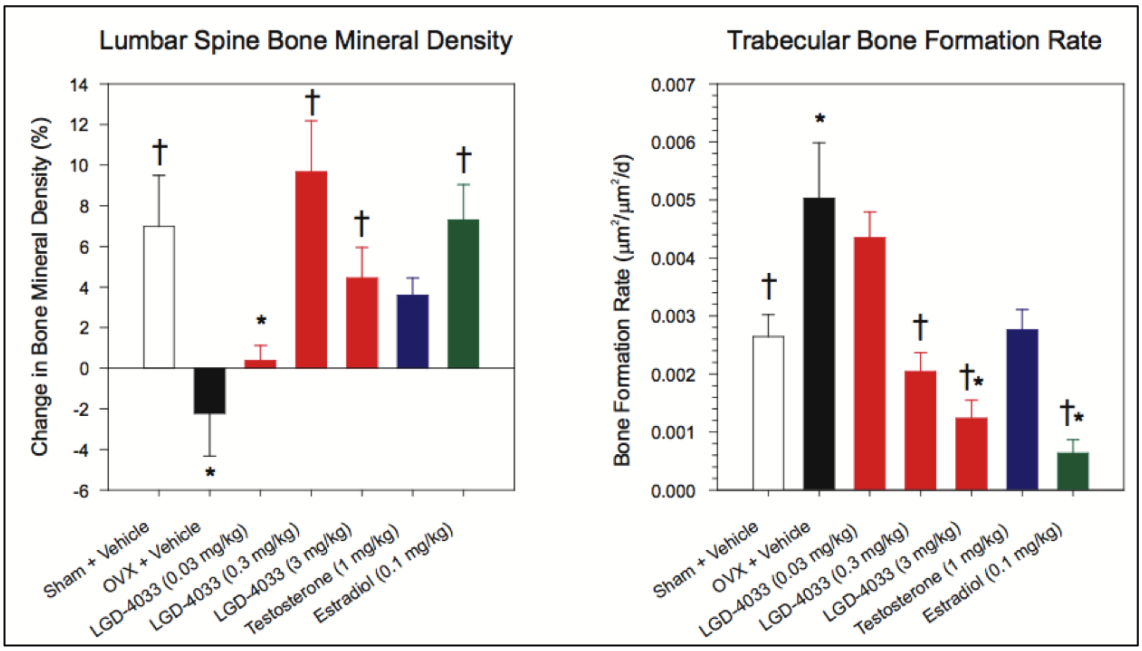
Interestingly, the tissue concentration of VK5211 was shown to be higher in prostate than in muscle (below left), however the activity of the drug was reduced in the prostate compared to muscle, as shown by a smaller prostate in

castrated rats treated with VK5211 (ORDX) than in sham operated rats that were intact (below right). The activity of VK5211 on muscle is exhibited by a larger weight of the levator ani (hip muscle) in castrated rats treated with VK5211 than in sham operated rats (below middle). Note that the graphs below identify VK5211 by its prior identification code, LGD4033.



Source: Vajda *et al*., 2009

VK5211 was also shown to be effective in a rat model of osteoporosis. Ovariectomized female rats were allowed to develop ostopenia for eight weeks before once-daily oral treatment with VK5211 for 12 weeks. Results showed that VK5211 increased lumbar spine BMD as effectively as estradiol and testosterone (below, left), and also significantly decreased trabecular bone turnover compared to placebo (below, right).



Source: Vajda *et al*., 2009

VK5211 Clinical Development Plan

Viking is developing VK5211 as a treatment for acute hip fracture, of which there are no approved therapies to treat patients experiencing loss of LBM or BMD nor are there approved therapies to facilitate improved functional performance following surgery. The company recently initiated a Phase 2 study in patients ≥ 65 years of age who have suffered a hip fracture within the past three to seven weeks. This will be a multicenter, randomized, parallel group, double blind, placebo controlled trial, where patients will be administered placebo or 0.5 mg, 1.0 mg, or 2.0 mg of VK5211 once-daily for 12 weeks (NCT02578095). A total of 120 patients are expected to enroll in the trial evenly split between the four treatment groups. The primary outcome of the trial is the change in LBM after 12 weeks of treatment. Secondary and exploratory endpoints include assessments of functional performance, quality-of-life, and activities of daily living. We anticipate topline results being available in the second half of 2016.

VK2809/VK0214

Thyroid Hormones

Thyroid hormones play a critical role in the regulation of metabolic rate, energy consumption, and lipid metabolism (Oetting *et al*., 2007). The predominant thyroid hormones, L-thyroxine (T4) and L-triiodothyronine (T3), are synthesized in the thyroid gland and released bound to thryoxine-binding globulin, albumin, and thyroid-binding prealbumin. Only small amounts of unbound thyroid hormones flow freely through the bloodstream, and it is this fraction that is available to enter target cells. Most of the effects of thyroid hormones are exerted through binding to the thyroid hormone receptors (TR). There are two major isoforms of TR, TRα and TRβ, which are encoded by separate genes. TRα and TRβ also have markedly different expression patterns, with TRα expression highest in the heart and brain while TRβ expression is highest in the liver (Bookout *et al*., 2006).

Excess thyroid hormone (hyperthyroidism), either through overactivation of the thyroid gland or delivery of exogenous hormone, can lead to tachycardia, muscle wasting, osteoporosis, fatigue, and anxiety (Webb, 2004). However, excess thyroid hormone can also result in some beneficial effects, such as reductions in serum LDL cholesterol and body fat. In addition, hypercholesterolemia was recognized early on as a side effect of hypothyroidism, which is a condition of insufficient thyroid hormones. These observations led to a study in psychiatric patients on the use of dried thyroid extract that showed it reduced serum cholesterol (Gofman *et al*., 1957). Follow-up studies with D-thyroxin showed that while it caused a decrease in LDL cholesterol, the side effects were so severe (in particular cardiac complications) that the use of thyroid hormones as therapeutics had to be abandoned (Coronary drug project, 1972). These results were the impetus to identify compounds that could provide the positive lipid lowering effects of thyroid hormones without the cardiac complications.

TRα and TRβ

Studies on genetically altered mice and patients with thyroid hormone resistance have given scientists a greater understanding for the differing roles of TRα and TRβ in regulating metabolism. Patients who are resistant to thyroid hormone have a mutation in TRβ that reduces the affinity of the receptor for T3 (Yen, 2003). This leads to an increase in circulating thyroid hormone levels, which is typically enough to restore normal TRβ activity in peripheral tissues (decreased affinity means that more thyroid hormone is necessary to elicit the same TRβ activity). However, a side effect of this increase in thyroid hormone levels is increased heart rate, suggesting that TRα regulates heart rate (since TRα would not require excess amounts of thyroid hormone to function properly, excess thyroid hormones causes excess activity of TRα).

Additional evidence for the roles of TRα and TRβ come from studies of “knock-out” mice whereby either TRα or TRβ was genetically removed, with the results showing a clear role for TRα in regulating heart rate (Wikström *et al*., 1998) and TRβ regulating serum cholesterol levels (Weiss *et al*., 2002; O’Shea *et al*., 2002). Thus, compounds that can selectively alter TRβ function with little to no effect on TRα could have a beneficial effect on lipid metabolism while avoiding deleterious cardiac side effects.

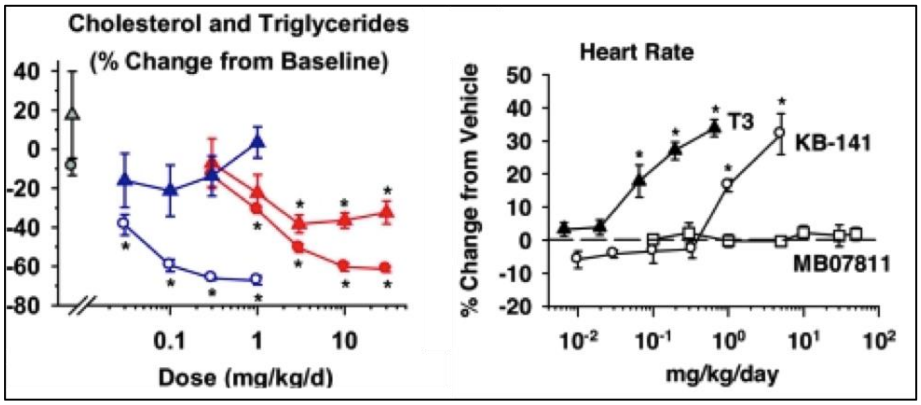
VK2809/VK0214

VK2809 and VK0214 are novel, orally available, selective TRβ agonists that are in development for adrenoleukodystrophy (ALD) and lipid disorders such as hypercholesterolemia and fatty liver disease. VK2809 ((2*R*,4*S*)-4-(3-chlorophenyl)-2-((3,5-dimethyl-4- (4′-hydroxy-3′-isopropylbenzyl)phenoxy)methyl)-2-oxido-(1,3,2)-dioxaphosphonane; formerly known as MB07811) was originally developed by Metabasis Therapeutics, Inc., which was acquired by Ligand in 2009. The compound has been tested in multiple preclinical models as well as two Phase 1 clinical trials.

While both compounds are TRβ agonists, VK0214 has a different pharmacokinetic and pharmacodynamic profile than VK2809 (shorter half-life but higher Cmax). In addition, the drug is activated by carboxyesterases, which are ubiquitously expressed in the body, thus potentially making the drug more suitable for a disease such as ALD, which is more diffuse than hypercholesterolemia or fatty liver disease.

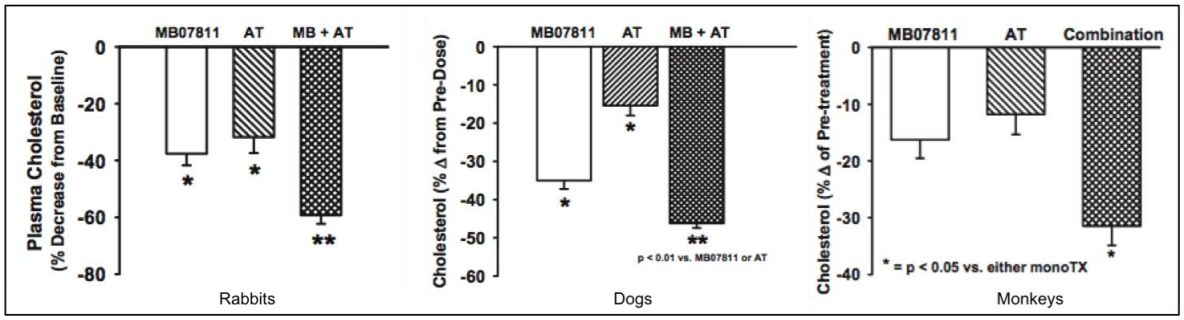
VK2809 is a prodrug of a potent TRβ agonist that is converted to the active compound through cleavage by the liver specific cytochrome P450 isoenzyme CYP3A4 (Erion *et al*., 2007). The activated form of the drug has approximately 16-fold higher affinity for TRβ (Ki = 2.2 nM) than for TRα (Ki = 35.2 nM). The following figures show that administration of VK2809 to rats caused a decrease in plasma cholesterol (lower left) with no effect on heart

rate (lower right). Note that in the following figures, the red lines indicate VK2809 (MB07811) results while results for another TRβ selective agonist are shown in blue; circles represent cholesterol level while triangles represent triglyceride level.



Source: Erion *et al*., 2007

The cholesterol lowering properties of VK2809 were further exhibited in multiple studies in rabbits, dogs, and monkeys (Ito *et al*., 2009). The following figures show that VK2809 (MB07811) was at least as effective in lowering plasma cholesterol as atorvastatin (Lipitor®) in all three species, and an additive effect exists with the combination of VK2809 and atorvastatin.



Adapted from: Ito *et al*., 2009

Mechanism of LDL-Lowering by TR Agonists

Importantly, the mechanism by which TR agonists lower cholesterol is distinct from statins. Statins work by inhibiting the rate-limiting enzyme in cholesterol biosynthesis, 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase, which leads to decreased hepatic cholesterol synthesis, enhanced LDL receptor cycling, and a slight increase in HDL levels (Deedwania *et al*., 2005). Thyroid hormones and TR agonists act by:

- Increasing expression of LDL receptors, which leads to enhanced clearance of serum LDL (Erion *et al*., 2007)
- Decreasing apolipoprotein B (ApoB) levels, which is the major protein constituent of LDL (Ladenson *et al*., 2010)
- Impacting several aspects of reverse cholesterol transport (Pedrelli *et al*., 2010), the net effect of which is to reduce LDL
- Enhancing synthesis of apolipoprotein A-1, the predominant protein of HDL (Hargrove *et al*., 1999)
- Increasing hepatic uptake of cholesterol from HDL by increasing activity of scavenger receptor class B type-1 (Johansson *et al*., 2005)
- Increasing the activity of liver cholesterol 7α hydroxylase, which converts cholesterol into bile acids for fecal excretion (Johansson *et al*., 2005)
- Inhibiting transcription of sterol regulatory element binding protein-1 (SREBP-1), which decreases fatty acid synthesis and reduces triglycerides (Erion *et al*., 2007)

In addition to lowering plasma cholesterol levels, VK2809 was also shown to reduce hepatic steatosis in rats (as is typically seen in non-alcoholic fatty liver disease, NAFLD) through increased hepatic fatty acid oxidation, with no evidence of liver fibrosis or other histological liver damage (Cable *et al*., 2009).

Hypercholesterolemia and Fatty Liver Disease

Polygenic hypercholesterolemia is the most common cause of elevated serum cholesterol levels and is caused by a combination of genetic susceptibility and one or more other factors, including diet, obesity, and sedentary lifestyle. In the U.S., the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) guidelines are most commonly used to determine optimum LDL cholesterol levels. The guidelines were originally published in 1988 and then updated in 2004 (Grundy *et al*., 2004) and define hypercholesterolemia as a blood cholesterol concentration of 240 mg/dL or more, with desirable concentrations as less than 200 mg/dL. For LDL cholesterol, a value of 160 mg/dL is considered high, with values greater than 190 mg/dL being considered very high. According to the CDC, there are approximately 70 million adults in the U.S. with elevated LDL cholesterol levels, but only 34 million of them are being treated and only 23 million have their condition under control. The most noteworthy consequence of elevated LDL cholesterol is increased coronary heart disease risk (Lewington *et al*., 2007).

Statins have become the therapy of choice for a large number of patients with hypercholesterolemia. The 2013 American College of Cardiology/American Heart Association Task Force guidelines identify four groups of patients who benefit the most from statin therapy:

1. Those with clinical atherosclerotic cardiovascular disease (ASCVD), such as acute coronary syndrome, history of myocardial infarction, stable or unstable angina, coronary revascularization, stroke presumed to be of atherosclerotic origin, and peripheral arterial disease or revascularization
2. Those with LDL cholesterol values of of 190 mg/dL or higher
3. Those with diabetes in persons aged 40-75 years and LDL cholesterol of 70-189 mg/dL
4. Those without clinical ASCVD or diabetes aged 40-75 years with LDL-C of 70-189 mg/dL with an estimated 10-year calculated Framingham risk score of 7.5% or higher

While statins have proven to be quite beneficial in treating hypercholesterolemia, they often have a number of side effects such as muscle pain, liver damage, digestive problems, and increased blood sugar.

Nonalcoholic fatty liver disease (NAFLD) is a type of fatty liver where there is deposition of fat (steatosis) in the liver brought on by something other than alcohol consumption and is often due to obesity. Approximately 10 to 20 percent of individuals in the U.S. have fat in their liver but no indication of inflammation. Nonalcoholic steatohepatitis (NASH) is inflammation and damage in the liver brought on by a buildup of fat and is the most severe form of NAFLD. NASH is an often “silent” liver disease as most people with NASH feel well and are not aware that they have a liver problem. Nevertheless, NASH can be severe and can lead to cirrhosis, in which the liver is permanently damaged and scarred and no longer works properly, liver failure, and hepatocellular carcinoma. NASH affects two to five percent of people in the U.S (NIDDK).

There are currently no treatment options available for those that develop NASH. Physicians typically advise NASH patients to lose weight (if they are overweight or obese), get more exercise, eat healthy, and avoid alcohol and unnecessary medications. While these are simply standard recommendations for maintaining a healthy lifestyle they can make a difference in patients with NASH. Losing weight typically leads to improved liver tests and may possibly reverse the disease, but usually only to a certain extent. In addition, very few people lose sufficient weight to impact their health (Fildes *et al*., 2015).

Experimental approaches currently under development for NASH include the use of antioxidants, such as Vitamin E, selenium, and betaine. There is usually an increased oxidative stress in the livers of NASH patients, thus these medications may work to lower the amount of oxidative species. Many NASH patients are insulin resistant, thus medicines such as metformin, rosiglitazone, or pioglitazone may increase patients sensitivity to insulin and reduce liver injury by better enabling a patient to control blood glucose and lipid levels. Additional therapies under development include experimental medications such as obeticholic acid (Intercept Pharmaceuticals), RP103 (Raptor Pharmaceuticals), GR-MD-02 (Galectin Therapeutics), and MN-001 (MediciNova).

VK2809 Clinical Data

VK2809 has been evaluated in two Phase 1 clinical trials, the first conducted in 2006 and a second Phase 1b trial conducted between 2007-2008. The Phase 1b trial was a 14-day, placebo controlled trial in patients with mild hypercholesterolemia (defined as baseline LDL cholesterol of at least 100 mg/dL). VK2809 was shown to be safe and well tolerated in doses ranging from 0.25 mg to 40 mg per day. No serious adverse events were reported and the frequency of adverse events in VK2809-treated subjects was similar to placebo-treated subjects. There were also no differences in heart rate, heart rhythm, or blood pressure between VK2809 and placebo-treated patients. The clinical trial results also showed dose-related reductions in fasting LDL cholesterol and fasting triglyceride

levels at day 14. Significant placebo-adjusted LDL cholesterol reductions from baseline were observed at doses of 5 mg and above and ranged from approximately 15%—41%, while placebo-adjusted triglyceride levels were reduced by more than 30% at doses of 2.5 mg and above. In addition, statistically significant reductions of lipoprotein a (Lp(a)) and apolipoprotein (Apo(B)), which are believed to be positively associated with a patient's risk of developing cardiovascular disease, were observed in certain cohorts. The table below gives a comparison of the Phase 1b efficacy results of VK2809 and data from existing hyperlipidemia treatments.

Drug	Class	LDL-C[1]	Triglycerides	Lp(a)	Apo-B	Safety, Tolerability, Other
VK2809, 10 mg	**TR-β**	**-27**	**-61**	**-55**	**-29**	**Expect safe, additive efficacy with statins; efficacy in statin-intolerant**
Niacin, 1500 mg	Nicotinic acid	-13	-25	-17	-13	Flushing, increased plasma glucose, liver toxicity, skeletal muscle toxicity
Ezetimibe, 10 mg	Cholesterol absorption inhibitor	-19	-8	-10	-14	Modest efficacy
Colesevelam, 3.8 g	Bile acid sequestrant	-15	+5	-	-12	Modest efficacy, gastrointestinal tolerability
Atorvastatin 20 mg	Statin	-47	-36	-	-38	Skeletal muscle toxicity/pain, potential elevation in diabetes risk
Fenofibrate, 145 mg	Fibrate	-18	-36	-	-28	Gallstones, risk of kidney dysfunction, skeletal muscle toxicity

Source: Viking Therapeutics, Inc.

Market Opportunity in Lipid Disorders

With only 50% of the 70 million U.S. adults with hypercholesterolemia being treated and only 50% of those patients having their condition under control, there exists a substantial population of patients who are either not being treated for hypercholesterolemia or not being treated effectively. As a class, sales of branded statin medications totaled approximately $11.5 billion in 2014 (EvaluatePharma), however generic competition has driven total revenues down since 2011, when Lipitor® (atorvastatin) lost patent protection. It should be noted that peak Lipitor® sales were approximately $13 billion per year, which suggests an enormous market for novel branded therapies.

There are approximately 15 million individuals who suffer from NASH in the U.S., and with no FDA approved therapies the opportunity for a successful NASH treatment is quite large. According to EvaluatePharma, sales of drugs for the NASH market could top $1.3 billion in 2020.

VK2809 Clinical Development Plan

Since prior data show excellent results in both the lipid-lowering setting and in models of fatty liver disease, Viking plans to conduct a Phase 2 trial to evaluate both potential indications. The company is planning to target patients with elevated cholesterol, fatty liver disease, and at least three risk factors for metabolic syndrome, which is considered a major driver for the onset of NASH. The primary endpoint will assess changes in LDL, with exploratory endpoints evaluating changes in liver fat content, inflammatory markers, and histological changes. Upon conclusion, the company hopes to be in a position to move forward in either hypercholesterolemia or NASH. Thus, it could be viewed as a two-in-one study – confirmatory on LDL and exploratory for fatty liver disease. We anticipate the study initiating in the fourth quarter of 2015 and topline results to be available in the fourth quarter of 2016 or first quarter of 2017.

Adrenoleukodystrophy

Adrenoleukodystrophy (ALD) is an X-linked genetic disorder caused by a mutation in the *ABCD1* gene that encodes ALDP, a peroxisomal membrane protein (Mosser *et al*., 1993). The defect leads to an accumulation of very long chain fatty acids (VLCFA) in almost all tissues, however the adrenal glands, testes, brain, spinal cord, and peripheral nerves are most affected clinically (Moser *et al*., 2001). While the accumulation of VLCFA would seem to be at the heart of the pathophysiological mechanism, the exact reason for tissue damage in those with ALD is

currently unknown. It is thought that the accumulation of VLCFA leads to a disruption in the cellular membrane and damage to the myelin sheath of neural cells. The damage leads to decreased motor coordination and function, visual and hearing disturbances, loss of cognitive function, and even death.

There is a wide heterogeneity in the clinical manifestations of ALD, with some patients experiencing rapid cerebral demyelination in childhood while others simply have myelopathy in adulthood. The two main sub-classifications for ALD are based on the presence or absence of brain inflammation:

- ✓ **Adrenomyeloneuropathy (AMN)**: AMN is the most frequent phenotype of ALD. AMN will affect all adult males with mutations in the *ABCD1* gene and approximately 65% of females. The first symptom of AMN typically appears in males between the ages of 20 and 30 years and almost always before the fifth decade of life. Women typically develop symptoms later in life than males. Symptoms include progressive stiffness and weakness in the legs, sphincter disturbances, and impotence. Severe motor neuron degeneracy typically develops over a span of three to 15 years and can often lead to lower limb paralysis. Approximately two-thirds of males will develop adrenocortical insufficiency (Addison's disease), while it is present in less than 1% of female carriers. Twenty percent of AMN males will develop a cerebral demyelinating form of the disease, although it is generally milder than cerebral demyelination in children.

- ✓ **Cerebral adrenoleukodystrophy (CALD)**: CALD is the most severe form of ALD and occurs in approximately 35-40% of males between the ages of five and 12 years. The earlier the age of onset is correlated with a more rapid progression of the disease. Patients are asymptomatic until cerebral demyelination develops on brain MRI. Initially, the demyelinating lesions are not inflammatory, and no neurological symptoms are present until suddenly the disease becomes inflammatory and at this point the disease progresses rapidly. A vegetative state will typically occur within two to five years with death occurring within 10 years. Approximately 65% of CALD patients will have adrenocortical insufficiency that can precede the onset of neurological symptoms by years or even decades.

Treatment of ALD

Allogenic hematopoietic stem cell transplantation (HSCT) is the only currently available effective treatment option as it has been shown to halt the progression of CALD, but only when performed at the early-stages of the disease (Miller *et al*., 2011). This is because HSCT can cause rapid progression of the disease initially after treatment before it is stabilized beginning approximately six months later. There are a number of risks associated with HSCT, including organ or tissue dysfunction, changes in quality of life, infections due to improper immune system reconstitution, and chronic graft versus host disease.

To overcome the limitations of allogenic HSCT, HSC gene therapy using patients' own cells was attempted (Cartier *et al*., 2012). In this procedure, HSC were purified from patients with CALD and a lentiviral vector was used to insert a functional copy of the *ABCD1* gene into the cells before reinfusing the cells back into the patient. Two patients were treated with this procedure, and after 14 and 16 months of follow-up neither patient has had further progression of the disease. A Phase 2/3 study of this therapy is currently underway.

Lorenzo's oil (LO) is a 4:1 mixture of glyceryl trioleate and glyceryl trierucate. Oral administration of the solution causes a rapid decrease in circulating levels of VLCFA in the bloodstream (Rizzo *et al*., 1989). This rapid decrease in circulating VLCFA levels led to the hope that LO could alter the clinical course of the disease. Unfortunately, multiple clinical trials did not show any effect of LO supplementation in patients who were already symptomatic when treatment was initiated, particularly those with CALD (van Geel *et al*., 1999; Aubourg *et al*., 1993). However, more recent trials have shown LO may have an effect in asymptomatic boys with normal MRI scans (Moser *et al*., 2005) and in slowing the progression of AMN (Koehler *et al*., 2005).

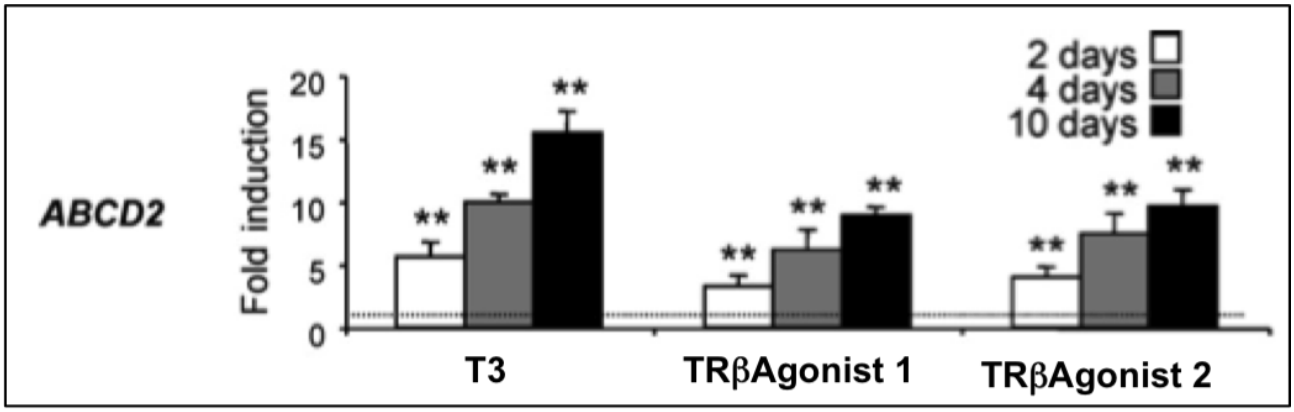
While a few treatment options do exist for ALD patients, there is still a pressing need for a more robust therapy that can offer treatment to a larger segment of the ALD population without unnecessary risks to the patient.

TRβ Agonists for the Treatment of ALD

ABCD1 is one of three genes encoding peroxisomal ABC-transporters, which includes *ABCD2* and *ABCD3*. ALDR is the protein encoded by *ABCD2*, and it shares 66% homology with ALDP, the protein encoded by ABCD1 (Holzinger *et al*., 1997). When ALDR was overexpressed in cultured fibroblasts from ALD patients, impaired peroxisomal beta-oxidation was restored (Netik *et al*., 1999), suggesting that ALDR activity could compensate for the loss of ALDP activity. In addition, when murine ALDR was ubiquitously overexpressed from a transgene in *Abcd1*-deficient mice, it normalized VLCFA levels in target tissues and rescued late-onset motor coordination

defects (Pujol *et al*., 2004). The reason that ALDR does not compensate for loss of ALDP function in ALD patients is because of complimentary expression of *ABCD1* and *ABCD2* (i.e., in tissues where *ABCD1* is expressed, *ABCD2* is not and vice versa) (Troffer-Charlier *et al*., 1998). Thus, while ALDR would appear to be able to replace the function of ALDP, it would be necessary to induce its expression in the tissues where it is not usually expressed.

Fibrates (Albet *et al*., 1997), thyroid hormones T3 and T4 (Fourcade *et al*., 2003), and 4-phenylbutyrate (Gondcaille *et al*., 2005) all stimulate the expression of *ABCD2* in the liver, thus proving that pharmacological induction of *ABCD2* expression is feasible. Furthermore, since T3 is able to induce expression of ABCD2 (through binding of TRβ), it stands to reason that a TRβ-specific agonist would also cause the same effect. In fact, TRβ-specific agonists have been shown to increase expression of *ABCD2* in a manner similar to T3 (Genin *et al*., 2009). The following figure shows the results of treating human HepG2 liver cells with either T3 or TRβ-specific agonists, with *ABCD2* expression being significantly increased compared to control treated cells (dashed line) after 2, 4, and 10 days of treatment. Thus, we believe there is ample evidence to support the development of either VK2801 or VK0214 as a treatment for ALD.



Source: Genin *et al*., 2009

Market Opportunity for ALD and Clinical Development Plan

In the U.S., there are approximately 8,000 patients suffering from ALD while in the E.U. there are approximately 12,000 patients. Since the only effective therapy currently available for these patients is HSCT, there exists an unmet medical need for less dangerous treatment options. In addition, since so few individuals suffer from this condition, Viking could apply for orphan drug designation from the FDA for whichever compound is advanced into clinical testing. Orphan drug designation carries a number of potential incentives for the company, including increased feedback from the FDA regarding clinical trial design, seven years of market exclusivity following approval for the treatment of ALD, tax credits, and a waiver of PDUFA fees. Lastly, therapeutics that treat orphan diseases typically enjoy premium pricing, often in excess of $300,000 per year for treatment.

Viking is planning to complete preclinical experiments in cell and animal models of ALD with both VK2809 and VK0214. Depending upon the results of those studies, the company will then move one of those compounds into an open label Phase 1 clinical trial in ALD patients in 2017. The trial, if pursued, would be expected to enroll ten to twelve patients and test up to three different doses of drug for safety and tolerability, as well as changes in VLCFA, functional status, and quality of life after six weeks of treatment. Since ALD is an orphan indication, positive results could lead to discussions with the FDA about moving straight into registration trials later in 2017 or 2018.

Additional Pipeline Programs Targeting Metabolic Diseases

While currently focusing on the development of VK5211 and VK2809/VK0214, the company also has a pipeline of three additional compounds that target metabolic diseases and anemia.

VK0612

VK0612 is a potent and selective inhibitor of fructose-1,6-bisphosphatase (FBP), an enzyme that catalyzes the rate-limiting step of gluconeogenesis (conversion of fructose-1,6-bisphosphate to fructose-6-phosphate). Gluconeogenesis is the process by which the body produces glucose from non-carbohydrate precursors. The drug is being developed for the treatment of type 2 diabetes, a disease in which the body is unable to properly respond to insulin, and blood glucose levels rise.

VK0612 has exhibited potent glucose-lowering effects in diabetic animal models and has been shown to be safe, well tolerated and have significant glucose-lowering effects in patients with type 2 diabetes. The drug has been studied in six Phase 1 clinical trials and one Phase 2a clinical trial in a total of over 250 patients. In addition, the drug exhibited the following positive potential advantages over existing type 2 diabetes therapies: the ability to lower fasting plasma glucose by as much as 58 mg/dL, a novel mechanism of action, encouraging safety and improved tolerability, and once daily dosing.

Pending future funding, the company is planning to conduct a Phase 2b clinical trial in patients with poorly controlled type 2 diabetes. We believe that were the drug shown to either lower hemoglobin A1c levels by 1% or more in a large cohort of patients or to be safely combined with metformin, that this would be enough to get a partnership with a larger pharmaceutical company to move the drug to Phase 3 testing.

Erythropoietin (EPO) Receptor Agonist Program

Viking is developing a series of orally available, small molecule agonists for the erythropoietin (EPO) receptor for the treatment of anemia, which is a decrease in red blood cells and is a typical side effect for patients with chronic kidney disease, cancer, and HIV/AIDS. Treatment for these patients currently consists of recombinant EPO or erythropoietin stimulating agents, however these agents have a number of serious side effects including an increased risk of cardiovascular complications and possibly an increase in mortality in cancer patients. The company is currently conducting preclinical studies and intends to file an IND to begin clinical testing of a lead compound at a future date.

Diacylglycerol Acyltransferase-1 (DGAT-1) Inhibitor Program

Viking is developing small molecule inhibitors of diacylglycerol acyltransferase-1 (DGAT-1) inhibitors for the potential treatment of obesity and dyslipidemia. Approximately 36% of U.S. adults are considered obese (CDC). DGAT-1 catalyzes the final and only committed step of triglyceride synthesis, which is essential for the formation of adipose tissue (Cases *et al*., 1998). Interestingly, DGAT-1 knockout mice (which do not have a functional DGAT-1 protein) are viable and still synthesize triglycerides, however the mice are lean and resistant to diet-induced obesity (Smith *et al*., 2000). Viking is working on compounds that selectively target the enterocyte, or intestinal absorptive cell, in the intestine, to inhibit triglyceride uptake, or in the liver, to inhibit *de novo* triglyceride synthesis. The company is continuing to conduct preclinical studies and will file an IND to begin clinical testing of a lead compound at a future date.

Master License Agreement

On May 21, 2014, Viking entered into a Master License Agreement with Ligand which granted Viking an exclusive, perpetual, irrevocable, worldwide, royalty-bearing right and license for VK5211, VK2809/VK0214, VK0612, compounds related to the EPO receptor program, and compounds related to the DGAT-1 program. As partial consideration for the licenses granted under the Master License Agreement, at the closing of Vikings Initial Public Offering (IPO), Ligand was issued 3,427,859 shares of common stock and an additional 228,105 shares of common stock upon closing of the over-allotment option related to the IPO. In addition, Viking will pay Ligand certain one-time, non-refundable milestone payments as follows:

- **VK5211**: An aggregate amount of up to $85 million per indication (up to two indications) upon the achievement of certain development and regulatory milestones and up to $100 million upon the achievement of certain sales milestones. In addition, an upper single digit royalty will be paid upon sales of VK5211.
- **VK2809/VK0214**: An aggregate amount of up to $75 million per indication (up to three indications) upon the achievement of certain development and regulatory milestones and up to $150 million upon the achievement of certain sales milestones. In addition, a low to middle single digit royalty will be paid upon sales of VK2809 or VK0214.
- **VK0612**: An aggregate amount of up to $60 million per indication (up to four indications) upon the achievement of certain development and regulatory milestones and up to $150 million upon the achievement of certain sales milestones. In addition, an upper single digit royalty will be paid upon sales of VK0612.
- **EPO program**: An aggregate amount of up to $48 million per indication (up to three indications) upon the achievement of certain development and regulatory milestones and up to $150 million upon the achievement of certain sales milestones. In addition, a middle to upper single digit royalty will be paid upon sales of any EPO compound.

- **DGAT-1 program**: An aggregate amount of up to $78 million per indication (up to two indications) upon the achievement of certain development and regulatory milestones and up to $150 million upon the achievement of certain sales milestones. In addition, a low to middle single digit royalty will be paid upon sales of any DGAT-1 compound.

Company Financials and Capital Structure

On May 4, 2015, Viking completed an IPO where a total of 3 million shares of common stock were sold at $8.00 per share. Upon closing of the IPO the company had raised a total of $22.1 million in net proceeds after deducting underwriting discounts and commissions. On May 26, 2015, the underwriters for the IPO exercised the full over-allotment option and purchased an additional 450,000 shares of common stock at $8.00 per share, which resulted in net proceeds to Viking of $3.3 million after deducting underwriting discounts and commissions. As of September 30, 2015, the company had approximately $17.5 million in cash and cash equivalents, which will be sufficient to fund operations into 2017.

At the end of the third quarter of 2015, the company had approximately 9.7 million shares of common stock outstanding, with Ligand owning approximately 35% of the total number of outstanding shares. Combined with the 0.8 million shares of restricted stock and the 0.4 million stock options outstanding, the company has a fully diluted share count of approximately 11 million shares.

Risks to Consider

Viking is very dependent on products and technologies in-licensed from Ligand: Vikings business is almost entirely dependent upon the technology licensed from Ligand. The Master License Agreement grants the company exclusive worldwide rights to VK5211, VK2809, VK0214, VK0612, and preclinical programs for anemia and lipid disorders. However, the intellectual property surrounding those programs is owned by Ligand, with the Master License Agreement giving Viking the rights to use that intellectual property. Ligand has the right to terminate the Master License Agreement under certain circumstances, including (1) Viking becomes insolvent or declares bankruptcy; (2) if Viking does not pay any amount owed to Ligand under the Master License Agreement; or (3) if Viking defaults on certain material obligations and fails to cure the default within a specified time frame.

Vikings drug candidates are still in the early stages of development: Currently, VK5211 is furthest along in development, as the company has recently initiated a Phase 2 clinical trial. While the drug has shown promise in previous clinical trials, there is no guarantee that positive results will be seen in the upcoming clinical trial. For VK2809/VK0214, the company has not yet selected which compound will be advanced for the treatment of ALD, as preclinical studies are still ongoing. VK2809 will be tested in a Phase 2 clinical trial in patients with hypercholesterolemia and fatty liver disease before the company decides which indication to pursue in later stage clinical trials.

Viking will need to raise additional capital in the future: While the company raised a substantial amount of money in the IPO, and had approximately $17.5 million in cash and cash equivalents at the end of the third quarter of 2015, that will not be sufficient to move any of the company's compounds all the way through clinical testing and approval by the FDA. We estimate that the current cash balance will fund Viking's operations into 2017, at which point the company will need to raise additional capital.

MANAGEMENT PROFILES

Brian Lian, PhD – President and Chief Executive Officer

Dr. Lian has served as President and Chief Executive Officer and as a Director since the company's inception in September 2012. Dr. Lian has over 15 years of experience in the biotechnology and financial services industries. Prior to joining Viking, he was a Managing Director and Senior Research Analyst at SunTrust Robinson Humphrey, an investment bank, from 2012 to 2013. At SunTrust Robinson Humphrey, he was responsible for coverage of small and mid-cap biotechnology companies with an emphasis on companies in the diabetes, oncology, infectious disease, and neurology spaces. Prior to SunTrust Robinson Humphrey, he was Managing Director and Senior Research Analyst at Global Hunter Securities, an investment bank, from 2011 to 2012. Prior to Global Hunter Securities, he was Senior Healthcare Analyst at The Agave Group, LLC, a registered investment advisor, from 2008 to 2011. Prior to The Agave Group, he was an Executive Director and Senior Biotechnology Analyst at CIBC World Markets, an investment bank, from 2006 to 2008. Prior to CIBC, he was a research scientist in small molecule drug discovery at Amgen, a biotechnology company. Prior to Amgen, he was a research scientist at Microcide Pharmaceuticals, a biotechnology company. Dr. Lian holds an MBA in accounting and finance from Indiana University, an MS and Ph.D. in organic chemistry from The University of Michigan, and a BA in chemistry from Whitman College.

Michael Morneau – Chief Financial Officer

Mr. Morneau has served as Chief Financial Officer since May 2014. Mr. Morneau has over 20 years of accounting and financial experience at public and private companies in the biotechnology and accounting industries. Prior to Viking, from 2009 to 2014, he was VP of Finance and Chief Accounting Officer at Trius Therapeutics, Inc., a subsidiary of Cubist Pharmaceuticals, Inc., a pharmaceutical company, following Cubist's acquisition of Trius in September 2013. Prior to Trius, from 2008 to 2009, he was Director of Lilly Research Labs Finance at Eli Lilly and Company, a pharmaceutical company. Prior to Eli Lilly, from 2006 to 2008, he was Director of Finance and Accounting at SGX Pharmaceuticals, Inc., a biotechnology company, which was acquired by Eli Lilly. Prior to SGX, from 2004 to 2006, he was Controller at Momenta Pharmaceuticals, Inc., a biotechnology company. Mr. Morneau earned his MBA and MA in accounting from New Hampshire College, and a BA in mathematics from the University of New Hampshire.

Rochelle Hanley, MD, FACP – Chief Medical Officer

Dr. Hanley has served as Chief Medical Officer since April 2013. Dr. Hanley is Board Certified in internal medicine and clinical pharmacology and has 20 years of drug development experience, primarily in diabetes and metabolic disorders. She is a fellow of the American College of Physicians and is the recipient of several awards and honors, including the Pfizer Medical Research Merit Award in 1984, NIH Physician Scientist from 1986 to 1991, Established Investigator, American Heart Association, from 1991 to 1993, and the NIH FIRST Award from 1991 to 1993. From 2011 to 2013, Dr. Hanley was an independent consultant to the pharmaceutical industry. Prior to that, she was Medical Director, Cardiovascular, Metabolic and Musculoskeletal Diseases at GlaxoSmithKline, or GSK, a pharmaceutical company, responsible for Asia Pacific research and development activities for albiglutide and darapladib, from 2008 to 2011. Prior to her position with GSK, from 2006 to 2008, she served as Chief Medical Officer for Quatrx Pharmaceuticals, a biotechnology company, managing the clinical program for ospemifene, for vaginal atrophy, which received U.S. approval in 2013. Prior to Quatrx, she was VP and Clinical Site Head, Ann Arbor at Pfizer, Inc., a pharmaceutical company. Prior to becoming Site Head, she was VP and Therapeutic Area Development Leader, Cardiovascular and Metabolic Diseases, Pfizer Global R&D. Dr. Hanley received her M.D. from the University of Michigan and a BA in molecular and cell biology from Smith College, and is licensed to practice medicine in Michigan and North Carolina (inactive).

VALUATION AND RECOMMENDATION

We are initiating coverage of Viking Therapeutics, Inc. (Nasdaq: VKTX) with a Buy rating and a price target of $15.00. Viking is a clinical stage biopharmaceutical company focused on developing treatments for metabolic and endocrine related disorders. We believe that Viking's products represent potential best-in-class treatments due to their unique mechanisms of action and strong safety profile in early clinical testing. With a market cap of less than $50 million, we believe the market does not fully appreciate the multiple billion-dollar opportunities Viking is pursuing, thus representing a compelling investment opportunity.

VK5211

The company's lead compound is VK5211, a non-steroidal selective androgen receptor modulator (SARM) that is being developed for maintenance or improvement of lean body mass (LBM), bone mineral density (BMD), and function in patients recovering from non-elective hip fracture surgery. SARMs are compounds that can interact with the androgen receptor (AR) in a tissue selective manner such that a positive effect is gained in muscle and bone while limiting unwanted side effects, such as unwanted hair growth, acne, or prostate growth. VK5211 has already exhibited a number of positive attributes that we believe increases the probability of clinical success:

- **Excellent Safety Profile**: VK5211 has been tested in three Phase 1 clinical trials in over 100 patients and thus far has proven to be safe and well-tolerated in all treated groups. This includes a group of elderly patients, which is likely to be representative of the hip fracture population.

- **Efficacy in Preclinical Studies**: VK5211 has been tested in a number of different preclinical animal models which showed >500-fold activity of the compound in muscle compared to prostate in rats, increased muscle size in castrated rats treated with VK5211, and increased BMD in rats treated with VK5211 in a rat model of osteoporosis.

- **Preliminary Signs of Clinical Efficacy**: In a Phase 1 clinical trial of VK5211 in 76 healthy men, treatment with VK5211 resulted in a statistically significant dose dependent increase in LBM along with an increase in strength and stair climbing power at the highest tested dose.

The company has recently launched a Phase 2 clinical trial of VK5211 in patients ≥ 65 years of age who have suffered a hip fracture within the past three to seven weeks. This will be a multicenter, randomized, parallel group, double blind, placebo controlled trial, with a total of 120 patients expected to enroll. The primary outcome of the trial is the change in LBM after 12 weeks of treatment. We anticipate topline results being available in the second half of 2016.

VK2809/VK0214

Thyroid hormones play a critical role in the regulation of metabolic rate, energy consumption, and lipid metabolism through binding of the thyroid hormone receptors (TR), of which two isomers exist (TRα and TRβ). The two isoforms have markedly different expression patterns, with TRα expression highest in the heart and brain while TRβ expression is highest in the liver. TRα is predominantly responsible for regulating heart rate while TRβ regulates serum cholesterol levels. Thus, compounds that can selectively alter TRβ function with little to no effect on TRα could have a beneficial effect on lipid metabolism while avoiding deleterious cardiac side effects.

Both VK2809 and VK0214 are selective TRβ agonists, with VK2809 being developed as a treatment for hypercholesterolemia and fatty liver disease and either VK2809 or VK0214 being developed for the treatment of the orphan indication adrenoleukodystrophy (ALD). VK2809 has shown promise as a treatment for hypercholesterolemia in multiple early stage clinical trials, particularly a Phase 1b clinical trial of hypercholesterolemia patients. In that trial, treatment with VK2809 was safe and well tolerated with no serious adverse events. At doses of 5 mg or more there was a significant reduction in LDL cholesterol of 15-41% along with reductions in triglycerides, lipoprotein A, and apolipoprotein B. We view the remarkable reduction in triglycerides as important (-61% at 10 mg dose), as we believe this could make the compound quite effective in fatty liver diseases such as nonalcoholic steatohepatitis (NASH), since most liver fat is composed of triglycerides.

ALD is an X-linked genetic disorder caused by a mutation in the *ABCD1* gene that encodes ALDP, a peroxisomal membrane protein. *ABCD1* is part of a gene family that includes *ABCD2* and *ABCD3.* The activity of ALDP is

disrupted in patients with ALD, however expression of the protein encoded by *ABCD2* can overcome this deficiency. TRβ agonists induce *ABCD2* expression and thus either VK2809 or VK0214 could be effective in treating the disease.

In order to maximize resources and obtain the most data possible, Viking is planning on conducting a Phase 2 clinical trial of VK2809 in patients with elevated cholesterol, fatty liver disease, and at least three risk factors for metabolic syndrome, which is considered a major driver for the onset of NASH. The primary endpoint will assess changes in LDL, with exploratory endpoints evaluating changes in liver fat content, inflammatory markers, and histological changes. Upon conclusion, the company hopes to be in a position to move forward in either hypercholesterolemia or NASH. Thus, it could be viewed as a two-in-one study – confirmatory on LDL and exploratory for fatty liver disease. We anticipate the study initiating in the fourth quarter of 2015 and topline results to be available in the fourth quarter of 2016 or first quarter of 2017.

For the treatment of ALD, Viking is planning to complete preclinical experiments in cell and animal models of ALD with both VK2809 and VK0214 before deciding which compound to move into clinical development. We anticipate a Phase 1 trial initiating in 2017 that would enroll ten to twelve patients and test up to three different doses of drug for safety and tolerability, as well as various qualities of ALD after six weeks of treatment. Since ALD is an orphan indication, positive results could lead to discussions with the FDA about moving straight into registration trials later in 2017 or 2018.

Valuation Methodology

We value Viking using a probability adjusted discounted cash flow model that takes into account potential revenues from the sale of VK5211 in treating patients suffering from hip fracture as well as the sale of VK2809 in NASH and either VK2809 or VK0214 in ALD. We are choosing to model VK2809 as a NASH treatment due to the fact that 1) there are no NASH treatments currently available, thus representing a large market opportunity for the company to pursue and 2) the compound showed a drastic reduction in triglycerides, which are the most abundant component of fat in the liver.

For VK5211, we model for a Phase 3 trial to initiate in 2017, a new drug application (NDA) filing in 2019, and approval of the drug in 2020. Given the fact there are no treatment options currently available to maintain or increase LBM following a hip fracture, we believe the drug will attain peak market share of 35% for the approximately 300,000 patients in the U.S. and 700,000 patients in the E.U. This translates into peak revenues of approximately $600 million in the U.S. and $1 billion in the E.U. We apply an 18% discount rate and a 33% probability of approval to arrive at a net present value for VK5211 of $89 million.

For VK2809 in NASH, we model for a Phase 3 trial to initiate in 2018, an NDA filing in 2020, and approval of the drug in 2021. While there are currently no treatment options available for NASH patients, there are a number of other compounds under development, thus we are estimating peak market share of 20%. We estimate peak worldwide revenues of greater than $2.5 billion, to which we apply an 18% discount rate and a 25% probability of approval to arrive at a net present value for VK2809 in NASH of $72 million.

For ALD, since it is an orphan indication we believe development can proceed relatively quickly and we model for an NDA filing in 2019 and approval in 2020. As an orphan indication, the drug would likely command premium pricing, thus we model for a yearly cost of $150,000 in the U.S. and $120,000 in Europe. That price may ultimately end up being too conservative as Kalydeco®, a treatment for the orphan disease cystic fibrosis, costs approximately $300,000 per year. We estimate peak market share for all patients with ALD at 40%, which translates into peak worldwide sales of approximately $450 million. We apply an 18% discount rate and a 20% probability of success to arrive at a net present value for VK2809/VK0214 in ALD of $25 million.

Combining the net present value for each of the company's development programs along with the current cash total and expected operating burn of $40 million we arrive at a net present value for the company of $164 million. Dividing this by the company's fully diluted share count of approximately 11 million shares leads to a fair value of approximately $15 per share, and we are assigning a 'Buy' rating to the stock.

PROJECTED FINANCIALS

Viking Therapeutics, Inc.
Income Statement

Viking Therapeutics, Inc.	2014 A	Q1 A	Q2 A	Q3 A	Q4 E	2015 E	2016 E	2017 E
VK5211 (Hip Fracture)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
VK2809 (Hypercholesterolemia)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
VK2809/VK0214 (ALD)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$22.2	$0.1	$1.1	$2.5	$2.5	$6.2	$8.0	$10.0
General & Administrative	$1.2	$0.3	$1.5	$1.8	$1.9	$5.5	$7.5	$9.0
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($23.5)	($0.5)	($2.6)	($4.3)	($4.4)	($11.8)	($15.5)	($19.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$1.6	($5.2)	($5.3)	($0.4)	($0.3)	($11.2)	($0.5)	($0.5)
Pre-Tax Income	($21.9)	($5.7)	($7.9)	($4.7)	($4.7)	($23.0)	($16.0)	($19.5)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($21.9)**	**($5.7)**	**($7.9)**	**($4.7)**	**($4.7)**	**($23.0)**	**($16.0)**	**($19.5)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($5.23)**	**($0.81)**	**($1.07)**	**($0.53)**	**($0.51)**	**($2.82)**	**($0.46)**	**($0.49)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	4.187	7.000	7.332	8.947	9.300	8.145	35.000	40.000

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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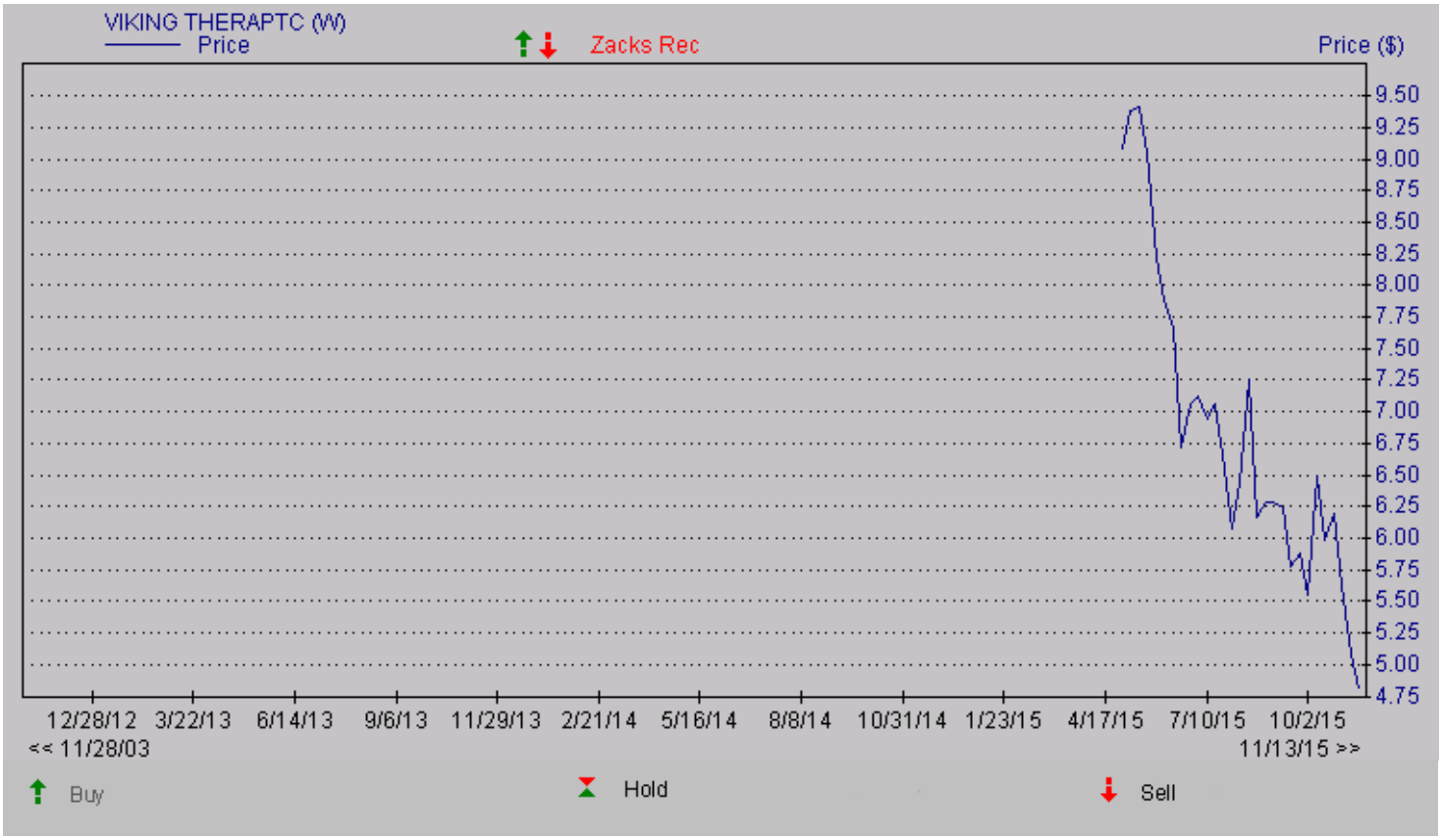

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