



UPDATE REPORT

Resverlogix

FDA Guidance and Potential in Dementia Creates Additional Upside



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Date: 24 July 2018

Name:	Resverlogix Corp.
Country:	Canada
Price:	CAD 2.41
ISIN Code:	CA76128M1086
Reuters Code:	RVX.TO
Market Cap (CAD m):	421.8
EV (CAD m):	421.8
Cash & cash eq. (CAD m):	40.0
Shares outstanding (m):	175.0
Volume:	157,603
Free float:	45%
52-week Range:	1.11-2.75

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



Executive Summary

- Resverlogix has developed an epigenetic drug development platform that has the potential to impact multiple diseases including high risk CVD in diabetes, chronic kidney disease (CKD), and neurodegenerative diseases such as dementia. 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 the past 6 months, Resverlogix has made important steps towards finalizing its pivotal Phase III BETonMACE trial with its leads product apabetalone in high risk CVD patients with Type 2 diabetes and low HDL. This trial started in November 2015 and exceeded full enrollment of 2,400 patients in March this year. The primary endpoint of the BETonMACE trial is designed to establish a relative risk reduction (RRR) of Major Adverse Cardiac Events (MACE), narrowly defined as a single composite endpoint of cardiovascular death, non-fatal myocardial infarction (MI) and stroke. Secondary pre-specified endpoints such as renal function (eGFR) in CKD Stage 3 patients and Cognition analysis via Montreal cognitive score (MoCA) are also planned.
- A prespecified interim analysis of MACE events is estimated to occur in the second half of this year. Previously, Apabetalone (RVX-208) has been successfully tested in about 1,000 patients in various clinical studies (ASSERT, SUSTAIN and ASSURE). The company has a planned Phase II 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 June, the FDA confirmed that if the Phase III BETonMACE study is successful, it will probably be enough to support the filing and approval of an NDA. The FDA's feedback is similar to that received previously from European authorities. Earlier this year, the study Data and Safety Monitoring Board (DSMB) completed a sixth safety review and recommended that the study should continue without any modifications.



- The need for new therapies that can actually improve the cognitive functions of patients with early Dementia/AD is mounting whereas the number of clinical trials to date that illustrated an improvement on cognition for this indication has been very limited. A pre-specified analysis of the phase III trial BETonMACE will examine the effects of apabetalone on cognitive function in patients at least 70 years of age using the Montreal Cognitive Assessment (MoCA). A specific target of this group will be those patients who have a baseline of below 26, which is indicative of mild cognitive decline. Upon completion of the study, it is estimated that approximately 460 patients will have undergone MoCA testing in the entire group and approximately 240 in the below 26 MoCA group, with a median exposure to study treatment of 20 months (range 6-36). The Company announced key presentations at the Alzheimer's conferences AAIC and CTAD conferences this summer and fall. Any improvement in cognition in the BETonMACE trial will be viewed as a very innovative approach as well as a positive step for the field, which is in dire need for new therapies.
- We have increased our valuation following very encouraging news from the FDA which encouraged us to lower the discount rate and increase the LOA for apabetalone in high risk diabetes and CKD patients. We also increased the number of potential patients by adding a Phase III subgroup of CVD patients with dementia/VCI. We believe that Resverlogix remains gravely undervalued at the current share price of CAD 2.34. We feel that the company's current total value should be CAD 3.3 billion, or CAD 19.00 per share. This represents a substantial upside from the current share price.



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.

Epigenetics and Apabetalone as First in Class BET Antagonist

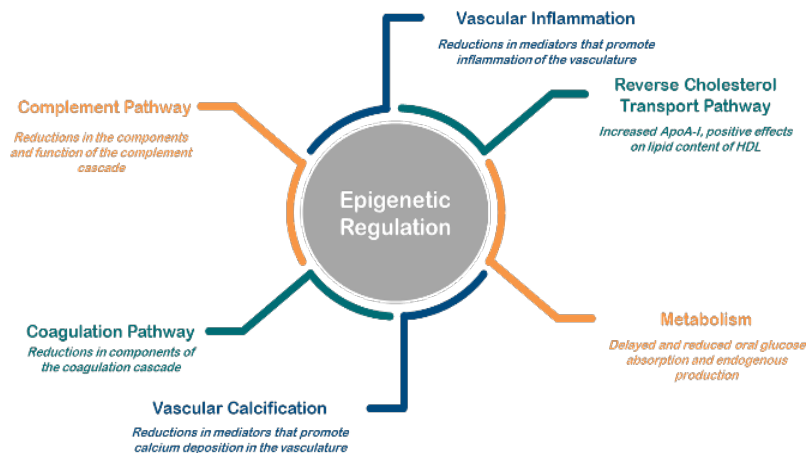
Apabetalone acts upon multiple pathways and genes that drive vascular risk such as: (i) reduction of key vascular inflammation and calcification markers, (ii) regulation of complement, coagulation and acute phase response cascades, known drivers in cardiovascular disease and MACE, (iii) enhancement of 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 prevents the reading of 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 and NLR, 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.



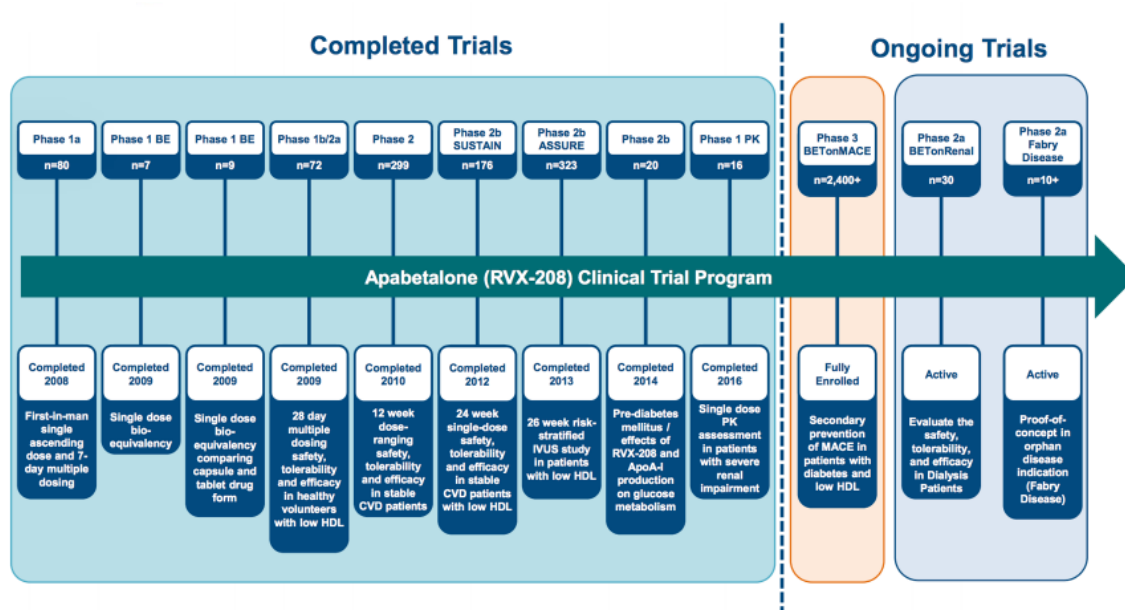
Epigenetic gene regulation governed by BET proteins is at the core of many CVD pathological processes – Apabetalone regulates the expression of genes and restores the function of pathways underlying the pathogenesis of multiple diseases

Source: Resverlogix

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 a co-morbidity. Further patient targeting will be performed by evaluation of a CKD subgroup and cognitive subgroup in the current Phase III BETonMACE trial. Apabetalone has been tested in over 2,400 patients in 19 countries, and clinical experience with apabetalone has demonstrated to date that select 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



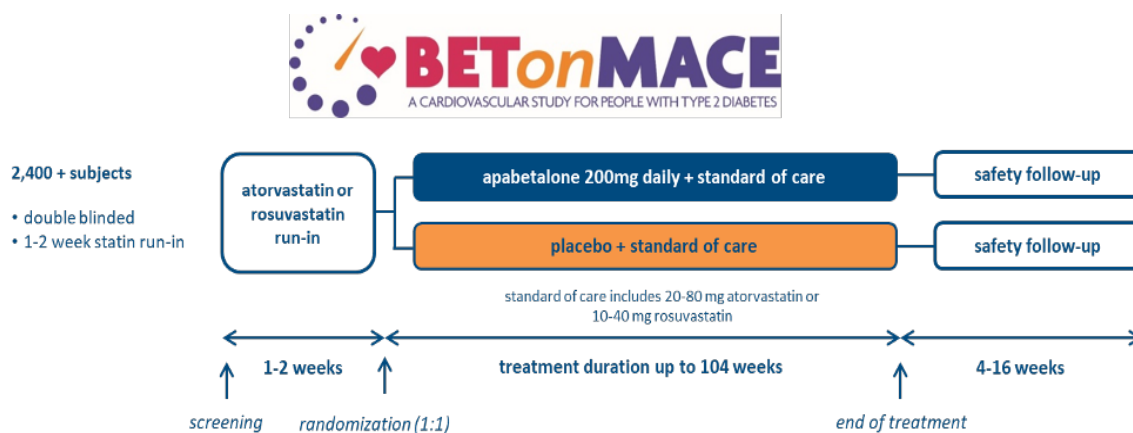
Source: Resverlogix



Apabetalone Phase III BETonMACE Clinical Trial in High Risk CVD Patients

In October 2015, Resverlogix initiated 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. Full enrollment of 2,400 patients was reached earlier this year. 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 other 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 approximately 8 per 100 patient years. This higher risk target patient group, approximately 3-5 times higher than other CVD outcome trial populations, allows 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 is being adjudicated by an independent committee and the study is being monitored by a data safety monitoring board. The trial is seeking a 25-30% reduction in MACE as compared to the placebo arm which is treated with best standard of care medicines such as beta blockers, high dose statins and dual platelet inhibitors.

Design of the BETonMACE Clinical Trial



Source: Resverlogix

The independent Data and Safety Monitoring Board for the BETonMACE trial completed six planned safety reviews of the trial (in August 2016, December 2016, March 2017, June 2017, and November 2017 respectively). On February 26, 2018, the 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. We feel however, that this might happen sooner with 125 primary MACE events. Topline data are expected towards the end of this year or early next year. **Furthermore, in June the FDA confirmed that if the Phase III BETonMACE study is successful, it will probably be enough to support the filing and approval of an NDA.** The FDA's feedback is similar to that received previously from European authorities.

BETonMACE is also examining 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 (mL/min/1.72 m²). 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 a total of approximately 300 CKD patients will be in the BETonMACE trial. The rationale for examining

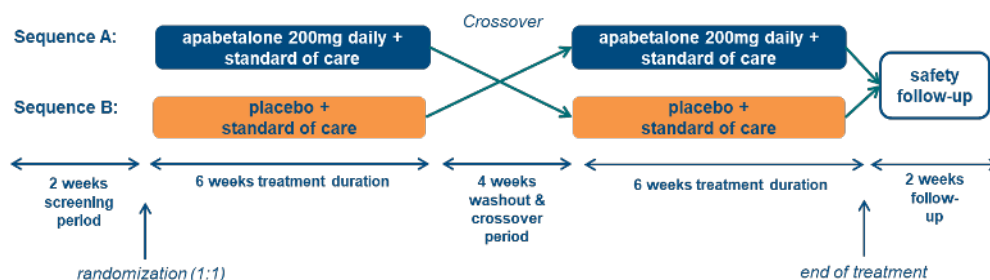


this important subgroup of patients is the eGFR data from the phase II ASSURE and SUSTAIN clinical trials and the proteomic data from the phase 1 PK clinical trial. These findings have been reported last year at the American Society of Nephrology (ASN) Kidney Week Conference and European Renal Association-European 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.

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

Resverlogix has a Phase IIa clinical study planned in patients with end-stage renal disease that are treated with hemodialysis. The primary objective of the study is 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



Source: Resverlogix

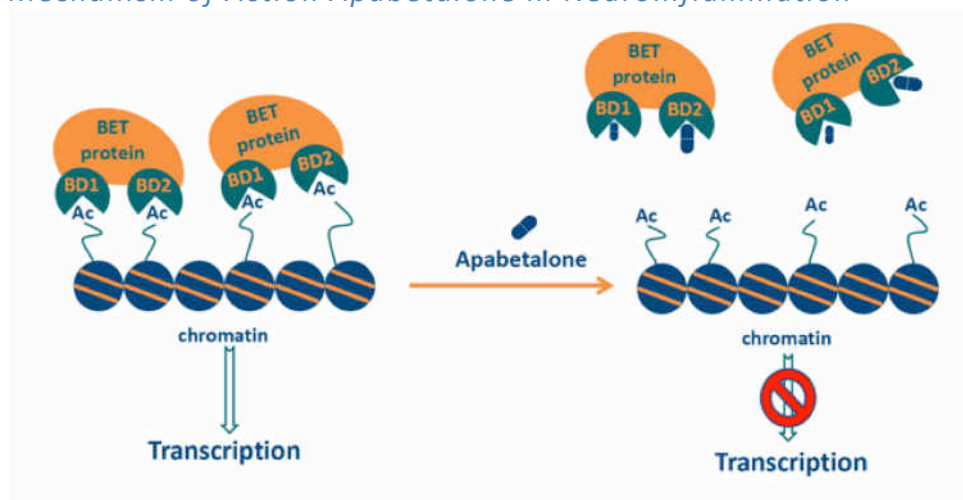


Late stage Chronic Kidney Disease (CKD) encompasses CKD stages 4 and 5. It can be alternatively defined as an estimated glomerular filtration rate (eGFR) of $<30 \text{ ml/min/1.73m}^2$. Reported in the 2016 United States Renal Data System (USRDS) Annual Report, approximately 1.4 million patients in 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 as Neurodegenerative Disease Opportunity

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 450-500 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.

Mechanism of Action Apabetalone in Neuroinflammation

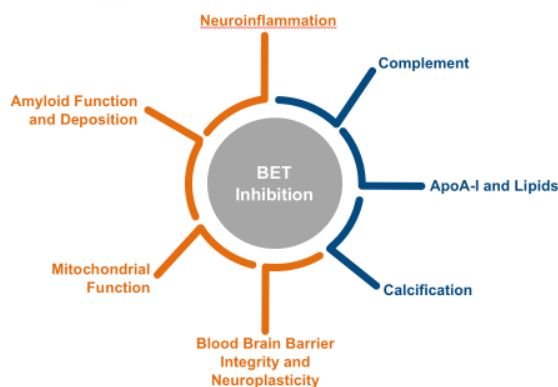


BET proteins such as BRD4, bind acetylated lysine (Ac) on proteins such as histones via bromodomains (BD) and recruit transcriptional machinery to drive expression of BET sensitive genes. Apabetalone inhibits BET bromodomains, causing release from chromatin and



downregulation of BET sensitive gene expression which may drive neuroinflammation and other key drivers of cognitive decline.

There is substantial evidence that histone acetylation plays a key role in memory consolidation and deregulated histone acetylation has been linked to neurodegenerative diseases such as Alzheimer's disease (AD). The histone acetylation landscape is shaped by the counteracting activity of so-called 'writer' and 'eraser' proteins that add or remove acetyl groups from histone proteins (see also earlier page 5 and 6). Histone deacetylases (HDACs) that constitute part of the 'eraser' activity in particular have gained increasing interest, since HDAC inhibitors were shown to ameliorate disease phenotypes in models for various neurodegenerative diseases. In contrast, there is only limited knowledge about the role of 'chromatin readers' that recognize combinatorial patterns of histone modifications and thus provide the essential link between histone changes and corresponding changes in cellular function. The Bromodomain Extraterminal (BET) subfamily of chromatin readers is highly specific toward acetylated histone tails. This is very interesting, as BRD2 and BRD4 preferentially bind H4K12ac. Moreover, H4K5ac and H4K12ac were specifically linked to memory function and age associated memory impairment



Source: Resverlogix

Calcification, plasticity, inflammation, and complement pathways have all been implicated in the progression of vascular cognitive impairment. Apabetalone has been shown to affect these key pathways by regulating specific proteins that are known risk drivers in vascular cognitive



impairment. Vascular Cognitive Impairment (VCI) is increased in cardiometabolic disease with no treatments available.

Recent findings indicate the importance of BET in cognitive impairment, including Alzheimer's disease (Liang, E. et al. 2018; Benito, E. et al. 2017; Magistri, M. et al. 2016). Exploratory serum proteomics studies from Phase II studies suggest BET inhibition affects several biological systems, including A β metabolism, blood-brain barrier integrity, mitochondria / energy, and neuroplasticity.

MoCA vs MMSE: MoCA is much more sensitive

The Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA), often used in clinical practice as a quick screen for Alzheimer disease (AD) or mild cognitive impairment (MCI), get high marks for diagnostic accuracy in a study of community-dwelling older adults, according to a study done by researchers from the University of Pennsylvania in Philadelphia. But the study also suggests that as a brief, stand-alone cognitive screening measure, the MoCA seems to be more sensitive than the more widely used MMSE. What's more, using the optimal cutoff score, the MoCA's classification accuracy exceeded that of the MMSE for differentiating MCI from healthy age-related changes. Researchers recruited 321 patients with AD, 126 with MCI, and 140 with healthy cognitive aging (HC) from the Penn Memory Center and Clinical Core of the University of Pennsylvania's Alzheimer's Disease Center. The researchers say their findings build on previous ones that the MoCA is a superior screen compared with the MMSE for detecting AD and MCI. "More striking" was the accuracy of the MoCA at differentiating MCI from HC. The MoCA was also more useful in a particularly challenging area: subtle transition in clinical status. The data suggest that the MoCA may be more sensitive to early changes in cognitive ability, as it includes more robust measures of visuospatial and executive functions, the researchers say. Because the MoCA shows a wider range of performances in AD and MCI than the MMSE does, the MoCA could be used to determine differing levels of severity or subtypes of MCI, they suggest. This is particularly important, they add, as the diagnosis of MCI or AD increases with age, and thus, performance on the MMSE or MoCA may systematically differ in an 80-year-old patient with MCI, compared with a 60-year-old patient with MCI.



Valuation Apabetalone: Upward Adjustment

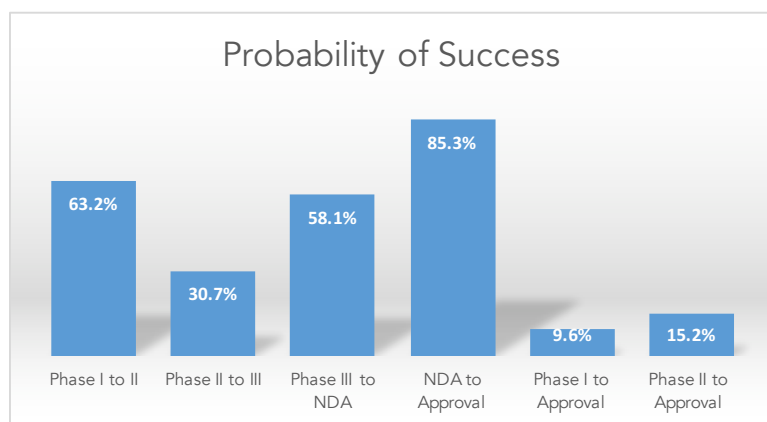
We have increased our valuation on Resverlogix to CAD 3.3 billion or CAD 19.00 per share from CAD 2,500 million or CAD 12.50 per share due to the fact that we have increased the LOA for Resverlogix' lead product apabetalone to 65% and reduced the discount rate used from 15% to 12% following the positive recommendation from the FDA regarding the ongoing Phase III BETonMACE trial (see earlier in this report). We also have taken into account the start of a Phase III trial with BETonMACE in a subgroup of VCI/Demetia in elderly with diabetes. This group of patients is estimated to be more than 3 million in the US, Europe and Japan together. 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.

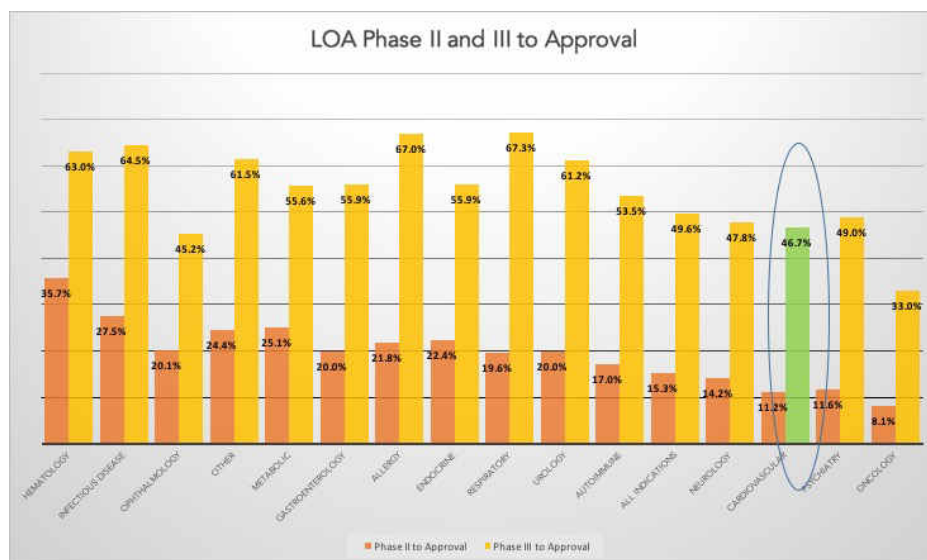
The Phase I transition success rate was 63.2% (n=3,582). As this Phase is typically conducted for safety testing and is not dependent on efficacy results for candidates to advance, it is common for this phase to have the highest success rate among the clinical phases across most categories analyzed in 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.

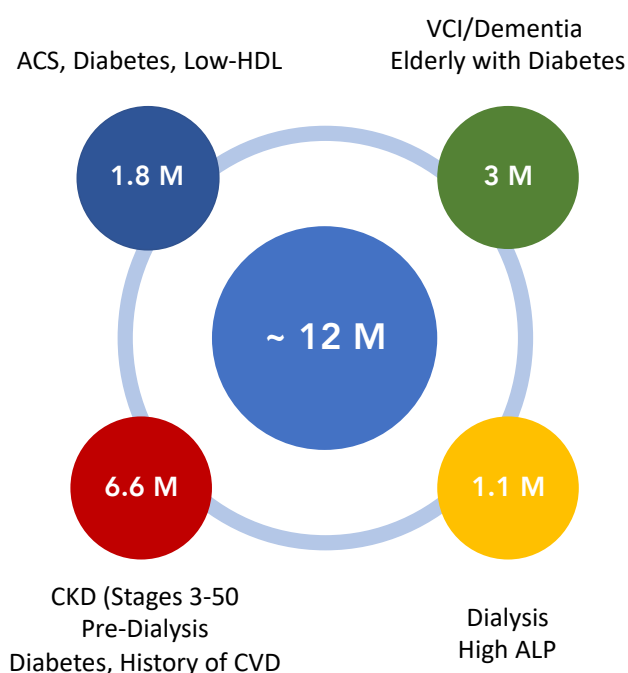


Key Value Assumptions

We have increased our value on apabetalone, and thereby Resverlogix as a whole from CAD 2.5 billion million to CAD 3.3 billion or CAD 19.00 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. We have increased our LOA following the positive recommendation of the FDA and EMA on the ongoing BETonMACE trial. We have also now included a potential Phase III for the cognition subgroup in BETonMACE. 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 full enrolment of all patients needed for the Phase III clinical trial we have increased the LOA to 65% from 55%. For the Phase IIA trial in CKD, we have assumed a LOA of 40%. The same LOA will be applicable for the VCI/Dementia trial

We expect an approval of apabetalone in the US, EU and Japan in 2021 for ACS, 2022 for CKD/Dialysis and 2023 for VCI/Dementia. We ascribe CAD 19.00 per share to apabetalone for high risk CVD, Diabetes mellitus, CKD and in VCI/dementia based on a risk-adjusted NPV analysis of the estimated net income in the next 10 years, assuming approval and market entries in 2021, 2022 and 2023 respectively. 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, VCI/Dementia, CKD Pre-Dialysis and Dialysis. 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 12 million high risk target patients in the top markets. Below are patient segmentation charts that outline the flow of these patients from the overall diabetes, high risk vascular, VCI and CKD patient groups.



Source: RVX internal projections

The total target patient population of **12.5** million patients eligible for apabetalone treatment represents a very significant group of residual risk patients.



Valuation apabetalone in ACS with Diabetes and Low HDL

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
MARKET SHARE US	0.6%	1.5%	3.0%	5.0%	7.0%	10.0%	12.0%	14.0%	16.0%	18.0%	19.0%
MARKET SHARE EU	0.5%	1.5%	3.0%	5.0%	7.0%	10.0%	12.0%	14.0%	16.0%	18.0%	19.0%
MARKET SHARE JAPAN	0.0%	0.2%	0.5%	1.2%	2.5%	4.0%	7.0%	10.0%	12.0%	14.0%	16.0%
REVENUES US (M)	\$24	\$60	\$121	\$201	\$281	\$402	\$482	\$563	\$643	\$724	\$764
REVENUES EU (M)	\$10	\$30	\$61	\$101	\$142	\$202	\$243	\$283	\$324	\$364	\$385
REVENUES JAPAN (M)	\$0	\$1	\$3	\$8	\$17	\$28	\$48	\$69	\$83	\$97	\$110
TOTAL REVENUES (M)	34	92	185	310	440	632	774	915	1,050	1,185	1,259
COGS 20%	\$6.8	\$18.4	\$37.0	\$62.1	\$88.1	\$126.4	\$154.7	\$183.0	\$210.0	\$236.9	\$251.8
GROSS PROFIT (M)	\$27.4	\$73.6	\$147.8	\$248.4	\$352.3	\$505.6	\$618.9	\$732.1	\$839.9	\$947.6	\$1,007.0
NET PROFIT (40%)	14	37	74	124	176	253	309	366	420	474	504
DISCOUNT RATE	0.64	0.57	0.51	0.45	0.40	0.36	0.32	0.29	0.26	0.23	0.20
Total NPV (USD m)											1,062
LOA 65% (USD m)											690
PER SHARE (CAD)											5.17

Valuation apabetalone in CKD and Dialysis

Year	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
MARKET SHARE US	0.6%	1.5%	3.0%	5.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%	20.0%
MARKET SHARE EU	0.5%	1.5%	3.0%	5.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%	19.0%
MARKET SHARE JAPAN	0.2%	0.5%	1.2%	2.5%	4.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%
REVENUES US (M)	\$74	\$185	\$370	\$617	\$864	\$1,234	\$1,604	\$1,975	\$2,221	\$2,468	\$2,468
REVENUES EU (M)	\$38	\$115	\$230	\$383	\$537	\$767	\$997	\$1,227	\$1,380	\$1,533	\$1,457
REVENUES JAPAN (M)	\$8	\$20	\$49	\$102	\$164	\$287	\$409	\$532	\$655	\$737	\$819
TOTAL REVENUES (M)	121	321	649	1,103	1,564	2,287	3,010	3,733	4,256	4,738	4,744
COGS 20%	\$24.1	\$64.1	\$129.9	\$220.5	\$312.9	\$457.5	\$602.1	\$746.7	\$851.3	\$947.7	\$948.7
GROSS PROFIT (M)	\$96.5	\$256.5	\$519.5	\$882.2	\$1,251	\$1,829.8	\$2,408.3	\$2,986.7	\$3,405.1	\$3,790.7	\$3,794.9
NET PROFIT (40%)	48	128	260	441	626	915	1,204	1,493	1,703	1,895	1,897
DISCOUNT RATE	0.57	0.51	0.45	0.40	0.36	0.32	0.29	0.26	0.23	0.20	0.18
Total NPV (USD m)											3,304
LOA 40% (USD m)											1,322
PER SHARE (CAD)											9.89



Valuation apabetalone VCI/Dementia in elderly with Diabetes

Year	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
MARKET SHARE US	0.6%	1.5%	3.0%	5.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%	20.0%
MARKET SHARE EU	0.5%	1.5%	3.0%	5.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%	19.0%
MARKET SHARE JAPAN	0.2%	0.5%	1.2%	2.5%	4.0%	7.0%	10.0%	13.0%	16.0%	18.0%	20.0%
REVENUES US (M)	\$36	\$90	\$181	\$302	\$422	\$603	\$784	\$965	\$1,085	\$1,206	\$1,206
REVENUES EU (M)	\$13	\$38	\$76	\$127	\$177	\$253	\$329	\$405	\$455	\$506	\$481
REVENUES JAPAN (M)	\$3	\$7	\$17	\$35	\$55	\$97	\$138	\$179	\$221	\$248	\$276
TOTAL REVENUES (M)	52	135	273	463	654	953	1,251	1,549	1,762	1,960	1,963
COGS 20%	\$10.3	\$27.1	\$54.7	\$92.5	\$130.9	\$190.5	\$250.2	\$309.8	\$352.3	\$392.1	\$392.5
GROSS PROFIT (M)	\$41.3	\$108.2	\$218.7	\$370.0	\$523.5	\$762.1	\$1,000.6	\$1,239.2	\$1,409.3	\$1,568.3	\$1,570.2
NET PROFIT (40%)	21	54	109	185	262	381	500	620	705	784	785
DISCOUNT RATE	0.51	0.45	0.40	0.36	0.32	0.29	0.26	0.23	0.20	0.18	0.16
Total NPV (USD m)											1,373
LOA 40% (USD m)											549
PER SHARE (CAD)											4.11



Scientific References Technology and Apabetalone

Below are a number of scientific references for Resverlogix' technology platform and on the effect of apabetalone in various studies.

- **Data on gene and protein expression changes induced by apabetalone (RVX-208) in ex vivo treated human whole blood and primary hepatocytes,**

Wasiak S, Gilham D, Tsujikawa LM, Halliday C, Norek K, Patel RG, McLure KG, Young PR, Gordon A, Kulikowski E, Johansson J, Sweeney M, Wong NC,

Data Brief. 2016 Jul 29;8:1280-8 <https://www.ncbi.nlm.nih.gov/pubmed/27570805>

- **Selective BET Protein Inhibition with Apabetalone and Cardiovascular Events: A Pooled Analysis of Trials in Patients with Coronary Artery Disease,**

Nicholls SJ, Ray KK, Johansson JO, Gordon A, Sweeney M, Halliday C, Kulikowski E, Wong N, Kim SW, Schwartz GG.

Am J Cardiovasc Drugs. 2018 Apr;18(2):109-115. . <https://www.ncbi.nlm.nih.gov/pubmed/29027131>

- **Benefit of Apabetalone on Plasma Proteins in Renal Disease,**

Wasiak S, Tsujikawa LM, Halliday C, Stotz SC, Gilham D, Jahagirdar R, Kalantar-Zadeh K, Robson R, Sweeney M, Johansson JO, Wong NC, Kulikowski E.

Kidney Int Rep. 2017 Dec 8;3(3):711-721. doi: 10.1016/j.ekir.2017.12.001. eCollection 2018 May.

<https://www.ncbi.nlm.nih.gov/pubmed/29854980>

- **Apabetalone Mediated Epigenetic Modulation is Associated with Favorable Kidney Function and Alkaline Phosphatase Profile in Patients with Chronic Kidney Disease,**

Kulikowski E, Halliday C, Johansson J, Sweeney M, Lebioda K, Wong N, Haarhaus M, Brandenburg V, Beddhu S, Tonelli M, Zoccali C, Kalantar-Zadeh K.

Kidney Blood Press Res. 2018;43(2):449-457. doi: 10.1159/000488257. Epub 2018 Mar 16.

<https://www.ncbi.nlm.nih.gov/pubmed/29566379>



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.

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