Epigenetics & BET Inhibition

Q1 2017 – Cowen Conference

TSX: RVX

Today's Agenda

1. **Corporate Overview**
2. **Market Opportunity**
3. **BET Inhibition Technology**
4. **Clinical Trial Updates**
5. **Key Market Research: Prescribers & Payers**
6. **Summary**

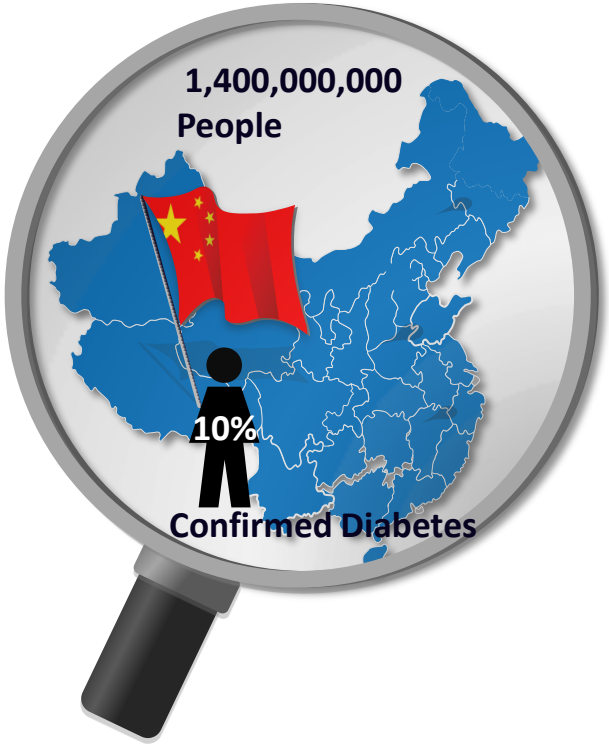
Safe Harbor

- 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 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 – RVX

Founded	**2001**
Ticker	**TSE-RVX**
Market Cap	**~$210 MM**
Shares Outstanding	**105.4MM** **~120MM fully diluted**
Cash Burn	**~$2.2 MM per month**
Top Shareholders	**Eastern Capital** **Shenzhen Hepalink** **NGN Capital**

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

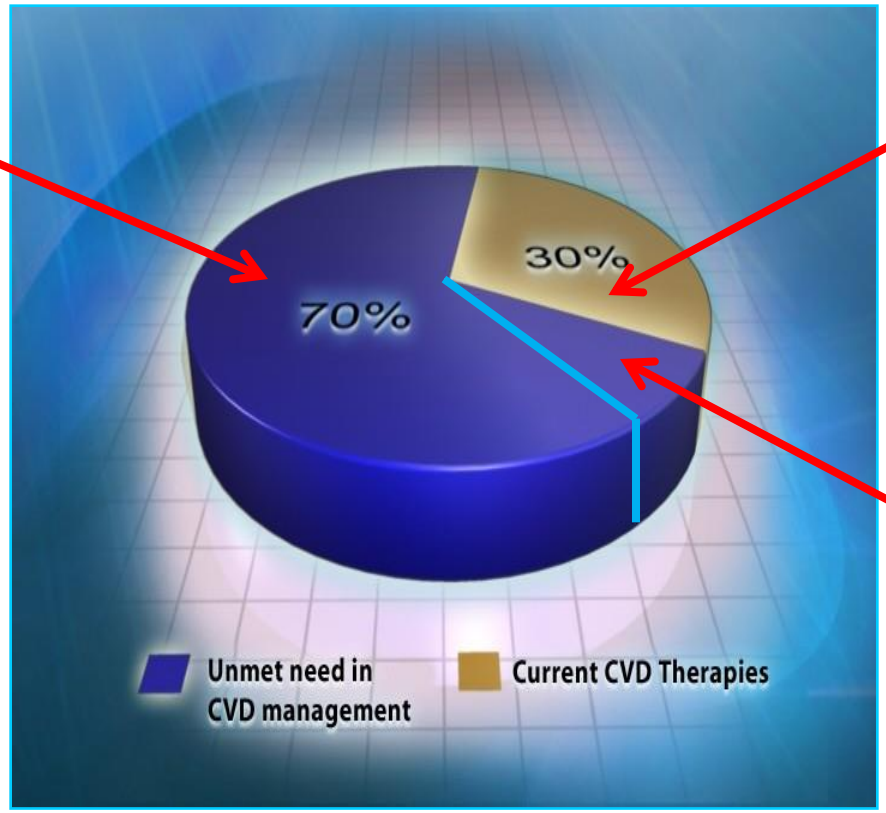
Market Opportunity

Unmet Need Segment is Still 70%

- 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



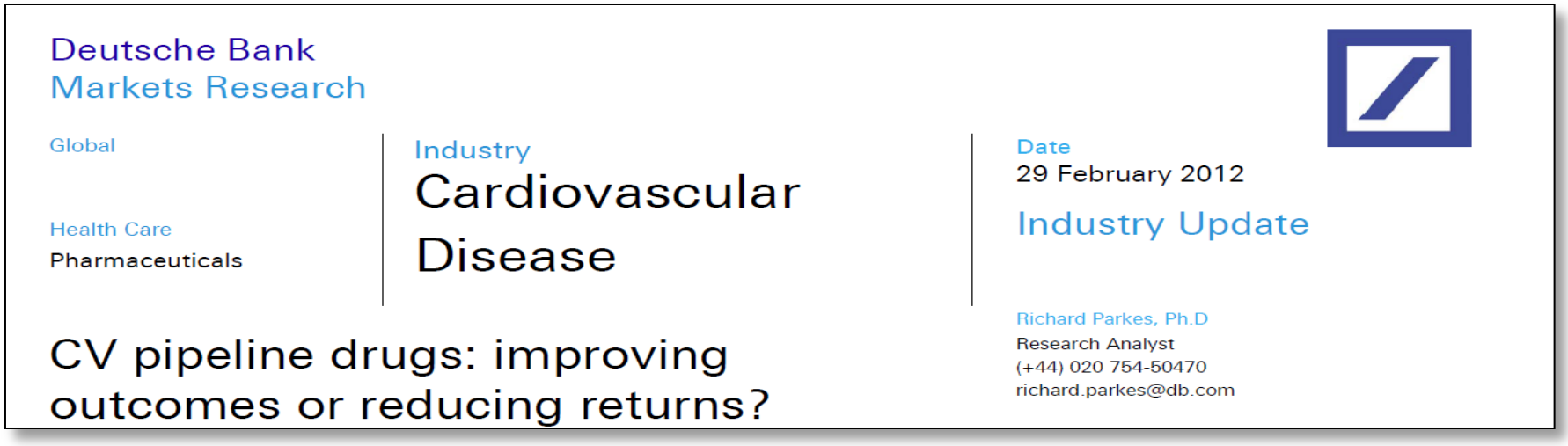
Current CVD Therapies

- 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

The Opportunity: Residual Risk in CVD Pipeline Value



Deutsche Bank
Markets Research

Global

Health Care
Pharmaceuticals

Industry
Cardiovascular Disease

Date
29 February 2012

Industry Update

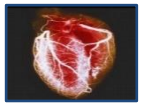
CV pipeline drugs: improving outcomes or reducing returns?

Richard Parkes, Ph.D
Research Analyst
(+44) 020 754-50470
richard.parkes@db.com

- Deutsche Bank estimates CVD Residual Risk Market worth **$90B**
- Strong pipeline value attributed for Phase 3 residual risk assets
  - **$13B Pipeline Value** for Torcetrapib (2006) Failed Phase 3
  - **$8B Pipeline Value** for Dalcetrapib (2012) Failed Phase 3
  - **$10B Pipeline Value** for Daralpadib (2014) Failed Phase 3
  - **$8B Pipeline Value** for Evacetrapib (2015) Failed Phase 3

Sources: Lehman Brothers - PharmaPipelines. 2007; Deutsche Bank - Cardiovascular Disease Industry Update. 2012

Current Target High Risk Vascular Patient Groups

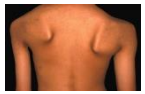


Phase 3: ACS with diabetes / low HDL – Peak Market 3,600,000

Phase 3 Sub Group: CKD pre-dialysis – Peak Market 4,500,000

Phase 2 Dialysis – Target Patient Market - Peak Market 1,300,000

Phase 3 Sub Group AD/MCI Diabetics – Peak Market 1,300,000



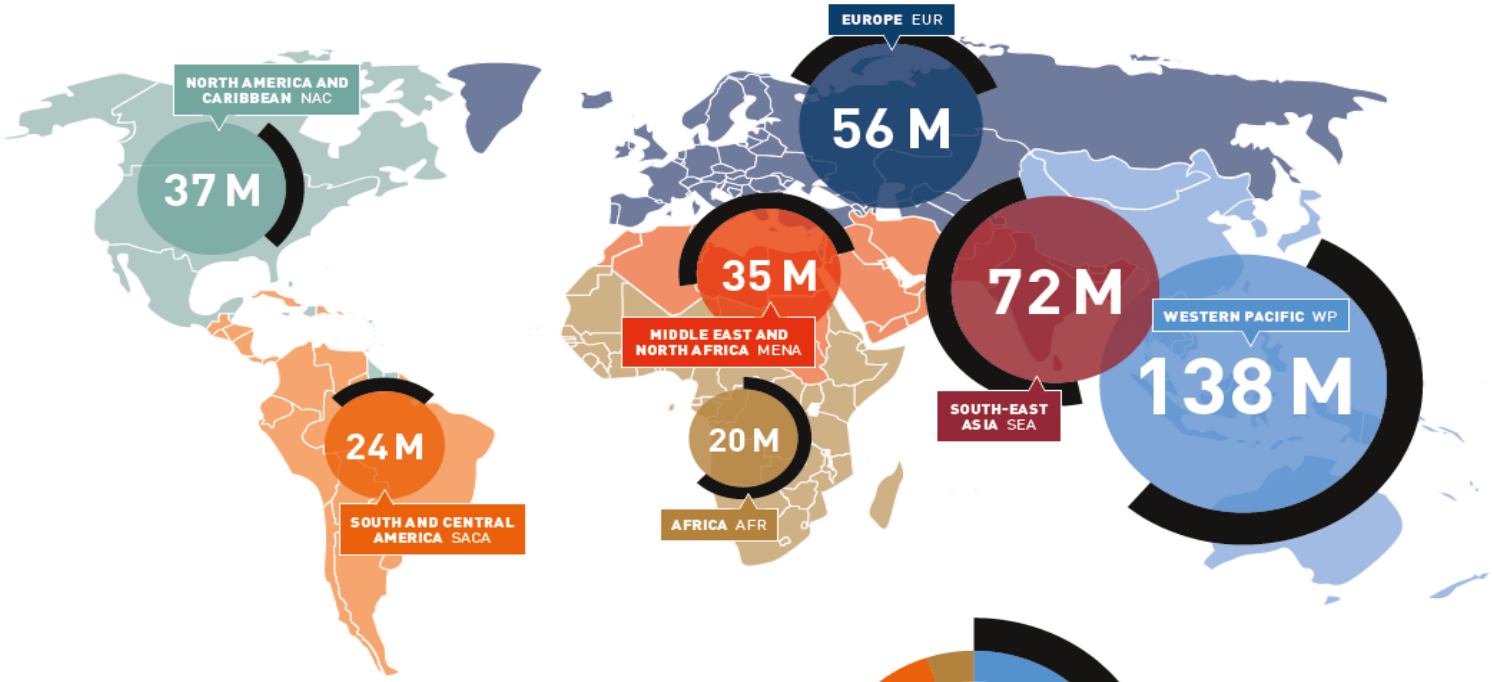
Phase 2 Orphan FSHD*/DMD/IgA Nephro – Peak Market 300,000+

Total Target High Risk Market opportunity: 10++ Million patients top 7 markets

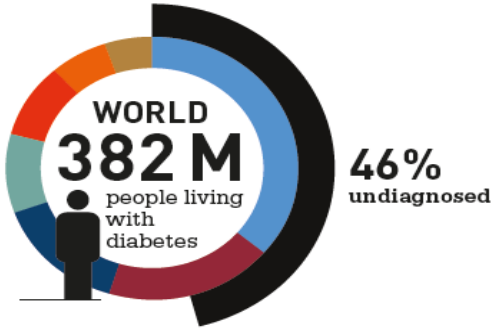
**FSHD market size outside of US only.*

70% Unmet Need in CVD Management: A Growing Problem - Diabetes

International Diabetes Federation 2013



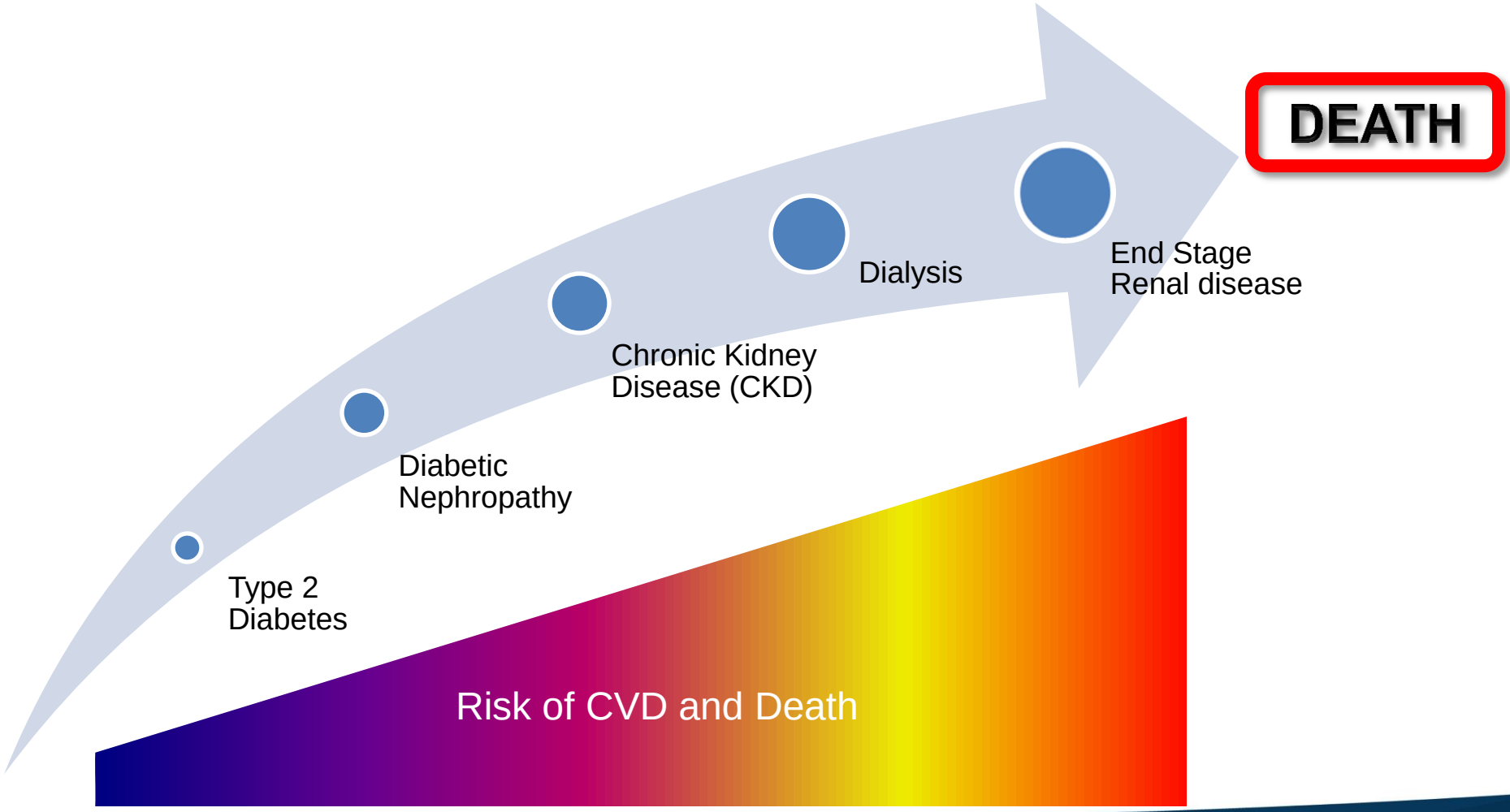
"Approximately 68% of patients with diabetes over the age of 65 will die from Cardiovascular disease (CVD)"



IDF Diabetes Atlas | Sixth edition

70% Unmet Need: Chronic Kidney Disease (CKD)

Type 2 diabetes patients have an increased risk for kidney risk and CVD events

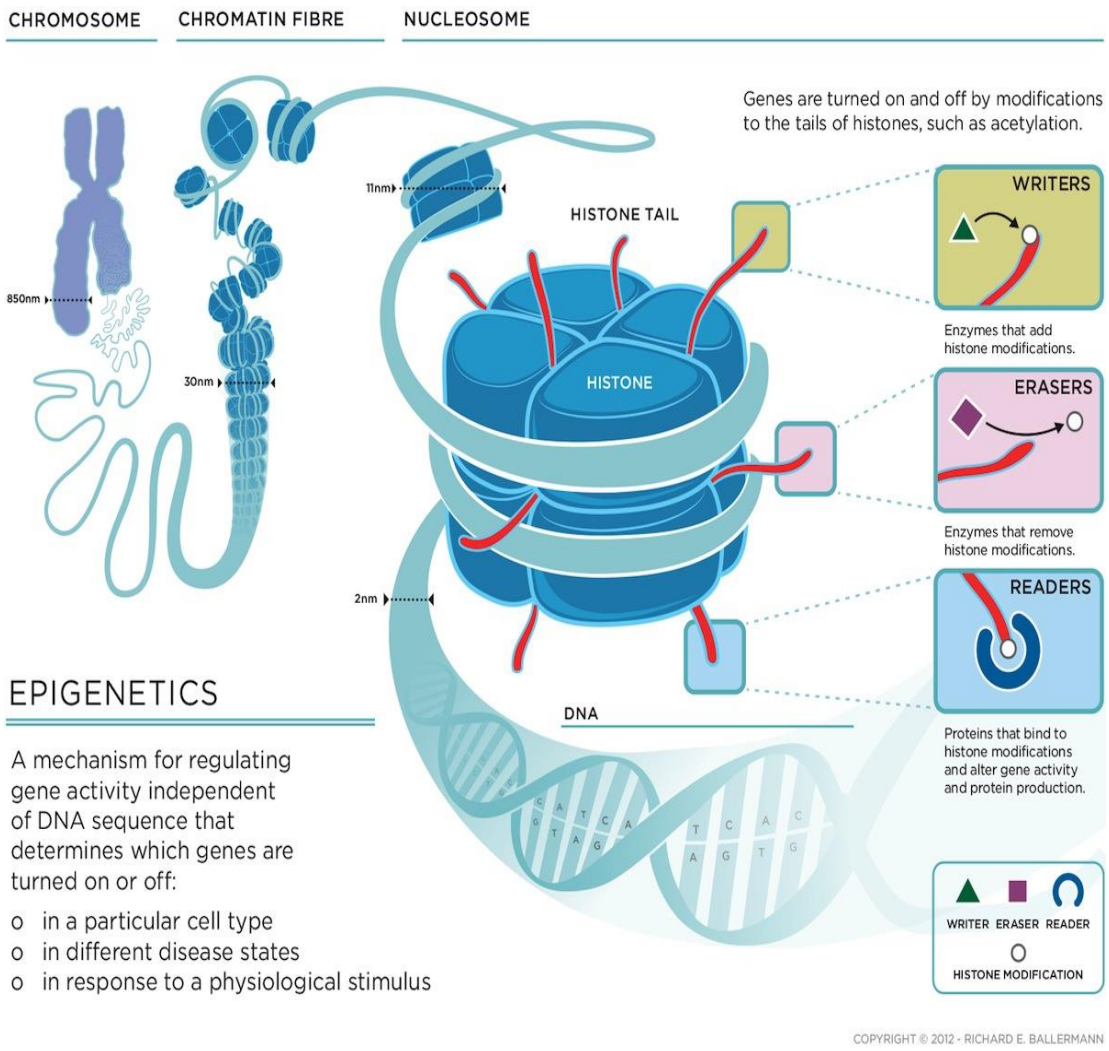


BET Inhibition Technology

Apabetalone: World Leading Epigenetic Drug

- 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 selectively and is the only clinical candidate in a phase 3 CVD outcome trial in high risk diabetes and CKD patients

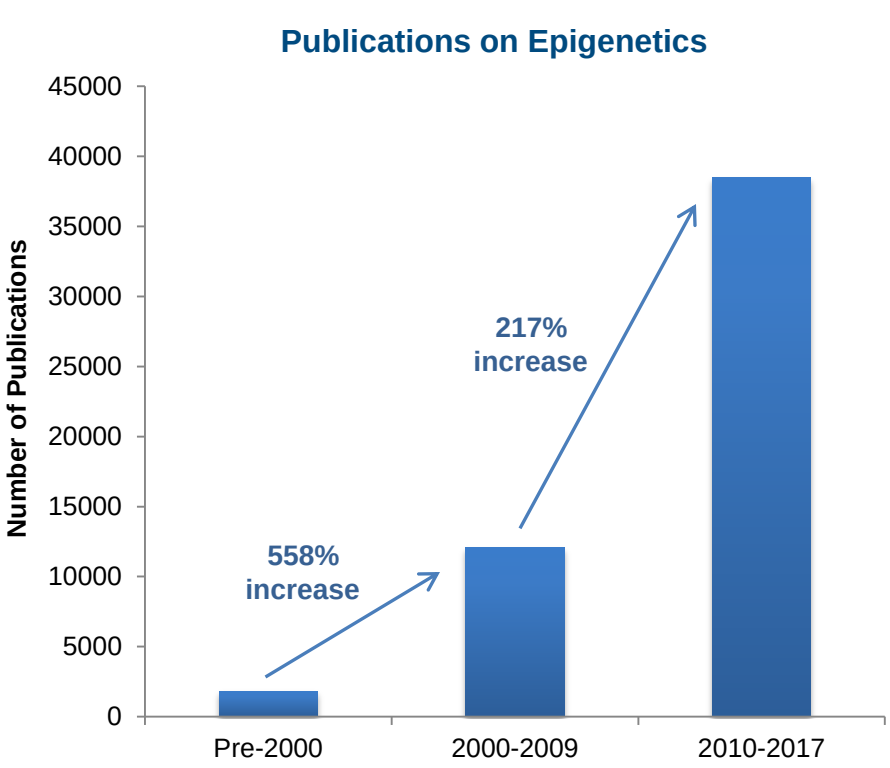
Epigenetics

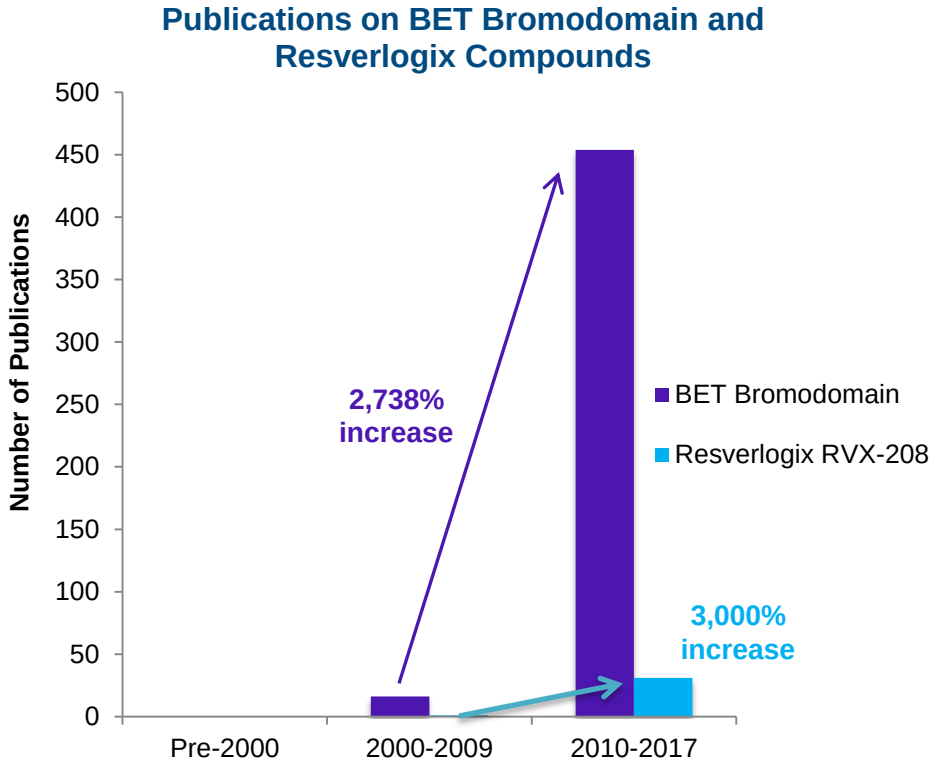


- The Epigenetic code refers to secondary modifications to chromatin components that regulate its activity
- Transcription is regulated by addition, removal or recognition of these modifications (writers, erasers, readers)
- Acetylation is associated with active transcriptional regions of chromatin
-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

Publications on Epigenetics and RVX

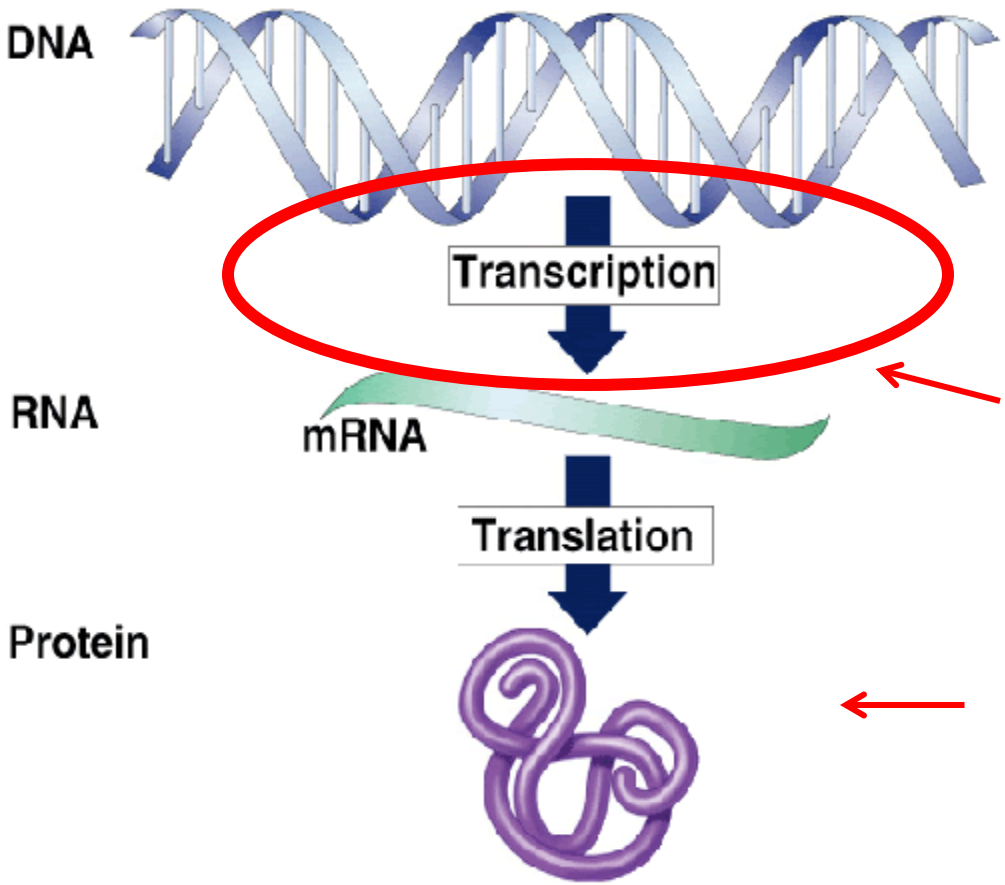
Dramatic growth of publications over the past decade in Epigenetics and BET Inhibition





Source: PubMed Database: Historical Review Q1 2017

Apabetalone Unique Mechanism



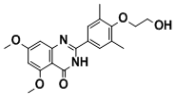
CRISPR: genome editing
The mechanism is based on cutting and pasting undesired/desired sequences into or out of the DNA, thereby altering the gene sequence and then re-introducing the modified DNA into the body

Apabetalone
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

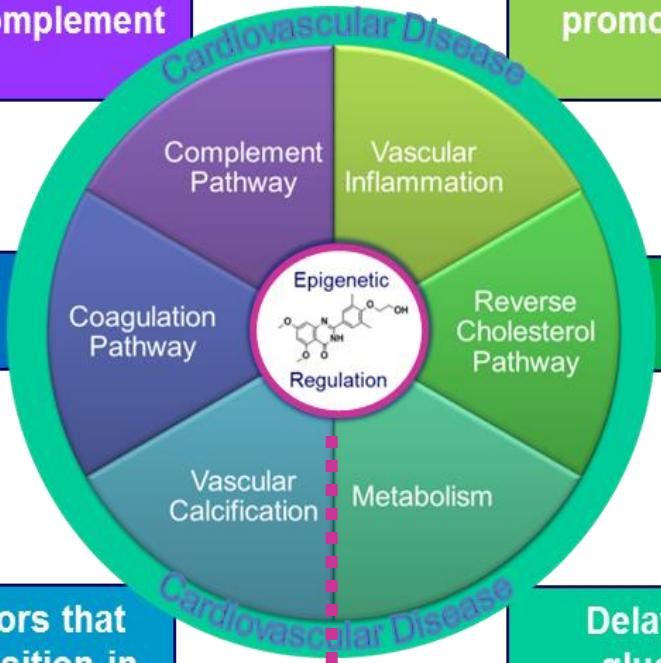
BET Inhibition Impacts Pathways that Drive CVD

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



Reductions in the components and function of the complement cascade

Reductions in mediators that promote inflammation of the vasculature



Reductions in components of the coagulation cascade

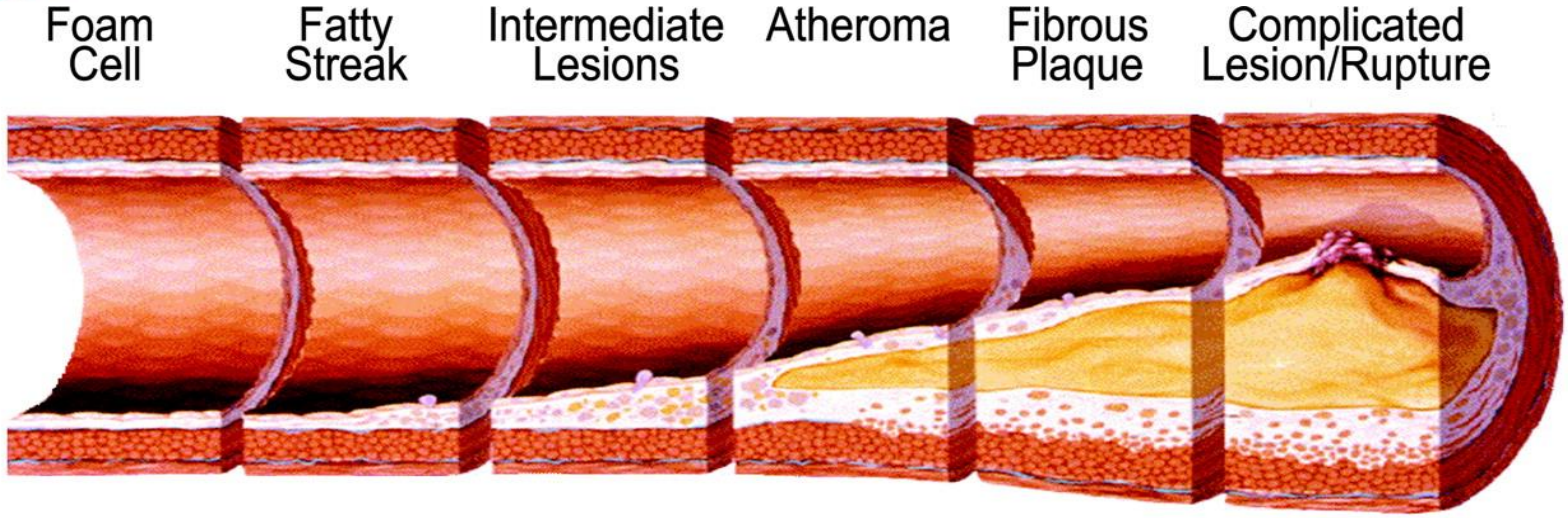
Increased ApoA-I, positive effects on lipid content of HDL

Reductions in mediators that promote calcium deposition in the vasculature

Delayed and reduced oral glucose absorption and endogenous production

Reduced incidence of MACE

Apabetalone Reduces Inflammation Key Driver of CVD Risk



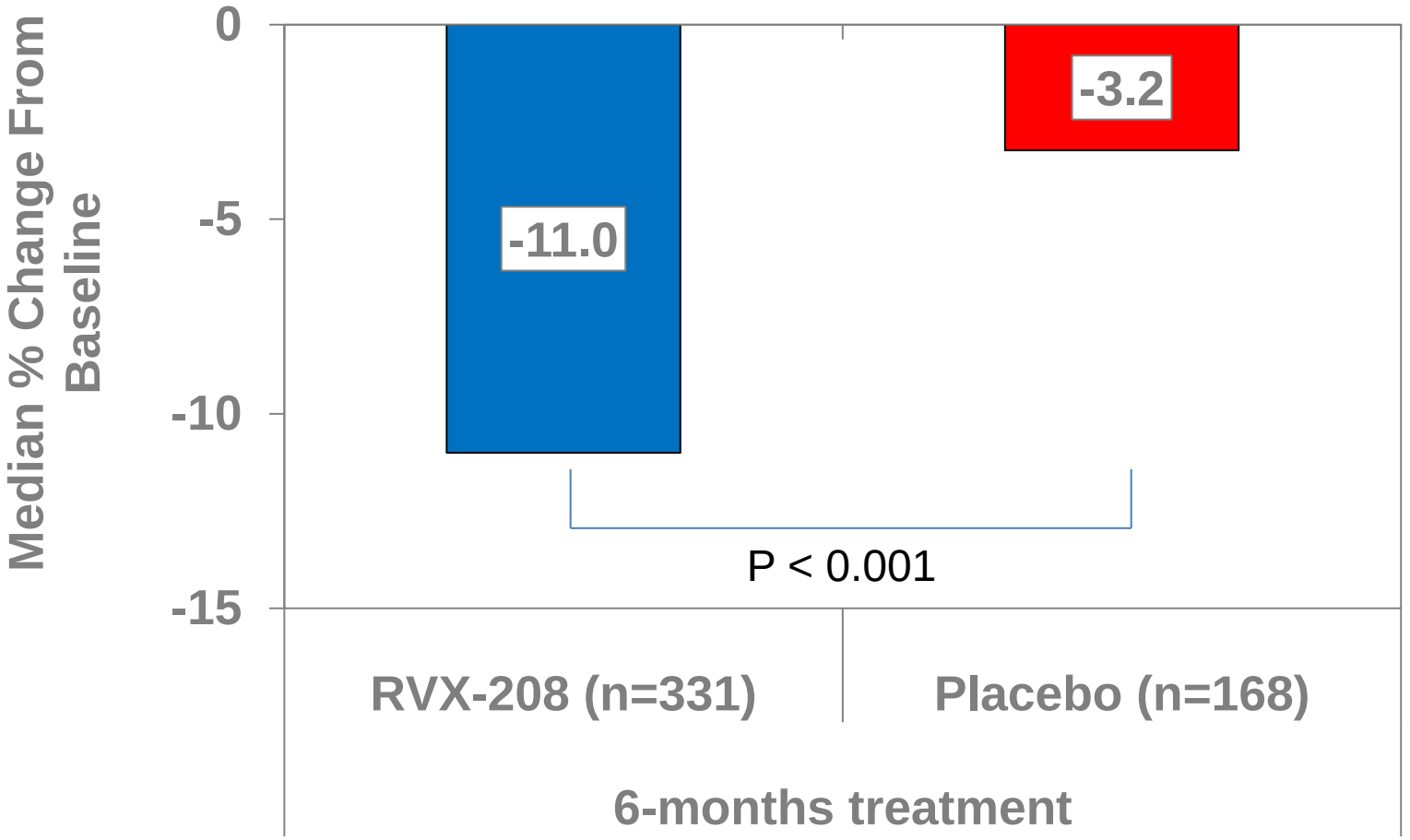
1°& Messenger Inflamm. Cyto/Chemokines	Cellular Adhesion Molecules	Plaque Destabilization		Plaque Rupture
IL-1	sICAM	IL-18*	MPO*	PAPP-A*
IL-6*	sVCAM	oxLDL*	MMPs*	sCD40L*
TNF-α	sSelectins	Lp-PLA$_2$*	MCP-1*	
IL-18*		GPx-1*	PIGF*	
MCP-1*				

Acute Phase Reactants

CRP*, sPLA$_2$*, SAA, Fibrinogen, WBCC

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

Apabetalone Improves Calcification Markers
ALP Reduction Impact



ALP & Outcomes in CKD: Literature Support

Strong independent literature on link between ALP and CKD outcomes and mortality
Large population studies demonstrating link between ALP and CKD

CLINICAL EPIDEMIOLOGY www.jasn.org

Serum Alkaline Phosphatase Predicts Mortality among Maintenance Hemodialysis Patients

Deborah L. Regidor,* Csaba P. Kovesdy,† Rajnish Mehrotra,‡§ Mehdi Rambod,*

AJKD
Original Investigation

Prognostic Importance of Serum Alkaline Phosphatase in CKD Stages 3-4 in a Clinical Population

Jonathan J. Taliercio, DO,[1] Jesse D. Schold, PhD,[1,2] James F. Simon, MD,[1] Susana Arrigain, MA,[2] Anne Tang, MS,[2] Georges Saab, MD,[3] Joseph V. Nally Jr, MD,[1,4] and Sankar D. Navaneethan, MD, MPH[1,4]

Outcome predictability of serum alkaline phosphatase in men with pre-dialysis CKD

Csaba P. Kovesdy[1,2], Vitalie Ureche[3], Jun L. Lu[4] and Kamyar Kalantar-Zadeh[5,6]

[1]Division of Nephrology, Salem Veterans Affa... Charlottesville, VA, USA, [3]Department of Me... USA, [5]Harold Simmons Center for Chronic Di... UCLA Medical Center, Torrance, CA, USA a...

Correspondence and offprint requests to: Csa...

Serum Alkaline Phosphatase and Phosphate and Risk of Mortality and Hospitalization

...Paul Muntner,† Maria Coco,* William Southern,* Irwin Lotwin,* ...and Michal L. Melamed*

...dicine, Montefiore Medical Center, Bronx, New York; and †University of Alabama at ...bama

Life Science Journal, 2011;8(4) http://www.americanscience.org

Bone Specific Alkaline Phosphatase and Cardiovascular Morbidity among Patients on Maintenance Hemodialysis

Emam Waked[1], Faten El Shanawani[2], Manar Raafat Amna Metwally[3], Ashraf Abdel- Khalek[3], Mona Hassan[2] and Hoda Abu taleb[4]

Nephrology[1], Clinical chemistry[2], Intensive care[3] and Environment research[4], Departments, Theodor Bilharz Research Institute, Giza, Egypt

Serum Alkaline Phosphatase and Mortality in African Americans with Chronic Kidney Disease

Srinivasan Beddhu,*† Xiulian Ma,† Bradley Baird,† Alfred K. Cheung,*† and Tom Greene*†

**Veterans Affairs Salt Lake City Healthcare System, Salt Lake City, Utah; and †Department of Medicine, University of Utah, Salt Lake City, Utah*

original article

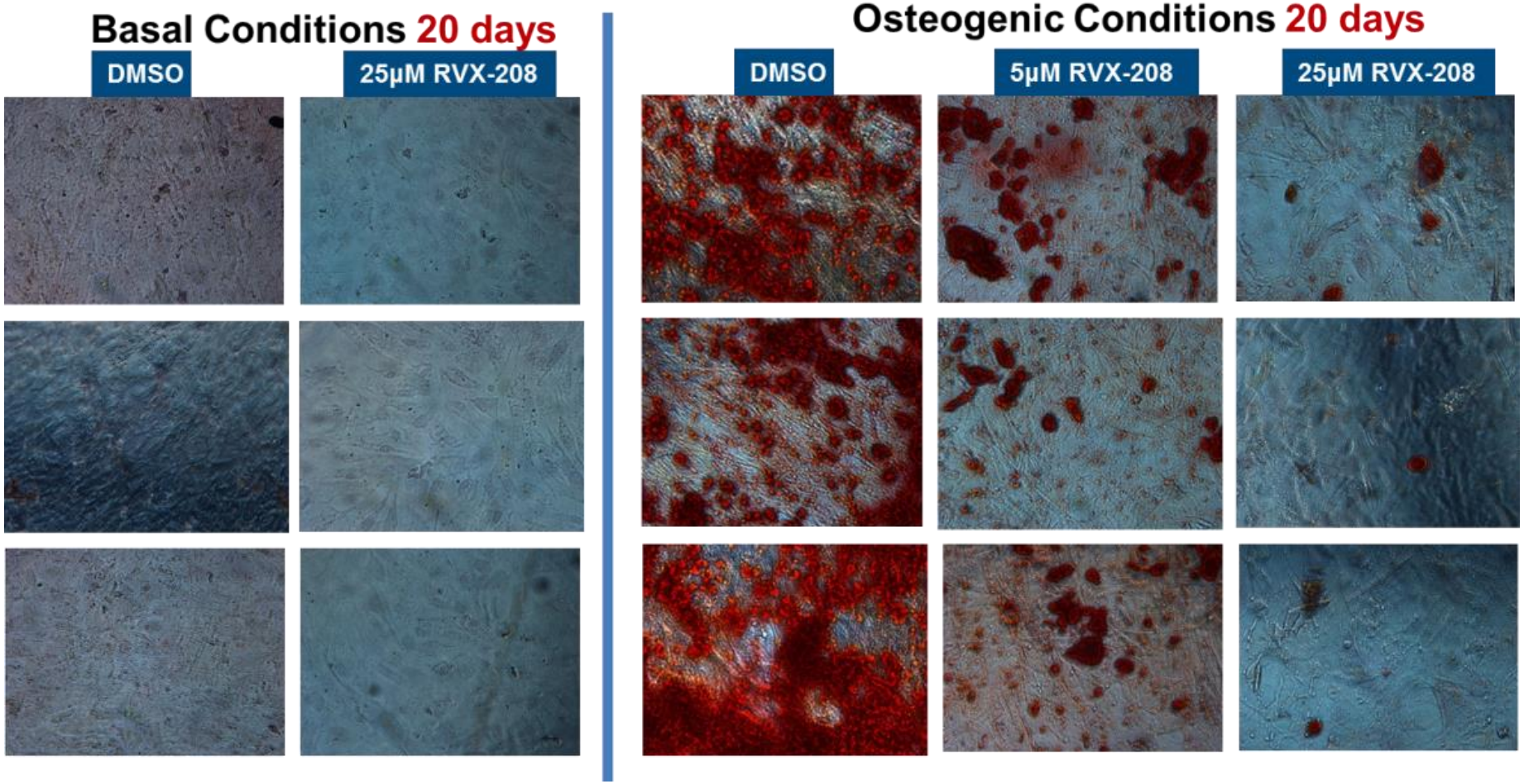
...ology

High alkaline phosphatase levels in hemodialysis patients are associated with higher risk of hospitalization and death

Margaret J. Blayney[1], Ronald L. Pisoni[1], Jennifer L. Bragg-Gresham[1], Juergen Bommer[2], Luis Piera[3], Akira Saito[4], Takashi Akiba[5], Marcia L. Keen[6], Eric W. Young[1,7] and Friedrich K. Port[1]

[1]Arbor Research Collaborative for Health, Ann Arbor, Michigan, USA; [2]Dialysis Center, University of Heidelberg, Heidelberg, Germany; [3]Hospital General Vall d'Hebron, Barcelona, Spain; [4]School of Medicine, Tokai University, Kanagawa, Japan; [5]Division of Blood Purification, Kidney Center, Tokyo Women's Medical University, Tokyo, Japan; [6]Amgen, Thousand Oaks, California, USA and [7]VAMC/University of Michigan, Ann Arbor, Michigan, USA

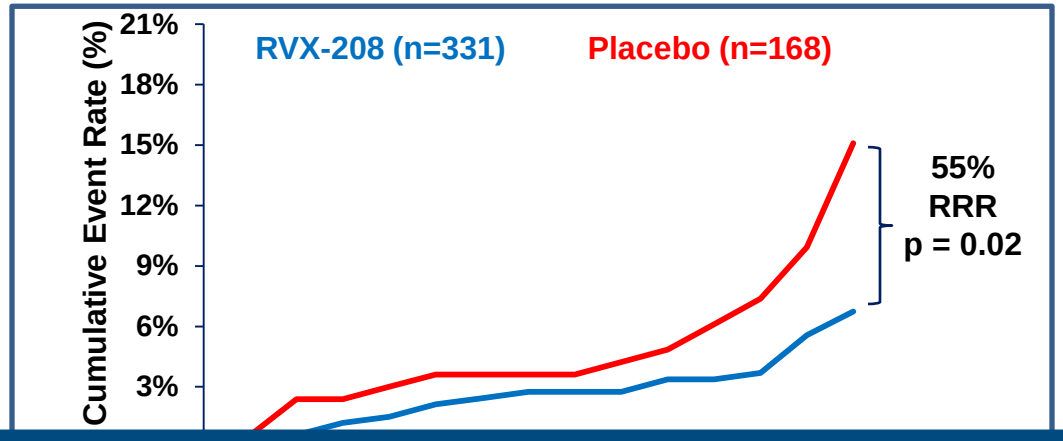
Apabetalone Reduces Expression of Calcification - Key Driver of CVD Risk



Apabetalone Clinical Results: MACE

Clinical Results: Efficient MACE Reduction

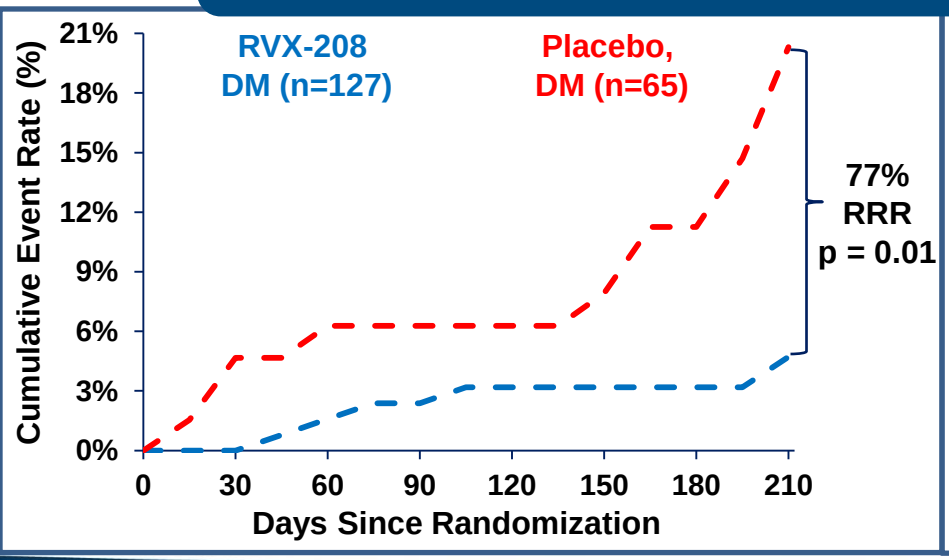
MACE: Major Adverse Cardiac Events including: death, myocardial infarction, stroke, coronary revascularization, hospitalization for acute coronary syndrome or heart failure

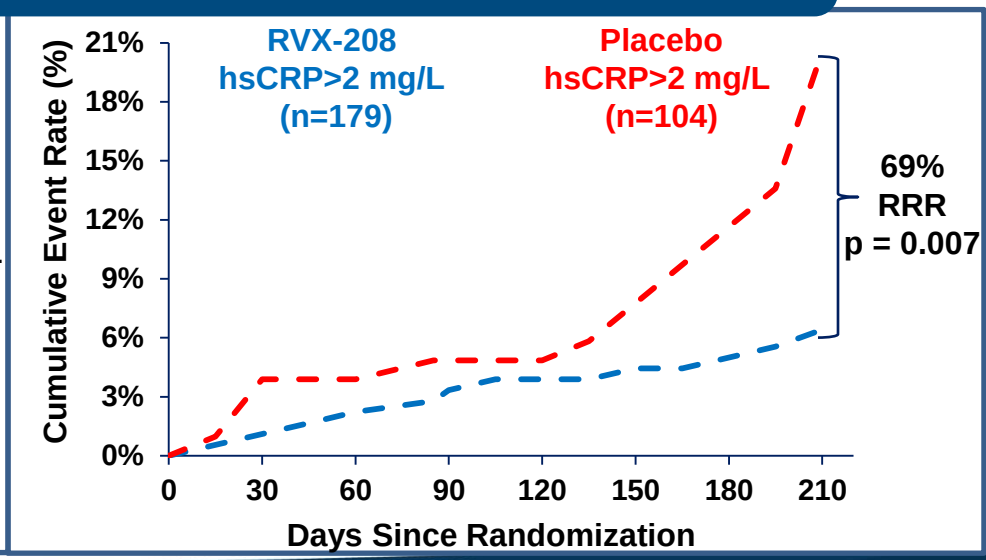


Note: Patients were censored at 30 days after the last dose of study medication.

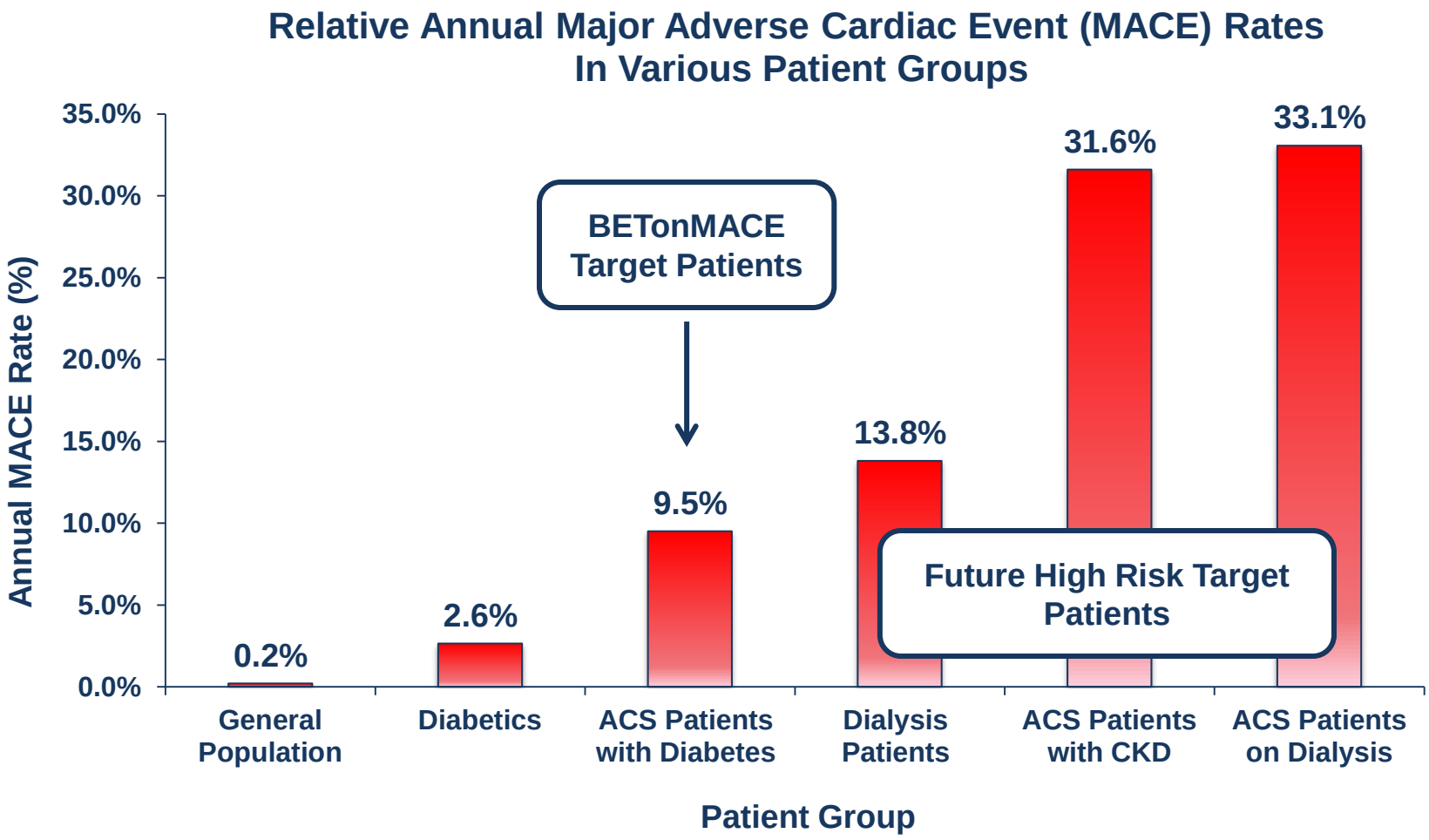
Source: *RVX data on file – ASSURE and SUSTAIN Safety Population. Log-Rank test for between group comparison*

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





Patient Enrichment Strategy
Initial 3 Target Indications (Diabetes, CKD, Dialysis)



Sources: Calculated from CDC Heat Disease Facts; Holden, SE. et al. 2015; White, WB. et al. 2013; Kim, H. et al. 2015; Cardarelli, F. et al. 2008; Okada, T. et al. 2008

World Leading Committee Members

CVD/Diabetes

Prof. Kausik K. Ray
Chair
Imperial College, London

Dr. Gregory G. Schwartz
Member
VA-Denver

Dr. Stephen Nicholls
Member
SAHMRI, Adelaide

Dr. Henry N. Ginsberg
Member
Columbia University

Dr. Peter P. Toth
Member
University of Illinois

Dr. Kamyar Kalantar-Zadeh
Member
Chair Nephrology UC Irvine

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

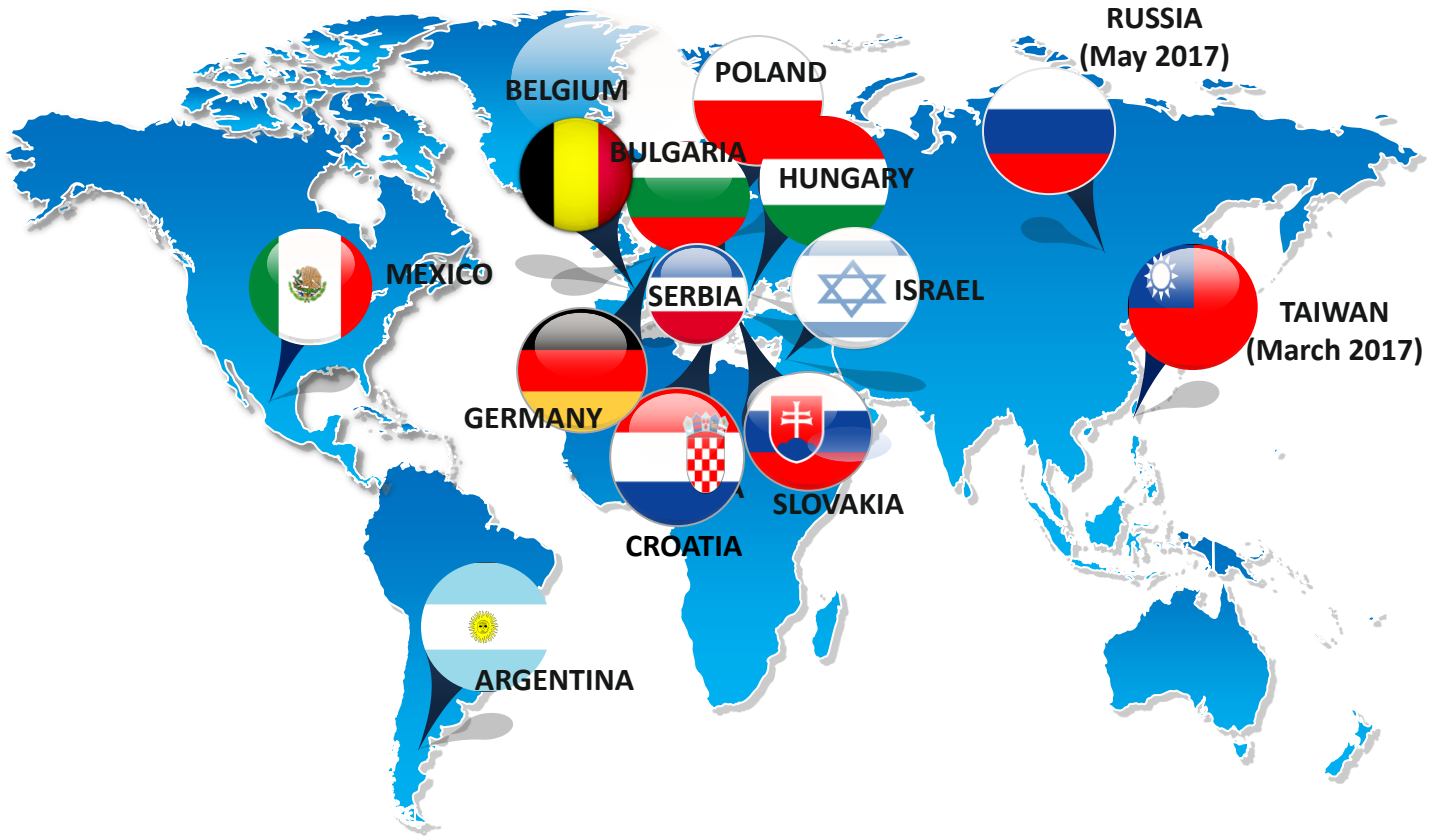
Dr. Marcello Tonelli
Member
University of Calgary Chair Medical Research

Dr. Srinivasan Beddhu
Member
University of Utah

BETonMACE and BETonRENAL Clinical Update

TSX: RVX

BETonMACE Commenced November 2015



Apabetalone has already been tested in over 1,000 patients in 18 countries around the world.

BETonMACE CV Outcomes Study Design

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

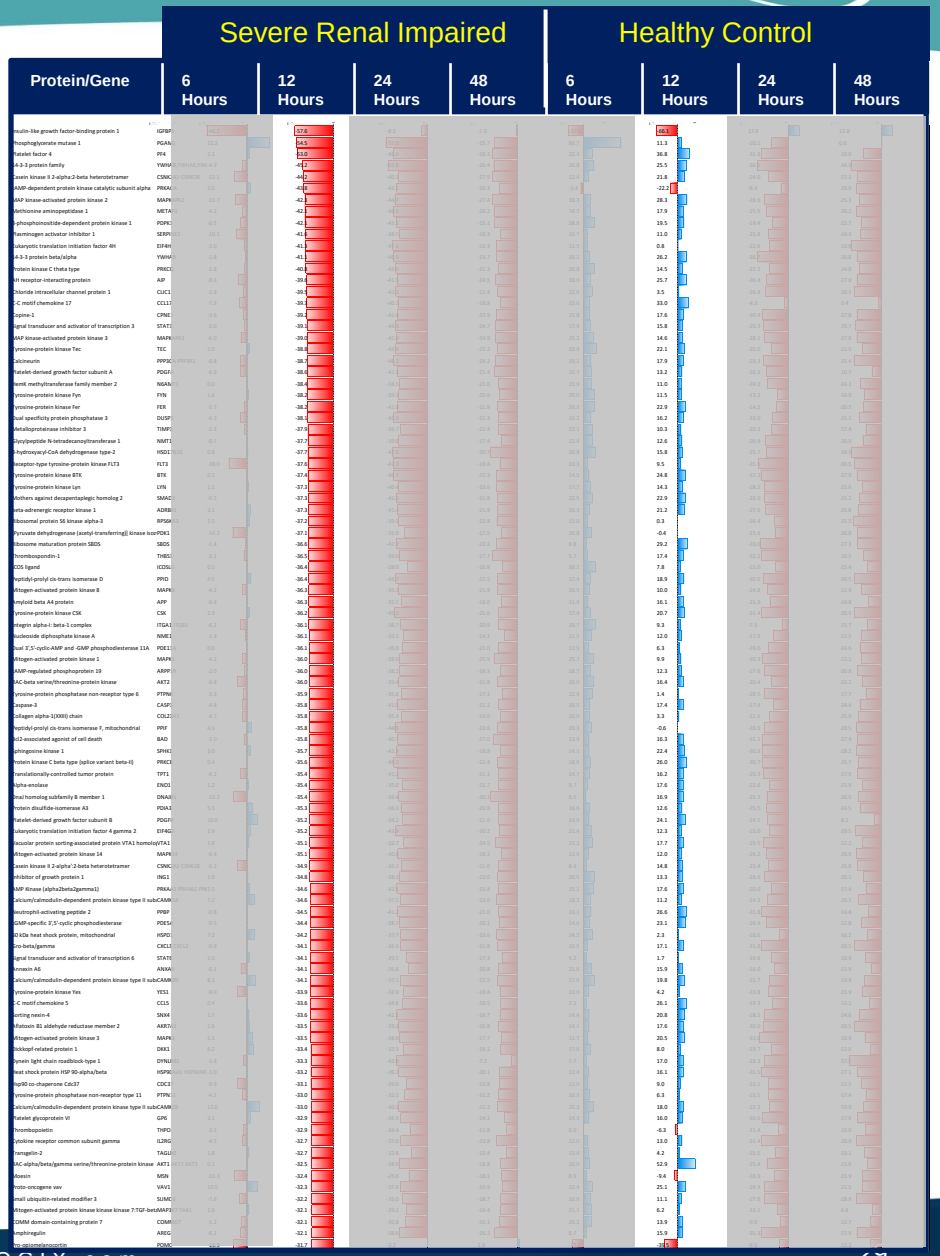
Time from randomization to the first occurrence of adjudication-confirmed MACE including:

- 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

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

Many key proteins known to drive CKD risk were already significant at12 hours post dose vs baseline



Commercial Opportunity:
Health Value Market Research

Apabetalone: Balanced for Success

THREE CRITICAL DEVELOPMENT SUCCESS FACTORS IN PLACE

INNOVATION

Resverlogix owns the worlds most advanced BRD4 epigenetics program

EFFICACY

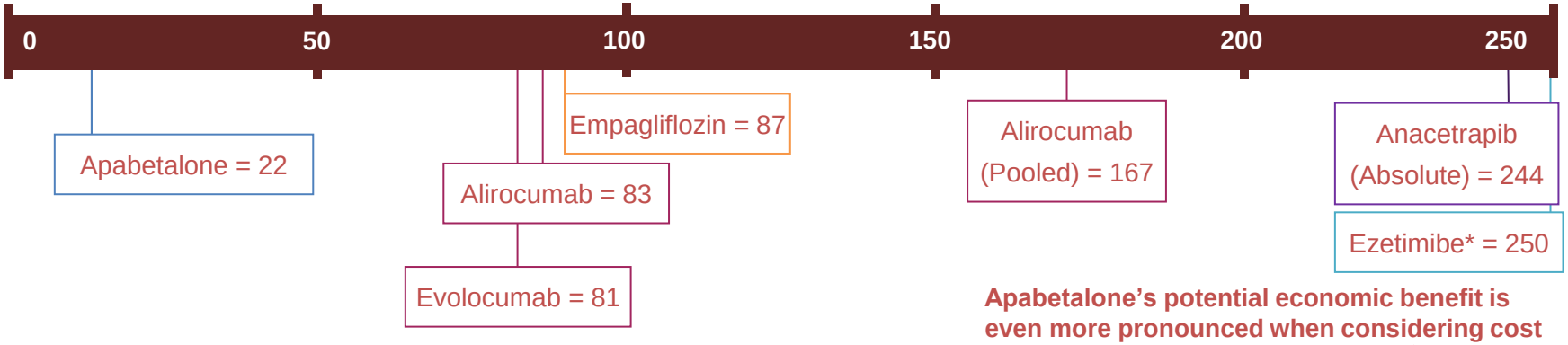
Clinical and safety data is continuing to suggest a successful program

PHARMACO-ECONOMICS

Payor groups response for BET program positive - seeking future results

BET NNT & Cost/Event Prevented Analysis
Vs. comparators in their respective patient populations

Number Needed to Treat (NNT) per MACE event prevented (1 Year Kaplan Meier Estimate unless otherwise specified)



Apabetalone's potential economic benefit is even more pronounced when considering cost of competitive PCSK9i products

Trial	Molecule	Trial Size	Treatment Duration (Years)	Absolute NNT/Yr	Kaplan Meier (KM) NNT/Yr	Tier 2 Planned Annual Medication Cost/Patient	Annual Cost per Event Prevented (KM)
SUSTAIN/ASSURE	**Apabetalone**	497	0.4 – 0.5	23	22	$2,400 - $4,200	**$52,800 - $92,400**
ASSERT/SUSTAIN/ ASSURE		798	0.25 – 0.5	11	22	$2,400 - $4,200	**$52,800 - $92,400**
ODYSSEY LONG-TERM	**Alirocumab**	2,338	1.6	97	83	$14,560	**$1,208,480**
POOLED ODYSSEY		3,459	1.6	NA	167	$14,560	**$2,431,520**
OSLER 1-2	**Evolocumab**	4,465	0.9	83	81	$14,100	**$1,142,104**
IMPROVE-IT	**Ezetimibe**	18,144	6.0	333	250*	$2,844	**~$711,000**
EMPA-REG OUTCOMES	**Empagliflozin**	7,042	3.1	194	87	$4,126	**$358,769**
DEFINE	**Anacetrapib**	1,612	1.5	244	NA	NA	NA

Note: Medication cost based on US WAC cost (PriceRx); Kaplan Meier estimates are based on digitized curves from publications
^No patient population standardization has been applied so additional population specific factors beyond severity can also influence NNT values
*1 year showed no benefit to calculate NNT; estimated by taking 5 year KM rate of 50 x 5 years

Price Band Research Report: Payer KOL Outreach

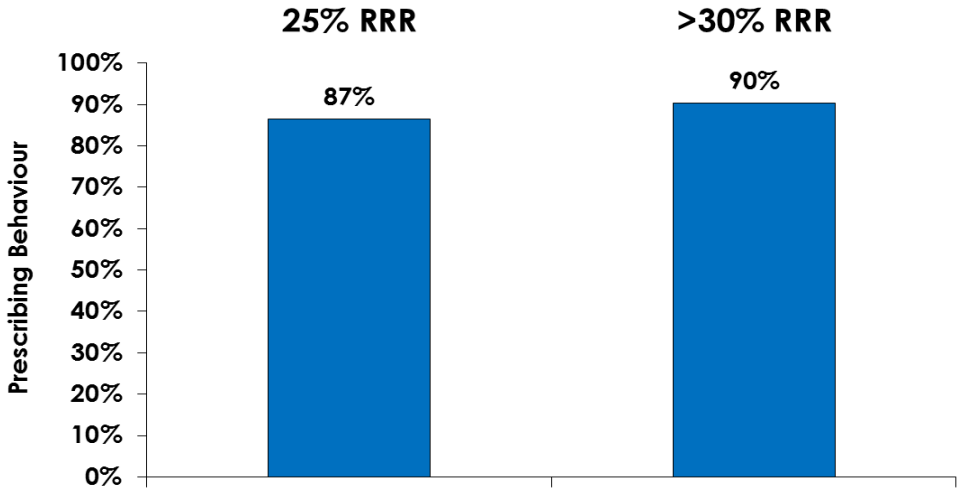
Organization	Lives Covered	MACE Reduction: Unmet need in Recent ACS and T2DM patients	MACE Reduction: Unmet need in CKD patients	ICER Threshold per annum
Payer 1	55 M	Moderate to High	Moderate to High	$ < 100,000
Payer 2	65 M	Moderate to High	Moderate to High	$ < 200,000
Payer 3	37 M	Moderate to High	Moderate to High	$ < 100,000
Payer 4	40 M	Moderate to High	Moderate to High	$ < 150,000
Payer 5	11 M	Moderate to High	Moderate to High	$ < 150,000

- 5 Payers - **208 million** lives covered, Key C Suite executives contacts – President, Chief Medical Directors, COO, Executive VP Pharmacy
- Pricing bands support average ICER Target Threshold of approximately **$140,000** USD
- Pricing bands support potential price of **$6,000 - $12,000** based on new enriched high risk patients

Prescribing Behaviour: Physician Survey Findings

- Based on responses from 1,920 primary care physicians (n=625), cardiologists (n=550), endocrinologists (n=420) and nephrologists (n=325)

If select BET inhibition in a large phase III prospective setting illustrates significant relative risk reduction of MACE, on top of standard of care, in diabetes patients with low HDL and an ACS co-morbidity, what would your level of interest be in prescribing this drug for the following risk reductions?



New Expanded Global SERMO Market Outreach Program Underway

Resverlogix Investment Highlights

- **Phase 3 Company** focused on significant unmet need in high-risk CVD patient population with novel BET therapeutic - **apabetalone**
- **Scarcity & Health Proposition Value** highly differentiated MOA first and only in class small molecule 9 year lead. Strong reimbursement positioning. IP until 2034
- **Market potential** – targeting high-risk patient groups – 10MM in top 7 markets
- **Indication Expansion** of apabetalone in high-risk (dialysis) CKD patients – Phase 2 clinical trials to commence in early 2017
- **Safety profile** - to date, over 1,200 patients treated with no significant safety issues