Resverlogix Corp.

BET inhibition for Global Vascular Risk

BIO-EUROPE Spring 2018 March 14th

Amsterdam, The Netherlands

TSX: RVX

Forward Looking Statements

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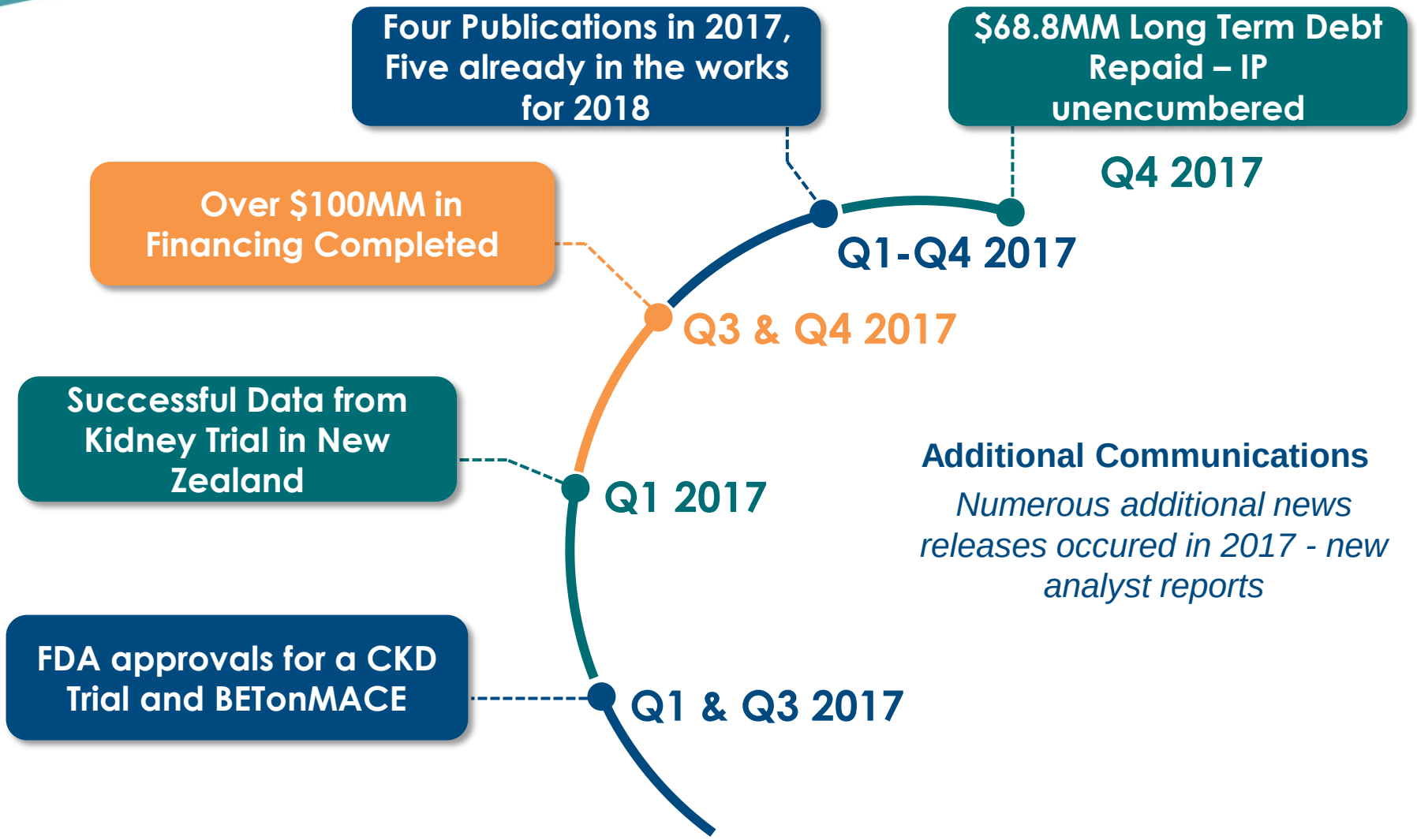
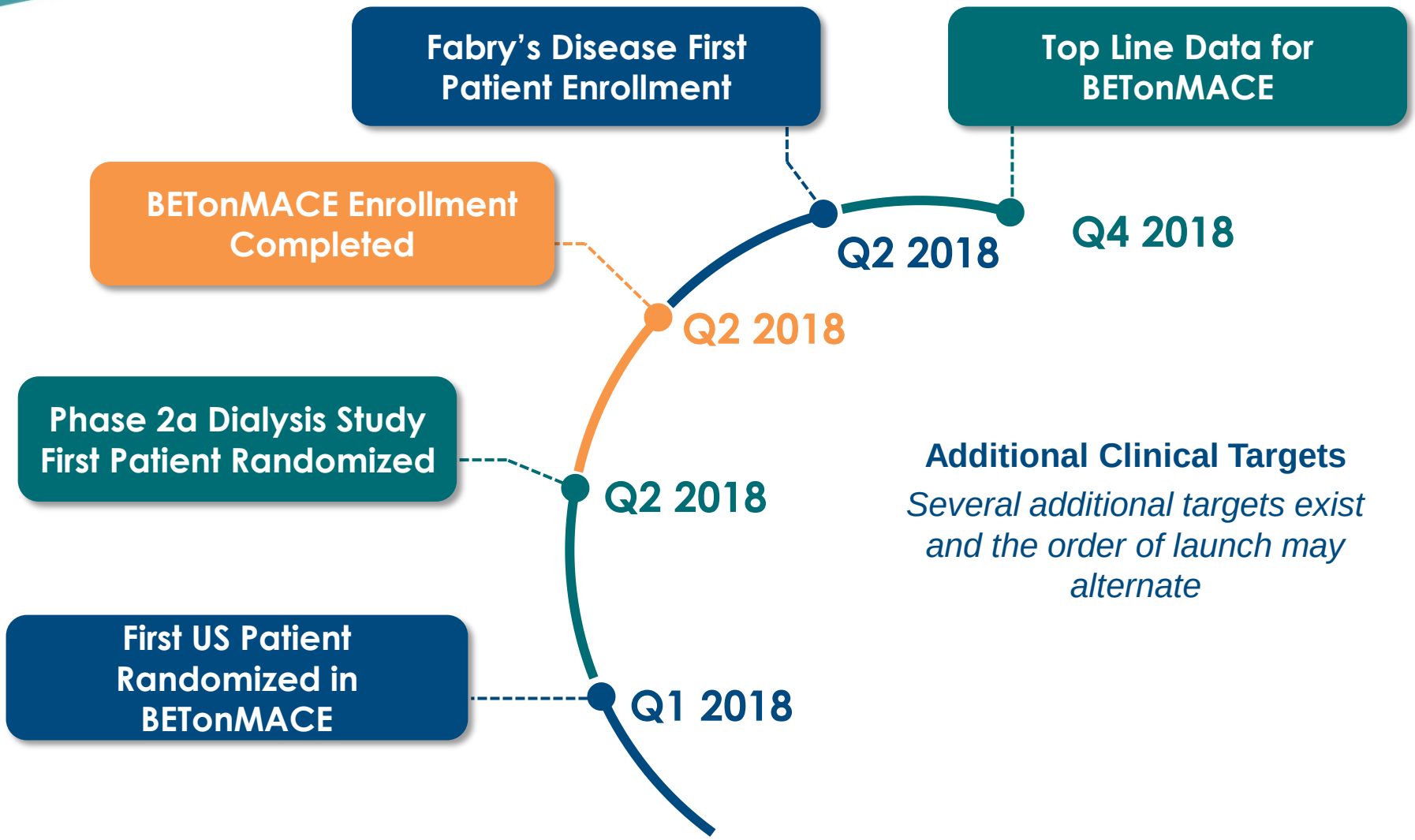
Apabetalone Development Highlights

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

2017 Major Accomplishments



Upcoming Clinical Year Estimates



Additional Clinical Targets

Several additional targets exist and the order of launch may alternate

BET Literature Impact Growing: CVD and Renal Risk

RESVERLOGIX

OPEN ACCESS Freely available online

PLOS ONE

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

Data in Brief 8 (2016) 1280–1288

Contents lists available at ScienceDirect

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Data Article

Data on gene and pr
induced by apabetal
treated human whol
primary hepatocytes

Sylwia Wasiak [a], Dean Gil
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Kevin G. McLure [a], Peter R
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Am J Cardiovasc Drugs
DOI 10.1007/s40256-017-0250-3

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ORIGINAL RESEARCH ARTICLE

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

KI REPORTS

Kidney International Reports

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Article in Press

Benefit of Apabetalone on Plasma Proteins in Renal Disease

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

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sson [b], Michael Sweeney [b],

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[1] · Dean Gilham[1] · Laura M. Tsujikawa[1] · Christopher Halliday[1] · Cyrus Calosing[1] · Ravi Jahagirdar[1] · Jan Johansson[2] · Michael Sweeney[2] · Norman C. Wong[1] · Ewelina Kulikowski[1]

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, Has Therapeutic Effects
tion and
Autoimmune Disease

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.)

BET Literature Impact Growing: Neurodegenerative Risk

Current Alzheimer Research, 2016, *13*, 985-995

BENTHAM SCIENCE

The BET-Bromodomain Inhibitor JQ1 Reduces Inflammation and Tau Phosphorylation at Ser396 in the Brain of the 3xTg Model of Alzheimer's Disease

Marco Magistri, Dmitry Velmeshev, Madina Makhmutova, Prutha Patel, Gregory C. Sartor, Claude-Henry Volmar, Claes Wahlestedt and Mohammad Ali Faghihi*

ELSEVIER

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

The BET/BRD inhibitor JQ1 attenuates diabetes-induced cognitive impairment in rats by targeting Nox4-Nrf2 redox imbalance

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Ershun Liang [a], Min Ma [b], Lei Wang [c], Xue Liu [a], Jinfeng Xu [d], Mingxiang Zhang [a, **], Ruixue Yang [a, *], Yuxia Zhao [a]

OPEN

Citation: Transl Psychiatry (2017) **7**, e1239; doi:10.1038/tp.2017.202

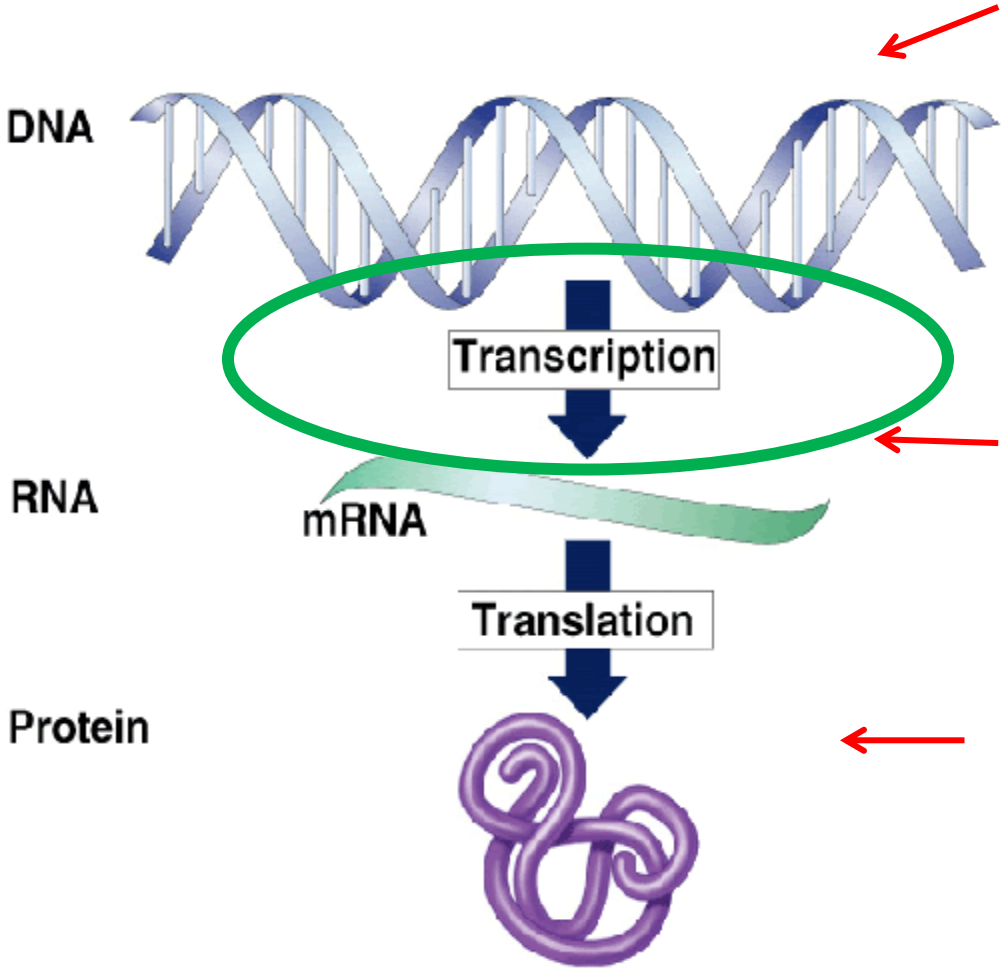
www.nature.com/tp

ORIGINAL ARTICLE

The BET/BRD inhibitor JQ1 improves brain plasticity in WT and APP mice

E Benito[1], B Ramachandran[2], H Schroeder[1], G Schmidt[3], H Urbanke[1], S Burkhardt[1], V Capece[1], C Dean[2] and A Fischer[1,4]

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

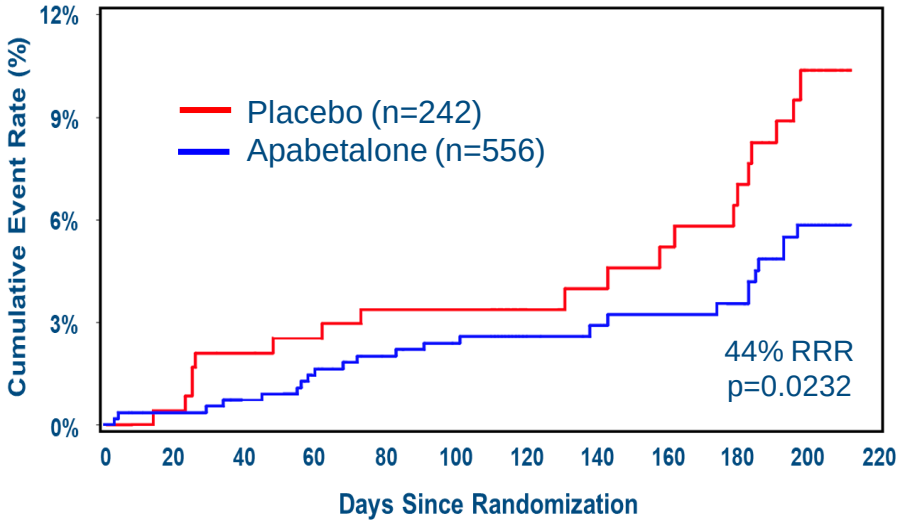
Apabetalone – reduces expression of disease mediators

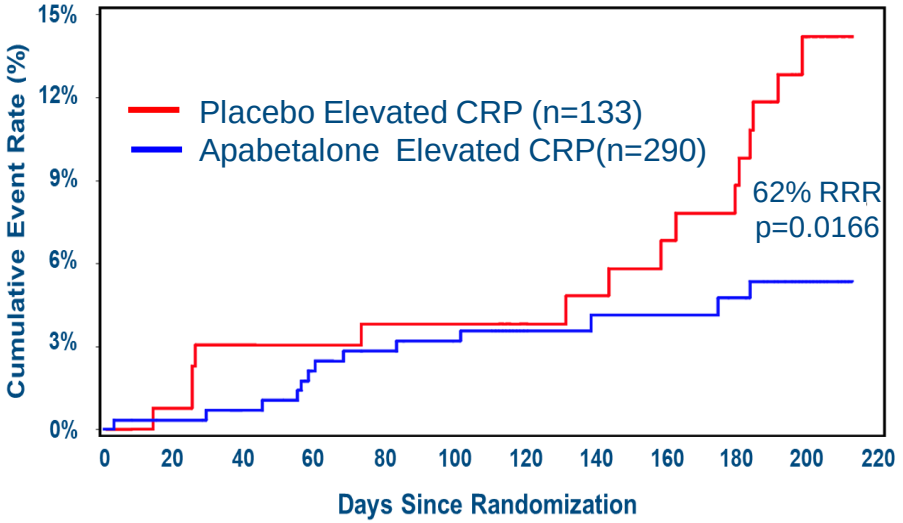
Protein Targeting

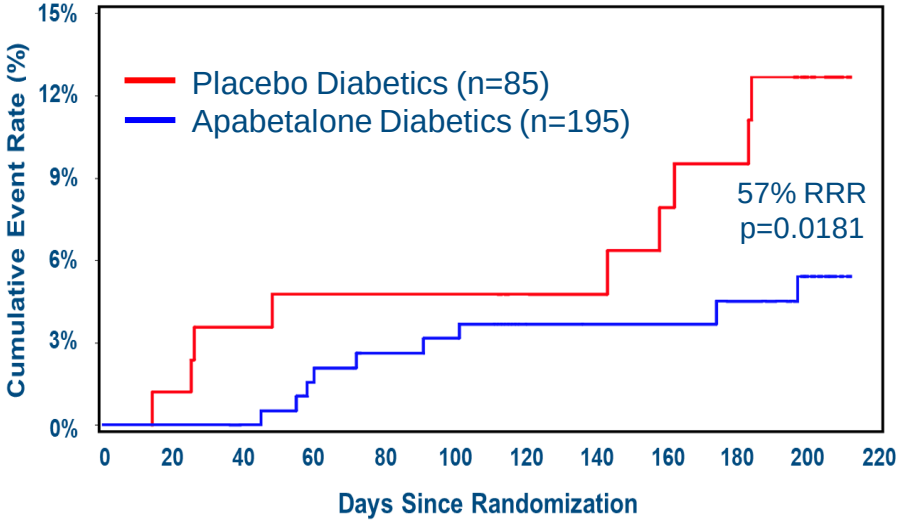
Focus on reducing or blocking the activity of **one** disease protein by using an inhibitor or antibody

Antibody or Inhibitor – blocks activity of one mediator of disease

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

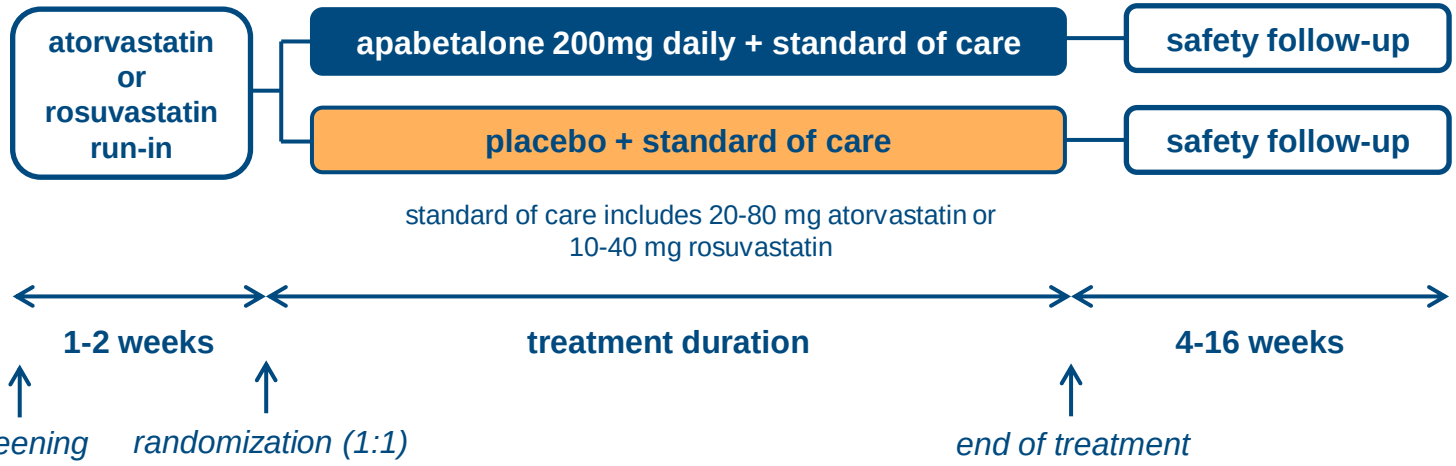
Decrease in MACE was most profound in patients who had a higher level of inflammation such as patients with diabetes

BETonMACE CV Outcomes Study Design

BETonMACE
A CARDIOVASCULAR STUDY FOR PEOPLE WITH TYPE 2 DIABETES

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

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 <40 mg/dL for males and <45 mg/dL for females

Primary Endpoint (CVD)

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 (RENAL)

- 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

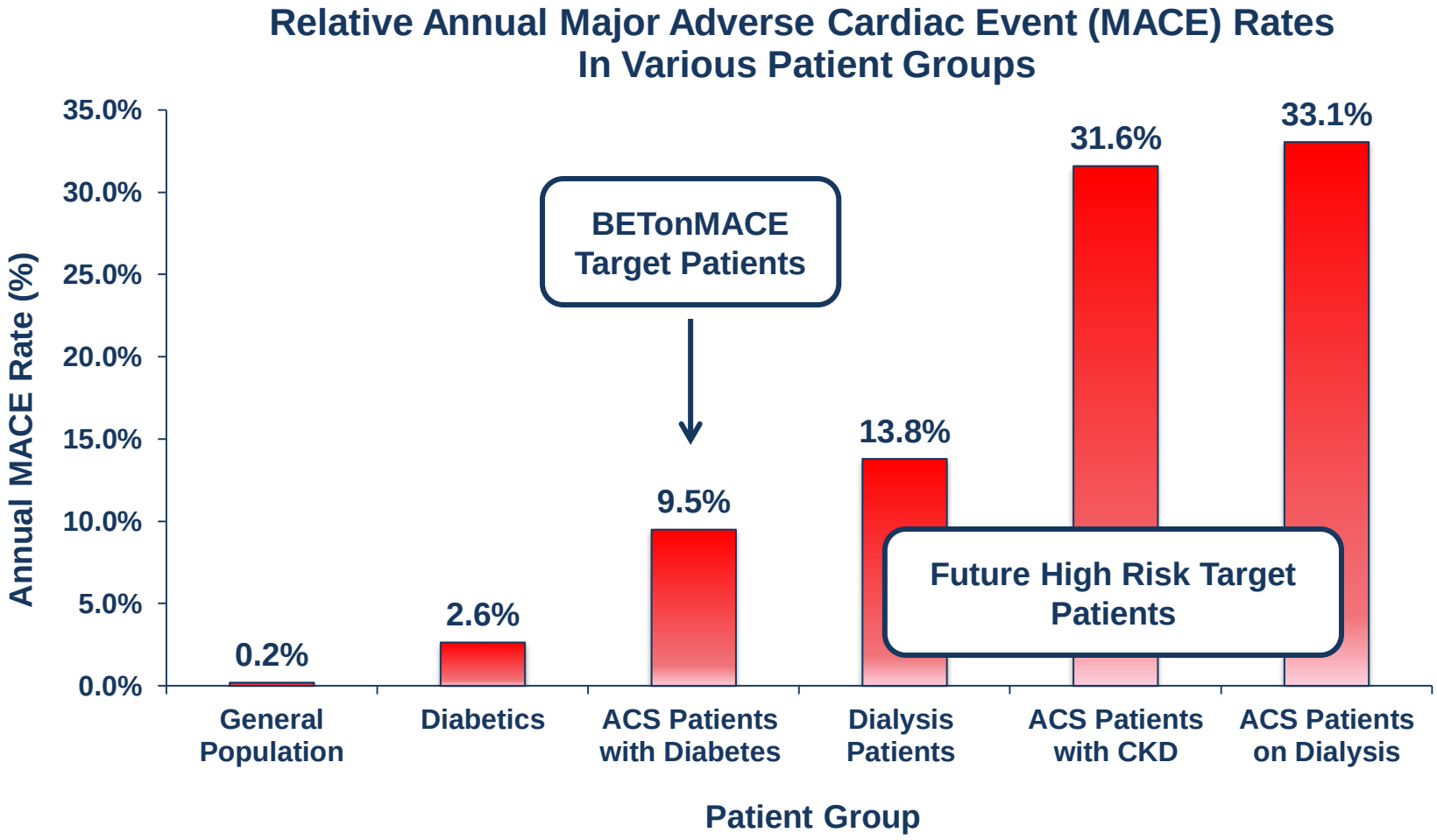
Exploratory Endpoint (NEURO)

- MoCA test on all patients 70 and over
- All patients and those with <26

BETonMACE Current Highlights

- ~ 98% 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 ≤ 25) approx. 275 patients
- Projected primary MACE rate still 8.0 per 100 patient years on top of aggressive standard of care (low LDL) = strong unmet need
- Even with aggressive statin therapy very high events illustrates CVD risk is more than just LDL

Patient Enrichment Strategy



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

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**

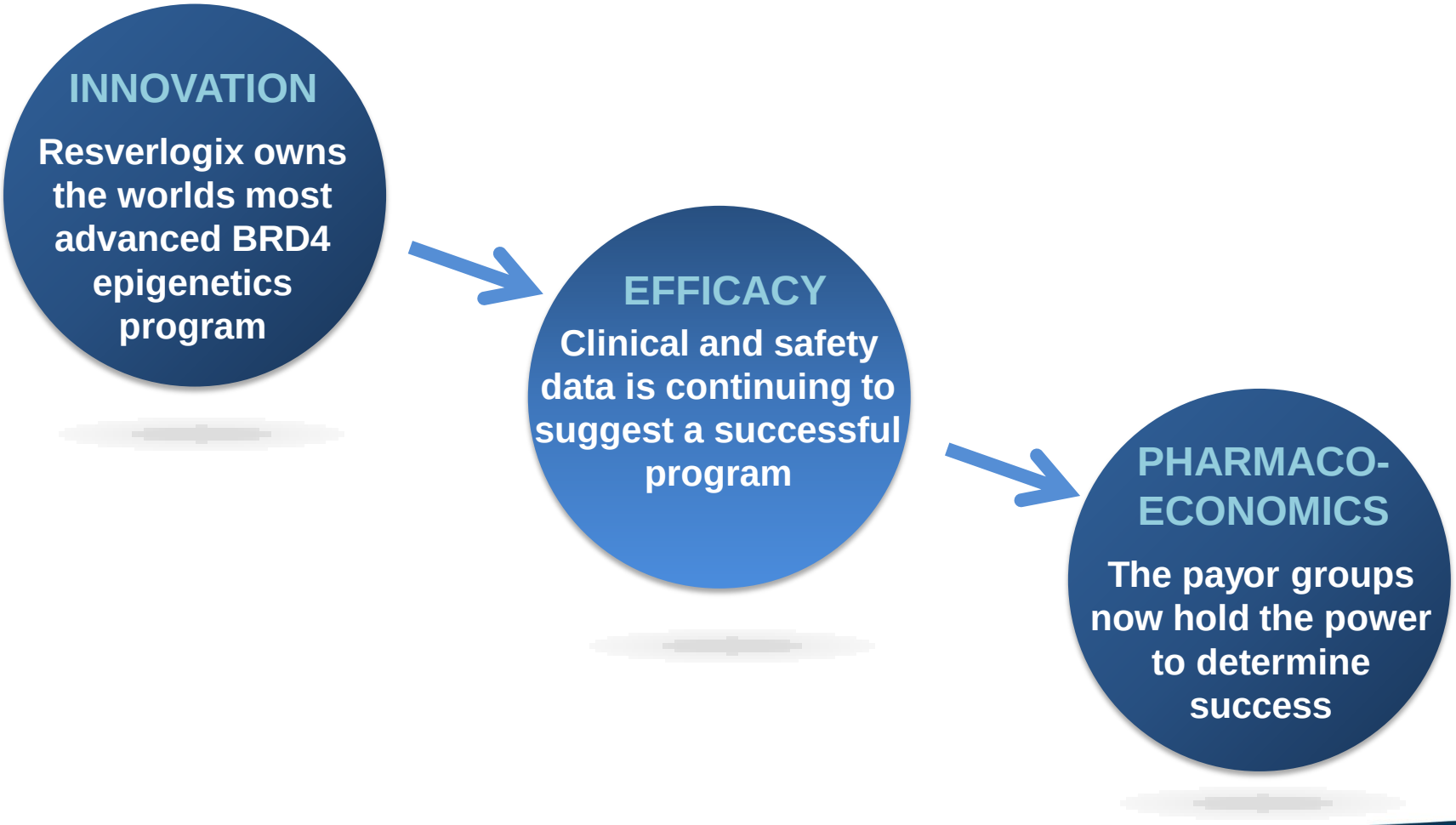
Expanded Programs

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

Improving Global Vascular Risk

Balanced for Success!

THREE KEY DEVELOPMENT TARGETS ARE IN PLACE



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 annual US price of **$5,000 - $8,000** based on new enriched high risk patients

Apabetalone Opportunity

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