

Resverlogix Corp.
Annual Meeting - Corporate Update
December 12, 2017 Calgary, AB

## Forward Looking Statements



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. 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 forwardlooking 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 Overview



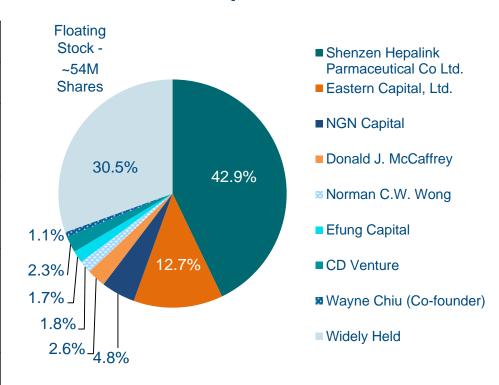
- Resverlogix Corp. (TSX:RVX) is a Calgary and San Francisco based clinical stage biotechnology company focused on the development of apabetalone
- Apabetalone (RVX-208) is a first-in-class small molecule selective BET bromodomain inhibitor, which acts via an epigenetic mechanism that can turn disease-causing genes off, thereby normalizing gene function
  - Apabetalone is the only selective BET bromodomain inhibitor in clinical trials
- Resverlogix has initiated clinical trial work for apabetalone in three indications:
  - Cardiovascular Disease (BETonMACE Trial) Phase 3
  - Chronic Kidney Disease (BETonRENAL Trial) Phase 2b
  - Fabry Disease Phase 2b

#### Capitalization and Financial Profile



Founded	2001
Ticker	TSX: RVX
Market Cap	~C\$425M
Long-Term Debt	C\$0.0M
Shares Outstanding	~175.0M
Cash Burn (Annual)	~C\$40.0M
Finance	\$87M - Closed Dec 2017

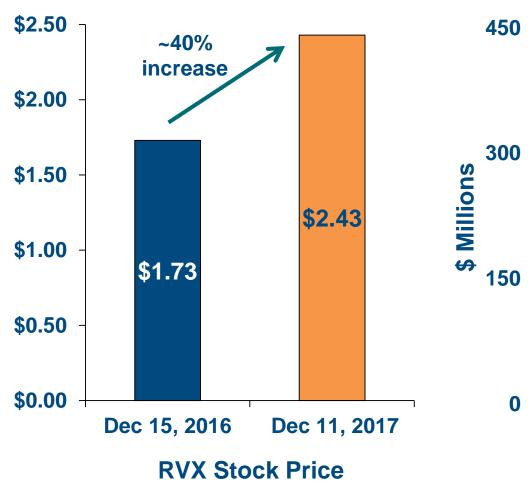
#### **RVX Top Shareholders**

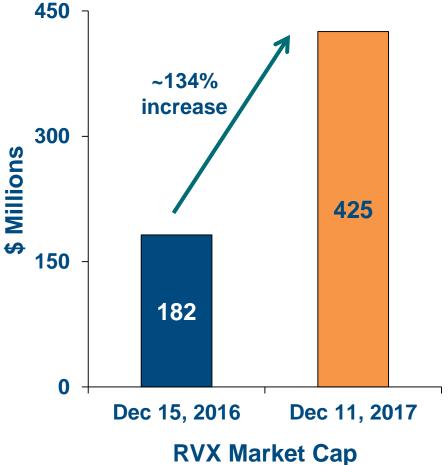


- RVX shareholder base consists of several long term investors who have been supportive over 10 years
- RVX maintains a diversified public market float of approximately 54M shares

#### RVX Stock Price and Market Cap

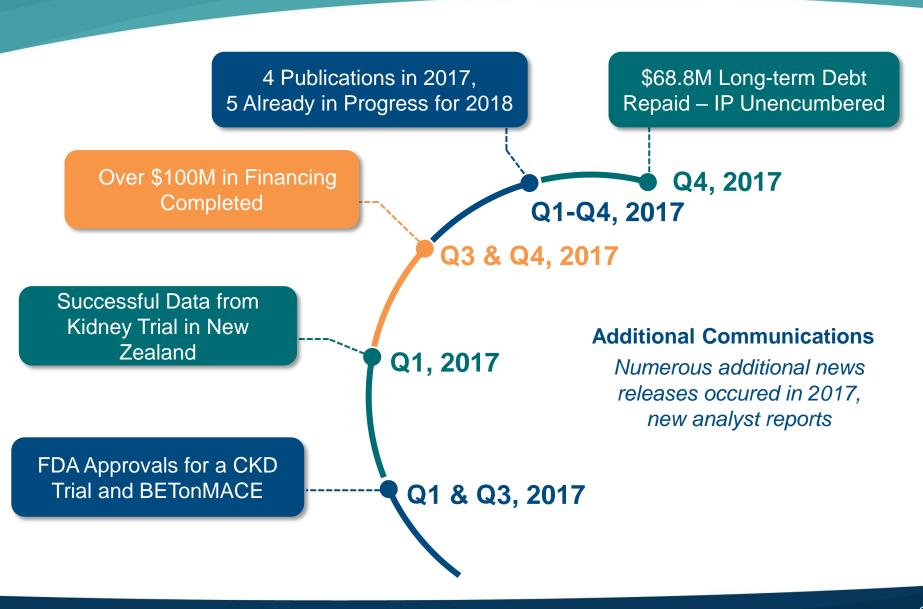






## 2017 - Major Accomplishments





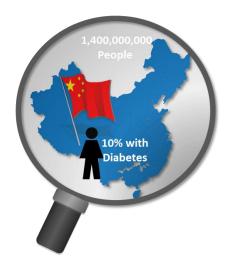
## Shenzhen Hepalink Partnership



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

RESVERLOGIX

Resverlogix – Shenzhen Hepalink Exclusive Licensing Agreement						
Compound	Apabetalone (RVX-208)					
Licensor	Resverlogix Corp.					
Licensee	Shenzhen Hepalink Pharmaceutical Co., Ltd.					
Territories	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>					



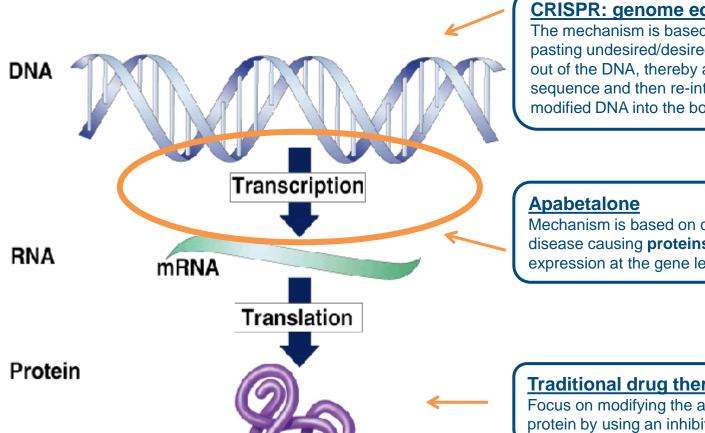




**Apabetalone and the BET Platform** 

#### Differentiation: Advanced Mechanism of Action





#### **CRISPR:** genome editing

The mechanism is based on cutting and pasting undesired/desired sequences into or out of the DNA, thereby altering the gene sequence and then re-introducing the modified DNA into the body

Mechanism is based on changing the levels of disease causing proteins by modulating their expression at the gene level

#### **Traditional drug therapies**

Focus on modifying the activity of one disease protein by using an inhibitor or antibody

#### Differentiation: RVX's BET Platform

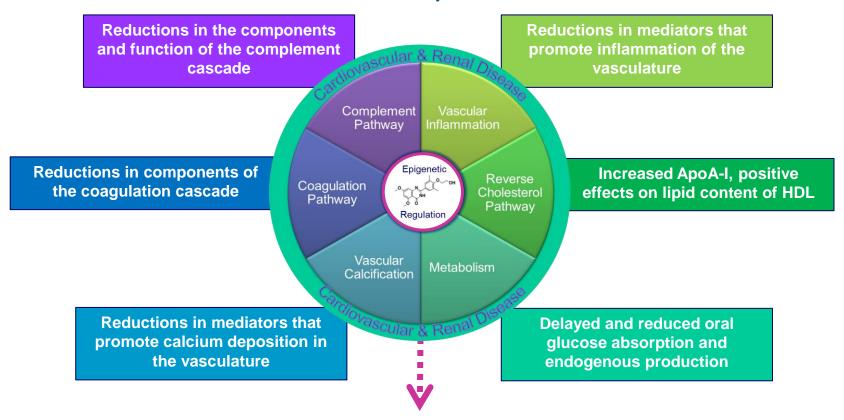


- Resverlogix has discovered compounds that bind the bromodomains of BET proteins with a high degree of specificity
  - Other BET programs hit multiple targets (BRD2, BRD3, BRD4, BRDT, etc.)
  - Our expertise in medicinal chemistry and epigenetics allows us to identify small molecules that target one or a specified subset of BET proteins
    - Resverlogix's apabetalone specifically targets BRD4
- Our Phase 2 clinical program provided us with the only blood bank of BET inhibitor-treated 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 provides a level of sophistication around BET inhibition that surpasses that of many others working in this area
- Specificity of Resverlogix's molecules improves the safety profile 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 side-effect profile acceptable for long-term treatment

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



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



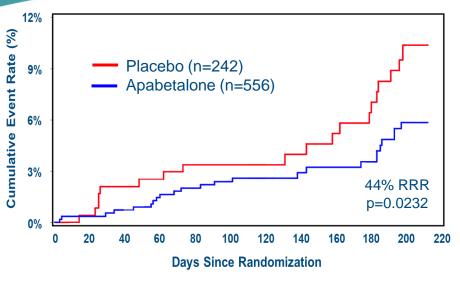
Reduced incidence of cardiac events and renal impairment

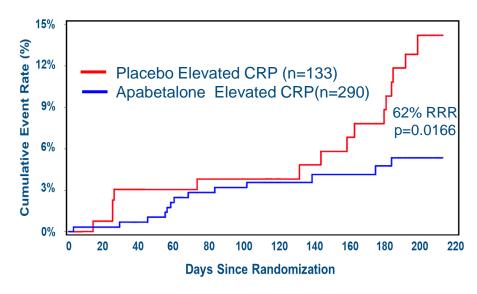


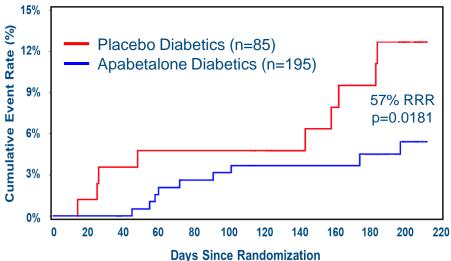
**BETonMACE Clinical Program Overview** 

# Nicholls et al. 2017: American Journal of Cardiovascular Drugs







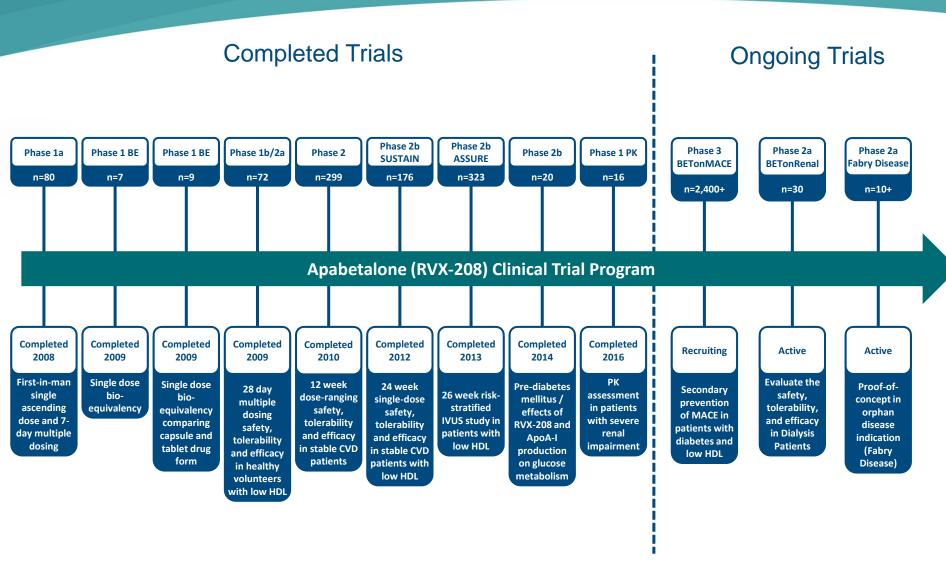


**MACE:** <u>Major Adverse Cardiac Events including: death, myocardial infarction, stroke, coronary revascularization, hospitalization for acute coronary syndrome or heart failure</u>

Decrease in MACE was most profound in patients who had a higher level of inflammation such as patients with diabetes

#### Apabetalone Clinical Trials to Date





#### CVD Program Moving Forward-BETonMACE CV Outcomes Study





#### 2,400 + **subjects**

- double blinded
- 1-2 week statin run-in



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
  - o Myocardial infarction (MI), unstable angina or percutaneous coronary intervention
- HDL < 1.04 for males and < 1.17 for females</li>

#### BETonMACE Commenced November 2015

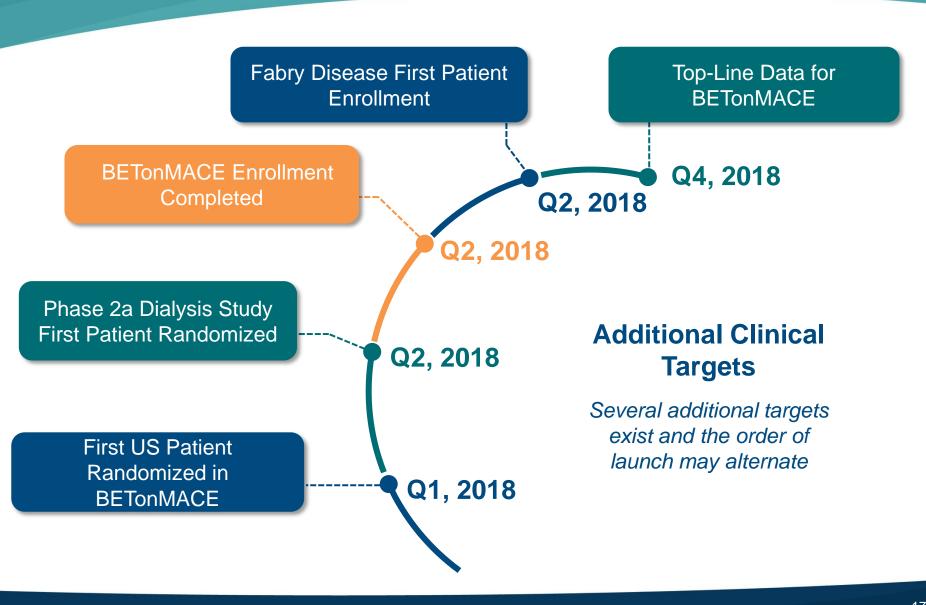




Apabetalone has already been tested in over 1,800 patients in 19 countries around the world.

## The Upcoming Clinical Year Estimates





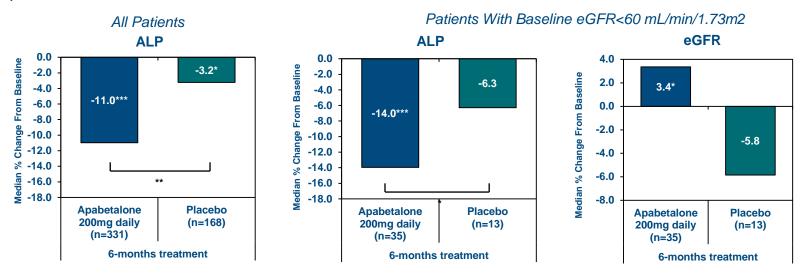


**Chronic Kidney Disease Clinical Program Overview** 

## Rationale for Chronic Kidney Disease (CKD) Program



Apabetalone has demonstrated reductions in alkaline phosphatase (ALP), a strong marker of CKD risk and improvements in eGFR in CKD patients (eGFR < 60 mL/min/1.73m²) with CVD in the phase 2 ASSURE and SUSTAIN trials.</li>



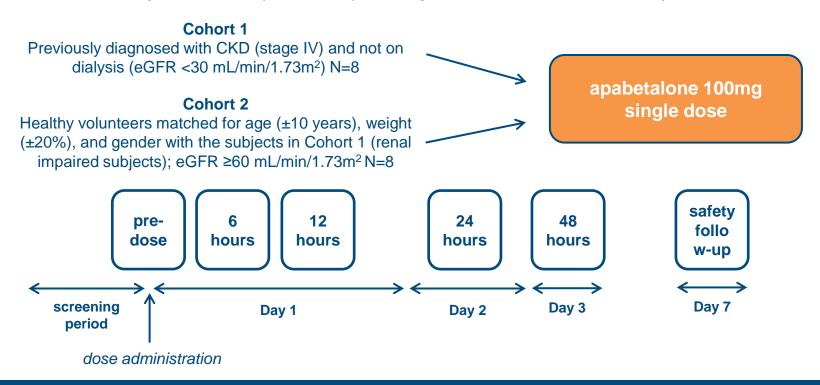
Data Presented in Keynote Address at the 2015 American Society of Nephrology Conference, San Diego

- 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)

## Kidney Disease: Phase I Study



A Phase I, open-label, parallel group study to evaluate the safety and pharmacokinetics of a single oral dose of apabetalone (RVX-208) in subjects with severe renal impairment



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

#### CKD Program - Phase 1 Data

#### Effect of Apabetalone on Differentially Expressed Proteins

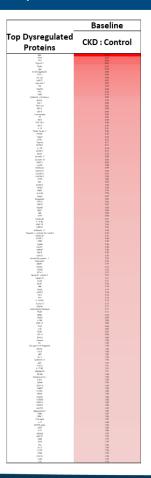


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288 proteins were different between the plasma of CKD patients and matched controls (red indicates higher protein levels in CKD/control)

CKD = Subjects with stage IV Chronic Kidney Disease

152 of the 288 differentially expressed proteins in the CKD patients were downregulated at 12 hours following one dose of apabetalone

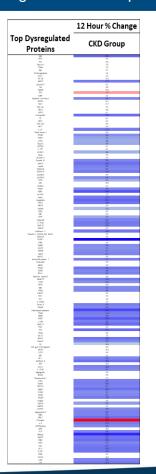


TSX: RVX



Blue = downregulated; white = no change; Red = upregulated

In CKD patients, one dose of apabetalone reduced CKD and CVD biomarkers that were dysregulated at baseline



## SOMAscan® Analysis of Plasma Proteome – Phase 1 Trial Apabetalone Reduces CVD and CKD Biomarkers

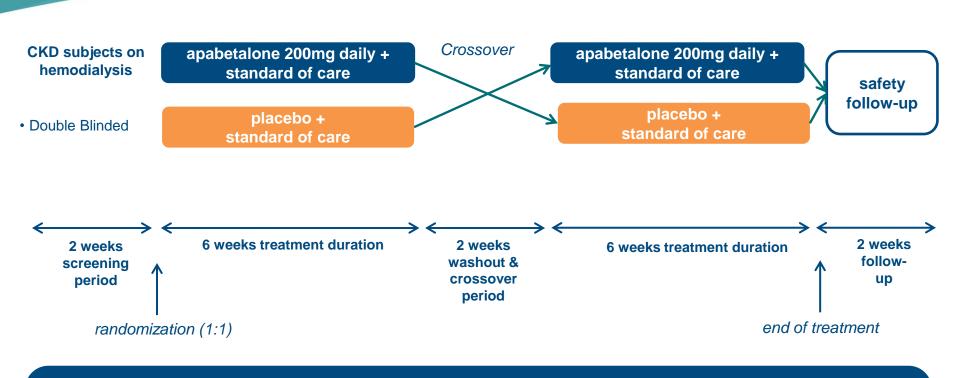


Protein Name		Gene Symbol	Subjects with CKD (stage IV) (n=8) treated with 100 mg apabetalone		Matched Control Subjects (n=8) treated with 100 mg apabetalone	
			% Δ from baseline at 12h	p-value	% Δ from baseline at 12h	p-value
Inflammation	Interleukin-6	IL6		0.05		NS
	Interleukin-1 alpha	IL1A		0.01		NS
	Interferon gamma	IFNG		0.04		NS
	TNF receptor superfamily member 1A	TNFRSF1A		0.05		NS
	C-reactive protein	CRP		0.04		NS
	Tumor necrosis factor	TNF		0.02		NS
Cell Adhesion	P-selectin	SELP		0.04		NS
	E-selectin	SELE		0.01		0.02
	Intercellular adhesion molecule 1	ICAM1		0.05		0.04
	Vascular cell adhesion protein 1	VCAM1		0.01		NS
Matrix Remodeling Calcification	Fibronectin	FN1		0.02		NS
	Stromelysin-1	MMP3		0.02		NS
	Stromelysin-2	MMP10		0.02		NS
Thrombosis	Osteopontin	SPP1		0.01		0.04
	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

#### Kidney Disease Program Clinical Advisory Board





**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



**Follow-on Compound Program Overview** 

#### **Expanding BETi Potential Targets**



- Pulmonary Arterial Hypertension: the effect of apabetalone on cells and in an animal model of PAH was positive
- Muscular Dystrophy/Facio Scapulo Humeral Dystrophy: testing apabetalone and other RVX compounds for target and biomarker engagement in muscle cells; also analyzing human muscle biopsies from diabetes patients treated with apabetalone
- **Fabry Disease:** ex vivo treatment of Fabry patient blood treated with apabetalone will analyze the effect on inflammatory mediators with plans to move into a safety/efficacy phase 2 study
- Neuroinflammation: direct effects of apabetalone demonstrate reduced inflammation and microglial activation
- PNH/Paroxysmal Nocturnal Hemoglobinuria: 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: proteomic analysis of data from CKD PK study to be published shortly supports studies in renal dialysis
- HIV-1 Latency: BET inhibitors have potential effects on reactivating HIV latency for therapeutic treatment

## **Expanding BETi Potential Targets**



www.nature.com/scientificreports



RESVERLOGIX.com

#### OPEN

# BET inhibitors RVX-208 and PFI-1 reactivate HIV-1 from latency

Panpan Lu<sup>1</sup>, Yinzhong Shen<sup>2</sup>, He Yang<sup>1</sup>, Yanan Wang<sup>1</sup>, Zhengtao Jiang<sup>1</sup>, Xinyi Yang<sup>1</sup>, Yangcheng Zhong<sup>1</sup>, Hanyu Pan<sup>1</sup>, Jianqing Xu<sup>2</sup>, Hongzhou Lu<sup>2</sup> & Huanzhang Zhu<sup>1</sup>

## Why Invest in Resverlogix?



- 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 2018
- Well established safety profile to date, over 1,800 patients treated with apabetalone with no significant safety issues
- Proven track record of funding development while minimizing shareholder dilution



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