

## Resverlogix Corp. (TSX:RVX) BIO International Convention San Diego, CA. June 2017

## **Forward Looking Statements**

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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", "anticipătes", "plans", "intends", "will", "should", "expects", "continue", "estimate", "forecasts" and other similar expressions. In particular, this news release includes forward looking information relating to the potential role of apabetalone in the treatment of cardiovascular disease (CVD), diabetes mellitus (DM), chronic kidney disease (CKD), end-stage renal disease treated with hemodialysis, Alzheimer's disease, Alkaline phosphatase (ALP), Fabry's disease, and Orphan diseases. Our actual results, events or developments could be materially different from those expressed or implied by these forward-looking statements. We can give no assurance that any of the events or expectations will occur or be realized. By their nature, 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 news release 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 Overview**

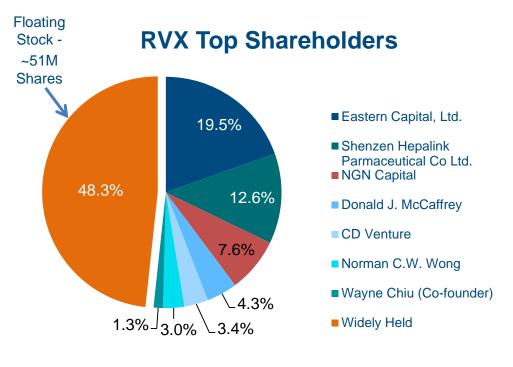


- Resverlogix Corp. (TSX:RVX) is a Calgary and San Francisco based clinical stage biotechnology company focused on the development of apabetalone
- Apabetalone (RVX-208) is a first-in-class small molecule selective BET bromodomain inhibitor, which acts via an epigenetic mechanism that can turn disease-causing genes off, thereby normalizing gene function
  - Apabetalone is the only selective BET bromodomain inhibitor in clinical trials
- Resverlogix has initiated clinical trials of apabetalone in three indications:
  - Cardiovascular Disease (BETonMACE Trial)
  - Chronic Kidney Disease (BETonRENAL Trial)
  - Fabry's Disease

# **Capitalization and Financial Profile**



Founded	2001
Ticker	TSE-RVX
Market Cap	~C\$150M
Debt	C\$68.8M
Shares Outstanding	105.4M 120M fully diluted



- RVX shareholder base consists of several long term investors who have been supportive over 10 years
- RVX maintains a diversified public market float of approximately 51M shares or ~\$100M

Note: Financial data on this slide has been updated at 10:30pm MT, June 19, 2017.

# Apabetalone Pipeline



COMPOUND	INDICATION	PRE-IND	IND	Phase 1	Phase 2	Phase 3
	Cardiovascular Disease		BE	TonMACE		
Apabetalone	Chronic Kidney Disease		BETonRE	ENAL		
	Fabry's Disease					
Follow-On Compounds	Orphan Diseases					



- Former Dean of the Faculty of Medicine at the University of Calgary
- Former Editor-in-Chief of the Canadian Journal of Cardiology
- Past President of the Canadian Cardiovascular Society and the Association of Canadian Medical Colleges, Vice President of the Inter-American Society of Cardiology.

DR. ELDON R. SMITH, OC, MD,

FRCPC, FCAHS, FAHA, FIACS

**Board of Directors Lead Director** 

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# Shenzhen Hepalink Partnership



Resverlogix's partnership with Shenzhen Hepalink represents the largest single molecule deal in the history of China



Compound	Apabetalone (RVX-208)
Licensor	Resverlogix Corp.
Licensee	Shenzhen Hepalink Pharmaceutical Co., Ltd.
Territory	China, Hong Kong, Taiwan, and Macau
Indications	Any approved indication
Deal Structure	<ul> <li>US\$35M in equity investments in Resverlogix</li> <li>&gt;US\$400M in projected future China sales milestones and licensing royalties</li> </ul>
Developmental Costs	<ul> <li>Shenzhen Hepalink is responsible for all developmental costs for the licensed territories</li> <li>This includes the cost of additional clinical trials in the licensed territories, regulatory applications, etc.</li> </ul>





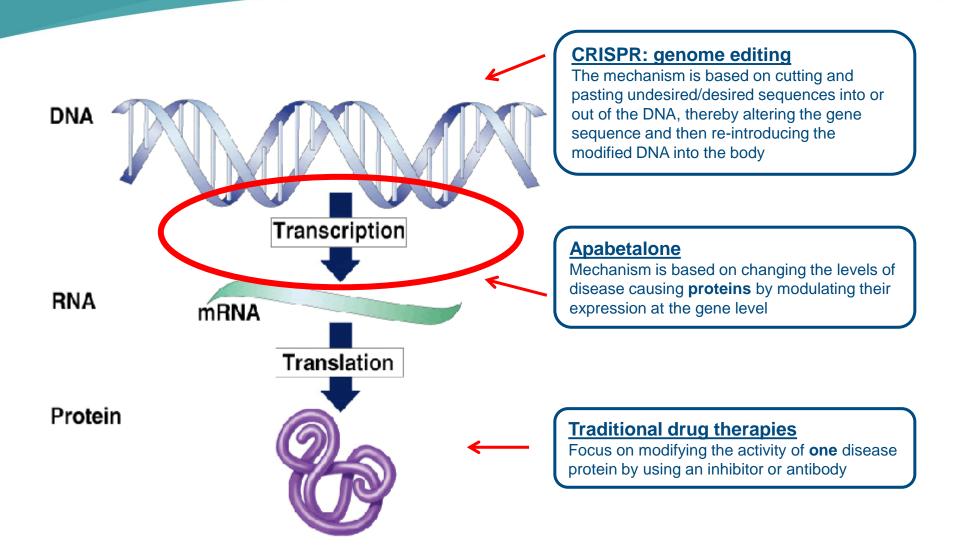


# **Apabetalone and the BET Platform**

# Differentiation: RVX's BET Platform



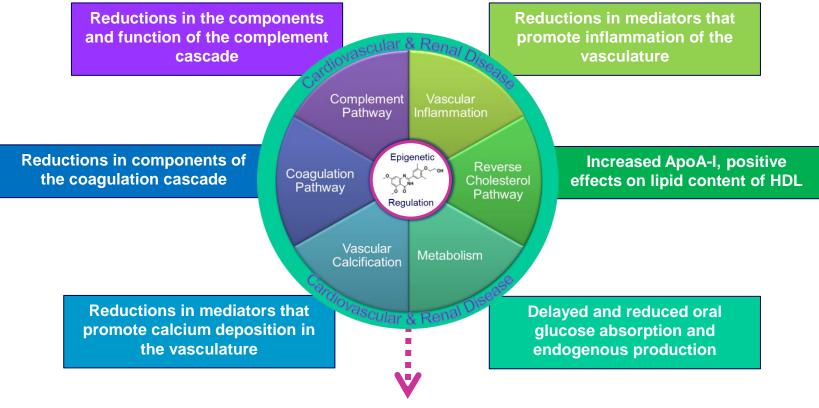
- Resverlogix has discovered compounds that bind the bromodomains of BET proteins with a high degree of specificity.
  - Other BET programs hit multiple targets (BRD2, BRD3, BRD4, BRDT, etc.)
  - Our expertise in medicinal chemistry and epigenetics allows us to identify small molecules that target one or a specified subset of BET proteins
    - Resverlogix's apabetalone product candidate specifically targets BRD4 BD2
- Our Phase 2 clinical program provided us with the only blood bank of BET inhibitortreated patients in the world
  - In-depth analysis such as proteomics, genomics, and pathway analysis revealed advanced knowledge of BET activities
  - The resulting knowledge from these activities provided a level of sophistication around BET that surpasses that of many others working in this area
- The specificity of Resverlogix's molecules avoids side effects seen when multiple targets
   are affected
  - BET programs in oncology can tolerate a high degree of side effects due to the nature of the disease being treated
  - Chronic conditions such as cardiovascular disease and renal impairment require treatments with a sideeffect profile acceptable for long-term treatment



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# BET Inhibition Impacts the Pathways that Drive Cardiovascular Disease and Kidney Diseases

Apabetalone, a bromodomain extra-terminal (BET) protein inhibitor, inhibits BRD4, thereby regulating the expression of genes and restoring the function of pathways underlying the pathogenesis of CVD and kidney disease

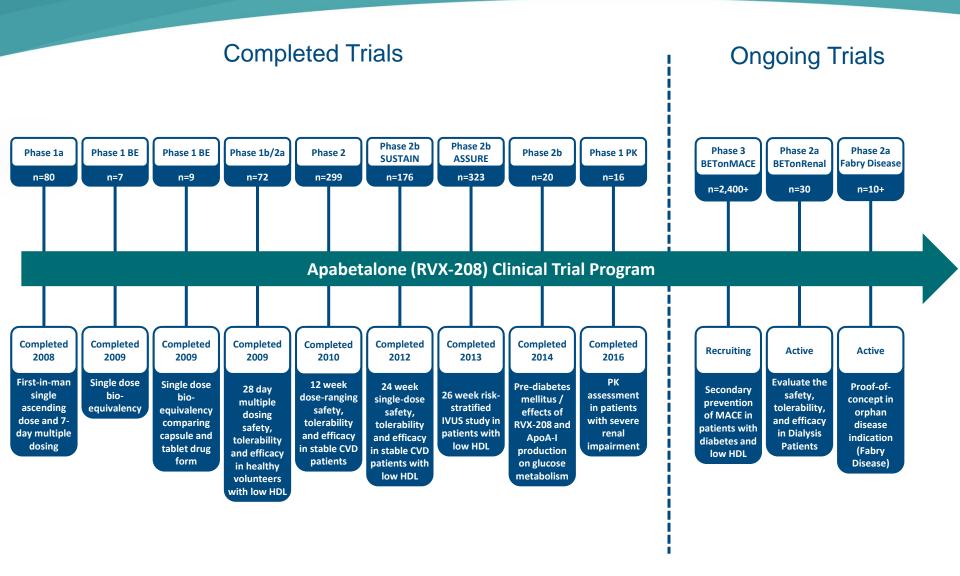


Reduced incidence of cardiac events and renal impairment

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# Apabetalone Clinical Trials to Date







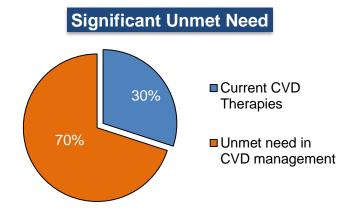
# **BETonMACE Clinical Program Overview**

# Rationale for Cardiovascular Disease Program



- Apabetalone has demonstrated a significant reduction in <u>Major Adverse</u> <u>Cardiovascular Events ("MACE")</u>, coupled with improvements in markers of vascular risk
  - Especially in those patients with
     Diabetes Mellitus in the Phase 2
     SUSTAIN and ASSURE trials
- Resverlogix believes that BET inhibition and apabetalone may have the potential to reduce the incidence of MACE
  - Particularly in patients with high risk CVD (recent acute coronary syndrome) and diabetes mellitus co-morbidity
- Resverlogix is currently investigating the potential for the following indication:
  - High Risk CVD Patients with low levels of HDL-C and diabetes mellitus
  - (Phase 3 BETonMACE)

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



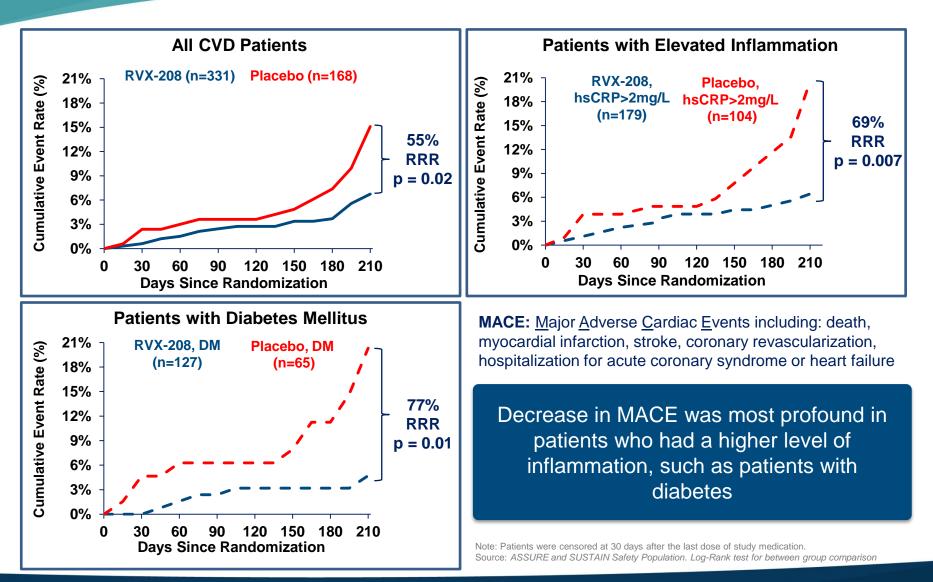
#### **Opportunity**

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

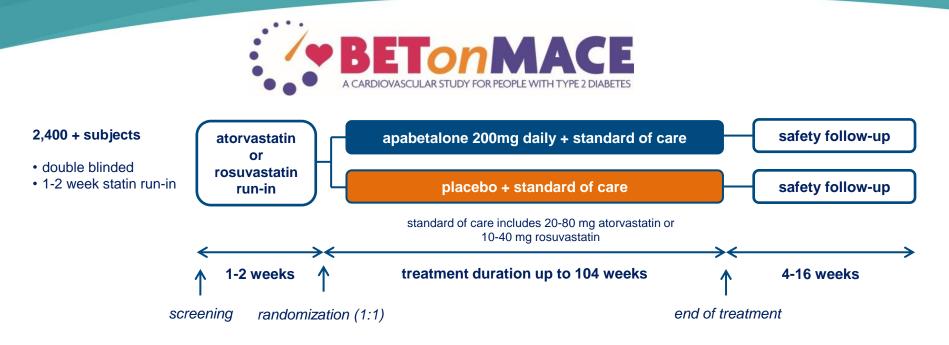
#### CVD Program - Phase 2 Data 499 Patients from the ASSURE & SUSTAIN Trials



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## CVD Program Moving Forward-BETonMACE CV Outcomes Study





The study is an event-based trial and continues until 250 narrowly defined MACE events have occurred

#### 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</li>

# **BETonMACE Clinical Steering Committee**



**Prof. Kausik K. Ray** Chair Imperial College, London Clinical trial expert

#### Dr. Henry N. Ginsberg Member Columbia University PI of ACCORD

**Dr. Gregory G. Schwartz** Member VA-Denver DSMB of RVX phase II trials



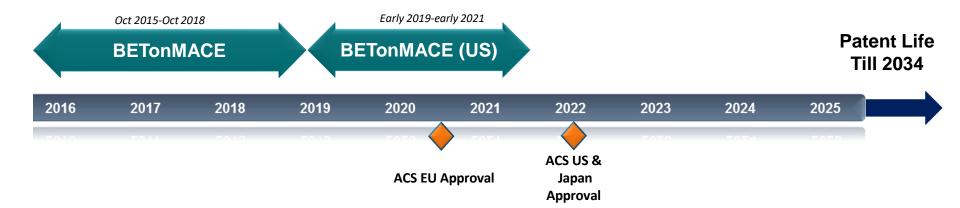
Dr. Peter P. Toth Member Univ. of Illinois Inflammation expert

#### **Dr. Stephen Nicholls**

Member SAHMRI, Adelaide PI of RVX phase II trials Dr. Kamyar Kalantar-Zadeh Member UC Irvine nephrologist and CKD expert

#### Apabetalone Timeline For CVD Indication

Apabetalone represents a unique opportunity for the expansion into the high vascular risk space and provides potentially unprecedented accretive value



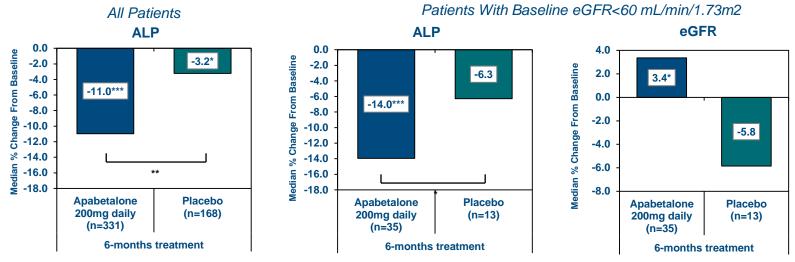
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# Chronic Kidney Disease Clinical Program Overview

#### Rationale for Kidney Disease Program

 Apabetalone has demonstrated reductions in alkaline phosphatase (a strong marker of CKD risk) and improvements in eGFR in CKD patients (eGFR < 60 mL/min/1.73m<sup>2</sup>) with CVD in the phase 2 ASSURE and SUSTAIN trials.



Data Presented in Keynote Address at the 2015 American Society of Nephrology Conference, San Diego

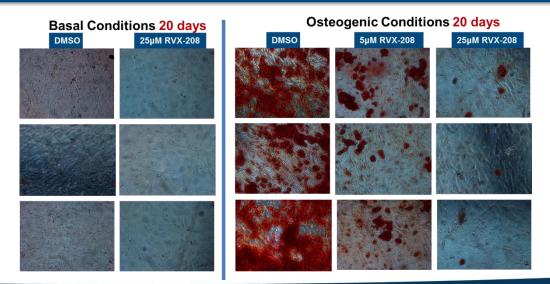
- Resverlogix believes that BET inhibition and apabetalone may have the potential to improve kidney function, as measured by eGFR, in patients suffering from various stages of kidney disease.
- Resverlogix is currently investigating the potential for expansion into specific kidney indications:
  - CKD (Stages 3a and 3b) patients, with a history of CVD (Phase 3 BETonMACE subgroup)
  - High Risk CKD Patients on Dialysis (Phase 2a BETonRenal study)

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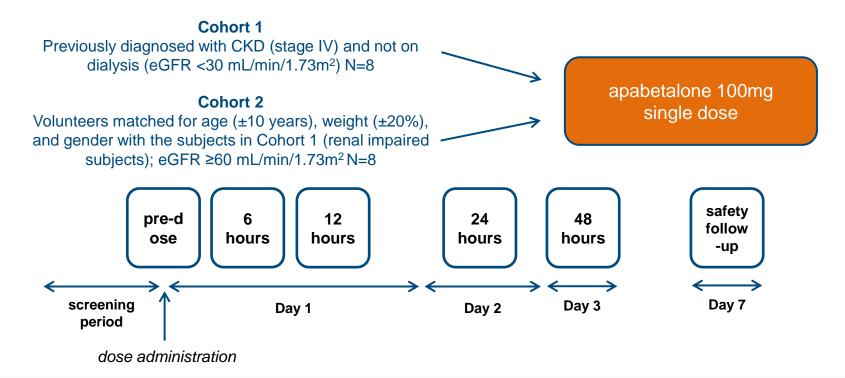
# Kidney Disease: Vascular Calcification

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- Coronary artery/vascular calcification is associated with all cause mortality, and cardiovascular events are the leading cause of mortality amongst patients with chronic kidney disease (CKD)
- Apabetalone treatment reduces expression of numerous proteins involved in vascular calcification in rat and human VSMCs in calcifying and osteogenic conditions, and in CVD patients

Apabetalone reduces calcium deposition in human VSMCs grown in osteogenic conditions

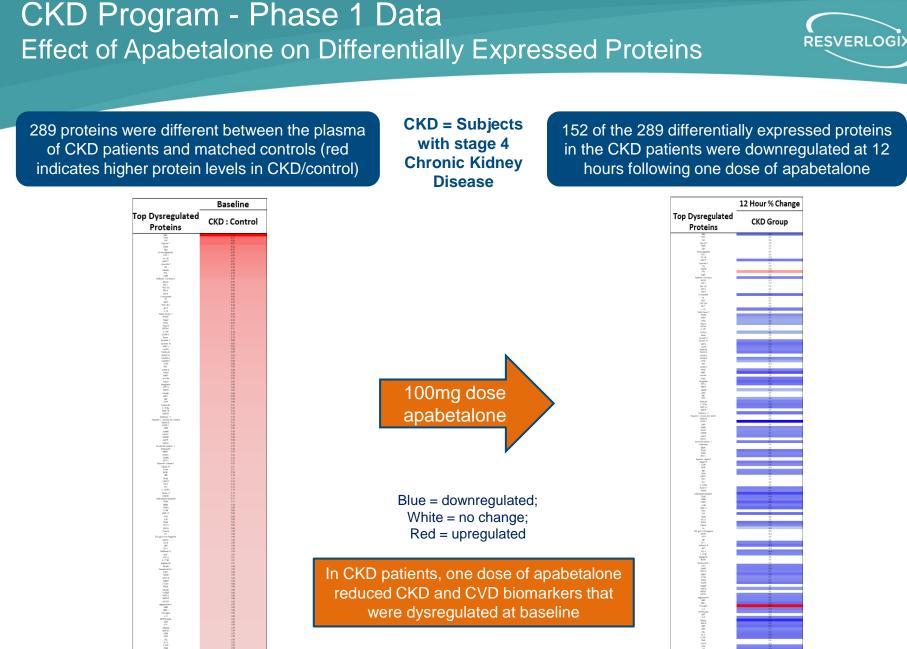


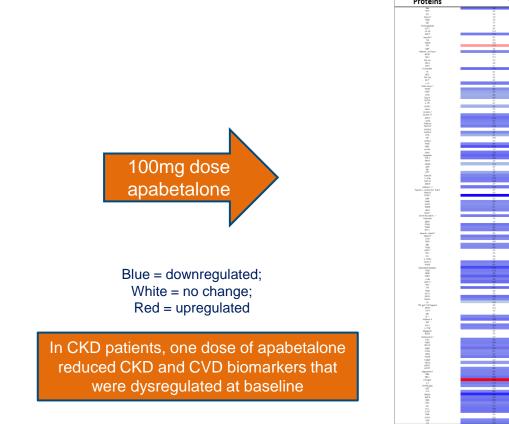
A Phase I, open-label, parallel group study to evaluate the safety and pharmacokinetics of a single oral dose of apabetalone in subjects with severe renal impairment



Trial demonstrated that apabetalone has a highly differential effect on protein levels based on disease status, healthy vs sick, reducing a variety of plasma proteins and downregulating pathways activated in the CKD cohort

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#### SOMAscan® Analysis of Plasma Proteome – Phase 1 Trial

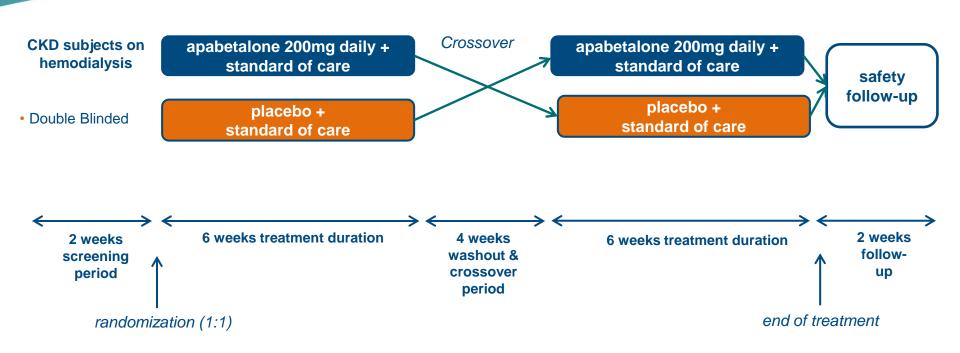
Apabetalone Reduces CVD and CKD Biomarkers

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	Protein Name	Gene	IV) (n=8) treated w	ubjects with CKD (stage /) (n=8) treated with 100 mg Apabetalone		Matched Control Subjects (n=8) treated with 100 mg Apabetalone	
		Symbol	% ∆ from baseline at 12h	p-value	% ∆ from baseline at 12h	p-value	
/	Interleukin-6	IL6		0.05	NS		
	Interleukin-1 alpha	IL1A		0.01	NS		
Inflammation	Interferon gamma	IFNG		0.04	NS		
minamination	TNF receptor superfamily member 1A	TNFRSF1A		0.05	NS		
	C-reactive protein	CRP		0.04	NS		
	Tumor necrosis factor	TNF		0.02	NS		
	P-selectin	SELP		0.04	NS		
Cell Adhesion	E-selectin	SELE		0.01		0.02	
	Intercellular adhesion molecule 1	ICAM1		0.05		0.04	
$\backslash$	Vascular cell adhesion protein 1	VCAM1		0.01	NS		
Matrix	Fibronectin	FN1		0.02	NS		
Remodeling Calcification	Stromelysin-1	MMP3		0.02	NS		
	Stromelysin-2	MMP10		0.02	NS		
	Osteopontin	SPP1		0.01		0.04	
Thrombosis	Plasminogen activator inhibitor 1	SERPINE1		0.04	NS		
	Tissue-type plasminogen activator	PLAT		0.01	NS		
	Urokinase-type plasminogen activator	PLAU		0.01	NS		
	D-dimer	FGA/B/C		0.05	NS		
	Urokinase plasminogen activator surface receptor	PLAUR		0.02	NS		

Apabetalone reduces markers of inflammation, cell adhesion, matrix remodeling, calcification and thrombosis in the CKD cohort after one dose and 12 hours

## **BETonRENAL Dialysis Study Design**



- The study is an sequential cross-over trial to evaluate the safety, tolerability, and efficacy of apabetalone in CKD patients on hemodialysis in addition to standard of care
- 30 CKD patients receiving standard regimens of hemodialysis three days per week
- · Clinical sites identified and prepared to begin patient enrollment

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## Kidney Disease Program Clinical Advisory Board





**Dr. Kamyar Kalantar-Zadeh** Chair *UC Irvine Chief Nephrology* 



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



Prof. Vincent Brandenburg Member University Hospital RWTH Aachen



Dr. Srinivasan Beddhu Member *University of Utah* 



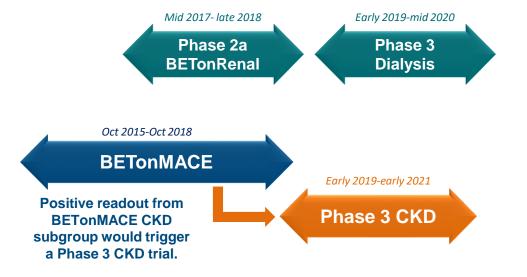
Dr. Carmine Zoccali Member University Pisa



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

#### Apabetalone Timeline For Kidney Indications





- BETonMACE subgroups will provide valuable insights into the top future indications for apabetalone
- Apabetalone represents a unique opportunity for the expansion into the high vascular risk space and provides potentially unprecedented accretive value

	2025	2024	2023	2022	2021	2020	2019	2018	2017	2016
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# Investment Highlights

Late Stage Trial	RVX is focused on significant unmet need in high-risk CVD, diabetes and CKD patient populations, with a phase 3 trial (BETonMACE) in CVD
Advanced R&D	Resverlogix's in-depth understanding of BET inhibitors and world-class medicinal chemistry allows it to develop candidates with better specificity, which affords the opportunity to target chronic disease through the BET pathway
Market Leader Targeting Unmet Need	Apabetalone expected to be indicated in several high-risk unmet need patient groups totaling over 10M patients in the top seven markets (US, 5 EU and Japan)
Established Safety Profile	Over 1,400 patients treated with apabetalone with no significant safety issues
Novel Mechanism of Action	Regulation of gene transcription, the turning on or off of various disease-causing genes, unlike the CRISPR approach of changing DNA
Quality Investor Base	Proven track record of attracting high quality and long term institutional investors

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