Zacks Small-Cap Research

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Viking Therapeutics, Inc.

(VKTX-NASDAQ)

VKTX: Encouraging Preclinical Data for VK0214 in Mouse Model of X-ALD…

Based on our probability adjusted DCF model that takes into account potential future revenues of VK5211, VK2809, and VK0214, VKTX is valued at $8/share. This model is highly dependent upon continued clinical success of those compounds and will be adjusted accordingly based upon future clinical results.

Current Price (09/27/16)	$1.29
Valuation	**$8.00**

OUTLOOK

On September 26, 2016, Viking Therapeutics, Inc. (VKTX) announced the presentation of positive proof-of-concept data for VK0214 in a preclinical model of X-linked adrenoleukodystrophy (X-ALD), an orphan neurodegenerative disease. In this study, treatment with VK0214 resulted in significant reductions in circulating levels of very long chain fatty acids (VLCFAs), a key biomarker of disease. The results are important due to the biochemical similarities displayed between this model and patients with X-ALD. Additional preclinical and IND-enabling studies are planned, with the company likely to file an IND and initiate clinical trials with VK0214 in the second half of 2017.

As a reminder, Viking will have data readouts from two Phase 2 clinical trials involving VK5211 for hip fracture and VK2809 in hypercholesterolemia and fatty liver disease in the second quarter of 2017.

SUMMARY DATA

52-Week High	**$6.90**
52-Week Low	**$1.18**
One-Year Return (%)	**-78.10**
Beta	**0.46**
Average Daily Volume (sh)	**146,283**
Shares Outstanding (mil)	**20**
Market Capitalization ($mil)	**$26**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**4**
Insider Ownership (%)	**20**
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 2016 Estimate	**-0.9**
P/E using 2017 Estimate	**-1.1**

Risk Level	**High,**
Type of Stock	**Small-Blend**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	0 A	0 A	0 A	0 A	0 A
2016	0 A	0 A	0 E	0 E	0 E
2017					0 E
2018					0 E

Earnings per Share

(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$1.40 A	- $1.07 A	-$0.53 A	-$0.57 A	-$3.68 A
2016	-$0.40 A	-$0.22 A	-$0.28 E	-$0.24 E	-$1.06 E
2017					-$0.89 E
2018					-$0.93 E

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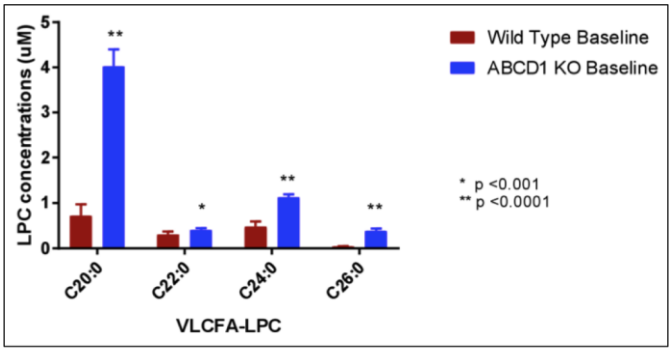
WHAT'S NEW

On September 26, 2016, Viking presented positive proof-of-concept preclinical data showing that VK0214 is active in a mouse model of X-linked adrenoleukodystrophy (X-ALD). Below we provide an overview of the data presented and the scientific rationale for pursuing this indication.

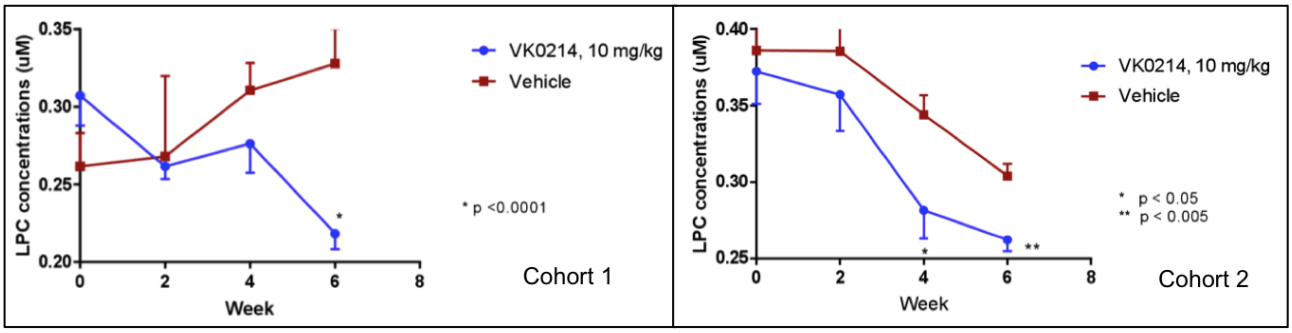
VK0214 Preclinical Data

To study the potential use of VK0214 in X-ALD, Viking tested VK0214 in the ABCD1 knockout (KO) mouse model, and while this model does not recapitulate the inflammation seen with severe forms of X-ALD, these mice do develop a phenotype similar to AMN with advanced age along with an accumulation of certain very long chain fatty acids (VLCFAs) in tissues and plasma (Lu *et al*., 1997). The following graph shows an accumulation of different VLCFAs in the blood of ABCD1 KO mice used in this experiment compared to wild-type controls. VLCFAs are denoted as "CX:Y" with "X" corresponding to the number of carbons in the fatty acid chain and "Y" corresponding to the number of double bonds in the chain.



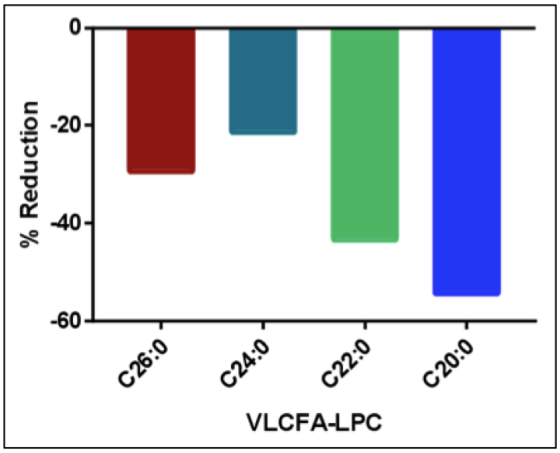
Source: Masamune *et al*., 2016

A pilot experiment was performed in 16 ABCD1 KO mice randomized 3:1 to receive VK0214 or placebo once daily for six weeks. Mice receiving VK0214 demonstrated rapid reductions in the mean level of C26:0, while control animals saw no reduction. After six weeks of treatment, mice receiving VK0214 had a 40% reduction in whole blood C26:0 levels relative to controls (*P*<0.0001). A second cohort of 20 mice randomized 1:1 to receive VK0214 or placebo for six weeks again showed a statistically significant decrease in C26:0 levels in mice treated with VK0214 (*P*<0.005). In the second cohort of mice, those receiving placebo also showed a reduction in C26:0 levels, which may have been due to the lipid-based nature of the vehicle, similar to results seen with Lorenzo's Oil.



Source: Masamune *et al*., 2016

Plasma taken from Cohort 2 mice was analyzed for the presence of different VLCFAs at two, four, and six weeks. The results show mean reductions of approximately 20-60% in the levels of C26:0, C24:0, C22:0, and C20:0 in mice treated with VK0214 compared to placebo at week six, as shown in the following figure. The importance of reducing shorter chain VLCFAs is unclear, however it may suggest a potential reduction in available substrates for elongation to the more problematic C24:0 and C26:0 VLCFAs, leading to even greater long term reductions in these longer chain VLCFAs.



Source: Masamune *et al.*, 2016

Overall, we believe the positive preclinical data reported here provide strong support for the development of VK0214 for X-ALD. The data presented by Viking are in alignment with the hypothesis that induction of *ABCD2* expression leads to increased metabolism and clearance of VLCFAs and treatment with VK0214 could represent a novel treatment options for X-ALD patients. The company is continuing work on characterizing the long-term impact of VK0214 treatment on VLCFA accumulation in tissues. We anticipate IND-enabling studies to continue and for the company to file an IND and initiate a clinical trial with VK0214 in the second half of 2017.

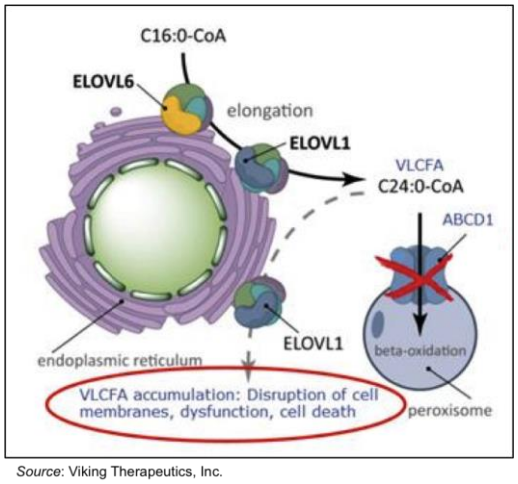
VK0214 and X-ALD Background

Viking is developing two novel, orally available, selective thyroid hormone receptor beta (TRβ) agonists, VK2809 and VK0214. 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). It is being developed for liver specific diseases such as hypercholesterolemia and fatty liver disease. An update on VK2809 was recently published and can be found here.

VK0214 is being developed for the treatment of X-ALD, an orphan neurodegenerative disease that affects approximately 8,000 individuals in the U.S. and 12,000 in Europe. In contrast to VK2809, VK0214 is a TRβ agonist that is activated by carboxyesterases that are ubiquitously expressed in the body. The drug also has a different pharmacokinetic and pharmacodynamic profile, thus potentially making the drug more suitable for a disease such as X-ALD, which is more diffuse than hypercholesterolemia or fatty liver disease.

X-ALD

X-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). ALDP functions to transport VLCFAs into peroxisomes for degradation via beta-oxidation, as shown in the following figure.



Source: Viking Therapeutics, Inc.

The defect in ALDP leads to an accumulation of VLCFAs 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 X-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 X-ALD, with some patients experiencing rapid cerebral demyelination in childhood while others simply have myelopathy in adulthood. The two main sub-classifications for X-ALD are based on the presence or absence of brain inflammation:

- ✓ **Adrenomyeloneuropathy (AMN)**: AMN is the most frequent phenotype of X-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).

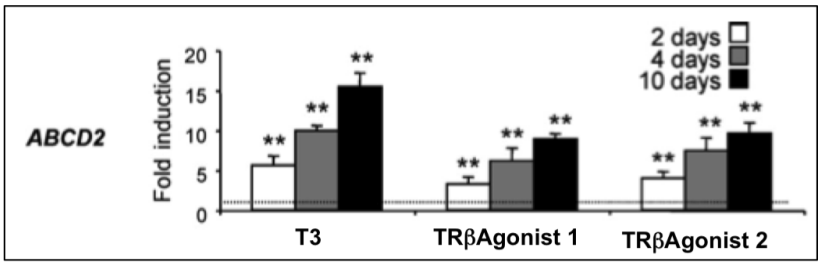
While a few treatment options do exist for ALD patients, there is still a pressing need for a more robust therapy that can offer treatment to a larger segment of the ALD population without unnecessary risks to the patient.

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 VK0214 as a treatment for X-ALD.



Source: Genin *et al*., 2009

Valuation and Conclusion

For valuation purposes, we have constructed a probability adjusted discounted cash flow model that takes into account potential revenues from VK5211 in hip fracture, VK2809 in NASH, and VK0214 in adrenoleukodystrophy (ALD).

We model for peak revenues for VK5211 of approximately $600 million in the U.S. and $1 billion in the E.U. based on compelling preclinical and early clinical data. Viking is expected to announce data from the ongoing Phase 2 study of VK5211 for the treatment of hip fracture in the second quarter of 2017.

We estimate potential peak worldwide revenues for VK2809 of $2.5 billion based upon the low level of adverse events seen with the drug in early clinical testing along with data that is just as good if not better than current treatment options for dyslipidemia. We anticipate topline results from the recently initiated Phase 2 study of VK2809 in hypercholesterolemia and fatty liver disease in the second quarter of 2017.

For ALD, since it is an orphan indication we believe 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, leading to estimated peak worldwide sales of approximately $450 million.

Based on these numbers, and using an 18% discount rate, we arrive at a valuation of $8/share. We continue to believe that Viking's shares are significantly undervalued. This is particularly evident on a comparative basis with Madrigal Pharmaceuticals, Inc. (MDGL), which is developing a Phase 2 ready TRβ agonist for the treatment of fatty liver disease. We believe Viking's TRβ agonists have potentially superior efficacy and fail to see why Viking is trading at approximately 1/5th the valuation of Madrigal. Small-cap biotech investors should take a serious look at Viking ahead of data readouts in the second quarter of 2017.

PROJECTED FINANCIALS

Viking Therapeutics, Inc.
Income Statement

Viking Therapeutics, Inc.	2015 A	Q1 A	Q2 A	Q3 E	Q4 E	2016 E	2017 E	2018 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	$7.0	$1.9	$2.4	$3.4	$2.9	$10.5	$13.5	$16.0
General & Administrative	$5.0	$1.4	$1.2	$1.5	$1.4	$5.5	$5.8	$6.0
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($12.0)	($3.3)	($3.6)	($4.9)	($4.3)	($16.0)	($19.3)	($22.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	($11.4)	($0.3)	($0.1)	($0.5)	($0.5)	($1.4)	($2.0)	($3.0)
Pre-Tax Income	($23.4)	($3.6)	($3.7)	($5.4)	($4.8)	($17.5)	($21.3)	($25.0)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($23.4)**	**($3.6)**	**($3.7)**	**($5.4)**	**($4.8)**	**($17.5)**	**($21.3)**	**($25.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($3.68)**	**($0.40)**	**($0.22)**	**($0.28)**	**($0.24)**	**($1.06)**	**($0.89)**	**($0.93)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	6.356	9.016	17.105	19.500	20.000	16.405	24.000	27.000

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

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