



## **Resverlogix**

BET Inhibition for Global Vascular Risk  
BIO CEO & Investor Conference  
New York, NY

February 12-13, 2018

TSX: RVX

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# Apabetalone Development Highlights



## Main Subject Matter

- Apabetalone, the only-in-class BET inhibitor (BETi), reduces key risk factors for high risk cardiovascular and renal patients resulting in reduction of Major Adverse Cardiac Events (MACE), observed renal improvement markers

## Advanced Mechanism

- Epigenetic modulation of gene expression makes BETi a novel approach
  - No known BETi competitor for next 9 plus years

## Confirmed Science

- Proteomics, genomics, pathway analysis, mechanism of action are all very well understood

## Clinical Evidence

- Phase 2b data – up to 62% RRR of MACE in high risk CVD patients
- Phase 3 BETonMACE trial 90% enrolled
  - CVD/CKD risk biomarkers tracked to date - positive

## Corporate Expansion

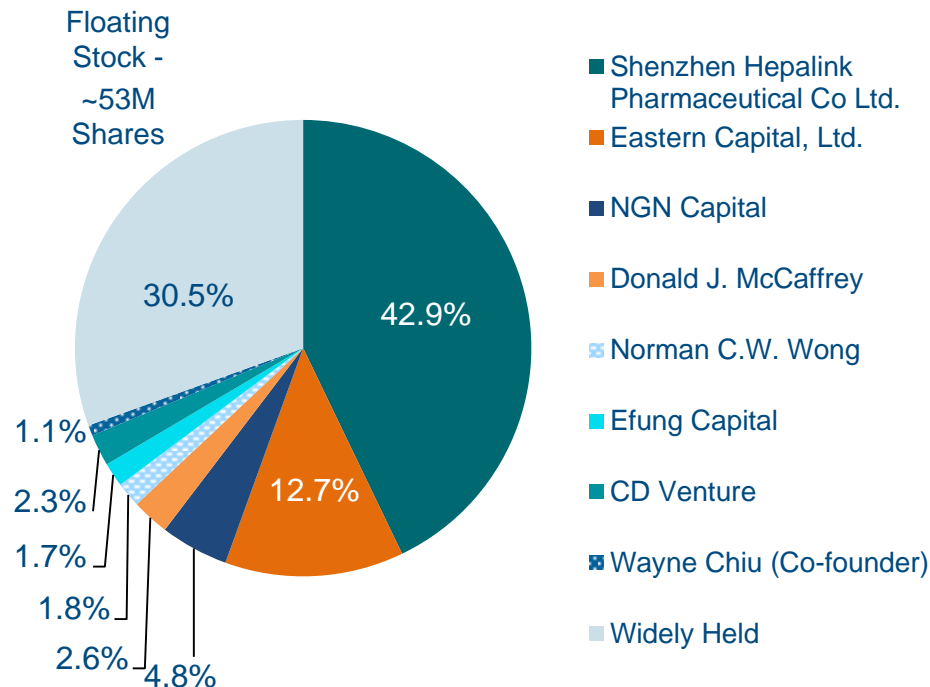
- Resverlogix corporate goal is to expand commercial partner program

# Capitalization and Financial Profile



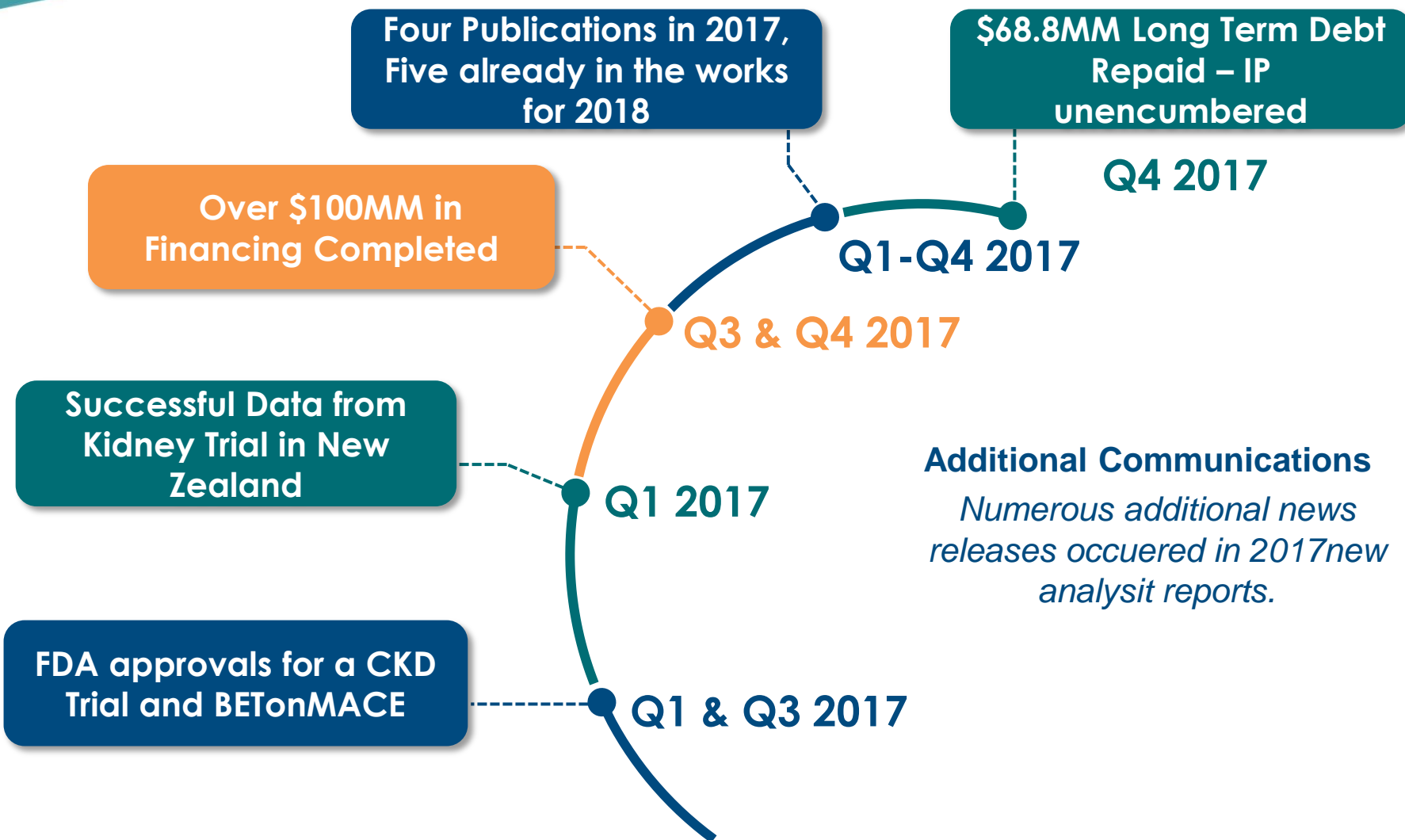
<b>Founded</b>	<b>2001</b>
<b>Ticker</b>	<b>TSX: RVX</b>
<b>Market Cap</b>	<b>~C\$300MM</b>
<b>Long Term Debt</b>	<b>~C\$0.0MM</b>
<b>Shares Outstand</b>	<b>175.04MM</b>
<b>Cash Burn (Annual)</b>	<b>~C\$40.0M</b>
<b>Finance</b>	<b>\$87MM – Announced October 2017</b>

## RVX Top Shareholders

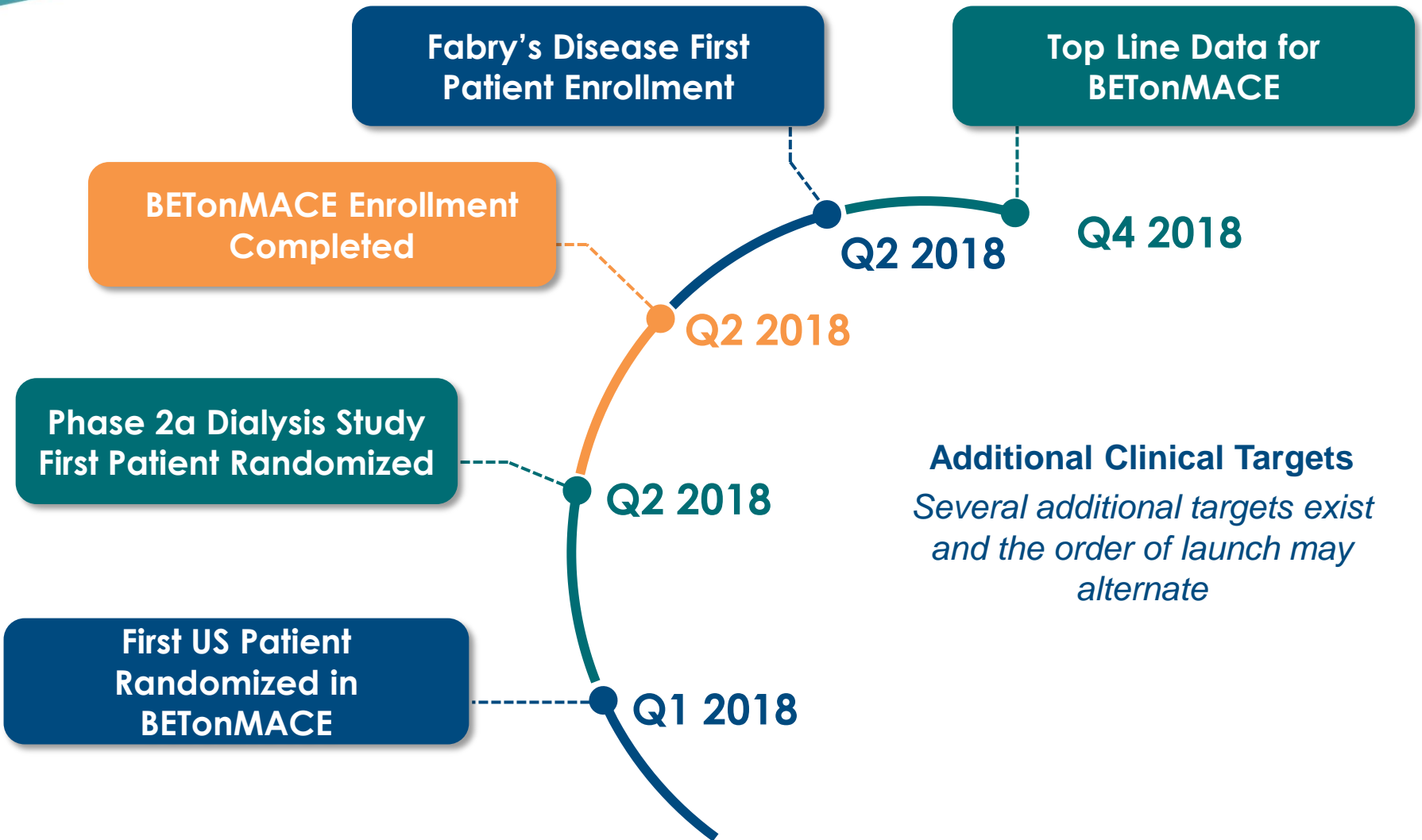


- RVX shareholder base consists of several long term investors who have been supportive over 10 years
- RVX maintains a diversified public market float of approximately 54M shares or ~\$130MM

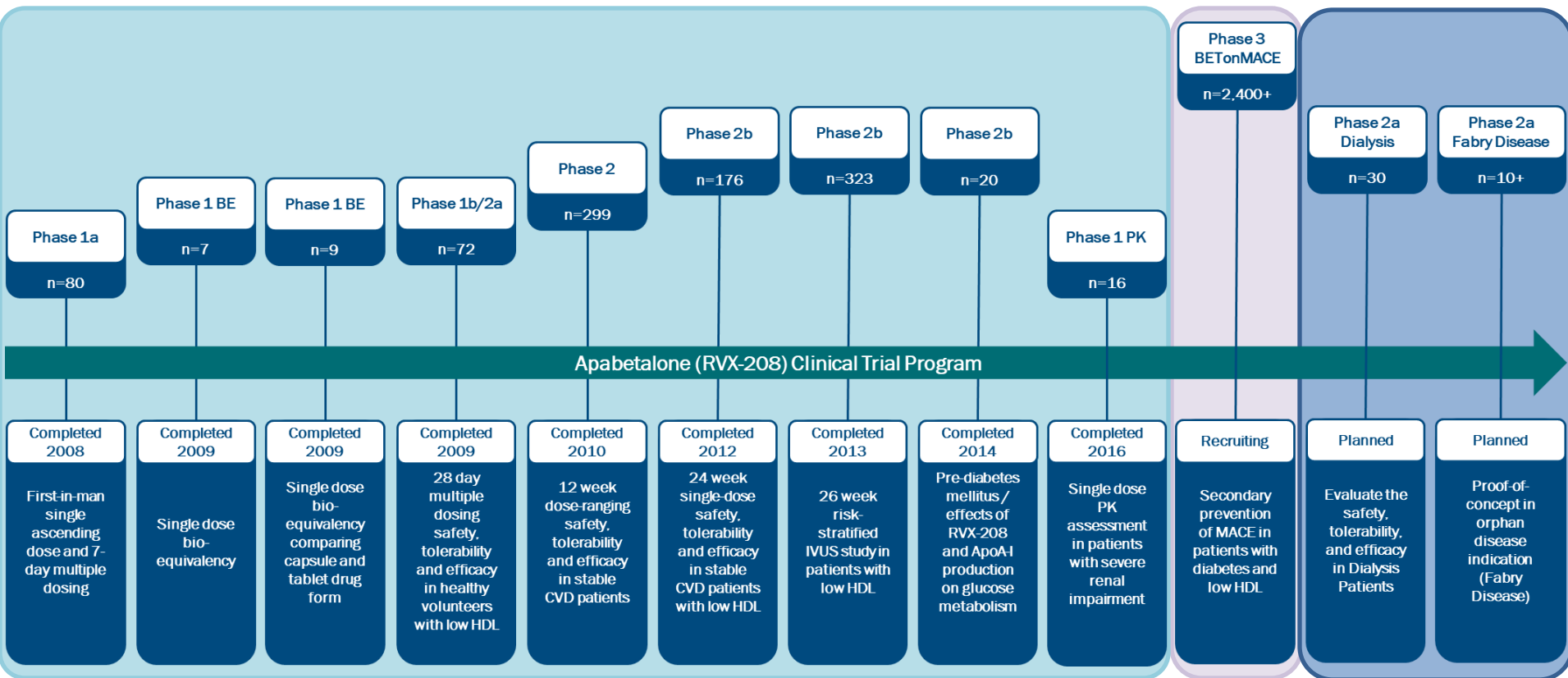
# 2017 Major Accomplishments



# Upcoming Clinical Year Estimates



# Apabetalone in the Clinic



Apabetalone has been tested in multiple clinical trials with a good safety and efficacy profile



# BET Literature Impact Growing: CVD and Renal Risk

## RVX-208, an Inducer of ApoA-I in Bromodomain Antagonist

Kevin G. McLure<sup>1</sup>, Ewelina Kulikowski<sup>1</sup>, Jan O. Johansson<sup>3</sup>, Norman C. Wong<sup>3</sup>, Ravi Jahagirdar<sup>1</sup>, Christopher Halliday<sup>1</sup>, Dean Gilham<sup>1</sup>, Sylwia Wasiak<sup>1</sup>, Michael Sweeney<sup>2</sup>

Data in Brief 8 (2016) 1280–1288



Contents lists available at ScienceDirect

Data in Brief

Data Article

Data on gene and protein expression induced by apabetalone in treated human whole primary hepatocytes

Sylwia Wasiak<sup>a</sup>, Dean Gilham<sup>a</sup>, Christopher Halliday<sup>a</sup>, Kevin G. McLure<sup>a</sup>, Peter R. Young<sup>a</sup>, Ewelina Kulikowski<sup>a</sup>, Jan O. Johansson<sup>b</sup>, Norman C. Wong<sup>a,\*</sup>

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<sup>b</sup> Resverlogix Corp., San Francisco, USA

Am J Cardiovasc Drugs  
DOI:10.1007/s40256-017-0250-3

### ORIGINAL RESEARCH ARTICLE

## Selective BET Protein Inhibition with Apabetalone and Cardiovascular Events: A Pooled Analysis of Trials in Patients with Coronary Artery Disease

Stephanie C. Stotz<sup>1</sup>, Ravi Jahagirdar<sup>1</sup>, Kevin G. McLure<sup>2</sup>, Jan O. Johansson<sup>3</sup>, Michael Sweeney<sup>4</sup>, Norman C. Wong<sup>3</sup>

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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](#)✉

J. of Cardiovasc. Trans. Res.  
DOI:10.1007/s12265-017-9755-z

ORIGINAL ARTICLE

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

Sylwia Wasiak<sup>1</sup>, Dean Gilham<sup>1</sup>, Laura M. Tsujikawa<sup>1</sup>, Christopher Halliday<sup>1</sup>, Cyrus Calosing<sup>1</sup>, Ravi Jahagirdar<sup>1</sup>, Jan Johansson<sup>2</sup>, Michael Sweeney<sup>2</sup>, Norman C. Wong<sup>1</sup>, Ewelina Kulikowski<sup>1</sup>✉

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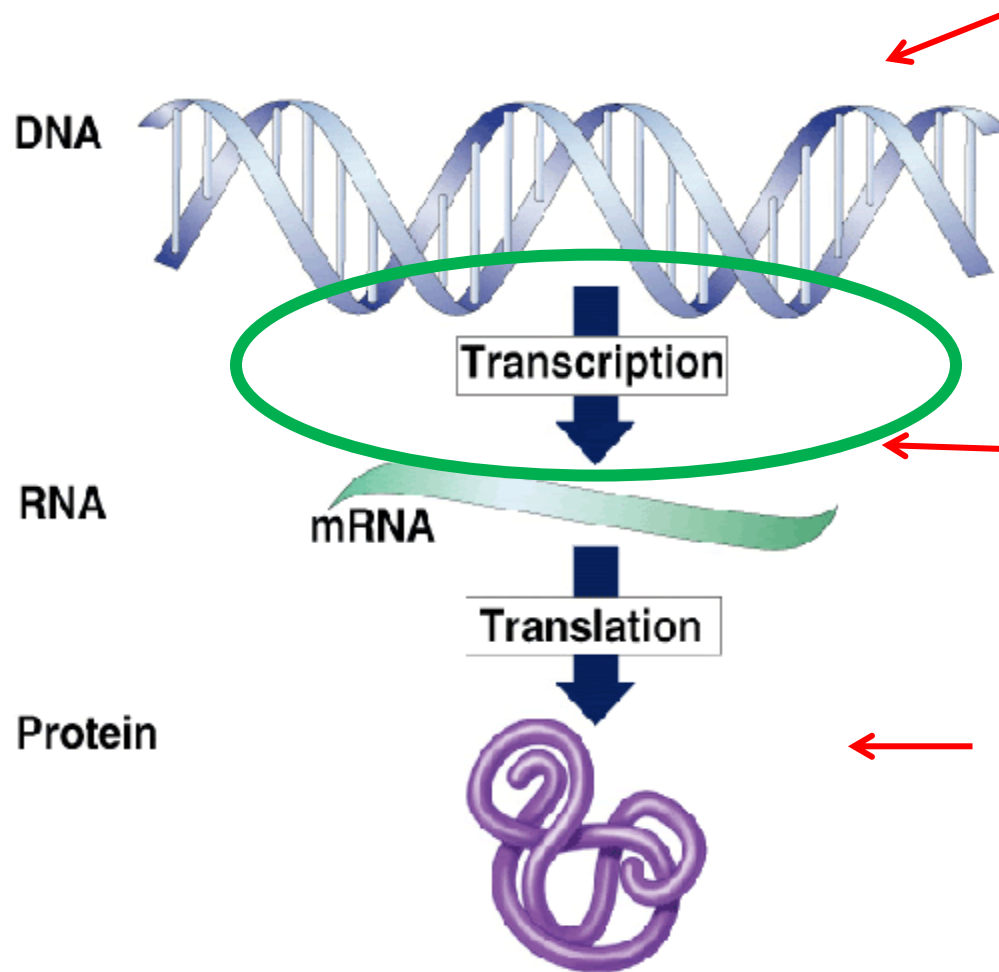
## Autoimmune Disease<sup>®</sup>

Ravi Jahagirdar, Sarah Attwell, Suzana Marusic, Alison Bendele, Narmada Shenoy, Kevin G. McLure, Dean Gilham, Karen Norek, Henrik C. Hansen, Raymond Yu, Jennifer Tobin, Gregory S. Wagner, Peter R. Young, Norman C. W. Wong, and Ewelina Kulikowski

Resverlogix Corporation, Calgary, Alberta, Canada (R.J., S.A., K.G.M., D.G., K.N., H.C.H., R.Y., J.T., G.S.W., P.R.Y., N.C.W.W., E.K.); Hooke Laboratories Inc., Lawrence, Massachusetts (S.M.); Bolder BioPATH Inc., Boulder, Colorado (A.B.); and Aravasc Inc., Sunnyvale, California (N.S.)



# Unique Mechanism of Action



## 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.

**CRISPR – gene editing within a cell sub population**

## Transcriptional Regulation

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

**Apabetalone – reduces expression of disease mediators**

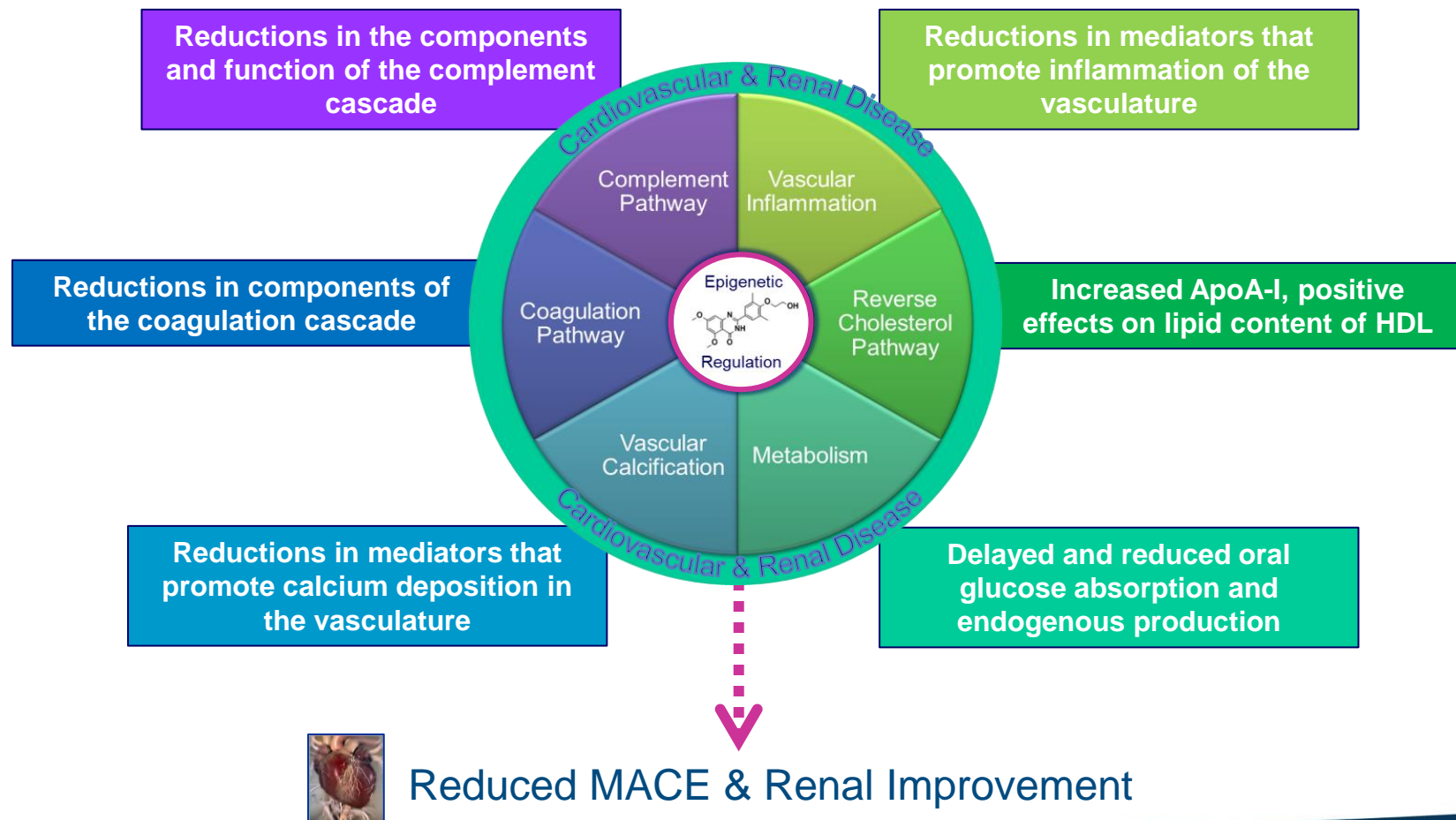
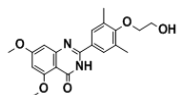
## Protein Targeting

Focus on reducing or blocking the activity of **one** disease protein by using an inhibitor or antibody

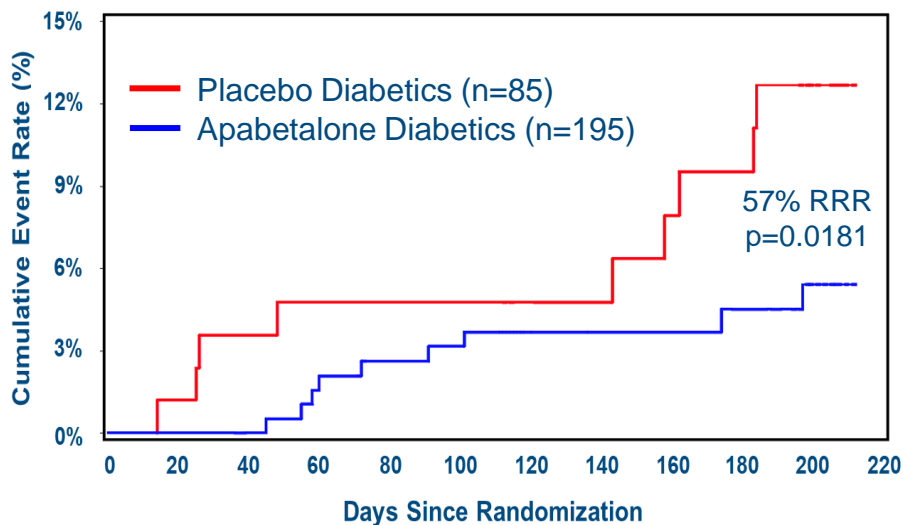
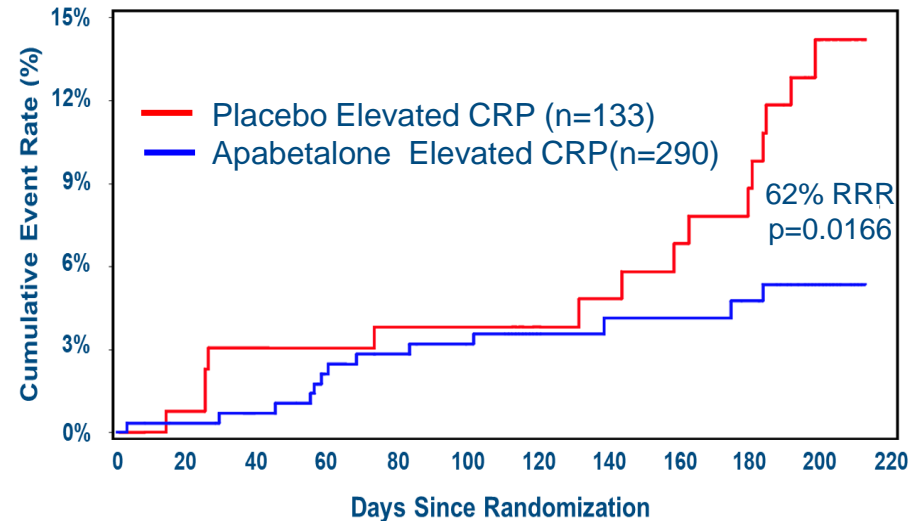
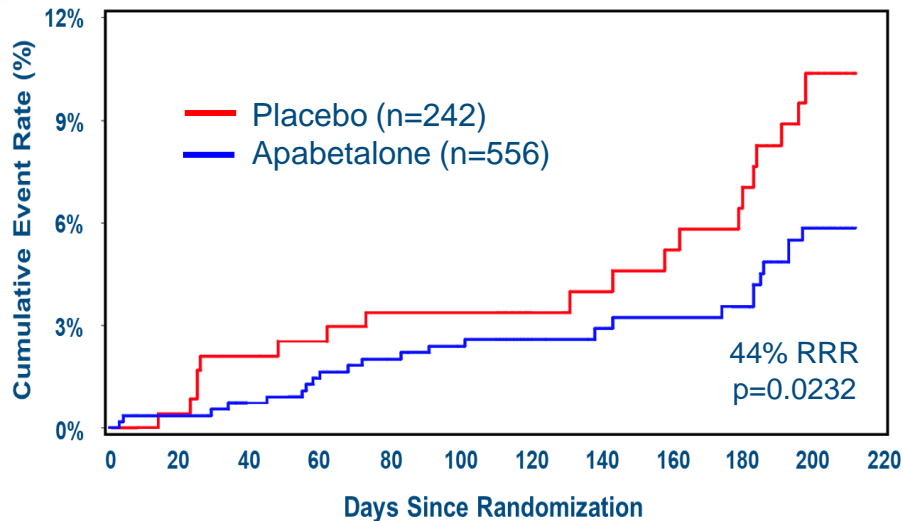
**Antibody or Inhibitor – blocks activity of one mediator of disease**

# 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



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



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

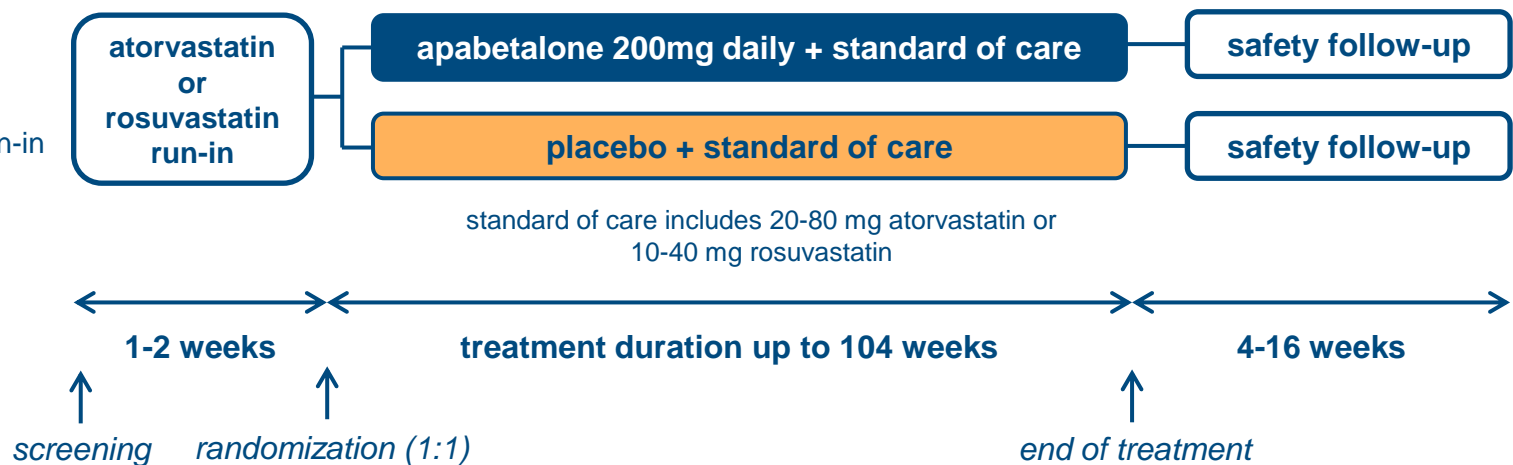
Decrease in MACE was most profound in patients who had a higher level of inflammation such as patients with diabetes

# BETonMACE CV Outcomes Study Design



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**

## **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 <40 mg/dL for males and <45 mg/dL 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

# Screening & Baseline Clinical Chemistry

## As of December 4, 2017



Parameter	N	Median (min, max)
Age	2,091	62 (33, 88)
Alkaline Phosphatase <sup>†</sup> , U/L	2,065	78 (5, 915)
HDL-C, mg/dL	2,074	33 (14, 47)
hsCRP <sup>†</sup> , mg/L	425	2.9 (0.2, 162.1)
Fibrinogen <sup>‡</sup> , mg/L	406	387 (92, 730)
LDL-C, mg/dL	2,057	65 (3, 232)
Apolipoprotein A-I <sup>†</sup> , mg/dL	415	118 (58, 179)
Glucose, mg/dL	2,074	135 (41, 555)
HbA1c, %	2,035	7.3 (4.5, 15.1)
Platelets, 10 <sup>9</sup> / L	1,976	248 (6, 989)
NLR, ratio	1,993	2.6 (0.6, 16.5)
Males	75.6% males	
Statin Allocation	52% atorvastatin	48% rosuvastatin

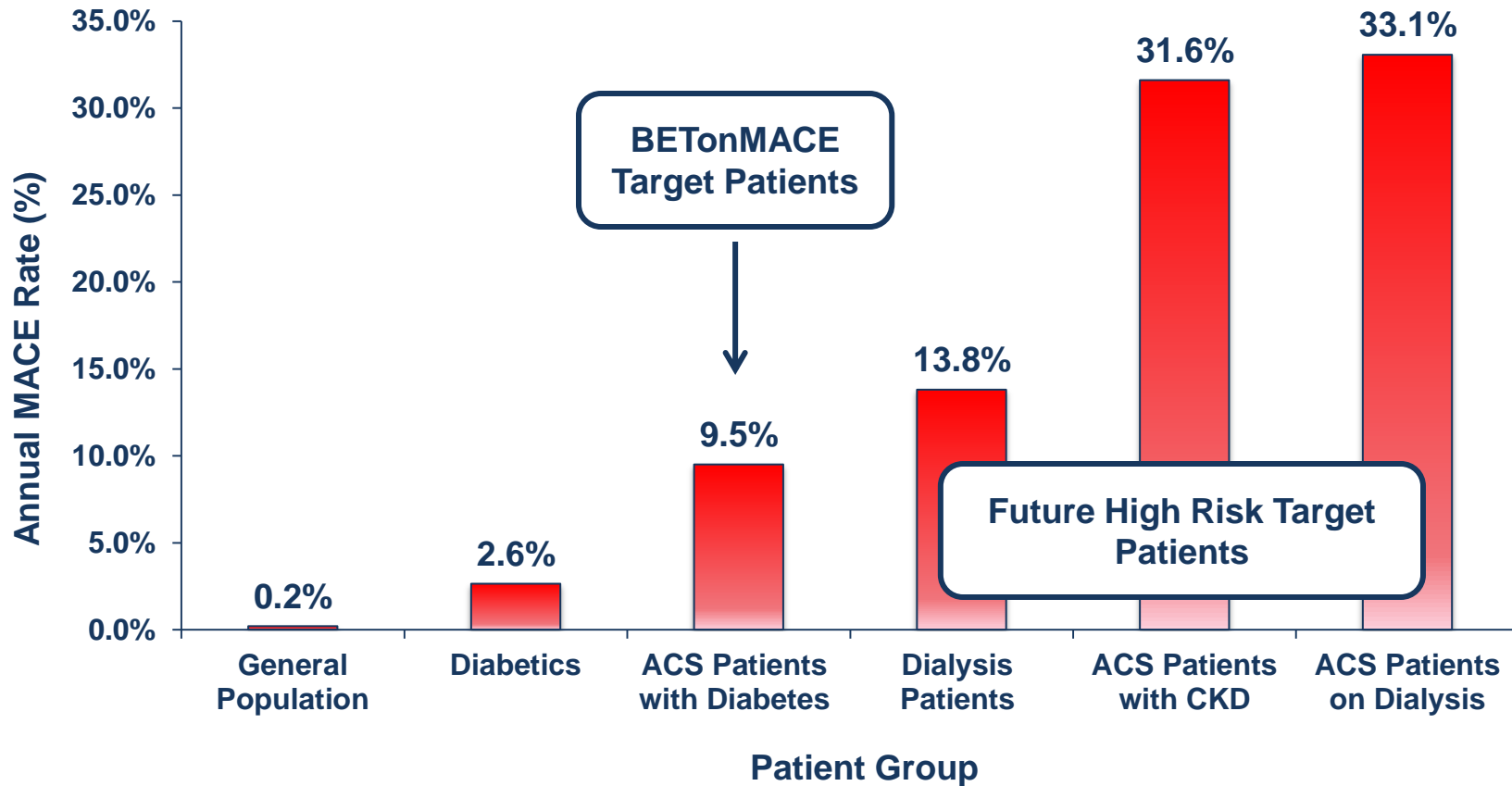
<sup>†</sup> results from visit 2/wk 0, whereas all other values are from visit 1/screening



- ~ 90% enrolled
- CKD Subgroup: ~11% of patients have eGFR<60 at screening
- Cognition Subgroup: ~18% of patients have completed MoCA at Baseline; Target patients are those with baseline MoCA  $\leq 25$
- Consistent data repeatable positive effects in key CVD and CKD biomarkers
- New data to target MoCA in elderly cognition subgroup (70 and over)
- Projected primary MACE rate still 8.0 per 100 patient years on top of aggressive standard of care = strong unmet need

# Patient Enrichment Strategy

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



Sources: Calculated from CDC Heart 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

# Market Opportunity Pathways



## Diabetes/ACS

- BETonMACE derived 2,400 patients
- MACE reduction
- **2-3 Million patients**



## CKD/ESRD

- BETonMACE sub population derived 300-400 patients
- Improved renal function in sub-group
- Reduced MACE
- Future trials in CKD Stage 3-4  
Diabetic Nephropathy  
ESRD
- **6 Million Patients**

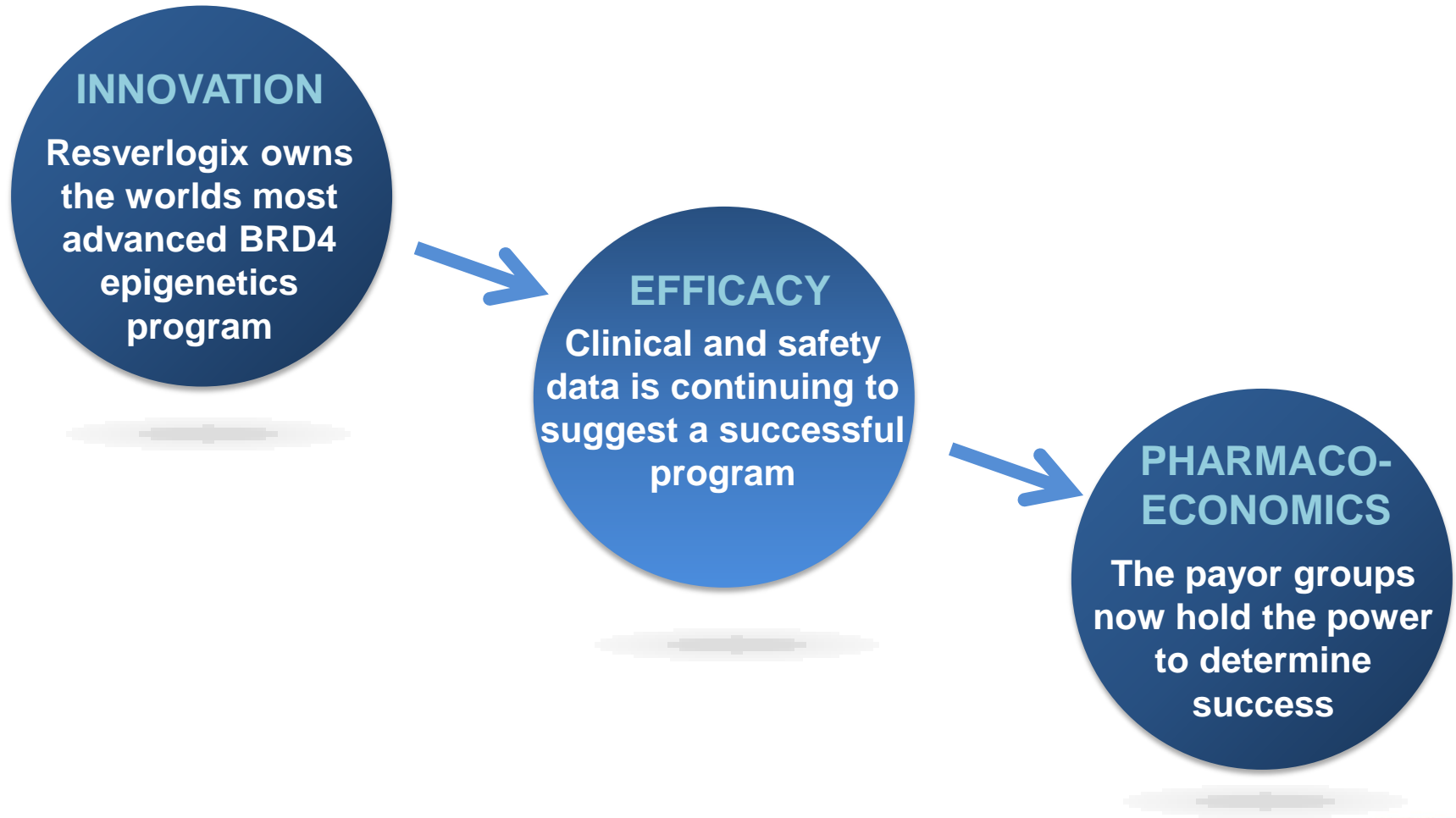


## Expanded Programs

- BETonMACE sub-population data analysis
- Cognition and dementia
- **2+ Million Patients**

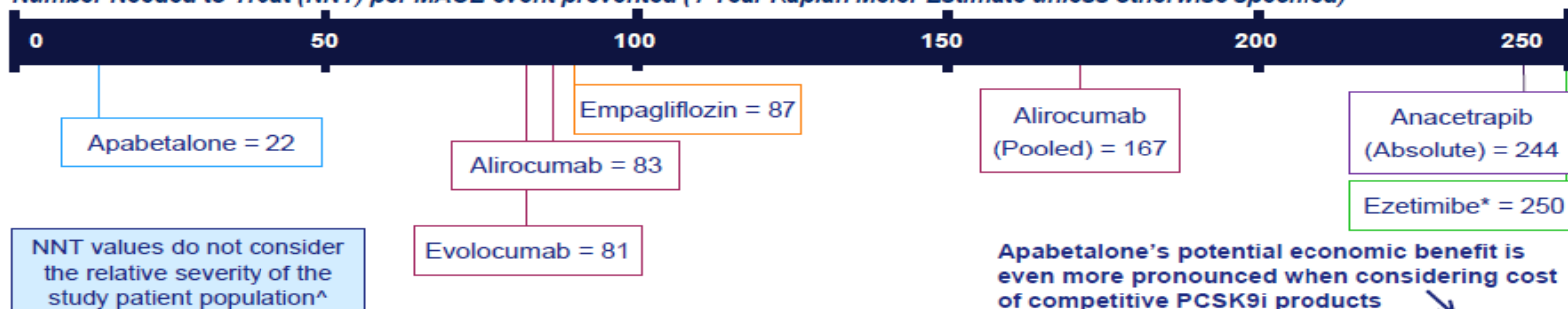


## THREE KEY DEVELOPMENT TARGETS ARE IN PLACE



Based on SUSTAIN/ASSURE, NNT and cost/event prevented were favourable versus comparators in their respective patient populations

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



Trial	Molecule	Trial Size	Treatment Duration (Years)	Absolute NNT/Yr	Kaplan Meier (KM) NNT/Yr	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

<sup>^</sup>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

Apabetalone HEOR Evidence Benchmarking - Final Results v4.0 Oct 2015

imshealth | brogan

RVX testing further price bands: Tier 3 based on higher risk populations

- RVX performed multiple outreach reports with leading US KOL payers for market pricing analytics
- Apabetalone target plan: higher risk CVD patients (e.g. Diabetes with recent ACS, CKD, Dialysis, Dementia) supported positive pricing and reimbursement with leading US payer groups
- Higher risk patients represent significantly increased burdens to healthcare systems on account of greater costs associated per patient per year
- Payer responses shows strong support for pricing value proposition falls within ICER range of \$140-175K USD. This ICER range represents superior value proposition versus current CVD risk competitors such as PCSK9s and SGLT2s
- Global pricing band planned by US market first, then European, Canada with applicable discounts



# Payer KOL Outreach: Key Payer Support



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-\$200,000** USD
- Pricing bands support average price of **\$6,000 - \$12,000** based on new enriched high risk patients

## Highlights

- Novel, first in class, technology – no competitor 8 – 10 years
- Clear science and clinical data supporting strong rationale for risk reduction
- Growing BET literature publications in CVD / Renal risk
- Strong KOL Payers and Prescriber support
- Transformative science and unprecedented commercial opportunity