



# Leading a New Paradigm in Cardiovascular Disease Management

Investor Presentation

January, 2020

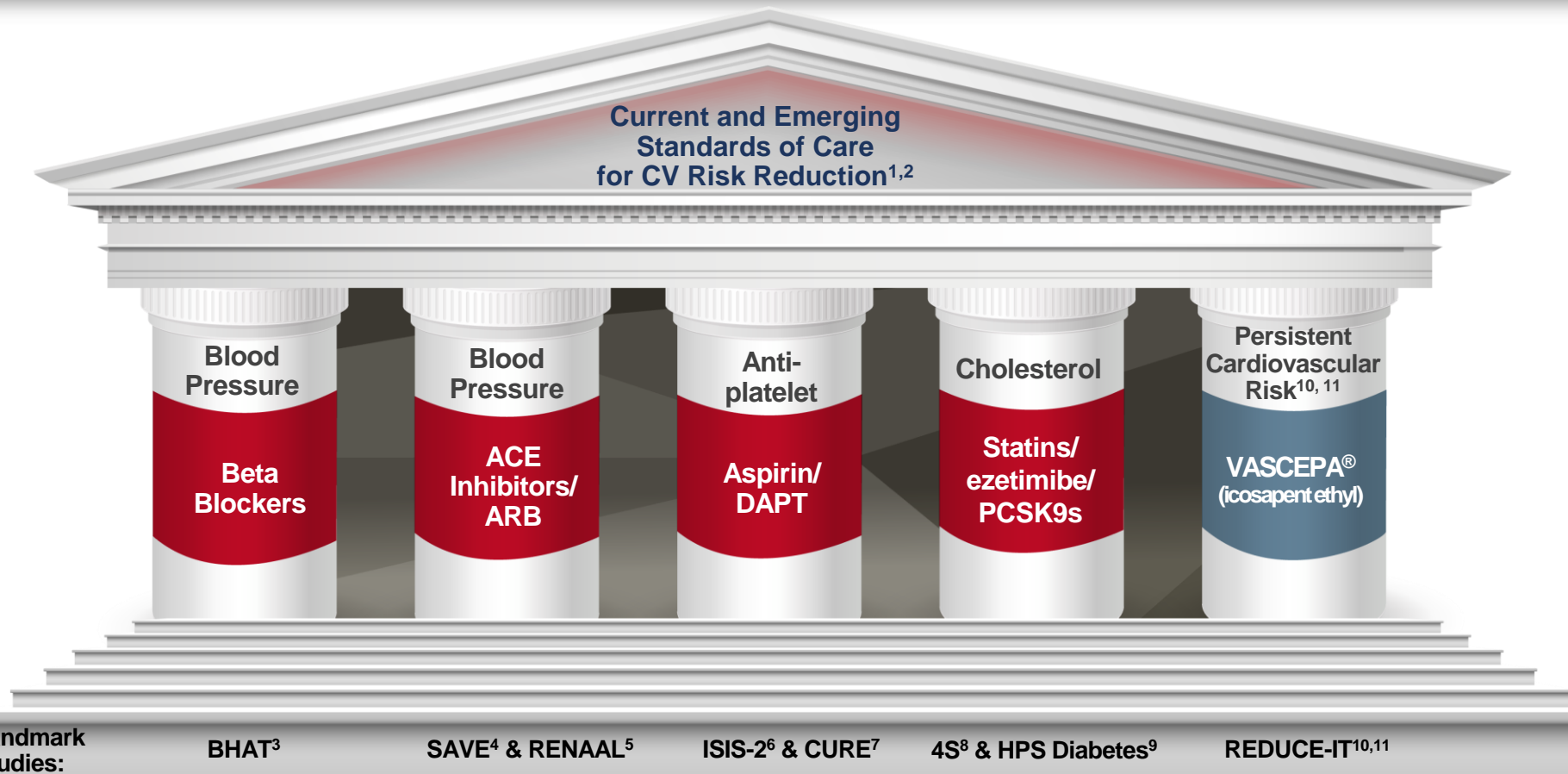
**Vascepa<sup>®</sup>**  
*(icosapent ethyl)*

## Forward-looking statements

This presentation contains forward-looking statements, such as those relating to the commercial potential of VASCEPA<sup>®</sup>, clinical and regulatory efforts and timelines, potential regulatory approvals, intellectual property, cash flow, and other statements that are forward-looking in nature and depend upon or refer to future events or conditions, including financial guidance and milestones. These statements involve known and unknown risks, uncertainties and other factors that can cause actual results to differ materially. Investors should not place undue reliance forward-looking statements, which speak only as of the presentation date of this presentation. Please refer to the “Risk Factors” section in Amarin’s most recent Form 10-Q filed with the SEC and cautionary statements outlined in recent press releases for more complete descriptions of risks in an investment in Amarin.

This presentation is intended for communication with investors and not for drug promotion.

# Amarin Working to Make VASCEPA® New Standard of Care



1) Current standards of care per American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2019;139(10):e56-e66; emerging standards of care, currently in medical guidelines, include ezetimibe, PCSK9s and Vascepa (icosapent ethyl) 2) Current standards of care per Jernberg T et al. *JAMA*. 2011;305(16):1677-1684; 3) Goldstein S. *Circulation*. 1983;67(6 pt 2):153-157; 4) SAVE 7) Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. *N Engl J Med*. 2001;345(7):494-502; 8) Scandinavian Simvastatin Survival Study Group. *Lancet*. 1994;344(8934):1383-1389; 9) Heart Protection Study Collaborative Group. *Lancet*. 2003;361(9374):2005-2016, 10) REDUCE-IT Investigators. *N Engl J Med*. 2019;380(1):11-22. 11) VASCEPA® {package insert}. Bridgewater, NJ: Amarin Pharma Inc.; rev 12/2019

# Cardiovascular Disease, the Most Damaging Disease in the Industrialized World

Problem: **cardiovascular (CV) disease** is an **enormous and worsening public health burden**

Unmet Need: **urgent need** to help more patients with CV disease; **significant persistent CV risk beyond cholesterol lowering**



Solution: In Dec'19, Amarin's **VASCEPA®** (icosapent ethyl) became **first and only drug approved** by U.S. Food and Drug Administration (FDA) for a new indication to **reduce persistent cardiovascular risk beyond statin therapy** in a broad group of high-risk patients as supported by REDUCE-IT®

- **Doubling** sales force size in the United States to 800 sales representatives
- Potential to help **millions of patients** based on new FDA approved indication
- Pursuing approvals for VASCEPA **internationally**

Significant growth prior to approval: Prior to this new FDA-approved indication **VASCEPA was already approved** for important niche market and had been prescribed over 8 million times

**Advantage of Being First** but not new: potential cost-effective high share of voice coupled with existing broad formulary coverage **positions VASCEPA for growth in multi-billion-dollar market**

## 2019 unaudited results

- Net total revenue of ~\$425M, an increase of ~85% over 2018
  - Reflects upper end of prior guidance
- Cash of ~\$645M believed adequate to get to cash flow positive from VASCEPA

## 2020 guidance

- Net total revenue projected to be between \$650M and \$700M
  - Growth to be primarily from U.S. sales of VASCEPA
  - U.S. VASCEPA sales growth to be driven by new FDA-approved label and expanded promotion
  - Branded direct to consumer (DTC) promotion to heighten mid'20 after OPDP approval
  - Quarterly variability anticipated to continue, including seasonal effects particularly in Q1

## International opportunities being advanced

- Canada (partnered): Recently approved in Canada for CV risk reduction (similar to U.S.)
- Europe: regulatory review expected to be completed in Q4'20
- China (partnered): clinical trial anticipated to be completed in Q4'20
- Middle East (partnered): marketed for TG lowering in Lebanon and United Arab Emirates with regulatory review underway in other countries

## ~65-75% persistent CV risk beyond historical standard of care<sup>1</sup>

- Controlled LDL-C doesn't eliminate CV risk; persistent CV risk often remains

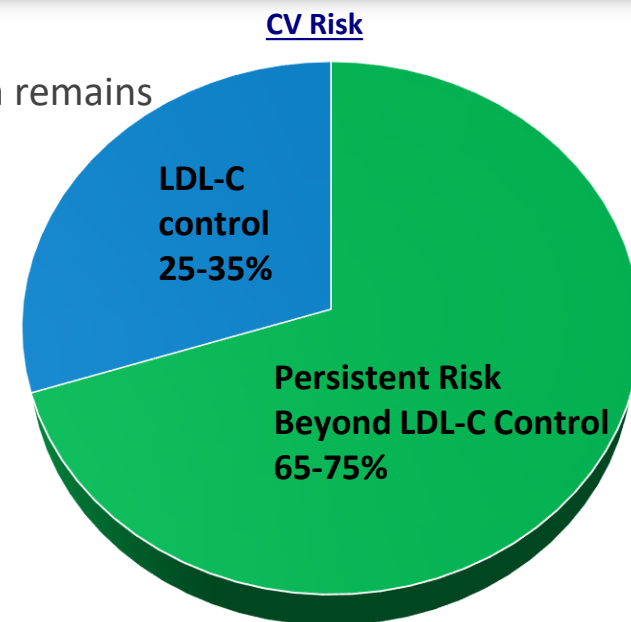
## Cardiovascular Disease: #1 cause of death in the U.S.

- One heart attack, stroke or CV death every 14 seconds<sup>2, 3</sup>
- Annual treatment cost \$555 billion; expected to double within twenty years<sup>4</sup>

## VASCEPA is first and only FDA approved therapy for treating persistent CV risk beyond statin therapy

## Millions of patients in the U.S. at risk

- ~38M patients are on statin therapy
  - ~12 million of these statin treated patients have TG  $\geq$ 150 mg/dL of whom more than half have established CV disease or diabetes and multiple risk factors
- ~4 to 8 million adults are statin intolerant and >40 million adults have high LDL-C levels and for various reasons don't take statin therapy<sup>5</sup>
  - A significant number of these statin intolerant and statin refusal patients could potentially benefit from VASCEPA



1) Ganda OP, Bhatt DL, Mason RP, Miller M, Boden WE. Unmet need for adjunctive dyslipidemia therapy in hypertriglyceridemia management. J Am Coll Cardiol. 2018. 2) American Heart Association. Heart Disease and Stroke Statistics – 2019 Update: A Report from the American Heart Association. Published Jan. 31, 2019. 3) American Heart Association: Heart Disease and Stroke Statistics -2019 At-a-Glance. 4) AHA: Cardiovascular Disease: A Costly Burden for America — Projections through 2035.htm, Jan. 20, 2017 [http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm\\_491543.pdf](http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_491543.pdf) 5) Newman, CB, Priess, D, FRCPath, et al. Statin Safety and Associated Adverse Events- A Scientific Statement From the American Heart Association. Feb. 2019

## VASCEPA has been robustly studied for more than a decade

- Clinical effects of VASCEPA are unique and can't be generalized to any other product
  - Multiple drugs from other companies have been studied and failed to show similar benefit

## Approved indications for VASCEPA in U.S.

- New indication (as of Dec'19):
  - “as an adjunct to **maximally tolerated statin therapy** to **reduce the risk of myocardial infarction, stroke, cardiovascular revascularization, and unstable angina requiring hospitalization** in adult patients with elevated triglyceride (TG) levels ( $\geq 150$  mg/dL) and
    - **established cardiovascular disease or**
    - **diabetes mellitus and 2 or more additional factors for cardiovascular disease**”
- Prior and continuing indication:
  - “as an adjunct to diet to reduce **TG levels** in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia”

## Broadly defined new indication enables broad physician discretion

- “Maximally tolerated statins” includes statin treated and statin intolerant patients
- “Established CV disease” includes patients with prior CV event (e.g., stroke, heart attack, revascularization) plus patients with coronary artery disease, peripheral artery disease, carotid disease and/or cerebrovascular disease
- “Diabetes mellitus” includes Type 1 and Type 2 diabetes; “two additional risk factors” could be any of age, obesity, hypertension, smoking history, low HDL, family history, renal dysfunction and other commonly accepted risk factors for CV disease



## REDUCE-IT Safety summary

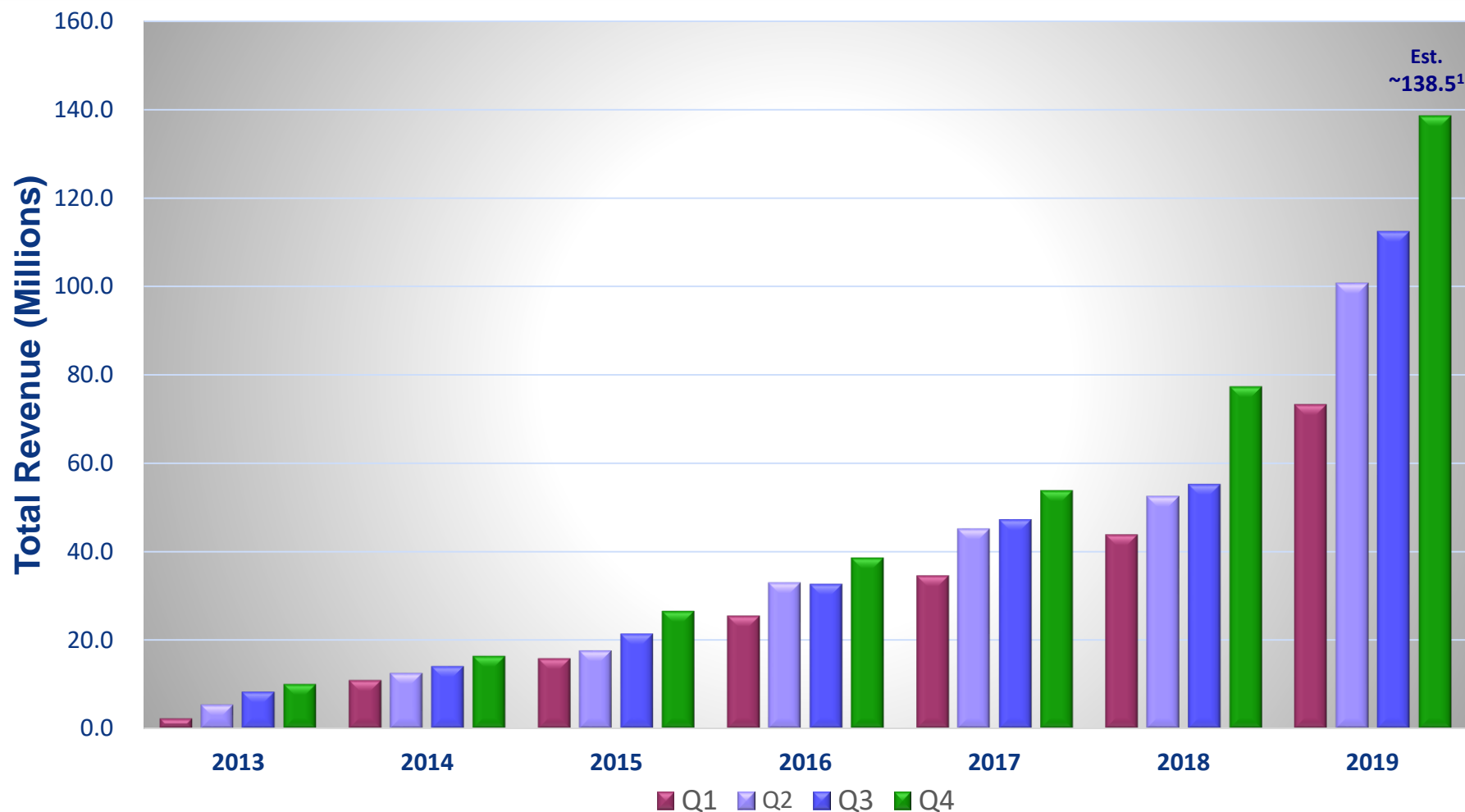
- Overall adverse event rates similar for both VASCEPA and placebo patients
  - Numerically more serious adverse events related to bleeding in VASCEPA patients (2.7% vs 2.1%)
  - Statistically, a significantly higher rate of hospitalization for atrial fibrillation or flutter in VASCEPA patients (3.1% vs 2.1%)

## Contraindications, Warnings, Precautions and AEs summary from FDA-approved label

- In cardiovascular risk patients, VASCEPA associated with increased risks:
  - Atrial fibrillation/flutter requiring hospitalization (3% vs 2%), particularly in patients with history of afib/flutter; and
  - Bleeding (12% vs 10%), with a greater incidence in patients on concomitant antithrombotics (e.g., aspirin, clopidogrel or warfarin)
- Unknown potential for allergic reaction in those allergic to fish or shellfish (not seen in REDUCE-IT or prior trials); as is typical for any drug product, VASCEPA would be contraindicated in patients with known sensitivity to VASCEPA or any of its components
- Common adverse reactions in REDUCE-IT (incidence  $\geq 3\%$  and  $\geq 1\%$  and more frequent than placebo) – musculoskeletal pain (4% vs 3%), peripheral edema (7% vs 5%), constipation (5% vs 4%), gout (4% vs 3%) and atrial fibrillation (5% vs 4%)



# Quarterly Total Net Revenue Growing; Data Primarily *Before* New FDA-Approved VASCEPA Indication



<sup>1</sup> 2019 unaudited results based on 2019 guidance revenue results at or slightly above annual net total revenue of \$410-\$425 million

- Normalized\* prescription growth of Vascepa driving increase in net total product revenue
- Seasonal factors, particularly in Q1 of each year, impact prescription levels; year over year comparisons may be most representative
- \* Normalized = 30-day supply of 4g VASCEPA daily

## Promotion transforming to CV risk reduction from niche TG lowering

- Initial feedback from healthcare professionals is positive

## Commercial expansion aligns with improved patient care

## Market experience provides foundation for growth

- Managed care coverage already broad; potential to improve
- >8M Rx for VASCEPA since launched for niche market in 2013

## U.S. launch plans underway for recently approved expanded VASCEPA label, including doubling sales force size

- Recruiting and training well underway to double US sales force size from ~400 to ~800 sales professionals in early 2020
  - Increasing U.S. physician targets to ~75k from ~50k and increasing sales call frequency
- Other promotional efforts also expanding, including plans for robust DTC promotion (subject to separate regulatory approval for branded promotion to consumers expected in mid'20)



## Broad industry relationships

- Numerous positive relationships with KOLs and industry groups
  - >100 scientific publications/posters supported in recent years; >50 in 2019 alone
  - Active in medical education programs and other forms of educational and promotional outreach
  - >100 letters written to FDA urging VASCEPA approval

## Supply capacity established and further expanding

- Multiple proven suppliers for VASCEPA
- Difficult and expensive product to learn to produce
  - Suppliers have facilities dedicated to production of VASCEPA
  - Purchasing supply in 2020 in excess of revenue guidance
    - Additional \$150 to \$200 million in supply will potentially be purchased in 2020 over 2019 levels
    - Creates added upside flexibility with little risk (supply has 4-year shelf life)



## Pricing and managed care coverage

- Seeking volume driven growth supported by affordable product pricing
  - Current pricing comparable to Lipitor® prior to it going generic; VASCEPA net pricing flat for past several years
  - Volume anticipated to grow based on new FDA approved label, expanded sales force and other promotion
- Managed care coverage has historically been good
  - Seeking to further improve coverage with affordable price, unique FDA-approved label, real world economic data which supports high cost of patients left untreated and third-party reports of cost-effectiveness

## Medical societies recognizing importance of REDUCE-IT results

- **National Lipid Association** issued new position statement recommending icosapent ethyl (VASCEPA) for appropriate high and very-high-risk patients with elevated triglycerides (135-499 mg/dL) (Sep'19)
- **European Society of Cardiology** and **European Atherosclerosis Society** jointly updated patient treatment guidelines to include icosapent ethyl (VASCEPA) to address high-risk cardiovascular patients with elevated triglycerides (135-499 mg/dL) (Sep'19)
- **American Heart Association** issued Scientific Advisory recognizing that elevated triglycerides may be a causal factor for CVD; that dietary supplements are not recommended, nor FDA approved, to treat medical conditions and that positive outcomes results were demonstrated in REDUCE-IT (Aug'19)
- **American Diabetes Association's** Standards of Medical Care updated to recommend that icosapent ethyl be considered for patients with diabetes and atherosclerotic cardiovascular disease or other cardiac risk factors on a statin with controlled LDL-C, but with elevated triglycerides (135-499 mg/dL) to reduce CV risk (Mar'19)

## Analyses show VASCEPA to be cost effective

- An independent drug price watchdog group, Institute for Clinical and Economic Review (ICER), released report that shows VASCEPA as cost effective for CV risk reduction (Oct'19)
- New analysis determined Icosapent Ethyl (VASCEPA) is highly cost-effective in patients from the REDUCE-IT study, and may even demonstrate cost-savings in the majority of simulations (Nov'19)

## Cardiovascular outcomes study results published in leading medical journals

- *The New England Journal of Medicine*
- *Journal of American College of Cardiology*
- *Circulation*

# VASCEPA CV Risk Reduction Has No Approved Competitors and Compares Well with Other Therapies



## VASCEPA number needed to treat (NNT): 21 for primary endpoint

- Low NNT combined with affordable price of VASCEPA should support continued broad managed care coverage
- For context, NNTs for other notable, but not competitive with VASCEPA, drugs:
  - Atorvastatin (Lipitor®)<sup>1</sup>: 45
  - Evolocumab (Repatha®)<sup>2</sup>: 67
    - No head-to-head study with these drugs
    - Study periods and study populations differ

## ~1 fewer MACE per 6 patients treated in total event analysis<sup>4</sup>

- Result helpful in pharmacoeconomic analysis

VASCEPA®  
REDUCE-IT<sup>3</sup>  
2018

20%  
CV Death<sup>3</sup>

25%  
RRR MACE<sup>3</sup>

21 NNT<sup>3</sup>

1) LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005; 352: 1425–35. 2) Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med*. 2017;376:1713. 3) Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med*. 2018. 4) Bhatt DL, Steg PG, Miller M, et al. Effects of Icosapent Ethyl on Total Ischemic Events: From REDUCE-IT. *J Am Coll Cardiol* 2019. epub ahead of print. <http://doi.org/10.1016/2019/03/01/j.jacc.2019.02.032>

# VASCEPA Demonstrated Largest CV Risk Reduction of Any Drug on Top of Statin Therapy



Endpoint	Relative Risk Reduction (RRR) on top of statin therapy	P-value
Primary Endpoint (5-point MACE)	↓ 25%	0.00000001
Key Secondary Endpoint (3-point “Hard” MACE)	↓ 26%	0.00000006
CV Death	↓ 20%	0.03
Heart Attack (Fatal or Nonfatal)	↓ 31%	0.0000005
Stroke (Fatal or Nonfatal)	↓ 28%	0.01

**“Icosapent Ethyl represents one of the most important developments in the prevention and treatment of cardiovascular disease since statins”**

- Deepak L. Bhatt, MD, MPH

Professor of Medicine at Harvard Medical School

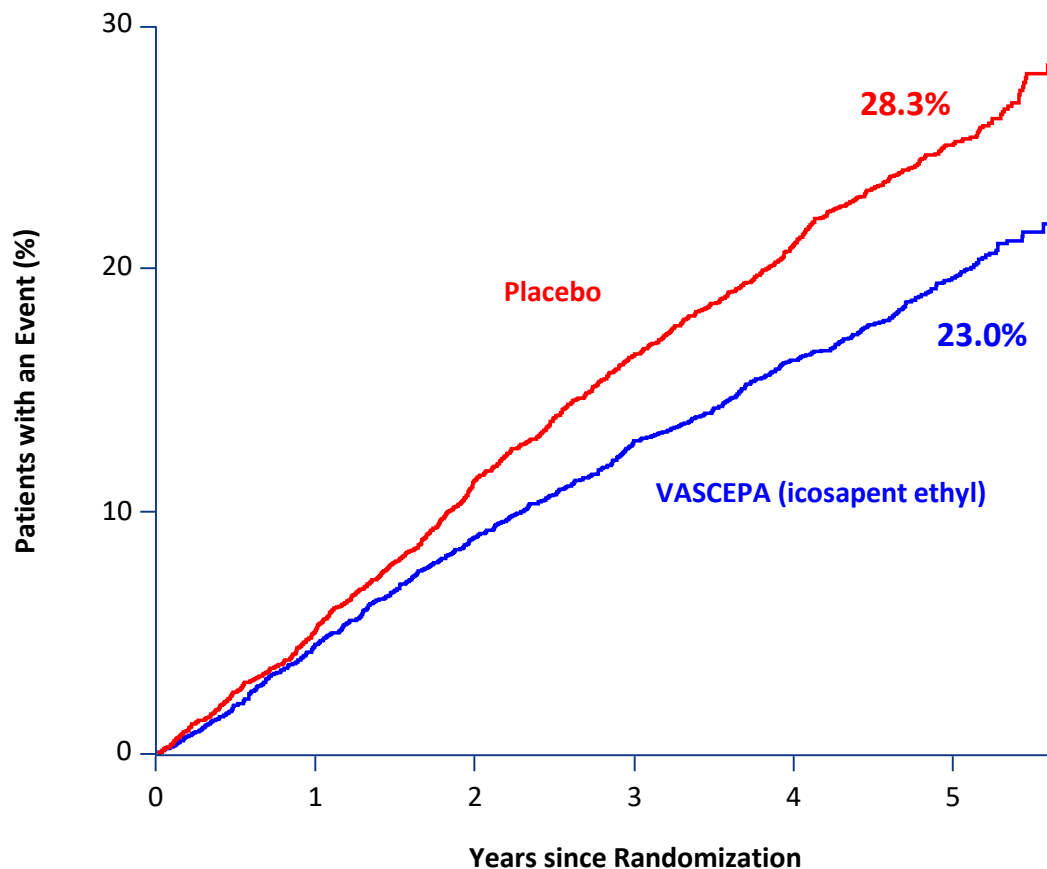
Executive Director of Interventional Cardiovascular Programs at Brigham and Women’s Hospital Heart and Vascular Center

Global Principal Investigator and Steering Committee Chair for REDUCE-IT

- Amarin advisory committee results press release November 14, 2019

MACE = major adverse cardiovascular events

# CV Event Curve for Primary Endpoint Separated at ~1 Year and Remained Separated Throughout Follow-up Period



**Hazard Ratio, 0.75**

(95% CI, 0.68–0.83)

**RRR = 24.8%**

**ARR = 4.8%**

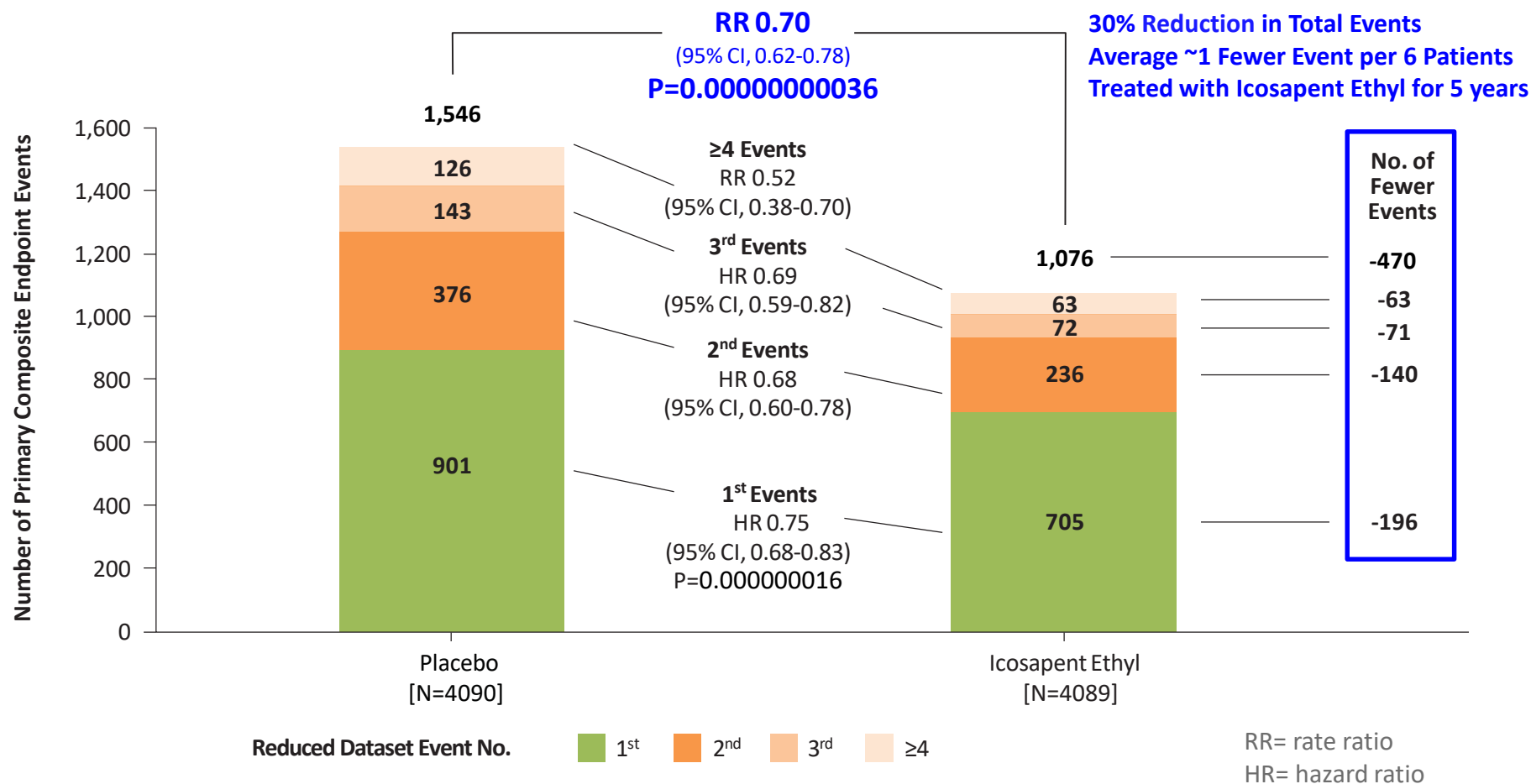
**NNT = 21** (95% CI, 15–33)

**P=0.00000001**

**CV event curve for key secondary endpoint (3-point MACE), not shown here, separated prior to 2 years and remained separated throughout follow-up period**



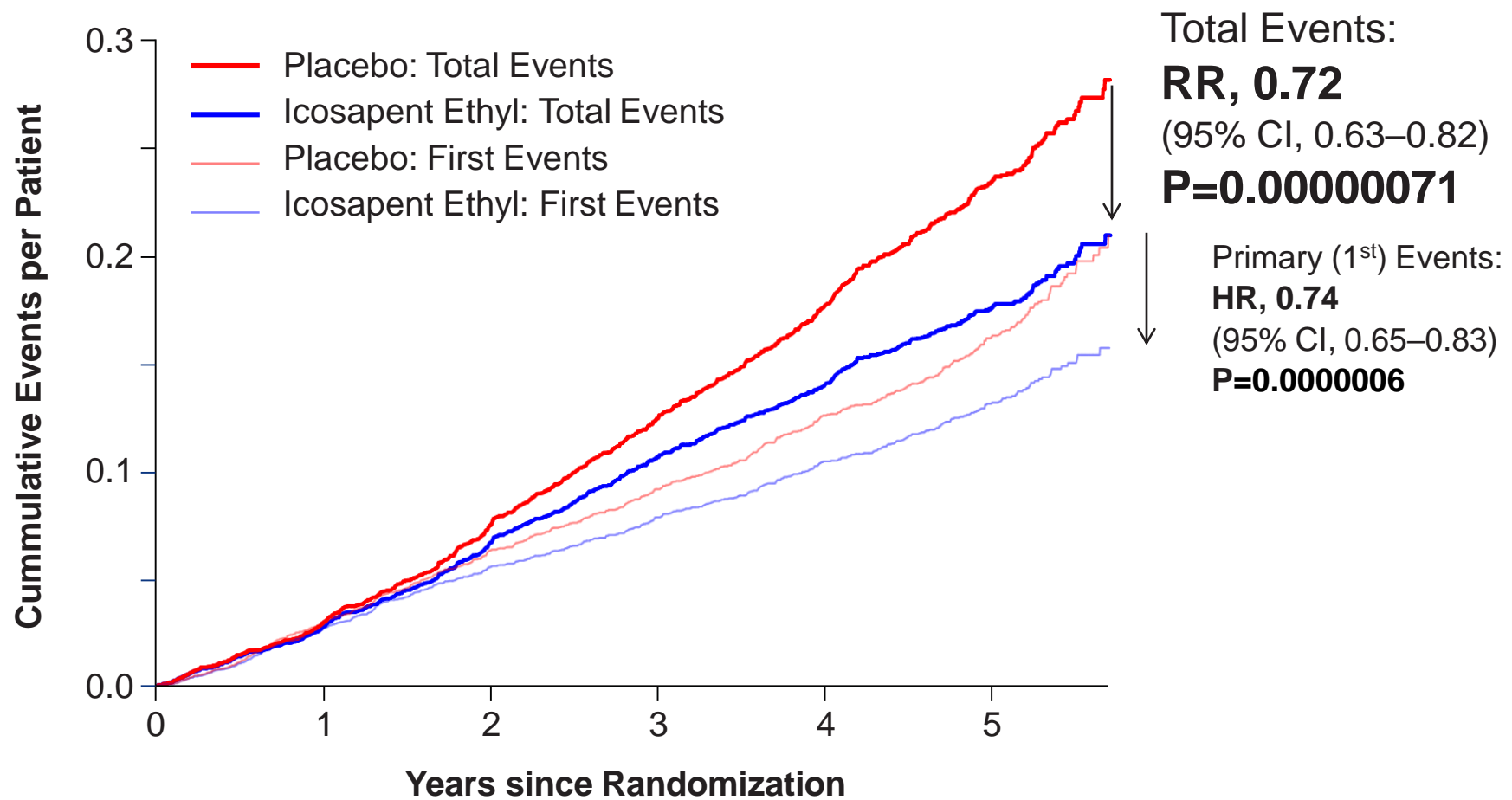
# MACE Continues to Be REDUCED Beyond 1<sup>st</sup> Events (25%, 32%, 31% and 48% for 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and ≥4th Events, Respectively)



# Total (First and Subsequent) Events

Key Secondary Endpoint (3 Point “Hard” MACE: CV Death, MI, Stroke)

Key Secondary Composite Endpoint



RR= rate ratio  
HR= hazard ratio

# 25% RRR on Top of Controlled LDL-C is Landmark Result

Class	CVOT	Relative Risk Reduction (RRR)	Positive CVOT	Peak Net Sales in U.S.
STATIN THERAPY				
Statins	Various	25-35%	✓	>\$20B - 2016
OTHER LDL-CHOLESTEROL LOWERING DRUGS <u>ON TOP</u> OF STATIN THERAPY				
Cholesterol Absorption Inhibitors	IMPROVE-IT	6%	✓	\$1.8B - 2007
PCSK9 Inhibitors	FOURIER	15%	✓	Recently Launched
	ODYSSEY	15%		
OTHER DRUGS <u>ON TOP</u> OF STATIN THERAPY				
Anti-Inflammatory	CANTOS	15%	✓	N/A
Omega-3 Mixture (Lovaza 1g/d)	ASCEND/VITAL	Not Significant	✗	\$1.0B - 2013
EPA (Epadel)	JELIS	19%	✓	N/A (in Japan only)
EPA (VASCEPA)	REDUCE-IT	25%	✓	TBD

25% RRR with VASCEPA from REDUCE-IT study is largest of any therapy on top of statins  
 Many other therapies failed trying to lower CV risk (e.g., CETP inhibitors, fibrates, niacin)  
 Lipitor (atorvastatin) lowers CV risk ~25%; REDUCE-IT effect is incremental to statins

# Science of Lipid Management and Clinical Effects of Omega-3 Fatty Acids Are Complex

**VASCEPA is unique proven prescription therapy developed over 10 years at cost of >\$500M**

## **Single active ingredient EPA (eicosapentaenoic acid)**

- Unique omega-3 molecule<sup>1</sup> derived from nature
  - New chemical entity designation by FDA for VASCEPA as pure EPA
  - Purity achieved while overcoming the fragility and stability issues associated with omega-3s
- Excludes saturated fats, omega-6s and other components in fish oil
- No known drug-drug interactions<sup>1</sup>

## **EPA is smaller than DHA in length and number of double bonds that influence activities**

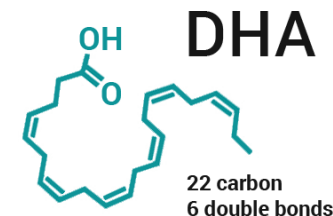
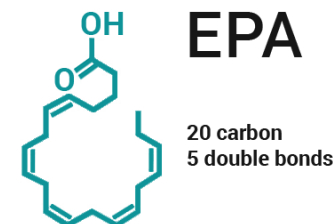
- Small molecule capable of entering and improving function of endothelial cells
- Doesn't inhibit clearance of LDL-C like DHA (docosahexaenoic acid)

## **Clinical effects of VASCEPA cannot be generalized to any other product**

- Distinction emphasized by FDA labeling and medical society recommendations

## **Omega-3s are easily oxidized or otherwise damaged**

- VASCEPA is expertly manufactured and encapsulated
- Demonstrated multi-year stability with consistent reproducibility



<sup>1</sup> VASCEPA® {package insert}. Bridgewater, NJ: Amarin Pharma Inc.; rev 12/2019

## United States

Initial indication (TG  $\geq$ 500 mg/dL)

- Teva, by agreement, may launch generic in Aug 2029
- Ongoing ANDA litigation with Dr. Reddy's and Hikma
  - Trial commencement date of Jan 13, 2020; court decision expected near end of March 2020
  - Amarin asserting and defending multiple patent claims

New expanded indication (CV risk reduction)

- Expecting 3-year regulatory exclusivity
- Multiple patents granted and being prosecuted with 2030 expiries
  - >20 of these granted patents added to Orange Book

## Europe

Pending approval, expecting

- Regulatory exclusivity for 10 years
- Patent protection from multiple patents granted and others are being prosecuted, earliest expiry date in 2033

## Canada

- Regulatory exclusivity for 8 years plus patent protection

## Rest of World

- Protection varies by country, including patents and potential regulatory exclusivity

# Capitalization Summary (Millions)

As of December 31, 2019 (Unaudited)



## Cash and Cash Equivalents

\$645

## Debt Obligations

### NOTES

\$ -

None

### ROYALTY-BEARING INSTRUMENT

\$52

10% of product revenue until fully paid

## Common Stock and Equivalent Shares

### COMMON/PREFERRED SHARES<sup>1</sup>

389

### OPTIONS AND RESTRICTED STOCK

23

### TOTAL IF ALL EXERCISED

412

## Tax Jurisdiction (primary)

Ireland

Loss carryforwards of ~\$800

<sup>1</sup> Includes 29 million common share equivalents issuable upon conversion of preferred shares



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