Epigenetics & BET Inhibition Corporate Update

BioPharm America
Boston, MA - September 26, 2017

TSX: RVX

Forward Looking Statements

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Outline

1. **Executive Summary & Background**
2. **Commercial Market Assessment: Planned Indications**
3. **BETonMACE Clinical Update**
4. **KOL Outreach / Commercial Opportunity**
5. **Clinical Steering Committees**
6. **Summary**

Executive Background

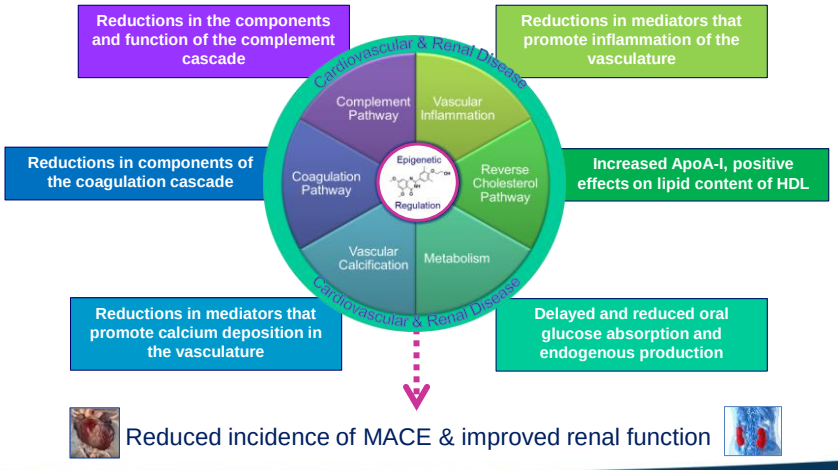
- Objective of today's presentation is to provide high level commercial assumptions, scientific and clinical data, and primary market research that provide near future rationale for **$50–$150 Billion lifetime revenue opportunity for apabetalone**
- Apabetalone is a **first and only in class BET inhibitor with patent life until 2034. High scarcity value with no competitors**
- Global market: four **planned indications**
  - Reducing MACE in ACS diabetes, patients
  - Reducing MACE in CKD patients with CVD risk profile & improvement in renal function
  - Reducing MACE and renal risk in dialysis patients
  - Improving cognition in elderly CVD/Diabetes patients

BET Inhibition MOA for High Risk Vascular Disease

- The multifactorial basis underlying high risk CVD in diabetes and CKD is driven by a wide rage on cellular responses including, vascular inflammation and calcification
- BET proteins, a major component of epigenetics, regulate these responses which drive CVD risk
- BET inhibition with apabetalone has been shown to represent a novel approach in the reduction of CVD risk and improved renal function on top of standard of care medicines

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

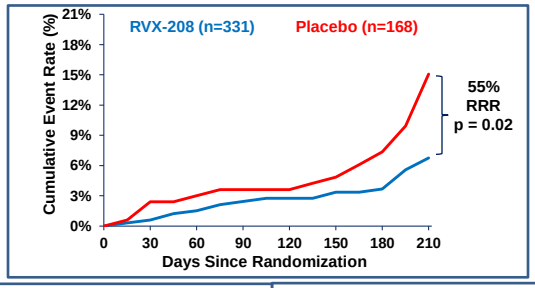
Apabetalone, a bromodomain extra-terminal (BET) protein inhibitor, inhibits BRD4, thereby regulating the expression of genes and restoring the function of pathways underlying the pathogenesis of CVD and kidney disease



Apabetalone Reduces Incidence of MACE

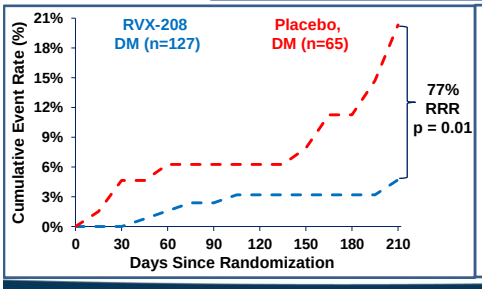
ASSURE and SUSTAIN Studies

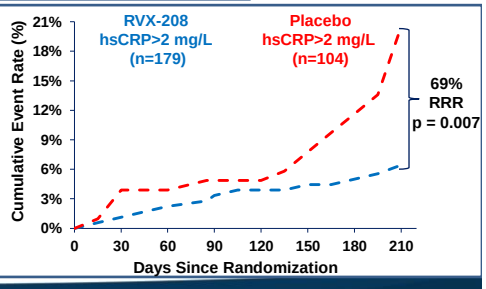
MACE: Major Adverse Cardiac Events including: death, myocardial infarction, stroke, coronary revascularization, hospitalization for acute coronary syndrome or heart failure



Note: Patients were censored at 30 days after the last dose of study medication. Log-Rank test for between group comparison

Source: Johannsson et al. European Heart Journal (2014); 35 (Abstract Supplement)
Puri et al. J Am Coll Cardiol. (2014); 63(12_S)





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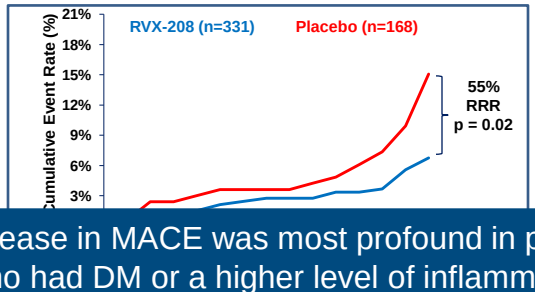

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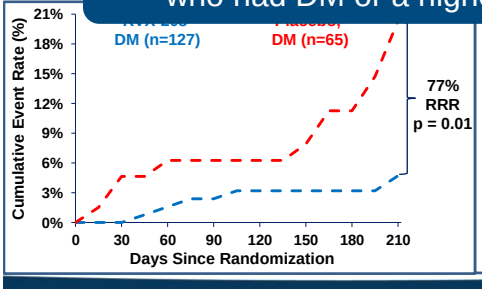
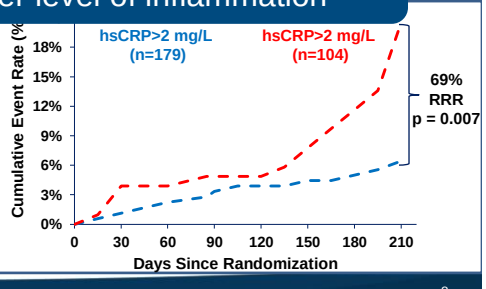
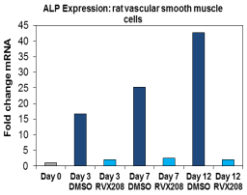
Decrease in MACE was most profound in patients who had DM or a higher level of inflammation

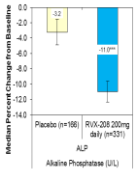


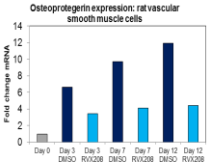


Kidney Disease: Vascular Calcification

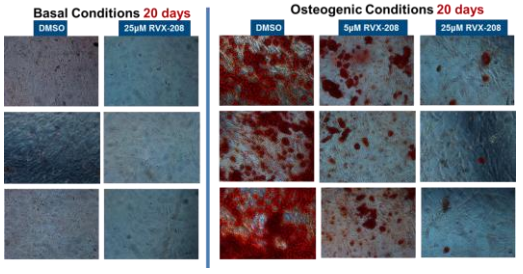
- Apabetalone treatment reduces expression of numerous proteins involved in vascular calcification in rat and human VSMCs in calcifying and osteogenic conditions, and in CVD patients

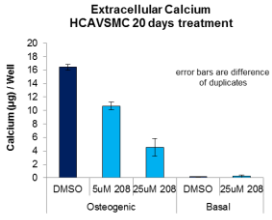






- Apabetalone reduces calcium deposition in human VSMCs grown in osteogenic conditions

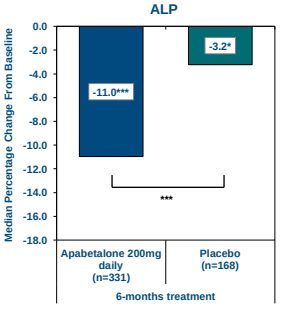


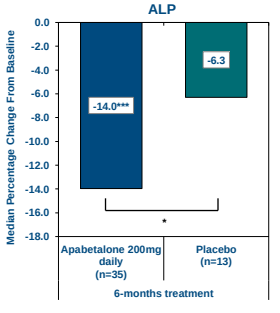


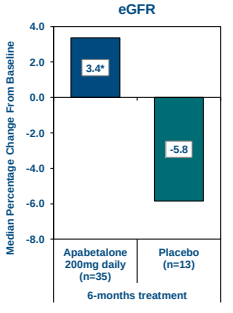
Kidney Disease: Reductions in ALP and Improvement in eGFR

- 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^2) with CVD in the phase 2 ASSURE and SUSTAIN trials.

All Patients *Patients With Baseline eGFR<60 mL/min/1.73m2*





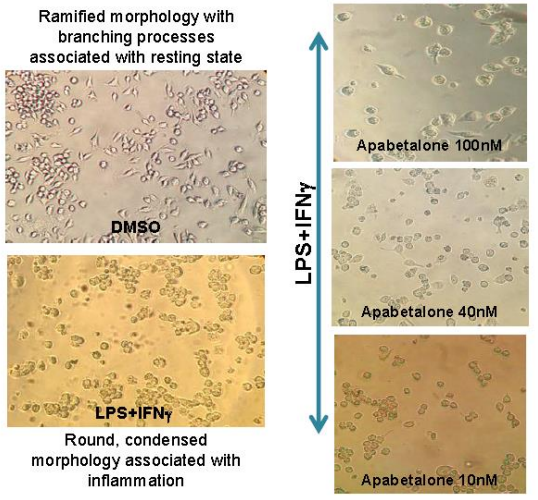


Wilcoxon signed-rank test for change vs. baseline and 2-sided Van Elteren test stratified by study for percent change in baseline vs. placebo * p<0.05; ** p<0.01; *** p <0.001

Neuroinflammation: AD/PD Presentation 2017

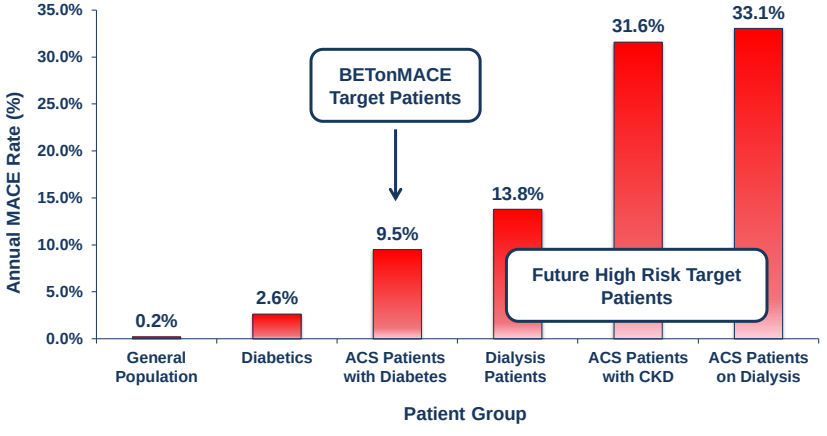
- Apabetalone reverses the inflammatory morphology acquired by stimulated microglia, consistent with suppression of the inflammatory response.
- Apabetalone promotes survival of microglia versus a comparator molecule.
- BET inhibition is a promising therapy that modulates multiple processes contributing to neurodegenerative disease.

Reversal of activated morphology by apabetalone



Targeted Patient Enrichment Strategy

Relative Annual Major Adverse Cardiac Event (MACE) Rates In Various Patient Groups



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

Targeting Market High Risk Vascular Patient Groups
Top Seven Markets

Phase 3: ACS with diabetes / low HDL – Peak Market 2,400,000

Phase 3 Sub Group: CKD pre-dialysis – Peak Market 5,500,000

Phase 2 Dialysis – Target Patient Market - Peak Market 1,200,000

Phase 3 Sub Group Dementia/MCI Diabetics – Peak Market 2,800,000

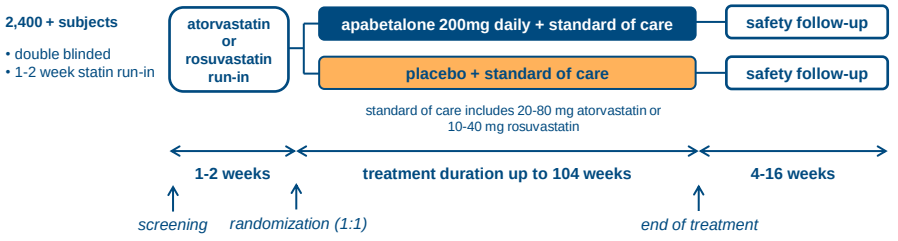
Phase 2 Rare/Orphan FSHD/IgA Nephro/PSKD – Peak Market 500,000+

Total Target High Risk Market opportunity: 12++ Million patients top 7 markets

BETonMACE Clinical Update

BETonMACE CV Outcomes Study Design

BETonMACE
A CARDIOVASCULAR STUDY FOR PEOPLE WITH TYPE 2 DIABETES



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

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

Exploratory Endpoint
MoCA in elderly patient 70 and over with focus on MoCA below 26

BETonMACE Subgroups/Summary

- **Pre-specified subgroup analyses for primary endpoint include:**
  - rosuvastatin/atorvastatin
  - ≤ 30 days/> 30 days post-acute coronary syndrome
  - LDL/HDL/TG's above and below median
  - HbA1c above and below median
  - eGFR ≥ 60 mL/min and < 60 mL/min
    - Also change in eGFR for all patients with eGFR <60 mL/min

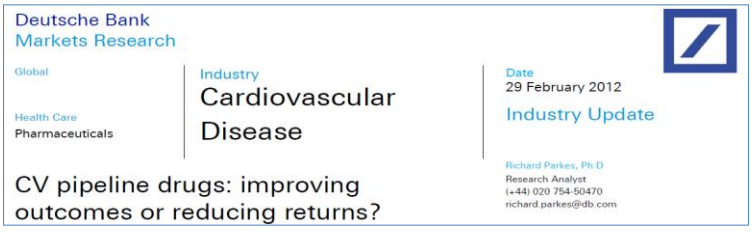
- **Planned exploratory subgroup analyses:**
  - Heart failure Stage 1-2
  - Cognition MoCA Score: Patients >70 years of age (MoCA<26)
  - Total all cause mortality

- **>1,800 patients dosed to date with 4 DSMB safety reviews and approvals**

Commercial Opportunity: KOL Outreach, Clinical Expansion

Historic Pipeline Value for CVD Risk Reduction Assets

- Deutsche Bank estimates CVD Residual Risk Market worth **$90B**
- Previous pipeline values attributed to Phase 3 residual risk assets
  - **$13B Pipeline Value** for Torcetrapib (2006) Failed mid Phase 3
  - **$8B Pipeline Value** for Dalcetrapib (2012) Failed mid Phase 3
  - **$10B Pipeline Value** for Daralpadib (2014) Failed Phase 3
  - **$8B Pipeline Value** for Evacetrapib (2015) Failed Phase 3
  - **$??B Value for Apabetalone (2018-2020) Multiple Phase 3 readouts**


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

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

Apabetalone: Balanced for Success

THREE CRITICAL DEVELOPMENT SUCCESS FACTORS IN PLACE

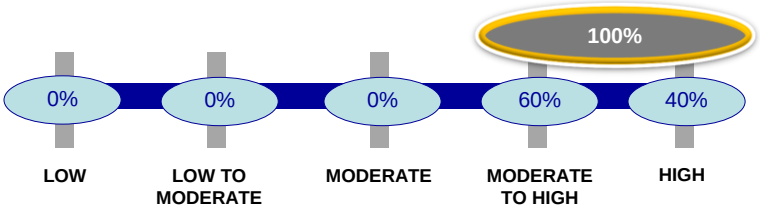
INNOVATION
Resverlogix owns the worlds most advanced BRD4 epigenetics program

EFFICACY
Clinical and safety data is continuing to suggest a successful program

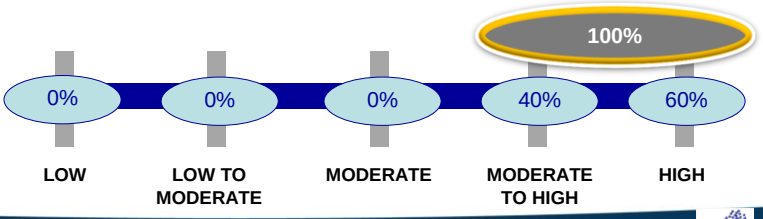
PHARMACO-ECONOMICS
Payor groups response for BET program positive - seeking future results

Commercial Metrics: Payer Analysis

Unmet medical need in reducing MACE in patients with recent ACS and T2DM



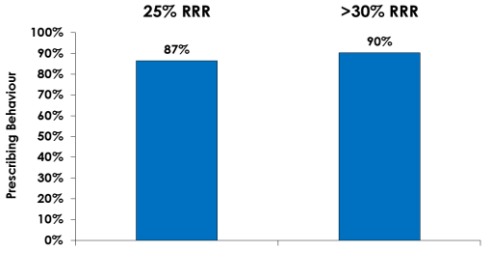
Unmet medical need in reducing MACE in patients with recent ACS and CKD



Commercial Metrics: Prescribing Behaviour: SERMO™ 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?



Expanded Global SERMO Market Outreach Program Underway

Commercial Metrics: Payer KOL Outreach Pricing Band Analysis

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 range of approximately **$140,000 -175,000** USD
- Pricing bands support average price of **$6,000 - $12,000** based on new enriched high risk patients

Commercial Metrics: ICER Analysis

Class	Trial	Patient Group	Size	Primary Endpoint	Primary MACE Reduction (RRR)	Annual No. Needed to Treat (NNT)	Annual Price (NHS - Europe Price) ($ USD)		ICER
Anti-Interleukin-1β Inhibitor	CANTOS Canakinumab	History of MI	10,061	nonfatal MI, nonfatal stroke, or cardiovascular death	50 mg = 7% (n.s.) 150 mg = 15% (p = 0.021) 300 mg = 14% (p = 0.031)	673	orphan drug price ~£69,000 per year discounted $10K per year	10,000	6,727,273
PCSK9 Inhibitors LDL Lowering	FOURIER Evolucumab	Athero CVD High CV risk	27,564	cardiovascular death, MI, stroke, hospitalization for unstable angina, or coronary revascularization	15% (p< 0.001)	147	wholesale price	5,840	856,460
	ODYSSEY LONG TERM Alirocumab	Heterozygous FH or with established CHD	2,341	death from coronary heart disease, nonfatal MI, fatal or nonfatal ischemic stroke, or UA requiring hospital	Post-Hoc Analysis on ODYSSEY OUTCOMES trial CV endpoint 48% (p = 0.02)	99	wholesale price	5,767	569,669
BET Inhibition	BETonMACE Apabetalone	recent ACS with T2DM and low HDL	2400	CV death, MI, or stroke	>25%	57	> 25% RRR	2,940	168,000
					>30%	48	> 30% RRR	3,360	160,000
					>35%	41	> 35% RRR	4,580	165,286
					>40%	36	>40% RRR	5,200	170,000

Apabetalone High Risk Vascular Expansion Plan

- BETonMACE contains specific patient subgroups that will provide insights into future indications to expand into
  - CKD patients (eGFR ≥ 60 mL/min and < 60 mL/min)
  - Cognition (MoCA score <26): Patients >70 years of age
- With respect to CKD patients (stages 3+), there has been an early signal from pooled Phase 2 studies (ASSURE & SUSTAIN) showing improvements in eGFR
- Therefore, positive subgroup readouts from BETonMACE would provide strong rationale for the commencement of Phase-3 CKD trials

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

Summary Highlights

Late Stage Trial	RVX is a phase 3 (BETonMACE) company focused on significant unmet need in high-risk CVD, diabetes and CKD patient populations.
Strong R&D	BET responsive activities including directional changes towards normalization of perturbed vascular inflammation, vascular calcification, complement and coagulation.
Market Leader Targeting Unmet Need	Apabetalone has potential in several high-risk unmet need patient groups totaling over 10MM patients in the top seven markets (US, 5EU and Japan).
Established Safety Profile	To date, over 1,800 patients have been treated with apabetalone with no significant safety issues. Four approved DSMB approvals to continue trial as is
Novel Mechanism of Action	First in class, only in class . Regulation of gene transcription and disease causing genes, unlike Crisper approach of changing DNA.
Strong Reimbursement Value	Robust Value Proposition Agreed by leading Payer groups