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TSX: RVX

Detailed Preliminary Results of BETonMACE

Strengthening Opportunities Through Positive Findings & Synergy

July, 2020

Forward Looking Statement

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Contact:

Donald McCaffrey
Email: don@resverlogix.com
Phone: 403-254-9252
Website: www.resverlogix.com

Executive Summary (1)

- **Very Encouraging Cardiovascular Disease Efficacy Results**
  - Narrow Miss on Primary Endpoint (CV Death, Non-fatal MI, and Stroke): 18% Hazard Reduction (HR: 0.82; 95% CI; 0.65-1.04) p=0.11
  - Trending MACE Improvements on Multiple Endpoints with Survival Curves Consistently Separating Early
  - Hit on Hospitalization for Congestive Heart Failure (CHF): 41% Hazard Reduction (HR: 0.59; 95% CI; 0.38-0.94) p=0.03

- **Primary Endpoint Hits in Prespecified Subgroups vs Top Standard of Care**
  - Impaired Renal Function: 50% Hazard Reduction (HR: 0.50; 95% CI; 0.26-0.96) p=0.03

- **Critically Important Finding, Patents Filed – Potential Synergy with New Generation of Diabetes Drugs**
  - Primary Endpoint in Patients Receiving SGLT2i
    - All SGLT2i's: 60% Hazard Reduction (HR: 0.40; 95% CI; 0.16-1.00) p=0.05 (non-QC'd)
    - Empagliflozin: 66% Hazard Reduction (HR: 0.34; 95% CI; 0.12-1.01) p=0.05 (non-QC'd)

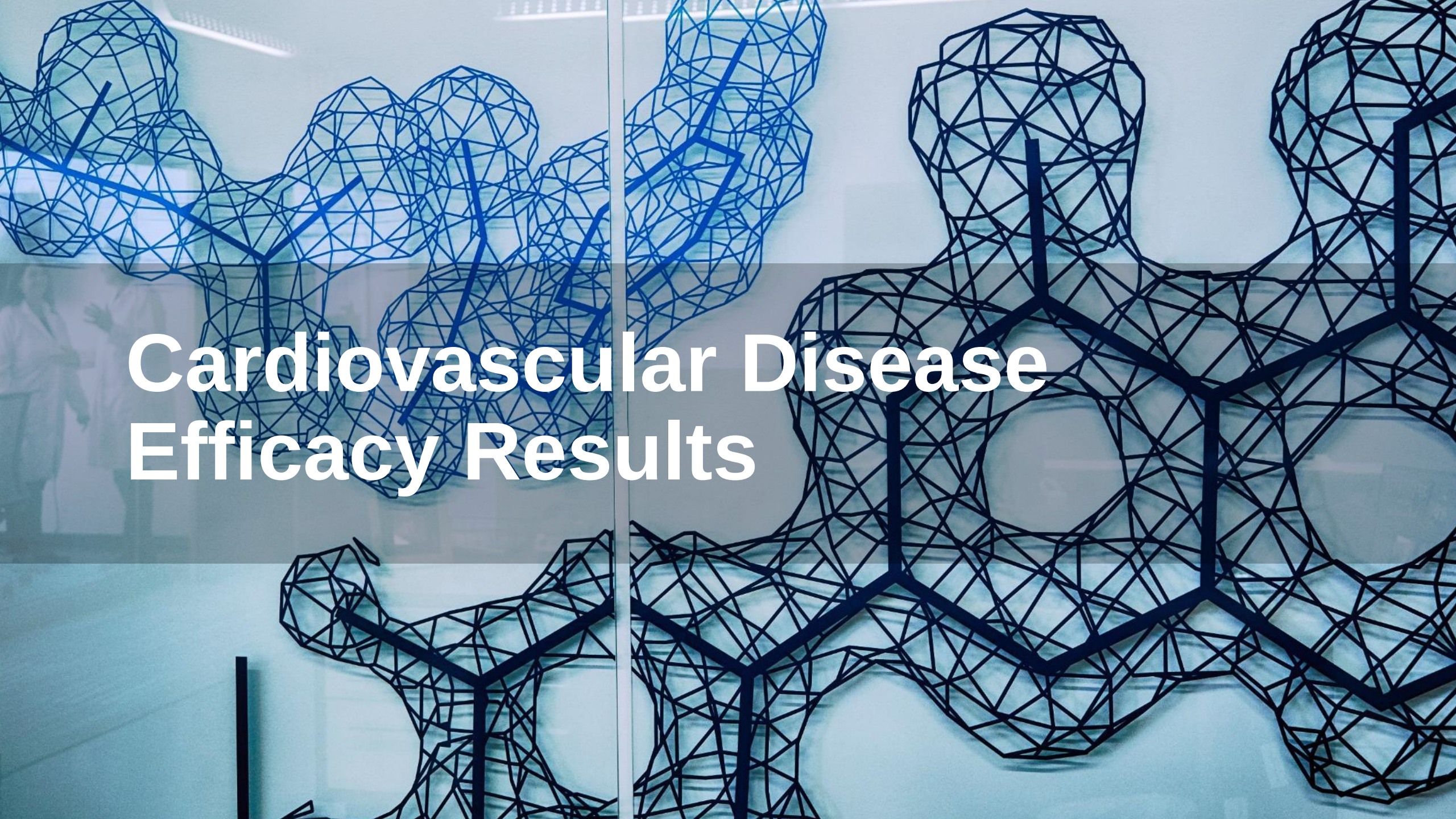
Executive Summary (2)

- **Apabetalone treatment illustrated statistically significant improvements versus placebo (+ top standard of care) in patients with a baseline MoCA <22 :**
  - 158% relative improvement in cognitive function in treated group compared to top standard of care placebo (comparing the mean change from baseline of the treated vs. untreated groups)
  - Significant and trending changes across treatment duration in ALP and HDL (biomarkers associated with cognitive risk) were observed in patients with a baseline MoCA<22

- **Significantly Enhanced Intellectual Property Position from Additional and Future Patent Filings**
  - Composition, use, and manufacturing, with long patent life for Apabetalone
  - Additional, important patent filings to come

- **Breakthrough Therapy Status Granted from FDA – February 2020**
  - Agreement reached with FDA for key aspects of apabetalone registration enabling study at June 2020 Meeting

- **Further Development of Apabetalone Well Underway Based on Key BETonMACE Findings**
  - Consider multiple paths forward (partnering for multiple indications and synergistic combination trials)



Cardiovascular Disease Efficacy Results

Primary Endpoint

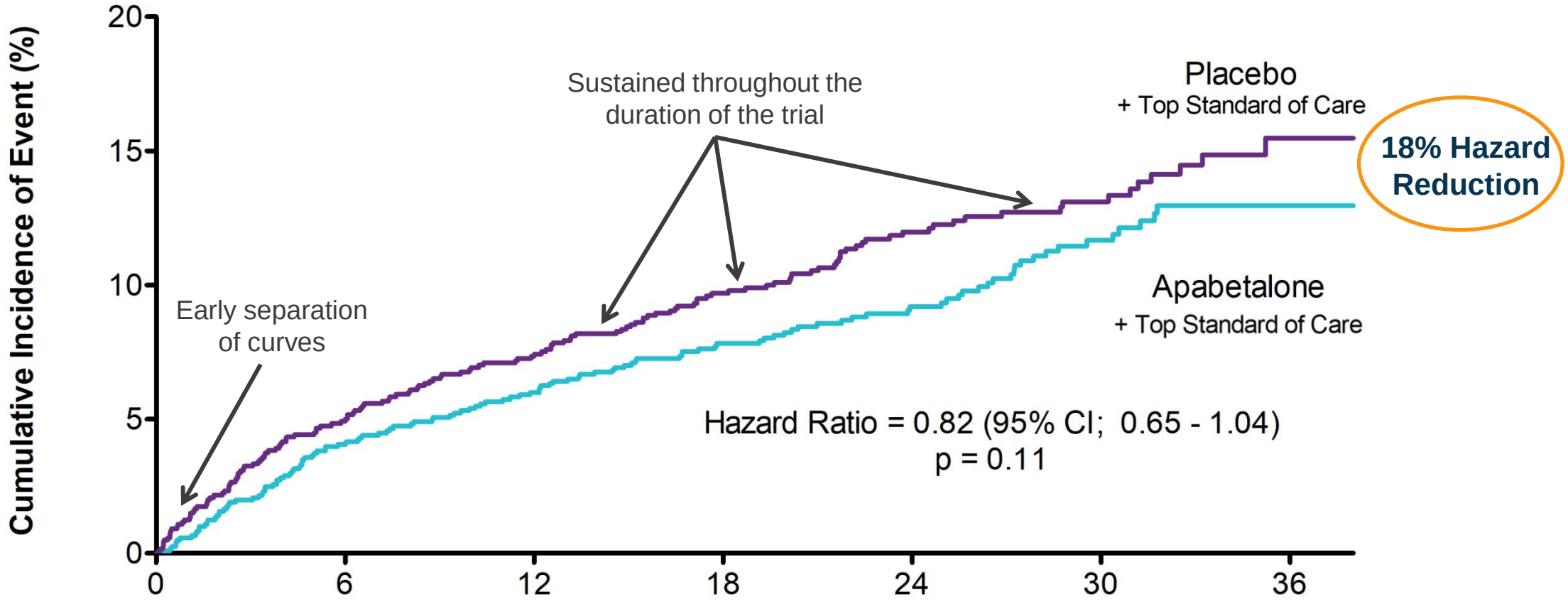
Primary Outcome Measure and Components

Major Adverse Cardiac Events

Endpoint, n(%)	Apabetalone (N=1212)	Placebo (N=1206)	HR (95% CI)	Log-rank p-value
MACE	**125**	**149**	**0.82 (0.65-1.04)**	**0.11**
Non-fatal MI	77	94	0.80 (0.59,1.08)	0.15*
Stroke	17	17	1.01 (0.52, 1.98)	0.99*
CV Death	45	55	0.81 (0.54, 1.19)	0.29*

***Nominal p value**

Primary Endpoint: CV Death, Non-fatal MI, and Stroke

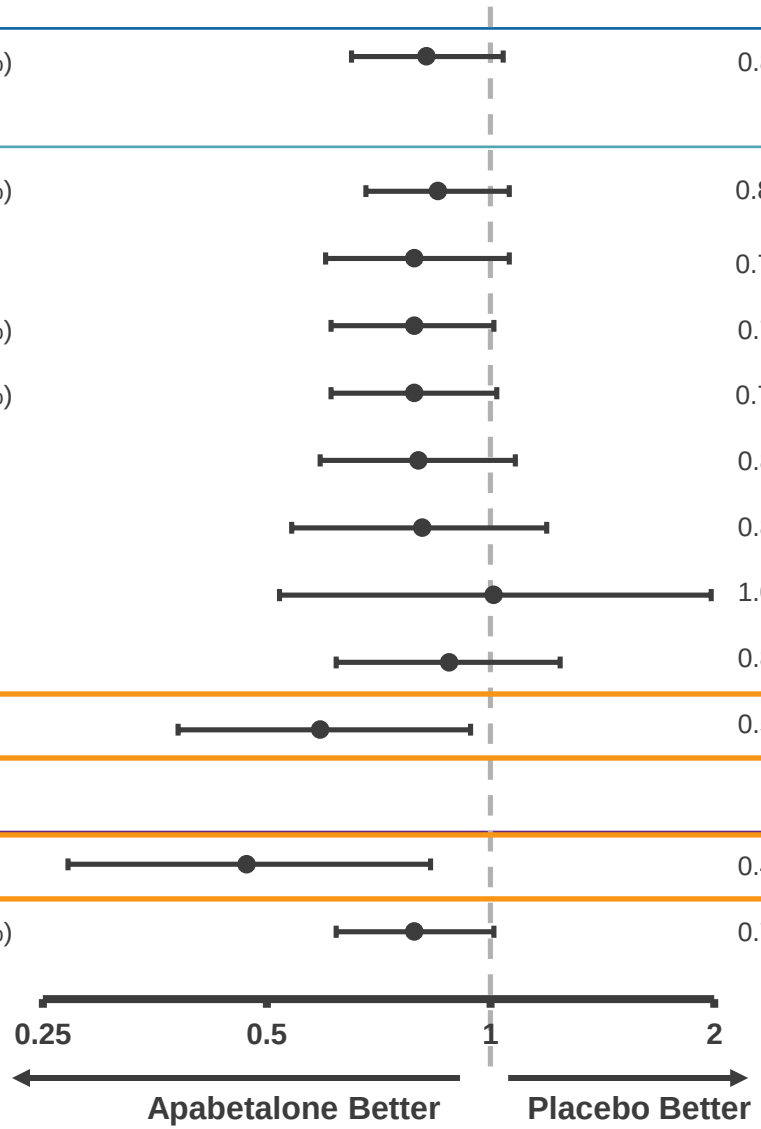


No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Secondary and Other Prespecified Endpoints

Cardiovascular Endpoints

Primary Endpoint	Apabetalone	Placebo	Hazard Ratio (95% CI)	P Value
	no. of events (%)			
First occurrence of primary endpoint: CV death, non-fatal MI and stroke	125 (10.3%)	149 (12.4%)	0.82 [0.65, 1.04]	0.11
Key Secondary Endpoints				
First occurrence of primary endpoint or hospitalization for unstable angina or urgent or emergency revascularization procedure	144 (11.9%)	166 (13.8%)	0.85 [0.68, 1.06]	
First and recurrent primary endpoint events	171	203	0.79 [0.60, 1.06]	
Cardiovascular death or non-fatal myocardial infarction	112 (9.2%)	139 (11.5%)	0.79 [0.61, 1.01]	
Coronary heart disease death or non-fatal myocardial infarction	110 (9.1%)	136 (11.3%)	0.79 [0.61, 1.02]	
Non-fatal myocardial infarction	77 (6.4%)	94 (7.8%)	0.80 [0.59, 1.08]	
Cardiovascular death	45 (3.7%)	55 (4.6%)	0.81 [0.54, 1.19]	
Stroke	17 (1.4%)	17 (1.4%)	1.01 [0.52, 1.98]	
All cause mortality	61 (5.0%)	69 (5.7%)	0.88 [0.62, 1.24]	
First hospitalization for congestive heart failure	29 (2.4%)	48 (4.0%)	0.59 [0.38, 0.94]	
Other Pre-specified Endpoints				
First and recurrent hospitalization for congestive heart failure	35	70	0.47 [0.27, 0.83]	
First occurrence of primary end point, excluding undetermined death	113 (9.3%)	140 (11.6%)	0.79 [0.62, 1.01]	



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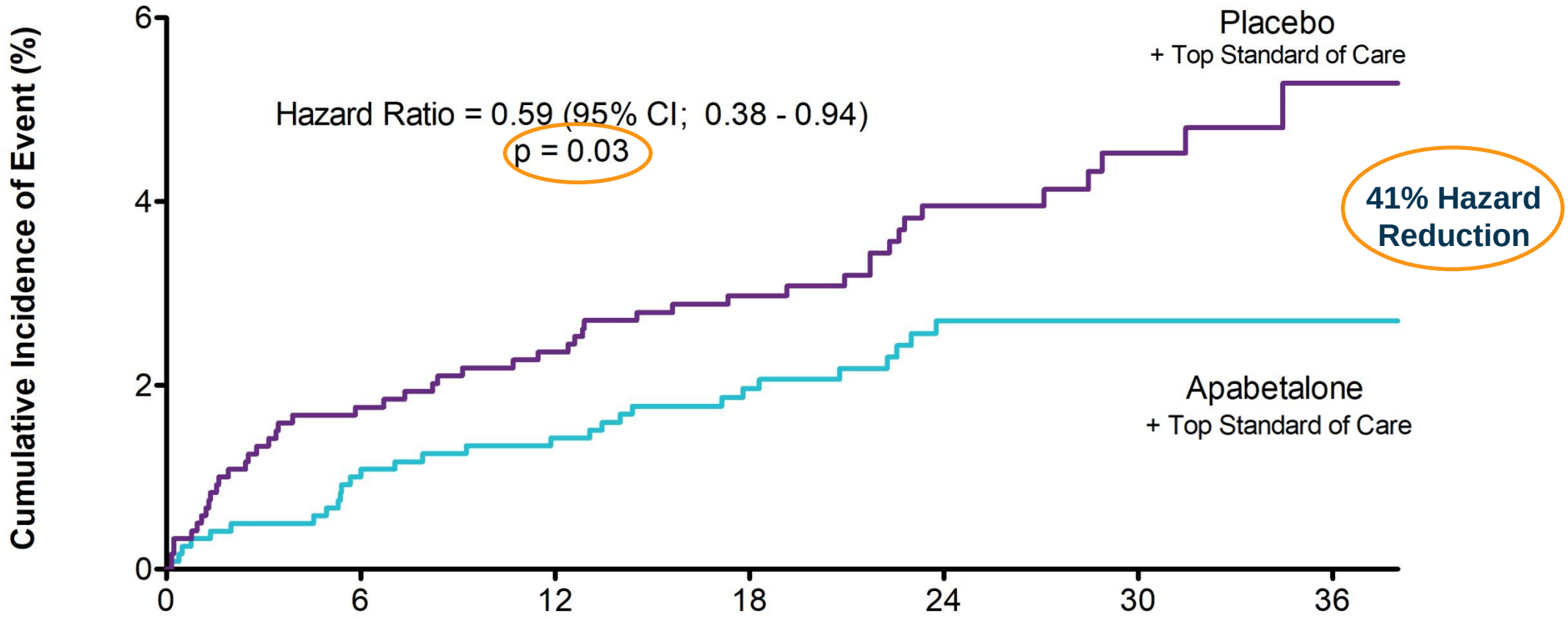
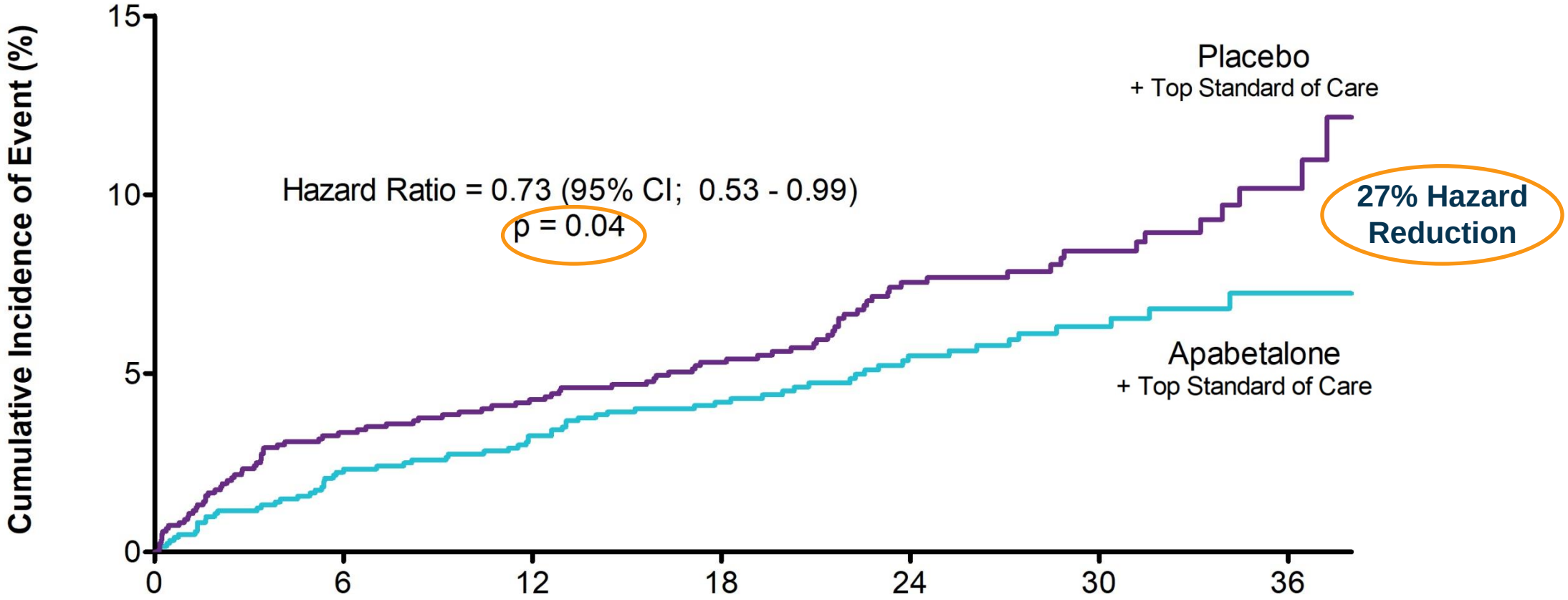
Hospitalization for Congestive Heart Failure (CHF)

Key Secondary Endpoint – First Hospitalizations for CHF



No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Exploratory Endpoint – First Hospitalizations for CHF and CV Death



No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Source: RVX Internal Analysis – Non-QC'd

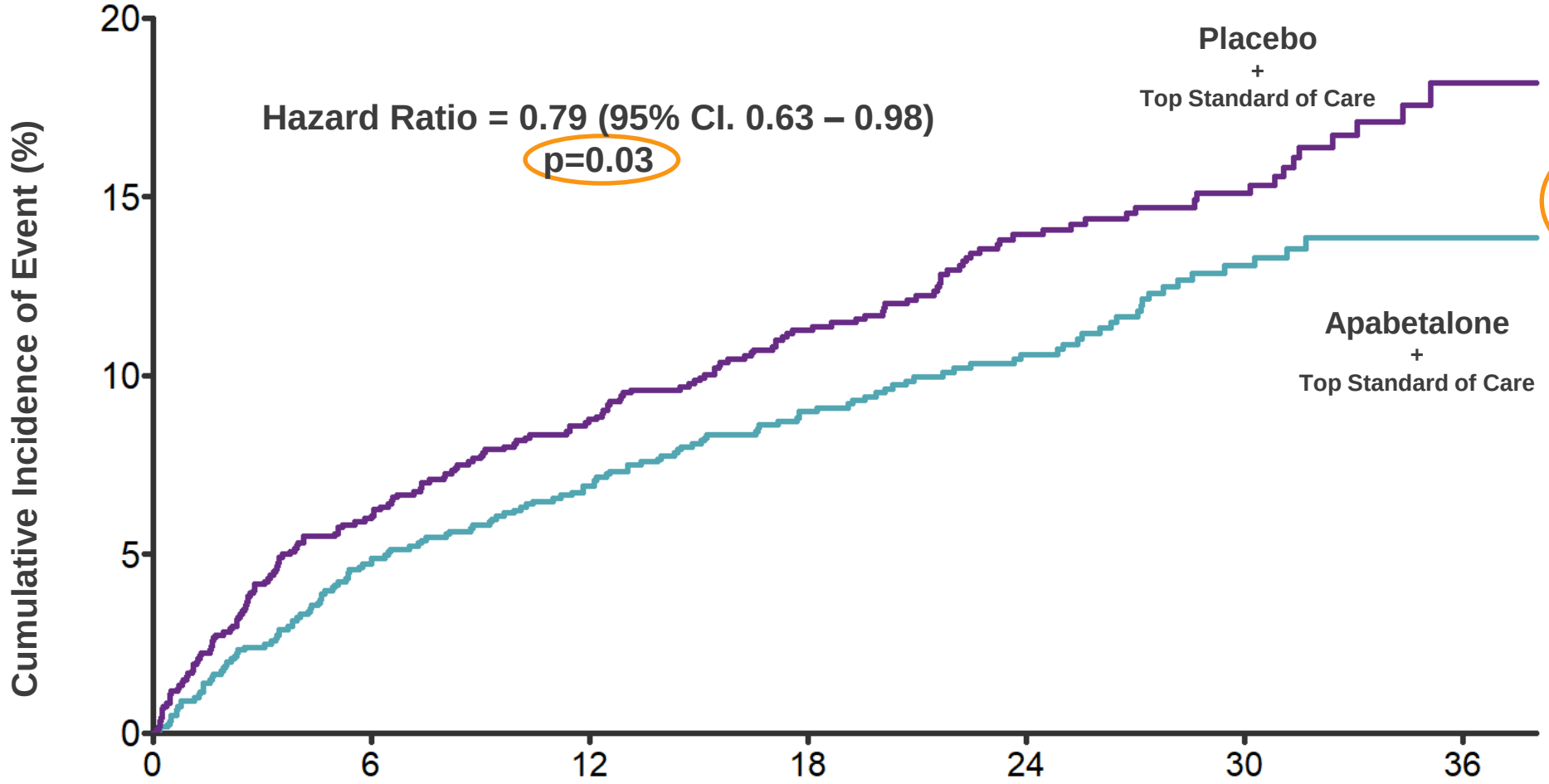
Non-fatal MI, Stoke, CV Death, and Hospitalization for CHF

Endpoint, n(%)	Apabetalone (N=1212)	Placebo (N=1206)	HR (95% CI)	Log-rank p-value
Composite	**139**	**173**	**0.79 (0.63, 0.98)**	**0.03***
Non-fatal MI	77	94	0.80 (0.59,1.08)	0.15*
CV Death	45	55	0.81 (0.54, 1.19)	0.29*
Stroke	17	17	1.01 (0.52, 1.98)	0.99*
Hosp. for CHF	29	48	0.59 (0.38, 0.94)	0.03*

Non-QC'd

***Nominal p value**

Non-fatal MI, CV Death, and Hospitalization for CHF – Survival Curve

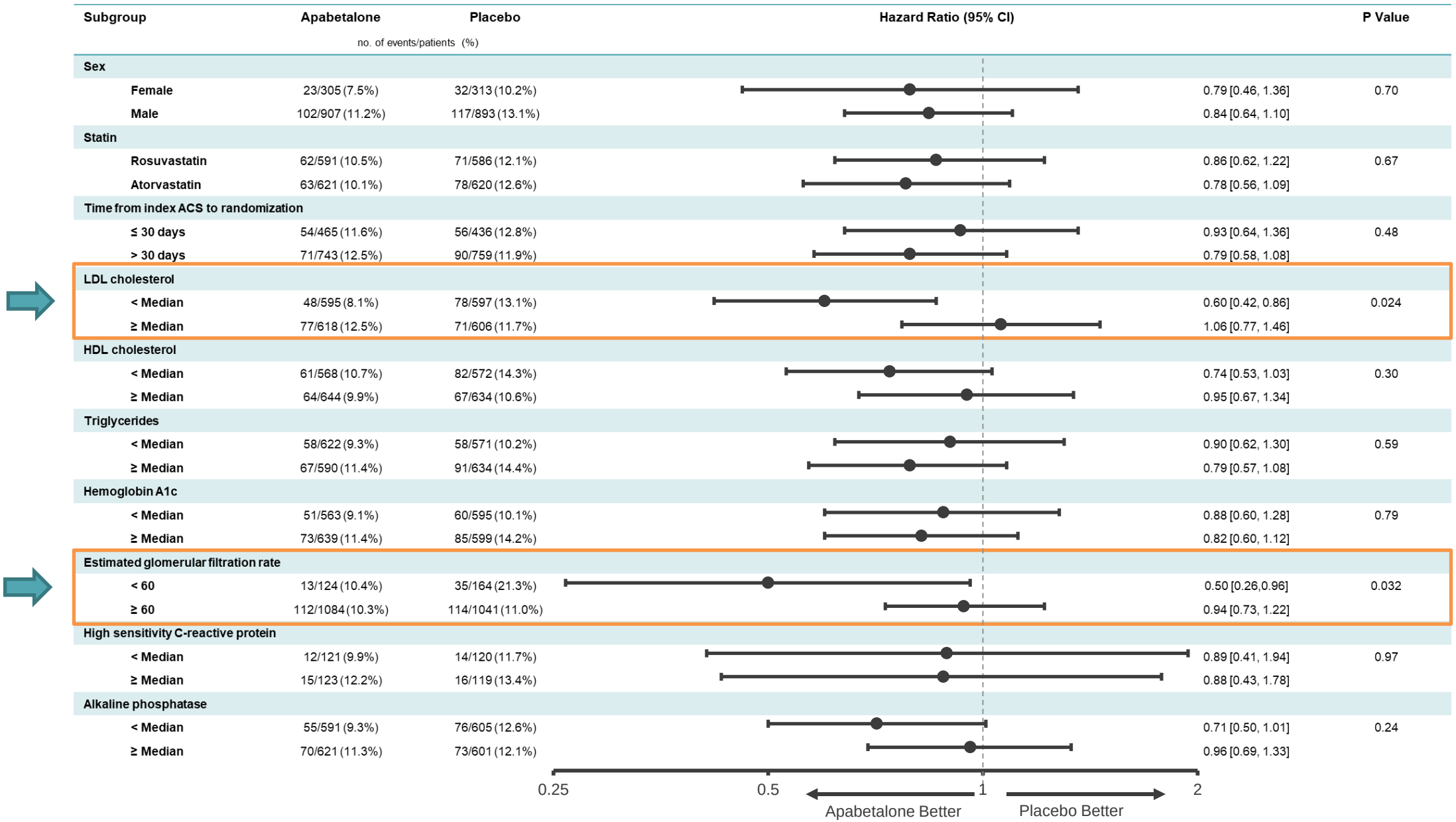


No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Source: RVX Internal Analysis – Non-QC'd


Prespecified Subgroups

Endpoint Significance Reached in Prespecified Subgroups



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Apabetalone Overperforms in Patients with Renal Impairment

(Baseline eGFR Below 60 mL/min)

Apabetalone Improved CVD Outcomes in Impaired Renal Subgroup

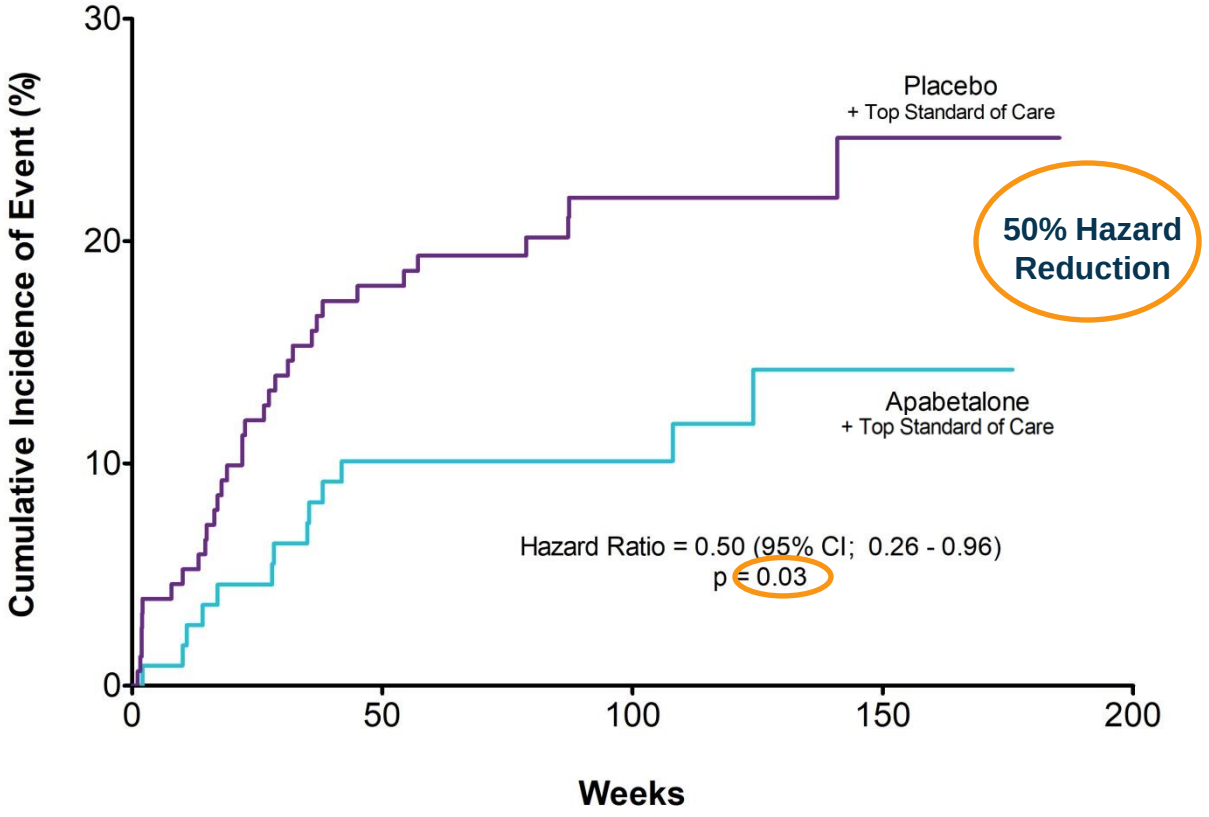
Baseline eGFR Below 60 mL/min

Endpoint	Hazard Ratio (95% CI)	P Value
CV Death, Non Fatal MI and Stroke		
eGFR < 60 mL/min	0.50 [0.26, 0.96]	0.03
eGFR ≥ 60 mL/min	0.94 [0.73, 1.22]	
CV Death, Non Fatal MI and Stroke (Excl. Undetermined Death)		
eGFR < 60 mL/min*	0.47 [0.26, 0.86]	0.01
eGFR ≥ 60 mL/min*	0.91 [0.69, 1.19]	
CV Death, Non Fatal MI, Hospitalization for CVD Event, and Stroke		
eGFR < 60 mL/min*	0.53 [0.30, 0.94]	0.03
eGFR ≥ 60 mL/min*	0.95 [0.74, 1.20]	
CV Death and Non Fatal MI		
eGFR < 60 mL/min*	0.53 [0.29, 0.98]	0.04
eGFR ≥ 60 mL/min*	0.88 [0.67, 1.15]	
Hospitalization for CHF		
eGFR < 60 mL/min*	0.36 [0.14, 0.93]	0.04
eGFR ≥ 60 mL/min*	0.73 [0.44, 1.22]	
Hospitalization for CVD Event		
eGFR < 60 mL/min*	0.28 [0.11, 0.73]	0.01
eGFR ≥ 60 mL/min*	1.00 [0.70, 1.45]	
Hospitalization for CHF and CV Death		
eGFR < 60 mL/min*	0.50 [0.25, 0.99]	0.05
eGFR ≥ 60 mL/min*	0.83 [0.59, 1.18]	

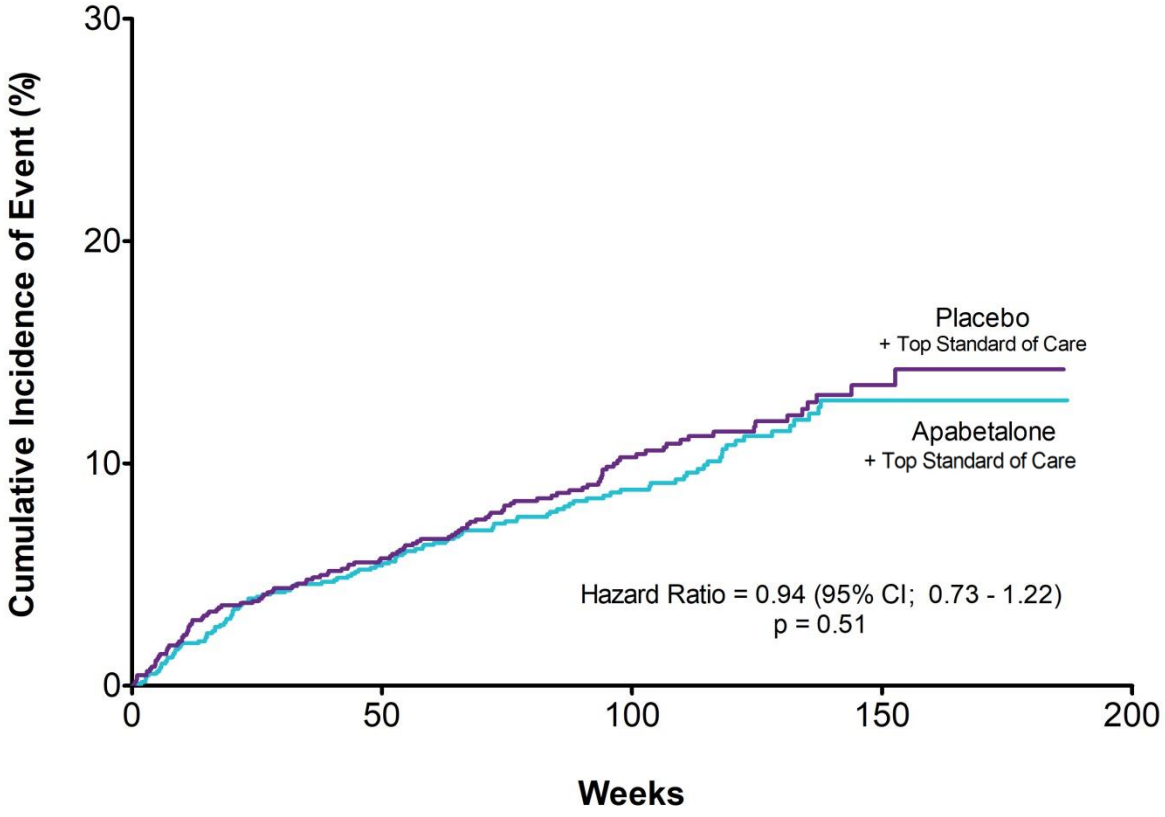
*Source: * RVX Internal Analysis – Non-QC'd*

Renal Subgroup – CV death, Non-fatal MI, and Stroke

Patients with eGFR < 60 at Baseline



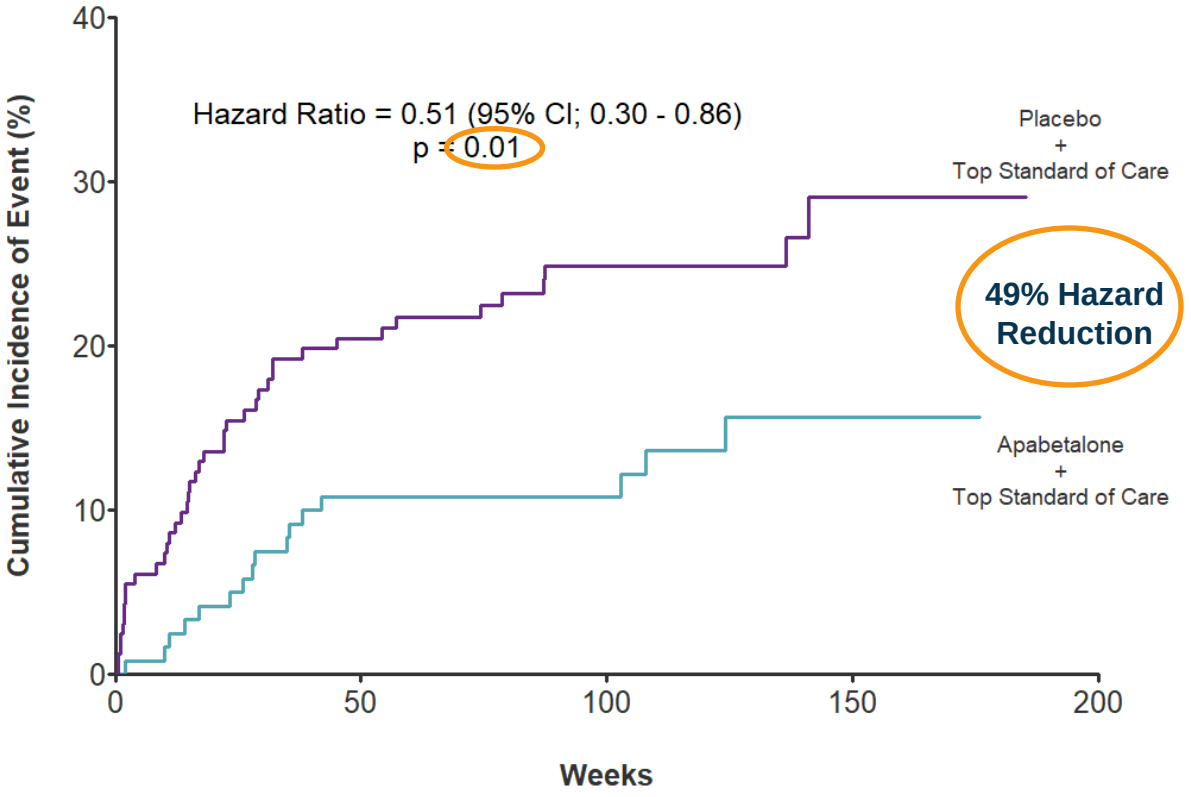
Patients with eGFR ≥ 60 at Baseline



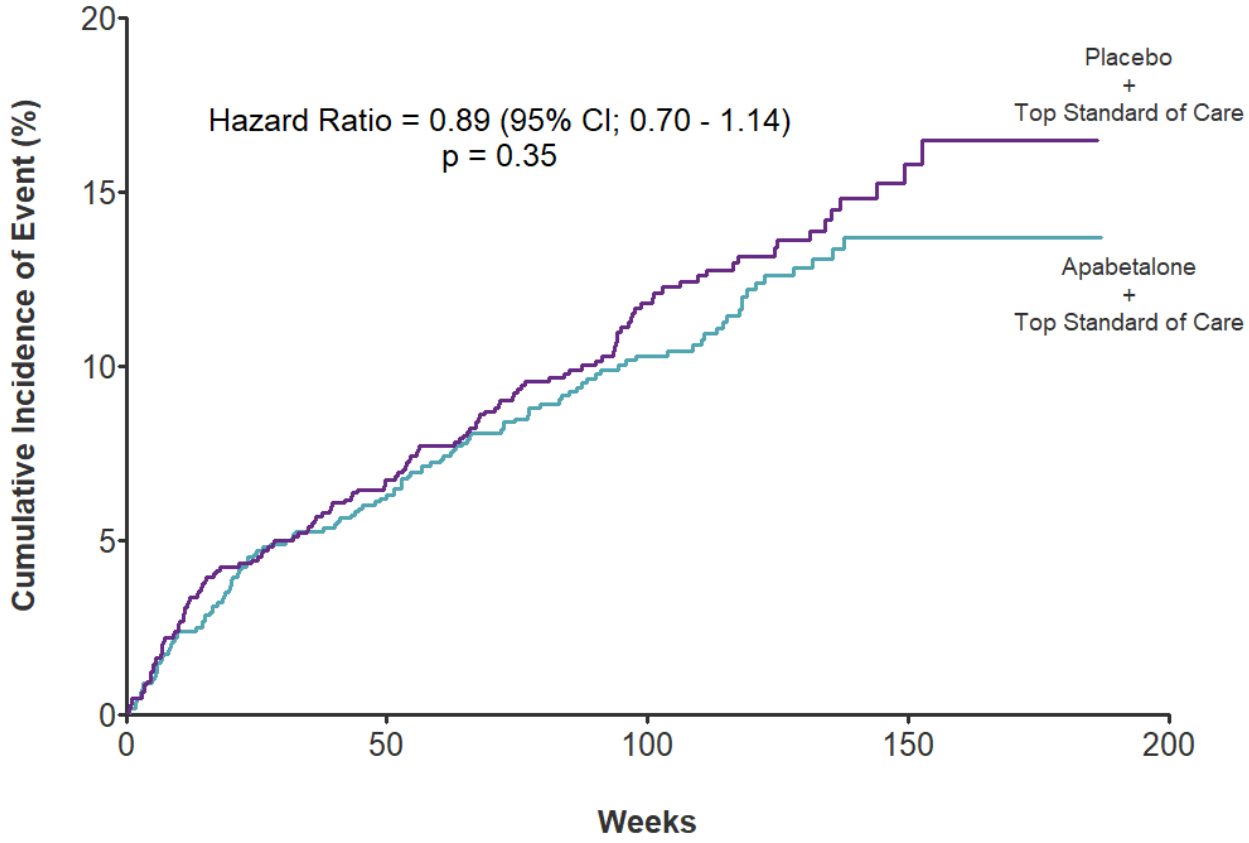
Source: RVX Internal Analysis – Non-QC'd

Renal Subgroup – CV death, Non-fatal MI, Stroke, and Hosp. for CHF

Patients with eGFR < 60 at Baseline



Patients with eGFR ≥ 60 at Baseline



Source: RVX Internal Analysis – Non-QC'd


Surprise Finding!
Potential Synergy with New Generation of Diabetes Drugs

Baseline Characteristics: Cardiovascular and Diabetes Medications

Cardiovascular and Diabetes Medications	Apabetalone (N=1212)	Placebo (N=1206)
Atorvastatin	621 (51.2)	620 (51.4)
Rosuvastatin	591 (48.8)	586 (48.6)
High intensity statin	1089 (89.9)	1092 (90.5)
ACE inhibitors/ angiotensin II blockers	1119 (92.3)	1110 (92.0)
Beta blockers	1103 (91.0)	1088 (90.2)
Antiplatelet agents	1196 (98.7)	1195 (99.1)
Dual antiplatelet agents	1057 (87.2)	1065 (88.3)
Metformin	1009 (83.3)	989 (82.0)
Insulin	445 (36.7)	464 (38.5)
Sulfonylureas	363 (30.0)	344 (28.5)
DPP4 inhibitors	181 (14.9)	178 (14.8)
SGLT2 inhibitors	150 (12.4)	148 (12.3)
GLP1 receptor agonists	41 (3.4)	45 (3.7)

Comparison to Other Major Therapeutic Classes

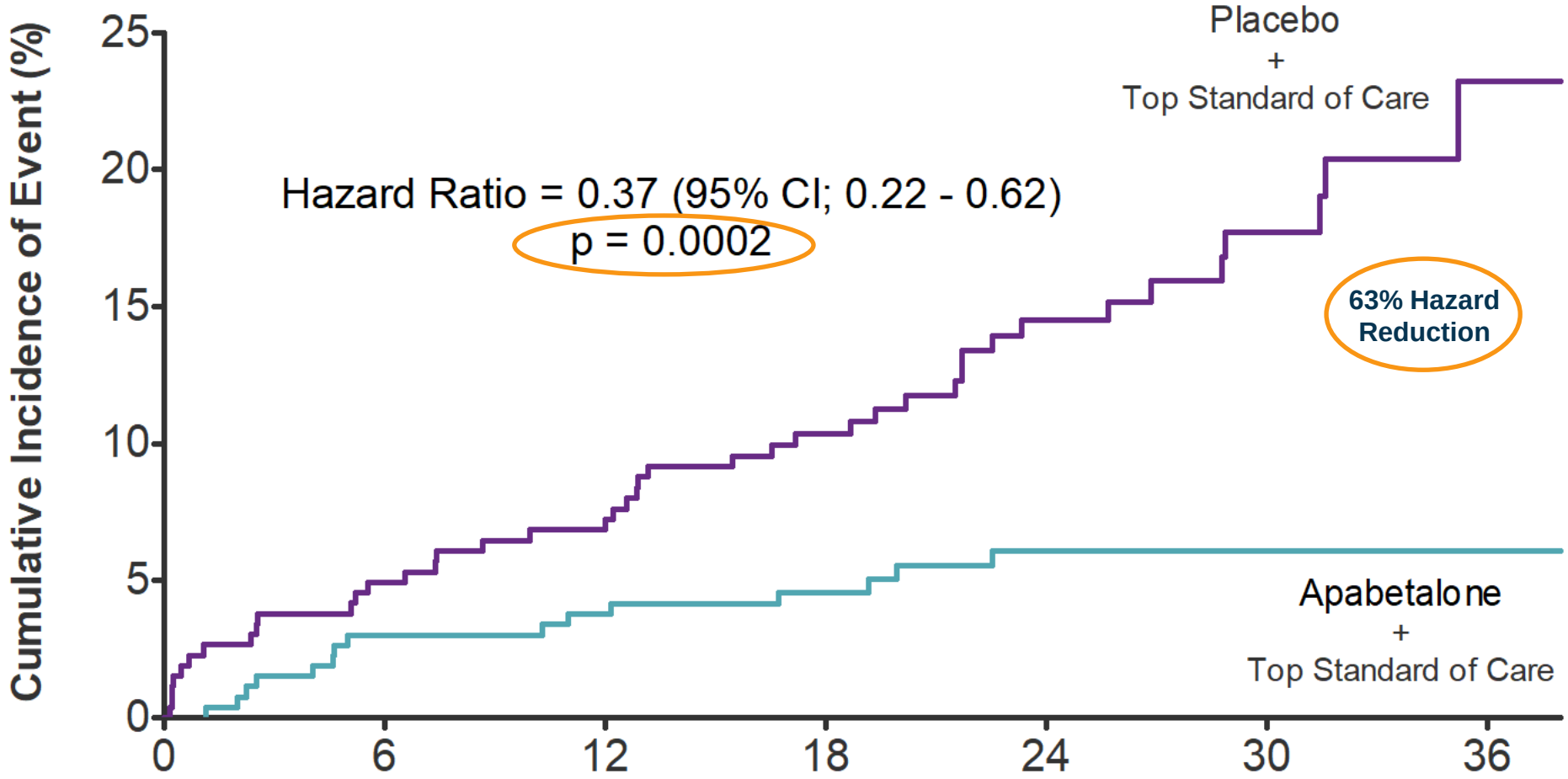
Impact on MACE in Patients with Type 2 Diabetes

Therapeutic	Trial Name	# Patients	Effect on MACE
Apabetalone	**BETonMACE**	**2,425**	**-18%***
Apabetalone + SGLT2i	**BETonMACE**	**298**	**-60%****
DDP-4 inhibitors[1,2]	CAROLINA	6,042	no effect
Insulin[3]	ORIGIN	12,537	no effect
SGLT2i[4]	CANVAS	10,142	-14%
PCSK9i[5]	ODYSSEY OUTCOMES	18,924	-15%
GLP-1 Receptor Agonists[6]	REWIND	9,091	-12% to -26%

*p-value = 0.11
**p-value = 0.05; patients receiving any SGLT2i during the study

1. Rosenstock, J et al. JAMA. (2019) Sep 19. doi: 10.1001/jama.2019.13772
2. Green, JB et al. N Engl J Med. (2015) 373:232–42. doi: 10.1056/NEJMoa1501352
3. ORIGIN trial Investigators, N. Engl. J. Med. (2012) 367, 319–328
4. Zelniker, TA et al. Lancet (2019) Jan 5;393(10166):31-39. doi: 10.1016/S0140-6736(18)32590-X.
5. Schwartz, GG et al. N Engl J Med (2018); 379:2097-2107 doi: 10.1056/NEJMoa1801174
6. Zelniker, TA et al. Circulation. (2019);139(17):2022-2031. doi: 10.1161/CIRCULATIONAHA.118.038868.

SGLT2i or DPP4i – CV death, Non-fatal MI, Stroke, and Hosp. for CHF



No. at Risk							
Placebo	264	250	243	209	143	86	25
Apabetalone	265	257	251	219	156	90	25

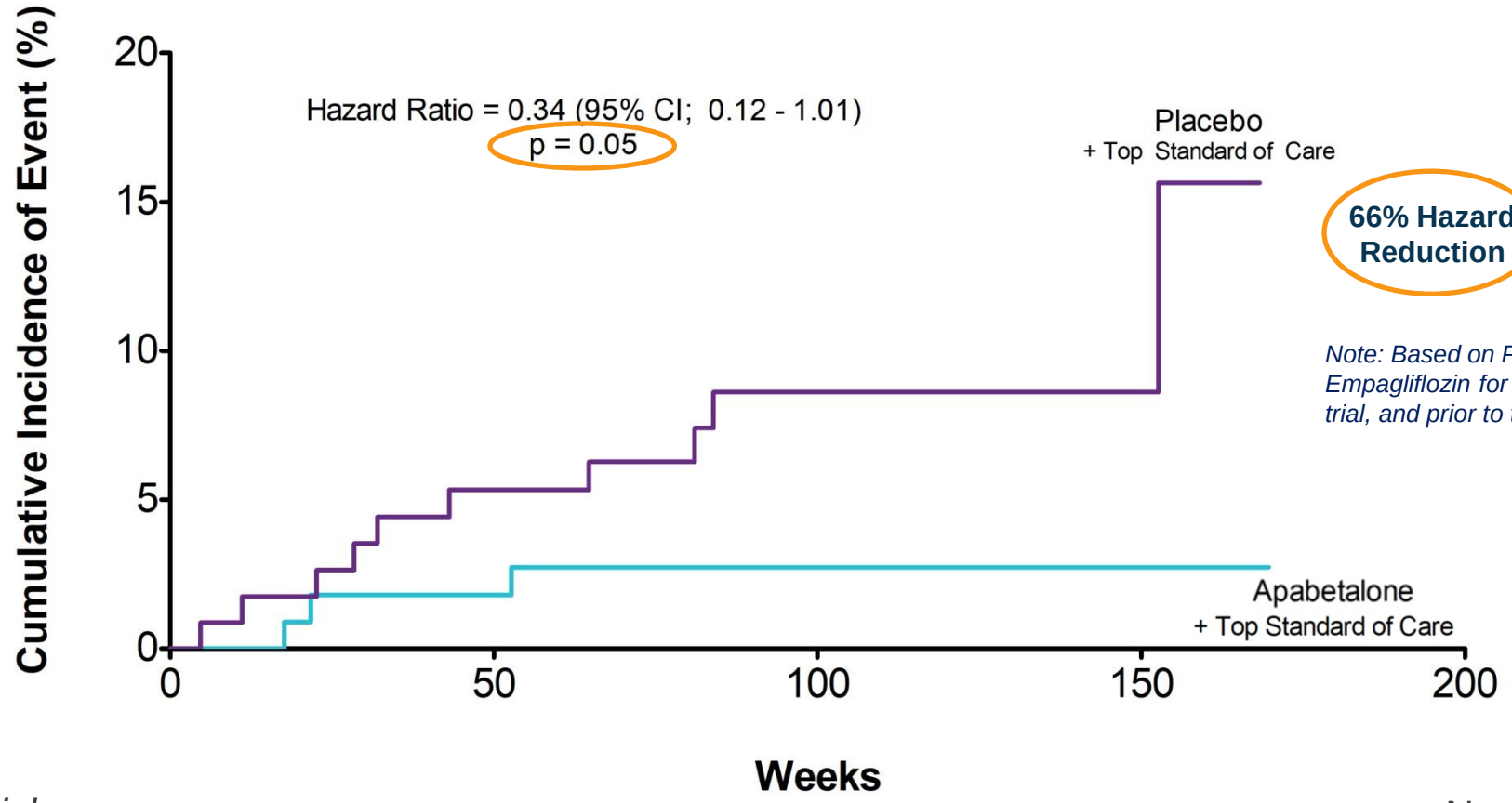
Source: RVX Internal Analysis – Non-QC'd

CVD Endpoints with SGLT2 Inhibitors

Endpoint, n(%)	Apabetalone (N=150)	Placebo (N=148)	HR (95% CI)
MACE CV death, non-fatal MI and stroke	5	13	0.40 (0.16, 1.00)
Hospitalization for Congestive Heart Failure (CHF)	1	2	0.49 (0.05, 4.73)
CV death, non-fatal MI stroke and hospitalization for CHF	5	15	0.35 (0.15, 0.85)
CV death, non-fatal MI and hospitalization for CHF	4	15	0.30 (0.12, 0.74)

Source: RVX Internal Analysis – Non-QC'd

Apabetalone and Empagliflozin (Jardiance)



Note: Based on Patients who were taking Empagliflozin for at least 30 days during the trial, and prior to their MACE

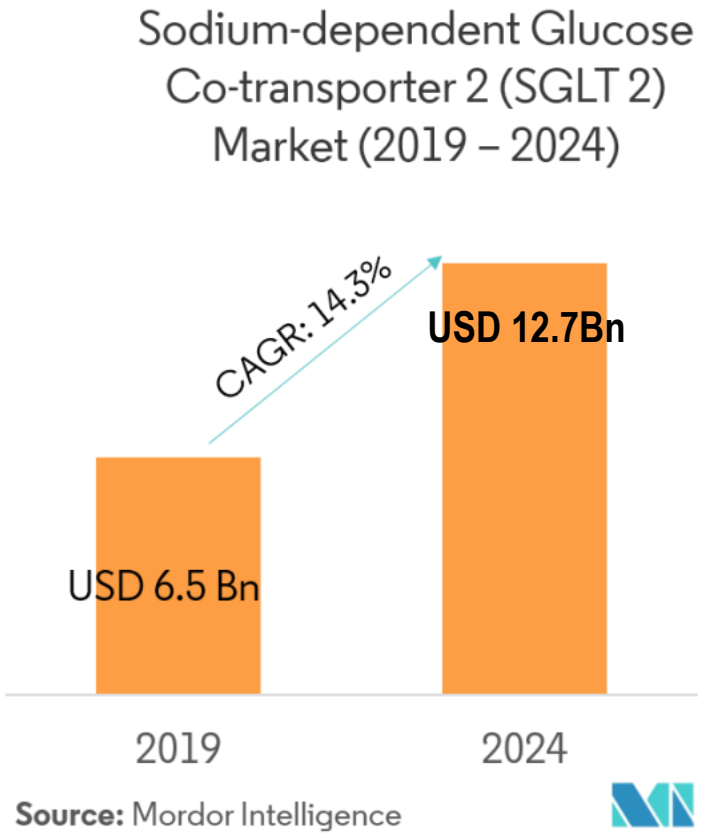
No. at Risk				
Apabetalone	113	108	67	13
Placebo	115	104	59	18

Narrowly Defined MACE:
- CV Death
- Non Fatal MI
- Stroke

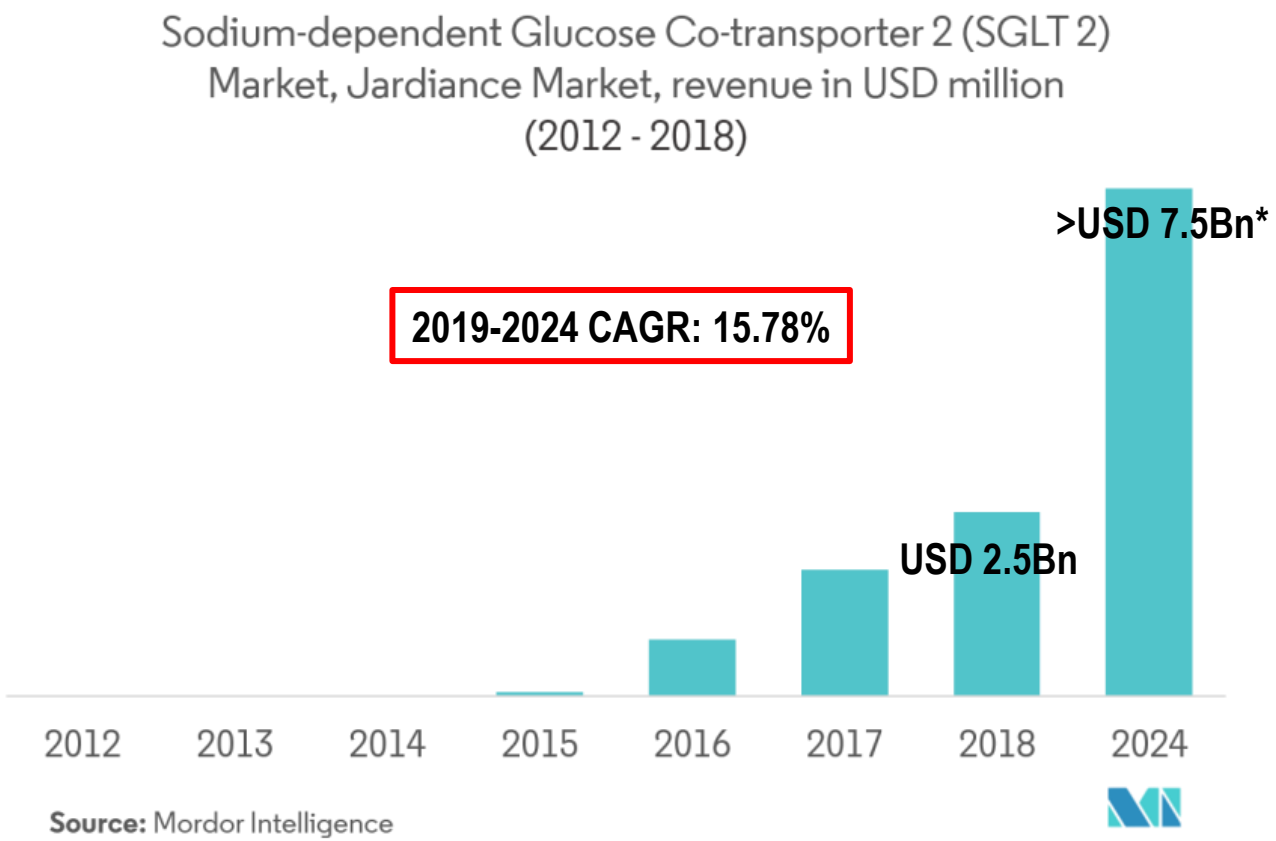
Source: RVX Internal Analysis – Non-QC'd

Market Growth of SGLT2 Inhibitors

Global Market Growth



Jardiance Market Growth



*Source: *RVX Internal Estimate*


Cognition Results

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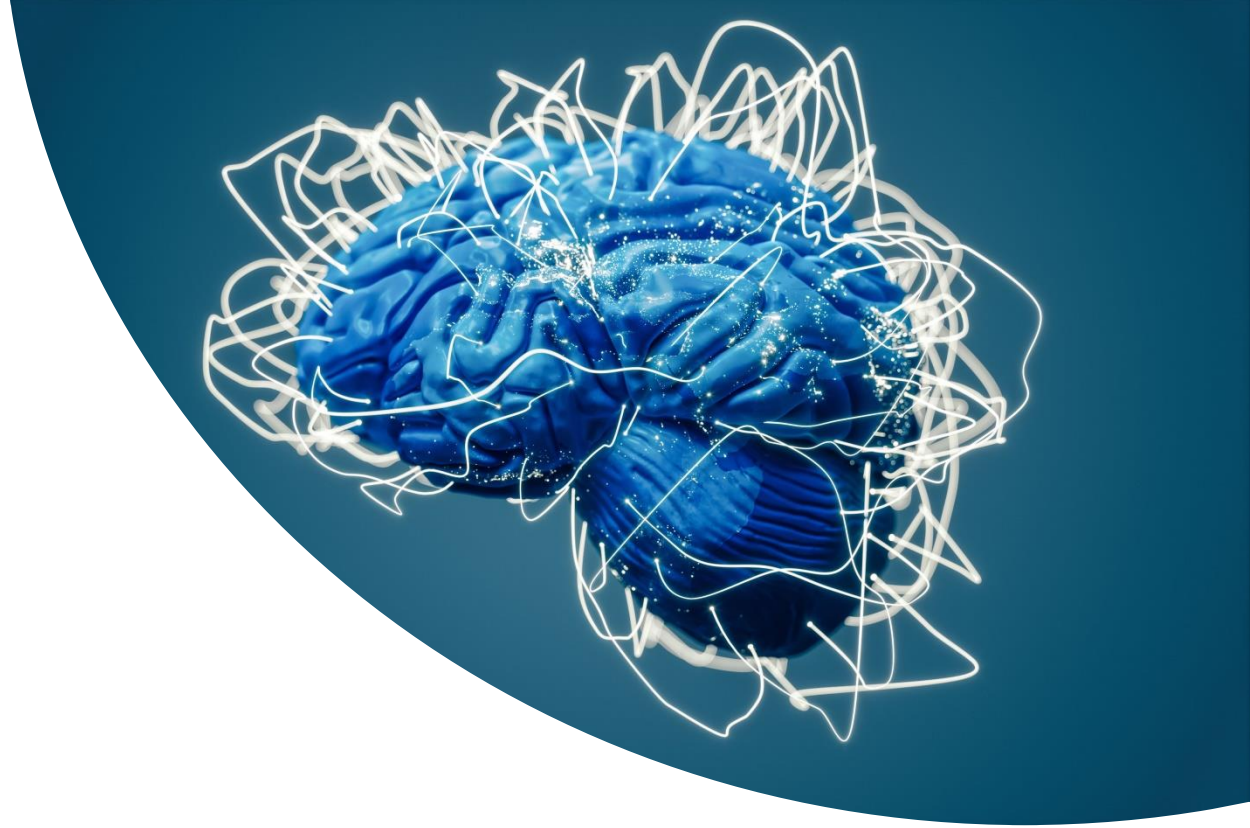
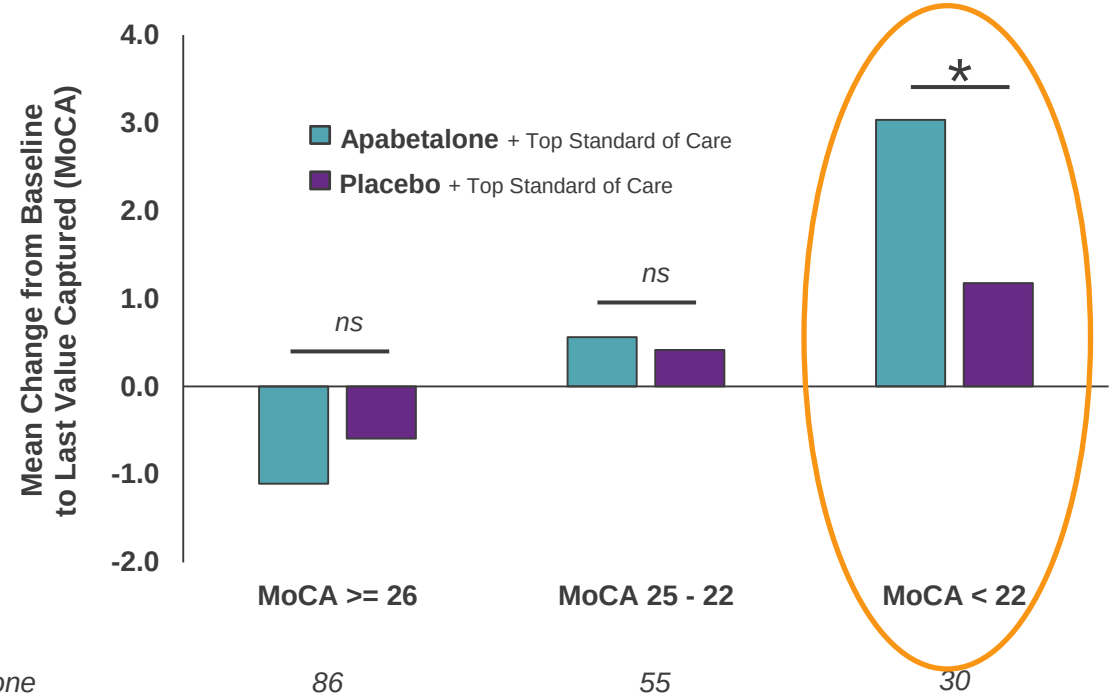


Montreal Cognitive Assessment (MoCA)

BETonMACE Cognition Findings - MoCA



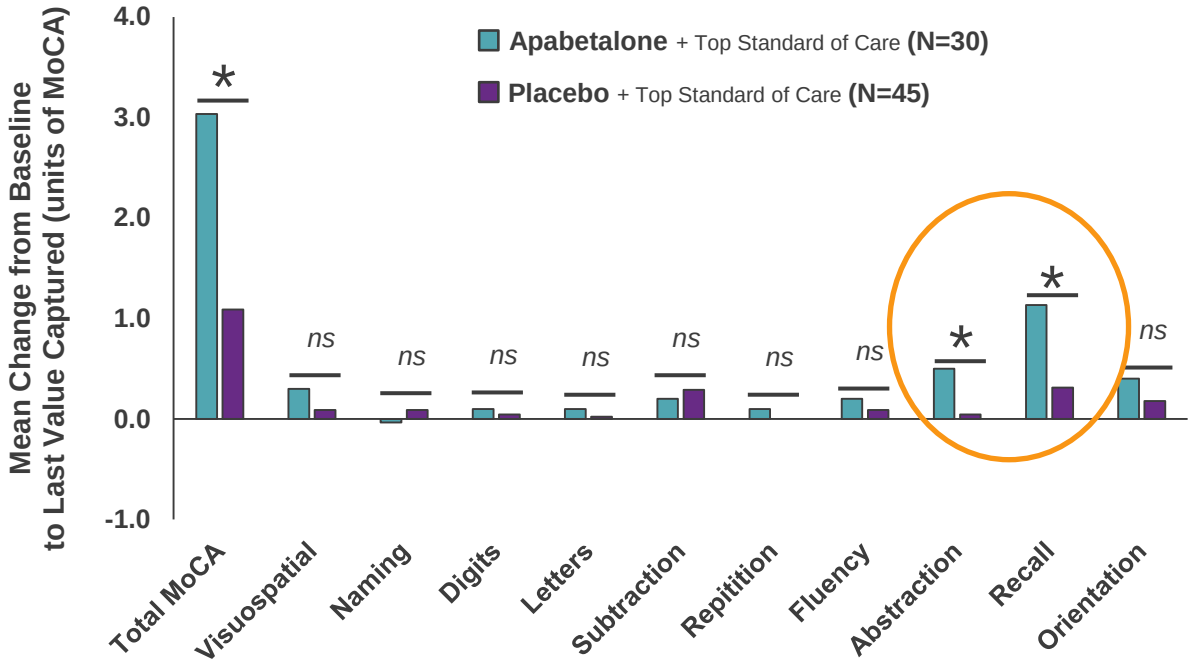
No.	MoCA >= 26	MoCA 25 - 22	MoCA < 22
Apabetalone	*86*	*55*	*30*
Placebo	*101*	*72*	*45*

*Treatment p-value calculated using two-sided t-test; * p=0.02*

- Apabetalone treatment **illustrates a statistically significant (*p=0.02) improvement versus placebo** in MoCA in patients with a **baseline MoCA below 22**
  - **158% relative improvement in cognitive function** over top standard of care placebo
  - **Study duration was the same between treatment groups**

Source: RVX Internal Analysis – Non-QC'd

MoCA Domains in Patients with Baseline MoCA <22



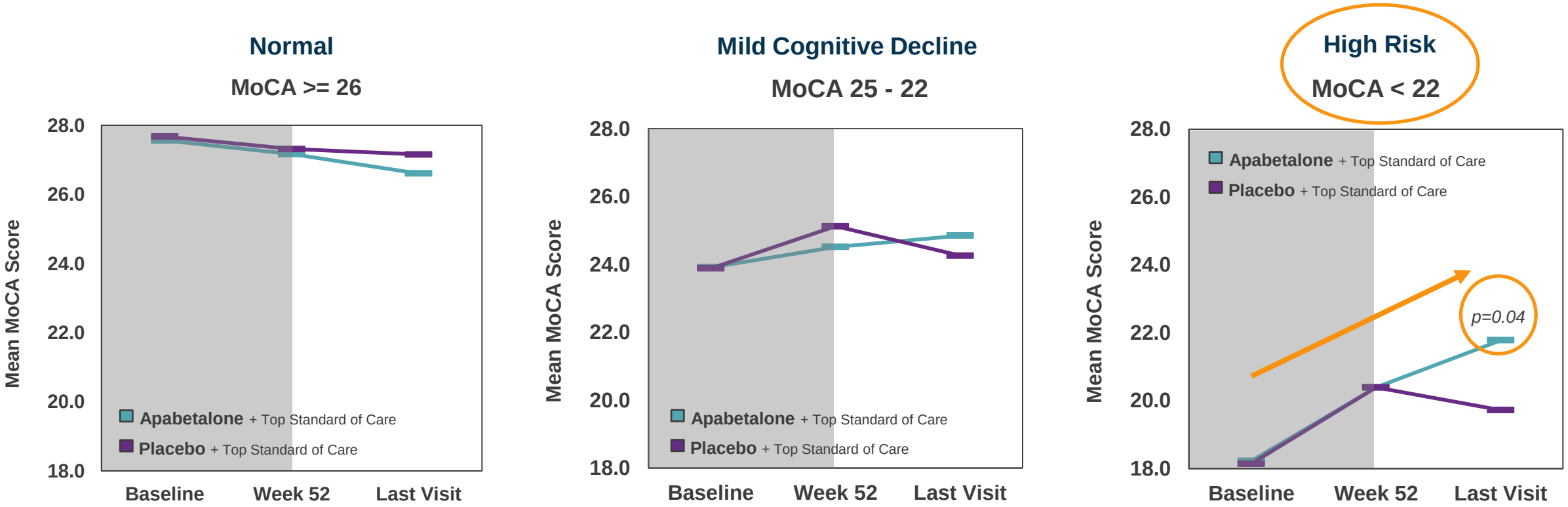
*Treatment p-value calculated using two-sided t-test; * p<0.05*

- Analysis of MoCA domains illustrates **a statistically significant improvement (*p<0.05) in the abstraction (conceptual thinking) and recall (memory) domains** in patients with a baseline MoCA < 22 with apabetalone treatment

Source: RVX Internal Analysis – Non-QC'd

BETonMACE Cognition Findings – Additional Analysis

- Apabetalone treatment illustrates a **trend in the improvement of cognition** when baseline MoCA was lower (MoCA < 22)



Treatment p-value calculated using two-sided t-test; p<0.05

Source: RVX Internal Analysis – Non-QC'd

Summary

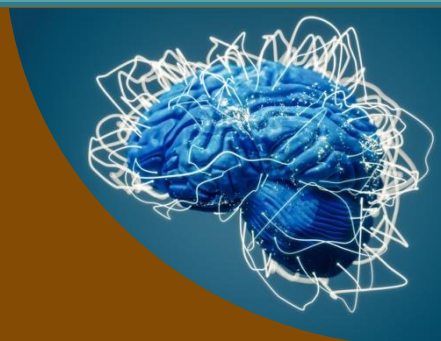
- CVD primary endpoint was narrowly missed **with consistent positive trend in key endpoints**
- Apabetalone **overperfomed in pre-specified renal subgroup,** reaching significance on multiple endpoints
- **Potential synergy discovered** between Apabetalone and SGLT2 inhibitors
- Apabetalone **significantly improved cognition** in patients with moderate to severe cognitive decline

Strengthening Opportunities Through Positive Findings & Synergy

Narrow MACE (with CHF)
24% Hazard Reduction
(HR: 0.76; 95% CI; 0.60-0.95)
p=0.02

Renal Subgroup
eGFR < 60 at Baseline
50% Hazard Reduction
(HR: 0.50; 95% CI; 0.26-0.96)
p=0.03

Apabetalone & SGLT2i (Empagliflozin)
66% Hazard Reduction
(HR: 0.34; 95% CI; 0.12-1.01)
p=0.05



Cognitive Function
Improved 158% in treated vs. placebo
(MoCA < 22 subgroup)
p=0.02

Source: RVX Internal Analysis – Non-QC'd

Near Term Commercialization Steps

In the near term we will continue our multi-point approach to progressing our corporate commercial value. This approach involves aggressive exploratory development of the following:

- Breakthrough Therapy Status Granted from FDA – February 2020
- Agreement reached with FDA for key aspects of apabetalone registration enabling study at June 2020 Meeting
- SGLT2i partnering discussions ongoing, key patent already filed
- Renal partnering discussions ASAP
- Congestive Heart Failure partnering discussions, already initiated
- Orphan partnering discussions initially focused on PAH and HIV only at this time. PAH enrollment has already commenced. HIV funding being derived from a yet to be named US based organization
- Cognitive Function partnering discussion in progress

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TSX: RVX

Detailed Preliminary Results of BETonMACE

Strengthening Opportunities Through Positive Findings & Synergy

January, 2020


Appendix

Study Design

BETonMACE Study Parameters

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 CV death or non fatal MI or stroke.

Key Inclusion Criteria

- Type 2 Diabetes Mellitus
  - HbA1c >6.5% or history of diabetes medications
- Acute coronary syndrome 7-90 days prior to the screening visit
  - Unstable angina (Limited to 25% of total participants) or acute myocardial infarction
- Low HDL cholesterol
  - <40 mg/dL (1.04 mmol/L) for males; <45 mg/dL (1.17 mmol/L) for females at the screening visit

Primary Endpoint

- Time to first occurrence of adjudication-confirmed triple MACE

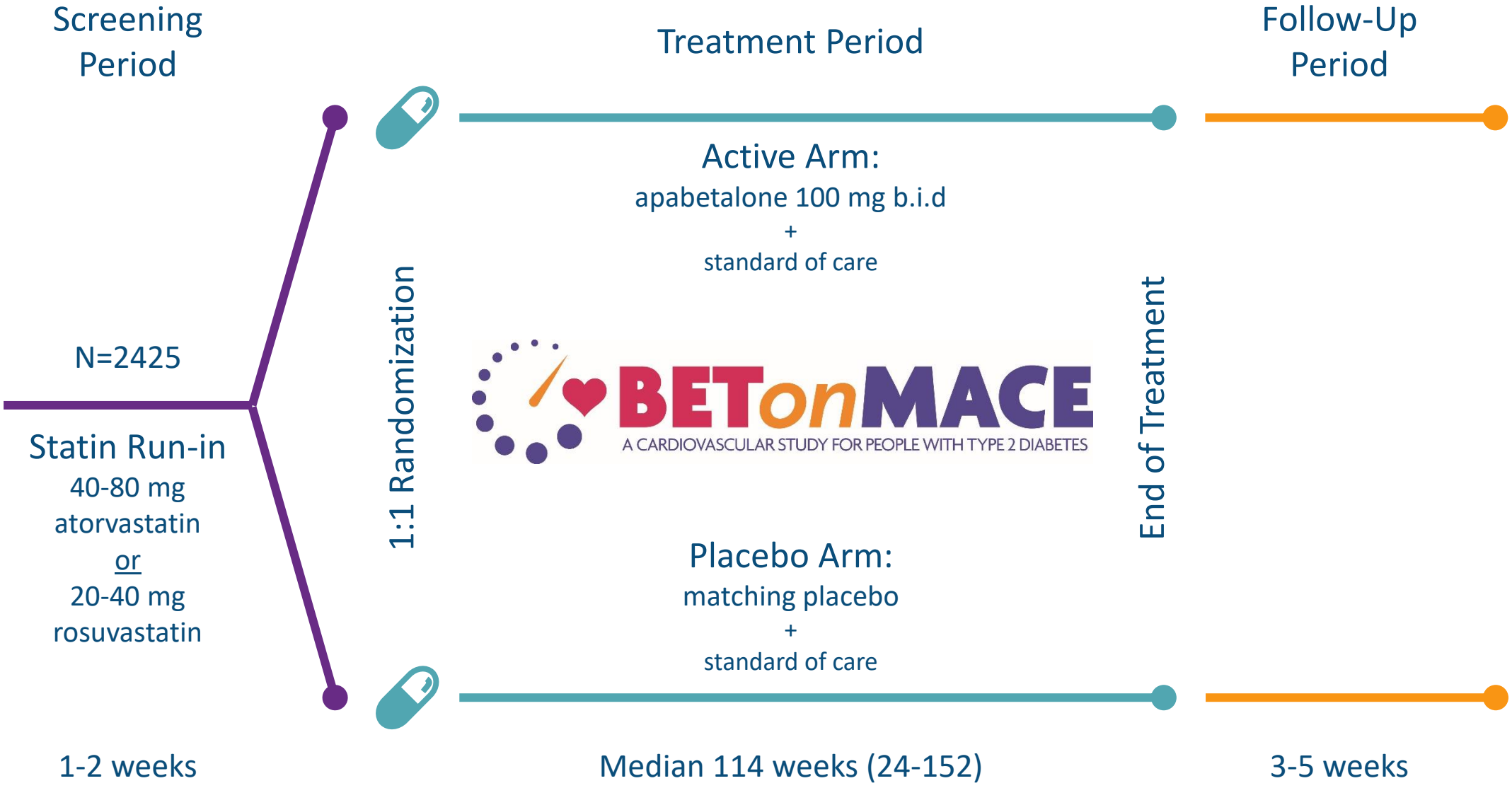
Key Secondary and Exploratory Endpoints

- Change in kidney function in chronic kidney disease sub-population
  - Baseline estimated glomerular filtration rate (eGFR) <60 mL/min/1.7m^2
- Change in Montreal Cognitive Assessment (MoCA)
  - Evaluated in at-risk sub-population (>70 years old at randomization)

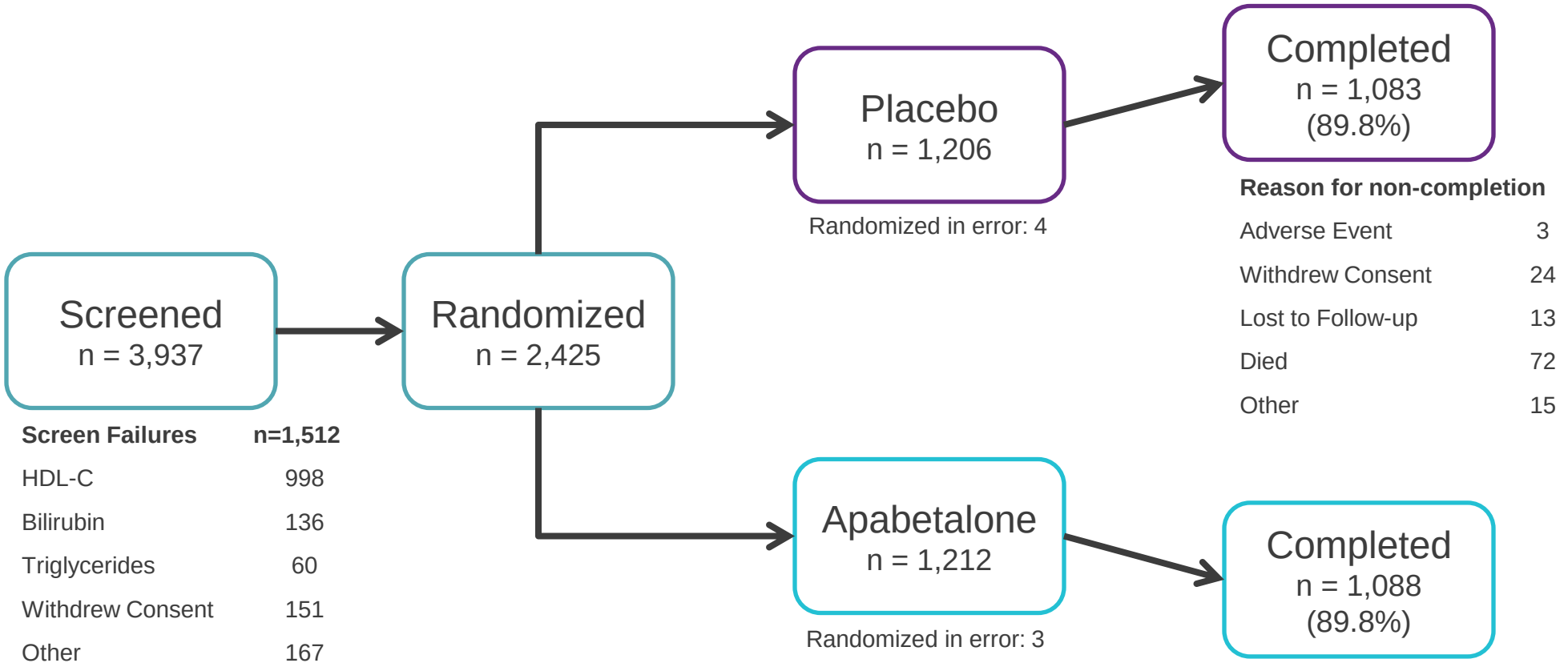
BETonMACE a Global, Multi-centered Clinical Trial

With 14 approved countries around the world,
BETonMACE included patients randomized at 220 different sites

BETonMACE Study Design



BETonMACE: Patient Disposition



Screen Failures	n=1,512
HDL-C	998
Bilirubin	136
Triglycerides	60
Withdrew Consent	151
Other	167

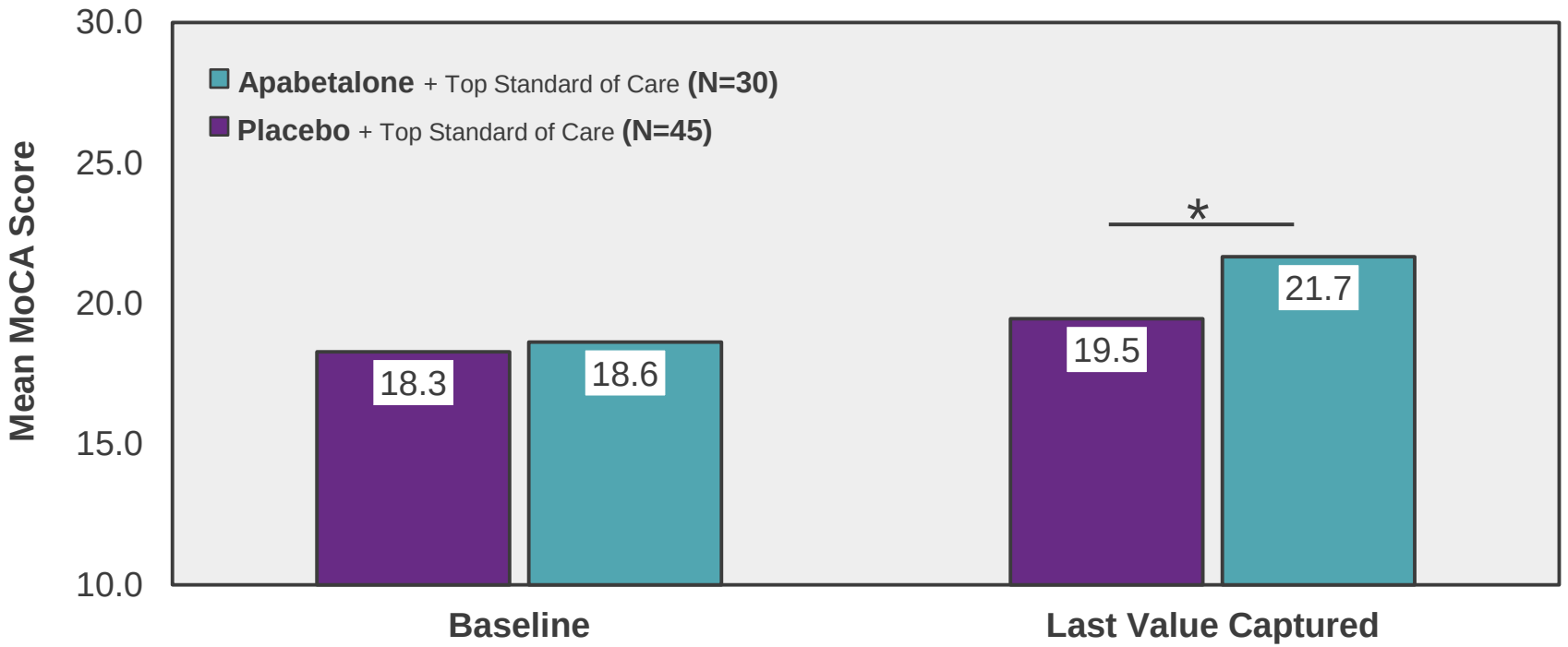
Reason for non-completion	
Adverse Event	3
Withdrew Consent	24
Lost to Follow-up	13
Died	72
Other	15

Reason for non-completion	
Adverse Event	2
Withdrew Consent	31
Lost to Follow-up	7
Died	61
Other	26

MoCA in Patients with Baseline MoCA <22

Baseline versus Last Value Captured

- **Study duration was the same between treatment groups**



Placebo = 702 days

Apabetalone = 701 days

*Treatment p-value calculated on change from baseline using two-sided t-test; * p<0.05*

- Apabetalone treatment **illustrates a statistically significant improvement versus placebo** in MoCA in patients with a **baseline MoCA below 22**

Preliminary Data; RVX Internal Analysis; November 2019

Baseline Characteristics

Overall Study Population

Baseline Characteristics, Prior Medical and Index ACS History

	Apabetalone (n=1212)	Placebo (n=1206)
Median age, yrs	62.0	62.0
Male sex- %	74.8	74.0
Body mass index, kg/m^2	30.2	30.3
Hypertension - %	89.4	87.8
eGFR Mean ± SD, mL/min/1.73m^2	104.9	101.7
Duration of diabetes – yrs	8.4	8.7
Index acute coronary syndrome – %		
Myocardial infarction	73.0	74.0
STEMI	38.4	38.6
NSTEMI	34.1	35.1
Unstable angina	26.7	25.0
PCI for index acute coronary syndrome	79.8	79.2
Time from index ACS to randomization – days	38	38

Baseline Characteristics: Cardiovascular and Diabetes Medications

Cardiovascular and Diabetes Medications (%)	Apabetalone (N=1212)	Placebo (N=1206)
Atorvastatin	51.2	51.4
Rosuvastatin	48.8	48.6
High intensity statin	89.9	90.5
ACE inhibitors/ angiotensin II blockers	92.3	92.0
Beta blockers	91.0	90.2
Antiplatelet agents	98.7	99.1
Dual antiplatelet agents	87.2	88.3
Metformin	83.3	82.0
Insulin	36.7	38.5
Sulfonylureas	30.0	28.5
DPP4 inhibitors	14.9	14.8
SGLT2 inhibitors	12.4	12.3
GLP1 receptor agonists	3.4	3.7

BETonMACE: Baseline Laboratory Parameters

Baseline Laboratory Parameters	Apabetalone (n=1212)	Placebo (n=1206)
Serum glucose, mg/dL	152.2 ± 60.7	150.7 ± 62.5
eGFR, ml/min/1.73m^2 †	104.9 ± 39.3	101.7 ± 38.6
Total cholesterol, mg/dL	134.8 ± 35.3	136.8 ± 38.2
LDL cholesterol, mg/dL	69.7 ± 29.8	70.9 ± 32.4
HDL cholesterol, mg/dL	33.3 ± 5.1	33.3 ± 5.1
Triglycerides, mg/dl	144.4 (110.7-194.9)	149.7 (116.0-201.9)
Alkaline phosphatase, U/L	83.3 ± 38.2	81.9 ± 34.8
Alanine aminotransferase, units/L	25.3 ± 14.3	25.4 ± 14.7
Total bilirubin, µmol/L	9.8 ± 4.2	9.9 ± 4.2
High sensitivity C-reactive protein §	2.9 (1.3-5.9)	2.7 (1.1-6.1)

† Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft Gault method, based on age and weight at baseline.
§ High-sensitivity C-Reactive Protein was assessed in only a subset of patients. Triglycerides expressed as median and IQR

Biochemical Parameters at 100 weeks and changes from baseline

Biochemical parameters	Apabetalone (N=1212)	Placebo (N=1206)	P value
HDL cholesterol, mg/dL	38.1 (+16.4%)	36.4 (+10.4%)	0.001
LDL cholesterol, mg/dL	69.6 (+11.5%)	72 (+14.9%)	0.35
eGFR, ml/min/1.73m^2	104.3 (-0.4)	105.2 (+2.1)	0.03
Alkaline phosphatase, U/L	77.6 (-4.8)	84.2 (+2.2)	0.003
Hemoglobin A1c, %	7.76 (+0.12)	7.76 (+0.04)	0.39
Serum glucose, mg/dL	161.1 (+9.2)	160.5 (+10.5)	0.74
hCRP §	2.2 (-17.1%)	2.3 (-16.2%)	0.74

§-only at centers in Hungary and Argentina

RESVERLOGIX

Safety Results

Top Line Data: Safety

Variable		Apabetalone (N=1212)	Placebo (N= 1207)
Adverse events - n (%)			
Patients with at least one adverse event		830 (68.5)	820 (67.9)
Adverse event leading to discontinuation		114 (9.4)	69 (5.7)
Serious adverse events – n (%)			
Patients with at least one SAE		354 (29.2)	339 (28.1)
Death		61 (5.0)	72 (6.0)
Cardiovascular deaths		34 (2.8)	42 (3.5)
Laboratory results – n (%)			
Liver Function	**ALT >3x ULN**	78 (6.4)	18 (1.5)
	ALT >5x ULN	40 (3.3)	9 (0.7)
	Bilirubin >2x ULN	7 (0.6)	9 (0.7)
Hy's law		0	0
Discontinuation due to LFT elevation – n (%)		35 (2.9)	11 (0.9)

- **Well tolerated with similar AE's and SAE's to placebo**
- **Rate raised LFT's >5xULN low and only 2.6 % greater than placebo**
- **No Hy's law cases reported by DSMB**

Top Line Data: Safety

Adverse Events, System Organ Classes with at least one AE > 2% incidence either group*

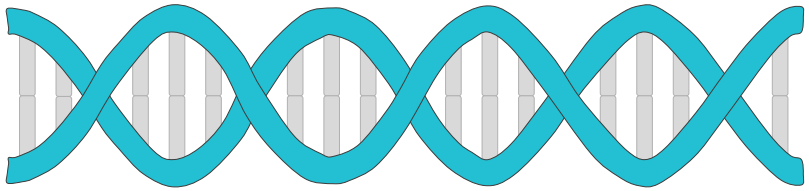
System Organ Class, Adverse Event	Apabetalone (N=1212)	Placebo (N= 1207)
Infections and Infestations	291 (20.6)	296 (19.3)
Nasopharyngitis	46 (3.8)	56 (4.6)
Urinary tract infection	58 (4.8)	40 (3.3)
Influenza	43 (3.5)	47 (3.9)
Bronchitis	25 (2.1)	32 (2.7)
Pneumonia	27 (2.2)	26 (2.2)
URTI	29 (2.4)	24 (2.0)
Cardiac Disorders	260 (19.1)	278 (21.2)
Angina	74 (6.1)	76 (6.3)
Angina unstable	58 (4.8)	41 (3.4)
Acute myocardial infarction	42 (3.5)	50 (4.1)
Cardiac failure	22 (1.8)	38 (3.1)
Gastrointestinal Disorders	186 (15.3)	170 (14.1)
Diarrhea	43 (3.5)	44 (3.6)
Abdominal pain	12 (1.0)	24 (2.0)
Nausea	26 (2.1)	7 (0.6)
Musculoskeletal	143 (11.8)	183 (15.2)
Myalgia	37 (3.1)	33 (3.7)
Back pain	17 (1.4)	28 (2.3)
Pain in extremity	15 (1.2)	26 (2.2)
Arthralgia	11 (0.9)	24 (2.0)
Metabolism and nutrition disorders	148 (12.2)	170 (14.1)
Diabetes mellitus	93 (7.7)	93 (7.7)
Vascular Disorders	135 (11.1)	142 (11.8)
Hypertension	72 (5.9)	72 (6.0)
Investigations	160 (13.2)	86 (7.1)
ALT increase	64 (5.3)	18 (1.5)
General Disorders	111 (9.2)	109 (9.0)
Non-cardiac chest pain	33 (2.7)	39 (3.2)
Blood and Lymphatic System Disorders	52 (4.3)	52 (4.3)
Anemia	36 (3.0)	40 (3.3)

Background Slides

BETonMACE: Background & Rationale

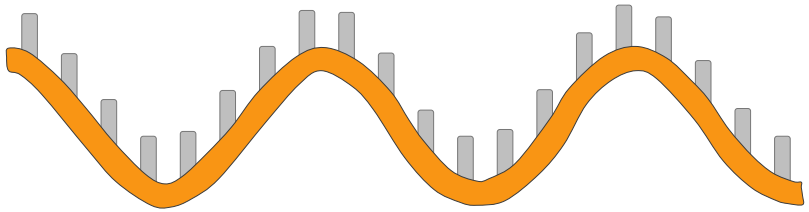
Apabetalone Mechanism of Action

DNA



Transcription

RNA



Translation

Protein

Genome Editing

Altering the sequence of DNA itself and then reintroducing **modified genes** into the body

*There are currently **no FDA-approved** therapies based on gene editing*

Transcriptional Regulation

Adjusting the levels of **multiple** disease proteins by modulating their expression at the gene level

***Apabetalone**, acting upstream of traditional pharmaceuticals, represents a **paradigm shift** in the treatment of chronic disease*

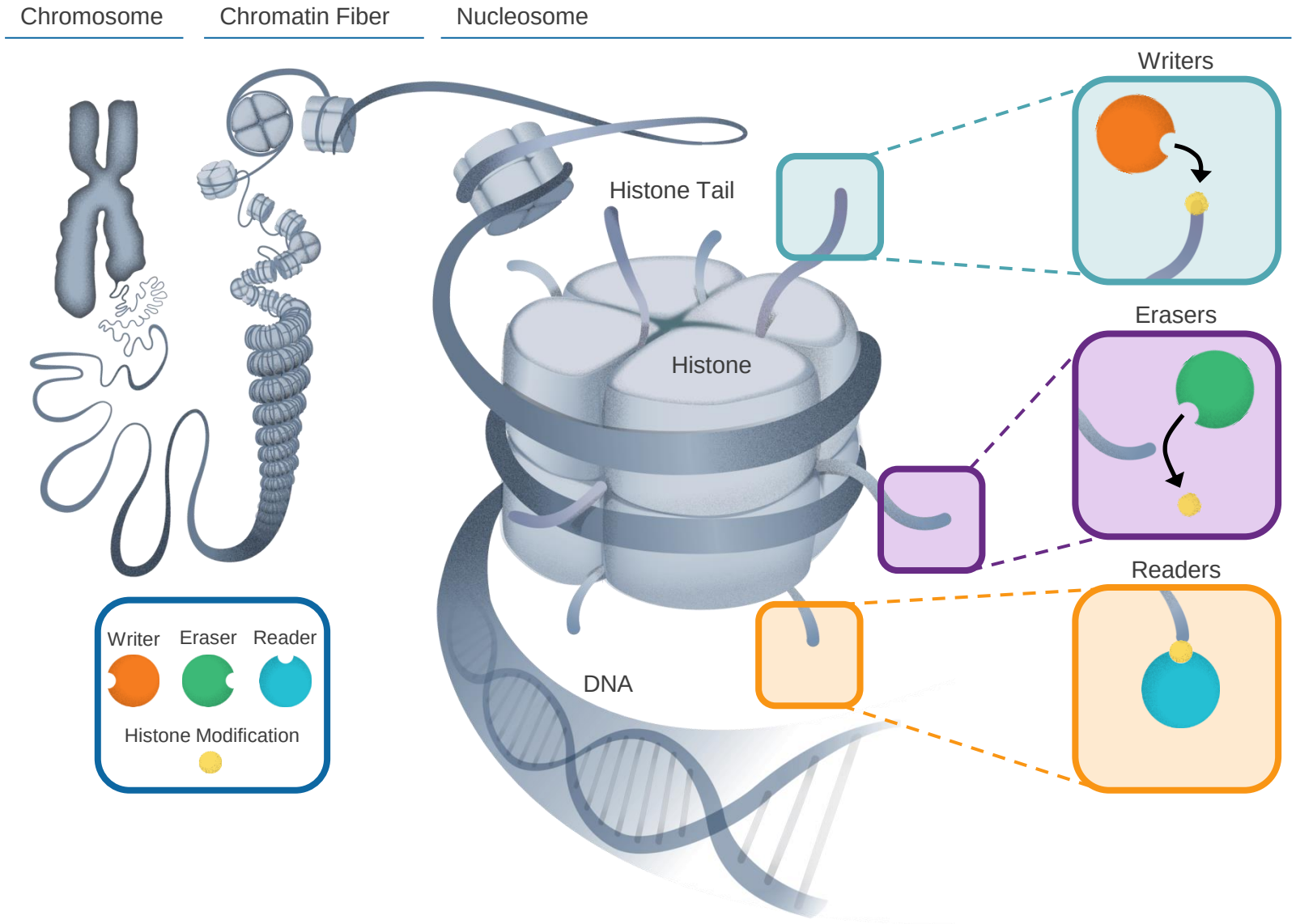
Protein Inhibition

Reducing or blocking the activity of **one** disease protein by using an inhibitor or antibody

Almost all **current therapeutics** function via protein inhibition

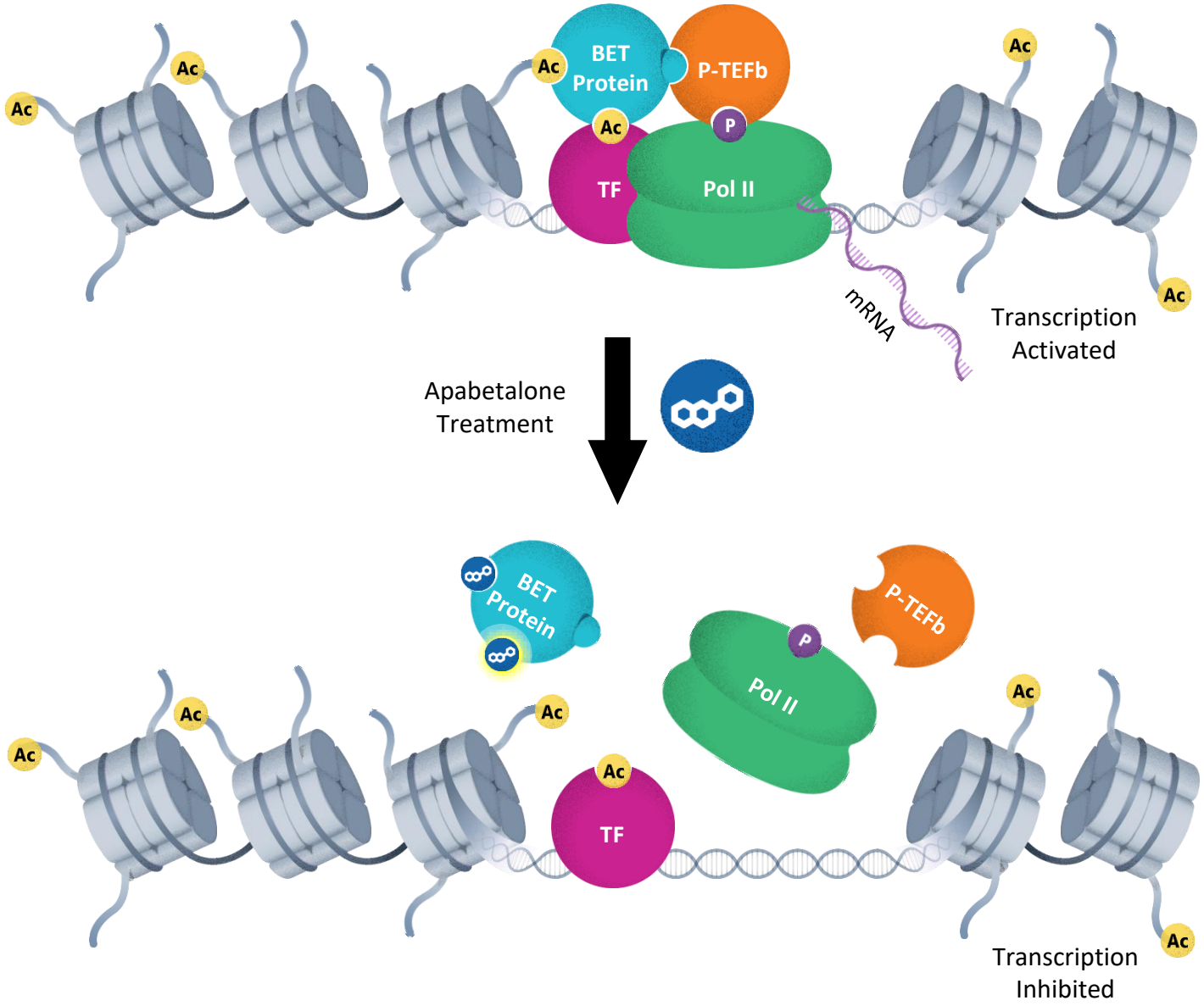
BETonMACE: Background & Rationale

Epigenetics Regulate Gene Activity



- Epigenetics refers to **modifications** to chromatin that regulate it's activity
- Transcription is regulated by **addition, removal, or recognition** of these modification
- **Acetylation** is associated with **active transcription** regions of chromatin
- **Bromodomain and Extraterminal Domain (BET)** proteins bind to acetylated histones and recruit additional transcription factors to drive gene expression

Apabetalone Mechanism of Action



Apabetalone Impacts the Pathways that Drive Disease

Apabetalone reduces the expression of multiple components of the **complement cascade**

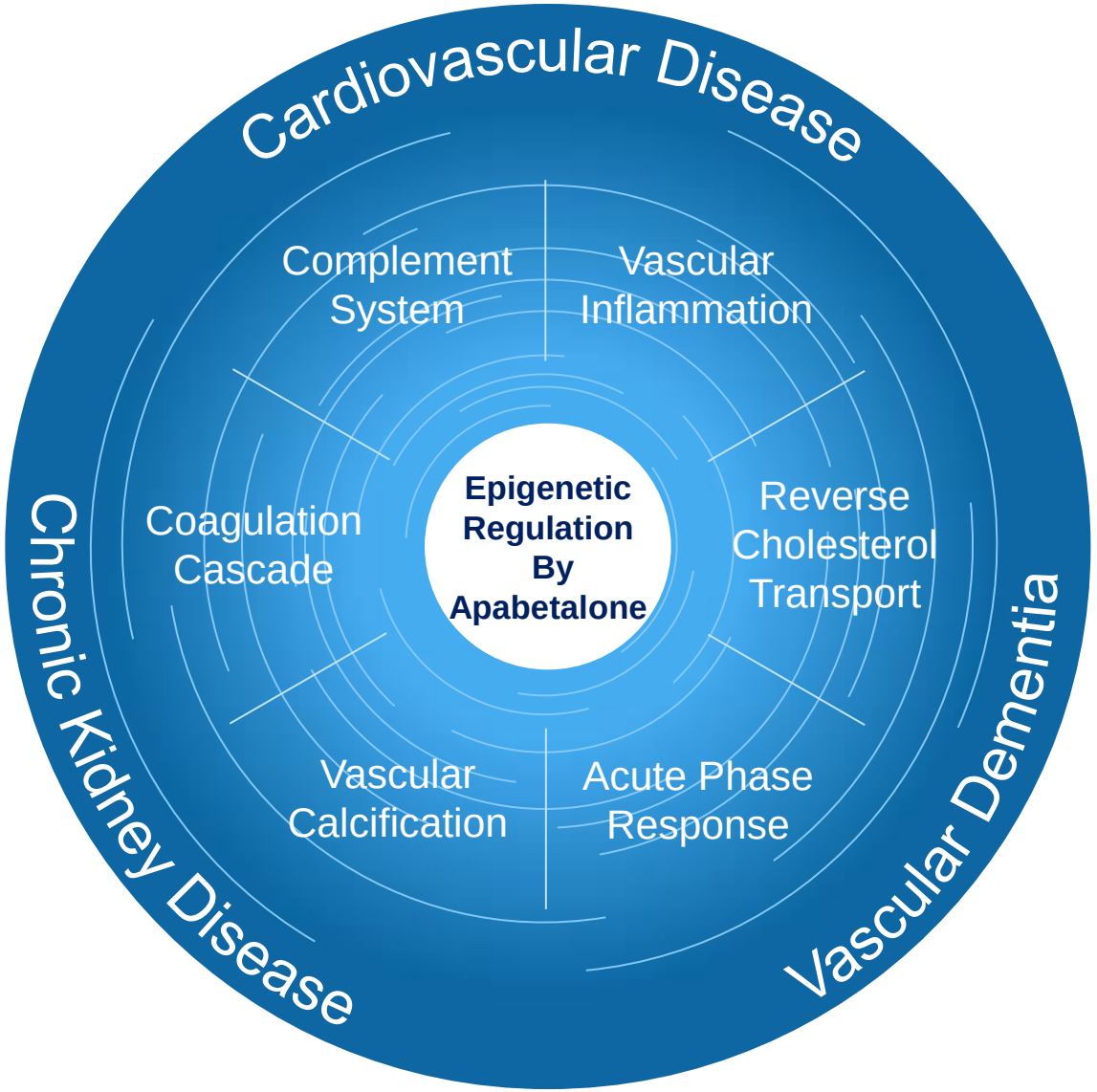
Wasiak et al. 2017

Apabetalone reduces the expression of several factors within the **coagulation system**

Wasiak et al. 2017

Levels of ALP, osteopontin and other drivers of **vascular calcification and fibrosis** are lowered by apabetalone

Gilham et al. 2019



Treatment with apabetalone **reduces mediators that drive endothelial activation**, monocyte recruitment and plaque destabilization

Tsujikawa et al. 2019

Apabetalone contributes to remodeling of the **HDL proteome and lipidome**, including increased ApoA-1 and HDL particle size

Jahagirdar et al. 2014

Apabetalone reduces markers of **systemic inflammation** including acute phase reactants

Wasiak et al. 2019 (Under Review)

Addressing Critical Unmet Needs

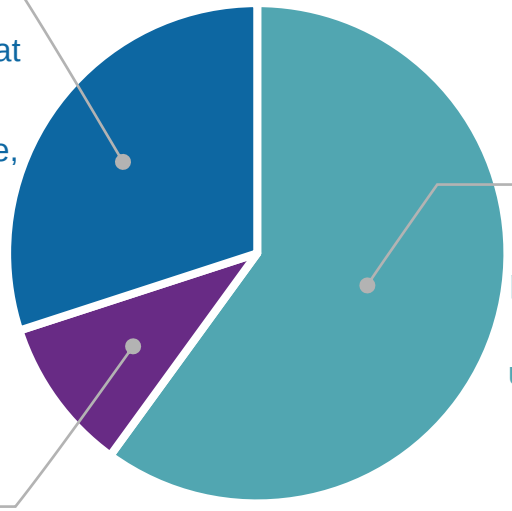
Cardiovascular Disease

Still the number one killer of both males and females and costs the US healthcare system over $500B per year

Current CVD Therapies - 30%

Statins are the top medication used to treat CVD

Despite maximized use, current therapies only manage about 30% of CVD events



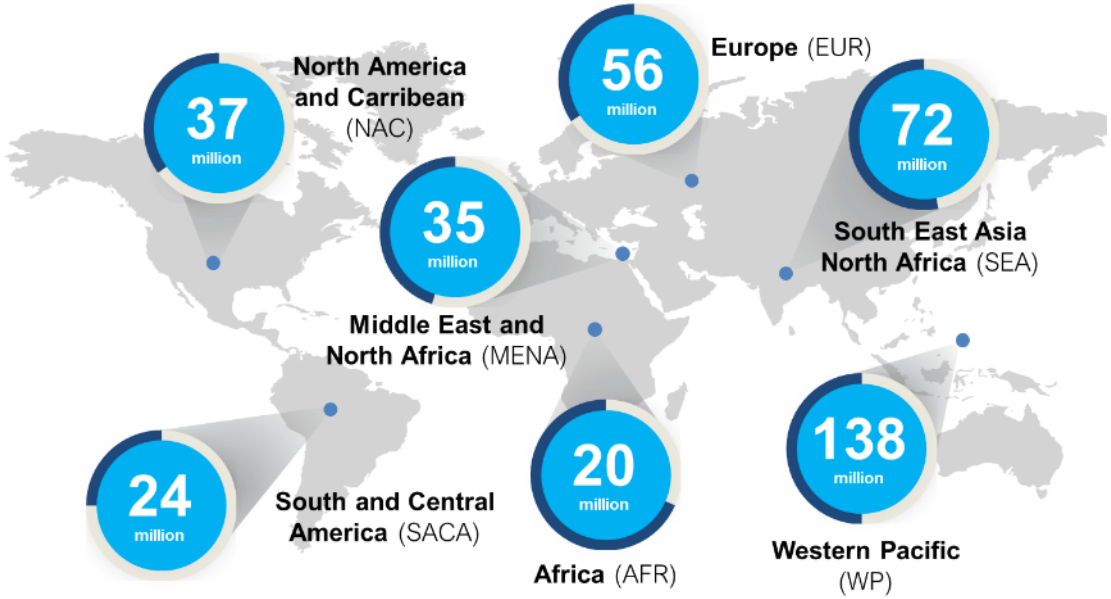
60% Opportunity

Huge market potential resides in the remaining 60% unmet need in CVD management

New LDL Modulators - 10%

Several new types of LDL modulators are in clinic. Leading are the very expensive PCSK9's

Diabetes Epidemic



Globally **382 Million** People living with diabetes

46% Undiagnosed

Diabetes prevalence; will increase by 55% in the next 30 years, with the Middle east region showing an increase of 96%.

IDF Diabetes Atlas | 6th edition