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October 2018 Research Report

Resverlogix

The Making of a mini-Humira?

Market Cap:	US\$440 million
Stock Price (10/2/18):	C\$3.05
Target Price:	C\$30

Note: Unless otherwise indicated, all dollar amounts are in USD.

About the Company

Resverlogix (RVX CN) is a Calgary, Canada based biotech company whose novel first in class epigenetic small molecule is focused on the needs of high-risk patients suffering from a combination of cardiovascular disease and diabetes mellitus.

Resverlogix is currently in the last stages of a Phase 3 trial with its drug called apabetalone. Its drug has the potential to significantly reduce the incidence of Major Adverse Cardiac Events (MACE) in such high-risk patients. Top line results are expected in the first few months of 2019. Resverlogix also believes that apabetalone can address other indications such as chronic kidney disease, and potentially dementia and Fabry Disease.

Our Thesis

Resverlogix's molecule is showing signs of having positive impact on several important indications with the potential of becoming the next mini-Humira. Based on excellent Phase 2 data on efficacy and safety, we believe that Phase 3 test results has a very high probability to confirm that RVX-208 remains safe and will meet its endpoint objective of reducing MACE events by at least 25% over standard of care medicines, along with other beneficiary impacts on chronic kidney disease, and potentially dementia. We believe that Resverlogix will most likely be bought out next year after its Phase 3 test results are fully analyzed, or, at the very least, will end up attracting a strategic partner for bringing to market its lead molecule.

Introduction

We are often bemused that when a medical breakthrough is announced, so many of them seem to impact a small number of people. Too many new drugs these days are targeting rare diseases or niche patient groups, with prices often being too high. Can a drug helping so few people really be worth THAT much, we wonder?

In contrast, Resverlogix is a company that addresses cardiovascular disease in a large high-risk patient group — people who have had a recent major adverse cardiac event (MACE), and who have diabetes — with a novel first-in-class small molecule. On top of that, their molecule (RVX-208) shows very promising data on addressing chronic kidney disease, an ailment for which there is no cure today. These are big addressable markets. Even more surprising, Resverlogix has no strategic partner right now.

To get an idea of what a successful result with a new therapeutic for cardiovascular disease could mean, we point to the recent results of the Phase 3 trial run by Amarin (AMRN US). Amarin's Vascepa medication showed a 25% relative risk reduction in MACE in its trials. That company's share price went from \$3 to \$20 within days. After a string of failed Phase 3 trials from other potential drugs, the medical profession badly needs to address a yawning gap in treating cardiovascular disease. Amarin proves that the stock market fully recognizes that.

What can support a belief that Resverlogix will not only be safe, but effective? First, there is mechanistic data analysis from earlier Phase 2 trials, showing very convincing data on early efficacy of cardiovascular disease relative risk reduction after only 26 weeks of treatment. Second, there have been seven successful data and safety monitoring board reviews with no change in protocol.

We see Resverlogix's small molecule having the potential to follow in the footsteps of Humira, the world's best-selling drug in 2017. While apabetalone will start off with a single indication, we believe it is highly likely that more indications will be approved over the next few years; exactly like Humira.

The 18-year long road for a company that started off with an interesting concept, and now is on the verge of becoming potentially the world's next important drug in the cardiovascular field, has been a long and hard one for Resverlogix. The road ahead is longer still, but far more lucrative.

RVX 208 - Apabetalone

The genesis of this drug was to meet the objective of boosting apolipoprotein A-I (ApoA-1), the major protein component of HDL-P, so that this would result in coronary plaque regression (like roto rooter for the plaque in your arteries). It is this primary endpoint that Resverlogix was targeting, that first caught our attention several years ago.

The molecule just missed its primary endpoint of plaque regression when the results came out in the 2013 ASSURE Phase 2b trial. However, upon further analysis from its entire Phase 2 program of three clinical trials — ASSERT, SUSTAIN and ASSURE — consistent and statistically significant relative risk reduction of MACE events were observed. MACE is described as a composite endpoint of nonfatal stroke, nonfatal myocardial infarction (a heart attack that did not kill), and cardiovascular death. This is the most important endpoint in cardiovascular disease risk.

These early Phase 2 trial results with its positive reports relating to MACE effects, as well improved kidney function data, led to a five-year effort for RVX to take the molecule through the current Phase 3 trial in efforts to convincingly prove the MACE reduction and kidney improvements observed in its Phase 2 program.

Before we explain the science, let's first understand the prize: the addressable market.

Addressable Market: High Risk Vascular Disease

Based on the results from its Phase 2 trials, Resverlogix decided to focus their Phase 3 trial on diabetes patients (HbA1c > 6.5% or history of diabetic medication) who have had a recent MACE event (7 to 90 days before screening) and low HDL-c (< 39 mg/dL). Across the eight top markets (US, Canada, Japan and top five EU countries), there are almost 2 million patients who have such conditions.

Resverlogix seeks to improve the high residual risk that remains in these patients even with standard of care medicines such as statins, beta blockers, aspirin, ACE inhibitors and Plavix. These are big markets. 65% of all deaths in people with diabetes are from cardiovascular diseases. 12% of all Americans have diagnosed or undiagnosed diabetes, while another 34% have prediabetes.

Resverlogix has prepared pre-specified secondary endpoints in BET on MACE for chronic kidney disease. The data to be produced from the Phase 3 trial will allow RVX to launch a Phase 2 trial for end stage renal disease (kidney failure) using eGFR to measure renal function.

RVX has another pre-specified endpoint of cognition, using the Montreal Cognitive Assessment tool (MoCA), in all patients in the BETonMACE trial age 70 and older. This is targeting vascular cognitive impairment, or dementia. Success here would be yet another inflection point for the molecule, as currently there are no therapeutic approaches in these areas that have clearly improved cognition.

From an addressable targeted high-risk therapeutic market of over 12 million, including cardiovascular disease, chronic kidney disease, end stage renal disease (kidney failure) and dementia, it is clear that Apabetalone is addressing critical large markets with high unmet need.

A potential price of \$5,000 per year and guidance from leading US payers for rapid reimbursement, gives one a sense of the immense commercial potential of this drug. Even if only 1 million patients start taking Apabetalone, that will generate \$5 billion a year in sales.

Below is a schematic that captures this opportunity.



Source: RVX Commercial Analysis

We have omitted off label use from the above table. From Phase 2 data, RVX-208 showed efficacy in a more general cardiovascular disease population. This suggests that the true addressable market for RVX-208 is far bigger than the more focused (although more desperate) patient population discussed here. This will provide significant option value for a potential buyer of Resverlogix. For now, we assign no value to this optionality.

The Science

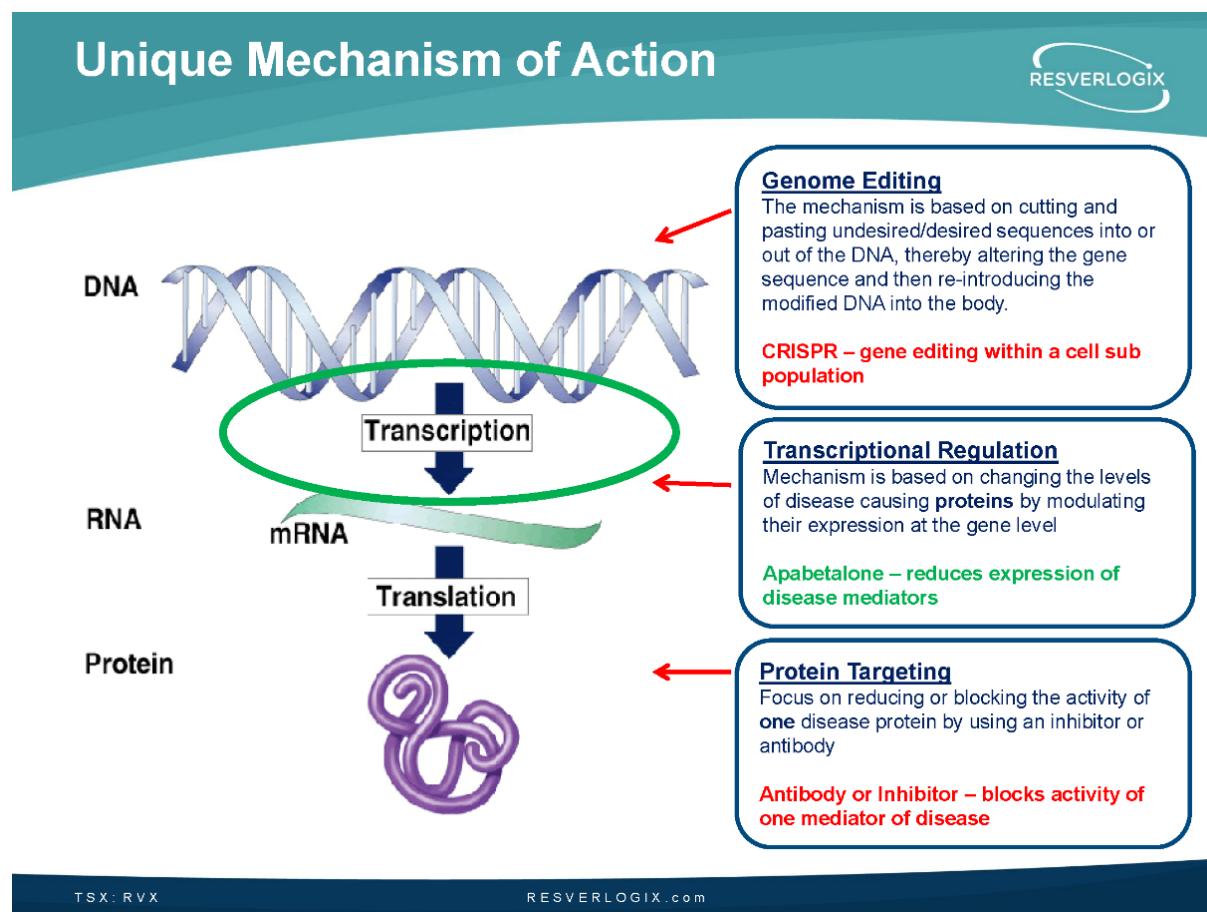
To better understand the science, start with cardiovascular disease. Medical science has to a large degree focused a large part of its efforts in reducing LDL cholesterol levels down to as low as possible, primarily through the use of statins and now PCSK9 inhibitors. However, this only appears to reduce the risk of cardiovascular disease by about 30%. Other approaches being tried out have mostly failed to reduce MACE during their Phase 3 trials, such as the CETP drug class.

Cardiovascular disease, chronic kidney disease and diabetes are diseases that are regulated by multiple pathways of risk. What is needed is a medicine that can impact multiple pathways at the same time (an epigenetic drug). Apabetalone is the only epigenetic molecule undergoing Phase 3 trials for cardiovascular disease right now (other epigenetic trials are in cancer). This suggests a lead of seven years for Resverlogix over potential competitive drugs.

The medical paradigm today uses a single molecular target for a single downstream effect. Epigenetic drugs through a single molecular target, concurrently modulate multiple biological processes contributing to a disease state.

Apabetalone, a single molecule for high-risk cardiovascular disease, has been shown to simultaneously target and improve the following processes: vascular inflammation, reverse cholesterol pathway, vascular calcification, metabolism, coagulation pathway, and complement pathway. Improvements in key risk markers such as a) an increase in ApoA-1, the key building block of new functional HDL, b) reduction of alkaline phosphatase, a reported key risk factor for vascular calcification, and c) reduction of vascular inflammation biomarkers including hsCRP and NLR, illustrate the multifactorial approach that this new molecule has illustrated to date.

Human DNA can be considered our hardware. Epigenetics can be considered the software. DNA contains the code that tells our cells what to do. This coded message, whether correct or faulty, is the same in every cell, and does not change with time. Epigenetic changes to the DNA allow the message in the genes to be turned up or down, like a dimmer switch.



Source: Resverlogix

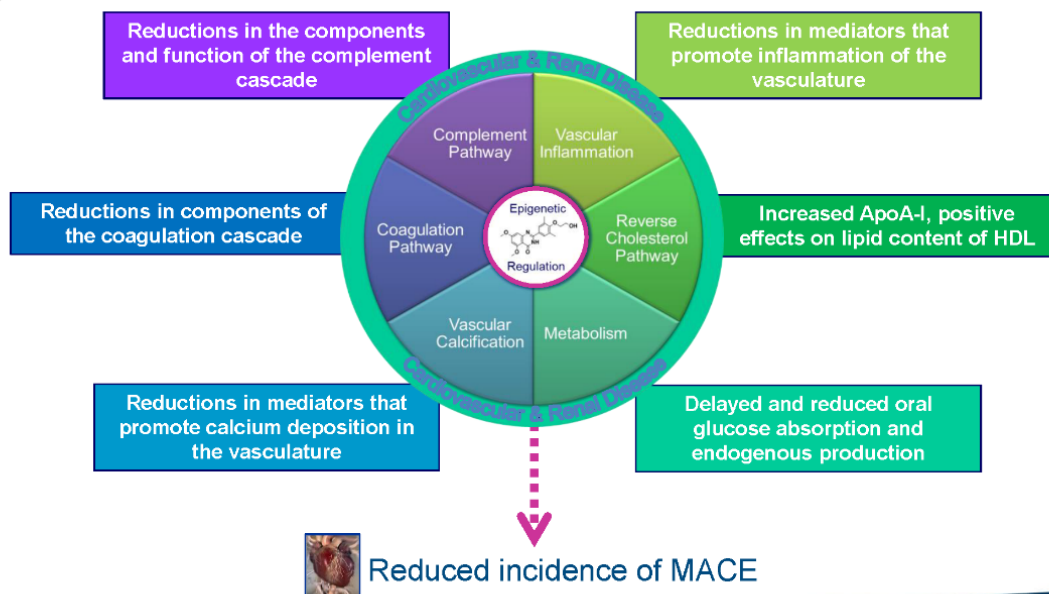
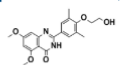
Apabetalone is based on targeting a group of BET (bromodomain and extra terminal) proteins. Each of these proteins contain two small regions called “bromodomains”, which play a role in regulating disease causing genes. Compounds that regulate the interaction of these domains may have favorable effects on reducing the level of proteins that play a role in disease.

BET inhibition results in the simultaneous modulation of multiple biological pathways via a single molecular target. RVX-208 preferentially binds to the second bromodomain of BET family members (BRD2, BRD3 and BRD4) with a 20-fold or higher selectivity for the second bromodomain versus the first bromodomain.

BET Inhibition Impacts the Pathways that Drive Cardiovascular Disease and Kidney Diseases



Apabetalone, a bromodomain extra-terminal (BET) protein inhibitor, regulates the expression of genes and restores the function of pathways underlying the pathogenesis of CVD and kidney disease



TSX: RVX

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Source: Resverlogix

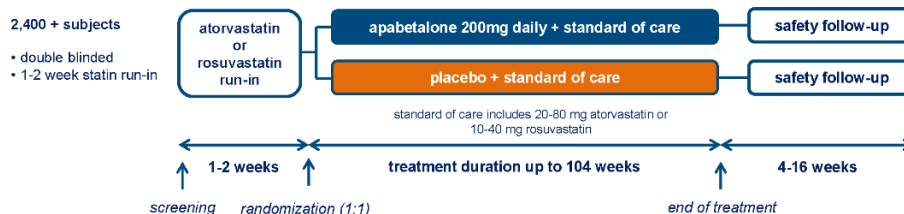
Resverlogix is looking at other potential markers regulated by BET inhibition. These ongoing efforts have positioned RVX as a world leader in its novel mechanistic target of select BET inhibition and epigenetic regulation. Interest in BET inhibition has grown substantially over recent years as an exciting new area of drug research. Leading global pharmaceutical companies such as Pfizer and others have dedicated research programs in the area. Resverlogix's foresight in investing in ongoing research into the area, including performing multiple proteome analysis of serum in patients from its Phase 2 program has provided new emerging pathways and proteins targets that are known driver of risk in cardiovascular and diabetic patients. The institutional knowledge gained by Resverlogix over the years, coupled with no known competitors in the BET space for vascular disease and long patent runways are considered strong reasons for potential buyers to pay even more for Resverlogix than what we forecast here.

The Ongoing Phase 3 Trial

Resverlogix launched its Phase 3 trial (BETonMACE) in October 2015, "Effect of RVX-208 on Time to Major Adverse Cardiovascular Events in High Risk Type 2 Diabetes Mellitus Subjects with Coronary Artery Disease". Top line results are expected in the first few months of 2019.

BETonMACE Phase 3 Trial

Enrollment Complete; Readout in Early 2019



The study is an event-based trial and continues until 250 narrowly defined MACE events have occurred

Key inclusion criteria

- Type II Diabetes Mellitus
 - HbA1c > 6.5% or history of diabetes medications
- CAD event 7 days - 90 days prior to screening
 - Myocardial infarction (MI), unstable angina or percutaneous coronary intervention
- HDL < 1.04 for males and < 1.17 for females

TSX: RVX

RESVERLOGIX.com

Source: Resverlogix

The trial is now fully enrolled with about 2,400 patients in 13 countries who are high risk cardiovascular patients with type 2 diabetes mellitus and low HDL. An estimated 12% to 15% of these patients also have chronic kidney disease. This is a double blind, randomized, parallel group, placebo controlled clinical trial to determine whether treatment of apabetalone combined with high dose Crestor or Lipitor and standard of care medicines increase the time to MACE, compared to treatment with Crestor or Lipitor alone.

Apabetalone Target Product Profile

High Risk ACS with Diabetes and Low HDL-C



High Risk Acute Coronary Syndrome (ACS) Patients with a Type II Diabetes Mellitus (DM) Comorbidity and Low High-Density Lipoprotein Cholesterol (HDL-C)		
Phase 3 BETonMACE	Primary Efficacy Endpoints	<ul style="list-style-type: none"> • Time to the first occurrence of Major Adverse Cardiovascular Events (MACE) defined as: <ul style="list-style-type: none"> ◦ CVD death; non-fatal myocardial infarction (MI); non-fatal ischemic stroke • Secondary endpoint includes: hospitalization for unstable angina, emergency revascularization procedures, and all-cause mortality
	Subgroups	<ul style="list-style-type: none"> • Assess potential improvement in kidney function, MACE, and renal serious adverse events (SAEs) (one time 40% or greater reduction in eGFR or doubling of serum creatinine) in population with baseline estimated GFR < 60 mL/min (stage 3+ CKD) <ul style="list-style-type: none"> ◦ Renal statistical analysis plan (SAP) in progress • Assess potential cognitive improvement based on a MoCA (Montreal Cognitive Assessment) in patients older than 70 years of age. <ul style="list-style-type: none"> ◦ Cognition statistical analysis plan (SAP) in progress
	Expected Efficacy Outcomes	<ul style="list-style-type: none"> • 30% relative risk reduction of MACE with statistical significance vs placebo with average treatment duration of 22- 24 months of treatment on top of current standard of care • Significant or trending results in defined subgroups such as CKD and cognition
	Unique Selling Points	<ul style="list-style-type: none"> • Novel mechanism of action with multi-factorial approach for the reduction of MACE in high risk ACS patients • Orally available small molecule with low projected COGS and price compared to monoclonal antibodies and peptides • Potential for alternate indications and increased accretive value based on subgroup analysis of BETonMACE, proteomic analyses of serum data from past Phase 2 trials, and early pre-clinical signals of genes associated with disease risk

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Source: Resverlogix

The primary endpoint is the time to first occurrence of MACE. The trial will continue until at least 250 MACE events have occurred. The trials will be considered a success if the endpoint improves on MACE incidence by 25%. Earlier Phase 2 trials showed far higher efficacy at over 40% relative risk reduction.

The company announced that it had received confirmation from the FDA that if the Phase 3 trial is successful, it is likely to support the filing and approval of a New Drug Application. This is similar to the feedback received from European authorities. This is a critical development as it takes RVX-208 one step closer to acceptance, once Phase 3 is a success.

Secondary endpoints include the hospitalization for cardiovascular disease events (unstable angina and revascularization procedures), changes in HDL and ApoA-I, changes in diabetes mellitus variables (glucose and glycated hemoglobin), changes in ALP, changes in kidney function as well as additional safety and tolerability of apabetalone.

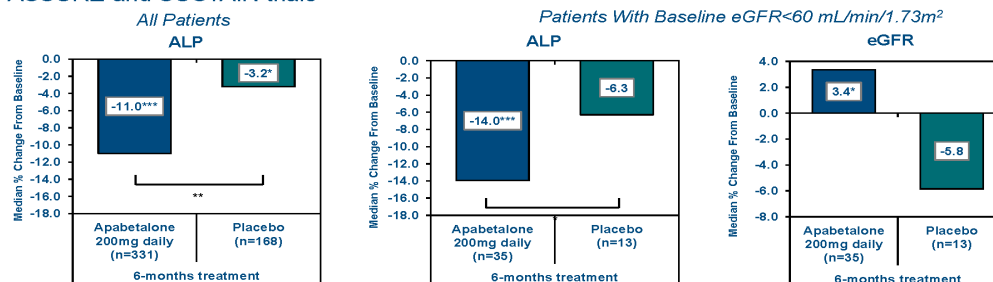
As noted above in our section on Addressable Market, after Phase 3 data has been analyzed, Resverlogix will conduct further Phase 2 tests on patients with end stage renal disease, as well as dementia.

In addition, after Phase 3 trial results are analyzed, Resverlogix plans to then conduct a proof of concept Phase 2a trial for Fabry disease, a rare and serious disease that results from the accumulation of a type of fat called GL-3 in blood vessels, the kidneys, the heart, the nerves and other organs.

Rationale for Kidney Disease Phase 2b/3



- Apabetalone has demonstrated reductions in alkaline phosphatase (a strong marker of CKD risk) and improvements in eGFR in CKD patients (eGFR < 60 mL/min/1.73m²) with CVD in the phase 2 ASSURE and SUSTAIN trials



Data Presented in Keynote Address at the 2015 American Society of Nephrology Conference, San Diego

- Resverlogix believes that BET inhibition and apabetalone may have the potential to improve kidney function, as measured by eGFR, in patients suffering from various stages of kidney disease
- Resverlogix is currently investigating the potential for expansion into specific kidney indications:
 - CKD (Stages 3a and 3b) patients, with a history of CVD (Phase 3 BETonMACE subgroup)
 - High Risk CKD Patients on Dialysis (Phase 2b BETonRenal study)

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Source: Resverlogix

Data from Previous Phase 2 Trials

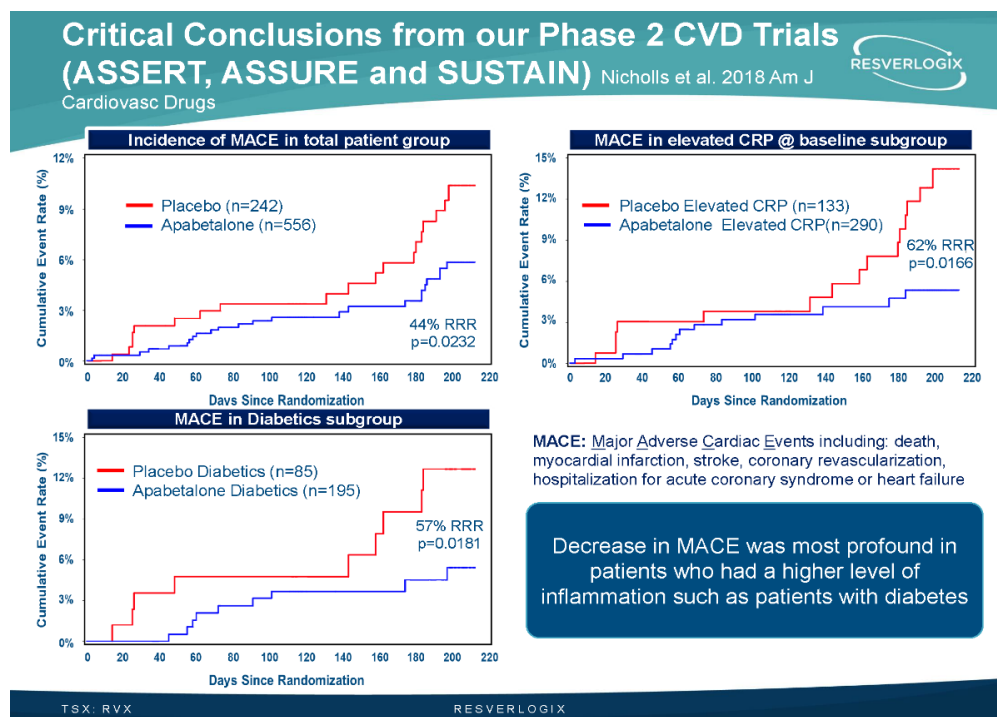
There were three clinical trials with a combined 1,001 subjects participating. 722 received treatment with RVX-208 while 279 received a placebo. Patients treated with RVX-208 had a less cumulative MACE rate of 5.9% versus 10.4% in the placebo treated group. In subgroups, the benefit of RVX-208 appeared more striking in patients with diabetes (5.4% vs 12.7%, $p=0.02$) and with baseline HDL-c <39 mg/dL (5.5 v 12.8%; $p=0.01$) or with baseline hsCRP levels > 2 mg/L (5.4% vs 14.2%; $p=0.02$). The relative risk reductions ranged from 44% to 62%. Such MACE data results are truly conclusive. The company reported that:

The actions of RVX-208 lowered atherogenesis by downregulating (8 of 11) pro-atherogenic genes but in contrast, upregulated (5 of 7) anti-atherogenic genes that control monocyte recruitment, migration and activation, macrophage function, inflammatory signaling and plaque stability.

Regarding toxicity: in one Phase 2 clinical trial, some patients had elevated serum enzymes (markers for liver injury); however other clinical tests indicated that there was no impairment in liver function and patients were asymptomatic for liver injury. Resverlogix has gone through seven data safety monitoring board reviews so far without any noted concerns for an ALT issue. Resverlogix has been instructed to continue the current BETonMACE trial with no changes to its protocol.

From the annual report, this is what they say worked in their trials:

Results demonstrated that apabetalone downregulates pathways that contribute to cardiovascular risk or MACE such as atherosclerosis, thrombosis and inflammation. Specifically, apabetalone downregulated the complement, fibrin clotting, acute phase response, cholesterol and fatty acid synthesis pathways, illustrating repression of most of the pathway components. Overactivation of the complement pathway and acute phase response participate in plaque development and destabilization. Fibrin clotting is fundamental in the formation of thrombi and emboli. Downregulation of these pathways by apabetalone may avoid catastrophic vascular events leading to vessel occlusion and death. Results for several components of the complement and coagulation pathways were verified by real-time PCR, a more sensitive and robust method of measuring mRNA expression, as well as using enzyme-linked immunosorbent assay ("ELISAs") to measure protein levels. Results were also recapitulated in human hepatocarcinoma cell lines and with BET inhibitors with different chemical scaffolds. In addition, in patients' plasma from the ASSERT, SUSTAIN and ASSURE clinical trials, apabetalone reduced levels of specific complement, coagulation and acute phase response proteins.



CKD Program - Phase 1 Data

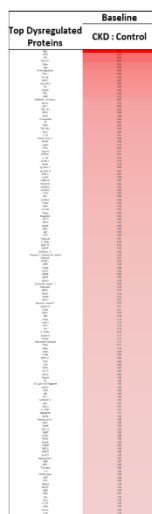
Effect of Apabetalone on Differentially Expressed Proteins



288 proteins were different between the plasma of CKD patients and matched controls (red indicates higher protein levels in CKD/control)

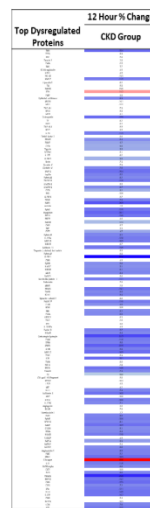
CKD = Subjects with stage 4 Chronic Kidney Disease

152 of the 288 differentially expressed proteins in the CKD patients were downregulated at 12 hours following one dose of apabetalone



Blue = downregulated;
white = no change;
Red = upregulated

In CKD patients, one dose of apabetalone reduced CKD and CVD biomarkers that were dysregulated at baseline



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SOMAscan® Analysis of Plasma Proteome – Phase 1 Trial

Apabetalone Reduces CVD and CKD Biomarkers



	Protein Name	Gene Symbol	Subjects with CKD (stage IV) (n=8) treated with 100 mg Apabetalone		Matched Control Subjects (n=8) treated with 100 mg Apabetalone	
			% Δ from baseline at 12h	p-value	% Δ from baseline at 12h	p-value
Inflammation	Interleukin-6	IL6		0.05	NS	
	Interleukin-1 alpha	IL1A		0.01	NS	
	Interferon gamma	IFNG		0.04	NS	
	TNF receptor superfamily member 1A	TNFRSF1A		0.05	NS	
	C-reactive protein	CRP		0.04	NS	
Cell Adhesion	Tumor necrosis factor	TNF		0.02	NS	
	P-selectin	SELP		0.04	NS	
	E-selectin	SELE		0.01		0.02
	Intercellular adhesion molecule 1	ICAM1		0.05		0.04
	Vascular cell adhesion protein 1	VCAM1		0.01	NS	
Matrix Remodeling Calcification	Fibronectin	FN1		0.02	NS	
	Stromelysin-1	MMP3		0.02	NS	
	Stromelysin-2	MMP10		0.02	NS	
	Osteopontin	SPP1		0.01		0.04
Thrombosis	Plasminogen activator inhibitor 1	SERPINE1		0.04	NS	
	Tissue-type plasminogen activator	PLAT		0.01	NS	
	Urokinase-type plasminogen activator	PLAU		0.01	NS	
	D-dimer	FGA/B/C		0.05	NS	
	Urokinase plasminogen activator surface receptor	PLAUR		0.02	NS	

Apabetalone reduces markers of inflammation, cell adhesion, matrix remodeling, calcification and thrombosis in the CKD cohort after one dose and 12 hours

TSX: RVX

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Source: Resverlogix

In summary, the data from Phase 2 trials is very clear: the molecule is safe and the trials successfully reduced MACE by large enough magnitudes to qualify for eventual FDA approval.

Management

Resverlogix was founded in 2001 by Donald McCaffrey and Dr. Norman Wong, both of whom are still at the company. McCaffrey is the CEO. Dr. Norman Wong is the author of more than 300 articles and abstracts and sits on over 40 international panels.

The best way to judge a biotech company is to check for peer acceptance of its trials. Who are the principal investigators? The very best scientists get to cherry pick projects they believe will have the best future. Professor Kaushik Ray was the senior principal investigator for the TOGETHER study looking at cardio metabolic risk in the vascular health checks of 250,000 in London. In addition, he is involved in eight ongoing trials in lipids and diabetes, as well as for ORION 1 assessing PCSK9 inhibition through RNA interference. Dr Ginsberg did the same for the landmark ACCORD LIPID trial. And the list goes on for Resverlogix's steering committee.

Financials

RVX has net debt of US\$20 million and a burn rate of US\$2.5 million a month. As a result, we expect RVX to need to raise more capital in the next few months.

Once again, its financing will depend on the results of Phase 3 test data.

Why is the valuation on RVX so low?

The market has an institutional memory for every stock. The record of Resverlogix has been detrimental to that memory. First, the company did not meet its stated endpoint goal of achieving plaque regression back in 2013. That was a huge shock to the market from which it took a long time to recover. If that was not bad enough, as a biotech company, RVX has had to raise capital non-stop. The market naturally does not take kindly to be continuously diluted. As recently as May 2018, the share price reached a low of \$1.10, far lower than levels seen for many years. It was a stock that had serially disappointed the market, and the market "forgot" about its very existence.

The credibility of the molecule is an issue for biotech analysts. Here is a drug that not only performs far better than existing therapies, in addition, it upends accepted medical wisdom. Most existing drugs are geared towards addressing one malfunctioning protein in the body. To have a proposed drug that will address several malfunctioning proteins through one small molecule, is difficult for many scientists to conceptually accept. This despite the fact that the data from Phase 2 testing is unequivocal and the drug has successfully gone through seven data and safety review boards. All this takes time for markets to absorb.

Another important reason for the market's current reluctance to revalue RVX is that the recent history of major Phase 3 trials of other promising drugs from other companies have failed. For example, Toretapib, Dalcetapib, Niacin trials were all stopped. All these efforts were focused on single protein targets. The market now has a show me attitude to all such tests. But the reaction to Amarin's Phase 3 test results show that the market will immediately revalue companies if the Phase 3 results are favorable.

Then there is the lack of analyst coverage, little trading volumes in the shares, and a Canadian stock market that is dominated by banks and commodity companies, not biotech. Therefore, what Makalu sees is a grossly undervalued special situations stock.

Is apabetalone the next mini-Humira?

Humira was initially approved in 2003 only for Rheumatoid Arthritis. With further clinical testing, it was later approved for additional indications, including psoriatic arthritis, Crohn's Disease and plaque psoriasis, among others. Sales for Humira went from \$1 billion in 2005 to over \$18 billion in 2017. Humira was the world's best-selling drug in 2017. Today, 1.4 million Americans have Rheumatoid Arthritis, a statistic comparable to the initial indication for RVX-208.

What is most interesting is that Abbott itself never expected such success. Their 2003 annual report forecast peak sales of \$1 billion from rheumatoid arthritis, and another \$1 billion from additional indications. Yet, by 2004, Humira was already being developed for six additional indications. If you were to calculate the discounted present value (5% discount rates) of the actual sales of Humira as calculated in 2002, then between 2003 and 2017, it adds up to \$60 billion. To make a 20% return on sales, it would have justified a nearly \$4 billion price to buy Humira from Abbott in 2003. Of course we know that profits grow much faster since margins on selling such drugs exceed 80%. Such calculations are admittedly rough and are meant more to provide a ballpark value to what a blockbuster drug can command.

All this is what we envision apabetalone to become. After cardiovascular disease, the next indication is chronic kidney disease and then dementia. Further down the line is Fabry disease and pulmonary arterial hypertension. While we can only estimate initial sales from RVX-208, we believe the potential to add more indicators make apabetalone the next mini-Humira.

What is the right price?

We believe Resverlogix will be bought out soon after its topline data comes out in 2019. Why isn't a company buying them out right now? The recent history of promising heart disease molecules failing in Phase 3 trials haunts potential buyers. In other words, RVX-208 results need to conclusively meet its MACE relative risk reduction target of 25% and is shown to remain safe. Executives at such potential buyers of Resverlogix would rather pay a lot more with a lot less uncertainty than the other way around.

For the buyer of Resverlogix, a key question is whether RVX-208 will be accepted by insurance companies, or will it go the way of PCSK9 inhibitors (simply too expensive to be acceptable to most insurance companies). Below is a table from 5 leading US Payers stating their ICER threshold of \$140,000 to \$200,000 to prevent one MACE event.

Organization	Lives Covered	MACE Reduction: Unmet need in Recent ACS and T2DM patients	MACE Reduction: Unmet need in CKD patients	ICER Threshold per annum
Payer 1	55 M	Moderate to High	Moderate to High	\$ < 100,000
Payer 2	65 M	Moderate to High	Moderate to High	\$ < 200,000
Payer 3	37 M	Moderate to High	Moderate to High	\$ < 100,000
Payer 4	40 M	Moderate to High	Moderate to High	\$ < 150,000
Payer 5	11 M	Moderate to High	Moderate to High	\$ < 150,000

Source: Resverlogix BIO 2018 Presentation

Since insurance companies are willing to pay for a MACE averted (\$100,000 to \$200,000), it then becomes a simple calculation to figure out how much a drug can get priced. The key unknown variable is relative risk reduction from apabetalone. The higher the reduction, the higher the price the drug can command. Based on numbers needed to treat (NNT) of about 25 to 60 (for a 40% and 25% RRR), the estimates indicate that \$5,000 price in the US should be acceptable.

In short, apabetalone is a very viable drug for a rapid reimbursement from health insurance companies, which in turn drives compelling commercial opportunity for the molecule.

Recent novel CVD therapeutic approach who have successfully completed Phase 3 trials provide a powerful example of this value inflection point. Amarin declared efficacy for 25% relative risk

reduction in MACE event with their purified fish oil over an average of 3.9 years treatment. Once this data came out their enterprise value grew from \$1 billion US to almost US\$6 billion in a matter of days. If we use that metric, Resverlogix can be argued to have a potential similar value of approximately \$30 US a share, which would be over ten times from today's enterprise value. While Amarin is a good comparison, it is not an apple to apple comparison. Amarin has a purified fish oil prescription medicine which can be used by a more general population with elevated triglycerides and or one of more cardiovascular risk factors.

Apabetalone has been planned to pursue high risk patients where the drug has compelling data of efficacy. These patients, having experienced a near death experience (ACS), a come to Jesus moment, have a very high compliance rate for ongoing use of the molecule. This in addition with potential use in chronic kidney disease and Dementia patients are additional markets where continuous and chronic dosing to take this drug are a must. This also makes for a very desirable commercial property from the seller of apabetalone's point of view. Like Humira, its use in future indications can easily expand with more clinical testing, allowing for even higher pricing of the molecule. Therefore, we see \$30 per share as the lower bound of what any drug company will pay for RVX.

We get a Net Present Value of about \$4 billion using conservative penetration rates for three indications. Almost 60% comes from the earliest indication (cardiovascular disease in diabetic and low HDL patients), another 30 percentage points from cardiovascular disease and chronic kidney disease patients, and the rest from Dementia. However, as we know, penetration rates can be much higher than our conservative estimates, and the potential for additional indications and off label use, can push estimated Net Present Value significantly higher.

Risks

Resverlogix's future depends on the results of its Phase 3 trial.

If, against all expectations (and particularly Phase 2 data), Phase 3 results do not meet the primary endpoint of MACE relative risk reduction, then the shares would be impacted negatively.

So far there have no toxicity concerns with Apabetalone in its current Phase 3 trial. Seven consecutive drug safety and monitoring review board reports have allowed the trial to continue with no changes in the clinical protocol. Such assessments provide an additional level of comfort that the drug to date is safe. Any unexpected data showing toxicity in Phase 3 may cause the FDA to ask Resverlogix to conduct more trials. This request, if it came, would significantly delay the ability of Resverlogix to apply for Apabetalone approval, and raise questions about the molecule.

Resverlogix will need more capital to continue its clinical trials. A failure of Phase 3 would severely curtail their ability to raise capital. The company expects to list on the NASDAQ, but a failure of this trial may make that a very difficult equity offering.

Summary

Resverlogix owns a novel first in class small molecule that is showing signs of having the potential to becoming the next mini-Humira.

Based on convincing Phase 2 data, we expect that Phase 3 results will show that Apabetalone remains safe and will most likely meet its endpoint of relative risk reduction of MACE events by at least 25%, along with other beneficiary impacts on chronic kidney disease patients and elderly patients with some form of cognition issues.

At the very least, we expect Resverlogix to have a strategic partner after successful Phase 3 test results are fully analyzed; most likely Resverlogix will get bought out for over \$30.

Resverlogix Data

Founded 2001 / listed 2005

Toronto XTSE

Calgary, Canada

GICS Classifications: Health Care / Pharmaceuticals, Biotechnology & Life Sciences / Biotechnology / Biotechnology

Auditor: KPMG LLP

Income Statement: Net Loss of US\$58 million

Balance Sheet: Net Debt of US\$20 million

Cash flow: Cash burn of US\$2.5 million a month

RVX STOCK PRICE FROM 2003 – Q3 2018



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