



TSX: RVX

**Resverlogix Corp.**  
**Corporate Presentation**  
February, 2019

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 may include forward looking information relating to the Phase 3 BETonMACE clinical trial, Phase 2a kidney dialysis clinical trial and Fabry Disease clinical trial, and the potential role of apabetalone in the treatment of CVD, DM, chronic kidney disease, end-stage renal disease treated with hemodialysis, neurodegenerative disease, Fabry disease, peripheral artery disease and other 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](http://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.

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## Snapshot

- Late-stage clinical biotechnology company that has built a **leadership position in epigenetics**
- Lead product candidate is **Apabetalone, a first-in-class small molecule selective bromodomain extra-terminal (BET) protein inhibitor** with broad applicability for cardiovascular, renal and other disease indications
- **Fully enrolled Phase 3** trial for secondary prevention of MACE in patients with diabetes (type 2) and low HDL
- Attractive safety profile, with **over 1,900 patients dosed** and eight successful DSMB readouts in Phase 3
- Addresses **critical unmet need with 12 million+ patients** in top 8 markets
- Robust intellectual property position for composition, use, and manufacturing, **with patent life ranging from 2027 to 2034**

## Profile

Listing	Toronto Stock Exchange: RVX
Market Cap	~C\$620M <sup>(2)</sup>   ~US\$473M <sup>(1)</sup>
Shares Outstanding	195M <sup>(2)</sup>

Note

1 Based on USD/CAD exchange rate of 1.31

2 As of January 31, 2019

# Our Clinical Development Pipeline



<u>Apabetalone Indication</u>	Pre-clinical	Phase 1	Phase 2 Ready	Phase 3	Status Est.
Acute Coronary Syndrome (ACS) - BETonMACE					<u>Initiation</u> : 2015 <u>Trial completion estimate</u> : H1 2019
Vascular Cognitive Dementia*					<u>Initiation</u> : H2 2019
Chronic Kidney Disease*					<u>Initiation</u> : H2 2019
Fabry's disease					<u>Initiation</u> : H2 2019
Pulmonary Arterial Hypertension					<u>Initiation</u> : H2 2019

\* To Initiate following BETonMACE trial completion

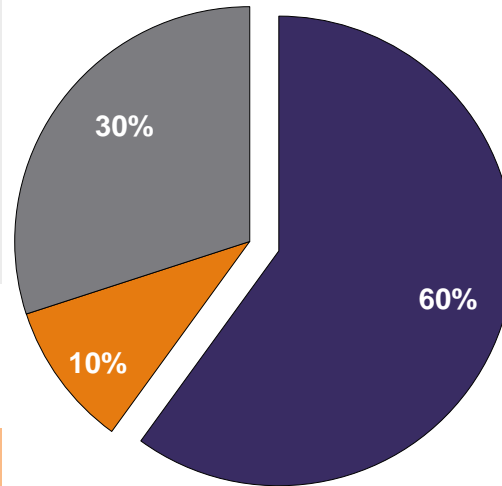


## Cardiovascular disease

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

### Current CVD Therapies

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



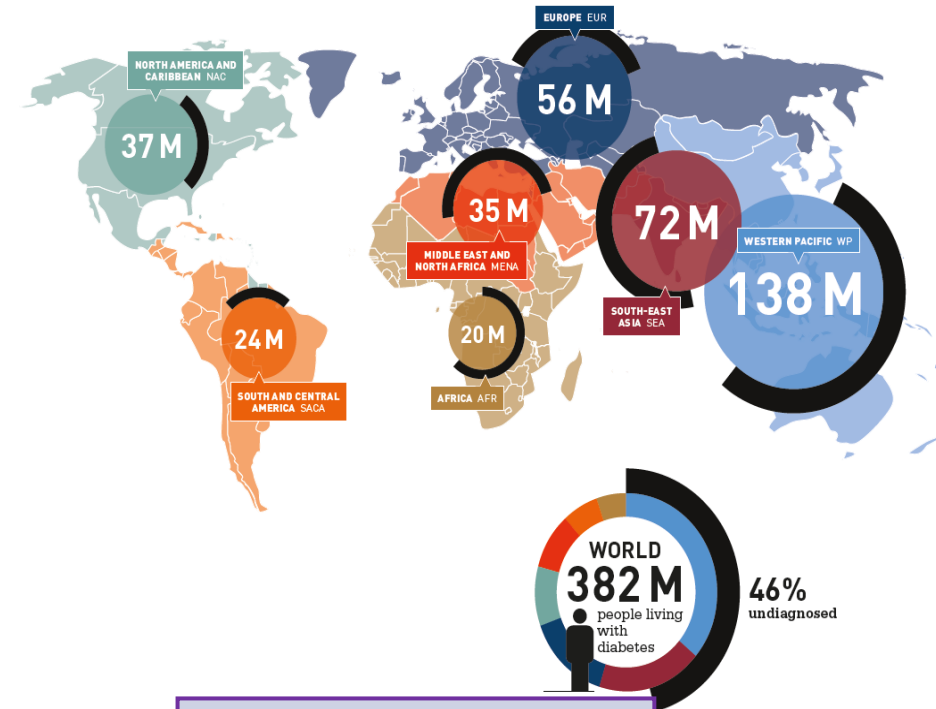
### New LDL Modulators

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

### Opportunity

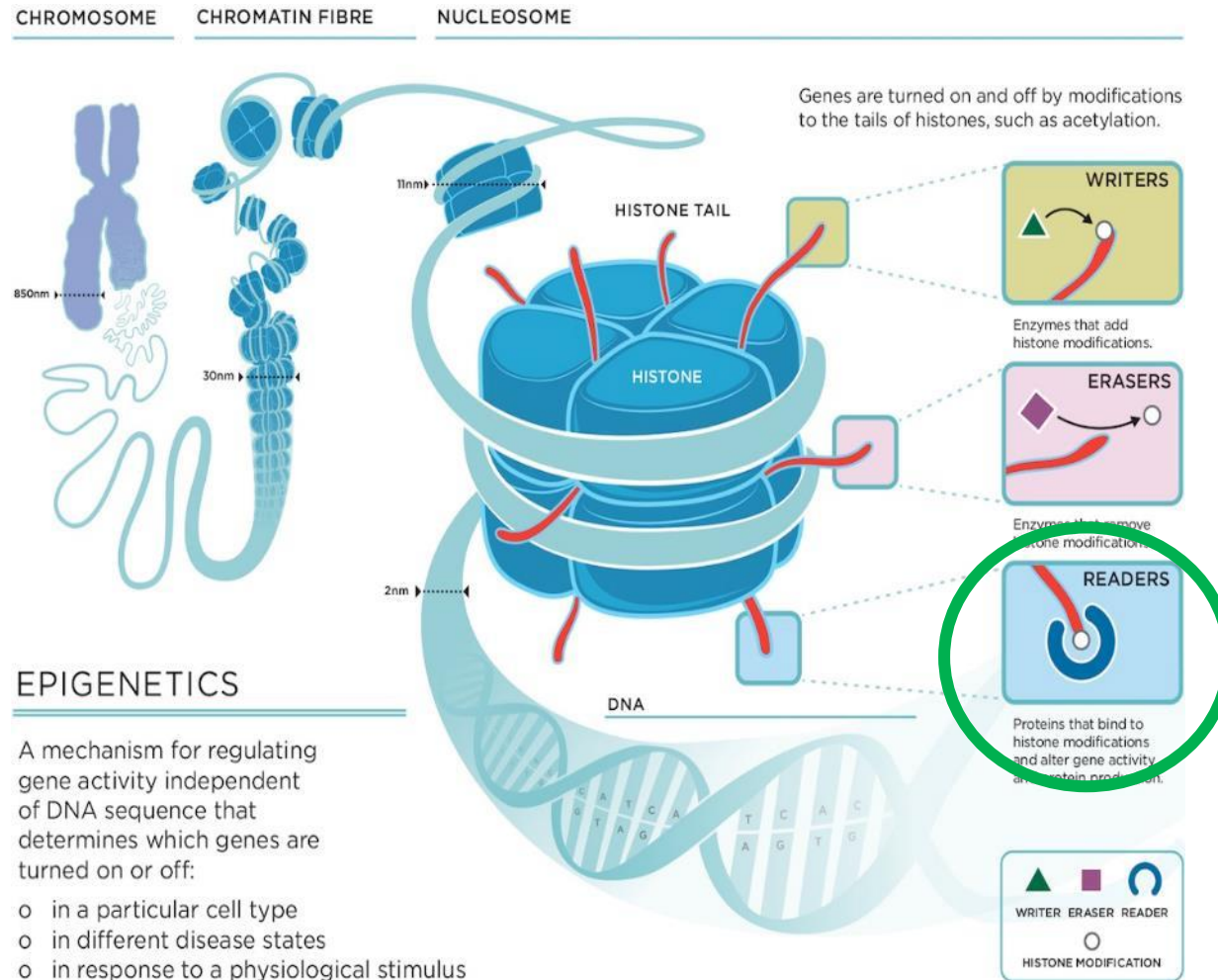
Huge market potential resides in the remaining 60% unmet need in CVD management

## The Diabetes Epidemic



**Diabetes prevalence will increase by 55% in the next 30 years, with the Middle east region showing an increase of 96%.**

IDF Diabetes Atlas | Sixth edition

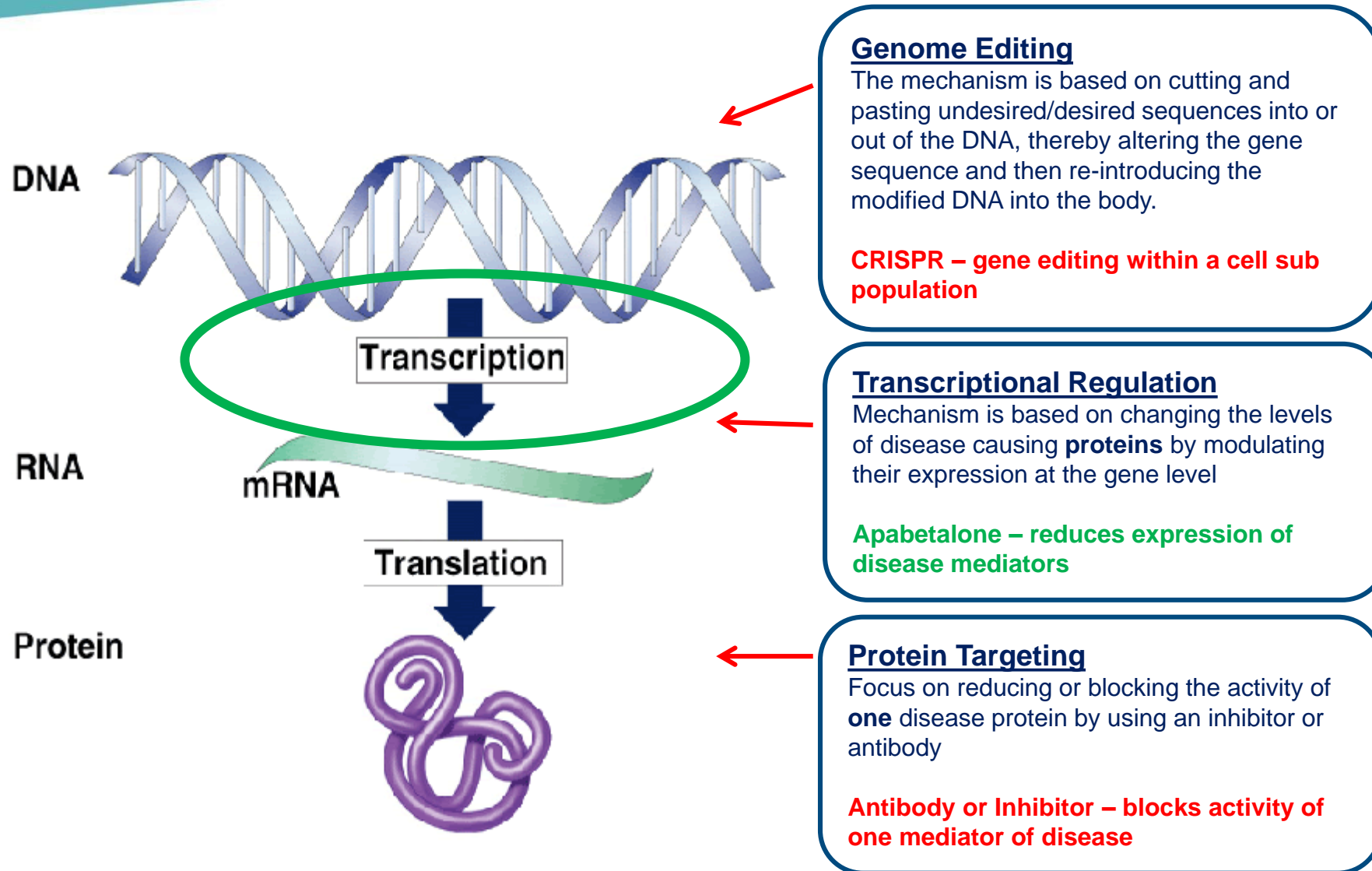


- The epigenetic code refers to modifications to chromatin components that regulate its activity
- Turning genes **on** or **off** is regulated by these modifications
- BET (Bromodomain and Extraterminal Domain) proteins recognize these modifications and turn genes **on**

COPYRIGHT © 2012 - RICHARD E. BALLERMANN

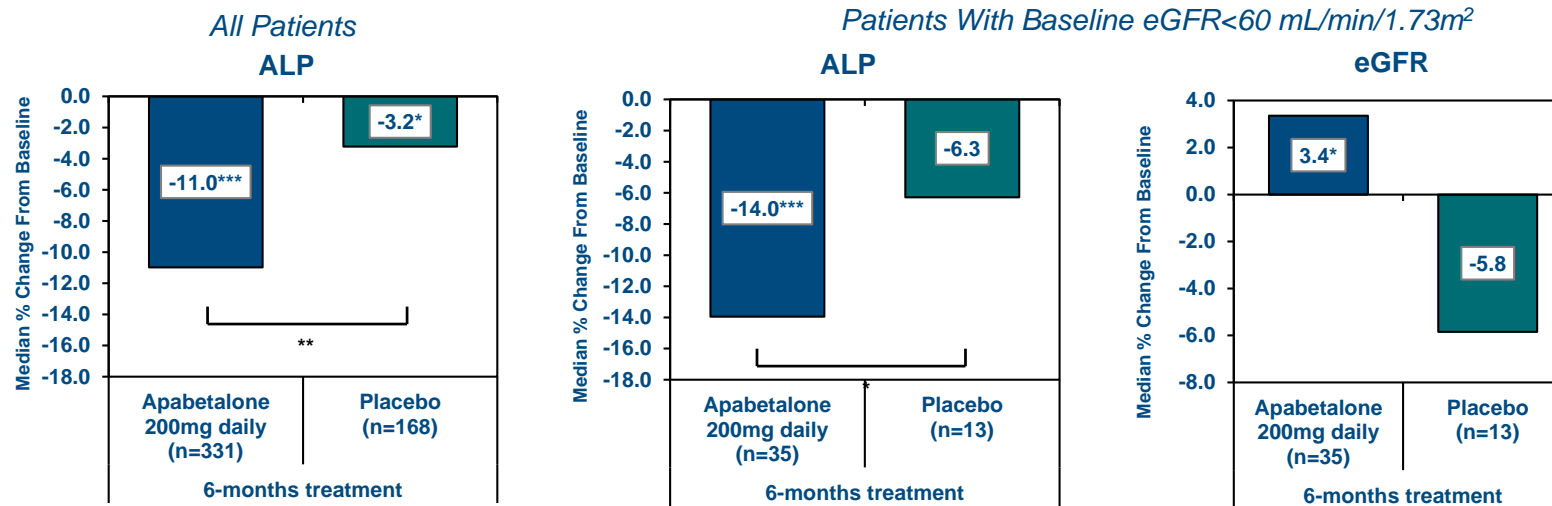
- Resverlogix has discovered compounds that **selectively** bind the bromodomains of BET proteins
  - Bromodomain selectivity: Resverlogix's Apabetalone selectively targets BD2
  - BET (BRD2, BRD3, BRD4) protein selectivity: Our expertise in medicinal chemistry and epigenetics allows us to identify small molecules that target one or a specified subset of BET proteins
- Our Phase 2 clinical program provided us with what was **the only blood bank of BET inhibitor-treated patients in the world**
  - In-depth analysis of proteomics, genomics, and pathways 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 properties of Resverlogix's molecules **avoid side effects seen with other BETi**
  - 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

# Unique Mechanism of Action





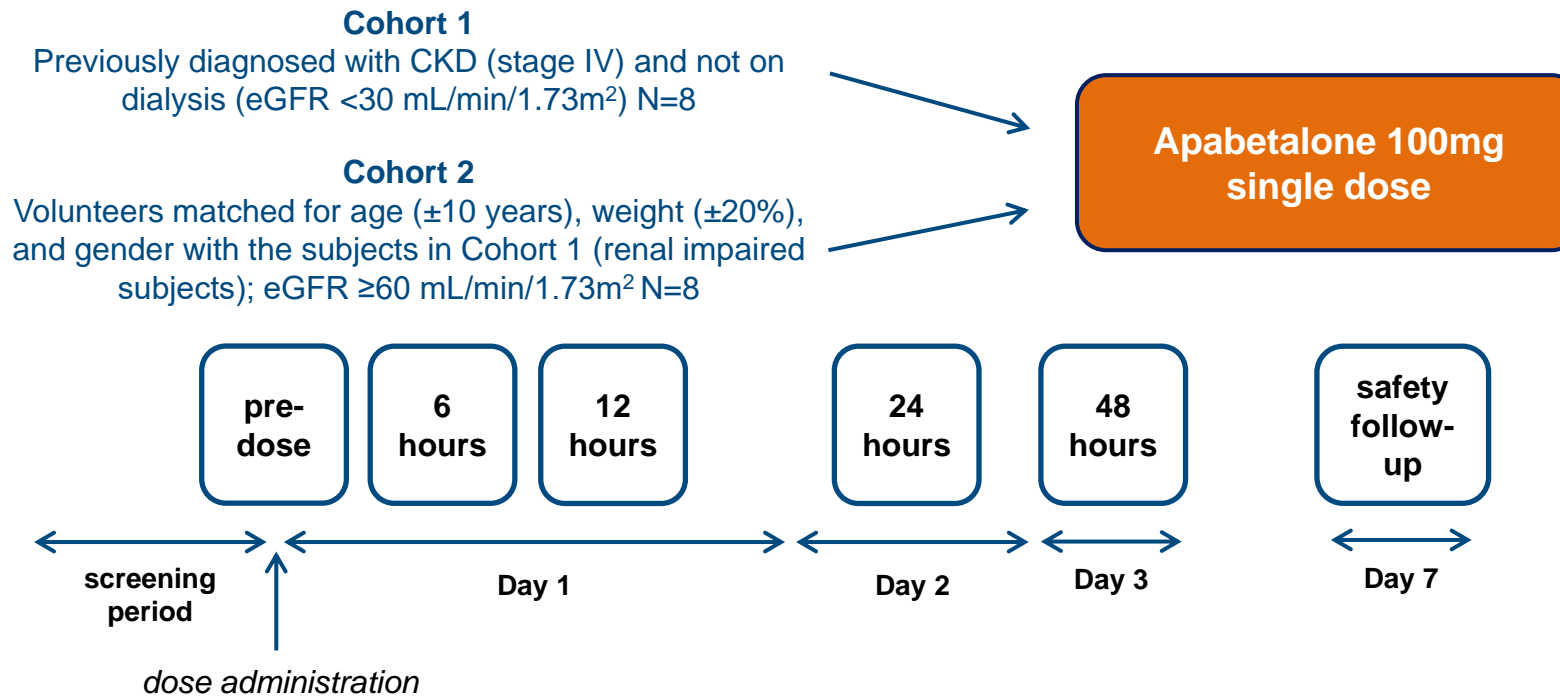
- Apabetalone has demonstrated reductions in alkaline phosphatase (ALP; a strong marker of CKD risk) and improvements in estimated glomerular filtration rate (eGFR) in CKD patients (eGFR < 60 mL/min/1.73m<sup>2</sup>) with CVD in the phase 2 ASSURE and SUSTAIN trials



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

- BET inhibition by 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 2b BETonRenal study)

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



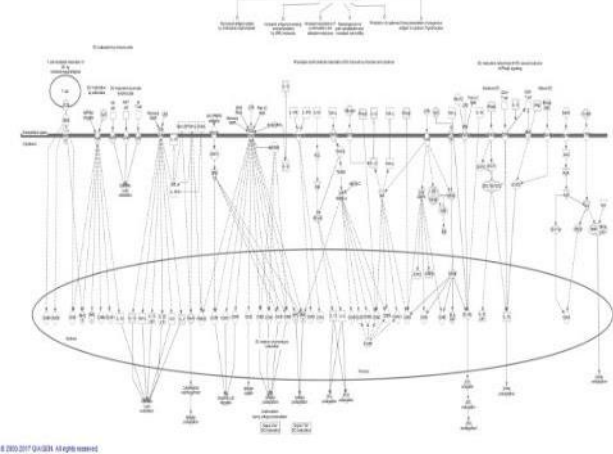
Trial demonstrated that Apabetalone has a highly differential effect on protein levels based on disease status, healthy vs sick, reducing a variety of plasma proteins and downregulating pathways activated in the CKD cohort

# SOMAscan® Analysis of Plasma Proteome in CKD Patients

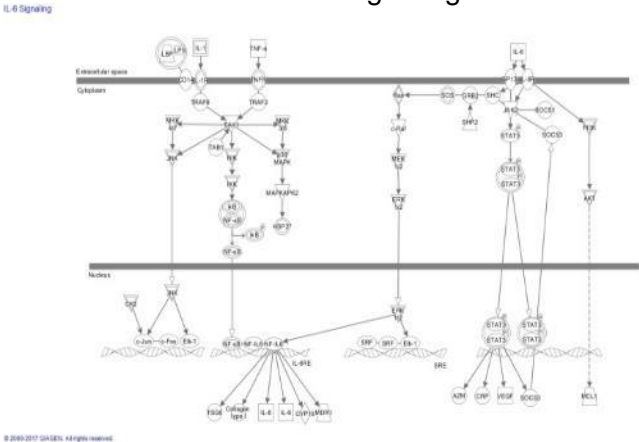
## IPA Canonical Pathways



Dendritic cell maturation



IL6 Signaling



**Prediction Legend**

more extreme in dataset

- Increased measurement (Yellow circle)
- Decreased measurement (Cyan circle)

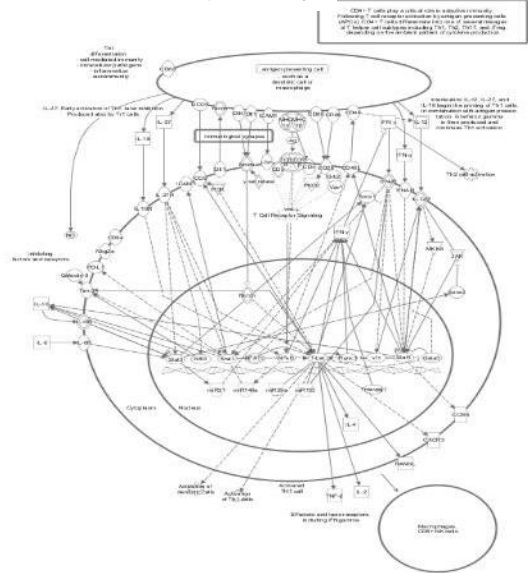
more confidence

- Predicted activation (Orange circle)
- Predicted inhibition (Blue circle)

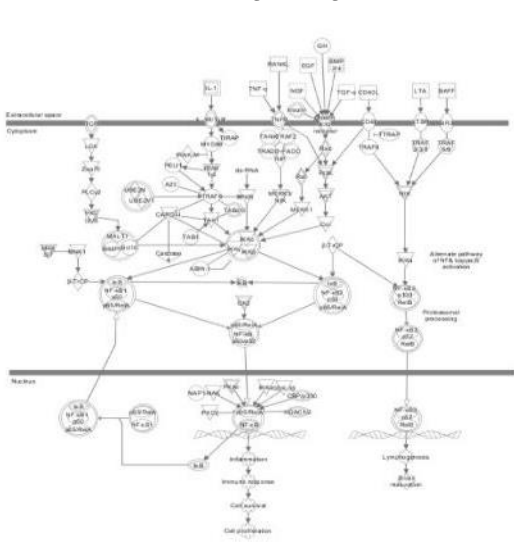
**Predicted Relationships**

- Leads to activation (Orange line)
- Leads to inhibition (Blue line)
- Findings inconsistent with state of downstream molecule (Yellow line)
- Effect not predicted (Grey line)

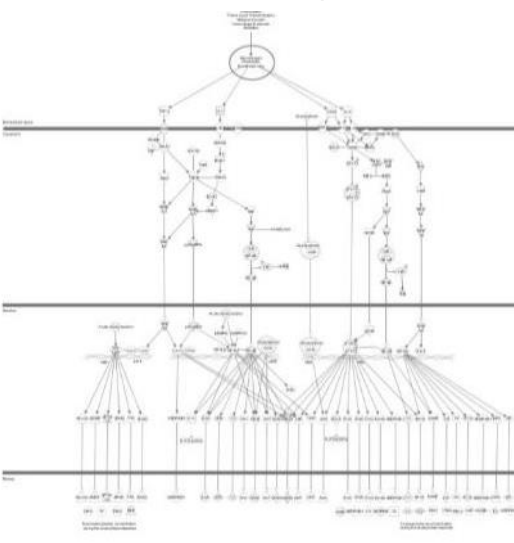
Th1 pathway



NF-kB Signaling



Acute Phase Response

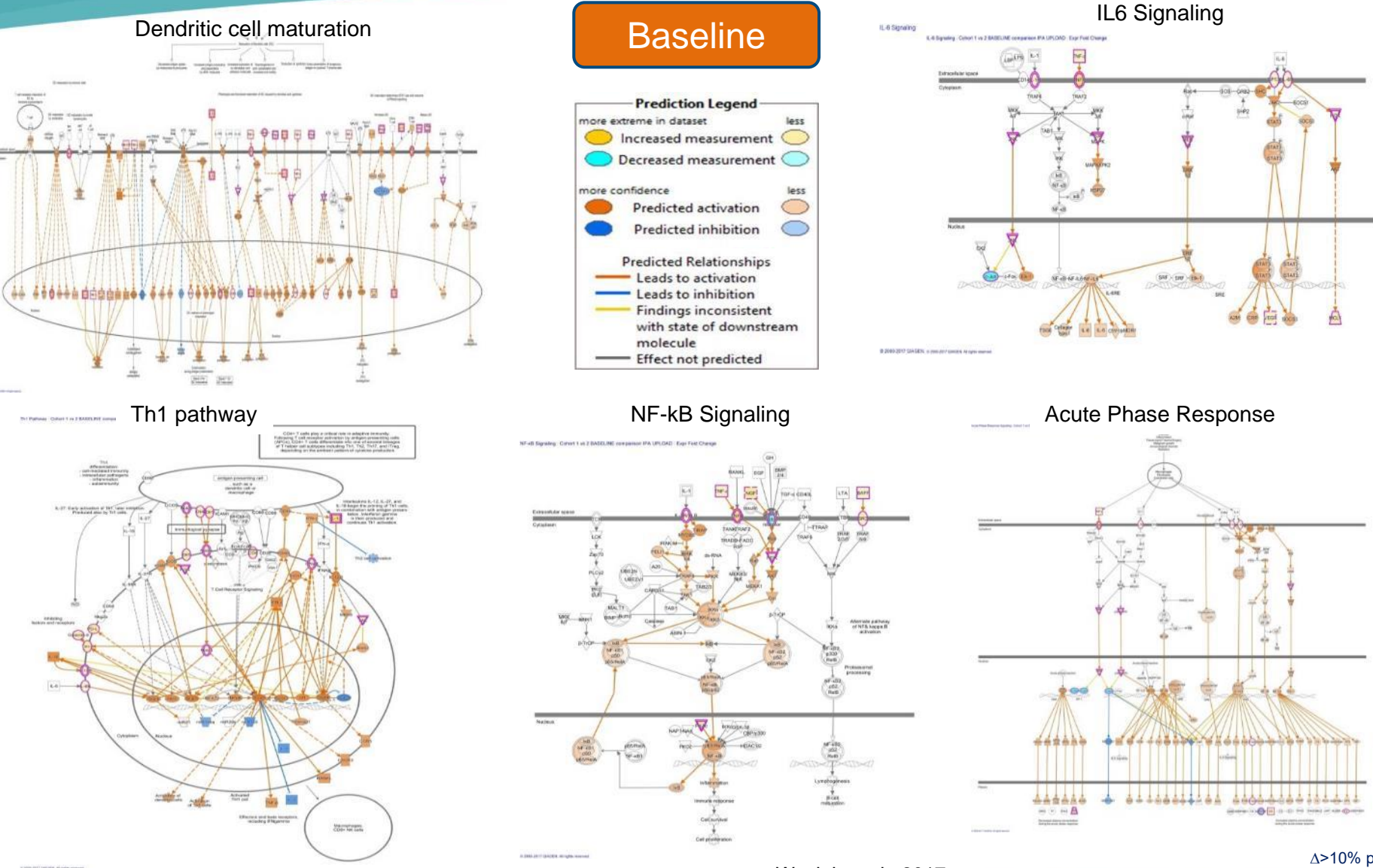


Wasiak et al., 2017

$\Delta > 10\%$   $p \leq 0.05$

# SOMAscan® Analysis of Plasma Proteome

## IPA Canonical Pathways: Top 5 Pathways Upregulated at Baseline



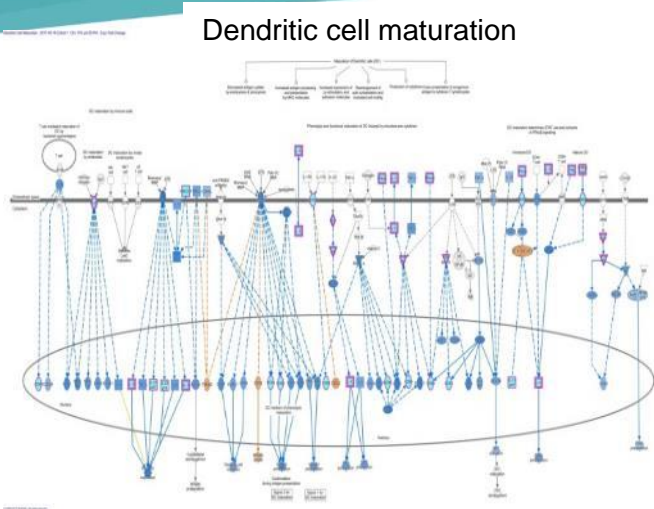
$\Delta > 10\%$   $p \leq 0.05$

Wasiak et al., 2017

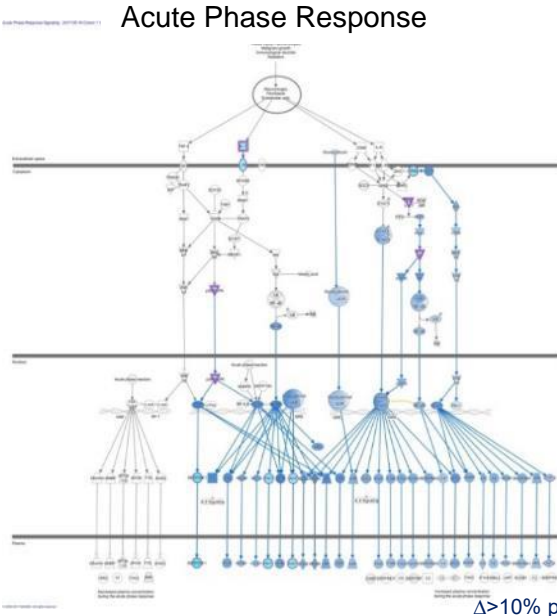
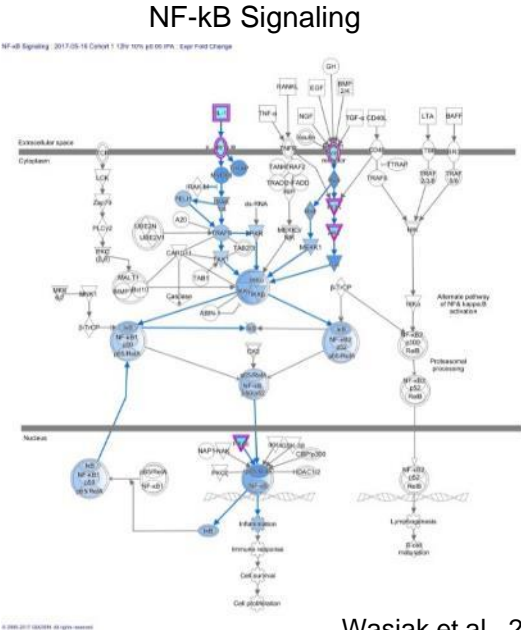
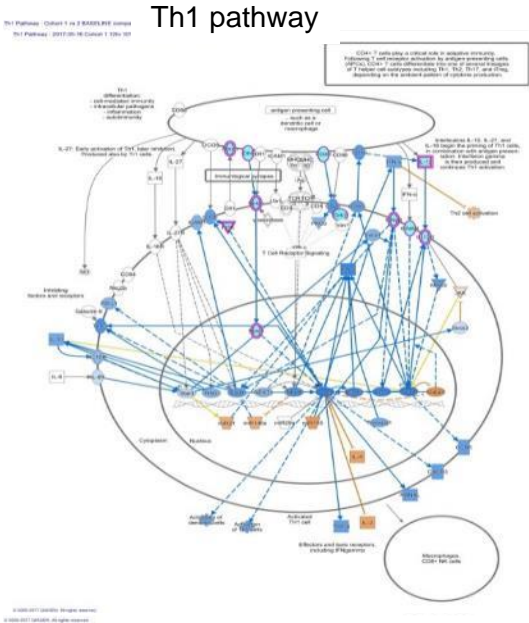
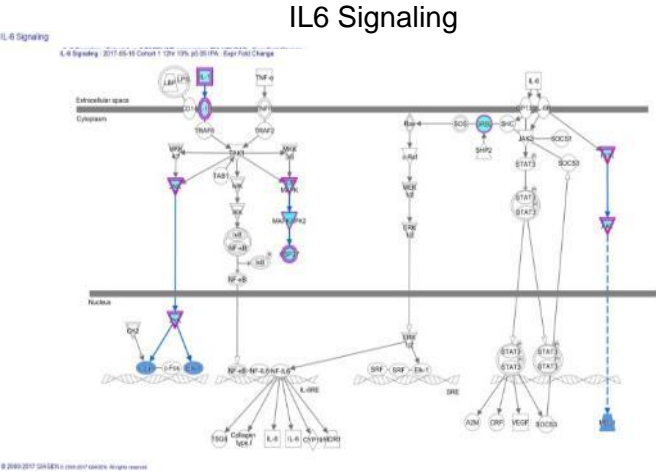


# SOMAscan® Analysis of Plasma Proteome

## IPA Canonical Pathways: Top 5 Pathways Downregulated with Apabetalone



Apabetalone



Wasiak et al., 2017

$\Delta > 10\%$   $p \leq 0.05$



# 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	<div><div></div></div>	0.05	NS	
	Interleukin-1 alpha	IL1A	<div><div></div></div>	0.01	NS	
	Interferon gamma	IFNG	<div><div></div></div>	0.04	NS	
	TNF receptor superfamily member 1A	TNFRSF1A	<div><div></div></div>	0.05	NS	
	C-reactive protein	CRP	<div><div></div></div>	0.04	NS	
	Tumor necrosis factor	TNF	<div><div></div></div>	0.02	NS	
Cell Adhesion	P-selectin	SELP	<div><div></div></div>	0.04	NS	
	E-selectin	SELE	<div><div></div></div>	0.01	<div><div></div></div>	0.02
	Intercellular adhesion molecule 1	ICAM1	<div><div></div></div>	0.05	<div><div></div></div>	0.04
	Vascular cell adhesion protein 1	VCAM1	<div><div></div></div>	0.01	NS	
Matrix Remodeling Calcification	Fibronectin	FN1	<div><div></div></div>	0.02	NS	
	Stromelysin-1	MMP3	<div><div></div></div>	0.02	NS	
	Stromelysin-2	MMP10	<div><div></div></div>	0.02	NS	
	Osteopontin	SPP1	<div><div></div></div>	0.01	<div><div></div></div>	0.04
Thrombosis	Plasminogen activator inhibitor 1	SERPINE1	<div><div></div></div>	0.04	NS	
	Tissue-type plasminogen activator	PLAT	<div><div></div></div>	0.01	NS	
	Urokinase-type plasminogen activator	PLAU	<div><div></div></div>	0.01	NS	
	D-dimer	FGA/B/C	<div><div></div></div>	0.05	NS	
	Urokinase plasminogen activator surface receptor	PLAUR	<div><div></div></div>	0.02	NS	

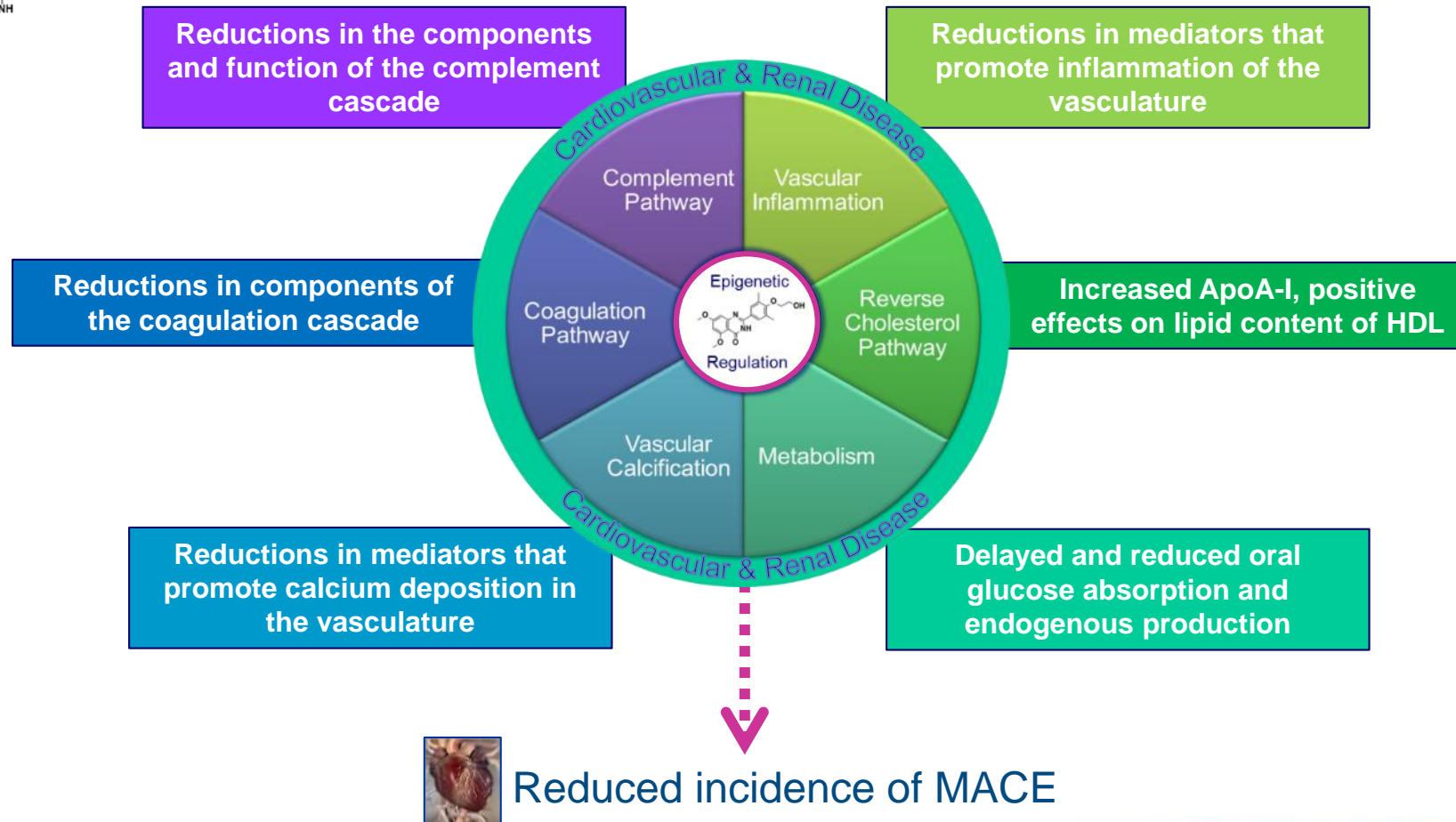
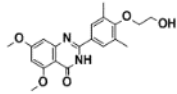
Apabetalone reduces markers of inflammation, cell adhesion, matrix remodeling, calcification and thrombosis in the CKD cohort after one dose and 12 hours

"NS": not significant

Wasiak et al., 2017

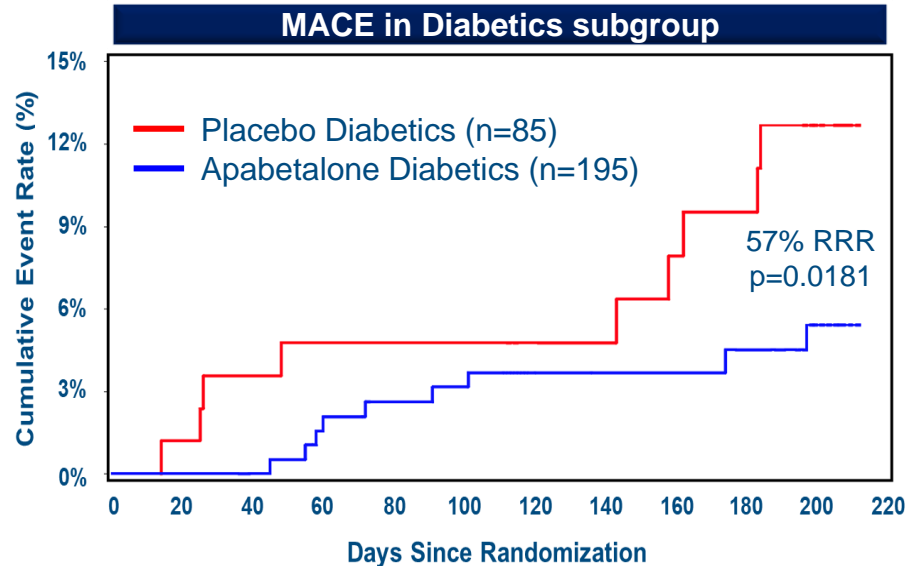
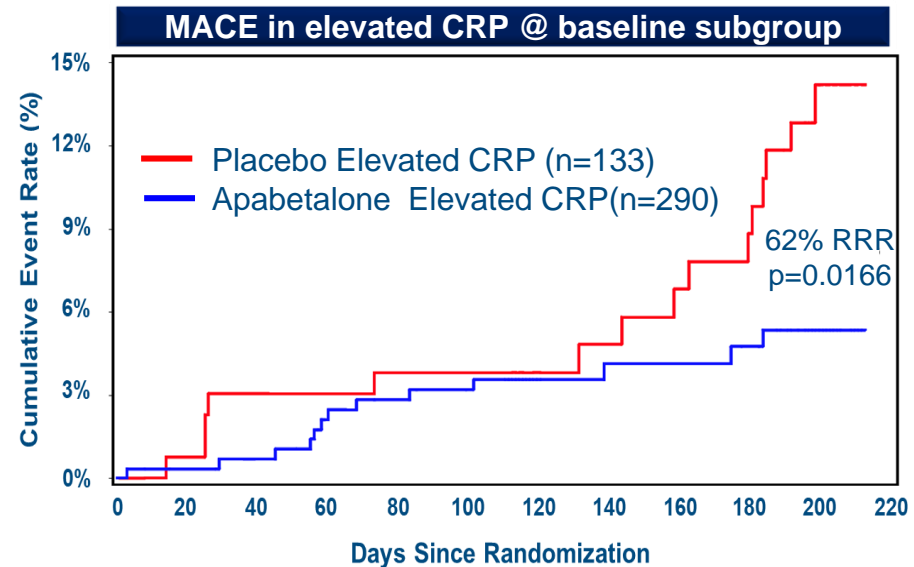
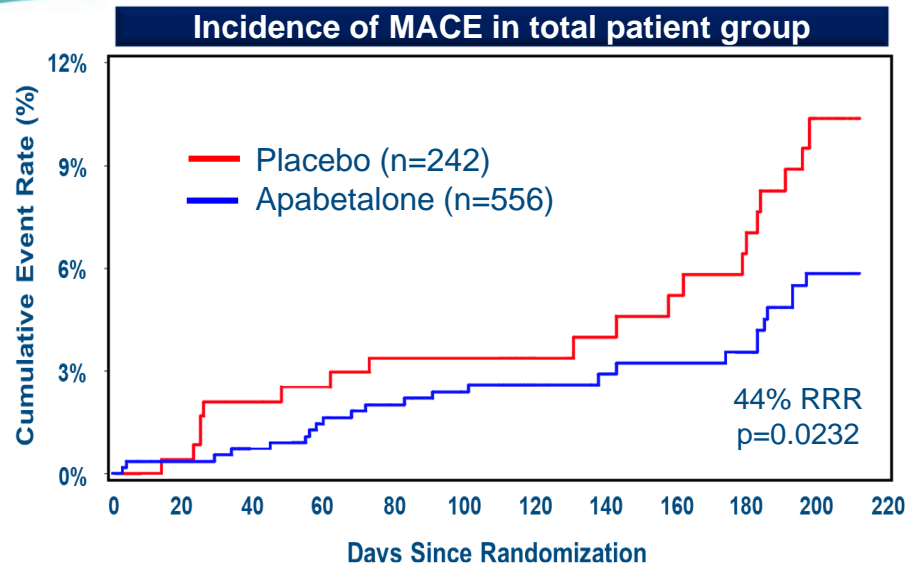
# BET Inhibition Impacts the Pathways that Drive Cardiovascular Disease and Kidney Diseases

Apabetalone, a bromodomain extra-terminal (BET) protein inhibitor, regulates the expression of genes and restores the function of pathways underlying the pathogenesis of CVD and kidney disease



# Critical Conclusions from our Phase 2 CVD Trials (ASSERT, ASSURE and SUSTAIN)

Nicholls et al. 2018 Am J Cardiovasc Drugs

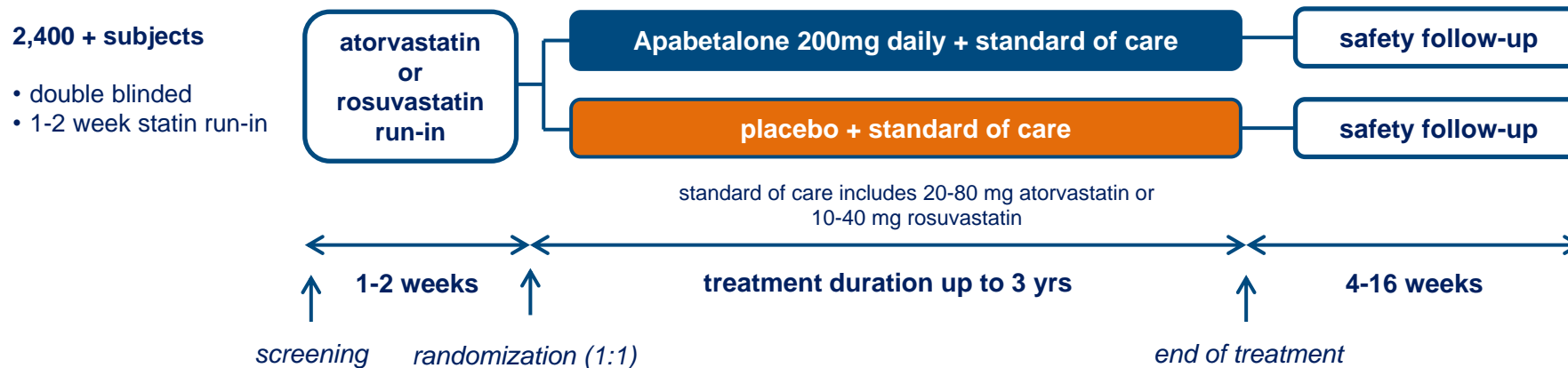


**MACE:** Major Adverse Cardiac Events including: death, myocardial infarction, stroke, coronary revascularization, hospitalization for acute coronary syndrome or heart failure

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

# BETonMACE Phase 3 Trial

Enrollment Complete; Trial completion expected H1 2019



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) or unstable angina with or without percutaneous coronary intervention to manage acute coronary syndrome
- HDL < 1.04 for males and < 1.17 for females

# Apabetalone Target Product Profile

High Risk ACS with Diabetes and Low HDL-C



## High Risk Acute Coronary Syndrome (ACS) Patients with a Type II Diabetes Mellitus (DM) Comorbidity and Low High-Density Lipoprotein Cholesterol (HDL-C)

Phase 3 BETonMACE	Efficacy Endpoints	<ul style="list-style-type: none"><li>Primary endpoint: Time to the first occurrence of Major Adverse Cardiovascular Events (MACE) defined as CVD death; non-fatal myocardial infarction (MI); non-fatal ischemic stroke</li><li>Secondary endpoints include: hospitalization for unstable angina, emergency revascularization procedures, and all-cause mortality</li></ul>
	Subgroup Analysis	<ul style="list-style-type: none"><li>Assess potential improvement in kidney function, MACE, and renal serious adverse events (SAEs) (one time 40% or greater reduction in eGFR or doubling of serum creatinine) in population with baseline estimated GFR&lt;60mL/min (stage 3+ CKD)</li><li>Assess potential cognitive improvement based on a MoCA (Montreal Cognitive Assessment) in patients older than 70 years of age</li></ul>
	Expected Efficacy Outcomes	<ul style="list-style-type: none"><li>30% relative risk reduction of MACE with statistical significance vs placebo with average treatment duration of 22- 24 months of treatment on top of current standard of care</li><li>Significant or trending results in defined subgroups such as CKD and cognition</li></ul>
Unique Selling Points		<ul style="list-style-type: none"><li>Novel mechanism of action with multi-factorial approach for the reduction of MACE in high risk ACS patients</li><li>Orally available small molecule with low projected COGS and price compared to monoclonal antibodies and peptides</li><li>Potential for alternate indications and increased accretive value based on subgroup analysis of BETonMACE, proteomic analyses of serum data from past Phase 2 trials and early pre-clinical work</li></ul>





Apabetalone has already been tested in over 1,900 patients in 18 countries around the world, 14 countries have already approved Phase 3 usage

# BETonMACE Clinical Trial Analysis Points and Time Lines



- 1 **Maintain existing safety** profile until trial completion, last dosing expected H1 2019
- 2 Trial completion – trial to continue until **250+ narrow MACE events have occurred**
- 3 Narrow, three point MACE event accumulation **stands at over 220**
- 4 **Adjudication of all** SAE MACE events expected to take two to three months post trial completion
- 5 **Top line data will** be announced after adjudication completion. Key subgroup analyses will also be released if available – Renal & Cognitive function
- 6 H2 2019 and beyond – full **outcomes, pre-specified endpoint data, safety results, and clinical implications** will be reported and published

## Clinical Advisory Board

**Prof. Kausik K. Ray**, BSc (hons), MBChB, MD, MPhil  
(Cantab), FACC, FAHA, FESC, FRCP;  
Chairman Imperial College

**Dr. Gregory G. Schwartz**, MD, PhD  
University of Colorado Denver

**Dr. Stephen Nicholls**, MBBS, PhD  
South Australian Health and Medical Research Institute

**Dr. Henry N. Ginsberg**, MD, FAHA  
Columbia University

**Dr. Peter P. Toth**, MD, PhD, FAAFP, FICA, FAHA,  
FNLA, FCCP, FACC  
CGH Medical Center

**Dr. Kamyar Kalantar-Zadeh**, MD, MPH, PhD, FAAP,  
FACP, FASN, FAHA, FNKF  
University of California Irvine

## Recent High Profile Publications

Apabetalone downregulates factors and pathways associated with vascular calcification – **Atherosclerosis 2018**

The Effect of Bromodomain and Extra-Terminal Inhibitor Apabetalone on Attenuated Coronary Atherosclerotic Plaque: Insights from the ASSURE Trial – **American Journal of Cardiovascular Drugs 2018**

Apabetalone Mediated Epigenetic Modulation is Associated with Favorable Kidney Function and Alkaline Phosphatase Profile in Patients with Chronic Kidney Disease – **Kidney and Blood Pressure Research 2018**

Benefit of Apabetalone on Plasma Proteins in Renal Disease- **KI Reports 2018**

Selective BET Protein Inhibition with Apabetalone and Cardiovascular Events: A Pooled Analysis of Trials in Patients with Coronary Artery Disease- **American Journal of Cardiovascular Drugs 2017**

Downregulation of the Complement Cascade In Vitro, in Mice and in Patients with Cardiovascular Disease by the BET Protein Inhibitor Apabetalone (RVX-208)- **Journal of Cardiovascular Translational Research 2017**

RVX-208, a BET-inhibitor for treating atherosclerotic cardiovascular disease, raises ApoA-I/HDL and represses pathways that contribute to cardiovascular disease- **Atherosclerosis 2016**

# Our First Three Initial Opportunities

Top 8 Markets (U.S., Top 5 EU, Japan & Canada)



Apabetalone is a first-in-class, small molecule that is a selective BET inhibitor that produces a specific set of biological effects with important benefits while maintaining a well described safety profile.

It is currently being evaluated for the following indications:

1

**High Risk Acute Coronary Syndrome (ACS) Patients with a Type II Diabetes Mellitus (DM) Comorbidity and Low High-Density Lipoprotein Cholesterol (HDL-C)**



**1.9 M Patients  
by 2032**

2

**High Risk Chronic Kidney Disease (CKD) Patients (Stages 3-5, Pre-Dialysis) with a Diabetes Mellitus Comorbidity and a History of Cardiovascular Disease (CVD)**



**6.6 M Patients  
by 2032**

3

**Dementia and Vascular Cognitive Dementia (MoCA score < 26) in Elderly (>65 years) Patients with Diabetes Mellitus Comorbidity and a History of CVD**



**3.2 M Patients  
by 2032**

- Complement Mediated Disease: orphan indication
- Neurofibromatosis – Malignant Peripheral Nerve Sheath Tumors (MPNST): orphan indication
- Pulmonary Arterial Hypertension: orphan indication
- Muscular Dystrophy/Facio Scapulo Humeral Dystrophy: orphan indication
- Fabry's Disease: orphan indication
- Vascular Cognitive Dementia
- HIV eradication



- Partnered Apabetalone in Greater China (China, Hong Kong, Taiwan and Macau) with Shenzhen Hepalink Pharmaceutical, a US\$3.1 billion market cap company listed in China
  - US\$35M initial equity investments in Resverlogix (total now exceeds US\$100M)
  - >US\$400M in projected future sales milestones and licensing royalties
  - Hepalink responsible for all development costs in Greater China
- Exclusive licensing agreement with Medison Pharma Ltd. for Apabetalone in Israel
  - >US\$100M in projected licensing royalties
- Discussing licensing opportunities in the Middle East / North Africa
- Exploring global licensing options (ex-Greater China and Middle East) for Apabetalone post Phase 3 readout

# Management Team



**Donald McCaffrey**  
**President & Chief Executive Officer**

- Co-founded Resverlogix in 2001 with Dr. Norman Wong
- Has over 40 years of corporate management experience, including over 18 years in drug discovery & development



**Dr. Norman C.W. Wong, M.D., FRCP,**  
**Chief Scientific Officer & Co Founder**

- Co-founded Resverlogix in 2001 with Donald McCaffrey
- Researches molecular actions of hormones related to the regulation of gene expression and pathogenesis of diabetes mellitus



**A. Brad Cann, CA, Chief Financial Officer**

- Has over 20 years of experience in a variety of financial and business roles
- Leads the Company's expanding financial activities supporting advancing scientific and clinical development



**Dr. Ewelina Kulikowski,**  
**PH.D., SVP, Research & Development**

- Joined in 2005 as Director of Research and Development
- Has been Involved in the development of lead drug RVX-208 from its discovery through to Phase 3 clinical development



**Dr. Michael Sweeney, M.D., SVP,**  
**Clinical Development**

- Cardiologist with extensive experience in pharmaceutical product development and marketing
- Has over 30 years in the pharmaceutical industry, including 11 years at Pfizer



**Kenneth Lebioda, BA, SVP, Business & Corporate Development**

- Has over 30 years of experience in the innovative pharmaceutical industry with leading global companies such as Bristol-Myers Squibb, Hoechst Marion Roussel and Marion Merrell Dow



**Dr. Jan O. Johansson, M.D., PH.D.,**  
**SVP, Medical Affairs**

- Has had a distinguished 35 year career in academia and in the pharmaceutical industry of which including various companies with expertise in the cardio-metabolic and neurological disease therapeutic area



**Dr. Henrik C. Hansen, PH.D., VP,**  
**Intellectual Property**

- Has over 17 years in drug discovery & development experience.
- Areas of expertise also include medicinal chemistry, process development and manufacturing of drug substances and products for clinical use



**Paul Moon, CPIR**  
**VP, Investor Relations and Communications**

- Has over 25 years of public company experience working in multiple industries, including: technology, financial services, real estate, international mining, and oil and gas

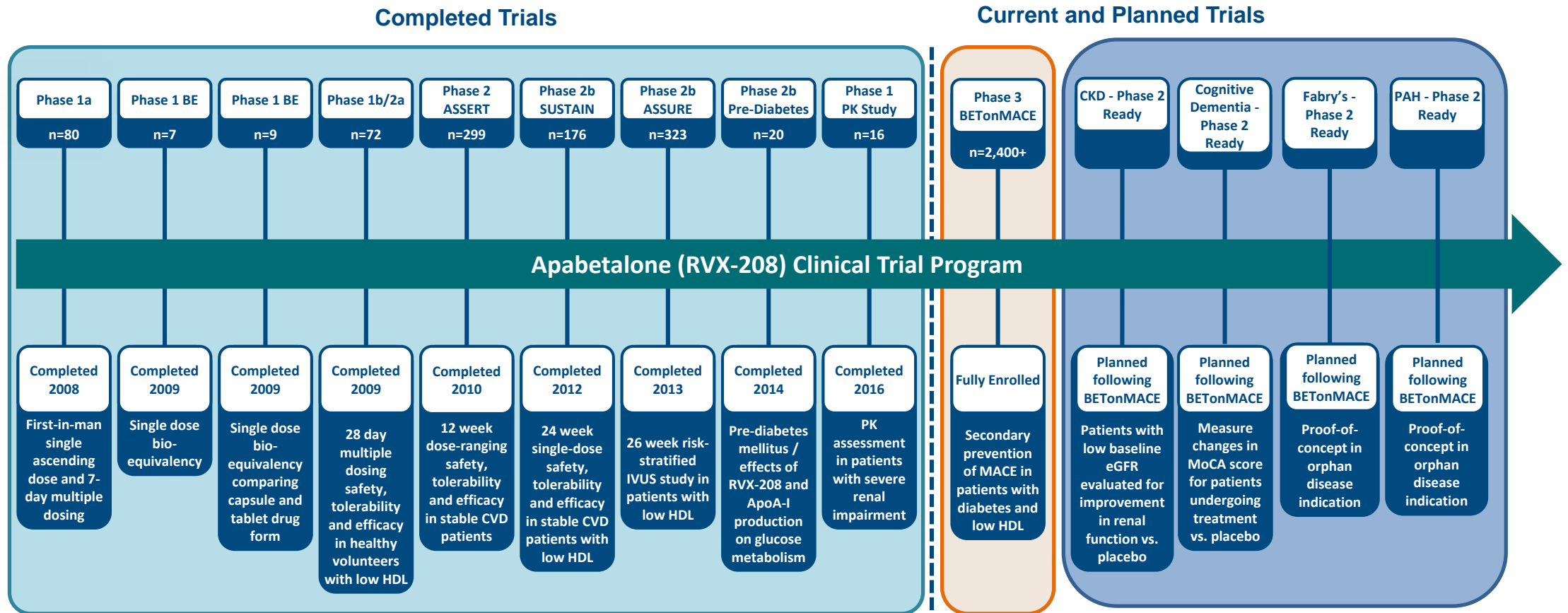
- 1 **Global leader** in epigenetic research and drug development
- 2 Apabetalone is a **first-in-class BET inhibitor** with potentially broad applicability across multiple disease indications
- 3 Addresses **critical unmet need with 12 million+ patients** in top 8 markets
- 4 Lead program has **completed enrollment of Phase 3 trial** for high risk CVD patient population
- 5 **Well established safety profile** – to date, over 1,900 patients treated with Apabetalone with no significant safety issues
- 6 **Proven track record** of funding development while minimizing shareholder dilution
- 7 Robust intellectual property position for composition, use, and manufacturing, **with patent life ranging from 2027 to 2034**





**Appendix**

# Apabetalone Clinical Trials To Date





OPEN ACCESS Freely available online

PLOS

## RVX-208, an Inducer of ApoA-I in Humans, Is a BET Bromodomain Antagonist

**Kidney  
& Blood Pressure  
Research**

Kidney Blood Press Res 2018;43:449-457

DOI: 10.1159/000488257

Published online: March 22, 2018

Accepted: March 13, 2018

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Original Paper

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

Ewelina Kulikowski<sup>a</sup> Christopher Halliday<sup>a</sup> Jan Johansson<sup>b</sup>  
Mike Sweeney<sup>b</sup> Kenneth Lebioda<sup>a</sup> Norman Wong<sup>a</sup> Mathias Haarhaus<sup>c</sup>  
Vincent Brandenburg<sup>d</sup> Srinivasan Beddhu<sup>e</sup> Marcello Tonelli<sup>f</sup> Carmine Zoccali<sup>g</sup>  
Kamyar Kalantar-Zadeh<sup>h,i,j</sup>

h Attwell<sup>1</sup>,  
t K. Suto<sup>2</sup>,

aryland, United States of Ar

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## Benefit of Apabetalone on Plasma Proteins in Renal Disease

Sylwia Wasiak<sup>5</sup>, Laura M. Tsujikawa<sup>5</sup>, Christopher Halliday, Stephanie C. Stotz, Dean Gilham, Ravi Jahagirdar, Kamyar Kalantar-Zadeh, Richard Robson<sup>6</sup>, Michael Sweeney, Jan O. Johansson, Norman C. Wong, Ewelina Kulikowski<sup>1,2</sup>  



Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: [www.elsevier.com/locate/atherosclerosis](http://www.elsevier.com/locate/atherosclerosis)



## Apabetalone downregulates factors and pathways associated with vascular calcification

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- Recent high profile publications illustrate apabetalone-induced activation of latent HIV-1 *in vitro and ex vivo*
- Suggest that Apabetalone synergistically reactivated latent HIV-1 and could combine with cART drugs to inhibit viral infection

Acta Pharmacologica Sinica

[www.nature.com/aps](http://www.nature.com/aps)



## ARTICLE

The BET bromodomain inhibitor apabetalone induces apoptosis of latent HIV-1 reservoir cells following viral reactivation

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# SCIENTIFIC REPORTS

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

Panpan Lu<sup>1</sup>, Yinzong 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>

# BET Technology Goes Mainstream

## Zenith Epigenetics

