



# Leading a New Paradigm in Cardiovascular Health Management

Investor Presentation  
April 2019

NASDAQ: **AMRN**

*Pure EPA*  
**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 FDA approvals, intellectual property, cash flow, and other statements that are predictive in nature and that 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. For example, as with any study result, further REDUCE-IT data assessment and data release by Amarin and FDA could yield additional useful information to inform greater understanding of the trial outcome. Investors should not place undue reliance on primary data or 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-K filed with the SEC and cautionary statements outlined in recent press releases for more complete descriptions of risks in an investment in Amarin.

## Presentation is for investors (not drug promotion)

This presentation is intended for communication with investors only.

Nothing in this presentation should be construed as promoting the use of Amarin’s product or product candidates.

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

Unmet Need: **urgent need** to help more patients with CV disease; **lowering cholesterol alone is not enough**



Solution: **Landmark positive CV outcomes trial results** of Amarin's **Vascepa®** shows it can effectively and safely lessen this enormous CV health burden

- Landmark global outcomes study **positions Vascepa to become first drug to cost-effectively help address residual CV risk beyond cholesterol management**
  - Unprecedented results presented at AHA and published in NEJM in Nov'18
- Amarin pursuing **expanded label and promotion for Vascepa** based on recent outcomes study results from REDUCE-IT™ trial and sNDA submission

Current Label: **Vascepa is already approved** for important niche market of treating patients with very high triglyceride levels  $\geq 500$  mg/dL

**Advantage of Being First** but Not New: potential cost-effective high share of voice coupled with existing broad formulary coverage **positions Vascepa well for growth in billion dollar market**

## Submission of sNDA to the FDA

- A supplemental new drug application (sNDA) was submitted to the U.S. FDA on Mar 28, 2019
  - Assuming standard 10-month review clock with PDUFA date near the end of Jan'20
  - PDUFA timing, including standard or priority or standard review determination, likely to be clarified by FDA by mid-June (anticipated communication 60-74 days from submission)
  - Preparing for advisory panel which is anticipated given large patient population that Vascepa (icosapent ethyl) is seeking to address based on the unprecedented results of the REDUCE-IT study

## American Diabetes Association's Standards of Medical Care updated to reflect REDUCE-IT results

- Recommendation added 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

## European Medicines Agency (EMA) update

- EMA confirmed omega-3 fatty acid mixture products that contain DHA at a dose of 1 g/day are not effective in preventing further heart problems after a heart attack
- Negative results of recent studies of omega-3 mixtures cited as reason for EMA update
  - REDUCE-IT results have not yet been presented to EMA, Vascepa is not an omega-3 mixture

## 30% reduction in total CV events (first and subsequent) with Vascepa in REDUCE-IT study

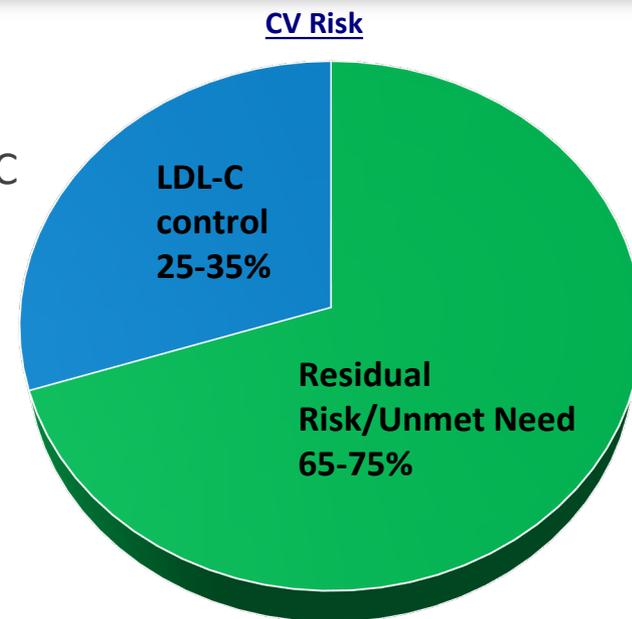
- *J Am Coll Cardiol* publication showing Vascepa benefits continue beyond first CV event
- Late-breaker presentation at the American College of Cardiology's (ACC) 68<sup>th</sup> Annual Scientific Session

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

- Controlled LDL-C does not eliminate CV risk
- Remaining residual CV risk high even with controlled LDL-C

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

- >800,000 deaths each year attributable to CV disease; more than all cancers combined<sup>2</sup>
- Annual treatment cost \$555 billion; expected to double within twenty years<sup>3, 4</sup>
- One death every 38 seconds

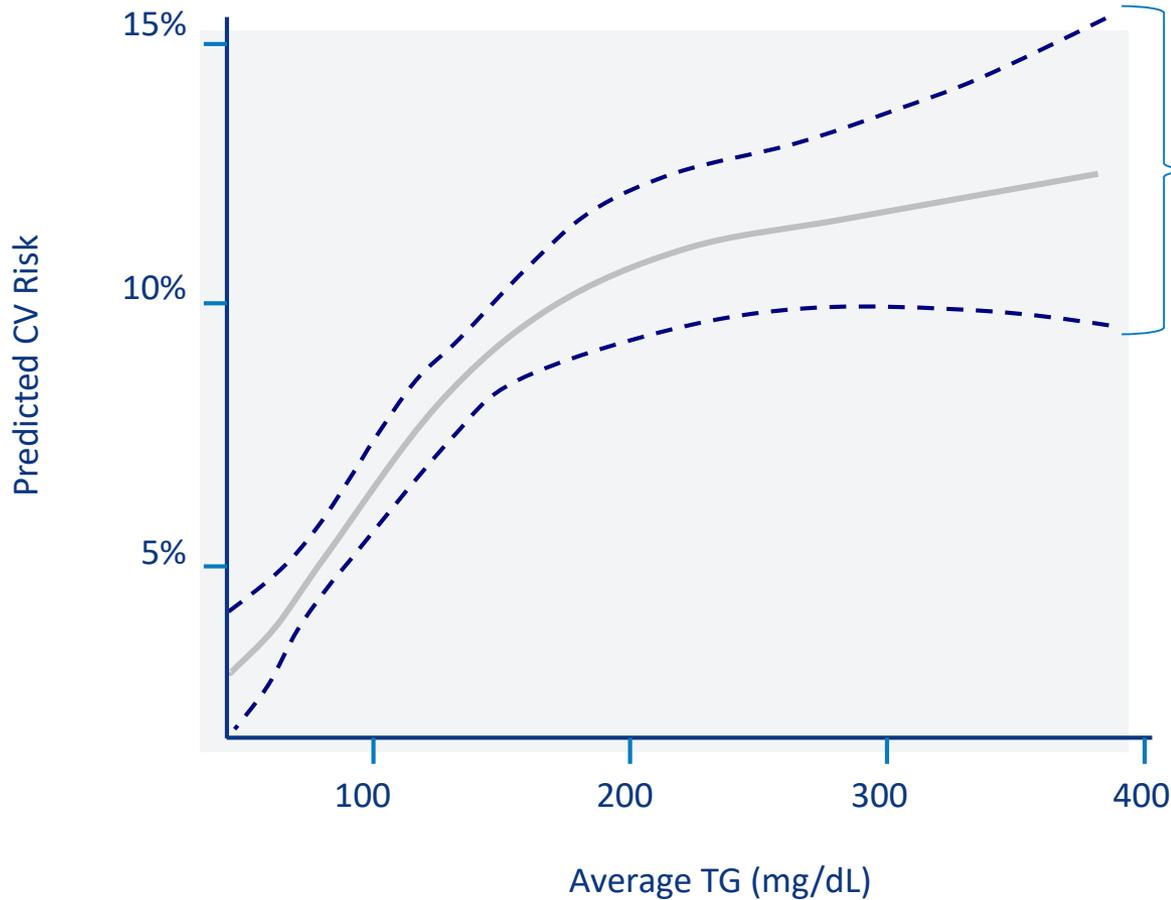


## No FDA approved therapy exists for treating CV risk in dyslipidemia patients beyond LDL-C

- ~38M patients in U.S. are on statin therapy
- >25% of adults in U.S. have CV risk factors beyond LDL-C (e.g. ~50M to 70M adults in U.S. have elevated triglycerides levels  $\geq 150$  mg/dL)
  - ~12M of these patients are already on statin therapy

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) AHA: Heart Disease and Stroke Statistics 2018 At-a-Glance 3) [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) 4) Centers for Disease Control and Prevention, <https://www.cdc.gov/nchs/fastats/leading-causes-of-death> AHA: Cardiovascular Disease: A Costly Burden for America — Projections through 2035.htm, January, 20, 2017,

# CV Risk Increases Across TG Levels up to ~150 mg/dL Above Which Risk Remains but the Relationship Flattens



Dashed lines reflect 95% confidence interval

Genetics studies support that TG levels are as well correlated to CV risk as are LDL levels

## Positive results reported in late '18 from REDUCE-IT cardiovascular outcomes study

- Evaluated Vascepa effects on statin-treated patients with residual elevated TG and other CV risks
- *The New England Journal of Medicine Journal Watch Cardiology* and the *American College of Cardiology* recognized REDUCE-IT™ results as top cardiovascular news for 2018
- Study conducted under a Special Protocol Assessment (SPA) agreement with FDA

## sNDA submitted on March 28, 2019

- Supplemental New Drug Application (sNDA) seeks expanded label for CV risk reduction
- Vascepa positioned to be first approved therapy to address above-described CV risk

## Expanding commercialization of Vascepa

- Amarin sales force at start of 2019 increased to 400 sales reps from 150 sales reps
  - Qualified promotion of outcomes study results commenced
- Further commercial expansion anticipated, including consumer promotion, after new label

## Increasing Vascepa revenues before and after REDUCE-IT results

- \$229 million in 2018 net total revenue
  - \$48.1 million growth over 2017 driven primarily by TRx growth (limited impact from REDUCE-IT on '18 revenue levels as REDUCE-IT results were presented and published late in 2018)
- \$350 million in 2019 net total revenue projected
  - Projection assumes no benefit in 2019 from expanded label

# Primary Endpoint Achieved in Vascepa Outcomes Study 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%	0.0000006
CV Death	↓ 20%	0.03
Heart Attack (Fatal or Nonfatal)	↓ 31%	0.000005
Stroke (Fatal or Nonfatal)	↓ 28%	0.01

**“This may be the biggest development in cardiovascular prevention since statins.”**

- Deepak L. Bhatt, MD, MPH

Professor of Medicine at Harvard Medical School

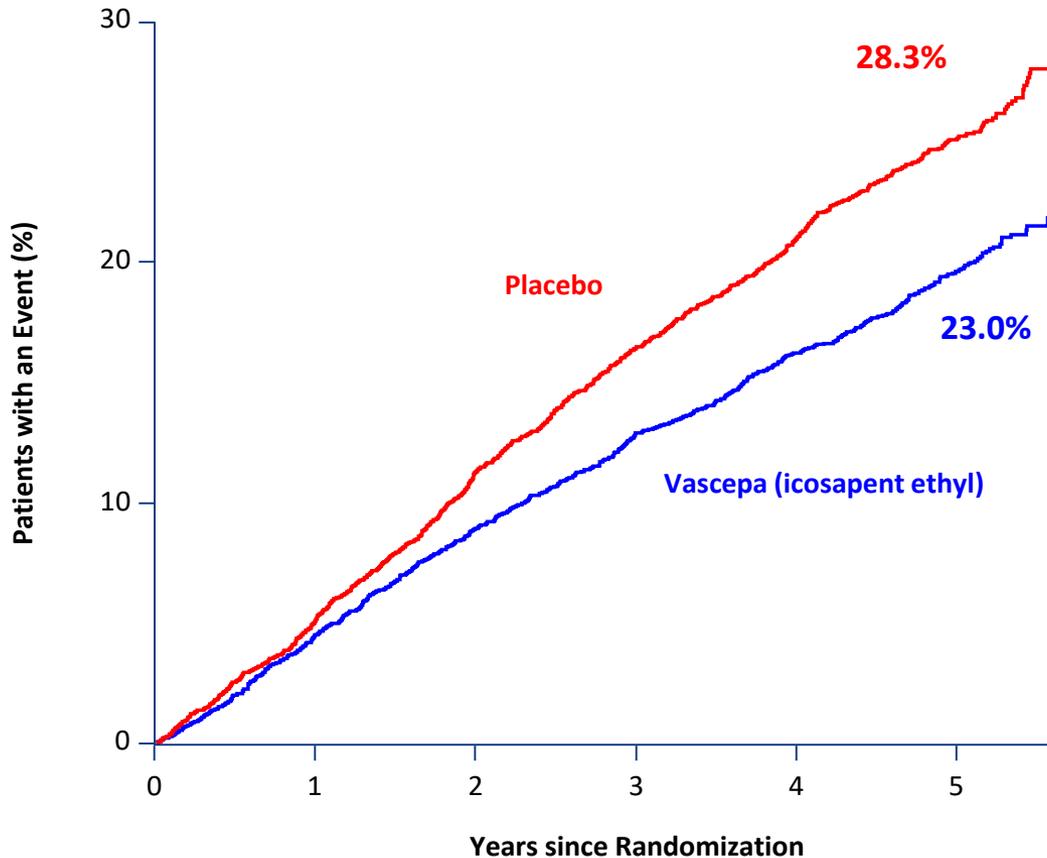
Executive Director of Interventional Cardiovascular Programs at Brigham and Women’s Hospital Heart and Vascular Center

Global Principal Investigator and Steering Committee Chair for REDUCE-IT

- Brigham and Women’s REDUCE-IT results press release November 10, 2018

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%**

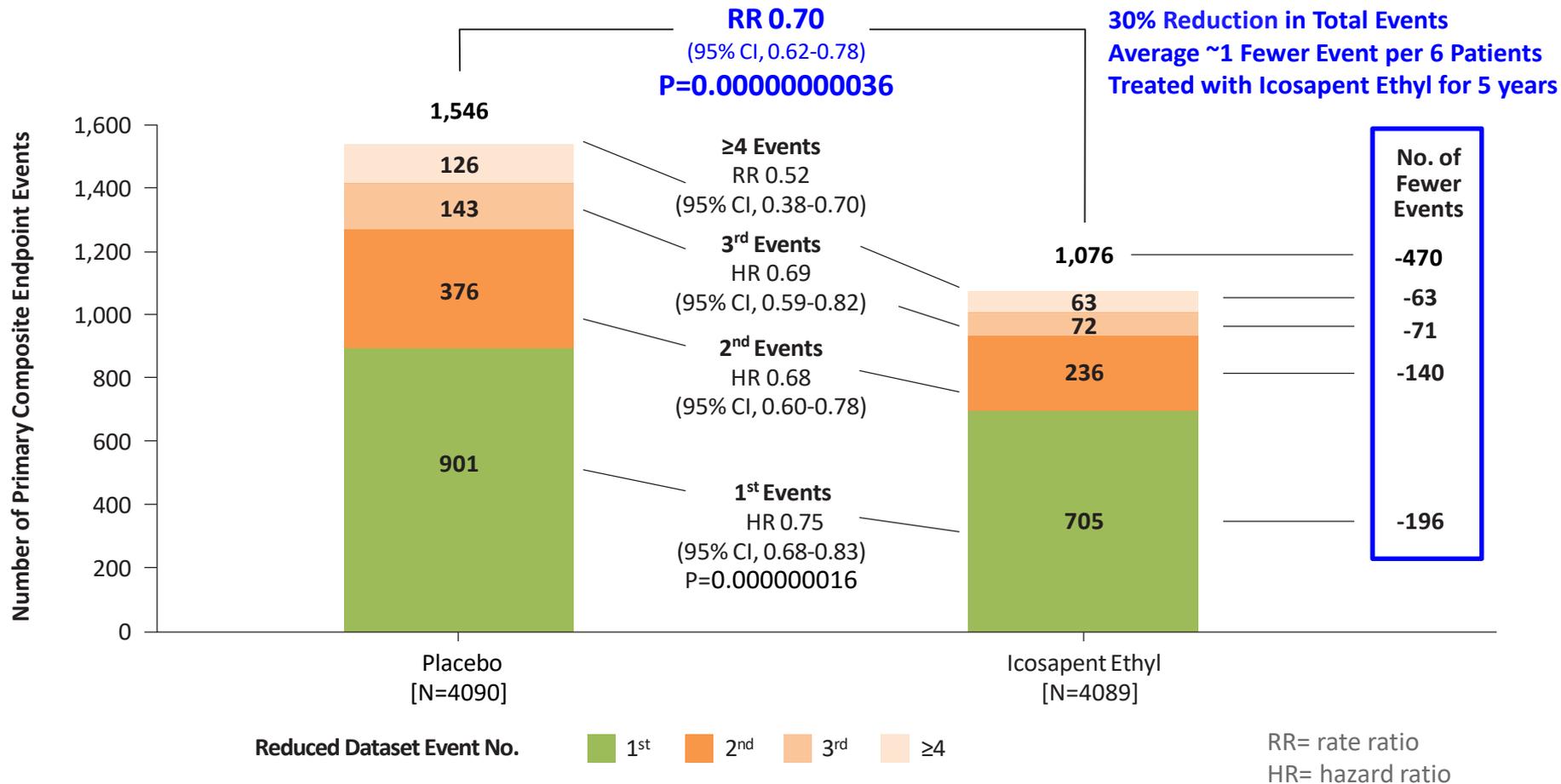
**ARR = 4.8%**

**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**

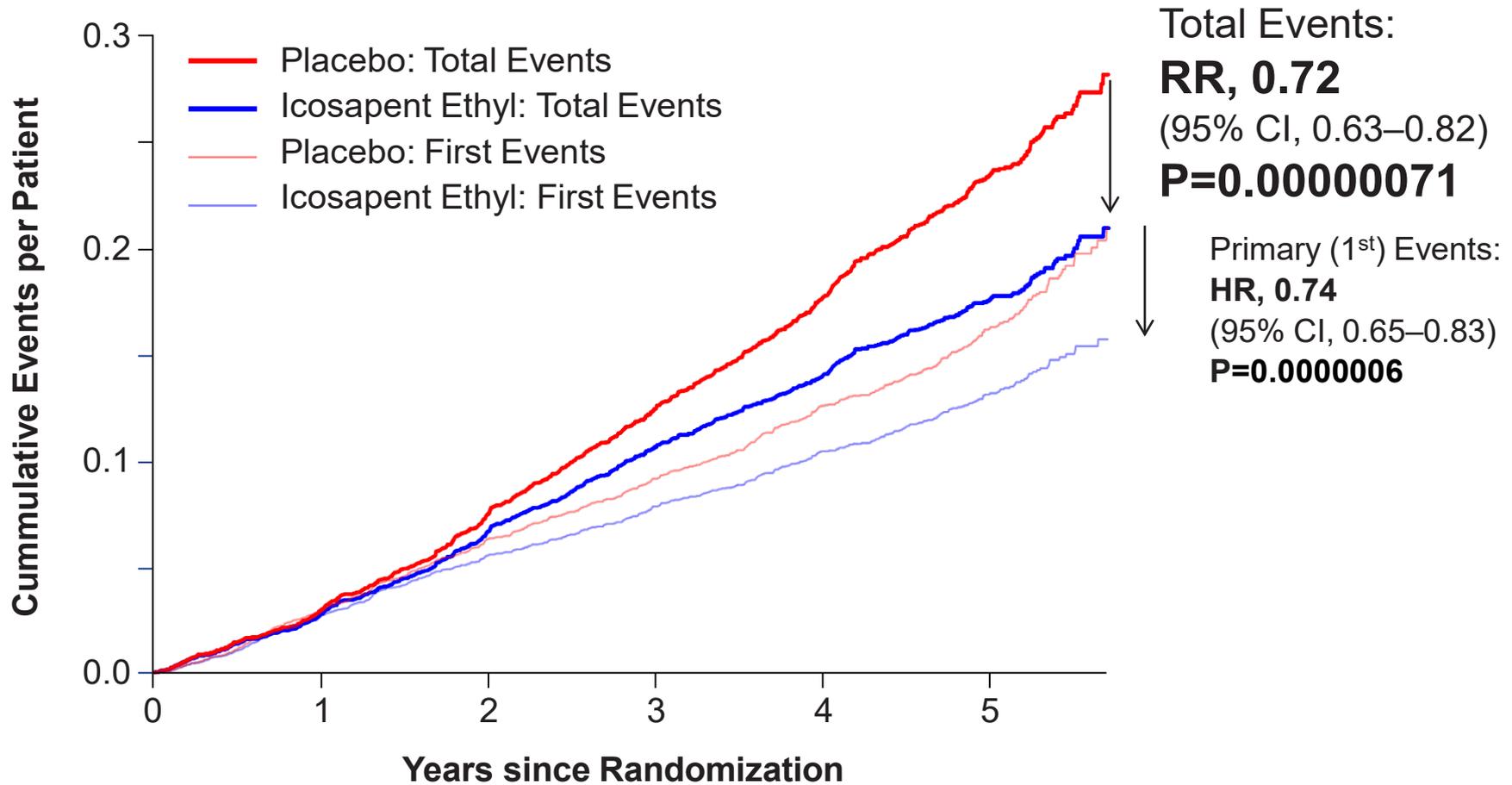
# MACE Continues to be REDUCED Beyond 1<sup>st</sup> Events (25%, 32%, 31% and 48% for 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> Events, Respectively)



# 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

## Positive results consistent across multiple subgroups including

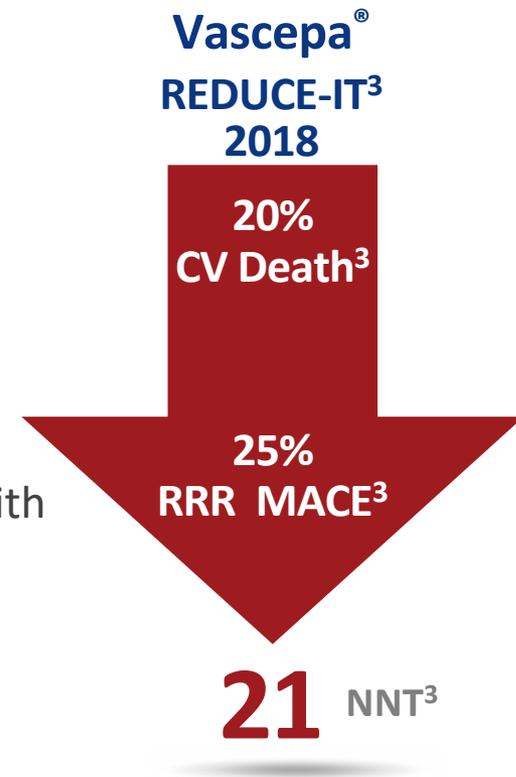
- Male/female
- Diabetes/no diabetes
- Secondary/primary prevention cohorts

## 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>®</sup>)<sup>1</sup>: 45
  - Evolocumab (Repatha<sup>®</sup>)<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 should be helpful in pharmacoeconomic analysis



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://www.onlinejacc.org/content/early/2019/03/01/j.jacc.2019.02.032>

## Reduction of CV events was similar for patients with TG levels above and below 150 mg/dL

- ~10% of patients enrolled had TG levels <150 mg/dL
- At 1 year ~36% of patients on Vascepa had TG levels <150 mg/dL
  - Primary endpoint RRR in such patients were 29% and 30% for TG  $\geq$ 150 mg/dL and <150 mg/dL

## REDUCE-IT was a clinical outcomes study not a TG lowering trial

- Median change in TG from baseline to year 1 for Vascepa vs. placebo was -19.7%
  - Similar to JELIS study, RRR exceeded TG reduction
- Median change in LDL-C from baseline to year 1 for Vascepa vs. placebo was -6.6%
  - RRR, as expected, was not likely significantly due to LDL-C modification

## Clinical effect of Vascepa cannot be generalized to any other product

- Early stage data show that Vascepa has multiple effects that extend beyond lipid-level modification including anti-thrombotic effects, anti-oxidant effects, antiplatelet or anticoagulant effects, membrane-stabilizing effects, effects on stabilization and/or regression of coronary plaque and inflammation reduction

## Overall adverse event rates in REDUCE-IT were similar across the statin plus Vascepa and the statin plus placebo treatment groups

- Overall patient population had numerous events reflecting their at-risk condition and need for medical care
- No significant differences between treatments in the overall rate of treatment-emergent adverse events or serious adverse events leading to withdrawal of study drug

## No Serious Adverse Event (SAE) $\geq$ 2% frequency and greater in Vascepa-arm

### Adverse Events (AE) greater in the Vascepa-arm, included:

- Peripheral edema (6.5% Vascepa-arm; 5.0% placebo-arm), atrial fibrillation (5.3% Vascepa-arm; 3.9% placebo-arm) and serious bleeding (2.7% Vascepa-arm; 2.1% placebo-arm)
- These events did not appear associated with increased MACE or other major issues
  - Peripheral edema increased without increase in heart failure
  - AFib increased but heart attack, cardiac arrest and sudden death each decreased >30%
  - Bleeding rates were characterized as low; no fatal bleeding assessed by investigators as related to Vascepa; no significant increases in hemorrhagic stroke, CNS bleeding or GI bleeding

# 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)
<b>EPA (Vascepa)</b>	<b>REDUCE-IT</b>	<b>25%</b>	<b>✓</b>	<b>TBD</b>

25% RRR with Vascepa 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

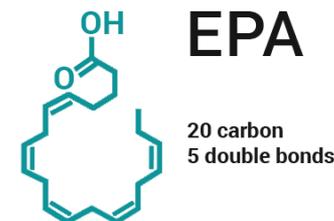
**Vascepa is unique proven prescription therapy developed over 10 years at cost of >\$500M**

## 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>

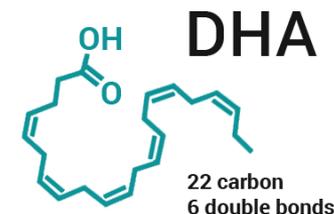
## EPA is smaller than DHA in length and number of double bonds that influence activities

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



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

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

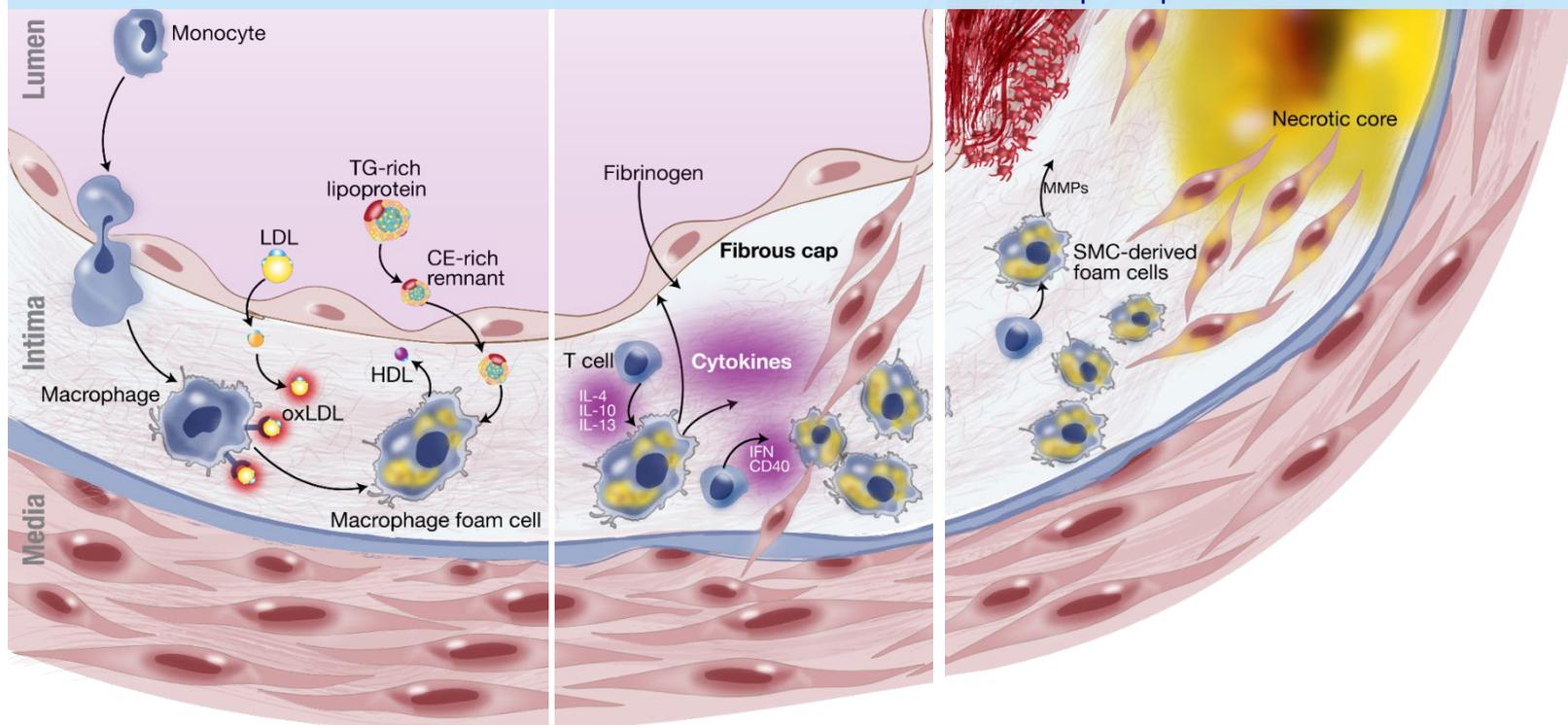


<sup>1</sup>See Vascepa® {package insert}. Bedminster, NJ: Amarin Pharma Inc.; 2017

# Mechanistic Effects of Vascepa's Active Ingredient on Multiple Atherosclerotic Processes Beyond Lipid Modification

## Multiple Processes Potentially Affected by EPA<sup>1</sup>

- Endothelial function
- Oxidative stress
- Foam cell formation
- Inflammation/cytokines
- Plaque formation/progression
- Platelet aggregation
- Thrombus formation
- Plaque rupture



The extent to which these or other pleiotropic effects of EPA may have contributed to the success of Vascepa in the REDUCE-IT study relative to other effects of EPA (e.g. lipid lowering) is under evaluation

## Priority focus on large U.S. market opportunity

## Transforming from niche to large outcomes-based opportunity

## Market experience provides foundation for growth

- Managed care coverage already broad
- >5M Rx for Vascepa since launched for niche market in 2013

## Expanding Vascepa promotion in 2019

- Expanded U.S. physician targets from ~20k to >50k
- Initial feedback from healthcare professionals regarding REDUCE-IT results broadly positive
- Targeted promotion based on Amarin's First Amendment decision and related FDA agreement reached in 2016 regarding communication of truthful and non-misleading information to healthcare professionals
  - Expand promotion further following label expansion



## Strengthening relationships

- Building relationships with KOLs and industry groups
  - >40 scientific publications/posters supported in 2018

## Supply capacity expanding

- Multiple proven suppliers for Vascepa
  - Capacity expanding to be able to support >\$1B in potential net Vascepa revenue in 2019 while actively evaluating options for further expansion

## Sustainable business

- Vascepa patents listed in the FDA's Orange Book expire in 2030
  - Teva, by agreement, may launch generic in August 2029
- NCE protection



## International expansion

- Vascepa approved for sale in Lebanon and United Arab Emirates
- Canadian partner received priority review status from Health Canada
- Regulatory approval for Vascepa in China being pursued
- Aiming in 2019 to submit application seeking approval for Vascepa in Europe
- Other geographies outside the United States to be pursued for Vascepa

## Before statin therapy

## Focus on LDL-C

Pre-Statins  
Cholesterol  
Resins

Cholesterol resins to  
LDL-C reduction to CV outcomes

STATINS  
PCSK9s  
Ezetimibe

## After statin therapy,

*modification of other lipid markers  
have not lowered CV risk*

~25% RRR on top of statins

Fibrates,  
Niacin,  
Omega-3  
Mixtures

Lipid biomarker modification (e.g., HDL,  
TGs) to CV event reduction with  
Vascepa's multiple effects

VASCEPA®

# Capitalization Summary (Millions)

As of December 31, 2018



<b>Cash and Cash Equivalents</b>	\$249
<b>Debt Obligations</b>	
NOTES	\$ - None
ROYALTY-BEARING INSTRUMENT <sup>1</sup>	\$89 10% of revenues until fully paid; no maturity date
<b>Common Stock and Equivalent Shares</b>	
COMMON/PREFERRED SHARES <sup>2</sup>	355 Preferred shares mirror common but non-voting
OPTIONS AND RESTRICTED STOCK	29
TOTAL IF ALL EXERCISED	384
<b>Tax Jurisdiction (primary)</b>	Ireland Loss carryforwards of ~\$800

<sup>1</sup> Represents face value of debt balance remaining to be paid in cash; a lower carrying value is reported for accounting purposes in accordance with U.S. GAAP

<sup>2</sup> Includes 29 million common share equivalents issuable upon conversion of preferred shares



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