



Update Report

Resverlogix

Clear Path Toward Profitability



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Name:

EV (CAD m):

52-week Range:

Date: 11 May 2016

Resverlogix Corp.

169.8

1.00-3.13

Country:	Canada
Price:	CAD 1.34
ISIN Code:	CA76128M1086
Reuters Code:	RVX.TO
Market Cap (CAD m):	141.0

Cash & cash eq. (CAD m): 40.0 Shares outstanding (m): 105.2 21,681 Volume:

Free float: 87%*)

*) Insider ownership is 41,8m shares or 38.8%

USD mln (ending April 30 th)	2014/15A	2015/16E	2016/17E
Total Revenues	-	-	-
Net (Loss)/Profit	(18.3)	(13.0)	(15.0)
Net loss per share (cents)	(0.22)	(0.12)	(0.14)
R&D costs	4.2	14.0	18.0
Cash increase/(decrease)	15.6	14.4	(8.0)
Cash and marketable sec.	16.2	30.0	22.0



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Executive Summary

- Resverlogix (RVX.TO) is a clinical stage cardiovascular company with an epigenetic platform technology that modulates protein production. The company is developing small molecules that selectively inhibit Bromodomain and Extra Terminal domain (BET) proteins, a new and emerging target for high risk vascular diseases. The company is the first to test the BET inhibition hypothesis as a new approach for reducing major adverse cardiovascular events (MACE) in high risk diabetes and CKD patients. To date the company holds a nine year lead in the field of epigenetic small molecules for vascular disease risk reduction.
- Resverlogix has a proprietary drug development platform that is based on targeting BET proteins. BET protein inhibitors have potential in many diseases including cardiovascular disease, neurodegenerative diseases and diabetes. The field of epigenetics is quickly growing and with it the understanding that both the environment and individual lifestyle can also directly interact with the genome to influence epigenetic change.
- Early significant observations of MACE reduction by a select BET inhibition epigenetic small molecule has been observed in back to back clinical trials. These findings are significant and intriguing, especially when these reductions were on top of standard of care medicines such as statin, antiplatelet and glucose lowering therapy. A resetting of new genes and pathways, via epigenetic mechanisms, potentially represent a novel approach to a currently high unmet need in high-risk CVD patients such as those with a recent acute coronary syndrome (ACS) and low HDL, diabetes and CKD.
- In October 2015, Resverlogix initiated a Phase III trial 'BETonMACE' with apabetalone (RVX-208). The main objective of the Phase III BETonMACE trial will be to confirm MACE reduction in high risk cardiovascular disease patients with type 2 diabetes and



low HDL. Approximately 15% to 20% of the target patient population is expected to also have chronic kidney disease (CKD). The primary endpoint is the time to first occurrence of Major Adverse Cardiac Events (MACE). Patient enrollment is ongoing as planned and all primary investigator meetings are now completed. This trial is estimated to have a minimum of 2,400 patients and 250 adjudicated primary major adverse cardiovascular events (MACE) of heart attack, stroke and death, in over 175 European and Latin American sites. Apabetalone (RVX-208) has already been successfully tested in about 1,000 patients in various clinical studies (ASSERT, SUSTAIN and ASSURE)

- Next to the start of the clinical Phase III trial BETonMACE, Resverlogix also announced that it intends to initiate an Orphan Disease Program which will target diseases where BET inhibition may hold a promising approach. Based on data that apabetalone modulates: 1) vascular inflammation, 2) complement pathway, 3) vascular calcification, 4) coagulation pathway, 5) acute phase response, and 6) Reverse Cholesterol Transport (RCT), all of which have been reported to play important roles in cardiovascular disease and a range of orphan diseases, BET inhibition may also hold promise for these additional important therapeutic markets. The company plans to initiate expansion into orphan diseases such as complement mediated areas or others affected by biological pathways noted above. A pilot trial is planned in one or more orphan diseases and an approval for apabetalone for any orphan disease would bring about additional accretive value for the epigenetics and BET inhibition approach through high value expanded indications. Orphan indications would expect to potentially speed up market introduction for the molecule more rapidly than the BETonMACE clinical trial.
- In 2015 Resverlogix successfully secured CAD 50 million via a license and equity agreement with China based Shenzhen Hepalink Pharmaceutical Co for China, Hong Kong, Taiwan and Macau. Resverlogix is eligible to receive sales based milestone payments from Hepalink ranging between USD 5 million and USD 90 million and



royalties based on sales. Total sales based milestones and royalties could reach in excess of USD 400 million.

- Based on our adjusted NPV valuation, we believe Resverlogix is substantially undervalued at the current share price of CAD 1.42. We have increased our valuation of Resverlogix to CAD 8.50 from CAD 5.85 per share. This represents a substantial upside from the current share price. The increase in valuation is based on the successful licensing deal with Shenzhen Hepalink Pharmaceutical Co., the initiation of the Phase III clinical trial BETonMACE as well as the commencement of other clinical research programs with apabetalone, specifically in orphan diseases.
- With a successful Phase III trial and considering the market potential for RVX-208, we feel that a very significant upside potential for RVX-208 and Resverlogix is attainable. The next trial will help position RVX-208 to have a similar or even superior accretive value to other CVD novel agents such as CETP and PSCK9 inhibitors. Future data based on a phase III outcome trial, BETonMACE, will provide important additional data to build sensitivity and more detailed value proposition and pharmacoeconomic models compared to other agents in development, CETP and PCSK9, in this important market of residual risk in high risk CVD patients with diabetes and CKD.



Company Profile

Resverlogix (RVX.TO) is a clinical stage cardiovascular company with an epigenetic platform technology that modulates protein production. Resverlogix is developing apabetalone (RVX-208), a first-in-class BET inhibition small molecule called apabetalone for the treatment of and efficient reduction of MACE in high-risk vascular patient groups such as diabetes and CKD. MACE is defined as heart attack, stroke, heart failure, PCI procedures and death. RVX-208 is the first select BET bromodomain inhibitor in a Phase III clinical trial that is targeted for vascular diseases. New compounds arising from Resverlogix's epigenetic drug development platform which function by inhibiting BET bromodomains, have the potential to provide a truly novel approach to vascular diseases risk and impact disorders that drive substantial costs to health systems globally. A growing number of reported publications on BET inhibition and its potential benefits for a variety of diseases make this Epigenetic drug target a novel and important new area of focus for the pharmaceutical industry.

The selective production of the proteins encoded by human genes is what leads to differences between cells, and the alteration of their levels can contribute to disease. Epigenetics, a mechanism for regulating gene activity to affect protein production, is becoming an important new field in biotechnology research and drug development. It encompasses mechanisms for regulating the production of proteins from genes without altering the genetic code. In cells, DNA is surrounded by proteins to form chromatin and ultimately human chromosomes. Epigenetics is the study of secondary modifications to DNA (without affecting the sequence) or its associated proteins, which alters their relative disposition, resulting in changes in gene transcription, the first step in producing the proteins that each gene encodes. With an increasing number of diseases being found to be associated with epigenetic factors, the epigenetics field holds a lot of promise for the development of new treatments of - often age-related - diseases ranging from neurodegenerative diseases and cardiovascular diseases to diabetes, renal diseases, cancer and a variety of orphan diseases as well.



Business Strategy

Given the high costs, long development times and high attrition rates associated with drug development, many biotechnology companies seek the assistance of a pharmaceutical partner to advance their products through clinical trials. Resverlogix maintains active discussions with potential pharmaceutical and biotech partners for its pharmaceutical drug candidates. The Company seeks partnership opportunities that will provide shareholders with the optimal value for their investment. New potential opportunities in orphan diseases, provides Resverlogix with important options for further value creation. Orphan clinical trials are usually much smaller and shorter than traditional larger CVD trials. Expansion into orphan markets provides the company with additional value potential by entering the market more quickly and also establishing a broader indication base for its lead molecule and follow-on compounds. In 2015, the company was successful in securing a partnership with China based Shenzhen Hepalink Pharmaceutical for a license on RVX-208 for all indications for China, Hong Kong, Taiwan and Macau for a total upfront investment of CAD 50 million and future China sales milestones and licensing royalties that could represent in excess of USD 400 million. We expect that Resverlogix will be able to make additional regional licensing deals that will give the company more early revenue possibilities. Deals in areas with high unmet medical need such as diabetes and CKD as well as initiation of quicker clinical trials for an orphan drug indication are likely to speed up revenue streams and value creation for the company markedly.



New Treatments Needed for High Risk CVD

As the global population pushes past 7 billion and more people reach old age, the number of deaths from cardiovascular diseases is on the rise. Cardiovascular diseases (CVD), the leading cause of premature death in the world, include heart attacks, strokes, and other circulatory diseases.

In the United States alone, over 16 million people have existing coronary heart disease (CHD), and another 6 million have suffered strokes. According to the World Health Organization more than 17.3 million people die each year from cardiovascular disease, representing one third of all global deaths. Of these, more than 40% are due to coronary heart disease. The remaining residual risk in CVD is still far too high. What needs to be highlighted is that this risk is on top of standard of care medicines such as lipid lowering agents, anti-thrombolytic agents and blood pressure lowering medicines. As a result new approaches to lowering this risk are needed.

Of all the indicators that are used for providing prognostic predictability for CVD risk, MACE (Major Adverse Cardiovascular Events) is the most important. Patients, physicians and CVD key opinion leaders look at MACE as the most impactful marker of CVD risk. MACE includes a variety of key markers of cardiovascular risk such as worsening angina, worsening of peripheral artery pain and ischemia, prevention of percutaneous stent procedures, hospitalization for cardiacrelated incidents, stroke, myocardial infarction and death. According to the 2016 AHA Statistics report, based on 2013 death rate data, more than 2,200 Americans die of CVD each day, an average of 1 death every 40 seconds. Many of these CVD patients will have some form of MACE during or after they have been diagnosed with CVD.

Reducing CVD Risk is more than addressing just lipids

Although the risk of cardiovascular disease in patients with diabetes and CKD can be partially managed through lifestyle modification and treatment with drugs to lower cholesterol, a



significant unmet need still exists as 70% of cardiovascular events still occur even with optimal LDL lowering therapy. This remaining residual risk is a major area of focus for the biopharmaceutical drug industry and specifically Resverlogix.

LDL Lowering

The LDL lowering hypothesis is being further tested in CVD risk with aggressive reduction of LDL to unprecedented levels such as 40-50mg/dl. Newly reported trials such ODYSSEY LONG TERM, PSCK9 LDL lowering approach via Alirocumab (ESC Barcelona 2014) and IMPROVE IT, cholesterol absorption LDL lowering approach via Ezetimibe (AHA Chicago 2014) have provided new information on the potential for very aggressive LDL lowering and its effects on efficient MACE reduction in CVD patients, on top of standard of care therapy. The following table illustrates the potential effect of additional lowering of LDL vs. BET inhibition and improvement of multiple risk pathways in high risk vascular patients:

Trial Analysis	Hypothesis	LDL Baseline	Trial Size	Treatment Duration Yr	Relative Risk Reduction	Number Needed Treat/yr
IMPROVE IT	LDL lowering 50mg/dl	60mg/dl	15000	7	6% (p<0.01)	350
ODYSSEY LONG TERM	LDL Lowering 40mg/dl	120mg/dl	2341	1.5	48% (p<0.02)	92
SUSTAIN/ ASSURE	BET Inhibition	90mg/dl	499	0.4-0.5	55% (p<0.02)	21

Although both IMPROVE IT and Odyssey Long Term were significant in lowering MACE in their respective trials, with a reported range of USD 2.5-14K a year treatment cost per patient, the cost to prevent an event could be argued to be somewhere in the area of USD 350-K to over 13ooK based on a simple analysis of NNT (number needed to treat) of annualized treatment therapy times annual treatment cost. It is critical to realize that when building a value proposition, the

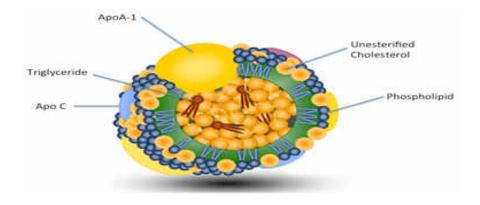


lower the NNT the better. If the current economic and value proposition for these LDL lowering technologies represents a standard range of NNT, reimbursement agencies could request stronger value evidence with significantly improved pricing thresholds. This is now evident in the large outcome trials that the PCSK9 developers have had to run for payer groups. Payer groups such as NICE and US Managed Care organizations are now demanding "value for money" if any new drugs are seeking rapid reimbursement, product positioning and uptake on their respective formularies. Apabetalone's multimodal mechanism of action on numerous pathways that drive vascular risk represent a highly differentiated and potentially more efficient way to addressing the need for a value proposition.

HDL and ApoA-I: Reverse Cholesterol Transport

An early focus biology and target of apabetalone was reverse cholesterol transport (RCT) and HDL and ApoA-I. The most abundant protein in HDL is ApoA-I and it serves as the building block for high-density lipoprotein (HDL or the "good cholesterol") particles. Increased production of ApoA-I protein results in the synthesis of new HDL particles. These newly synthesized HDL particles are more 'functional' because of their ample capacity to remove cholesterol from atherosclerotic plaques. The efflux of cholesterol from the plaque to HDL is called reverse cholesterol transport (RCT). The goal of enhanced RCT with newly synthesized HDL is to remove cholesterol from plaque in the arteries, subsequently regressing atherosclerosis. ApoA-I production versus other approaches such as CETP therapeutics, are the only technologies to date to efficiently remove and regress atherosclerotic plaque in high risk CVD patients, specifically over a short treatment.





Source: Resverlogix

Although RCT is an important biology, BET inhibition via apabetalone, has been reported to modulate and improve additional biology pathways that drive vascular risk such as inflammation, complement, thrombolytic and calcification pathways. These will be discussed in subsequent sections.

Alkaline Phosphatase

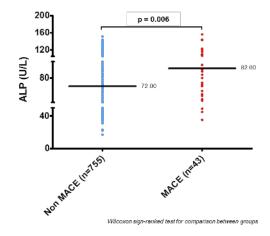
One emerging risk marker that does not focus on lipids or LDL lowering is alkaline phosphatase. It is a widely reported risk marker for MACE in patients with diabetes and CKD. Below is a table of one such study reported in 2011 of The American Journal of Medicine, Krishnamurthy et al, in over 15,000 patients with diabetes. This study is one of many that highlight the link and risk associated with elevated ALP and added CVD risk in patients with diabetes. Elevated ALP has been reported in numerous publications with vascular calcification and an increased incidence of heart failure and CKD.



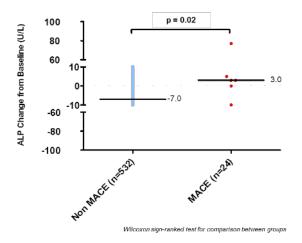
Table 1 Baseline Characteristics by Serum Alkaline Phosphatase Quartiles					
	Serum Alkaline Phosphatase Quartiles				
	<69 (U/L)	69-83 (U/L)	84-101 (U/L)	102-952 (U/L)	<i>P</i> -Value
Serum alkaline phosphatase (U/L)	57 ± 0.30	76 ± 0.10	92 ± 0.20	126 ± 1.0	
Age (years)	40 ± 0.4	44 ± 0.6	46 ± 0.6	48 ± 0.6	<.001
Men (%)	39 (37-41)	50 (47-52)	56 (53-58)	53 (51-56)	<.001
African American (%)	10 (9-11)	10 (9-12)	10 (9-12)	13 (11-14)	.199
Clinical characteristics					
Myocardial infarction (%)	1.8 (1.5-2.3)	2.7 (2.1-3.5)	4.3 (3.3-5.7)	5.9 (4.9-7.2)	<.001
Stroke (%)	1.1 (1.0-1.5)	1.4 (1.2-1.9)	2.3 (1.8-3.0)	3.0 (2.7-4.5)	<.001
Congestive heart failure (%)	1.0 (0.7-1.4)	1.3 (0.9-1.7)	2.4 (1.8-3.2)	4.2 (3.4-5.7)	<.001
Malignancy (%)	3.0 (2.4-3.7)	3.4 (2.5-4.4)	4.0 (3.2-4.9)	4.7 (3.7-6.0)	.045
Diabetes mellitus (%)	3.8 (3.2-4.6)	5.5 (4.2-6.5)	7.7 (6.5-9.1)	14 (12.4-15.8)	<.001

Source: Krishnamurthy et al. The American Journal of Medicine (2011) 124, 566.e1-566.e7.

Emerging in Resverlogix's data is a new nexus of pathways and biology's that appear to be improved by select BET inhibition and apabetalone. To date the early data support that several new pathways and risk markers of vascular risk are modulated thus creating a new hypothesis for BET inhibition and early observations of MACE reduction in high risk patients. This nexus of biology's that are apparently improved by apabetalone treatment represent a new treatment paradigm for high risk. Early evidence of apabetalone's impact on ALP and its relationship to CVD risk and MACE was presented at ASN in San Diego in November of last year. At the Keynote Presentation by Dr. Kam Kalandar Zadeh, Chief of Nephrology at University of Irvine California outlined the long standing relationship with reduced ALP and reduced risk for MACE in CKD populations as well as the correlation observed in Resverlogix's reported trials on ALP and MACE. Below is a graph which outlines baseline ALP characteristics of patients who experienced MACE vs those who did not have a MACE in the RVX clinical Phase 2 program.



In addition Dr. Zadeh reported change characteristics of ALP and observed MACE correlation as well in the RVX-208 treatment group.



Consistency within the data indicates that the early effects of BET inhibition on reducing ALP and observed correlation on MACE may provide further evidence that CVD risk will be impacted by apabetalone in novel ways. These findings provide new potential indications of even higher risk renal patients for the Company for apabetalone.



Vascular Inflammation

Reported by Libby in "Clinical Cardiology New Frontiers" atherosclerosis, what was formerly considered a bland lipid storage disease, has moved beyond lipids and actually involves an ongoing inflammatory response. Recent advances in basic science by many have established a fundamental role for inflammation in mediating all stages of this disease from initiation through progression and, ultimately, the thrombotic complications of atherosclerosis. These new findings provide important potential links between risk factors the mechanisms of MACE and the potential emerging role of BET inhibition. Data provided from the Company have also shown that markers of inflammation such as hsCRP are reduced in human patients. Additional inflammation and cytokine markers such as haptoglobin, IL-18 and VCAM-1 were also reduced in animal models vs. placebo by apabetalone, reported in Atherosclerosis 2014, Jahagirdar et al. Emerging evidence on multiple risk pathways and markers that affect CVD risk are now being viewed in new models that may predict more accurate and efficient outcomes of patients with acute coronary syndromes, diabetes and CKD.

CETP Dead and Buried

While statins are effective and represent the current mainstay of treatment, it is clear that new treatment options are needed, particularly in high-risk patients who rarely achieve guideline-recommended targets. Clearly, patients who have already had a heart attack are at high risk. Therefore novel options are particularly needed for these patients. An important clinical trial in the past few years has been the IMPROVE IT trial of Merck, which examined the outcomes in patients with Acute Coronary Syndrome (ACS). Primary objective was to evaluate the clinical benefit of Simvastatin/Ezetimibe and Simvastatin. Over a period of seven years, no less than 18,000 patients were enrolled. The trial only showed an improvement of the relative risk reduction of MACE by 6.4% over a 5 year period. This is a far too weak of a signal for efficient MACE reduction and the number needed to treat (NNT) is approximately 350 to prevent one



MACE outcome. The absolute risk reduction (ARR) in the trial was approximately 2%. This means that for every 100 patients treated, 98 of them are not getting any benefit. Many view these results as a confirmation of the hypothesis that, when it comes to LDL cholesterol, "lower is better". Others further speculated that these results would cause the FDA to become more lenient in approving all LDL-lowering drugs in advance of having to prove by way of an IMPROVE-IT-style outcome study that such a new LDL-lowering agent would share Vytorin's risk-reducing profile. However, we believe it is definitely not at all certain that the FDA will move in such a direction.

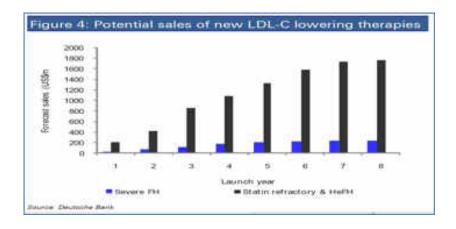
According to the February 2012 Cardiovascular Disease Pipeline Healthcare report from Deutsche Bank, the residual risk marketplace for CVD and MACE in high risk populations was estimated with a large potential market opportunity range of USD 4-90 billion. Their detailed analysis of current products included several new categories of drugs such as CETP, PLA2, IL-1 Beta, antisense Apo B-100 gene and PCSK9, all new approaches and risk biomarkers that progressed into Phase III trials that focused on MACE outcomes. The report provided a detailed market opportunity analysis of all these new approaches and the potential sales of:

- new therapeutics that address excess CV risk and
- new LDL lowering therapies

The market potential is broken down in the following graphs.



The report illustrated a much stronger value proposition to new approaches that reduced MACE in high risk groups versus LDL lowering noted in the next graph.



The failure of several of these approaches post the launch of this report, Dalceptrapib (Roche) May 2012, Darapladib (GSK) October 2012 and Evacetrapib (Eli Lilly) highlighted the lack of any signal or efficacy in reducing MACE with CETP and PLA2. Eli Lilly announced last year it was to discontinue studies of Evacetrapib after it failed to reduce rates of major cardiovascular events, including heart attack, stroke, angina or cardiovascular death. In early April 2016 the Cleveland Clinic released further data on the Phase III trial (Accelerate Study, enrolled 12,000 patients). The



researchers found that not only did it not reduce CV events, but that this came despite reducing levels of low-density lipoprotein (LDL, or "bad" cholesterol) by 37% and raising levels of highdensity lipoprotein (HDL, or "good" cholesterol) by 130%. The data also revealed that hypertension was significantly increased with evacetrapib--a highly concerning adverse event given the patient population. Improving HDL via CETP inhibition had been seen as the great hope of this next-generation class of statins. The drug more than doubled HDL and lowered LDL levels by as much as many statins--but had no effect on cardiac events. Just looking at the effects a therapy has on cholesterol levels doesn't always translate into clinical benefits. The trial raises questions about the benefits of raising HDL and the future of this class of drugs. Lilly has already moved on from this failure, but these data will be a blow for Merck and Amgen, who are both continuing to develop their versions of cholesteryl ester transfer protein (CETP) inhibitors, despite three huge failures in the area from Pfizer all the way back in 2006 after deaths were reported, and more recently from Roche in 2012 and Lilly last year.

The idea is that CETP deficiency is cardioprotective, but these three late-stage studies just have not backed this up. In fact, evacetrapib was thought to be the most promising approach because it is a potent CETP inhibitor that lacks the toxicity of former failed meds, but it too still did not help CV patients and increased hypertension. The study's researchers concluded: "Despite widespread use of statins, many patients continue to experience cardiovascular events. Therefore, considerable efforts have been put into investigating whether the protective benefits of HDL cholesterol could be targeted as a form of therapy."

Merck's ongoing REVEAL study for anacetrapib may just reveal something many are already expecting: failure. "Merck's drug is the fourth shot on goal for CETP inhibitors, but with disappointment or lack of success for the other agents you have to be increasingly pessimistic about the class of drugs. The same goes for Amgen, whose CETP inhibitor TA-8995, acquired from its USD 1.6 billion deal with Dezima in 2015, will potentially undergo mid-stage testing. In



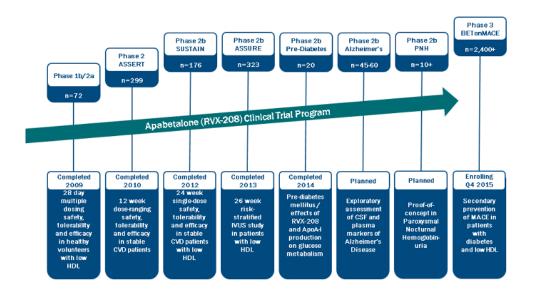
addition another new entrant into CETP, DalCor, is trying a genetic approach to risk reduction in CVD utilizing CETP genotypes. DalCor Pharmaceuticals, has recently moved forward with this approach, which was based on a post-hoc review from the DalOUTCOMES trial. Here they observed a 37% broad 5 point MACE reduction in a small genetic subset of patients. This data was taken from a total of 38 reported broad MACE events over an approximate 5 year treatment period. Upon detailed review of the data it was interesting to note that these genotype AA patients had an overall less event rate versus the other genoptype patient groups within the DalOUTCOMES trial. By having even less events than the total DalOUTCOMES population the targeted genotype population in DalCor's approach would be even less enriched for MACE events and as a result would potentially have an even lower value proposition argument for Payers.



Clinical Overview Apabetalone (RVX-208)

Resverlogix' lead drug candidate is apabetalone (RVX-208), an oral first-in-class BET inhibition small molecule apabetalone for the treatment of and efficient reduction of MACE in high-risk vascular patient groups such as diabetes and CKD. Apabetalone is the first select BET bromodomain inhibitor in clinical trials that is targeted for vascular diseases. New compounds arising from Resverlogix's epigenetic drug development platform function by inhibiting BET bromodomains have the potential provide a truly novel approach to vascular diseases risk and impact disorders that drive substantial costs to health systems globally.

Resverlogix has performed numerous clinical trials to date. It has learned from these trials to target patients with RVX-208 and Crestor with low HDL and diabetes.

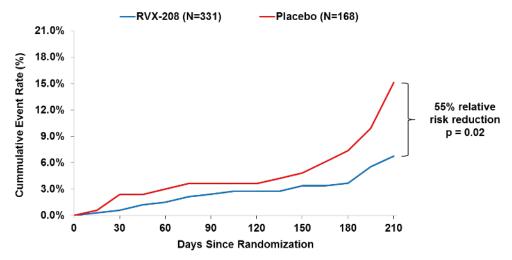


Source: Resverlogix



Extensive analysis on early MACE was performed in the Company's Phased IIb program of almost 500 patients. MACE was a pre-specified endpoint in the statistical analysis plan (SAP) in ASSURE. ASSURE revealed a MACE reduction on treatment vs placebo of p value <0.09, trending towards significance. This early positive finding from ASSURE helped direct the larger post hoc analysis for both trials. Over a period of 24 and 26 weeks a total of 35 MACE events were reported in both the SUSTAIN and ASSURE trials combined. Patients treated with RVX-208 in both studies reported 6.7% MACE events while patient in the placebo group reported a total of 15.1% (p=0.02). This 55% reduction of events was reported on January 8, 2014 in a Company press release.

Relative Risk Reduction of MACE in ASSURE and SUSTAIN Clinical Trials



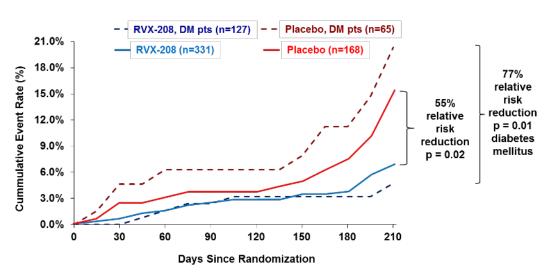
ASSURE and SUSTAIN Safety Population. Log-Rank test for between group comparison. Patients were censored at 30 days after the last dose of study medication.

Further analysis of patient segments, those with elevated vascular inflammation, (CRP >2.0), a known risk marker for vascular inflammation, were reported at ACC 2014. Dr. Puri, from the Cleveland Clinic, reported an observed 70% reduction in MACE (p<0.02.). These findings in patients with elevated vascular inflammation risk prompted the company to perform additional



exploratory analysis in patients with elevated risk. One such group that provided important additional information were those with diabetes mellitus. In several large epidemiological reports diabetes patients have up to twice the amount of MACE versus conventional CVD risk patient groups.

Diabetes patients are known to have higher risk of CVD events than the general CVD population. Analysis of this enriched group again a more marked reduction of MACE, up to 77%, in the RVX-208 treated group versus placebo. The data was presented at the ESC in Barcelona in 2014 at - "State of the Art – Innovation in Acute Coronary Syndrome Session".



Relative Risk Reduction of MACE in ASSURE and SUSTAIN Clinical Trials

ASSURE and SUSTAIN Safety Population. Log-Rank test for between group comparison. Patients were censored at 30 days after the last dose of study medication.

Source: Resverlogix ESC 2014 Presentation

Analysis from multiple high risk patient groups in the Company's Phase IIb program illustrate that RVX-208', apabetalone, in early treatment programs of up to 26 weeks have marked reduction on MACE. These consistent findings of MACE reduction add to the future opportunity for the "select BET inhibition approach" for patients with high residual risk. The Company continues to perform



detailed analysis of additional proteins and markers of interest to further elucidate expanded biological plausibility for MACE reduction observed to date. In addition the Company is expected to complete an exhaustive protein analysis which will further add to its proprietary human BET clinical database and knowhow in BET inhibition. This new information will add to the Company's lead position in Epigenetics and BET inhibition for expanded clinical indications such as renal and orphan diseases.

SUSTAIN Clinical Trial (Completed)

Resverlogix started enrollment and dosing of 176 patients for the SUSTAIN trial in September 2011. Enrollment was completed in November 2011 and dosing was completed in May 2012. In August 2012 the company announced that SUSTAIN met its primary and secondary endpoints.

SUSTAIN was a 24-week, multi-center, double-blind, randomized, parallel group, placebo controlled clinical trial conducted in South Africa. 176 subjects with established CVD who continue to have a high-risk for recurrent CVD events were enrolled. All subjects in SUSTAIN had a low level of HDL-C and were receiving standard of care therapy that included up to 40 mg Atorvastatin (Lipitor®) or 20 mg Rosuvastatin (Crestor®). Subjects received 200 mg/day of RVX-208 or placebo in order to assess lipid trends and safety. In addition, other biomarkers of reverse cholesterol transport were examined. The primary endpoint of SUSTAIN was the change in HDLC from baseline after receiving RVX-208 for 24 weeks vs. placebo. Secondary endpoints included change in ApoA-I, LDL-C, non-HDLC, apoB, TG and HDL subclasses. RVX-208 significantly increased HDL-C (p=0.001), the primary endpoint of the SUSTAIN trial. SUSTAIN also successfully met secondary endpoints, showing increases in levels of ApoA-I (p=0.002) and large HDL particles (p=0.02), both believed to be important factors in enhancing reverse cholesterol transport activity. The SUSTAIN trial also showed that increases in ALTs reported in previous trials were infrequent and transient with no new increases observed beyond week 12 of the 24-week trial.



Findings drawn from SUSTAIN included:

- Low baseline HDL and low baseline ApoA-I were the best responders; and
- There was 1 MACE event in treated subjects vs 6 in placebo

ASSURE Clinical Trial (Completed)

In September 2011, Resverlogix began activating study sites for ASSURE and, in November 2011, it commenced enrollment and dosing of patients in ASSURE. In September 2012, Resverlogix completed enrollment (of 323 patients) in the ASSURE trial. In June 2013, the company announced that ASSURE did not meet its primary endpoint but met its secondary endpoints.

In September 2013, the full analysis set data was published. It showed that the below median HDL (<39 mg/dL) baseline population consisted of 92 patients who were taking either Rosuvastatin (Crestor®) or Atorvastatin (Lipitor®) together with RVX-208. Those patients taking Rosuvastatin (Crestor®) and RVX-208 had a highly statistically significant Percent Atheroma Volume (PAV) plaque regression of -1.43% with probability value of p<0.002, versus baseline. This PAV regression exceeded the trial's pre-specified PAV endpoint (-0.6%) by more than two-fold. Those patients taking Atorvastatin (Lipitor®) together with RVX-208 had a PAV plaque progression of +0.19% with a non-significant probability value versus baseline. In November 2013, Resverlogix announced two additional results from ASSURE. The first showed statistically significant improvements in coronary IVUS atheroma measurements and MACE in patients with a high (>2.0 mg/dL) serum high sensitivity C-Reactive Protein ("hsCRP"). Secondly, initial findings illustrated that the actions of RVX-208 pointing to less vulnerability of the atherosclerotic plaque for rupture.



On January 16, 2014, Resverlogix announced new information arising from ongoing analysis of data from both the SUSTAIN and ASSURE trials in atherosclerotic patients with high risk for recurrent events. This analysis, performed by an independent biostatistical analysis firm, focused on the potential benefit of RVX-208 to impact MACE over a short time period of six months. When MACE data (n=499) from both SUSTAIN and ASSURE trials were combined, it demonstrated that treatment with RVX-208 lead to a significant reduction in MACE. RVX-208 treated patients (n=331), had less cumulative events of 6.7% vs. 15.1% (p=0.02) in the placebo treated group (n=168). Furthermore, in patients who had elevated CRP > 2.0mg/dL (n=283) the benefit of RVX-208 treatment of patients (n=179) appeared more striking with a cumulative event rate of 6.4% vs. 20.5% (p=0.007) in the placebo group (n=104). This was the first reported evidence that apabetalone appeared to work better in patients who had an inflamed vasculature. The Company intends to further provide future analysis for all three Phase 2 clinical trials for MACE in treated versus placebo groups. If consistent findings of reduced MACE from all three clinical trials hold, this would further provide evidence that BET inhibition is a promising new approach for risk reduction in important market segments of diabetes and CVD.

ASSERT Clinical Trial (Completed)

ASSERT was a 13-week randomized, double-blind, placebo-controlled, multi-center US study with 299 patients enrolled with stable coronary artery disease. The primary endpoint of the study was increased plasma ApoA-I levels compared to placebo group after three months of dosing of RVX-208. Other objectives were to examine the safety and tolerability of RVX-208 and to compare the dose and time response relationship for ApoA-I as well as to examine key reverse cholesterol markers involved with HDL functionality.

In November 2010, Resverlogix announced top line results of the ASSERT Phase 2 clinical trial. The ASSERT trial data demonstrated that the three key biomarkers in the reverse cholesterol transport process showed dose dependent and consistent improvement. The trial showed dose-



dependent increases, though not statistically significant, in ApoA-I, the trial's primary endpoint. The trial also showed statistically significant increases in HDL cholesterol including alpha1 particles or functional HDL, and highly statistically significant increases in large HDL particles. RCT is a pathway by which accumulated cholesterol is transported from the arterial wall to the liver for excretion, thus reducing and/or preventing atherosclerosis. In the high dose, ApoA-I achieved a 5.6% increase with a statistical value of p=0.06 versus placebo. Across all subjects, ApoA-I showed a trend to increase in higher doses with statistical significance of p=0.035. ApoA-I and other HDL particles continued to be increasing at the end of the 12 week study. Both the 8.3% HDL cholesterol increase and the 21.1% large particle HDL increase were highly statistically significant, p<0.01 and p<0.001 respectively. These pronounced HDL related increases via ApoA-I production are important as they take place later in the reverse cholesterol transport chain of events and strongly indicate the potential for plaque regression.

Findings drawn from ASSERT included:

- Data illustrated that 200 mg/day of RVX-208 was the optimal dose, based on safety and efficacy;
- Data illustrated that those patients with a low level of HDL-C at baseline had a better response for HDL-C and ApoA-I increases when treated with RVX-208; and
- Data illustrated that the best response were those patients given RVX-208 in combination with non-max doses of second generation statins such as Rosuvastatin (Crestor®) or Atorvastatin (Lipitor®).

These key findings contributed to determining a therapeutics window and targeted patient group for RVX-208.



Pre-Diabetes (Completed)

In October 2012, Resverlogix initiated an exploratory Phase 2 clinical trial in patients with prediabetes mellitus to examine the effects of RVX-208 and ApoA-I production on glucose metabolism. Dosing concluded in March 2014. On July 23, 2014, the company announced that the preliminary results of the trial. The investigators postulated that the RVX-208 induced rise in ApoA-I/HDL-C may impact pancreatic insulin secretion and thereby lower blood glucose (detected using an oral glucose tolerance test).

Patients (n=23) with pre-diabetes mellitus (also called metabolic syndrome) were given 200 mg/day RVX-208 for a short duration of only 4 weeks. The preliminary results were not consistent with their hypothesis. However, this finding was useful in understanding the ASSURE data because for RVX-208 to reduce blood glucose in patients with diabetes mellitus required at least 12 weeks of treatment. Analysis of data from the trial beyond preliminary results reported here is planned to include; HDL abundance, lipidomics, platelet aggregation, monocyte activation and neutrophil adhesion.

Phase III BETonMACE (Enrollment ongoing)

In October 2015, Resverlogix announced the commencement of the Phase III BETonMACE trial to confirm MACE reduction by apabetalone as shown in the Phase II trials SUSTAIN and ASSURE in high risk patients with coronary artery disease and type 2 Diabetes Mellitus. Approximately 15% of the patient population will also have chronic kidney disease (CKD). The primary endpoint is the time to first occurrence of MACE. In November dosing has begun in this double blind randomized placebo controlled trial at a dose of 100mg twice daily or matching placebo in combination with standard of care statin therapy administered to type 2 diabetes patients. Key inclusion criteria are type 2 diabetes and a recent coronary event. Standard of care statin therapy will be of a daily dose of either atorvastatin (Lipitor) 20-80mg or rosuvastatin (Crestor) 10-40mg.



This combination treatment period will continue for up to 104 weeks and will be conducted in more than 150 European. A minimum of 2,400 patients will take part in the trial and the trail is expected to be completed in October 2018 or until at least 250 MACE events have occurred. To date patient recruitment is going as planned. The Company aims to show a 25-30% MACE reduction with apabetalone as compared to the placebo and the current standard of care statin therapy.

Resverlogix is planning to review various sub groups such as a planned 15-20% of patients who are expected to have stage 3-4 chronic kidney disease and up to 10% are expected to have peripheral artery disease. If these sub populations, within the BETonMACE trial, reveal positive results then a Pharma partner would have expanded indications to pursue and build further accretive value for the molecule. The Company also intends to perform a cognitive function assessment for all patients over the age of 70. These subgroups will be analyzed in the statistical analysis plan. Positive data in these subgroups would indicate that further clinical trials could be initiated providing additional important patient market segments for the molecule.

Commencement of Orphan Disease Program

In September 2015, the company announced the initiation of an Orphan Disease Program with initial early data on complement markers. New data generated by Resverlogix and others have demonstrated that BET inhibition and the BRD4 target has effects on multiple biological pathways that underlie several orphan diseases. Specifically, apabetalone and its target BRD4 has been shown to modulate biological pathways and markers known to play a role in a variety of orphan indications. Based on these findings, Resverlogix plans to expand proof-of-concept trial or trials in several orphan indications such as complement mediated diseases and potentially others. Apabetalone, RVX-208 has been shown to modulate components calcification, complement and coagulation pathways both *in vitro*, *in vivo* and in the plasma of select patients treated with RVX-208 (from the ASSURE clinical trial). The Company also has communicated that



it is completing a large protein analysis where it will further reveal new pathways and proteins of interest that BET modulates. New areas of interest that may be clarified by this analysis may provide further guidance into other areas of interest such as renal orphan diseases.

Preclinical testing on other BET inhibitors in the Resverlogix library demonstrates similar effects on important markers in complement, coagulation as well as other pathways which as known to play a role in other orphan diseases. These compounds are under consideration as follow on compounds for additional orphan diseases. Apabetalone is expected to move into some form of pilot orphan study in 2016. An approval of apabetalone in any orphan indication such as PNH or others could get the drug likely earlier to the market and would be additional source of early revenues for the company.

PNH is a rare, acquired, life-threatening disease of the blood characterized by destruction of red blood cells by the complement system, a part of the body's intrinsic immune system. This destructive process is a result of a defect in the formation of surface proteins on the red blood cell, which normally function to inhibit such immune reactions. Since the complement cascade attacks the red blood cells throughout the circulatory system, the hemolysis is considered an*intravascular* hemolytic anemia.

aHUS is a chronic, ultra-rare disease characterized by thrombotic microangiopathy (TMA), the formation of blood clots in small blood vessels throughout the body, causing a reduction in platelet count (thrombocytopenia) and life-threatening damage to the kidney, brain, heart and other vital organs. Approximately 60 percent of patients with aHUS require dialysis, a kidney transplant or die within a year of diagnosis, despite currently available care. The majority of patients with aHUS who receive a kidney transplant experience severe complications of the disease, and more than 90 percent of these patients experience failure of the donor kidney. aHUS is caused by uncontrolled activation of the complement system. When naturally occurring

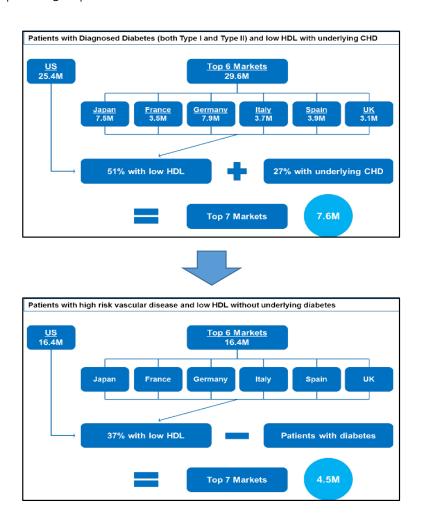


complement inhibitors are absent or do not function normally, the complement system becomes chronically uncontrolled, causing ongoing inflammation and blood clots in vital organs in patients with aHUS, uncontrolled complement activation results in an ongoing risk of sudden and catastrophic life-threatening complications. Recent publications of BET inhibition and BRD4 effects in additional orphan diseases such as neurofibramotis (NR), (Patel et al. Cell, 2014), exemplifies additional important research into the potential of epigenetics and BET inhibition for a variety of orphan diseases. If the Company moves successfully into any of these orphan areas would illustrate a positive value milestone for RVX's BET technology lead.



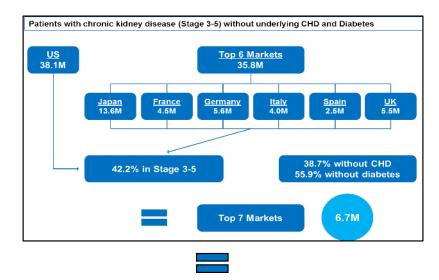
Valuation Apabetalone: Blockbuster potential

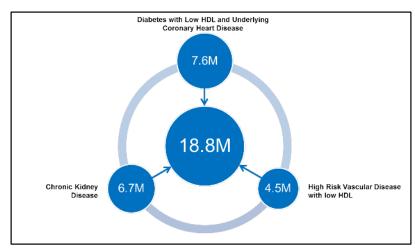
Apabetalone is targeting specific patients with high residual risk for increased MACE: patients with low HDL and Diabetes and CKD. This group of patients represents a very significant patient population of approximately 18 million patients in the top seven markets. Below are patient segmentation charts that outline the flow of these patients from the overall diabetes, high risk vascular and CKD patient groups.











Source: RVX iInternal projections based AHA 2015 statistics, 2014 IDF Atlas, 2013 US RDS CKD Report, patient population studies

The total target patient population of 18.8 million patients eligible for RVX-208 treatment represents a very significantly group of residual risk patients. Detailed notes of patient segment modeling are contained within the appendix.



Current Unmet Need in Diabetes: Apabetalone Value Proposition

Diabetes therapy for the past several decades has been developed around lowering glucose and hb1AC. Below is a detailed table highlighting this approach does little to reduce large vessel disease, namely MACE in patients with diabetes. Resverlogix intends to test this hypothesis for risk reduction in these patients coupled with CKD and other high risk vascular patients such as PAD and stroke, with apabetalone therapy.





Study	Population	Size	Findings
UK Primary Retrospective Study <i>Maru et al 2005</i>	Newly Diagnosed Diabetes patients	25,690	Use of metformin, insulin & SU therapy illustrates increased HF CVD risk
ADVANCE Patel et al 2008	Diabetic patients worldwide	11,140	No significant reduction in cardiovascular outcomes with intensive glycemic control
ACCORD Ginsberg et al 2008	History of CVD event or high risk for CVD event	10,251	Intensive glucose lowering significantly increases risk of cardiovascular (HR 1.35; 95%CI) and all-cause mortality (HR 1.22; 95%CI) compared with standard therapy
VADT Duckworth et al 2009	Veterans	1,791	No significant reduction in cardiovascular outcomes with intensive glycemic control
EXAMINE White et al 2013	Diabetics with ACS	5,380	No increase or benefit on MACE
SAVOR – TIMI 53 Scirica et al 2013	Diabetes with CVD	16,492	No increase or decrease in MACE but increase in HF hospitalization
DPP-4 Meta Analysis Wu et al 2014	Diabetic patients worldwide	55,141	No CVD harm or benefit and significant increase in heart failure outcomes

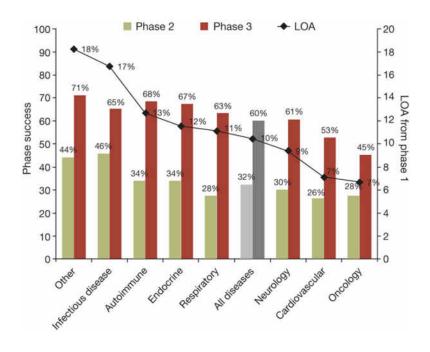
A risk reduction of MACE in this important patient group would represent an important breakthrough for diabetes and CKD globally. CKD patients with stage 3 are estimated to be approximately 15% of diabetes patients while PAD and stroke would account for an additional 10%. Key assumption modeling takes this into account for patient segmentation.

Key Value Assumptions

We have increased our value on Apabetalone, and thereby Resverlogix as a whole from CAD 500 million to CAD 900 million or CAD 8.50 per share. The increase in valuation is based on the commencement of the Phase III trial BETonMACE as well as the start of the Orphan Disease Program for some form or orphan disease in a risk-adjusted net present value analysis of income



from RVX-208. RVX-208 clearly has blockbuster potential. We choose not to value the company's total technology platform and potential additional indications for apabetalone. We feel that potential value of its platform and additional indications offers an additional upside potential. With the commencement of a large Phase III clinical trial we have increased the probability of success to 58% from 54%. The success rate is based on an independent survey executed by Nature Biotechnology in 2014¹. See also the graph below.



Source: Nature Biotechnology, 2014

As noted earlier we believe that with a successful Phase III BETonMACE trial, efficient NNT to reduce MACE events, and considering the market potential for RVX-208 the upside pipeline potential for Resverlogix should be in line with earlier reported agents such as CETP with bull case model reporting up to USD 10 Billion in revenue potential, as mentioned in the Deutsche Bank 2012 Report.

¹ Clinical development success rates for investigational drugs, Nature Biotechnology 32 40-51 (2014)



We expect an approval of apabetalone in the US in 2020 as well as approval in the EU and Japan. We ascribe CAD 7.50 per share to apabetalone for high risk CVD, Diabetes mellitus and CKD based on a risk-adjusted NPV analysis of estimated its net income in the next 10 years, assuming approval and a 2020 launch. An approval of apabetalone for any Orphan Diseases expected to be up to two years earlier provided positive data. We ascribe CAD 1.00 per share to apabetalone and RVX's development pipeline for Orphan drug market potential. We subscribe an estimated peak market share of 40% in any indication.

Currently, one of the most expensive approved therapy for Orphan disease is in PNH. Soliris of US based company Alexion was approved by the FDA in 2007 for the treatment of PNH. Soliris blocks the complement system that destroys red blood cells in PNH patients. The blocking of the complement system (as part of the immune system) increases the risk of infections. Therefore patients that receive Soliris are required to get vaccinated with a meningococcal vaccine. According to the international PNH Registry, Soliris is only received by 25-30% of PNH patients due to its extremely high price of USD 440,000 per year. Sales of Soliris in 2015 amounted to USD 2.6 billion. We therefore agree that with apabetalone's reported modulation of complement biology this approach could potentially be a successful treatment for PNH and filling a large unmet medical need for patients with this rare disease. We would estimate a 20-25% cost-of-goods and a 20-25% discount rate.

We make use of a probability adjusted NPV, which is dependent on the success rate and development stage of apabetalone. The total market potential for apabetalone is large and based on the potential number of patients in the US, EU and Japan. Any future expansion into this or other orphan markets would add significant value to the BET hypothesis for high risk diseases.



SWOT

Strengths

Strong patent position with its lead compound RVX-208

Significant scarcity value – 8-9 lead in BET inhibition (no known BET competitor)

Strong management and human therapy development expertise

Novel and highly differentiated approach to impacting residual risk in diabetes and CKD

Vast expertise in CVD, diabetes and neurodegenerative disease

Sufficient access to finance its clinical program with RVX-208

Weaknesses

Ongoing liver safety analysis for new BET therapeutic class

Operating losses cumulating year-on-year

Delay pipeline development RVX-208

Opportunities

Profitable Partnerships and license agreements with large pharmaceuticals

Blockbuster potential RVX-208

Favourable early pharmacoeconomics modelling with RVX-208

Threats

Uncertainty about the outcome of clinical trial of the products

Higher level of expenditure than budgeted

Potential ongoing clinical trials needed in CVD



Patent Position

Resverlogix devotes significant resources to ensure protection of ideas and inventions related to the core areas of its business. The Company's strategy is to build a strong patent portfolio around its core technology that is important to the development of leading edge medicines. Resverlogix' strategy is to be the first to identify, isolate, and patent therapeutic agents with commercial importance, as well as, to seek out and license intellectual property believed to be useful in connection with potential products, and to control public disclosures. Resverlogix' intellectual property portfolio covers compositions, methods and treatments for a number of indications related to its core technology. The company owns and/or has rights to more than 10 patent families, comprising more than 30 issued patents, including nine in the US, as well as more than 60 pending patent applications in different jurisdictions. The intellectual property around apabetalone includes claims covering composition, method of use, manufacturing, and combinations.

Patent Overview Apabetalone/RVX-208

Patent Number	Title	Expiry Date
US 8,053,440 (Composition claims)	Compounds for the prevention and treatment of cardiovascular disease	August 2030
US 8,889,698 (Use claims)	Compounds for the prevention and treatment of cardiovascular disease	September 2031
US 8,114,995 (Manufacturing)	Process for high throughput DNA methylation analysis	April 2030
US 8,884,049 (Manufacturing)	Highly sensitive method for the detection of cytosine methylation patterns	October 2033
China No. 2007 8 0052349.8	Compounds for the Prevention and Treatment of Cardiovascular Disease	February 2027
China No. ZL 2009 8 0106586.7	Methods of Preparing Quinazolinone Derivatives	June 2029



Financials

For the first nine months till 31 January 2016, Resverlogix reported a net loss of USD 8.9 million compared to a net loss of USD 1.6 million in the same period last year. During the nine months ended January 31, 2016, gross R&D expenditures totalled USD 9.4 million (2015: USD 2.4 million).

Total cash at the end of the period amounted to USD 30 million (CAD million). The company successfully entered into an equity investment and a license of RVX-208 for all indications with China based Shenzhen Hepalink Pharmaceutical Co. for China, Hong Kong, Taiwan and Macau. Under the terms of the transaction, Hepalink subscribed for 13,270,000 Resverlogix common shares and 1,000,000 common share purchase warrants, for aggregate proceeds of approximately CAD 35 million, or CAD 2.67 per unit. Each warrant is exercisable into one common share at CAD 2.67 per share for a period of five years. After giving effect to the transaction, Hepalink will hold approximately 12.69% of Resverlogix's common shares. The common shares and warrants issued to Hepalink will be subject to a three year lock-up period. Also, as previously announced, effective April 4, 2016, Mr. Shawn Lu of Hepalink USA Inc. was appointed to the board of directors of the Company.

In addition, to the Hepalink transaction, Eastern Capital Limited ("Eastern") 5,600,000 common shares and 422,005 common share purchase warrants for aggregate consideration of approximately CAD 15 million, or CAD 2.67 per unit. Therefore, total equity investment by Hepalink and Eastern exceeds CAD 50 million. Eastern holds 14,965,307 shares of Resverlogix which represents 17.46% of the 85,699,287 common shares outstanding before giving effect to any outstanding warrants. Eastern currently holds 7,578,232 common share purchase warrants of Resverlogix. Assuming all warrants are exercised before giving effect to the transaction, Eastern will hold approximately 24.17% of the common shares outstanding. After giving effect to the transaction, assuming all warrants held by Eastern are exercised, Eastern



would hold 28,565,544 common shares of Resverlogix representing 25.38% of Resverlogix's issued and outstanding common shares.

Resverlogix intends to use the net proceeds to fund its:

- research and development activities (alone or through strategic collaboration) including clinical development (including clinical trials and the clinical development of our product candidates), non-clinical development, research, discovery, chemistry and regulatory costs;
- repayment of outstanding indebtedness and/or payment of interest thereon;
- general and administrative expenses, capital expenditures, working capital needs and other general corporate purposes.

Profit & Loss Statement (USD mln)

For nine months ended	Jan 31 2016	Jan 31 2015A
Revenues	-	-
R&D Costs	2.458	9.384
Tax Credits	(0.034)	(0.018)
General & administrative expenses	3.035	3.055
Finance costs (income)	(2.344)	(7.062)
Gain on distribution	(13.650)	()
Loss (income) before income taxes	10.041	(0.517)
Income Taxes	(0.005)	0.043
Net Loss (Income)	10.036	(1.626)



Consolidated statement of cash flows

	Jan 31 2016A (9 months)	Jan 31 2015A (9 months)
Cash flow from operating activities	(17.438)	(7.724)
Cash flow from investing activities	(0.491)	(0.811)
Cash flow from financing activities	35.186	27.717
Cash and cash equivalents at beginning of the period	16.211	0.590
Net change in cash and cash equivalents	13.716	16.423
Cash and cash equivalents at the end of the period	29.927	17.013

Consolidated Balance Sheet

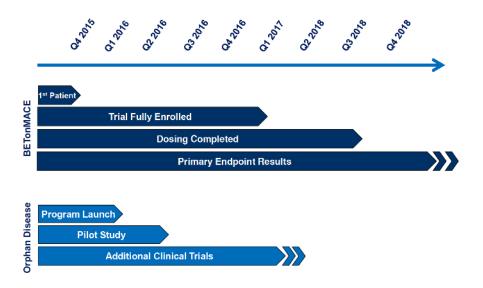
	Jan 31 2016A	Jan 31 2015A
Cash and cash equivalents	29.927	16.211
Current Assets	38.625	18.749
Non Current Assets	2.856	2.407
Total Assets	41.481	21.156
Current Liabilities	11.994	22.346
Total Liabilities	88.570	94.883
Total Equity	(47.089)	(73.727)



Upcoming Milestones & Catalysts

For 2016, a number of important catalysts for the share price are expected. We believe that the company will be able to sign additional license agreements comparable with the agreement made with Shenzhen Hepalink Pharmaceutical Co. in China and The Territories. Any additional partner or license agreements would provide the company with an early revenue stream and an important source of capital to finance its ongoing and potential expanded clinical program with apabetalone.

Another source of capital would be an IPO on NASDAQ to increase its visibility to the investment community and thereby increase its share price.



Next to these potential catalysts, important milestones will be expected from its ongoing BETonMACE clinical trial and the start of clinical trials for apabetalone in PNH or another Orphan indication.



Glossary

Acute Coronary Syndrome ("ACS")

a term used for any condition brought on by the sudden reduced blood flow to the heart. Acute coronary syndromes may include a heart attack, unstable angina. The first sign of acute coronary syndrome can be sudden stopping of your heart (cardiac arrest). Acute coronary syndrome is often diagnosed in an emergency room or hospital.

Acute Phase Response Cascade

a series of systemic events that occur within hours of an inflammatory stimulus. The most important component of this response comprises the acute phase proteins. Acute phase response takes place in response to a variety of stimuli including bacterial infection, trauma and myocardial infarction.

Alpha1 HDL

mature lipid-rich particles that are involved in reverse cholesterol transport whereby cholesterol is removed from cell membranes to the liver for excretion.

Apabetalone

generic name of RVX-208

ApoA-I Therapeutic Field

the prevention, treatment or mitigation of any disease via the administration of a Pharmaceutical Agent that results in therapeutic relevant elevation in the plasma levels of ApoA-I that in a predictable model of ApoA-I expression, using either a human or nonhuman primate model, the Pharmaceutical Agent is demonstrated to have at least a seven percent (7%) increase in humans and fifty percent (50%) increase in nonhuman primates in the ApoA-1 plasma level in two consecutive weeks of treatment using less than 30 milligrams – b.i.d. (60 milligrams per day) of the Pharmaceutical Agent per kilogram of the weight of the subject;

Apolipoprotein

the protein combined with a lipid to form a lipoprotein, a

component of HDL and LDL.

ApoA-I

the apolipoprotein component of the HDL particle.



Atherosclerosis a disease in which the deposition of lipids and plaque in

arteries

results in the hardening and decrease of arterial lumen size.

the deposit or accumulation of lipid containing plaques in the Atherosclerotic Plaque

arterial wall(also known as atheroma).

BET proteins Bromodomain and ExtraTerminal domain proteins that contain

> bromodomains, which regulate gene transcription through binding to acetylated lysines within the histones bound to

DNA.

Bioavailability the degree and rate at which a drug is absorbed into a living

system or is made available at the site of activity after

administration.

Biopharmaceuticals a medical drug developed by biotechnology to improve human

or animal health.

a series of events that culminate in the formation of a bloodclot Coagulation Cascade

> and its subsequent breakdown. This process is controlled by a signaling cascade consisting of coagulation factors which

interact and activate each other.

Complement Cascade the complement system contains a network of tightly

> regulated proteins that together are a key part of the innate immune system response. The principal roles of complement include defending against invading pathogens, bridging innate and adaptive immunity, eliminating immune complexes and the

products of inflammatory injury.

Coronary artery disease ("CAD") the most common type of heart disease. It is the leading cause

> of death in the United States in both men and women. CAD occurs when arteries that supply blood to heart muscle become hardened and narrowed. This is due to the buildup of cholesterol and other material, called plaque, on their inner

walls.



Cardiovascular Disease (CVD)

a group of diseases of the heart and blood vessels

Cholesterol

a fatty molecule essential for normal body functions, including the production of hormones and bile acids; it is also an important component of a cell membrane.

Contract Research Organization

"CRO" an organization (commercial, academic or other), contracted by the sponsor to conduct research or development activities.

Chromatin

the combination of DNA and proteins that make up the contents of the nucleus of a cell. The primary functions of chromatin are: to package DNA into a smaller volume to fit in the cell, to strengthen the DNA to allow mitosis and meiosis and prevent DNA damage, and to control gene expression and DNA replication. The primary protein components of chromatin are histones that compact the DNA.

Clinical Trial/Study

a research study in human subjects to evaluate a new drug, medical device, biologic or other intervention under a strictly controlled scientific setting.

Chronic Kidney Disease ("CKD")

a progressive loss in renal function over a period of months or years, also known as chronic renal disease (CRD). Chronic kidney disease is also associated with other chronic diseases such as diabetes and or cardiovascular disease. Profession guidelines classify the severity of chronic kidney disease in five stages, with stage 1 being the mildest and usually causing few symptoms and stage 5 being a severe illness with poor life expectancy if untreated. Stage 5 CKD is often called end stage renal disease.

Deoxyribonucleic Acid ("DNA")

the material inside the nucleus of cells that carries genetic information.

Diabetes Mellitus

the most common metabolic disease and currently is a worldwide epidemic fueled by the wave of modernization swiping across much of the developing countries. There are two types of diabetes, Type-1 and Type-2. The difference



between these two types of diabetes is that there is an absence of insulin (Type-1) or a deficiency in the amount of insulin (Type-

2). While Type-1 affects less people and mostly younger individuals, Type-2 most commonly accounts for roughly 90% of the cases. The cause of Type-1 Diabetes is believed to lie in defects within the immune system. In the pathogenesis of Type-2, there is direct connection between dietary habits, sedentary life styles and obesity. One of the most feared consequences of either form DM is that it is one of many major risk factors leading to the development of CVD, the number one cause of premature death in modern societies.

Enzyme

a protein that acts as a catalyst in mediating and accelerating a specific chemical reaction.

Epigenetics

the study of heritable traits not caused by a change in the genetic code. These are typically mediated through secondary modifications to the DNA and its bound proteins, which regulate expression of genes contained within the DNA.

Food and Drug Administration

the United States governmental agency responsible for the approval, manufacture, usage and sale of food, human diagnostics and therapeutic products.

Gene

a sequence of DNA encoding a protein.

Good Manufacturing Practice (GMP)

the international set of regulations, codes and guidelines for the manufacture of drugs, medical devices, diagnostics and food products.

High-density Lipoprotein (HDL)

a complex of lipids and proteins (ApoA-I) that function in the transport of cholesterol away from the tissues to the liver and is associated with a decreased risk of atherosclerosis and coronary heart disease (also known as "good cholesterol").

Histones

highly alkaline proteins found in eukaryotic cell nuclei that package and order the DNA into structural units called nucleosomes. Histones are the chief protein components



of chromatin. acting as spools around which DNA winds, and play role in gene regulation.

IND-Enabling Studies

is a toxicology package, including general acute and repeated-dose toxicity and genotoxicity studies, and safety pharmacology studies, conducted under GLP and in accordance with the International Conference of Harmonization guideline (M3(R1)) to support the filing of an IND application (21.CFR.312). Initiation of the toxicology package will occur when protocols have been written and a contract laboratory has been contracted to conduct the studies.

Investigational New Drug (IND)

the application submitted to the FDA prior to being tested in humans in clinical trials.

Low-density Lipoprotein (LDL)

a complex of lipids and proteins (ApoB) that function by transporting cholesterol to the tissues, in particular the arteries, and is associated with an increased risk of atherosclerosis and coronary heart disease (also know as "bad cholesterol").

Lipids

fatty substances, including cholesterol and triglycerides that are present in cell membranes and body tissues.

Lipoproteins

a complex of proteins and lipids that are the principal means by which fat and cholesterol is transported in the blood; major lipoproteins are low-density lipoproteins (LDL) and high-density lipoproteins (HDL).

MACE

Major Adverse Cardiovascular Events a commonly used end point for cardiovascular research. MACE is a composite of clinical events that usually are measured in clinical trials of cardiovascular patients. It may include a variety of end points such as death, myocardial infarction (heart attack), stroke, worsening angina, hospitalization for heart disease and

New Drug Application ("NDA")

the documentation submitted to the FDA, Health Canada or other local regulatory authorities to obtain approval to market a new drug.



Pharmacodynamics the study of the biological actions of a drug in the body,

specifically the relationship between how much drug is present

and its effects.

Pharmacoeconomics the scientific discipline that compares the value of one

> pharmaceutical drug or drug therapy to another. It is a subdiscipline of Health economics. A pharmacoeconomic study evaluates the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, efficacy or enhanced

quality of life) of a pharmaceutical product.

Pharmacokinetics the study of how a drug is absorbed, distributed, metabolized

and eliminated (ADME) by the body over time.

Pharmacology the study of pharmacological agents and their origin, nature,

properties and effects on living organisms.

Phase 1 Clinical Trial a smaller scale trial, where a drug is first tested on a small

number of healthy human volunteers to evaluate the drug's

safety, schedule, dose, pharmacokinetics and

pharmacodynamics (an approximate 1-2 year time trial).

Phase 2 Clinical Trial a study in patients (not healthy volunteers) with the main

objective to establish a safe and efficacious dose for phase 3

clinical trials.

Phase 3 Clinical Trial a study or studies in a defined patient population designed to

> demonstrate effect to support use for a special indication, for example treatment of patients with previous coronary artery disease to prevent the occurrence of a major adverse coronary.

Phosphorylation the process by which an phosphate functional group is

transferred onto a molecule.

Preclinical Studies the studies conducted in animals to evaluate the toxic effects,

> pharmacokinetics and metabolism of a drug to provide evidence for safety, efficacy and bioavailability of the drug prior

to its administration to humans in clinical studies.



PCSK9 Proprotein convertase subtilisin/kexin type 9 is an enzyme that

has medical significance because it functions in cholesterol homeostasis. PCSK9 binds to a domain of the LDL receptor, inducing degradation. Reduced levels of the LDL receptor result in decreased metabolism of LDL, and thus increased LDL

levels, a known risk factor for CVD.

Reader, writer, eraser proteins that bind to histone modifications and alter gene

activity and protein production (reader); enzymes that add histone modifications (writer); enzymes that remove histone

modifications (eraser).

RVX-208 Resverlogix' drug candidate for the treatment of

atherosclerosis in patients at high risk for cardiovascular

disease.

Statin a class of drugs that block cholesterol production in the body

by inhibiting an enzyme called HMG-CoA reductase.

Toxicology the study of the harmful effects of substances in the body,

including the level of toxicity, the mechanism by which toxicity

occurs and how it can be controlled.



Appendix

Diabetes with Low HDL and Underlying Coronary Heart Disease Market Assessment- Notes and Assumptions

- Note 1 Recent estimates from the International Diabetes Federation, published in the IDF Diabetes Atlas, show the prevalence of diagnosed diabetes (both Type I and Type II) in males and females aged from 20-79. These estimates do not include patients with undiagnosed diabetes and impaired glucose tolerance. The prevalence from the United States is entered as the "US Patient Population".
- Note 2 Resverlogix includes France, Germany, Italy, Japan, Spain and the United Kingdom as the Top 6 markets outside of the US. Recent estimates from the International Diabetes Federation, published in the IDF Diabetes Atlas, published in the IDF Diabetes Atlas, show the prevalence of diagnosed diabetes (both Type I and Type II) in males and females aged from 20-79. These estimates do not include patients with undiagnosed diabetes and impaired glucose tolerance. The prevalence from each country is totaled to determine the "Top 6 Markets Patient Population".
- Note 3 According to the International Diabetes Federation, published in the IDF Diabetes Atlas, there were 382 million people living with diabetes worldwide in 2013.

 It is projected that, that number will increase to 592 million by 2035. Assuming a consistent growth rate during that time period, the prevalence of diabetes will increase by 2.01% per annum on average worldwide.
- Note 4 Resverlogix estimates that the percentage of diabetes patients with low HDL is 51.3%. The following references were used to determine the percentage of diabetes patients with low HDL. In a population of patients with type 2 diabetes (n = 7,692) in 12 eastern Massachusetts outpatient practices nearly half (49.5%) of patients had low HDL cholesterol (<40 mg/dl for men, <50 mg/dl for women). In a population of patients receiving treatment for dyslipidemia under the care of specialist physicians in 11 European countries (Pan-European Survey) (n= 8,545), where 45.2% of the patients had type II diabetes, the prevalence of low HDL (<40 mg/dl for men, <50 mg/dl for women) was 33% in men and 40% in women. The average prevalence of low HDL (when taking into account the weighting of each group) is 35%. In two randomized, placebo-controlled studies, FIELD (n=9,795) and ACCORD (n=5,518), in which the inclusion criteria was type II diabetes, 59.0% had low HDL (<40 mg/dl for men, <50 mg/dl for women) and 65.2% had low HDL (≤40 mg/dL), respectively. A weighted average was used to determine the above mentioned RVX estimate of the percentage of diabetes patients with low HDL.
- Note 5 Resverlogix estimates that the percentage of diabetes patients with underlying coronary heart disease (CHD) is 26.9%. The following references were used to determine the percentage of diabetes patients with underlying coronary heart disease. In a population of patients with type 2 diabetes (n = 7,692) in 12 eastern Massachusetts outpatient practices 26.7% of patients were listed as having CVD clinical characteristics. In two randomized, placebo-controlled studies, FIELD (n=9,795) and ACCORD (n=5,518), in which the inclusion criteria was type II diabetes, 21.8% had previous CVD clinical characteristics and 36.5% had experienced a previous CVD event, respectively. A weighted average was used to determine the above mentioned RVX estimate of the percentage of diabetes patients with underlying CHD.
- Note 6 The projections do not include the patient populations of Brazil, Russia, India and China (BRIC) or Middle East and North Africa (MENA). The percentage of patients in these markets that can afford the therapeutic is undeterminable; however Resverlogix estimates that this number represents a small fraction of the total patient population.



High Risk Vascular Disease with low HDL- Excl. Diabetes Market Assessment- Notes and Assumptions

- Note 1 According to the Heart Disease and Stroke Statistics- 2014 Update (AHA Report), the prevalence of patients who have suffered an MI in the US is 7.6M and the prevalence of patients diagnosed with angina pectoris in the US is 7.8M. The combined prevalence of patients with CHD is 15.4M.
- Note 2 Management's internal projections extrapolate the market size for the Top 6 Markets (Japan and 5EU) to be equivalent to that of the US.
- **Note 3** BioMedTracker uses an annual average growth rate (AAGR) of 1.23% for the 7 major markets for the incidence of atherosclerosis. Management annual target population growth rate is 1.23%.
- Note 4 RVX-208 is currently being developed for the indication of secondary prevention of major adverse cardiovascular events (MACE) in patients with high risk vascular disease (including diabetes) and low HDL. In order to determine the percentage of patients in this target market that have low levels of HDL, two populations were examined. The first was the general adult population. According to the Total and High-density Lipoprotein Cholesterol in Adults: National Health and Nutrition Examination Survey, 2009–2010, 21.3% of adults had low HDL (below 40 mg/dL). The second was patients who have previously experienced a MACE event. The following references were used to determine the percentage of coronary heart disease patients with low HDL. 55.8% of patients who presented with ACS have HDL-C below 40 mg/dL. 52.6% of NSTEMI ACS patients had HDL-C below 40 mg/dL (E). 49.7% of NSTEMI patients aged >65 years had HDL-C below 40 mg/dL. Based on these studies, the average percentage of ACS and coronary heart disease patients with low HDL-C is 52.7%. The rationale for using both the general population and patients who have experienced a MACE lies in the notion that once a patient recovers from a MACE, they will still be receiving chronic treatment of RVX-208, and thus their HDL levels may be more reflective of the general population. Using both the adherence from the general population and patients who have experienced a cardiovascular event, management calculated the average of the two patients populations. Management estimated prevalence of low HDL in high risk vascular disease patients is 37.0%.
- Note 5 In the diabetes prevalence projection model, the patient prevalence of diabetes with low HDL and underlying cardiovascular disease in the US is projected. These patients are subtracted from these estimates to eliminate overlap between the patient groups.
- Note 6 The projections do not include the patient populations of Brazil, Russia, India and China (BRIC) or Middle East and North Africa (MENA). The percentage of patients in these markets that can afford the therapeutic is undeterminable; however Resverlogix estimates that this number represents a small fraction of the total patient population.



Chronic Kidney Disease- Excl. CHD and Diabetes Market Assessment- Notes and Assumptions

- Note 1 Recent estimates from the National Center for Chronic Disease Prevention and Health Promotion Division of Diabetes Translation revealed that 16.0% of US adults aged 20 years and older have CKD. The U.S. Census Bureau estimated that the US population in 2013 was 316,128,839 and that 71.8% of the total population are >20 years of age. RVX estimates that the total number of patients with CKD in the US is approximately 36M patients.
- Resverlogix includes France, Germany, Italy, Japan, Spain and the United Kingdom as the Top 6 markets outside of the US. The prevalence of chronic kidney disease in each country was reviewed in a systematic review in 2008. The prevalence of CKD in the UK was estimated in the NEOERICA Project in 2007. France and Germany did not have analyses performed in the study and thus the prevalence rate of the 3 other european countries, Italy, Spain and the UK was averaged and used as an estimated prevalence. The populations for each country were taken from the World Bank database. RVX estimate of approximately 34M CKD patients in the top 6 markets excluding the US is consistent with the notion that doubling the US patient population reflects a rough estimate of the other top 6 markets.
- **Note 3** According to the US Census Bureau, the growth rate of the general american population between 2010 and 2013 was 2.4%. RVX estimates a similar growth rate for the top 6 markets.
- Note 4 According to the National Kidney Foundation, 39.4% of CKD patients are at stage 3, 1.83% are at stage 4 and 0.92% are at stage 5. These numbers were obtained from the NHANES III study which illustrated the prevalence of each stage of CKD in the general population. These rates were adapted to the prevalence of each stage within the CKD population by RVX.
- Note 5 According to the USRDS Annual Data Report, the Atlas of Chronic Kidney Disease in the United States, 38.7% of CKD patients did not have any type of underlying cardiovascular disease (congestive heart failure, acute myocardial infarction and cerebrovascular disease). In the same report, the prevalence of various risk factors in the NHANES population is illustrated. In the CKD patients, 40.1% had diabetes, thus indicating that 59.9% did not have the underlying comorbidity. Similar rates in the top 6 markets are estimated by RVX.
- Note 6 The projections do not include the patient populations of Brazil, Russia, India and China (BRIC) or Middle East and North Africa (MENA). The percentage of patients in these markets that can afford the therapeutic is undeterminable, however Resverlogix estimates that this number represents a small fraction of the total patient population.



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Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.

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