

# Resverlogix Corp. Corporate Breakthroughs

December 22, 2020 – AGM Presentation



# Forward Looking Statement

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 BETonMACE2 clinical trial, COVID-19 planned trial, vascular cognitive dementia, chronic kidney disease, fabry disease and pulmonary arterial hypertension clinical trials, and the potential role of apabetalone in the treatment of high-risk cardiovascular disease, diabetes mellitus, 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.

## Contact

Donald McCaffrey

Email: [don@resverlogix.com](mailto:don@resverlogix.com)

Phone: 587-390-8887

Website: [www.resverlogix.com](http://www.resverlogix.com)

# Resverlogix at a Glance

- Resverlogix Corp. is a Canadian public company developing an advanced cardiovascular drug called apabetalone. We are pioneering a technology that has the ability to turn multiple disease-causing genes on or off. No actual change to the human DNA occurs. Our exciting breakthrough technology places Resverlogix as a world leader in utilizing “**epigenetics**” to regulate disease-causing genes.
- Apabetalone, was awarded **FDA Breakthrough Therapy Designation (BTD) in Feb. 2020**. This is the highest designation that a drug can receive from the FDA. BTD has only been awarded to 130 drugs previously and apabetalone is the first drug ever for mainstream cardiovascular development.
- Apabetalone’s unique approach has been tested in over **4,200 man years of treatment** and has demonstrated its positive biological effects on patients with diseases such as;
  - Cardiovascular disease (CVD),
  - Diabetes mellitus (DM)
  - Chronic kidney disease (CKD).
  - Non-Alcoholic Fatty Liver disease (NAFLD)
  - Vascular Dementia
  - Pulmonary Arterial Hypertension
  - COVID-19

Stock Symbol	TSX: RVX
Market Cap	~\$240MM <sup>1</sup>
Shares Outstanding	234MM <sup>1</sup>

1. As at December, 2020



## **Resverlogix Announces Apabetalone Treatment Prior to SARS-CoV-2 (COVID-19) Exposure Significantly Reduces Viral Infection – Confirms Plans for COVID-19 Clinical Trial**

*Latest publication confirms BET inhibitors reduce the levels of critical receptors used by SARS-CoV-2 (COVID-19) to gain entry into cells, thereby reducing viral infection*

CALGARY, December 22, 2020 - Resverlogix Corp. ("Resverlogix" or the "Company") (TSX:RVX) is pleased to announce recent published findings in the high-impact journal, Proceedings of the National Academy of Sciences (PNAS), that further supports other 2020 publications and provides new evidence for the therapeutic potential of BET inhibitors in the treatment of COVID-19. A publication titled: "*Targeting transcriptional regulation of SARS-CoV-2 entry factors ACE2 and TMPRSS2*", highlights the important role that host cell receptors play in enabling viral entry into cells, and presents direct evidence that BET inhibitors reduce SARS-CoV-2 (the scientific name for the virus responsible for COVID-19) infection by inhibiting the expression of these receptors. The publication also acknowledges Resverlogix and the Company's plans to confirm the hypothesis with a clinical trial utilizing its advanced BET inhibition technology.

The publication can be viewed using the following [LINK](#).

The findings are consistent with recent in-house studies performed by Resverlogix which demonstrated that [apabetalone](#) inhibits the expression of angiotensin-converting enzyme 2 (ACE2), the receptor utilized by the novel coronavirus to enter human cells. Further, preliminary data from collaborators – working with live coronavirus in multiple cell models – suggest apabetalone treatment prior to SARS-CoV-2 (COVID-19) exposure significantly reduces viral infection.



### RESEARCH ARTICLE



## **Targeting transcriptional regulation of SARS-CoV-2 entry factors ACE2 and TMPRSS2**

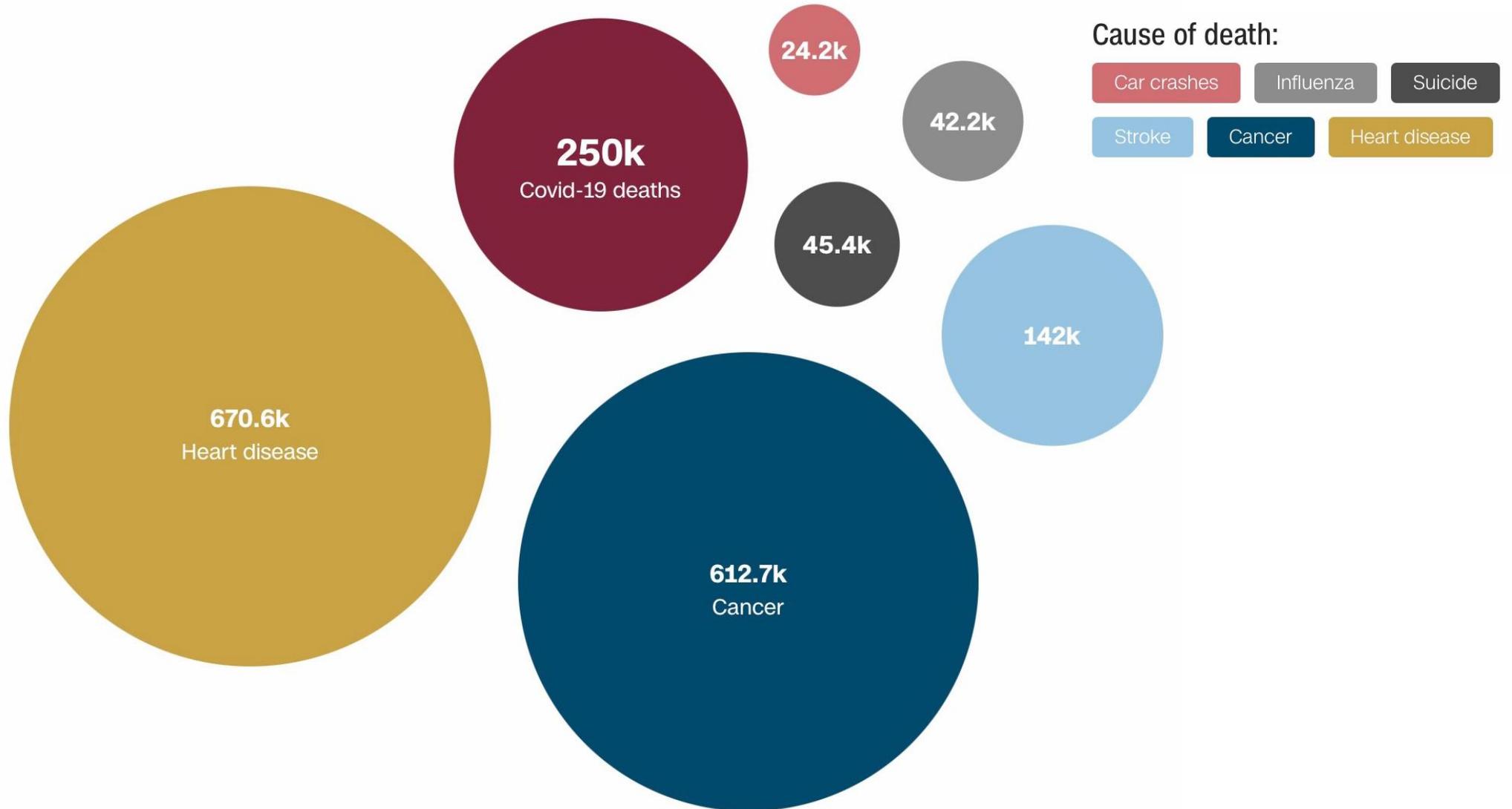
 Yuanyuan Qiao,  Xiao-Ming Wang, Rahul Mannan,  Sethuramasundaram Pitchiaya, Yuping Zhang,  Jesse W. Wotring, Lanbo Xiao, Dan R. Robinson,  Yi-Mi Wu, Jean Ching-Yi Tien, Xuhong Cao, Stephanie A. Simko, Ingrid J. Apel, Pushpinder Bawa, Steven Kregel, Sathiya P. Narayanan,  Gregory Raskind, Stephanie J. Ellison, Abhijit Parolia, Sylvia Zelenka-Wang, Lisa McMurry, Fengyun Su,  Rui Wang, Yunhui Cheng, Andrew D. Delekta,  Zejie Mei, Carla D. Pretto, Shaomeng Wang,  Rohit Mehra, Jonathan Z. Sexton, and Arul M. Chinnaiyan

PNAS January 5, 2021 118 (1) e2021450118; first published December 11, 2020;  
<https://doi.org/10.1073/pnas.2021450118>

Contributed by Arul M. Chinnaiyan, November 18, 2020 (sent for review October 16, 2020; reviewed by William L. Dahut and Nicholas Nickols)

# Number of US Deaths Due to Current Diseases in 2020

Posted on CNN - Nov. 2020



Source: US Centers for Disease Control, National Highway Traffic Safety Administration

Graphic: Daniel Wolfe, CNN

# Near Term Events & Planning



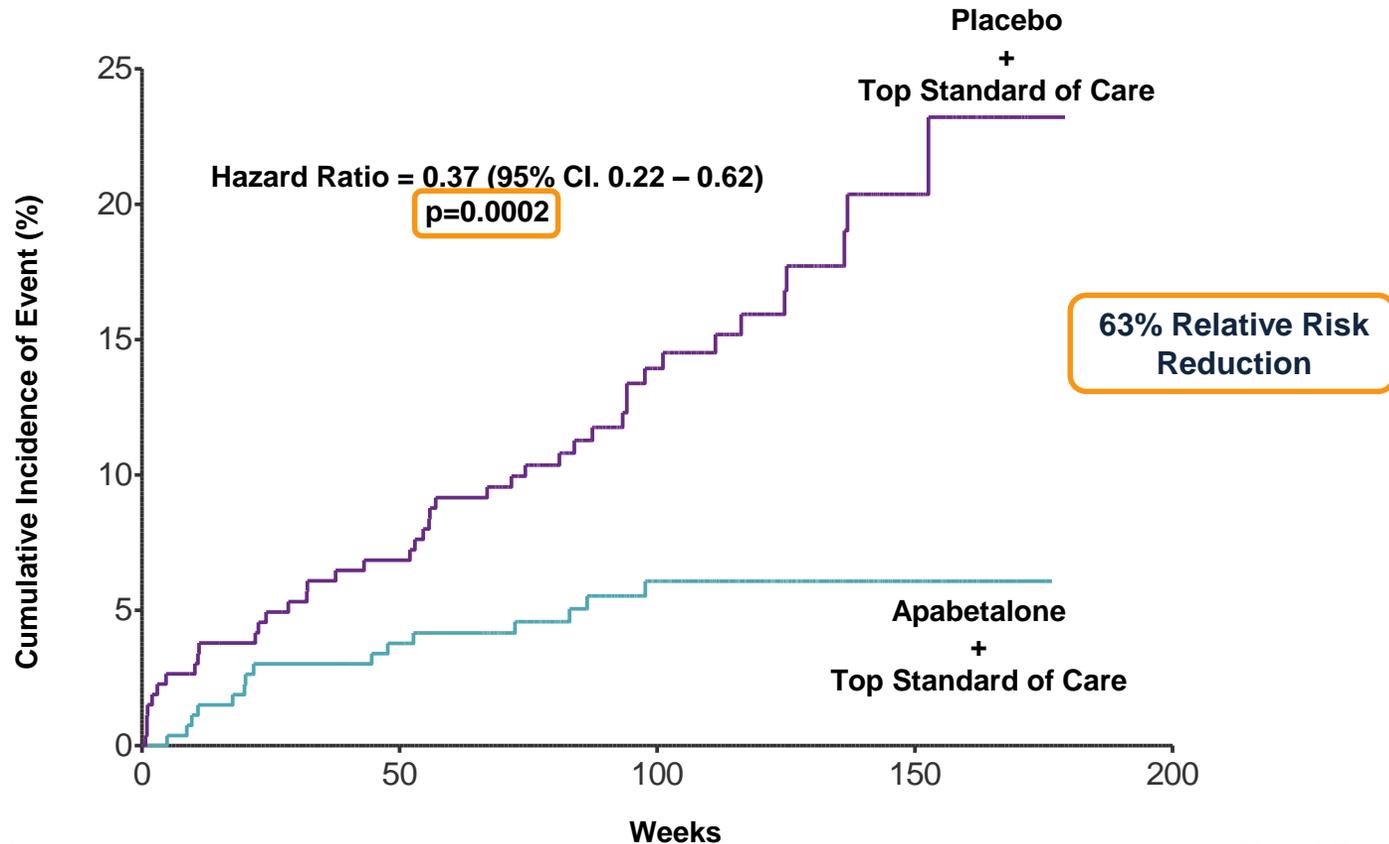
- The US **FDA and Resverlogix** have now confirmed the final BETonMACE2 clinical plans.
  - Filing of a New Drug Application (NDA) with the FDA is possible following unequivocal efficacy at **an interim analysis** of BETonMACE2 – potentially 2022
  - All or most BETonMACE2 patients to receive top standard of care, including **SGLT2 inhibitors**
  - BETonMACE2 to significantly increase enrichment of chronic kidney disease (**CKD**) patients
- **Partnering Option** - Resverlogix is advancing its ongoing negotiations with Major Pharmaceutical companies to determine a suitable partner, structure and trial design for co-developing apabetalone. Timing of completion is somewhat dependent on COVID-19, causing delays of large clinical trials globally. Co-development discussions with numerous pharma's include the following:
  - Resverlogix expects to receive a **significant** upfront payment upon completion
  - The Phase 3b clinical trial will be funded by a partnering company – Trial designs in discussion range in cost from **\$60MM to \$150MM US dependent on the trial size, length and overall design**. Backup options for funding include the sale of royalties or internal financing from current investors
- **COVID-19** early clinical trial results could be available as early as Q1, 2021. The trial is being designed as a small fast program designed to confirm the recent scientific data regarding BETi and COVID-19
- **Pulmonary Arterial Hypertension (PAH)** clinical trial data should be available in the first half of 2021. This trial has been on and off again due to the strain of COVID 19 on pulmonary units. Data is still compiling and will continue to do so until the trial can be deemed completed

# Required Drug Qualities for Successful Commercialization

- **Efficacy**, does the drug work? ✓
- **Safety**, is the drug safe in general populations? ✓
- **Regulatory Approvability**, will the FDA or EMA approve the drug based on safety and efficacy? ✓
- **Mechanism of Action (MOA)**, a deep understanding of how the drug works must be demonstrable. ✓
- **Publications**, a wide body of third party reviewed peer publications must be readily available. ✓
- **Strategic Commercial Pathway**, a clear commercial pathway with payer group support must be present. ✓

*We have mountains of proof for all of the above, please see some examples in the following slides.*

# Efficacy - The Drug Works! Trials Confirmed a Highly Significant Reduction in Death, Heart Attacks and CHF



No. at Risk	Weeks				No. of Events
	0	50	100	150	
Placebo	264	244	151	36	42
Apabetalone	265	253	169	41	15

- The effect of the co-administration of apabetalone and SGLT2 or DPP4 inhibitors – quantified by CV death, non-fatal MI, stroke and hospitalization for congestive heart failure (CHF) – illustrated a significant reduction of events compared to placebo and SGLT2 or DPP4 inhibitors
  - HR = 0.37 (95% CI, 0.22–0.62; p=0.0002)
- Apabetalone was well tolerated with similar rates of adverse events compared to placebo

*Top standard of care includes: high intensity statins, ACE inhibitors/angiotensin II blockers, beta blockers, antiplatelet agents*

*RVX Internal Analysis January 2020*

**Apabetalone treatment led to a significant 63% RRR of MACE and hospitalization for Congestive Heart Failure (CHF) compared to placebo in patients receiving SGLT2 or DPP4 Inhibitors**

# FDA Approves Breakthrough Therapy Designation



“A breakthrough therapy designation is for a drug that treats a serious or life-threatening condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies.”

**FDA Website**



IND 76487

**GRANT –  
BREAKTHROUGH THERAPY DESIGNATION**

Resverlogix Corp.  
Attention: Barry Calvarese  
Consultant, Regulatory Affairs  
44 Montgomery Street, Suite 4010  
San Francisco, CA 94104

Dear Mr. Calvarese:

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for apabetalone (RVX000222).

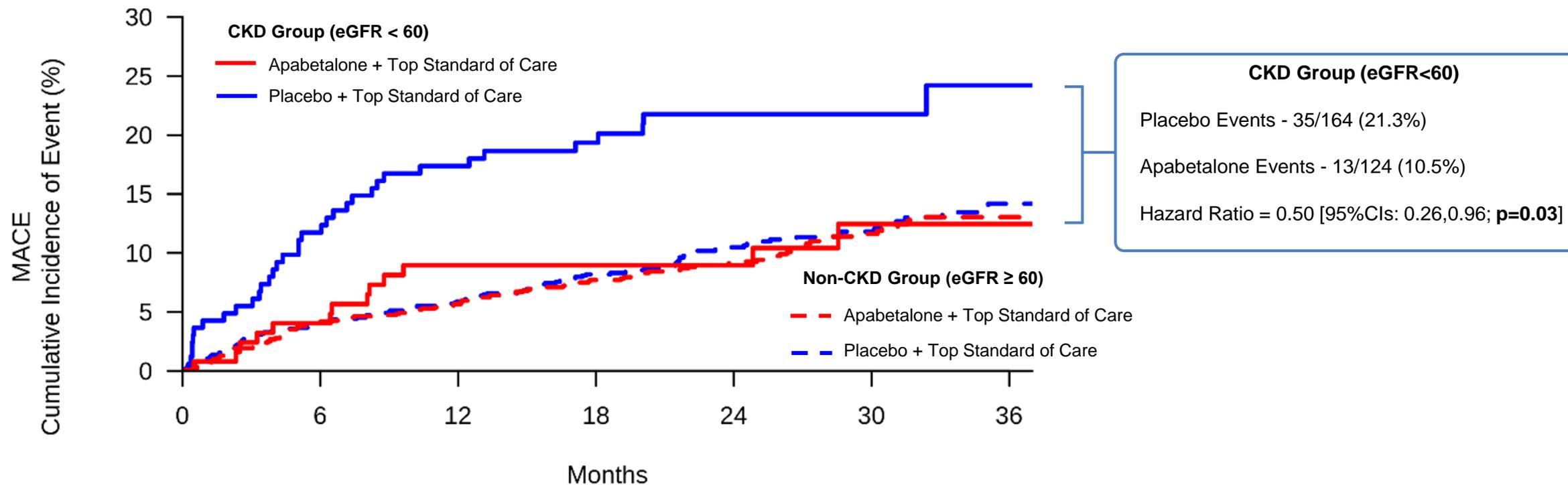
We also refer to your December 4, 2019, request for Breakthrough Therapy designation. We have reviewed your request and have determined that apabetalone, in

As the result of very safe and promising data the FDA granted Resverlogix the coveted **Breakthrough Therapy Designation**

# Kaplan-Meier Estimates by CKD/Non-CKD for MACE

## Apabetalone Compared to Placebo

A



**No. at Risk**

eGFR < 60	288	259	240	207	146	85	20
eGFR ≥ 60	2125	2022	1971	1675	1163	691	192

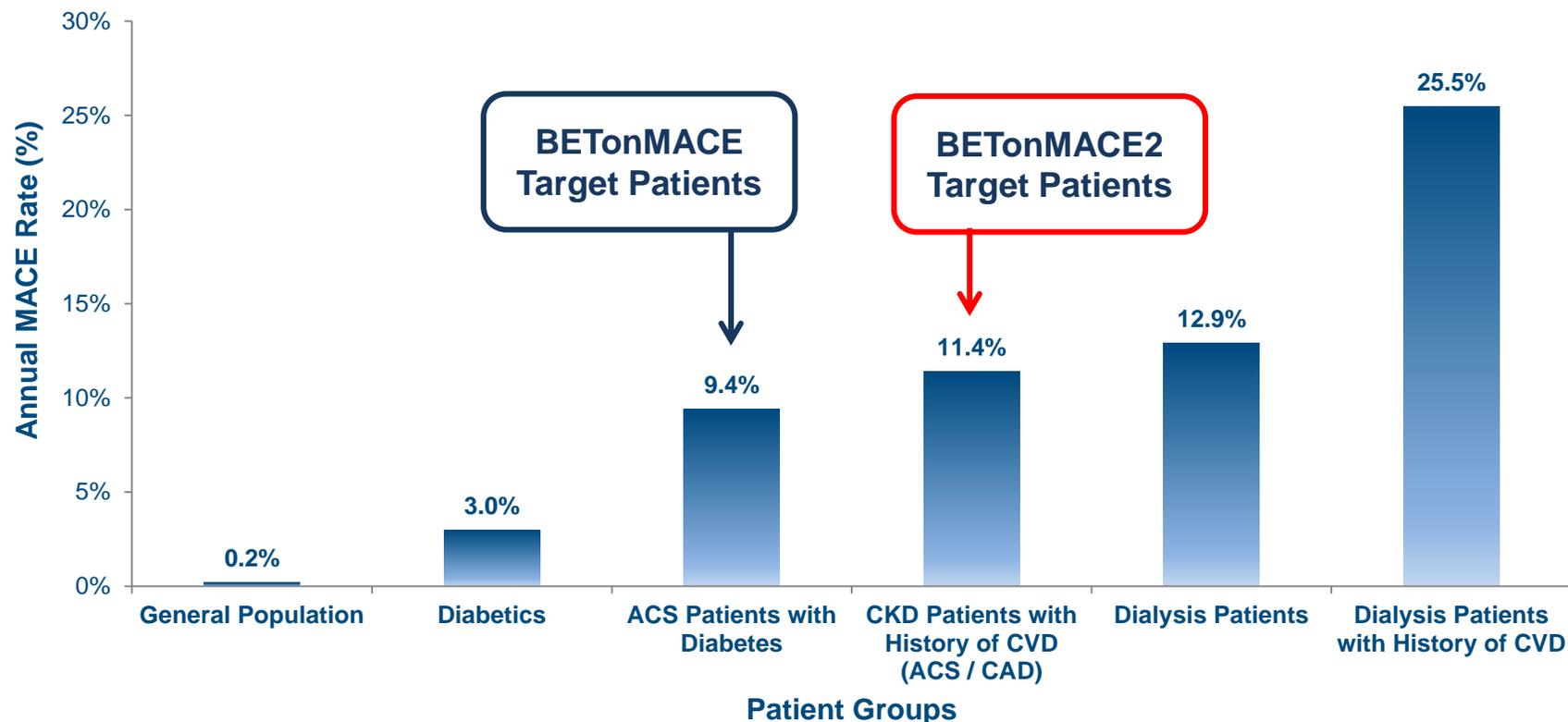
Source: Kalantar-Zadeh et al 2020; Apabetalone in CKD and MACE; publication pending

**Apabetalone treatment led to a significant 50% relative risk reduction of MACE compared to placebo in patients with CKD**

# Patient Enrichment Strategy: Target High Residual Risk



Relative Annual of Major Adverse Cardiac Events (MACE) in Target Patient Groups



Calculated from:

General Population: CDC Heart Disease Facts;

Diabetics: ACCORD (2008); ADVANCE (2010); SAVOR-TIMI (2013); EXAMINE (2013); EMPA-REG (2015); LEADER (2016); SUSTAIN-6 (2016); CANVAS (2016); EXSCEL (2017);

ACS – Diabetes: TRITON-TIMI 28 (2008); PLATO (2010); PROSPECT (2012); EXAMINE (2013); PEGASUS-TIMI 54 (2016); Taiwan ACS Registry(2017);

CKD – ACS / CVD: PPP (2004); VA-HIT (2004); CREDO (2008); Kang, YU. (2009); PLATO (2010); Liu, Y. (2014); Miller-Hodges, E. (2018);

Dialysis: 4D (2005); FOSIDIAL (2006); AURORA (2009); Eckardt, KU. (2015);

Dialysis – ACS: Liu, Y. (2014); Alushi, B. (2017)

# Mechanism of Action - Unique, Effective, Highly Advanced!

## How Does Drug Development Work?

### Epigenetic Regulation - New

Due to disease, environment or diet a patients original DNA messages can be corrupted before it is replicated into mRNA. Our epigenetic approach has demonstrated the ability to impact hundreds of compromised proteins in a safe manor. **No competitors.**

**Apabetalone** – basically resets the original DNA message and reduces numerous metabolic disease mediators, potentially including Covid-19 factors.

### Protein Targeting – Standard Drug Approach

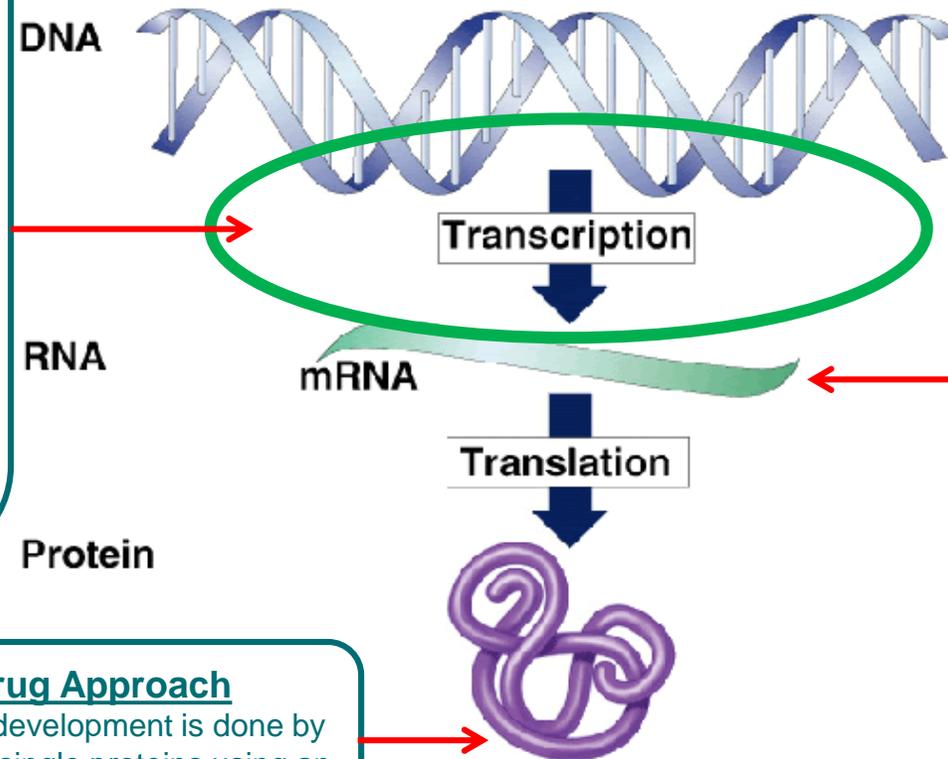
Approximately 95% of standard drug development is done by either down regulating or up regulating single proteins using an inhibitor or antibody. **Tens of thousands of competitors.**

### 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. **Dozens of competitors.**

### Messenger RNA

This new approach of altering mRNA has recently made some advances as significant improvements in oligonucleotide delivery have been realized. A promising approach in vaccinations but still only deals with one protein issue at a time. **Dozens of competitors.**

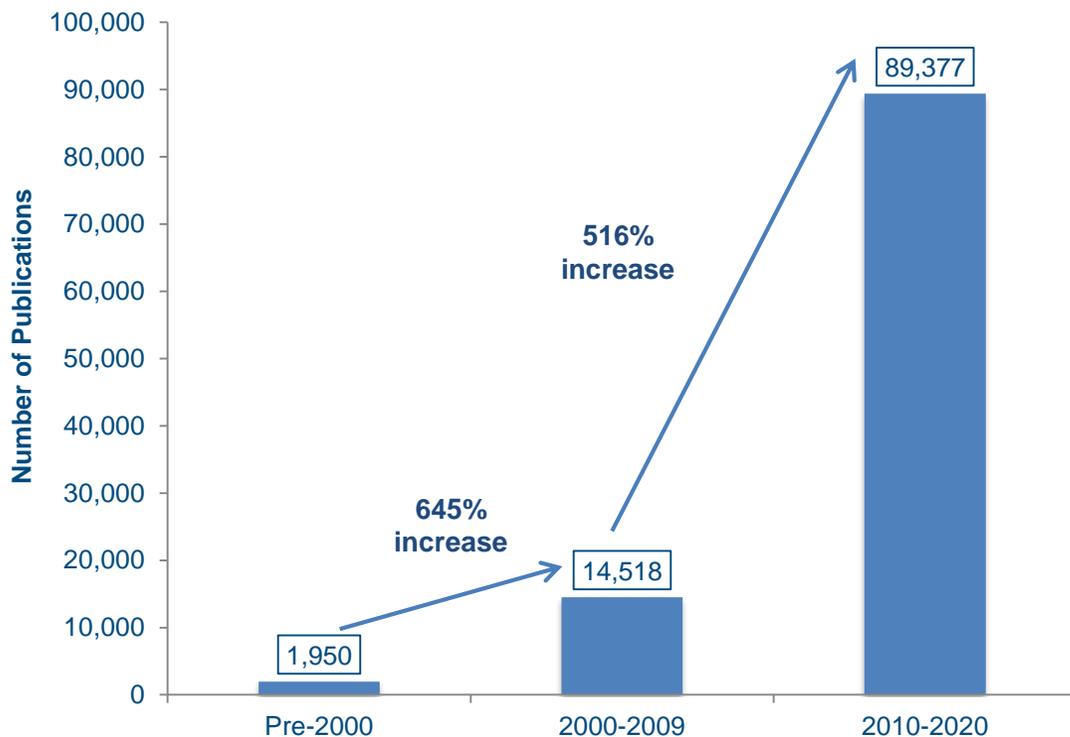


# Publications on Epigenetics and RVX

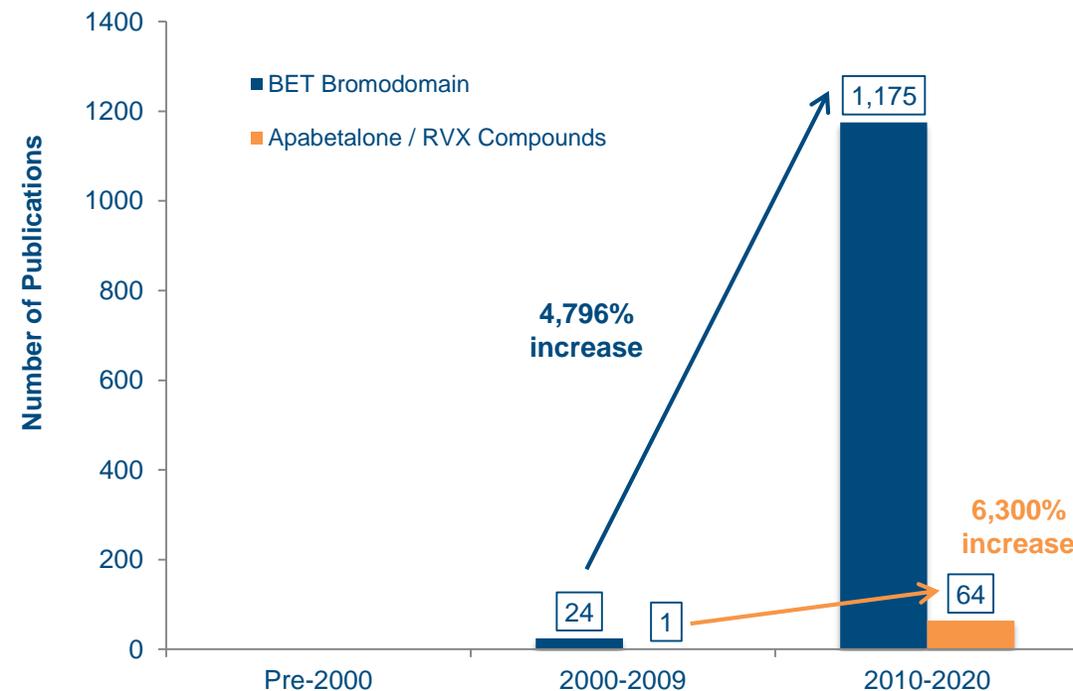


## Dramatic growth of publications over the past decade in Epigenetics and BET Inhibition

### Publications on Epigenetics



### Publications on BET Bromodomain and Resverlogix Compounds



Source: PubMed Database: Historical Review Q1 2020

As of May 25<sup>th</sup>, 2020

# Safety- BETonMACE Nov. 2015 to Sept. 2019



IND 76487

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As the result of very safe and promising data the FDA granted Resverlogix the coveted **Breakthrough Therapy Designation**. Apabetalone has already been tested in over 1,900 patients in 18 countries around the world, 14 countries have approved Phase 3 usage

# Strategic Commercial Pathway - Global Vascular Opportunity



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:

- |          |  |   |                                |
|----------|--|---|--------------------------------|
| <b>1</b> | <b>High Risk Acute Coronary Syndrome (ACS) Patients with a Type II Diabetes Mellitus (DM) Comorbidity and Low High-Density Lipoprotein Cholesterol (HDL-C)</b>       |    | <b>1.5 M+ Patients by 2032</b> |
| <b>2</b> | <b>High Risk Chronic Kidney Disease (CKD) Patients (Stages 3-5, Pre-Dialysis) with a Diabetes Mellitus Comorbidity and a History of Cardiovascular Disease (CVD)</b> |    | <b>4.0 M+ Patients by 2032</b> |
| <b>3</b> | <b>High Risk End Stage Renal Disease (ESRD) Patients with Elevated Alkaline Phosphatase (ALP) (&gt;80 U/L)</b>   |    | <b>1.0 M+ Patients by 2032</b> |
| <b>3</b> | <b>Vascular Cognitive Dementia (MoCA score &lt; 26) in Elderly (&gt;65 years) Patients with Diabetes Mellitus Comorbidity and a History of CVD</b>                   |  | <b>1.5 M+ Patients by 2032</b> |

# Additional Indication Targets

- Complement Mediated Disease: orphan indication
- Neurofibromatosis – Malignant Peripheral Nerve Sheath Tumors (MPNST): orphan indication
- Pulmonary Arterial Hypertension (PAH): orphan indication – **In progress now**
- Muscular Dystrophy/Facio Scapulo Humeral Dystrophy: orphan indication
- Fabry Disease: orphan indication
- Vascular Cognitive Dementia
- HIV eradication
- Covid -19, interruption of replicating mechanisms such as BRD4 and ACE2 - **In progress now**

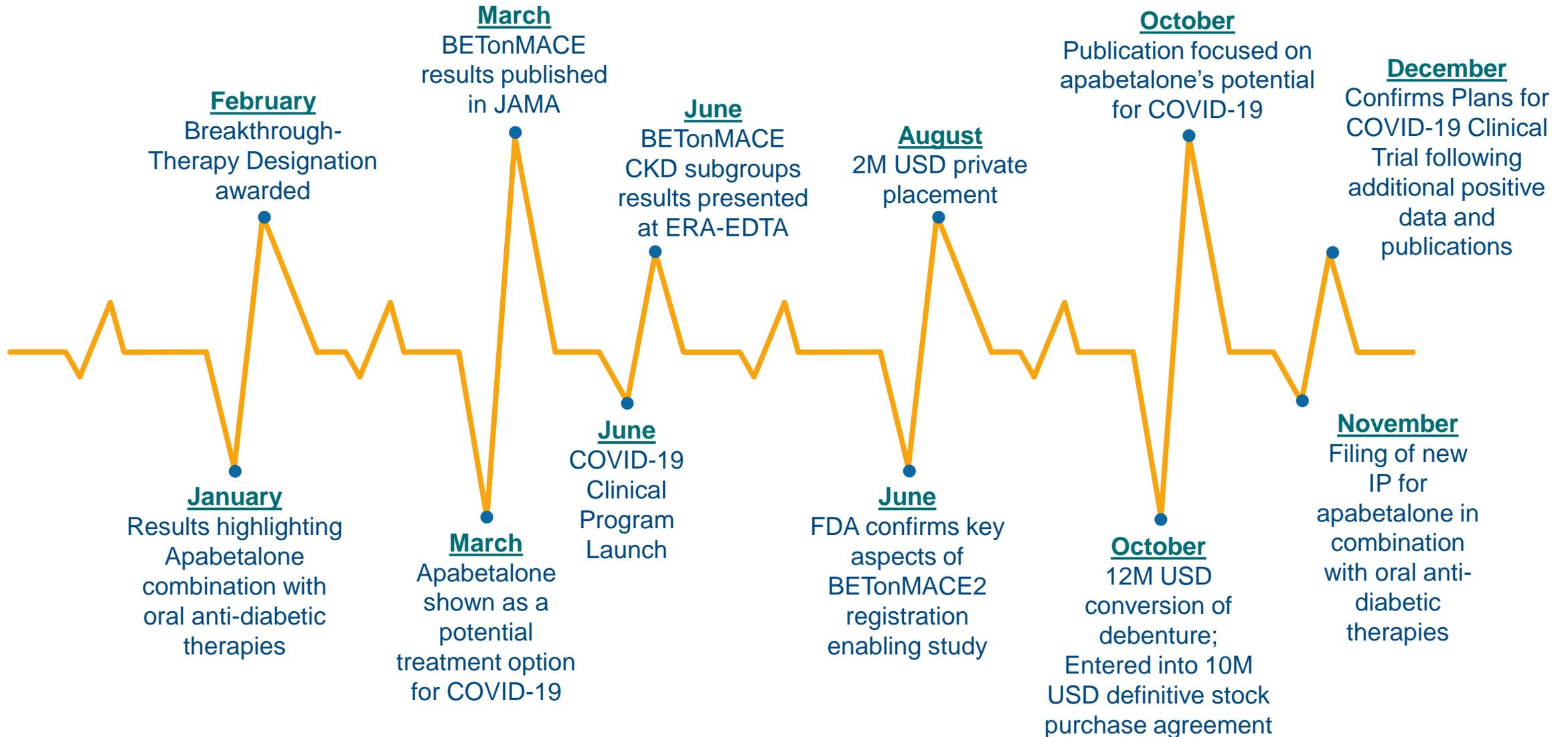


# Intellectual Property Update & 2020 Key Corporate Milestones



- **Resverlogix has filed three patent applications for the observed effects in BETonMACE of apabetalone in combination with the leading anti-diabetes treatments, sodium-glucose co-transporter-2 (SGLT2) inhibitors**
- **SGLT2 inhibitor combination provisional patent application filed 5 November 2019; converted to PCT application Nov. 4, 2020**
  - Title: Prevention of Major Adverse Cardiac Events In Diabetes Patients With Low HDL Through Combination Therapy With Sodium-Glucose Co-Transporter-2 Inhibitors And RVX-208
- **DPP4 combination provisional patent application filed 1 January 2020**
  - Title: Prevention of Major Adverse Cardiac Events In Diabetes Patients With Low HDL Through Combination Therapy With Dipeptidyl Peptidase 4 Inhibitors And RVX-208
- **SGLT2 inhibitor combination provisional patent application filed 30 October 2020**
  - Title: Methods For Improving Renal Function With a Combination of a BET Bromodomain Inhibitor And a Sodium Dependent Glucose Transport 2 Inhibitor
- **SGLT2 inhibitor combination provisional patent application filed 30 October 2020**
  - Title: Methods For Lowering HbA1c Level With a Combination of a BET Bromodomain Inhibitor And a Sodium Dependent Glucose Transport 2 Inhibitor
- **These patents may provide apabetalone with exclusivity through 2039/2040 when given in combination with the SGLT2 inhibitor anti-diabetes treatments which are emerging as the standard of care in high-risk diabetes patients**

# Resverlogix 2020 Key Milestones



# 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 20 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 20 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**  
**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

# Questions & Answers

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