

Resverlogix Corp. Q1 2017 - Corporate Update BIO-Europe Spring, March 21, 2017

### Today's Agenda

- 1. Corporate Overview
- 2. Technology Review
- 3. BETonRENAL Clinical Trial Update
- 4. **BETonMACE Clinical Update**
- 5. Financial Position & Opportunities

#### 6. Market Opportunity

This presentation may contain certain forward-looking information as defined under applicable Canadian securities legislation, that are not based on historical fact, including without limitation statements containing the words "believes", "anticipates", "plans", "intends", "will", "should", "expects", "continue", "estimate", "forecasts" and other similar expressions. In particular, this presentation includes forward looking information relating to the Company's clinical trials and the potential role of apabetalone in the treatment of CVD, DM, chronic kidney disease, Orphan diseases, and peripheral artery disease. Our actual results, events or developments could be materially different from those expressed or implied by these forward-looking statements are subject to numerous assumptions and risk factors including those discussed in our Annual Information Form and most recent MD&A which are incorporated herein by reference and are available through SEDAR at www.sedar.com. The forward-looking statements contained in this presentation are expressly qualified by this cautionary statement and are made as of the date hereof. The Company disclaims any intention and has no obligation or responsibility, except as required by law, to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

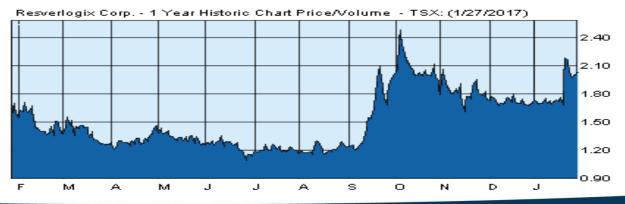




#### Corporate Review – Financial Profile

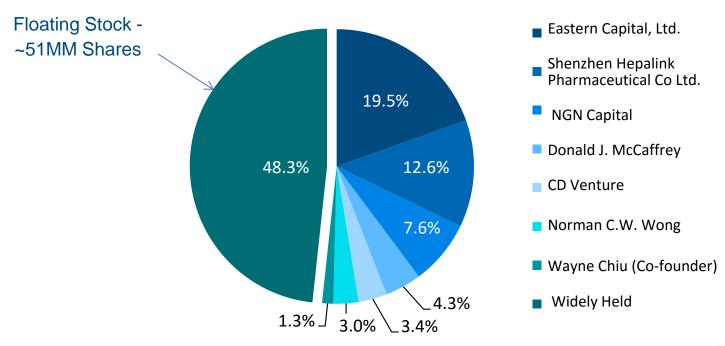


Founded	2001
Ticker	TSE-RVX
Market Cap	~\$250 MM
Shares Outstanding	105.4MM ~120MM fully diluted
Cash Burn	~\$2.0 MM + per month



#### **Top Shareholders & Available Float**

- RVX shareholder base is highly concentrated and relatively shallow
- Implies that the "float" (actual shares available for trading) is limited to ~51MM shares



#### **RVX Top Shareholders**

RESVERLOG

### **Resverlogix Partnership**





- Shenzhen Hepalink & Resverlogix announced a major licensing & milestone deal that could exceed USD \$450MM
- Largest single molecule deal in China history
- Apabetalone targets 140 MM China diabetes & CKD patients
- The market is 10% of the population and growing at 15% per year

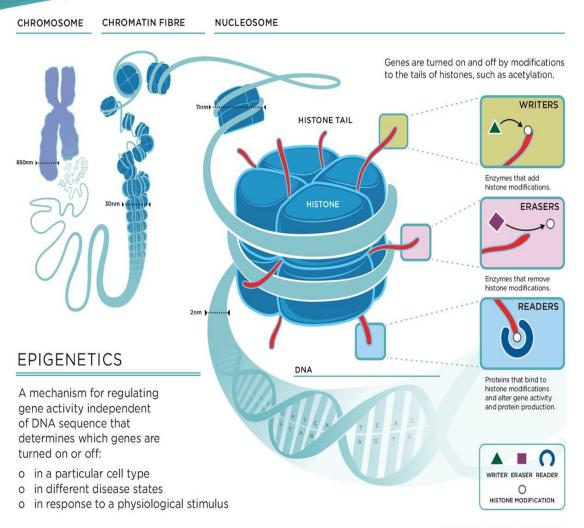


**Technology Review** 

- CVD and CKD are multifactorial diseases driven by dysregulated genes and pathways, such as inflammation and calcification
- BET proteins (epigenetic readers) regulate the genes and pathways underlying this pathology
- Apabetalone inhibits BET proteins and is the only clinical candidate in a phase 3 outcomes trial in CVD or CKD.
- The BETonMACE trial is 50% enrolled and is designed to reconfirm marked MACE reductions observed in previous trials.

## **Epigenetics**

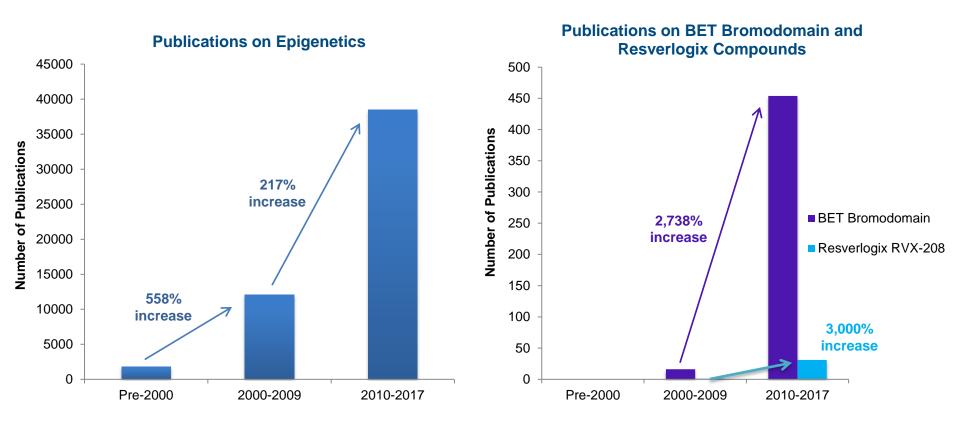




- The Epigenetic code refers to secondary modifications to chromatin components that regulate its activity
- Transcription is regulated by addition, removal or recognition of these modifications (writers, erasers, readers)
- Acetylation is associated with active transcriptional regions of chromatin
- BET (Bromodomain and Extraterminal Domain) proteins bind to acetylated lysines on histones and recruit additional transcription factors

COPYRIGHT © 2012 - RICHARD E. BALLERMANN

#### Dramatic growth of publications over the past decade in Epigenetics and BET Inhibition



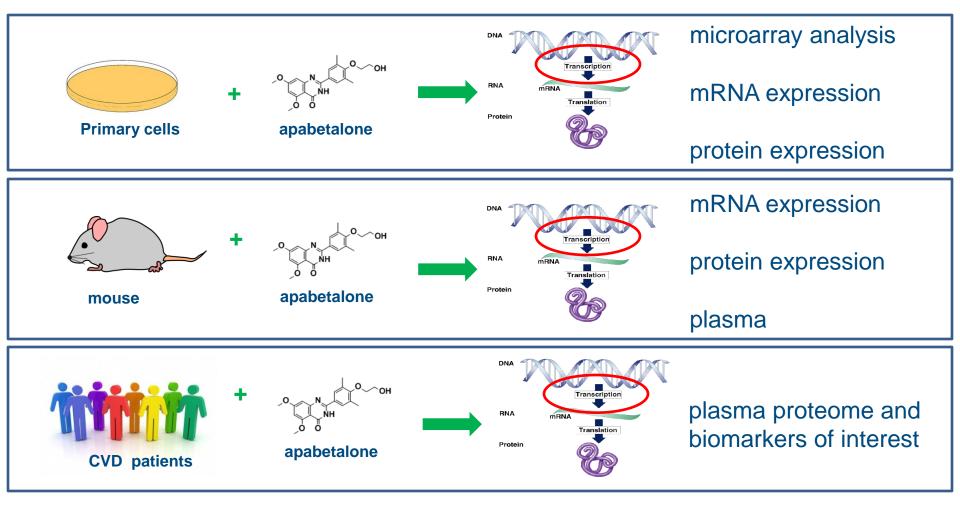
Source: PubMed Database: Historical Review Q1 2017

RESVERLOG

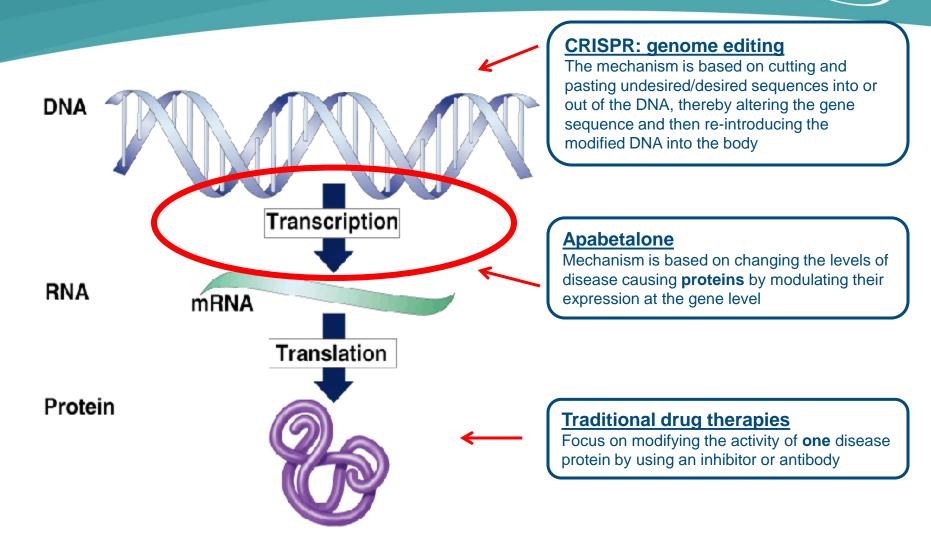
## **Studies in BET Inhibition**



#### Studies in cells, animals and humans

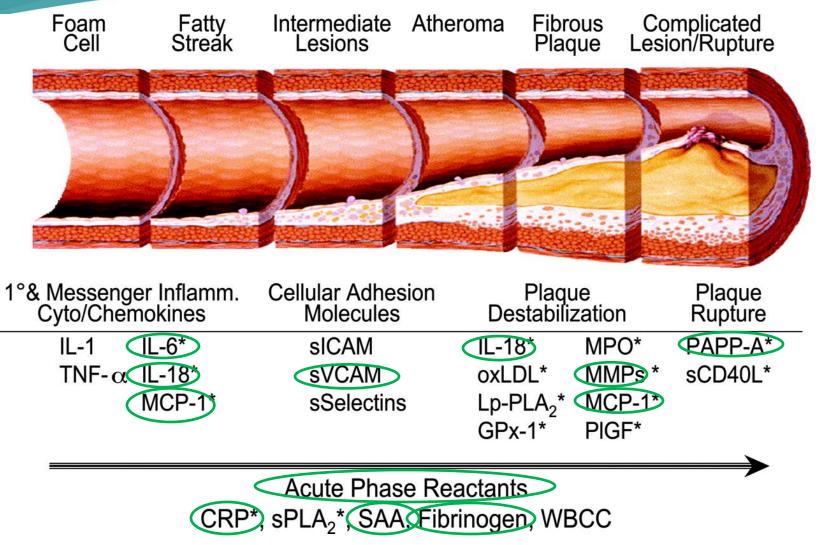


#### Apabetalone's Advanced Mechanism



RESVERLOGI

## Inflammation in Cardiovascular Disease



RESVERLOGI

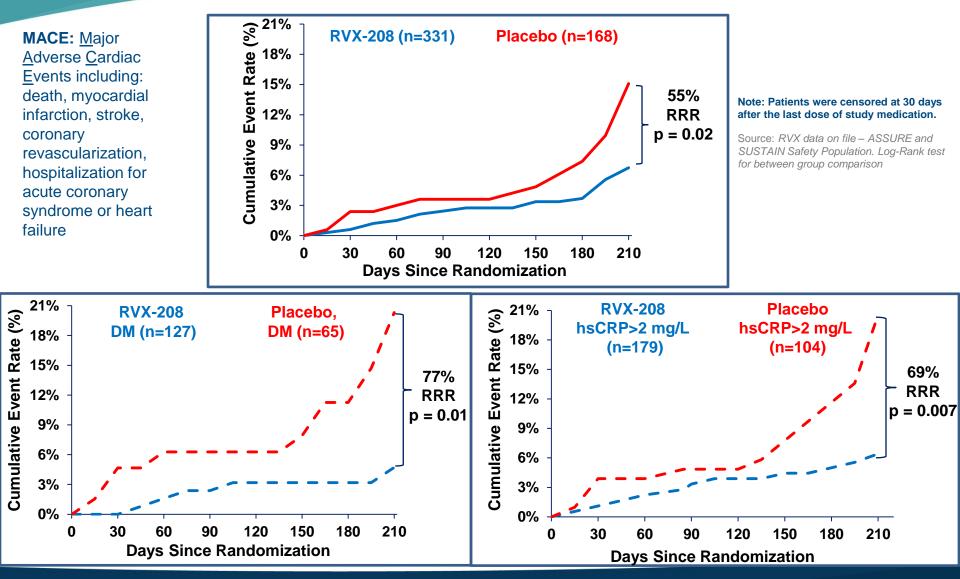
Source: Koenig, W. and Khuseyinova, N. (2007). "Biomarkers of Atherosclerotic Plaque Instability and Rupture." Arterioscler Thromb Vasc Biol; 27: 15-26



**Examples of Detailed Science Compilation** 

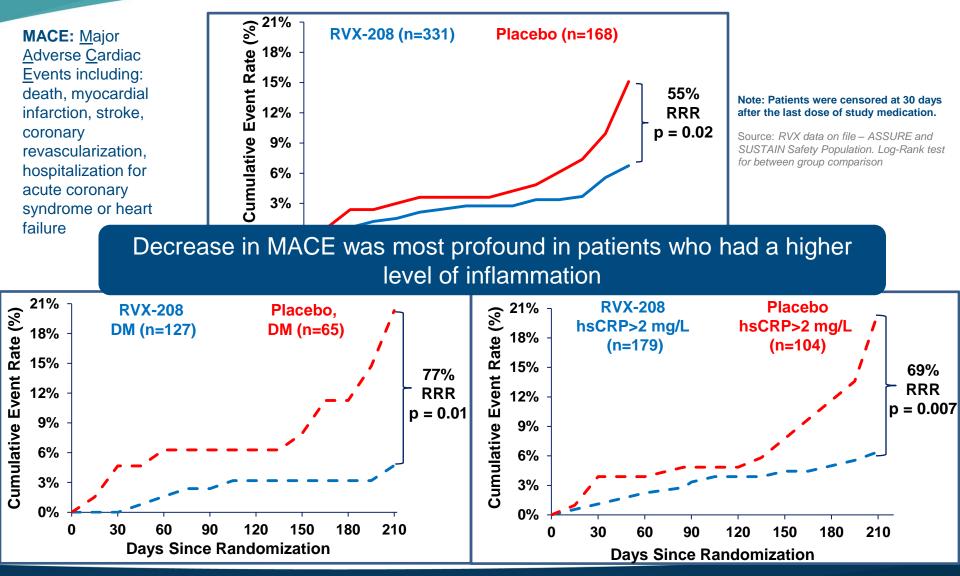
# Strong Clinical Trial Data Indicated a Diverse Mechanism of Action





# Strong Clinical Trial Data Indicated a Diverse Mechanism of Action

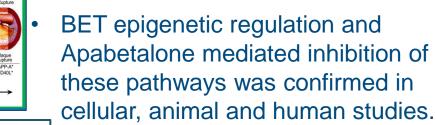




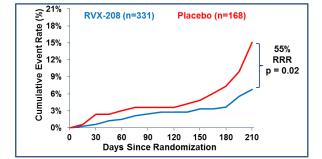
PLA \* SAA Fibringen WRC

### Apabetalone: BET Inhibition Targets Processes Driving CVD Disease Pathology

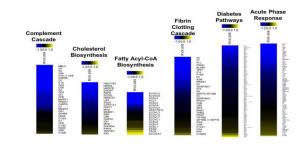
- Based on data generated in phase 2 studies, Apabetalone treatment resulted in a reduced incidence of MACE (Major Adverse Cardiac Events) in CVD patients (especially with Diabetes)
- Arrays from primary human hepatocytes and human whole blood demonstrated marked effects on numerous pathways that drive CVD

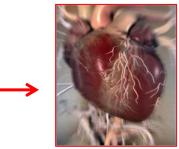


- complement and coagulation
- vascular inflammation
- acute phase response
- vascular calcification
- reverse cholesterol transport
- diabetes and glucose metabolism.



RESVERLOG





Cardio/Renal Disease

## Current & Ongoing Studies Support Alternate Indications

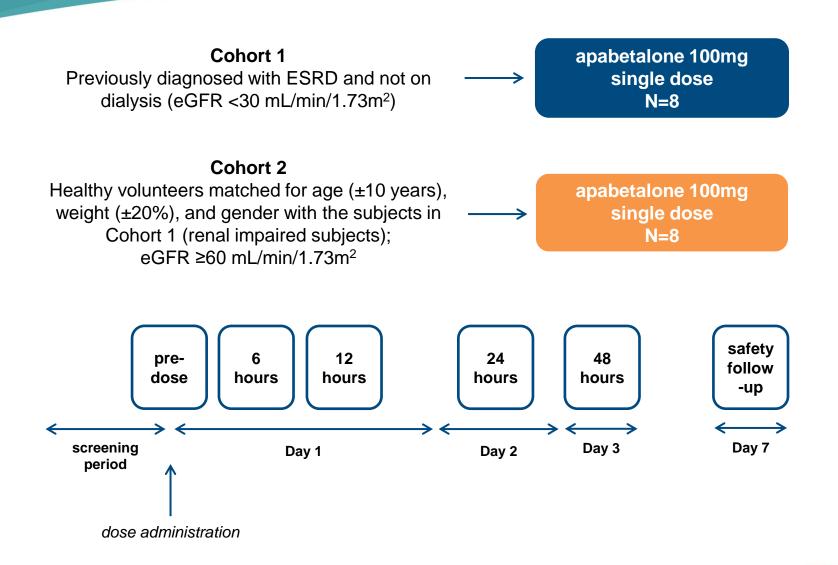


- <u>Neurofibromatosis Malignant Peripheral Nerve Sheath Tumors (MPNST)</u>: studies have examined the effect of apabetalone, in vitro and in vivo, on MPNST (potential orphan indication)
- **Pulmonary Arterial Hypertension:** studying the effects of apabetalone on primary lung SMCs was positive, animal study of the effect of apabetalone on top of standard of care
- <u>Muscular Dystrophy/Facio Scapulo Humeral Dystrophy</u>: We have tested apabetalone and ~20 alternate RVX compounds for target and biomarker engagement in muscle cells, we are also analyzing human muscle biopsies from patients treated with apabetalone
- <u>Calciphylaxis/Calcification</u>: due to positive in vitro data animal studies of calcification are ongoing (also supports CVD)
- Fabrys Disease: arranging ex-vivo treatment of Fabry patient blood, to analyze the effect of apabetalone on inflammatory mediators to move into a safety/efficacy Phase 2 study
- <u>Neuroinflammation</u>: direct effects of apabetalone demonstrate reduced inflammation and microglial activation with drug treatment and no detrimental effects on neurons – animal study 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 have been initiated
- Chronic Kidney Disease (CKD): proteomic analysis of data from CKD PK study is ongoing
- <u>Characteristics of BET Inhibitors</u>: studies investigating PK/tissue distribution of apabetalone and other BET inhibitors are underway, new scientist hired to investigate distribution, formulation and route of administration of BETi for other indications and target organs



**BETonRENAL Clinical Update** 

## Phase 1 CKD PK Study Design



RESVERLOG

### Proteomic Analysis of CKD PK Study



Top 100 proteins from Somalogic, ranked by magnitude of effect at 12 hours post dose vs baseline, compare biomarkers of severe renally impaired patients versus healthy controls

		Severe Renal Impaired				Healthy Control			
Protein/Gene	6 Hours	12 Hours	24 Hours	48 Hours	6 Hours	12 Hours	24 Hours	48 Hours	
realin-like growth factor-binding protein 1	IG1071	574		-1.0	37.0	46.1	12.8	12.1	
hosphoglycerate mutase 1 Yatelet factor 4	PGAN1 22.2 PF4 2.2	54.5	-44.5			11.3 36.8		-20.0	
14-3-3 protein family Casein kinase II 2-alpha:2-beta heterotetramer	YWHAR, YMHAR, YMHAR, YMHAR, P	-42	-42.3			25.5		-34.3	
AMP-dependent protein kinase catalytic subunit alpha MAP kinase-activated protein kinase 2	PREACE 10	-01-	-12			-22.2		-29.0	
Aethionine aminopeptidase 1	META71 -6.2	-42	-45			17.9		-28.2	
I-phosphoinositide-dependent protein kinase 1 Tauminoeen activator inhibitor 1	POPIC 6.5	42	-01			19.5		-32.7	
Sukaryotic translation initiation factor 4H 4-3-3 protein beta/alpha	DF4H -3.0	41.1	-41.4			0.8		-33.9	
Protein kinase C theta type	YWH 5 -1.5 PRKC1 -2.5	-40.	-44.9			26.2		-26.8	
AH receptor-interacting protein Chloride intracellular channel protein 1	AP -8.3 CUCI -8.8	-39.4	-41.5			25.7		-27.9	
-C motif chemokine 17	CC117 -7.3	-39.	-42.2			33.0		-3.4	
Copine-1 Rgnal transducer and activator of transcription 3	CPNE -3.6 STAT2 -2.0	-39.	-41.4			17.6		-27.8	
WAP kinase-activated protein kinase 3 Tyrosine-protein kinase Tec	MAPROVIS -6.0 TEC 2.0	-32.0	-42			14.6 22.1		-27.8	
alcineurin	PPP2C A 9792323 -6.5	-31.7	-40,2			17.9		-21.5	
Natelet-derived growth factor subunit A femK methyltransferase family member 2	PDGFA -6.9 NGANTI 0.0	-38.4	-41.5			13.2		-10.7	
Tyrosine-protein kinase Fyn	PW 1.5	-36.2	-22.2			11.5		-18.9	
Tyrosine-protein kinase Fer Dual specificity protein phosphatase 3	FER -2.7 DUSP1 -6.3	-362	-413			22.9 16.2		-20.5	
Metalloproteinase inhibitor 3 Dycylpeptide N-tetradecanoy/transferase 1	TIMPS -2.3	-37.9	-35.7			10.3		-17.4	
-hydroxyacyl-CoA dehydrogenase type-2	HSD17030 0.0	-37.7	-4/5			15.8		-34.5	
Receptor-type tyrosine-protein kinase FLT3 Tyrosine-protein kinase BTK	FLT3 -18.0 BTX 0.1	-37.5	-42			9.5 24.8		-30.5	
Tyrosine-protein kinase Lyn	LYN 1.1	-37.3	-42.4			14.3		-21.6	
Nothers against decapentaplegic homolog 2 sets-adrenergic receptor kinase 1	SMADO -0.5 ADRECI -0.1	-37.3	-42.4			22.9		-35.2	
libosomal protein 56 kinase alpha-3	R7528/A3 2.5	-37.2	-32.2			0.3		-31.5	
Ebosome maturation protein SBDS	5805 -1.4	-36.6	-12			29.2		-27.3	
Thrombospondin-1 CDS ligand	THES: -3.1 ICOSLO 0.5	-36.5	-22.0			17.4		-20.5	
Veptidyl-prolyl cis-trans isomerase D Vitoger-activated protein kinase 8	PPID 4.0 MAPIO 4.2	-36.4	-41 2			18.9 10.0		-30.5	
kmyloid beta A4 protein	APP -0.4	-36.3	-35.3			16.1		-14.9	
Tyrosine-protein kinase CSK ntegrin alpha-l: beta-1 complex	CSK 2.3 ITGA1 (TOE1 -6.2	-36.2	-45_1			20.7		-30.5	
Nucleoside diphosphate kinase A	NME1 -1.4	-36.1	-33.2			12.0		-22.5	
Dual 3',5'-cyclic-AMP and -GMP phosphodiesterase 11A Vitogen-activated protein kinase 1	PDE12A 0.5 MAPIC -4.2	-36.1 -36.0	-35.0			6.3 9.9		-20.6	
AMP-regulated phosphoprotein 19 IAC-beta serine/threonine-protein kinase	A899:0 -2.0 AKT2 -0.0	-36.0	-38.2			12.3 16.4		-26.8	
Yrosine-protein phosphatase non-receptor type 6	PTPNO -3.3	-35.9	-35.8			14		-17.7	
Caspase-3 Collagen alpha-1(XXXI) chain	CASP2 -4.3 COL22A3 -4.7	-35.5	-412 -35.4			17.4		-26.4	
Peptidyl-prolyl cis-trans isomerase F, mitochondrial Icl2-associated agonist of cell death	PPIF 4.5	-8.1	-44			-0.6		-28.5	
phingosine kinase 1	SPHQ 1.0	-35.7	-42			22.4		-20.2	
Protein kinase C beta type (splice variant beta-li) Pranslationally-controlled tumor protein	PRICE 0.4 TPT1 -6.2	-856	-42			26.0		-26.7	
Upha-enclase	EN01 1.2 DNAE1 -11.2	-35.4	-35.0			17.6		-21.9	
Inal homolog subfamily 8 member 1 Yotein disulfide-isomerase A3	DNA811 -13.2 PDNA3 5.5	-354	-35.3			16.9		-26.5	
Natelet-derived growth factor subunit B Sukaryotic translation initiation factor 4 gamma 2	PDGFI 10.6	-852	-34.2			24.1		42	
facuolar protein sorting-associated protein VTA1 homol	o/VTA1 1.8	-35.1	-12.7			17.7		-22.2	
Witogen-activated protein kinase 14 Casein kinase II 2-alpha'2-beta heterotetramer	MAPICA -0.4 CSNIC A2 CSNI28 -0.2	-351	-42.4			12.0		-28.5	
nhibitor of growth protein 1 AMP Kinase (alpha2beta2gamma1)	ING1 1.0	216-	-38.3			13.3 17.6		-20.1	
alcium/calmodulin-dependent protein kinase type II su	bCAMB <sup>CA</sup> A	-34.5	-37.5			11.2		-26.1	
Keutrophil-activating peptide 2 GMP-specific 3',5'-cyclic phosphodiesterase	PPEP 0.8 PDES4 0.5	-34.5	-41.2			26.6 23.1		-14.8 -22.8	
KO kDa heat shock protein, mitochondrial Gro-beta/gamma	HSPD 7.2	-34.2	-37.7			2.3		-16.2	
imal transducer and activator of transcription 6	STATE 2.0	-34.1	-22.5			1.7		-18.4	
kropsin A5 Jakium/caimoduilin-dependent protein kinase type II su		-341	-25.6			15.9		-11.9	
Tyrosine-protein kinase Yes	YES1 -0.0	-31.9	-32.9			42		-21.9	
C motif chemokine 5 jorting nexin-4	CCLS 0.4 SNX4 1.7	-115	-34.6			26.1 20.8		-11.1	
Matoxin 81 aldehyde reductase member 2	ARE7/12 2.8 MAPI0 5.1	-115	-32.2			17.6 20.5		-20.5	
Witogen-activated protein kinase 3 Dickkopf-related protein 1	003 6.2	-31.4	-11.1			8.0		-12.8	
Dynein light chain roadblock-type 1 feat shock protein HSP 90-alpha/beta	DYNU 22 -3.8	-111	-12			17.0		-37.	
tip90 co-chaperone Cdc37	CDC3 -0.9	-111	-23.0			9.0		-22.5	
Calcium/calmodulin-dependent protein kinase type II su	6CAN9/21 12.5	-31.0	-42.3			18.0		-17.4	
Yatelet glycoprotein VI hromboopietin	GP6 1.1 THPD -1.5	-32.9	-35.5			16.0		-27.6	
Cytokine receptor common subunit gamma	1285 -4.5	-32.7	-37.0			13.0		-28.9	
Transgelin-2 IAC-alpha/beta/gamma serine/threonine-protein kinase	TAGUIZ 1.8 AKTI AKTZ AKT3 0.2	-32.7 -32.5	-22.6			4.2 52.9		-19.1	
Voesin hoto-oncoene vav	MSN -12.3	-12.4	-25.6			-9.4		-21.9	
imall ubiquitin-related modifier 3	VAV1 505 SUMC0 -7.6	-32.2	-35.0			11.1		-28.9	
Witogen-activated protein kinase kinase kinase 7:TGF-be COMM domain-containing protein 7	COM/107 -5.2	-12.1	-23.2			6.2 11.9		-0.8 -12.7	
kraphiregulin Im-aniamalaraaratin	AREG -6.2	-32.1	-33.0			15.9		-27.9	

### World Leading Committee Members



#### **CKD/Dialysis**



Dr. Kamyar Kalantar-Zadeh Chair UC Irvine Chief Nephrology



**Prof. Vincent Brandenburg** Member *University Hospital RWTH Aachen* 



Dr. Carmine Zoccali Member *University Pisa* 



**Dr. Marcello Tonelli** Member *University of Calgary Chair Medical Research* 

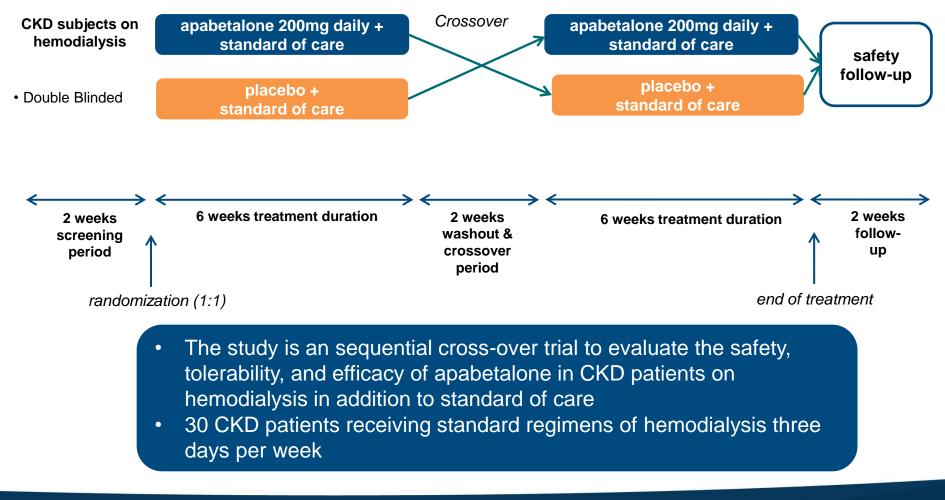


Dr. Srinivasan Beddhu Member *University of Utah* 



**Dr. Mathias Haarhaus** Member *Karolinska University Hospital* 

#### Phase 2 Renal Study Design: Primary Endpoint Change in ALP



RESVERLOG

#### FDA Interactions: Cardio/Renal Division

- Filed for a Type B Meeting early fall 2016
- Completed Type B Meeting late fall 2016, face to face in Washington
- Received positive feedback on trial design and positive instructions to enhance the program without affecting the IND filing timeline
- New Cardio/Renal IND on track for Q1 2017



**BETonMACE Clinical Update** 

## **BETonMACE Commenced November 2015**



Apabetalone has already been tested in over 1,400 patients in 18 countries around the world.

RESVERLOGIX



#### Primary Objective

To evaluate if treatment with apabetalone as compared to placebo increases time to the first occurrence of triple MACE. Triple MACE is defined as a single composite endpoint of: 1) CV Death or 2) Non-Fatal MI or 3) Stroke.

#### Key Inclusion Criteria

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

#### **Primary Endpoint**

Time from randomization to the first occurrence of adjudication-confirmed triple MACE defined as a single composite endpoint of: 1) CV Death or 2) Non-Fatal MI or 3) Stroke.

#### Secondary Endpoint

Time from randomization to the first occurrence of adjudication-confirmed MACE including:

- revascularization and unstable angina
- changes in apoA-I, apoB, LDL-C, HDL-C, and TG
- changes in HbA1c, fasting glucose, and fasting insulin
- changes in ALP and eGFR



**Market Opportunity** 

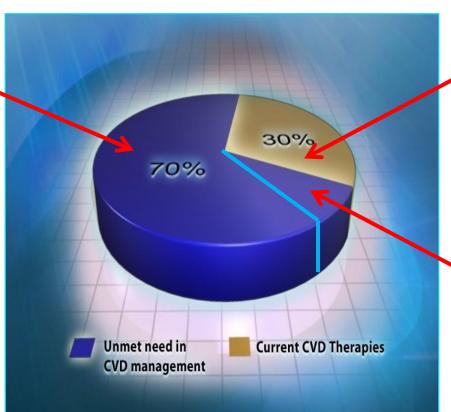
### Unmet Need Segment is Still 70%

RESVERLOGIX

 Cardiovascular disease is still the number one killer of both males and females and costs the US healthcare system over \$500B per year

#### **Opportunity**

 Huge market potential resides in the remaining 70% unmet need in CVD management



#### Current CVD Therapies

- Statins are the top
  medication used to treat
  CVD
- Despite maximized use, current therapies only manage about 30% of CVD events

#### New LDL Modulators

 Several new types of LDL modulators are in clinic.
 Leading are the very expensive PCSK9's

#### Tier 2 Valuation Example: Acute Coronary Syndrome Indications Risk-Adjusted NPV Projections

$\frown$
RESVERLOGIX

Milestone Valuations	Scenario i >25% RRR			Scenario ii >30% RRR		
	ACS + Diabetes	ACS + CKD	Total	ACS + Diabetes	ACS + CKD	Total
Phase III EU	<u>\$ 1,044</u>	<u>\$ 717</u>	<u>\$    1,761</u>	<u>\$    1,351</u>	<u>\$ 921</u>	<u>\$ 2,272</u>
Phase III EU Completion	<u>\$    2,363</u>	<u>\$   1,554</u>	<u>\$ 3,917</u>	<u>\$ 3,015</u>	<u>\$ 1,967</u>	<u>\$ 4,982</u>
Market Approval EU + Phase III US	<u>\$ 2,686</u>	<u>\$   1,763</u>	<u>\$ 4,449</u>	<u>\$ 3,422</u>	<u>\$ 2,225</u>	<u>\$ 5,647</u>
Market Approval EU + Phase III US Completion	<u>\$ 3,458</u>	<u>\$ 2,243</u>	<u>\$    5,701</u>	<u>\$ 4,394</u>	<u>\$ 2,831</u>	<u>\$ 7,225</u>
Full Market Approval	<u>\$ 3,828</u>	<u>\$ 2,474</u>	<u>\$    6,302</u>	<u>\$ 4,862</u>	<u>\$ 3,121</u>	<u>\$ 7,983</u>

#### **Data Value Indications**

- i. RRR >25% in BETonMACE; \$3,600/yr; market penetration 60%
- ii. RRR >30% in BETonMACE; \$4,200/yr; market penetration 64%

#### Assumptions

- 1. Ramp to peak 7 years
- 2. 2021 market entry in EU; 2023 market entry in US
- 3. Japan to follow EU registration path
- 4. NPV calculated on net operating income at a 15% discount rate
- 5. Patent life 2034/35

 $\mathsf{T}\,\mathsf{S}\,\mathsf{X}:\;\mathsf{R}\,\mathsf{V}\,\mathsf{X}$ 

(in USD millions unless otherwise noted)

- Phase 3 company focused on significant unmet need in <u>high-risk CVD</u> patient population with lead therapeutic - apabetalone
- Market leader with significant potential targeting high-risk unmet need in several patient groups Over 10MM patients in top 7 markets
- Advancing development of apabetalone in high-risk (dialysis) CKD patients – Phase 2 clinical trials to commence in early 2017
- Well established safety profile to date, <u>over 1,400 patients</u> treated with apabetalone with no significant safety issues
- Proven track record of funding development while minimizing shareholder dilution



Resverlogix Corp. Q1 2017 - Corporate Update BIO-Europe Spring, March 21, 2017