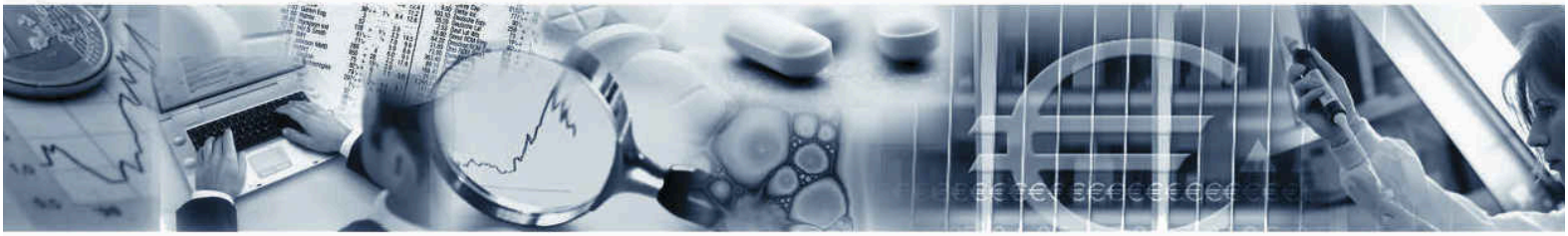

Update Report

Resverlogix

Debt Removal Reduces Risk Profile

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Date: 16 January 2018

Name:	**Resverlogix Corp.**
Country:	**Canada**
Price:	**CAD 2.00**
ISIN Code:	**CA76128M1086**
Reuters Code:	**RVX.TO**
Market Cap (CAD m):	**350.0**
EV (CAD m):	**340.0**
Cash & cash eq. (CAD m):	**10.0*)**
Shares outstanding (m):	**175.0**
Volume:	**64,842**
Free float:	**45%**
52-week Range:	**1.23-2.47**

*** this includes the CAD 87m private placement with Shenzhen Hepalink**

USD m (ended 04/30)	2014/15A	2015/16A	2016/17A
Total Revenues	-	-	-
Net (Loss)/Profit	(18.323)	(19.715)	(46.210)
Net loss per share (pence)	(0.22)	(0.20)	(0.44)
R&D costs	4.185	15.681	29.875
Cash increase/(decrease)	15.621	11.898	(26.754)
Cash and marketable sec.	16.211	28.109	1.355

Contents

Executive Summary

- Resverlogix (RVX.TO) is a clinical stage cardiovascular company with an epigenetic platform technology that modulates protein production. The company is developing apabetalone (RVX-208), a first-in-class, small molecule that is a selective BET (bromodomain and extra-terminal) inhibitor. BET bromodomain inhibition is an epigenetic mechanism that can regulate disease-causing genes. Apabetalone is the first and only therapeutic in the BET inhibitor class that preferentially targets the second bromodomain (BD2) of BET protein 4, called BRD4. 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 CVD patients with diabetes and CKD. It also is expected to offer substantial benefits for patients with end-stage renal disease treated with hemodialysis, neurodegenerative diseases such as dementia, Fabry disease, peripheral artery disease and other orphan diseases, while maintaining a well described safety profile. To date the company holds a nine year lead in the field of epigenetic small molecules for vascular disease risk reduction.

- Resverlogix has developed an epigenetic drug development platform that has the potential to impact multiple diseases including atherosclerosis, diabetes, autoimmune diseases, cancer, and neurodegenerative diseases. This platform targets BET proteins that play a vital role in the epigenetic regulation of transcription of particular genes. The renewed interest in epigenetics has led to new findings about the relationship between epigenetic changes and a host of disorders including various cancers, mental retardation associated disorders, immune disorders, neuropsychiatric disorders and pediatric disorders.

- In October 2015, Resverlogix initiated a Phase III clinical trial "BETonMACE" with apabetalone in high-risk CVD patients with type 2 diabetes mellitus and low HDL. The primary endpoint is the time to first occurrence of MACE. Secondary endpoints such as renal function (eGFR) in CKD patients are also planned. The company received regulatory approval to open clinical investigator sites in all planned countries. Resverlogix has enrolled more than 2,100 of the planned 2,400 patients. An interim analysis is planned after 188 primary MACE events have

been adjudicated. Previously, Apabetalone (RVX-208) has been successfully tested in about 1,000 patients in various clinical studies (ASSERT, SUSTAIN and ASSURE). The company expects to initiate a Phase IIa kidney dialysis trial designed to evaluate biomarker changes and safety parameters in up to 30 patients with end-stage renal disease treated with hemodialysis.

- In the past few months, the company was successful to raise a total of CAD 97 million, of which CAD 87 million came from a private placement with its business partner Shenzhen Hepalink in China. The net proceeds were used to repay the company's CAD 68.8 million secured loan with the remainder to be used to fund R&D activities including its ongoing Phase III BETonMACE trial. End of October, Resverlogix announced that it entered into a Right of First Refusal Agreement with Hepalink USA in connection with the licensing of the right to develop pharmaceutical products containing RVX-208 in the US until April 15, 2019. Hepalink USA paid a CAD 8 million fee.

- **We have increased our valuation based on a lower discount rate and an increased LOA for apabetalone in high risk diabetes and CKD patients. With no outstanding long-term debt on its balance sheet, we feel that the risk profile of the company is reduced considerably. We believe that Resverlogix remains gravely undervalued at the current share price of CAD 2.00. We feel that the company's current total value should be CAD 2.5 billion, or CAD 14.75 per share. This represents a substantial upside from the current share price.**

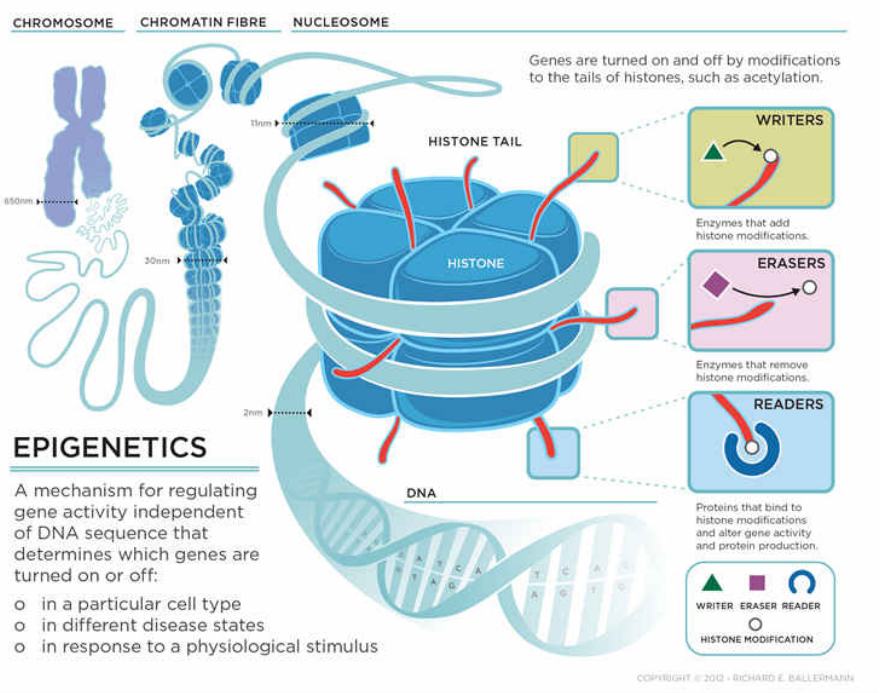
Company Profile & Technology

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. Apabetalone 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.

Resverlogix has developed an epigenetic drug development platform that has the potential to impact multiple diseases including atherosclerosis, diabetes, CKD, autoimmune diseases, cancer, and neurodegenerative diseases. This platform targets BET proteins that play a vital role in the epigenetic regulation of transcription of particular genes. BET proteins are often called 'readers' of the histone/chromatin structure.

Epigenetic Mechanism of Action



Source: Resverlogix, Richard E. Ballermann

Epigenetics and Apabetalone as First in Class BET Antagonist

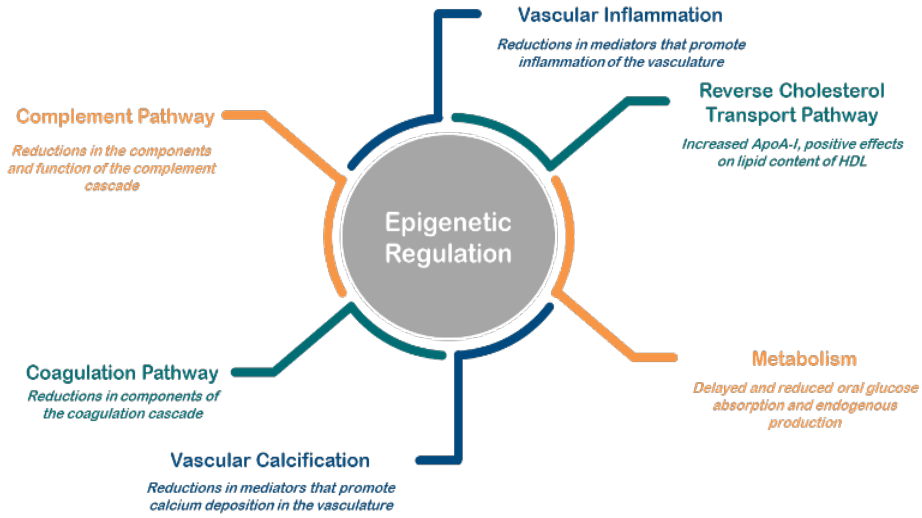
Apabetalone acts upon multiple pathways and genes that drive vascular risk such as: (i) reduction of key vascular inflammation markers, (ii) regulation of complement, coagulation and acute phase response cascades, known drivers in cardiovascular disease and MACE, (iii) enhancement of reverse cholesterol transport, and (iv) lowering of key markers of metabolic risk. Apabetalone is the first small molecule to act through a novel epigenetic mechanism that regulates gene transcription to regulate these biological pathways. Epigenetics is a new frontier in the search of

treatment of human diseases. Although genes are encoded within the DNA, the tight regulation of this information requires epigenetic mechanisms. To understand these mechanisms we begin by sharing that nuclear chromatin is comprised of DNA complexed with histones and other proteins. When histone proteins coat the DNA to form chromatin, it looks like beads on a string. Chromatin is a dynamic structure that may be open or closed. But for DNA to be transcribed the chromatin must be open. The transition from the close to open confirmation is mediated by the addition or removal of modifications such as phosphorylation, methylation or acetylation at specific amino acids within the histones. These processes are the writing and erasing part of the so-called epigenetic code.

Apabetalone does not write or erase but reads the acetylation of specific lysines in the histones found in actively transcribed regions of DNA. This is another key component of epigenetics. Apabetalone is an oral selective BET protein inhibitor. These proteins contain two small conserved regions called bromodomains. Each bromodomain has a pocket that combines to or read a specific acetylated lysine found at some n-terminus of some histones. When this interaction occurs, a different region at the BET protein can recruit other components important for controlling gene transcription. Thus, when a BET protein is anchored to chromatin via its chromodomain to an acetylated lysine, this complex recruits additional proteins that regulate transcription, which can lead to selective, increases and decreases in mRNA. Apabetalone binds to the same pocket of the bromodomain as the acetylated lysine of histones. And in so doing causes the BET protein to be released from chromatin thus altering transcription.

This action of apabetalone leads to an improvement of multiple pathways that play a role in vascular risk previously noted. Improvement in key risk markers such as: i) an increase of ApoA-1, the key building block of new functional HDL; ii) a reduction of alkaline phosphatase, a reported key risk factor for vascular calcification, and; iii) a reduction of vascular inflammation biomarkers including hsCRP, highlight the multifactorial approach that this new molecule has illustrated to date. Discovery of the molecular target of apabetalone has enabled Resverlogix to obtain a high-resolution structure of apabetalone bound to the bromodomain and to devise biochemical assays

that that will hasten the discovery of additional compounds. Potential new select BET inhibition compounds may provide attractive opportunities for potentially treating many additional diseases including neurodegenerative and orphan diseases.



Epigenetic gene regulation governed by BET proteins is at the core of many CVD pathological processes – Apabetalone regulates the expression of genes and restores the function of pathways underlying the pathogenesis of multiple diseases

Source: Resverlogix

Business Strategy & Partnerships

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 high risk renal diseases as well as rare and orphan diseases, provides Resverlogix with important options for further value creation. Renal function and orphan clinical trials are usually much smaller and shorter than traditional larger CVD trials. Expansion into these high risk markets provides the company with additional value potential by commercializing the molecule more quickly and also establishing a broader

indication base for its BET inhibition technology platform. We expect that Resverlogix will be able to make additional regional licensing deals that will give the company more early revenue possibilities and monetize the asset in a variety of markets. Deals in areas with high unmet medical need such as CVD, 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.

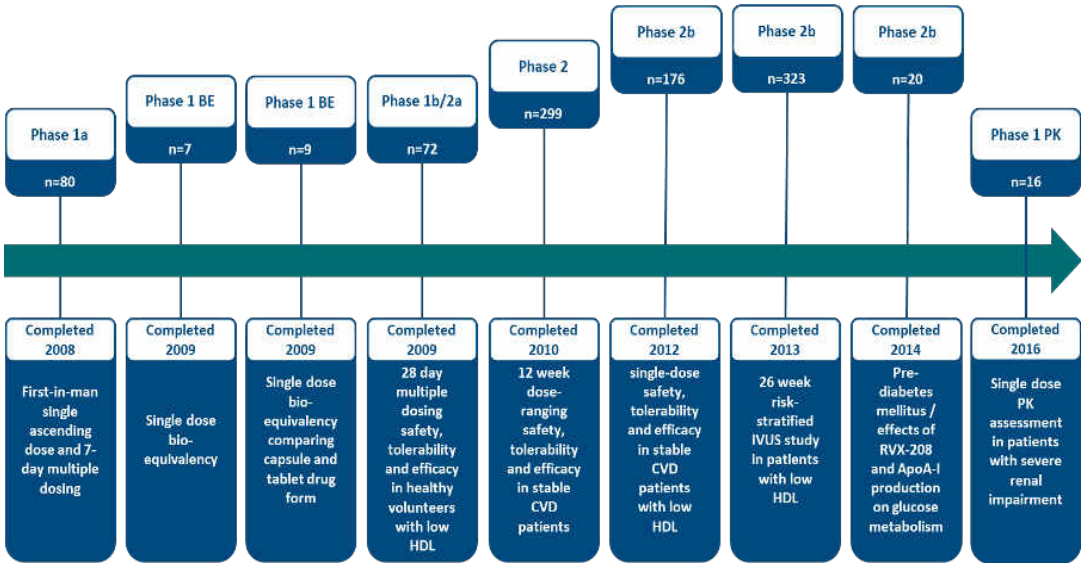
Partnership Shenzhen Hepalink Pharmaceutical Co., Ltd

In April 2015, Resverlogix and Shenzhen Hepalink Pharmaceutical Co., Ltd., a leading global life science company, entered into one of the largest strategic partnerships for a single molecule for high-risk cardiovascular disease patients including those with diabetes and CKD. A definitive agreement was completed in July 2015 where Resverlogix is eligible to receive sales-based milestone payments from Hepalink, each ranging from USD 5 million to USD 90 million and Royalties based on net sales. In addition, Hepalink will pay Resverlogix a royalty based on net sales. Total sales based milestones and royalty payments have an estimated potential in excess of USD 400 million. In October 2017, Resverlogix entered into a Right of First Refusal Agreement with Hepalink USA Inc. Under the Agreement, Hepalink USA was granted a right of first refusal in connection with the licensing of the right to develop, manufacture and commercialize pharmaceutical products containing apabetalone in the United States until April 15, 2019. Hepalink USA paid CAD 8 million to Resverlogix in consideration for the right of first refusal granted. In December 2017, Resverlogix closed a CAD 87 million private placement with Shenzhen Hepalink Pharmaceutical Co., Ltd. The offering was primarily be used to repay the Company's CAD 68.8 million secured loan which was repaid in December and fund R&D activities.

Pipeline: Focus on Apabetalone

Resverlogix has performed numerous clinical trials to date. It has learned from these trials to target patients with high risk vascular disease defined as those with CVD with a diabetes and low HDL aco-morbidity. Further patient targeting will be performed by evalution of a CKD subgroup and congitive subgroup in the current Phase III BETonMACE trial. Apabetalone has been tested in over 1,800 patients in 19 countries, and clinical experience with apabetalone has demonstrated that BET inhibitors can be both safe and effective. Apabetalone is the first select BET bromodomain inhibitor in clinical trials for high risk vascular diseases. New compounds arising from Resverlogix's epigenetic drug development platform 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.

Clinical Trial Overview of Apabetalone



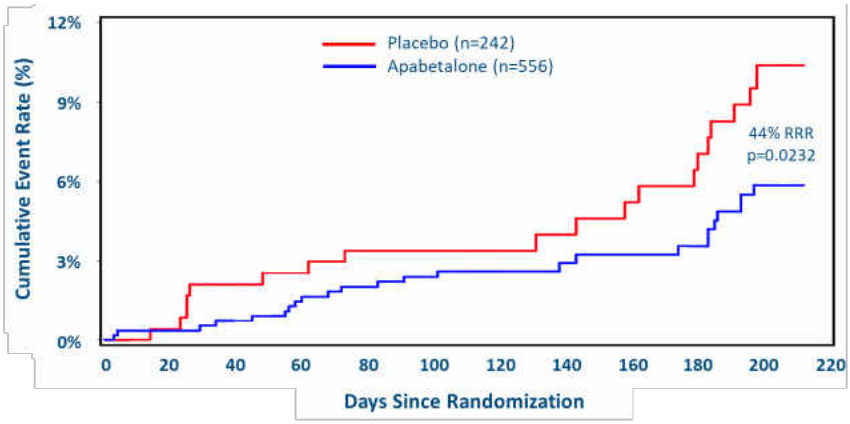
A total of 1,001 subjects have participated in its completed clinical trials, of which 722 received treatment with apabetalone and 279 received placebo. Three Phase II studies in patients with cardiovascular disease and one Phase II study in patients with pre-diabetes have been completed.

1) The ASSERT study enrolled 299 patients. Findings demonstrated by ASSERT included:
   - 200 mg/day of apabetalone was the optimal dose, based on safety and efficacy;
   - Patients with a low level of HDL-C at baseline had a better response for HDL-C and ApoA-I increases when treated with apabetalone; and
   - Best response were observed in those patients given apabetalone in combination with second generation statins such as Rosvastatin (Crestor®) or Atorvastatin (Lipitor®).
2) The SUSTAIN study enrolled 176 patients. Findings demonstrated by SUSTAIN included:
   - Low baseline HDL and low baseline ApoA-I were the best responders; and
   - There was one MACE event in subjects treated with apabetalone compared to six in subjects treated with placebo.
3) The ASSURE study enrolled 323 patients. Findings demonstrated by from ASSURE included:
   - Low baseline HDL were the best responders;
   - Elevated baseline hsCRP were strong responders; and
   - There were fewer MACE events in subjects treated with apabetalone (7.4%) vs. subjects treated with placebo (13.8%).
4) The Pre-diabetes study enrolled 20 patients. Findings demonstrated by from this study included:
   - Short duration of apabetalone treatment had effects on glucose metabolism; and
   - Both the reduction in glucose absorption and production are expected to be of benefit in patients with prediabetes mellitus.

These key findings contributed to determining a therapeutic window and targeted patient group for apabetalone.

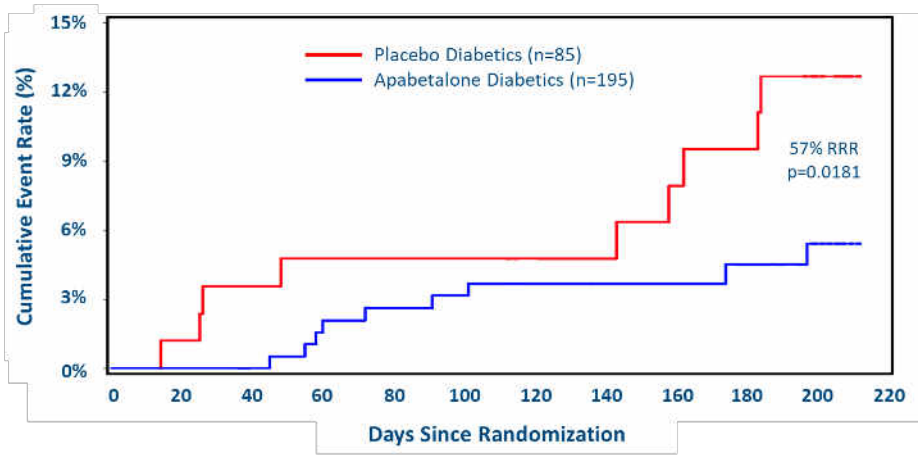
Based on our clinical trials, we have developed a broader and more integrated view of the effects of treatment with apabetalone across the vascular and coronary artery disease spectrums with safety and efficacy results for up to six months of treatment.

MACE Reduction in Resverlogix CVD Program- Analysis of Data from the ASSURE, SUSTAIN *and ASSERT* Phase II Clinical Trials



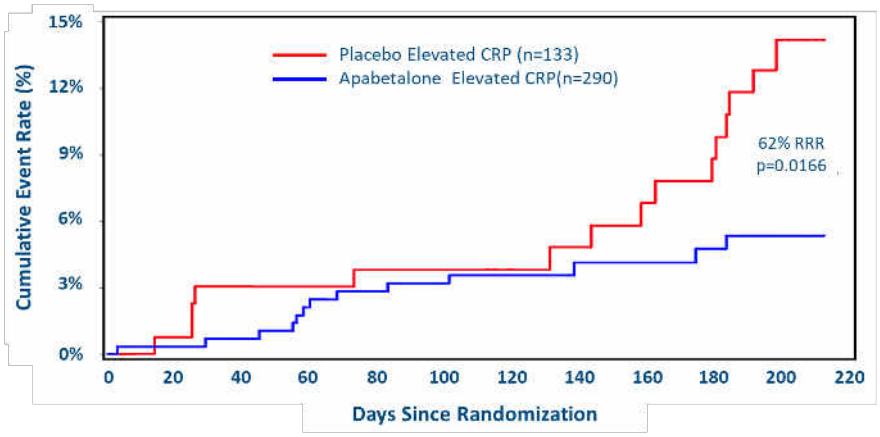
Time to first cardiovascular event in patients treated with placebo and apabetalone in patients with CVD from the ASSERT, SUSTAIN and ASSURE clinical trials

Source: Nicholls et al. 2017 Am J Cardiovasc Drugs



Time to first cardiovascular event in patients treated with placebo and apabetalone in patients with CVD stratified according to diabetes from the ASSERT, SUSTAIN and ASSURE clinical trials

Source: Nicholls et al. 2017 Am J Cardiovasc Drugs



Time to first cardiovascular event in patients treated with placebo and apabetalone in patients with CVD stratified according to baseline high-sensitivity C-reactive protein level from the ASSERT, SUSTAIN and ASSURE clinical trials

Source: Nicholls et al. 2017 Am J Cardiovasc Drugs

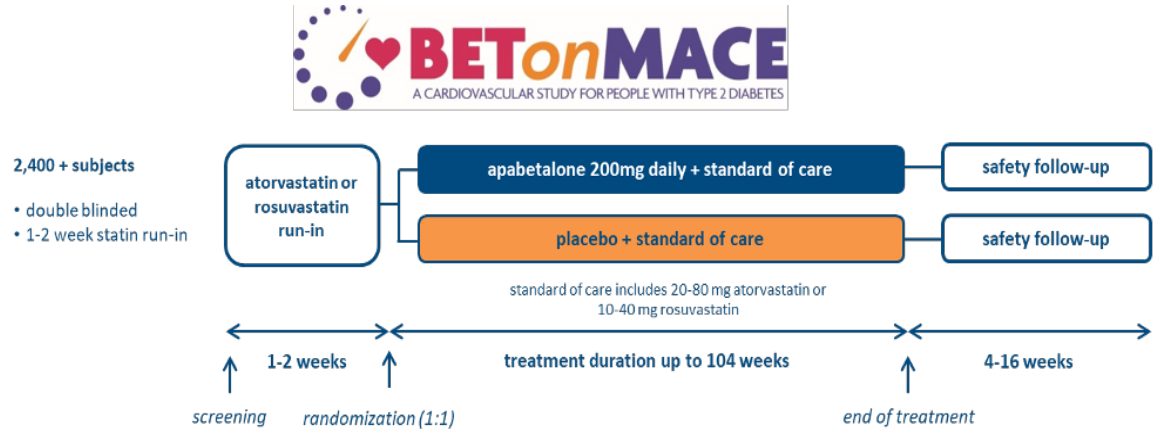
This peer reviewed publication of all three Phase II clinical trials with apabetalone further confirms the potential of the molecule's ability to impact MACE in high risk CVD and diabetes patients. This data provided the rationale for the target patient group for the Company's Phase III plans.

Apabetalone Phase III BETonMACE Clinical Trial in High Risk CVD Patients

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 ASSURE, SUSTAIN and ASSERT clinical trials. The BETonMACE study, "Effect of RVX-208 on Time to Major Adverse Cardiovascular Events in High-Risk Type 2 Diabetes Mellitus Subjects with Coronary Artery Disease" is a large international multi-center, double-blind, randomized, parallel group, placebo-controlled clinical trial to determine whether treatment with apabetalone in combination with rosuvastatin or atorvastatin increases the time to MACE compared to treatment with rosuvastatin or atorvastatin alone. In order to be eligible to participate in the study, patients must have documented history of type 2 diabetes, experienced a recent MACE and have low levels of HDL (<40 mg/dL for males and <45 mg/dL for females). All subjects will remain on a high-dose statin therapy (atorvastatin or rosuvastatin), and best standard of care treatments such as, beta blockers, ACE inhibitors and dual platelet inhibitors. Patients are randomized to either apabetalone 100 mg b.i.d. (twice daily) or matching placebo with continued statin treatment. This treatment period

continues for up to 104 weeks. The company anticipates that a minimum of 2,400 patients will be enrolled. The study is an event-based trial and will continue until at least 250 MACE events have occurred. The primary endpoint of the BETonMACE trial is designed to show a relative risk reduction of MACE, narrowly defined as a single composite endpoint of CV death, non-fatal myocardial infarction and stroke. As compared to recent larger CVD outcome trials (FOURIER, REVEAL and EMPA-REG), BETonMACE has an important differentiation in that its target patient group has a more enriched and much higher estimated MACE (CV death, non-fatal MI and stroke) rate of 8 per 100 patient years. This higher risk target patient group provides the Company with the potential to power the trial accordingly with smaller patient numbers. Primary outcome measures will be time to first occurrence of MACE. MACE will be adjudicated by an independent committee and the study will be monitored by a data safety monitoring board. The trial is seeking a 25-30% reduction in MACE as compared to the placebo arm.

Design of the BETonMACE Clinical Trial



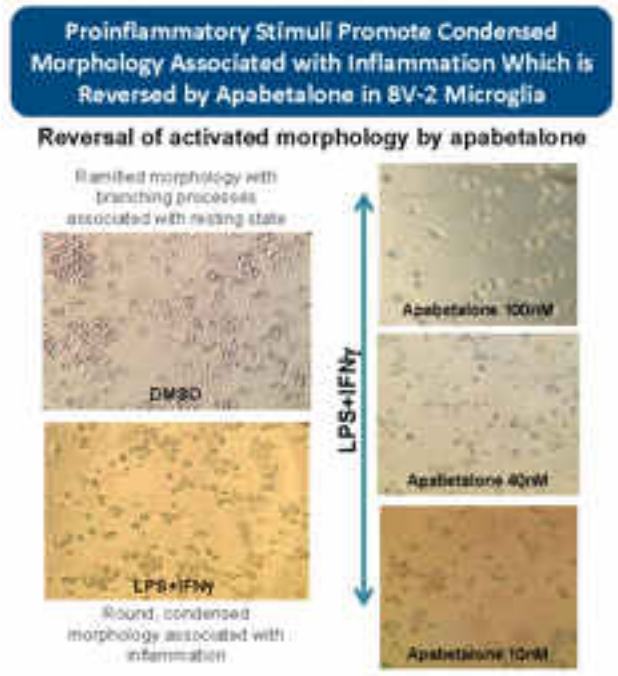
Source: Resverlogix

The independent Data and Safety Monitoring Board for the BETonMACE trial completed four planned safety reviews of the trial (in August 2016, December 2016, March 2017 and June 2017, respectively). On November 1, 2017, the independent DSMB confirmed that consistent with the previous DSMB reviews, the BETonMACE study should continue as planned without any

modifications and permits the trial to remain on schedule. The DSMB will conduct additional periodic reviews and a futility analysis is planned after 188 primary MACE events have been adjudicated. To date, more than 2,100 patients are enrolled in BETonMACE. Full enrollment is now anticipated in 2018H1.

BETonMACE will also examine a subgroup of CKD patients. Approximately 12-15% of the patient population is anticipated to have stage 3A and 3B CKD which is defined as an eGFR below 60. Important secondary endpoints such as MACE reduction and renal function in CKD patients will be included in the statistical analysis plan. The company anticipates that at total of approximately 300-350 CKD patients will be in the BETonMACE trial. The rationale for examining this important subgroup of patients is the eGFR data from the phase 2 ASSURE and SUSTAIN clinical trials and the proteomic data from the phase 1 PK clinical trial. These findings have been reported at the American Society of Nephrology (ASN) Kidney Week Conference and European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Congress. Any reported delay of onset or improvement of renal function would be an important secondary readout for the product position of apabetalone.

BETonMACE will also examine cognition in a subgroup of elderly patients. Patients 70 years of age or older are required to complete the Montreal Cognitive Assessment (MoCA) test at the beginning and end of the study. Approximately 15-20% of the patient population is anticipated to be included in this subgroup. This subgroup represents the equivalent of conducting a large Phase IIb dementia clinical trial within BETonMACE. The company anticipates that a total of approximately 450-550 elderly patients in the BETonMACE trial. The rationale for examining this important subgroup of patients is the mechanism of action of apabetalone and its effects on neuroinflammation. These findings have been reported at the International Conference on Alzheimer's and Parkinson's Diseases (ADPD). Any delay of cognitive decline or improvement of cognition, measured with MoCA within this patient group would provide rationale for expansion into neurodegenerative indications.



Results: After pro-inflammatory stimulation, microglia cells acquired the condensed morphology associated with a pro-inflammatory phenotype. In a dose dependent fashion, treatment with apabetalone reversed microglia back to a ramified, resting phenotype.

Source: Resverlogix ADPD Poster Presentation 2017

Apabetalone Phase I PK Clinical Trial in Patients with Severe Renal Impairment

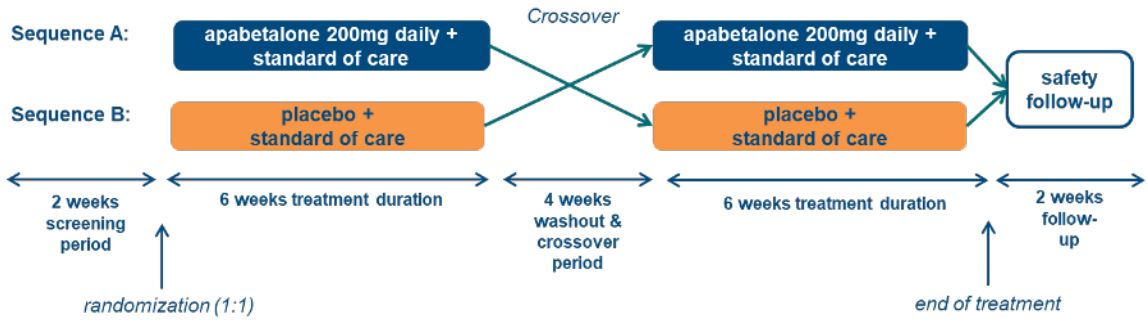
In late 2016, the company announced the collection of data from the New Zealand based Phase I PK study with apabetalone in patients with severe renal impairment. The primary objective of the Phase I study was met by demonstrating that apabetalone treated patients with severe renal impairment have the same favorable PK traits and safety profile as has been observed in previous apabetalone trials. With these positive results the company plans to proceed with more advanced renal impairment and dialysis trials. In early 2017, preliminary results from the Phase I PK study in late stage CKD patients were published. The data showed remarkable results in reducing acute phase proteins as well as inflammation protein biomarkers in patients with late stage CKD versus healthy control patients. It is believed that this is the first time in medical history that a direct connection of this type can be made between epigenetic regulation and its

potential for positive disease impact. Protein data was collected following a single oral administration of 100mg of apabetalone before and after multiple time points in both cohorts. Protein levels of 289 proteins were significantly different at baseline between the two groups ($p<0.05$). Initial findings from this study revealed a highly differential protein signature at baseline between CKD patients and controls. Following a single dose administration of apabetalone in the late stage CKD patients, the levels of multiple plasma proteins were changed within 12 hours after dosing, demonstrating a fast onset of drug action. Analysis of the changes in protein levels at the 12-hour time point revealed that, in the late stage CKD patients, 33 percent of proteins had statistically significant changes ($p<0.05$) compared to only 10 percent in the controls. Of these significant proteins, several established renal biomarkers such as interleukin 6 (IL6) and osteopontin, were regulated positively with respect to disease severity and progression. Ongoing expanded analysis of this exploratory data is also planned which will look at Ingenuity Pathway Analysis (IPA). The quick onset of action and improvement of reported CKD risk factors are encouraging for us in the planned expansion beyond the current cardiovascular and diabetes program. Detailed data has been submitted for peer reviewed publications.

Apabetalone Phase II Clinical Trial in Patients with End-Stage Renal Disease Treated with Hemodialysis

In February, Resverlogix received positive guidance from the FDA on the design of the company's proposed protocol for its Phase IIa kidney dialysis trial. The primary objective of the study will be to evaluate if treatment with apabetalone in combination with standard of care (SoC) decreases alkaline phosphatase in comparison to placebo and SoC. In light of guidance received from the FDA, the Phase IIa study design will be separated in two parts. Part A will involve a single-dose pharmacokinetic (PK) study in eight patients receiving hemodialysis. The PK results from Part A will influence the dose selection for Part B. Part B will be a double-blind, randomized, placebo-controlled, sequential cross-over study with apabetalone, and is designed to evaluate biomarker changes and safety parameters with apabetalone in up to 30 patients with end-stage renal disease treated with hemodialysis and elevated ALP (>80 U/l).

Design of Part B of the Phase 2a Clinical Trial in Patients with End-Stage Renal Disease Treated with Hemodialysis



Source: Resverlogix

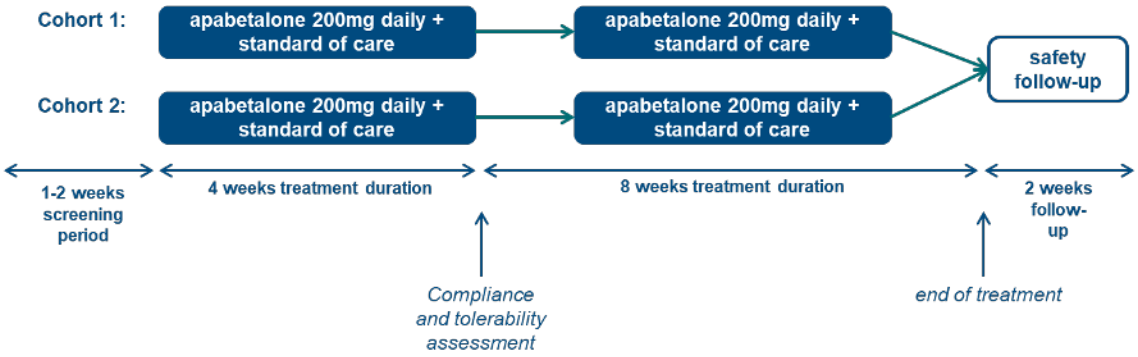
Late stage Chronic Kidney Disease (CKD) encompasses CKD stages 4 and 5. It can be alternatively defined as an estimated glomerular filtration rate (eGFR) of <30 ml/min/1.73m^2. Reported in the 2016 United States Renal Data System (USRDS) Annual Report, approximately 1.4 million patients in the US have advanced CKD, 474,000 of which are on dialysis treatment. According to the USRDS, advanced CKD cost the US healthcare system approximately USD 17 billion in 2014, with an average cost exceeding USD 28,000 per patient. Additionally, dialysis treatment costs the US Medicare system approximately USD 28 billion with an average cost exceeding USD 80,000 per year. Currently there are no known agents that reduce MACE and maintain or improve renal function in CKD or dialysis patients.

Apabetalone Phase II Clinical Trial in Fabry Disease

Resverlogix has received approval from Health Canada, Therapeutic Products Directorate, to proceed with a clinical trial with apabetalone in patients with Fabry disease. This is an open-label, exploratory clinical study to assess the patient safety and effect on key biomarkers of apabetalone in subjects with Fabry disease for up to 16 weeks. The study population will consist of two cohorts. Cohort 1: Patients with Fabry disease receiving enzyme replacement therapy (ERT). Cohort 2: Patients with Fabry disease not receiving ERT. The primary objective of the study is to evaluate the safety and tolerability of apabetalone in patients with Fabry disease. Secondary

objectives include evaluating the effect of apabetalone in subjects with Fabry disease as determined by change in key biomarkers including alkaline phosphatase (ALP), high-sensitivity C-reactive protein (hs-CRP), and other well-known markers for chronic kidney disease. In addition, an ex vivo study of apabetalone treated Fabry Disease blood is planned.

Design of the Phase 2a Clinical Trial in Patients with Fabry Disease



Source: Resverlogix

Orphan Disease Indications

In September 2015, the company announced the initiation of an Orphan Disease Program with initial early data on complement markers. 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 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 apabetalone (from the ASSURE clinical trial).

- *Pulmonary Arterial Hypertension*

Due to the positive effects of apabetalone treatment on primary lung smooth muscle cells (SMCs), an animal study of the effect of apabetalone on top of standard of care in pulmonary arterial hypertension is ongoing.

- *Muscular Dystrophy/facio scapula humeral dystrophy*

Resverlogix has tested apabetalone and a variety of other RVX compounds for target and biomarker engagement in muscle cells, The Company is also analyzing human muscle biopsies from patients treated with apabetalone. Additional work is ongoing.

- *Paroxysmal nocturnal hemoglobinuria (PNH)*

Due to positive data on the effect of apabetalone on the complement cascade, plans to start a safety/efficacy trial in this population.

- *Neuroinflammation*

Direct effects of apabetalone demonstrate reduced inflammation and microglial activation with drug treatment and no detrimental effects on neurons. Additional work is ongoing.

Competitive Landscape in 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 cardiac-related 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

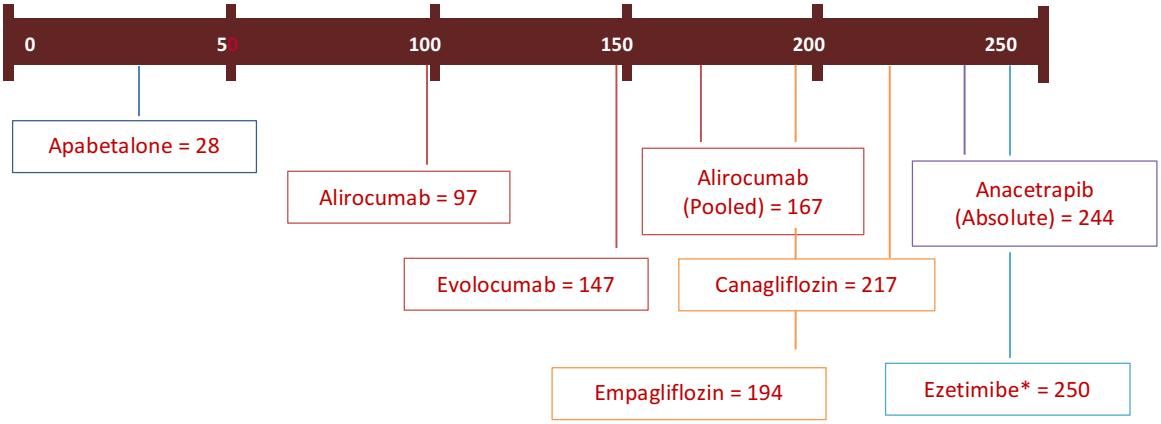
The LDL lowering hypothesis is being further tested in CVD risk with aggressive reduction of LDL to unprecedented levels such as 40-50mg/dl. Newly reported trials such ODYSSEY LONG TERM, PSCK9 LDL lowering approach via Alirocumab (ODYSSEY OUTCOMES 2017), Evolocumab (FOURIER 2017), and cholesterol absorption LDL lowering approach via Ezetimibe (IMPROVE IT 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. early 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	15,000	7	6% (p<0.01)	333
ODYSSEY LONG TERM	LDL Lowering 40mg/dl	120mg/dl	2,341	1.5	48% (p<0.02)	97
FOURIER	LDL Lowering	92mg/dl	27,564	2.2	15% (p<0.001)	147
ASSURE, SUSTAIN and ASSERT	BET Inhibition	85mg/dl	798	0.25-0.5	44% (p<0.02)	28 (6-months)

Although IMPROVE IT, ODYSSEY LONG TERM and FOURIER 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 350,000 to almost USD 1 million. This is based on a simple analysis of number needed to treat (NNT) annually, multiplied by the treatment cost over one year. It is critical to realize that when building a value proposition with health system payors, the lower the NNT the better. If the current economic and value proposition for these LDL lowering technologies has a range of NNT from 100-300, reimbursement agencies would most likely request stronger value evidence with significantly improved pricing thresholds. Payor groups, such as NICE UK (National Institute of

Clinical Excellence) and ICER US (Institute for Clinical and Economic Review), are now demanding "value for money" for new drugs seeking rapid reimbursement. In their September 2017 Economic Analyses for PCSK9 Inhibitor Evolocumab, ICER states, "the value-based price benchmarks, or the range in which the cost of evolocumab would align with its benefit to patients, was found to be substantially lower than initially calculated, at $1,725 – $2,242 for annual treatment costs versus $5,300 – $7,600 in [their] initial report. To meet the revised value-based price benchmark, evolocumab would need to be discounted 85% – 88% from the current wholesale acquisition cost (WAC) of $14,523 annually". 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 value proposition. The new reported early MACE findings (Nicholls et al 2017) from the Company's entire Phase II Program provide plausibility for a much more efficient impact on CVD risk versus novel approaches to LDL-lowering.

Number Needed to Treat (NNT) per MACE event prevented (1 Year Kaplan Meier Estimate unless otherwise specified)



Compared to other CVD risk improvement therapies, such as the PCSK9 inhibitors which are retail priced at near USD 14,000 per year, estimates for the annual treatment cost of apabetalone are planned at approximately USD 7,000 per year. When examined in terms of its potential economic benefit, the cost for apabetalone to prevent one cardiovascular event is even more

striking with an ICER (Incremental Cost Efficiency Ratio) range of USD 140,000-200,000. This level makes the implicit assumption that the potential relative risk reduction of apabetalone is greater than 25%.

To further assess the potential value of apabetalone in the high-risk target diabetes and CKD patients in BETonMACE, Resverlogix commissioned additional studies in 2016 from top US payers covering over 200 million lives. The focus of this analysis was to assess the cost threshold range that several of the major pharmacy benefit managers in the US market would be willing to pay to prevent one MACE event. The new analysis found that an average incremental cost efficiency ratio score (ICER) of USD 140,000 to prevent one event was seen as appropriate by US Payors for the higher risk patients targeted in BETonMACE. This score represents a substantial increase of 50% than the earlier reported KM score reported above for apabetalone in its initial US Payer assessment back in 2015. In recent Tier 3 pricing models (>5K USD per year), the molecule is now positioned to be more appropriately priced for higher risk CVD, diabetes and CKD patients. Further pharmacogenomics and health value analysis work is planned by the company for apabetalone to ensure it is well positioned to provide a strong health value proposition to key stakeholders including future pharmaceutical partners and payors alike.

Financials

For the quarter ended October 31 2017, Resverlogix reported a net loss of USD 10.9 million compared to a net loss of USD 15.2 million in the same period last year. Expenses for the period totaled to USD 9.6 million (2016: USD 7.6 million) including R&D expenses of USD 8.4 million. Clinical costs totaled approximately USD 4.6 million (2016: USD 3.6 million), including USD 4.4 million on the BETonMACE clinical trial net of cost recoveries, reflecting the continued progression and expansion of the trial (2016: USD 3.0 million on the BETonMACE clinical trial and USD 0.3 million on the Renal PK trial), USD 0.1 million on regulatory costs (primarily related to the BETonMACE clinical trial) (2016: USD 0.1 million) and USD 0.1 million (2016: USD 0.2 million) of other clinical costs including sample analysis, consultants and insurance. BETonMACE costs included those related to country selection, investigative site evaluation; central lab start-up, set-up of electronic systems, training, site initiation visits, and patient recruitment.
As at October 31, 2017, the company had USD 0.7 million of cash, USD 12.1 million of trade and other payables, and USD 3.9 million of accrued interest and fees. However, upon writing this report, the cash position was improved substantially with the outstanding debt fully paid.

On June 20, 2017, the company issued a total of USD 7.5 million (CAD 10 million) of equity units pursuant to a private placement and prospectus offering. Eastern and Hepalink purchased 1,617,980 and 1,333,333 equity units, respectively at a price of CAD 1.80 per unit pursuant to a private placement for gross proceeds of USD 4.0 million (CAD 5.3 million). Other subscribers purchased an additional 2,552,489 equity units at a price of CAD 1.80 per unit pursuant to a prospectus offering for gross proceeds of an additional USD 3.5 million (CAD 4.6 million). Each equity unit consists of one common share and one common share purchase warrant. Each warrant is exercisable at a price of CAD 2.05 per underlying common share for a period of four years from the closing of the private placement and prospectus offering. Also, the maturity date of the company's CAD 68.8 million loan was extended from August 28, 2017 to December 26, 2017. Early December, Resverlogix closed its previously announced private placement of 60,416,667 equity units to Shenzhen Hepalink Pharmaceutical Co. Ltd. (Hepalink) at a price of CAD 1.44 per unit for gross proceeds of USD 87 million. Each unit was comprised of one

common share and 0.082759 of a common share purchase warrant. Each full warrant is exercisable at a price of CAD 1.64 per share for a period of four years from the closing of the offering.

After giving effect to the private placement, the Company has a total of 175,040,756 common shares issued and outstanding. Hepalink holds 75,020,000 common shares and 7,333,333 common share purchase warrants which represents 42.86 percent of the common shares outstanding before giving effect to any outstanding warrants and 45.16 percent of the outstanding common shares assuming the exercise by Hepalink of its warrants. The net proceeds was primarily used to repay the USD 68.8 million secured loan, which means that the company is now debt free.

Profit & Loss Statement (USD mln)

For 2nd quarter 2017/18 ended Oct 31 (USD m)	Oct 31 2017A	Oct 31 2016A	2017A FY	2016A FY
Revenues	-	-	-	-
R&D Costs	8.440	6.346	29.875	15.681
General & administrative expenses	1.141	1.253	4.269	4.326
Finance costs (income)	1.281	7.551	11.983	(0.303)
Loss (income) before income taxes	10.862	15.150	46.127	19.704
Income Taxes	0.013	0.015	0.083	0.011
Net Loss (Income)	***10.875***	***15.165***	***46.210***	***19.715***

Consolidated statement of cash flows

For 2nd quarter 2017/18 ended Oct 31 (USD m)	Oct 31 2017A	Oct 31 2016A	2017A FY	2016A FY
Cash flow from operating activities	(12.032)	(11.550)	(22.669)	(21.422)
Cash flow from investing activities	(0.124)	(0.393)	(1.053)	(1.153)
Cash flow from financing activities	11.485	(2.274)	(2.380)	35.183
Cash and cash equivalents beginning period	1.355	28.109	28.109	16.211
Net change in cash and cash equiv.	(0.644)	(15.314)	(26.754)	11.898
Cash and cash equiv. end of period	0.711	12.795	1.355	28.109

Consolidated Balance Sheet

(USD million)	Oct 2017A	April 2017A
Cash and cash equivalents	1.907	1.850
Current Assets	5.325	5.654
Non-Current Assets	4.445	5,213
Total Assets	**9.770**	**10.867**
Current Liabilities	82.010	69.736
Total Liabilities	128.510	112.436
Total Equity	(118.840)	(101.569)

Valuation Apabetalone: Upward Adjustment, Reduced Risk Profile

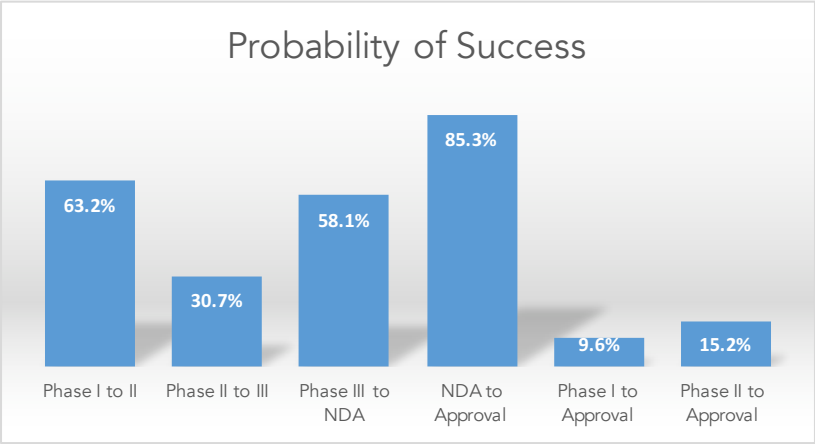
We have increased our valuation on Resverlogix to CAD 2.5 Billion or CAD 14.25 per share from CAD 1,300 million or CAD 12.50 per share due to the fact that we have increased the LOA for Resverlogix' lead product apabetalone to 55% and reduced the discount rate used from 15% to 12% following the repayment of its CAD 68.8 million loan, leaving the company with no outstanding long-term debt. At this moment we do not address value to the other programs in Resverlogix's pipeline. This is a potential upside for the company.

Phase Success and Likelihood of Approval (LOA)

In estimating a value for the clinical programs with apabetalone, we made use of several studies that were done on the clinical development success rates for investigational drugs to measure success rates for investigational drugs. We analyzed individual drug program phase transitions from January 1, 2006 to December 31, 2015. For the ten years studied, 9,985 transitions in the Biomedtracker database were analyzed. A phase transition is the movement out of a clinical phase – for example, advancing from Phase I to Phase II development, or being suspended after completion of Phase I development. These transitions occurred in 7,455 clinical drug development programs, across 1,103 companies (both large and small), making this the largest study of its kind. With this broad set of data, we aimed to capture the diversity in drug development across levels of novelty, molecular modalities, and disease indications. Only company-sponsored, FDA registration-enabling development programs were considered; investigator-sponsored studies were excluded from this analysis.

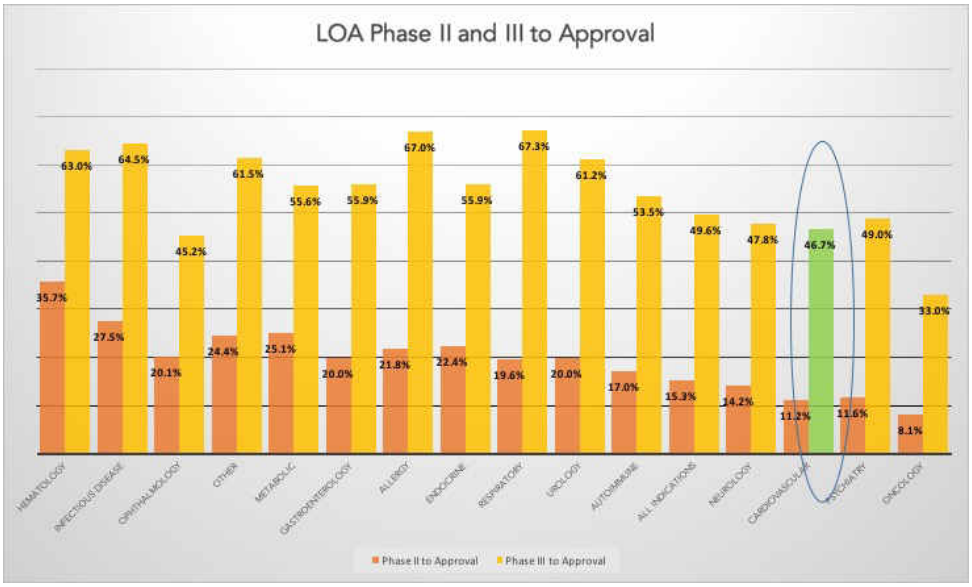
The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted for safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in this report. Phase I success rates may also benefit from delayed reporting bias, as some larger companies may not deem failed Phase I programs as material and thereby not report them in the public domain. The Phase II transition success rate (30.7%, n=3,862) was substantially

lower than Phase I, and the lowest of the four phases studied. As this is generally the first stage where proof-of-concept is deliberately tested in human subjects, Phase II consistently had the lowest success rate of all phases. This is also the point in development where industry must decide whether to pursue the large, expensive Phase III studies and may decide to terminate development for multiple reasons including commercial viability. The second-lowest phase transition success rate was found in Phase III (58.1%, n=1,491). This is significant as most company-sponsored Phase III trials are the longest and most expensive trials to conduct. The probability of FDA approval after submitting a New Drug Application (NDA) or Biologic License Application (BLA), taking into account re-submissions, was 85.3% (n=1,050). Multiplying these individual phase components to obtain the compound probability of progressing from Phase I to U.S. FDA approval (LOA) reveals that only 9.6% (n=9,985) of drug development programs successfully make it to market (see graph below)



Source: BIO Industry Analysis

Major disease areas were segmented according to the convention used by Biomedtracker, and categorized 21 major diseases and 558 indications for the 2006-2015 timeframe. As can be seen in the graphs below, there is a wide range of Likelihood of Approval (LOA) from Phase III.



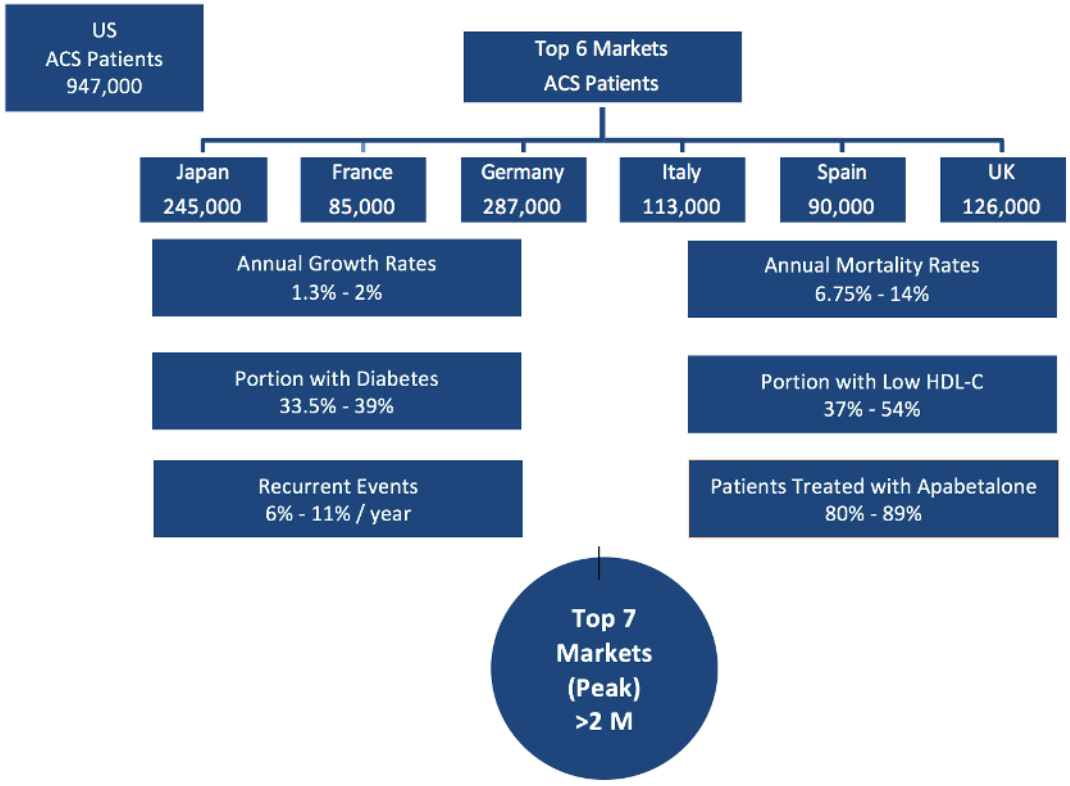
Key Value Assumptions

We have increased our value on Apabetalone, and thereby Resverlogix as a whole from CAD 1,300 million to CAD 2.6 billion or CAD 14.75 per share. The increase in valuation is based on the ongoing successful enrolment of the Phase III trial BETonMACE as well as reducing the discount rate. Apabetalone clearly has blockbuster potential. We choose not to value the company's total technology platform and potential additional indications for apabetalone. We feel that the potential value of its platform and additional indications offer an additional upside potential. With the enrolment of more than half the needed patients for the Phase III clinical trial we have increased the probability of success to 55% from 46%.

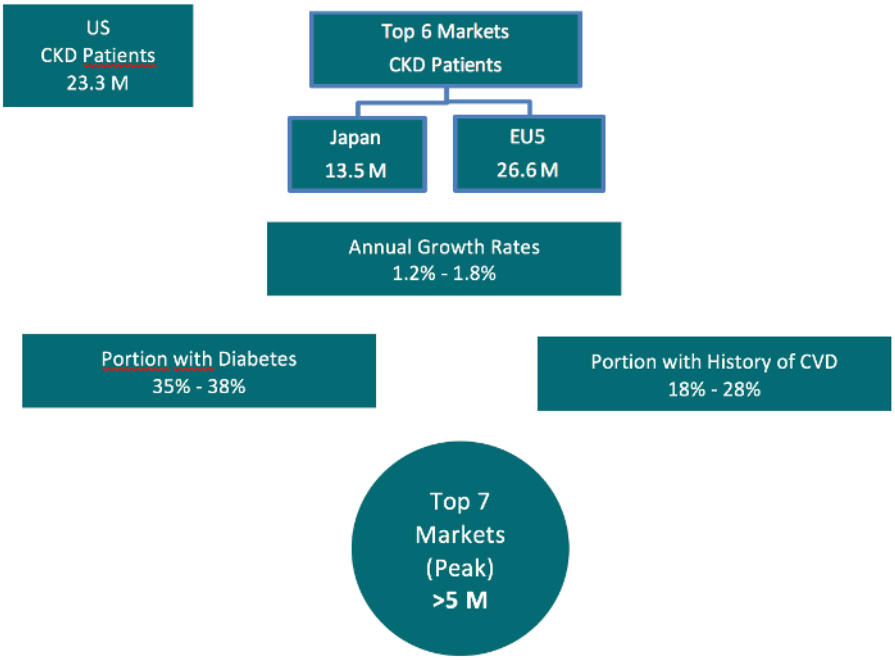
We expect an approval of apabetalone in the US, EU and Japan in 2021. We ascribe CAD 14.25 per share to apabetalone for high risk CVD, Diabetes mellitus and CKD based on a risk-adjusted NPV analysis of the estimated net income in the next 10 years, assuming approval and a 2021 launch. An approval of apabetalone for any Orphan Diseases is expected to be up to one year earlier provided positive data.

Apabetalone is targeting specific patients with high residual risk for increased MACE: patients with low HDL and Diabetes, and CKD. Expansion into ESRD and CKD will continue to add important therapeutic patients with very high CVD events and extremely poor renal function. These groups of patients represent a very significant patient population of potentially 8 million high risk target 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.

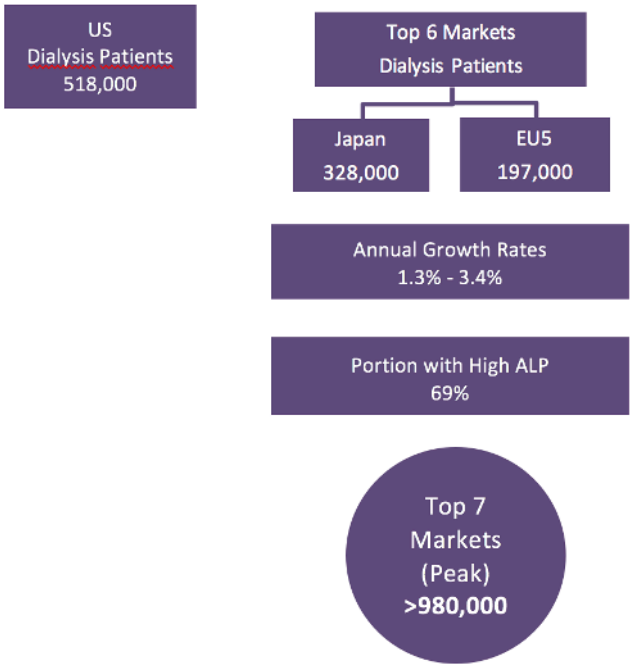
High Risk ACS Patients with Diabetes Mellitus Comorbidity and Low HDL-C

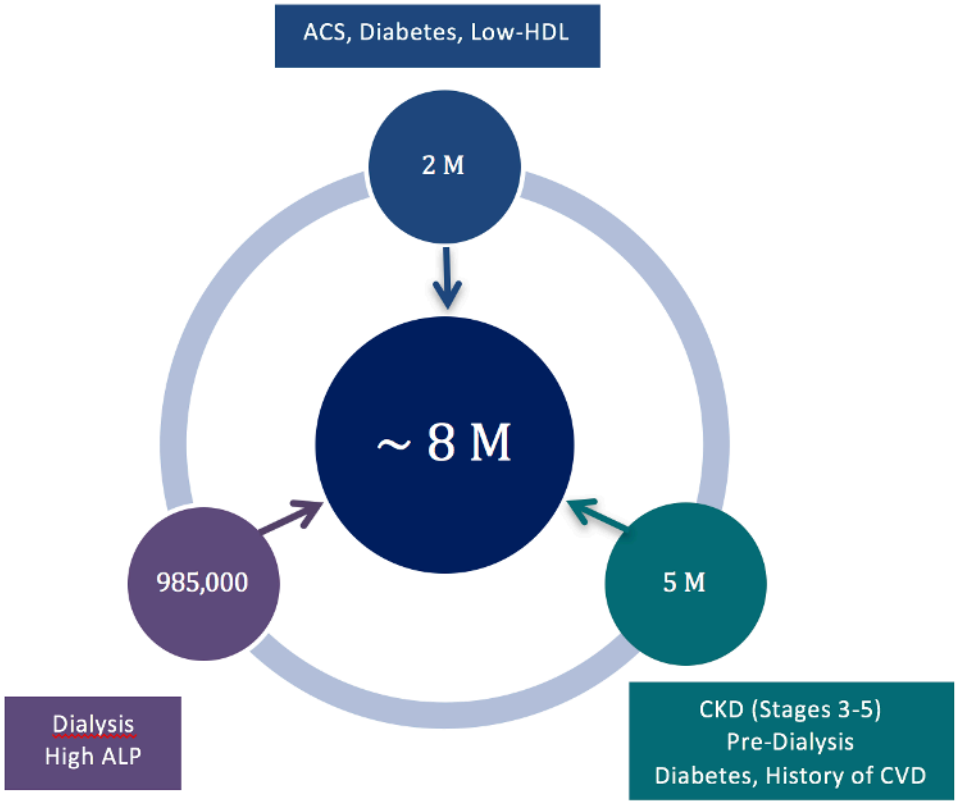


High Risk CKD Patients (Stages 3-5, Pre-Dialysis) with Diabetes Comorbidity and History of CVD



High Risk CKD Patients on Dialysis with High ALP (> 80 U/L)



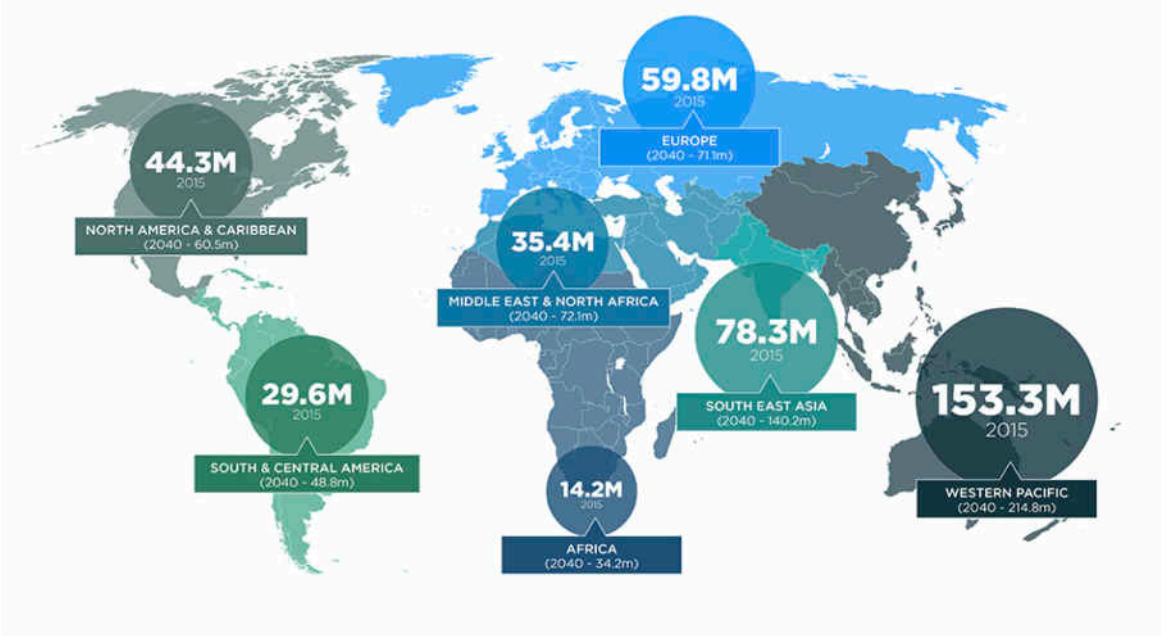


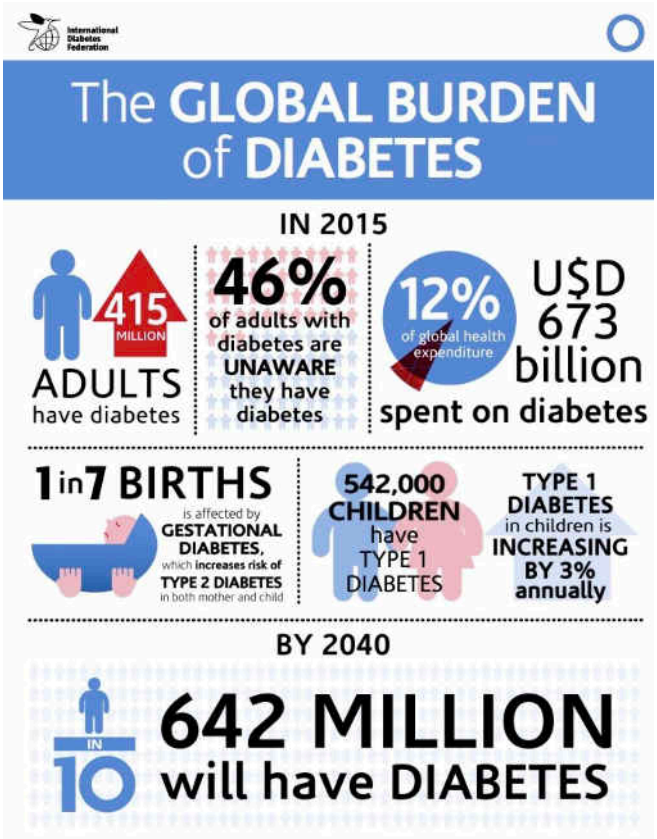
Source: RVX internal projections

The total target patient population of **8.2** million patients eligible for apabetalone treatment represents a very significant 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 how 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.


59.8M
2015
EUROPE
(2040 - 71.1m)
44.3M
2015
NORTH AMERICA & CARIBBEAN
(2040 - 60.5m)
35.4M
2015
MIDDLE EAST & NORTH AFRICA
(2040 - 72.1m)
78.3M
2015
SOUTH EAST ASIA
(2040 - 140.2m)
153.3M
2015
WESTERN PACIFIC
(2040 - 214.8m)
29.6M
2015
SOUTH & CENTRAL AMERICA
(2040 - 48.8m)
14.2M
2015
AFRICA
(2040 - 34.2m)


International Diabetes Federation
The GLOBAL BURDEN of DIABETES
IN 2015
415 MILLION
ADULTS have diabetes
46% of adults with diabetes are UNAWARE they have diabetes
12% of global health expenditure
U$D 673 billion spent on diabetes
1 in 7 BIRTHS is affected by GESTATIONAL DIABETES, which increases risk of TYPE 2 DIABETES in both mother and child
542,000 CHILDREN have TYPE 1 DIABETES
TYPE 1 DIABETES in children is INCREASING BY 3% annually
BY 2040
IN 10
642 MILLION will have DIABETES

Valuation apabetalone key markets

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	
No of eligible patients US, EU & Japan (m)	8.2										
Market penetration markets	50-60%										
Market share US	0.6%	1.5%	3.0%	5.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%	
Market Share EU	0.0%	0.5%	1.5%	3.0%	5.0%	7.0%	10.0%	13.0%	16.0%	18.0%	
Market share Japan	0.0%	0.2%	0.5%	1.2%	2.5%	4.0%	7.0%	10.0%	13.0%	16.0%	
Total Revenues (USD m)	92	281	608	1,072	1,604	2,297	3,139	3,981	4,671	5,275	
Margin 40%	37	112	243	429	641	919	1,256	1,593	1,868	2,110	
WACC 12%	0.64	0.57	0.51	0.45	0.40	0.36	0.32	0.29	0.26	0.23	
NPV (USD m)	23.3	63.7	123.2	193.9	259.1	331.3	404.3	457.8	479.5	483.5	
Total NPV (USD m)											**3,665**
LOA 55% (USD m)											**2,016**
PER SHARE (CAD)											**14.75**

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.*
Atherosclerotic Plaque	*the deposit or accumulation of lipid containing plaques in the 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.*
Coagulation Cascade	*a series of events that culminate in the formation of a bloodclot 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.*
ESRD	***Define End Stage Renal Disease and poetnail market of 2million + patients***
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 sub-discipline 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 I 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 II 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 III 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 a 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.**
Note 2	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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