Initiating Coverage Report

RESVERLOGIX

Epigenetics
&
Select BET Inhibition

A New approach to
High Risk Diabetes and Chronic Kidney Disease

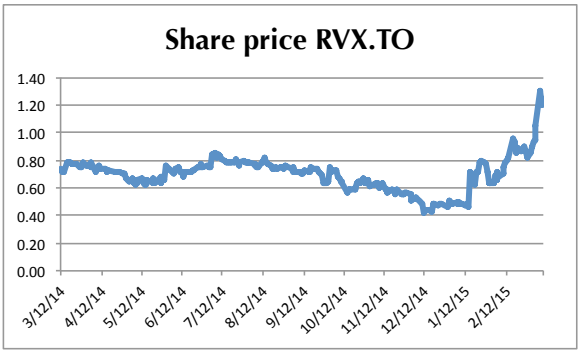
EXECUTIVE SUMMARY

Price Target: **CAD 5.85**

Date: 16 March 2015

Country:	**Canada**
Price:	**CAD 1.80**
ISIN Code:	**CA76128M1086**
Reuters Code:	**RVX.TO**
Market Cap (CAD m):	**154.3**
EV (CAD m):	**178.6**
Cash & cash eq. (USD m):	**17.0**
Shares outstanding (m):	**85.35**
Volume:	**90,438**
Free float:	**100%**
52-week Range:	**0.41-1.93**

USD mln	2013A	2014A	2015E
Revenues	-	-	-
Net (Loss)/Profit	(43.8)	55.1	(5.0)
Net profit (loss) per share	(0.58)	0.69	(0.06)
R&D costs	28.8	9.8	5.0
Cash increase/(decrease)	9.9	(16.8)	14.4
Cash and marketable sec.	17.4	0.6	15.0



Chief Research Analyst

Marcel Wijma MSc

+1 (917) 460 6185 (US)

+31 (6) 8489 2954 (NL)

m.wijma@leeuwenhoeck.com

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 secondary prevention in 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 an nine year lead in the field of Epigenetic small molecules for vascular disease risk reduction.

- In March 2014, the company presented a Poster, authored by Cleveland Clinic (Puri et al), at the American Cardiology Congress. Patients with CVD and elevated CRP >2.0 had a 70% relative reduction of MACE over 24 and 26 weeks of treatment. This observed early beneficial effect of RVX-208 in patients with elevated CRP could explain that the molecule had novel anti-inflammatory vascular effects in addition to the ability to raise ApoA-I and HDL.

- In September 2014, the company announced at the European Society of Cardiology that patients with CVD arising from atherosclerosis when given RVX-208 had a 55% relative risk reduction of MACE over 24 and 26 weeks or treatment. This beneficial effect of RVX-208 on patients with diabetes mellitus was more marked with a 77% reduction. These reductions may be a result from the ability of RVX-208 to significantly improve new specific biomarkers of CVD risk measured in the SUSTAIN and ASSURE trials. One additional risk marker for MACE, namely alkaline phosphatase (ALP), was also discussed at the oral presentation further enlightening the broader effect that BET inhibition has on multiple pathways of vascular risk. RVX-208 was highly efficacious in lowering ALP, a marker of vascular calcification, versus placebo.

- 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 an Epigenetic small molecule with select BET inhibition 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 and diabetes therapies.. A resetting of new genes and pathways, via epigenetic mechanisms, potentially represent a novel line of attack to badly needed risk reduction in high-risk CVD patients such as those with low HDL, diabetes and CKD.

- Atherosclerosis, a key underlying marker for CVD risk, is another focus for the pharmaceutical industry. This therapeutic segment exceeds USD 38 billion in costs in the US annually. 335 million lipid-regulating prescriptions were written in 2010 (IMS Health) with statins, the most commonly prescribed class of LDL-cholesterol-lowering drugs, achieving USD 16 billion in sales. Data presented by Resverlogix at ESC in Barcelona observed more robust regression of atherosclerosis in target patient groups, specifically those with low HDL and taking the co-medication of rosuvastatin. Moving forward the Company will employ a combination strategy with rosuvastatin to capitalize on these Certain important news expected in the next 12 months could drive the stock up. This includes announcement of a new larger clinical trial or trials that would offer a novel approach, different from additional LDL lowering, targeted at CVD risk reduction in high-risk patient groups. Additional publications in new therapeutics areas such as CKD and or diabetes. Announcement of new mechanisms of action and pathways that drive risk in patients with diabetes and CKD. The addition of new key opinion leaders (KOLs) in

the areas of CVD, diabetes and CKD diseases. The potential for additional smaller and or orphan indications.

- In the last year, Resverlogix was successful to secure an additional USD 30 million from a Citibank loan. The total loan agreement with Citibank was thereby increased to USD 68.8 million, which will be repayable upon maturity by the end of August 2017. Resverlogix also closed a USD 2.3 million private placement with existing shareholder NGN BioMed Opportunity II and others. We believe the Company's cash will be sufficient to fund all of the Company's planned business operations for more than the next year as well has the ability to raise additional funds for ongoing and additional clinical development of RVX-208. The Company may raise additional capital through other sources such as prospectus offerings and/or private placements.

- Based on our adjusted NPV valuation, we believe **Resverlogix** is substantially undervalued at the current share price of CAD 1.80. Using our valuation model, the Company's current value is CAD 500 million, or CAD 5.85 per share. This represents an enormous upside from the current share price. The valuation is based on the development of its potential blockbuster RVX-208 and its purported early efficiency in reducing MACE.

- 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 from 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, which are currently underway in this important excess residual risk market of high risk CVD such as diabetes and CKD patients.

Company Overview

Resverlogix (RVX.TO) is a clinical stage cardiovascular company with an epigenetic platform technology that modulates protein production. Resverlogix is developing RVX-208, a first-in-class BET inhibition small molecule apabetalone for the treatment of secondary prevention 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 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.

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, has recently emerged as a promising 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. Epigenetics represents an important new area of drug development and is now a hallmark of several complex pathologies, including metabolic disorders, cardiovascular and neurological diseases. Epigenetic protein and enzyme molecular targets are positioned as promising targets for therapeutic intervention.

MACE: The Most Important CVD risk marker

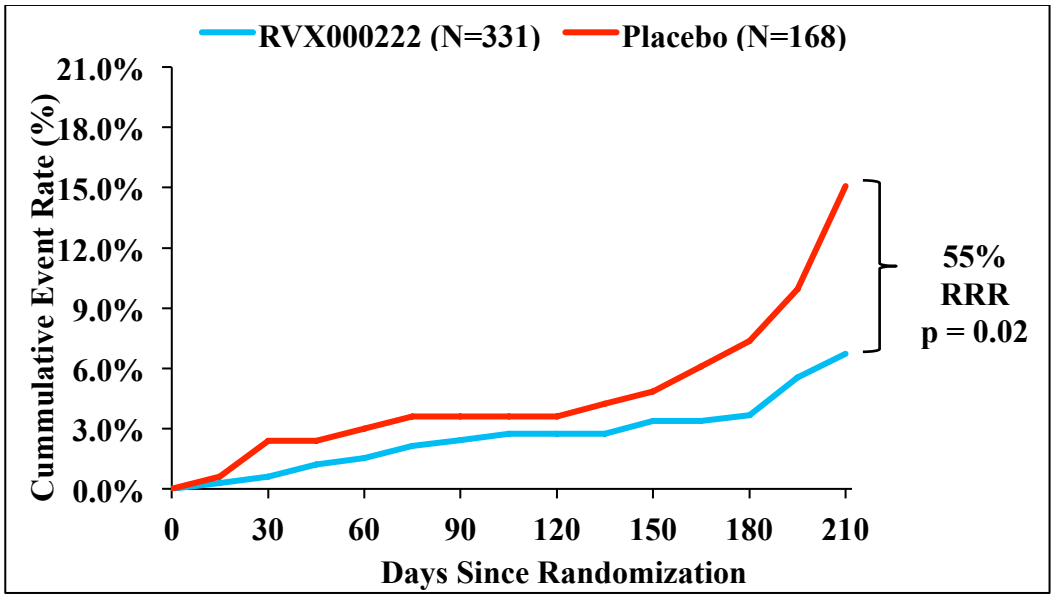
Of all the biomarkers that are used for providing prognostic predictability for CVD risk, MACE (Major Adverse Cardiovascular Events) is the most important! Patients, Physicians and CVD Key Opinion Leaders look at MACE as the most impactful marker of CVD risk. MACE includes a variety of key markers of 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 2013 AHA Statistics report, based on 2010 death rate data, more than 2,150 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.

As the leading cause of death in the United States, CVD is responsible for 1 in every 4 deaths or approximately 600,000 deaths annually. Important risk factors for heart disease include elevated blood pressure, dyslipidaemia and lifestyle factors such as obesity, physical inactivity and smoking. As such, the American Heart Association/American College of Cardiology guidelines for risk reduction involve a comprehensive approach to management of the disease. These recommendations include lifestyle modifications such as smoking cessation, daily physical activity, and dietary/weight management, and therapeutic interventions to control blood pressure, lipid profile, and platelet activity are also recommended.

RVX-208: Early Reported Effect on MACE

Extensive analysis on early MACE was performed in the Company's Phase IIb program of almost 500 patients. 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 6.5% MACE events while patient in the placebo group reported a total of 13.4% (p=0.02). This 55% reduction of events was reported on January 8, 2014 in a Company press release.

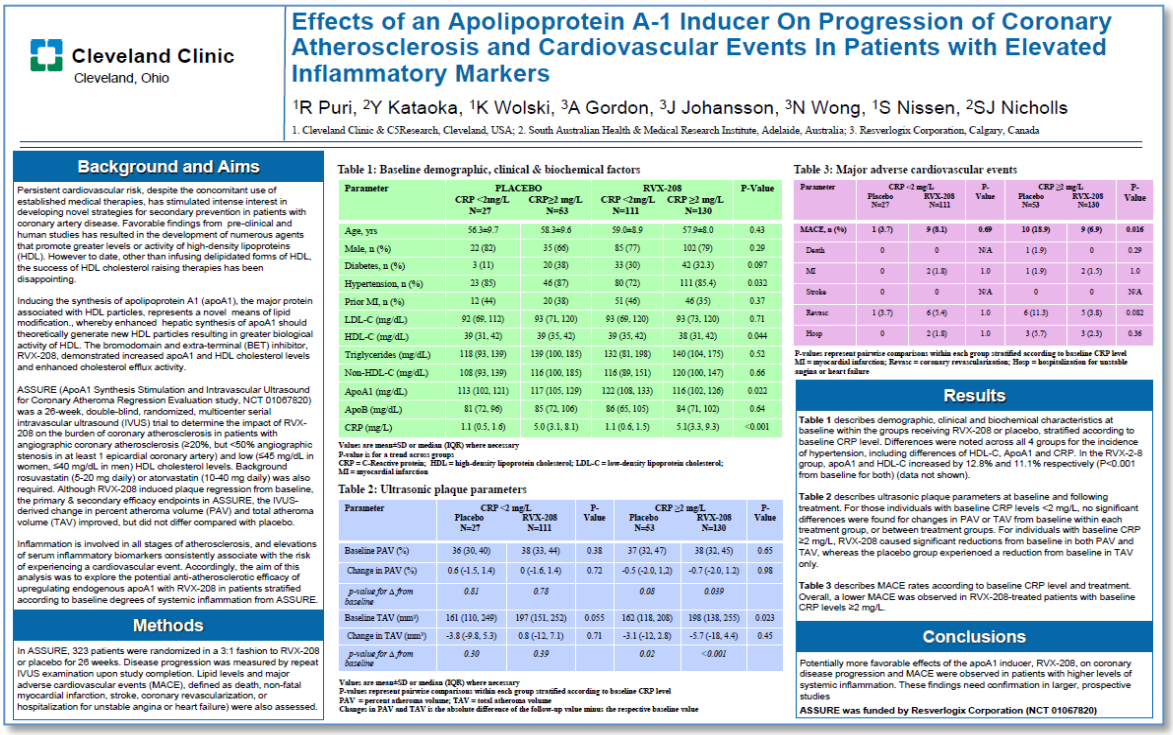
MACE in Patients Treated with RVX000222 (All Patients)



Source: RVX data on file – ASSURE and SUSTAIN Safety Population. Log-Rank test for between group comparison. Relative risk reduction is calculated based on Kaplan-Meier estimates of event rate.

Further analysis of patient segments, those with elevated vascular inflammation, (CRP >2.0), a known risk marker for vascular inflammation, were reported at ACC 2013. Dr. Puri reported an observed 70% reduction in MACE from the Cleveland Clinic ($p<0.02$.)

MACE in Patients Treated with RVX000222 (Subgroup of Patients with elevated hsCRP)



Cleveland Clinic
Cleveland, Ohio

Effects of an Apolipoprotein A-1 Inducer On Progression of Coronary Atherosclerosis and Cardiovascular Events In Patients with Elevated Inflammatory Markers

[1]R Puri, [2]Y Kataoka, [1]K Wolski, [3]A Gordon, [3]J Johansson, [3]N Wong, [1]S Nissen, [2]SJ Nicholls

1. Cleveland Clinic & CSResearch, Cleveland, USA; 2. South Australian Health & Medical Research Institute, Adelaide, Australia; 3. Resverlogix Corporation, Calgary, Canada

Background and Aims

Persistent cardiovascular risk, despite the concomitant use of established medical therapies, has stimulated intense interest in developing novel strategies for secondary prevention in patients with coronary artery disease. Favorable findings from pre-clinical and human studies has resulted in the development of numerous agents that promote greater levels or activity of high-density lipoproteins (HDL). However to date, other than infusing delipidated forms of HDL, the success of HDL cholesterol raising therapies has been disappointing.

Inducing the synthesis of apolipoprotein A1 (apoA1), the major protein associated with HDL particles, represents a novel means of lipid modification., whereby enhanced hepatic synthesis of apoA1 should theoretically generate new HDL particles resulting in greater biological activity of HDL. The bromodomain and extra-terminal (BET) inhibitor, RVX-208, demonstrated increased apoA1 and HDL cholesterol levels and enhanced cholesterol efflux activity.

ASSURE (ApoA1 Synthesis Stimulation and Intravascular Ultrasound for Coronary Atheroma Regression Evaluation study, NCT 01067820) was a 26-week, double-blind, randomized, multicenter serial intravascular ultrasound (IVUS) trial to determine the impact of RVX-208 on the burden of coronary atherosclerosis in patients with angiographic coronary atherosclerosis (≥20%, but <50% angiographic stenosis in at least 1 epicardial coronary artery) and low (≤45 mg/dL in women, ≤40 mg/dL in men) HDL cholesterol levels. Background rosuvastatin (5-20 mg daily) or atorvastatin (10-40 mg daily) was also required. Although RVX-208 induced plaque regression from baseline, the primary & secondary efficacy endpoints in ASSURE, the IVUS-derived change in percent atheroma volume (PAV) and total atheroma volume (TAV) improved, but did not differ compared with placebo.

Inflammation is involved in all stages of atherosclerosis, and elevations of serum inflammatory biomarkers consistently associate with the risk of experiencing a cardiovascular event. Accordingly, the aim of this analysis was to explore the potential anti-atherosclerotic efficacy of upregulating endogenous apoA1 with RVX-208 in patients stratified according to baseline degrees of systemic inflammation from ASSURE.

Methods

In ASSURE, 323 patients were randomized in a 3:1 fashion to RVX-208 or placebo for 26 weeks. Disease progression was measured by repeat IVUS examination upon study completion. Lipid levels and major adverse cardiovascular events (MACE), defined as death, non-fatal myocardial infarction, stroke, coronary revasoularization, or hospitalization for unstable angina or heart failure) were also assessed.

Table 1: Baseline demographic, clinical & biochemical factors

Parameter	PLACEBO CRP <2mg/L N=27	PLACEBO CRP≥2 mg/L N=83	RVX-208 CRP <2mg/L N=111	RVX-208 CRP ≥2 mg/L N=130	P-Value
Age, yrs	56.3±9.7	58.3±9.6	59.0±8.9	57.9±8.0	0.43
Male, n (%)	22 (82)	35 (66)	85 (77)	102 (79)	0.29
Diabetes, n (%)	3 (11)	20 (38)	33 (30)	42 (32.3)	0.097
Hypertension, n (%)	23 (85)	46 (87)	80 (72)	111 (85.4)	0.032
Prior MI, n (%)	12 (44)	20 (38)	51 (46)	46 (35)	0.37
LDL-C (mg/dL)	92 (69, 112)	93 (71, 120)	93 (69, 120)	93 (73, 120)	0.71
HDL-C (mg/dL)	39 (31, 42)	39 (35, 42)	39 (35, 42)	38 (31, 42)	0.044
Triglycerides (mg/dL)	118 (93, 139)	139 (100, 185)	132 (81, 198)	140 (104, 175)	0.52
Non-HDL-C (mg/dL)	108 (93, 139)	116 (100, 185)	116 (89, 151)	120 (100, 147)	0.66
ApoA1 (mg/dL)	113 (102, 121)	117 (105, 129)	122 (108, 133)	116 (102, 126)	0.022
ApoB (mg/dL)	81 (72, 96)	85 (72, 106)	86 (65, 105)	84 (71, 102)	0.64
CRP (mg/L)	1.1 (0.5, 1.6)	5.0 (3.1, 8.1)	1.1 (0.6, 1.5)	5.1(3.3, 9.3)	<0.001

Values: are mean±SD or median (IQR) where necessary
P-value is for a trend across groups
CRP = C-Reactive protein; HDL = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol;
MI = myocardial infarction

Table 2: Ultrasonic plaque parameters

Parameter	CRP <2 mg/L Placebo N=27	CRP <2 mg/L RVX-208 N=111	P-Value	CRP ≥2 mg/L Placebo N=53	CRP ≥2 mg/L RVX-208 N=130	P-Value
Baseline PAV (%)	36 (30, 40)	38 (33, 44)	0.38	37 (32, 47)	38 (32, 45)	0.65
Change in PAV (%)	0.6 (-1.5, 1.4)	0 (-1.6, 1.4)	0.72	-0.5 (-2.0, 1.2)	-0.7 (-2.0, 1.2)	0.98
p-value for Δ from baseline	*0.81*	*0.78*		*0.08*	*0.039*	
Baseline TAV (mm³)	161 (110, 249)	197 (151, 252)	0.055	162 (118, 208)	198 (138, 255)	0.023
Change in TAV (mm³)	-3.8 (-9.8, 5.3)	0.8 (-12, 7.1)	0.71	-3.1 (-12, 2.8)	-5.7 (-18, 4.4)	0.45
p-value for Δ from baseline	*0.30*	*0.39*		*0.02*	*<0.001*	

Values: are mean±SD or median (IQR) where necessary
P-values: represent pairwise comparisons within each group stratified according to baseline CRP level
PAV = percent atheroma volume; TAV = total atheroma volume
Changes in PAV and TAV is the absolute difference of the follow-up value minus the respective baseline value

Table 3: Major adverse cardiovascular events

Parameter	CRP <2 mg/L Placebo N=27	CRP <2 mg/L RVX-208 N=111	P-Value	CRP ≥2 mg/L Placebo N=53	CRP ≥2 mg/L RVX-208 N=130	P-Value
MACE, n (%)	1 (3.7)	9 (8.1)	0.69	10 (18.9)	9 (6.9)	0.016
Death	0	0	N/A	1 (1.9)	0	0.29
MI	0	2 (1.8)	1.0	1 (1.9)	2 (1.5)	1.0
Stroke	0	0	N/A	0	0	N/A
Revasc	1 (3.7)	6 (5.4)	1.0	6 (11.3)	5 (3.8)	0.082
Hosp	0	2 (1.8)	1.0	3 (5.7)	3 (2.3)	0.36

P-values: represent pairwise comparison within each group stratified according to baseline CRP level
MI = myocardial infarction; Revasc = coronary revascularization; Hosp = hospitalization for unstable angina or heart failure

Results

Table 1 describes demographic, clinical and biochemical characteristics at baseline within the groups receiving RVX-208 or placebo, stratified according to baseline CRP level. Differences were noted across all 4 groups for the incidence of hypertension, including differences of HDL-C, ApoA1 and CRP. In the RVX-2-8 group, apoA1 and HDL-C increased by 12.8% and 11.1% respectively (P<0.001 from baseline for both) (data not shown).

Table 2 describes ultrasonic plaque parameters at baseline and following treatment. For those individuals with baseline CRP levels <2 mg/L, no significant differences were found for changes in PAV or TAV from baseline within each treatment group, or between treatment groups. For individuals with baseline CRP ≥2 mg/L, RVX-208 caused significant reductions from baseline in both PAV and TAV, whereas the placebo group experienced a reduction from baseline in TAV only.

Table 3 describes MACE rates according to baseline CRP level and treatment. Overall, a lower MACE was observed in RVX-208-treated patients with baseline CRP levels ≥2 mg/L.

Conclusions

Potentially more favorable effects of the apoA1 inducer, RVX-208, on coronary disease progression and MACE were observed in patients with higher levels of systemic inflammation. These findings need confirmation in larger, prospective studies

ASSURE was funded by Resverlogix Corporation (NCT 01067820)

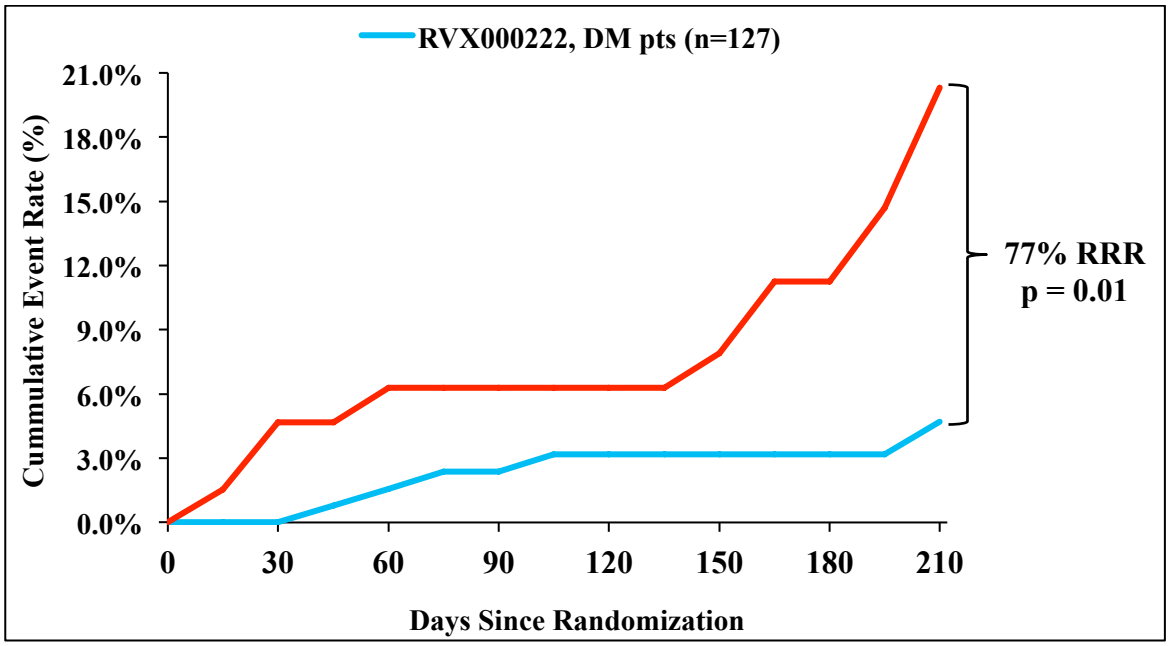
Data Reported ACC 2014: Puri et al Cleveland Clinic – MACE p <0.02

These findings in patients with elevated vascular inflammation risk prompted the company to perform additional exploratory analysis in patients with elevated risk. On 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 at - *"State of the Art – Innovation in Acute Coronary Syndrome Session"*.

MACE in Patients Treated with RVX000222 (Subgroup of Patients with Diabetes Mellitus)



Source: RVX data on file – ASSURE and SUSTAIN Safety Population. Log-Rank test for between group comparison. Relative risk reduction is calculated based on Kaplan-Meier estimates of event rate.

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 biological plausibility of these findings will be further analysed to elucidate the potential mechanism or mechanisms driving this risk reduction.

CVD Risk: More than just lipids

Although the risk of cardiovascular disease in patients with diabetes and CKD can be 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

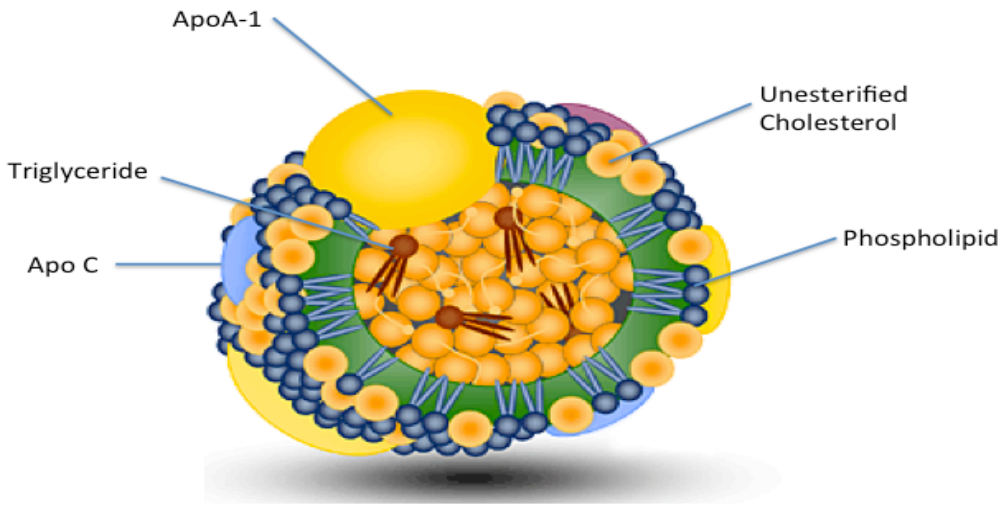
The LDL lowering hypothesis is being further tested in CVD risk with aggressive reduction of LDL lowering to unprecedented levels such as 40-50mg/dl. Newly reported trials such ODYSSEY LONG TERM, PSCK9 LDL lowering approach via Alirocumab (ESC Barcelona 2014) and IMPROVE IT, cholesterol absorption LDL 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	50% (p<0.02)	92
SUSTAIN ASSURE	BET Inhibition	90mg/dl	493	0.4-0.5	45% (p<0.02)	21

Although both IMPROVE IT and Odyssey Long Term were significant in lowering MACE in their respective trials with a reported USD 5-8K a year treatment cost per patient the cost to prevents an event could be argued to be somewhere in the area of USD 500-700K per event based on a simple analysis of NNT (numbers needed to treat) based on annualized treatment therapy. It is critical to realize that when building a value proposition, the lower 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. Payer groups such as NICE and US Managed Care organizations such as now demanding “value for money” if any new drugs are seeking rapid reimbursement, product positioning and uptake on their respective formularies.

HDL and ApoA-I: Reverse Cholesterol Transport

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 will result 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, 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

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%. 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 bad 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.

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)	*P*-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 RVX-208. 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 RVX-208 treatment represent a new treatment paradigm for high risk.

Vascular Inflammation

Reported by Libby in "Clinical Cardiology New Frontiers" Atherosclerosis, formerly was considered a bland lipid storage disease, has moved beyond on 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 Haptoglobn, IL-18 and VCAM-1 were also reduced in animal models vs. placebo by RVX-208, 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.

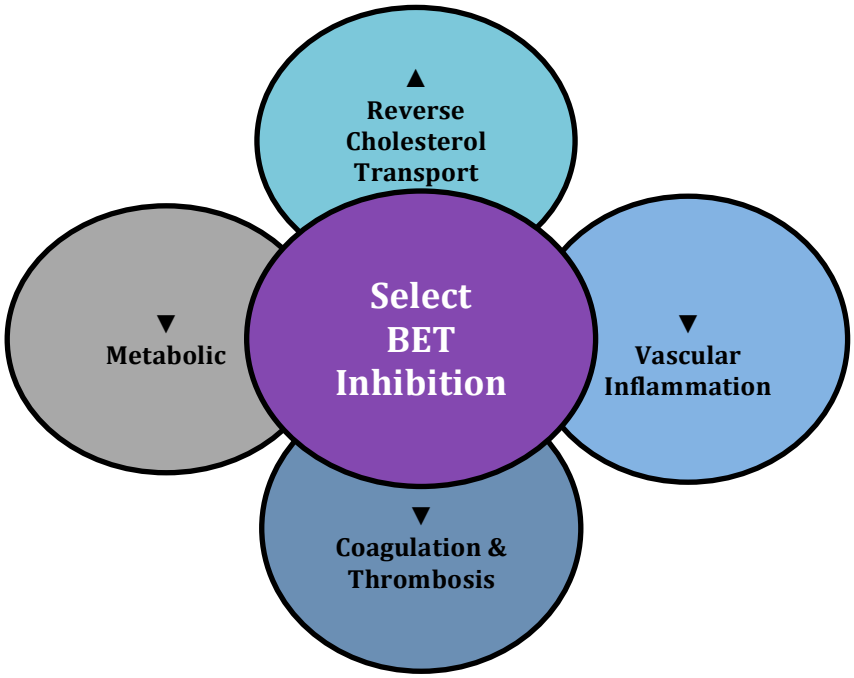
Mean Levels of serum cytokines

Group	Haptoglobin	VCAM-1	IL-18
Vehicle	128	2311	9.9
RVX-208	47	1911	7.8
P – value	0.001	0.004	0.056

Source: Atherosclerosis 2014: R.Jahagirdar

Certain treatments that reduce coronary risk and have clear relationships with

reduced vascular inflammation and other markers of vascular risk may offer a new way of thinking to tackling the number one killer of patients in the US and worldwide. A single target, BET inhibition, and multiple pathway approach is novel and highly differentiated in the field of secondary prevention of MACE and reducing vascular risk. If observed again prospectively in an larger clinical setting a "efficient" BET approach to reduce MACE versus single target approached such as LDL and glucose reduction for patients with high residual risk such as diabetes and CKD patients will be highly sought after. The following Venn-diagram illustrates the potential multiple pathways of risk that BET inhibition by RVX-208 have reported, thus providing a biological plausibility of the early marked reduction of MACE observed thus far in the PHASE IIb SUSTAIN and ASSURE clinical trials.



RVX-208: Clinical Overview

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. Final planning stages for its Phase III trial BETonMACE, will focus on secondary prevention of MACE.

Overview Clinical Trials RVX-208

Trial	Summary	Patients	Status	Initiated	Data Release
Phase III	MACE reduction BETonMACE	1600-3200	Pending	TBD	TBD
Phase IIb	Alzheimer's disease	45-60	Pending	TBD	TBD
Phase IIb	Pre-diabetes mellitus/effects of RVX-208 and ApoA-I production on glucose metabolism	20	Completed	2012Q4	2014Q3
Phase IIb ASSURE	26 week risk stratified IVUS study in patients with low HDL	323	Completed	2011Q2	2013Q2
Phase IIb SUSTAIN	24 week single dose safety, tolerability and efficacy in stable CVD patients with low HDL	176	Completed	2011Q3	2012Q3
Phase II ASSERT	12 week dose ranging safety, tolerability and efficacy in stable CVD patients	299	Completed	2009Q4	2010Q4
Phase Ib/IIa	28 day multiple dosing safety, tolerability and efficacy in healthy volunteers with low HDL	72	Completed	2008Q3	2009Q3
Phase I BE	Single dose bio-equivalency comparing capsule and tablet drug form	9	Completed	2009Q3	N/A
Phase I BE	Single dose bio equivalency	7	Completed	2009Q3	2009Q4

Phase Ia	First in man single ascending dose and 7-day multiple dosing	80	Completed	2007Q4	2008Q1

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.

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.

ASSERT Clinical Trial (Phase II 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.

Clinical Trial Pre-Diabetes: (completed)

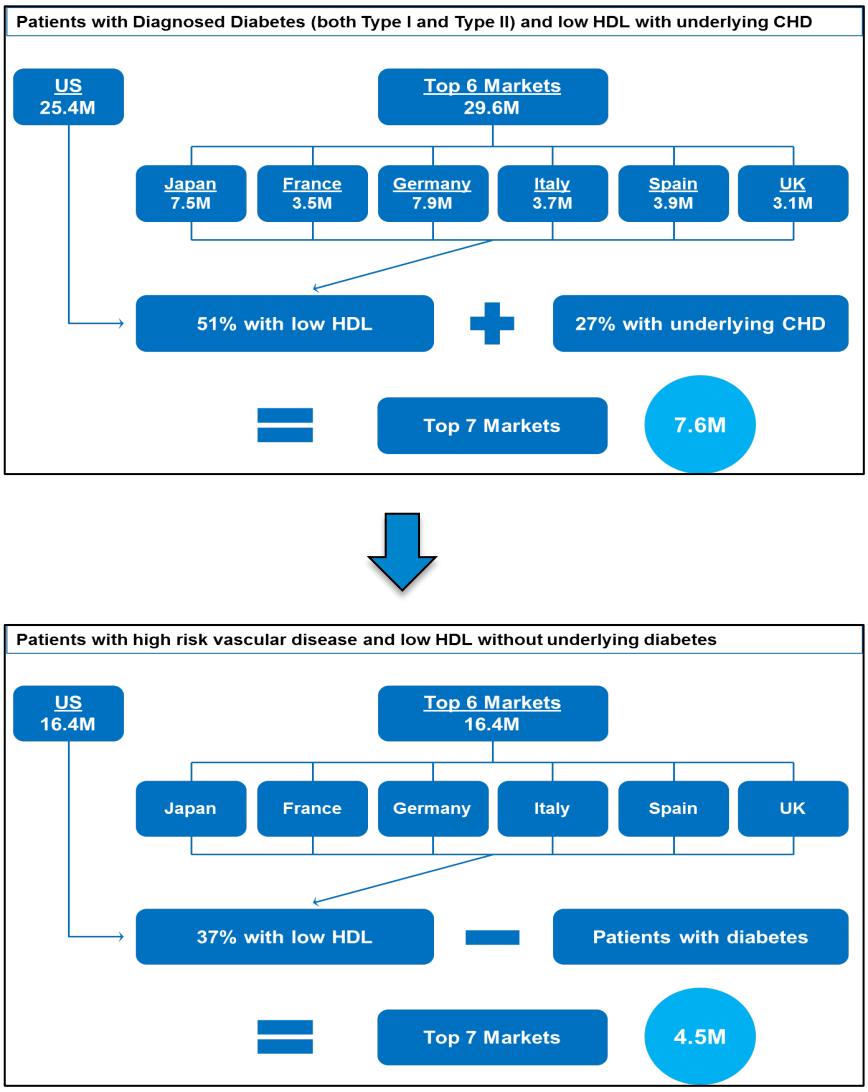
In October 2012, Resverlogix initiated an exploratory Phase 2 clinical trial in patients with pre-diabetes mellitus to examine the effects of RVX-208 and ApoA-I production on glucose metabolism. Dosing concluded in March 2014. On July 23, 2014, the company announced that the preliminary results of the 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).

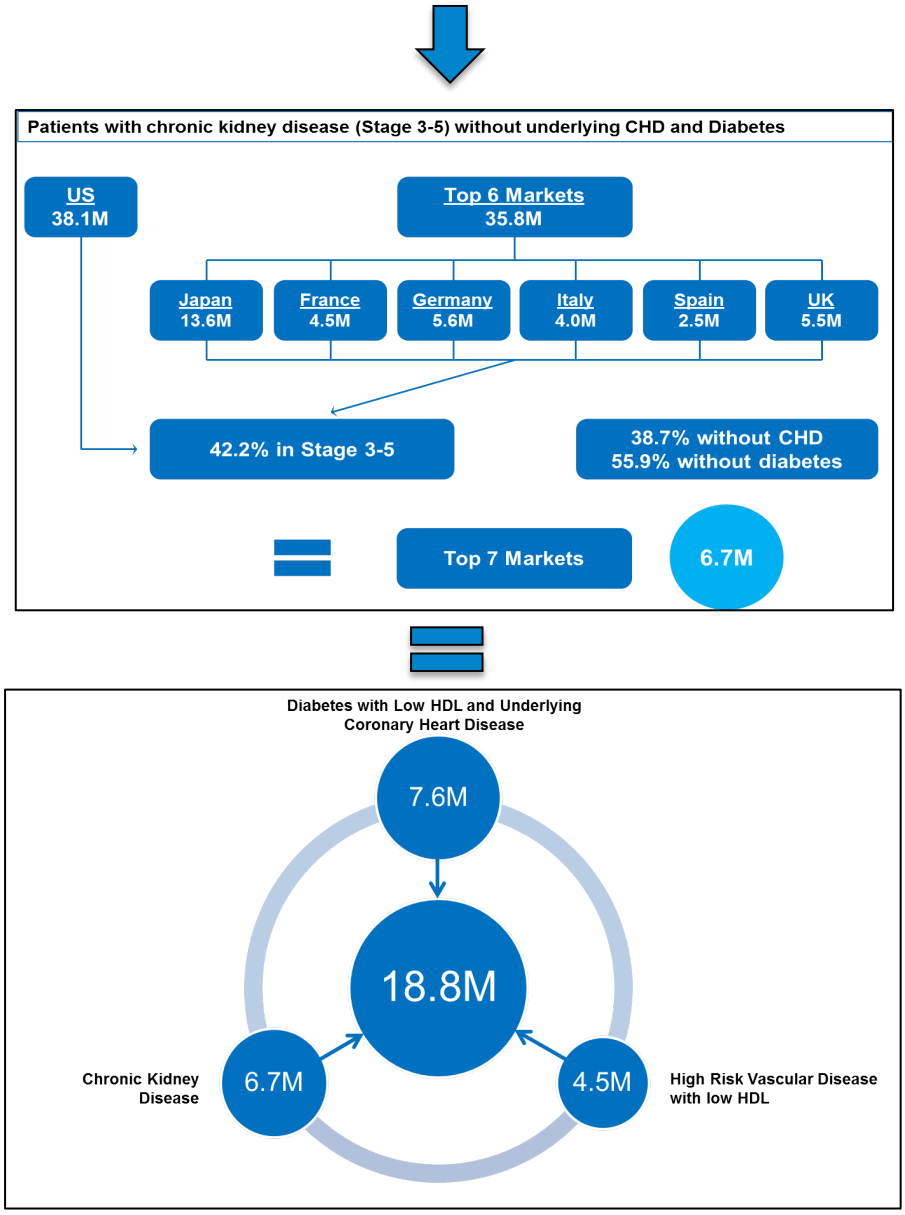
Phase III BETonMACE (MACE-Related Trial – Pending)

Resverlogix intends to reconfirm in a larger prospective setting with patients that have modifiable vascular disease (i.e. low HDL-C and diabetes) positive effects on markers of vascular risk and reduction of MACE. Confirmation of this trial would establish a very strong value proposition for a Phase III registration trial, which would incorporate MACE as the primary endpoint. The planned trial will have a minimum of 1600 patients up to 3200 patients with and a planned average of 18 months of treatment duration.

RVX 208 Valuation: Blockbuster potential

The Company 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 Internal projections based AHA 2015 statistics, 2014 IDF Atlas, 2013 US RDS CKD Report and current patient population studies

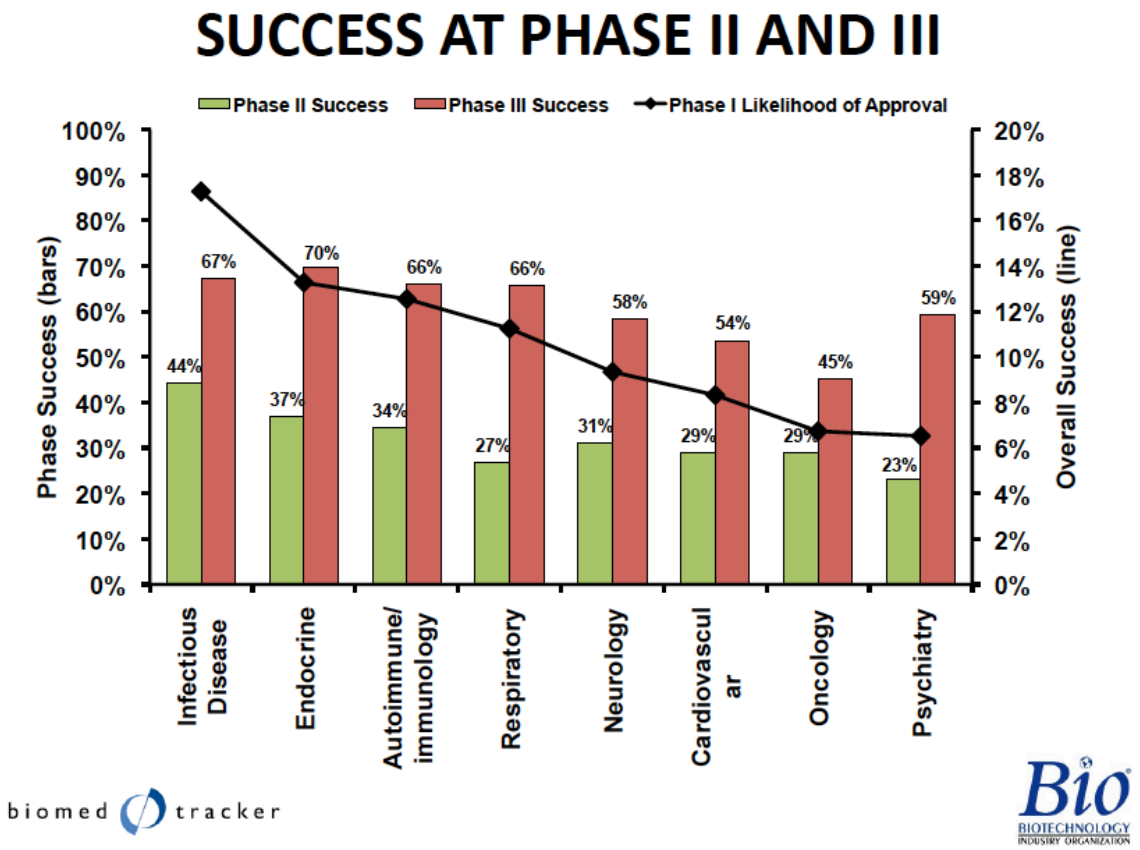
The total target patient population of **18.8** million patients eligible for RVX-208 treatment represents a very significantly group of residual risk patients. Detailed notes of patient segment modeling are contained within the appendix.

Key Value Assumptions

We value RVX-208, and thereby Resverlogix as a whole at CAD 500 million or CAD 5.85 per share. This is based on 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 RVX-208 and therefore only to make a valuation of the current clinical pipeline of RVX-208. We feel that potential value of its platform and additional indications offers an additional upside potential. With the start of a large Phase III clinical trial we estimate a probability of success of 54%. This is based on an independent survey executed by BioMedTracker and BIO in 2012[1]. See also the graph below.

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, Deutsche Bank 2012 Report.

1 Clinical Development Success Rates for Investigational Drugs, Pharma CI2012



We expect an approval of RVX-208 in the US in 2018 as well as approval in the EU and Japan. We ascribe CAD 5.85 per share to RVX-208 based on a risk-adjusted NPV analysis of estimated its net income in the next 10 years, assuming approval and a 2018 launch.

We estimate a 20% cost-of-goods and a 20% discount rate. We make use of a probability adjusted NPV, which is dependent on the success rate and development stage of RVX-208.

The total market potential for RVX-208 is large and based on the potential number of patients in the US, EU and Japan.

SWOT Analysis

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 modeling 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

Analyst: Marcel Wijma MSc
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.

Disclaimer
The facts stated and the opinion and prognoses given in this publication are based on data and information considered to be reliable and have been carefully worked into our analyses and prognoses. However, no guarantee can be given as to their fairness, accuracy or completeness. Van Leeuwenhoeck Institute. does not accept responsibility or liability in any way in respect to the information stated herein. Van Leeuwenhoeck Institute does not hold or have positions in securities as referred to in this publication.

The views expressed in this publication accurately reflect the analyst's personal views on the subject securities or issuer. Neither the analyst's compensation nor the compensation received by Van Leeuwenhoeck Institute is in any way related to the specific recommendations or views contained in this publication.

Any investments referred to herein may involve significant risk, are not necessarily available in all jurisdictions, may be illiquid and may not be suitable for all investors. The value of, or income from, any investments referred to herein may fluctuate and/or be affected by changes in exchange rates. Past performances are not indicative for future results. Investors should make their own investment decisions without relying on this publication.

Only investors with sufficient knowledge and experience in financial matters to evaluate the merits and risks should consider an investment in any issuer or market discussed herein and other persons should not take any action on the basis of this publication.

Information, opinions or recommendations contained in this publication are submitted solely for advisory and information purposes. The information used and statements of fact made, have been obtained from sources considered reliable, but we neither guarantee nor represent the completeness or accuracy. Such information and the opinions expressed are subject to change without notice. This publication is not intended as an offering or a solicitation of an offer to buy or sell the securities mentioned or discussed.

Van Leeuwenhoeck Institute does not accept any equity compensation. Reports are performed on behalf of the public, and are not a service to any company. The analysts are responsible only to the public, and are paid in advance to eliminate pecuniary interests and insure independence.

Periodic Research reports and research notes on this Company are available at our web site: www.leeuwenhoeck.com