



## Leading a New Paradigm in Cardiovascular Health Management

Leerink Partners Global Healthcare Conference  
February 16, 2017

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>, Amarin's product development, 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, clinical trials are inherently risky and the REDUCE-IT study may not be successful. Investors should not place undue reliance on 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 Annual Report on Form 10-K and Quarterly Report on Form 10-Q filed with the SEC for a more complete description of risks of an investment in Amarin.

## Presentation is for investors (not drug promotion)

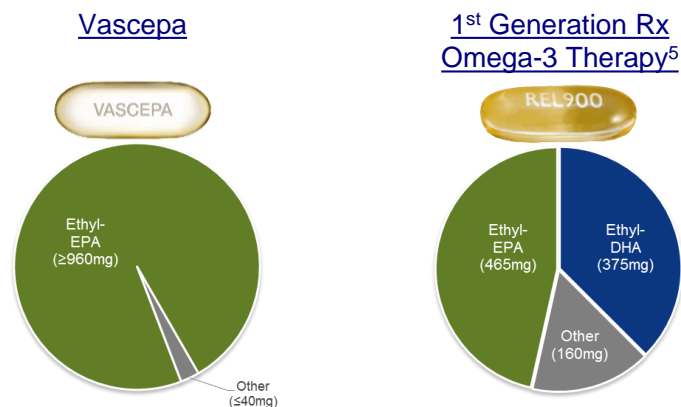
This presentation is intended for communication with investors only.

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

## Pure eicosapentaenoic acid (EPA) Vascepa

- Lowers triglyceride (TG) levels in patients with elevated TG levels
- Does not raise LDL-C (bad cholesterol)
- Favorable effect on other clinically relevant endpoints
- Safety comparable to placebo<sup>1</sup>

Both the amount and type of omega-3 fatty acid are important for TG lowering<sup>2</sup>

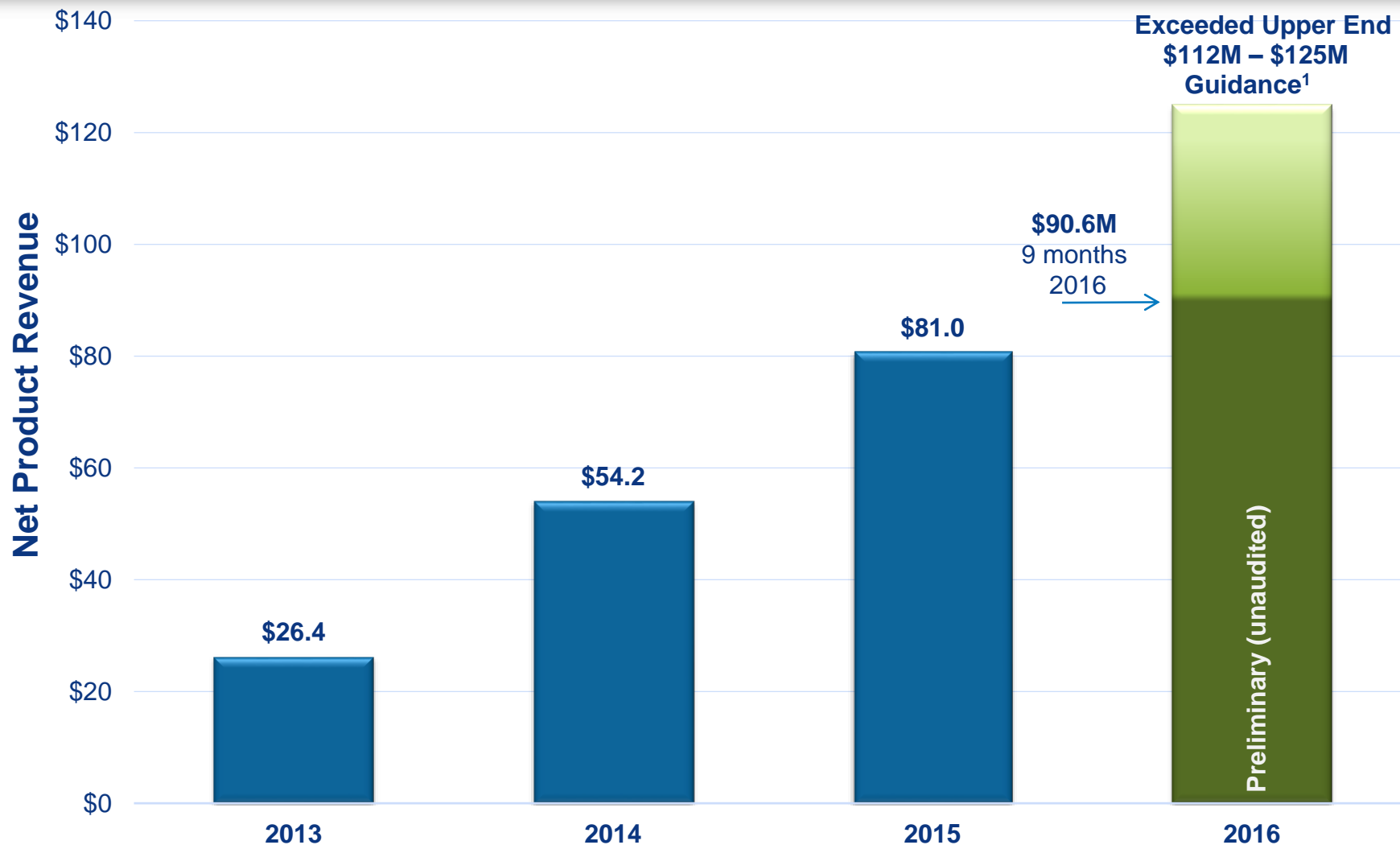


- Each 1-g capsule of Vascepa contains at least 96% EPA and no DHA<sup>3,4</sup>
  - DHA has been correlated with increases in LDL-C<sup>6,7</sup>

1. Use with caution in patients with known hypersensitivity to fish and/or shellfish. Only reported adverse reaction across the clinical profile for Vascepa with an incidence >2% and greater than placebo in Vascepa-treated patients was arthralgia (2.3% for Vascepa, 1.0% for placebo)

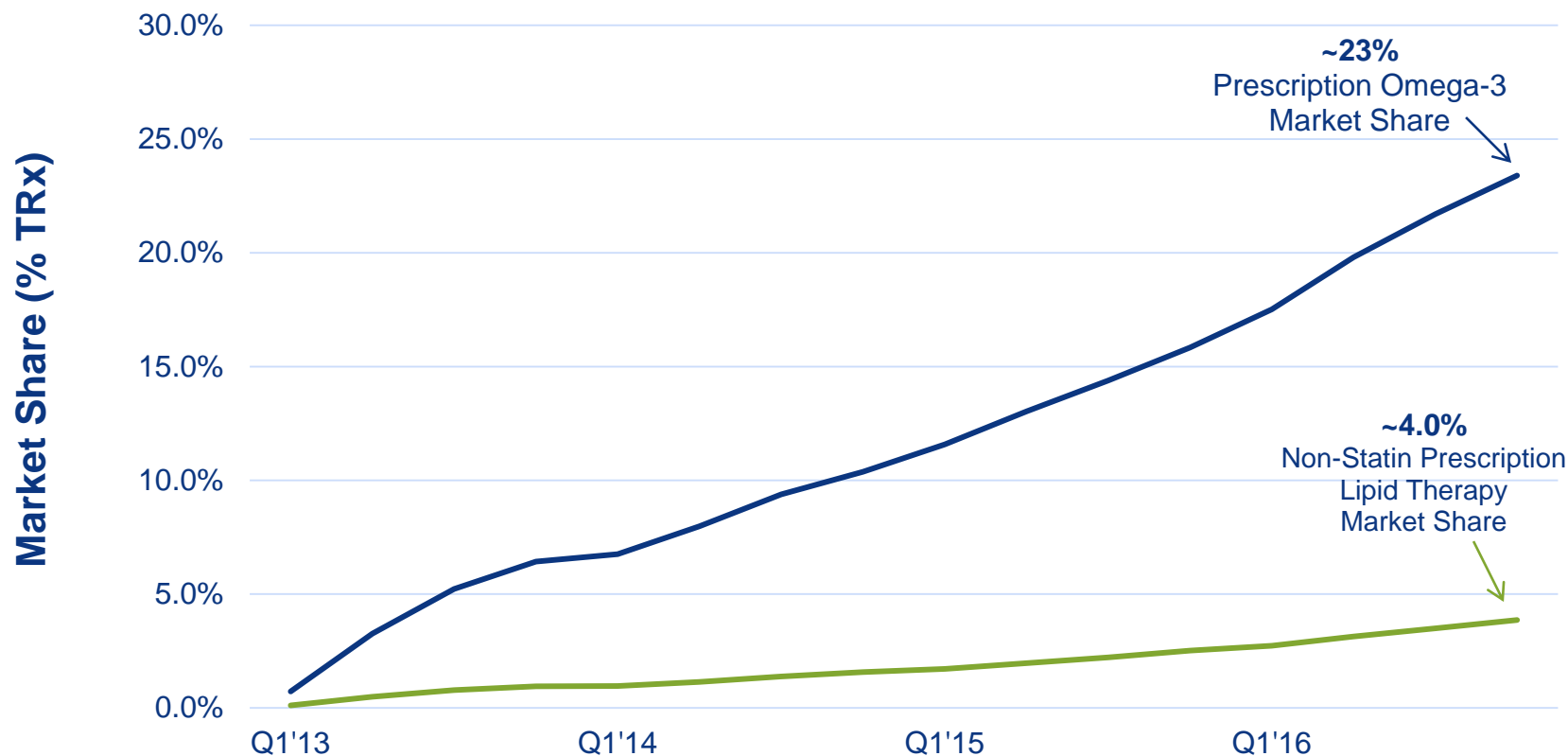
2. Miller M et al. *Circulation*. 2011;123(20):2292-2333; 3. VASCEPA [package insert]. Bedminster, NJ: Amarin Pharma, Inc; 2016; 4. Ballantyne CM et al. *Am J Cardiol*. 2012;110(7):984-992; 5. Bays HE et al. *Expert Rev Cardiovasc Ther*. 2008;6(3):391-409; 6. Jacobson TA et al. *J Clin Lipidol*. 2012;6(1):5-18; 7. Wei MY, Jacobson TA. *Curr Atheroscler Rep*. 2011;13(6):474-483. No head to head studies conducted

# Vascepa Net Product Revenues (\$Millions)



<sup>1</sup>Result for 2016 unaudited; 2016 revenues for GAAP purposes, including channel growth, estimated to modestly exceed \$125M; revenues, excluding approximately \$3-\$6 million of channel growth, are estimated to be in upper end of \$112 to \$125 million guidance range

# Vascepa Share of Market Is Growing



- Considerable growth opportunity remains
- Market share is higher in called upon targets than overall market share illustrated above

## U.S. Commercial

- Net product revenue grew >50% to exceed \$125 million (unaudited)
- Prescriptions increased by >50%; total patients on therapy >100,000
- Managed care coverage expanded to >140 million lives on tier 2 unrestricted
- Gross margin percentage increased to mid-70's from mid-60's

## International

- Added commercial partner in Middle East; advanced regulatory filings in China

## R&D

- Progressing on schedule in REDUCE-IT cardiovascular outcomes study
  - Enrollment complete at 8,175 patients
  - Nearing in H1'17 onset of 80% of targeted 1,612 primary major adverse cardiovascular events

## Cash Position and Balance Sheet

- Ended 2016 with \$98 million cash (\$112 million pro forma with Jan'17 debt restructure\*)
- Reduced debt by \$135 million (inclusive of Jan'17 debt restructure)

\*In January 2017, \$15 million in debt was paid off concurrent with the issuance of \$30 million in new debt; leading to ~\$112 million pro forma cash balance, after issuance costs

## U.S. Commercial

- Net product revenue forecast at \$155 to \$165 million; quarterly variability to continue

## International Expansion

- Clarity on China regulatory path expected from China FDA
- At least one country in Middle East expected to allow commencement of Vascepa sales

## R&D

- Onset of 1,612th primary major adverse cardiovascular event, the target for REDUCE-IT completion, expected to occur near end of 2017; results publication expected in 2018
  - Interim look at safety and efficacy (based on ~80% of events) expected in Q3'17; trial expected to continue to completion; onset of 80% of targeted 1,612 primary major adverse cardiovascular events likely in H1 2017

## Cash

- Commercial operations, excluding costs of REDUCE-IT and financing (interest & royalty), expected to be cash flow positive for full-year 2017

|  | <u>Today</u>               | <u>Post REDUCE-IT</u><br>(assumes success) |
|--|----------------------------|--|
| Approved Promotion                       |                            |  |
| Based on surrogate biomarkers            | Yes                        | Yes  |
| Based on global outcomes study           | No (none for any comp. Rx) | <b>Yes</b>                                 |
| Population covered in label <sup>1</sup> |                            |  |
| TG $\geq$ 500 mg/dL                      | Yes                        | Yes - 3.8M patients                        |
| TG 200-499 mg/dL                         | No <sup>2</sup>            | <b>Yes - 36M patients</b>                  |
| TG 150-199 mg/dL                         | No                         | <b>Yes - 30M patients</b>                  |
|  |                            | <b>70M<sup>4</sup></b>                     |
| Sales reps (U.S.)                        | 135 <sup>3</sup>           | <b>400 to 500</b>                          |

<sup>1</sup>Population data from NHANES [The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on High Blood Cholesterol In Adults (Adult Treatment Panel III) JAMA. 2001 May. 285 (19): 2486-97]; populations of TGs <500 mg/dL being studied in statin treated patients with persistent high TGs

<sup>2</sup>Current Vascepa label based on successful MARINE phase 3 study; under special agreement with FDA reached in 2016 qualified off-label promotion allowed including results of successful ANCHOR phase 3 study but label not expanded

<sup>3</sup>Current Amarin sales force targets approximately 20K physicians; additional outreach provided under co-promotion agreement with Kowa Pharmaceuticals America

<sup>4</sup>Population numbers include both patients on and not on statin therapy

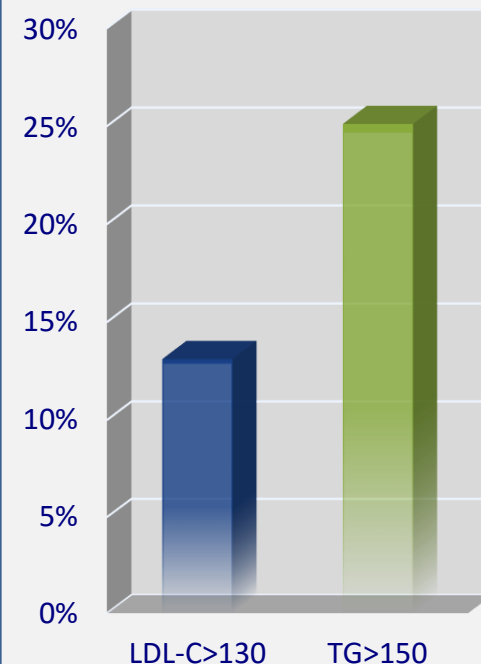


<5% of patients with elevated TGs are currently treated with prescription therapy

No prospective multi-national outcomes study ever conducted in population of patients who despite statin therapy have elevated TG levels

- Prior generation lipid lowering therapies focused on raising HDL-C (fenofibrates and nicotinic acid) or not ideally suited due to effect of raising LDL-C (fenofibrates and DHA containing omega-3) and other side effects
- Vascepa uniquely positioned for success
  - Broad favorable effect on lipids (e.g. TG levels) and lipoproteins
  - EPA has multiple other positive pleiotropic effects (e.g. anti-inflammation, reduces/slows plaque formation)
  - Safety and tolerability profile
  - Oral
  - Affordable price

**LDL-C AND TG PREVALENCE IN ADULTS (U.S.)**

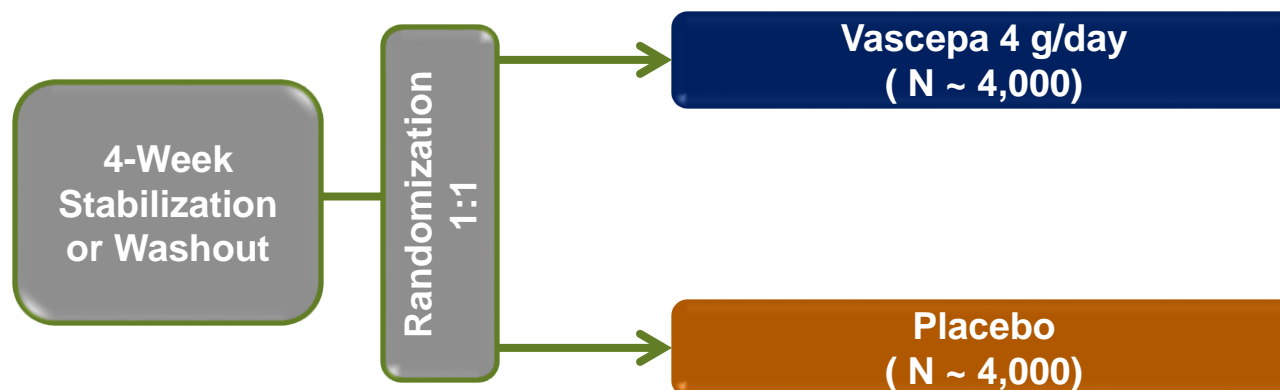


Source: NHANES 2009-2012

REDUCE-IT CV outcomes trial designed to address this void

# REDUCE-IT: Blinded Events Based Outcomes Assessment of CV Risk Reduction vs. Placebo

8,175 Patients (enrollment complete)



## Primary endpoint - time to first occurrence of composite MACE

- MACE (major adverse cardiovascular events): CV death; non-fatal MI; non-fatal stroke; coronary revascularization; and hospitalization for unstable angina (caused by myocardial ischemia, determined by invasive or non-invasive testing)
- All events adjudicated by independent, blinded, Clinical Endpoint Committee
- >30 pre-specified secondary and tertiary endpoints

## Designed under Special Protocol Assessment (SPA) agreement

## Robustly powered study designed for 90% power to detect 15% relative risk reduction

- Assumes 1,612 primary endpoint events across a 4-5 year median patient follow-up period
- As with other long term outcomes trials, actual study power may be higher or lower driven by typical factors such as the relative risk reduction observed between the treatment groups, the number of events observed at study completion and the aggregate time over which patients are studied

# Data Supporting Potential for REDUCE-IT Success

(in addition to positive Phase 3 studies of Vascepa)



## Same active ingredient (EPA) successful in JELIS, large Japanese outcomes study

- 19% reduction ( $p=0.011$ ) in CV events in overall population (which didn't have high TGs)
- 53% reduction ( $p=0.043$ ) in CV events in subgroup with TG  $\geq 150$  mg/dL and HDL-C  $< 40$  mg/dL
  - REDUCE-IT design differences vs. JELIS include: higher EPA dose; lower LDL-C enrollment target; patients from 11 countries; and enriched, persistent high TG patient population; JELIS was open label, randomized with blinded endpoint analysis; unstable angina contributed more significantly to JELIS results than expected for REDUCE-IT

## Multiple recent large genetic studies suggest TG and LDL-C levels are similar predictors of CHD

- Do et al.: genes regulating TG and LDL-C levels correlated strongly with coronary heart disease (0.40 and 0.39, respectively;  $p < 0.0001$ ) vs. HDL-C having weak correlation (0.04;  $p = 0.32$ )

## Lower TG levels correlated with lower CHD risk when LDL-C is well controlled

- PROVE-IT (Lipitor/Pravachol): Analysis of all patients well controlled for LDL ( $< 70$  mg/dL) in which patients with TG  $< 200$  mg/dL were associated with 40% lower risk of recurrent CHD events vs TG  $\geq 200$  mg/dL

## Subsets of patients in clinical outcomes studies evaluating therapies that lower TG levels have shown benefit in subset populations of patients with baseline elevated TG, despite failed trials

- ACCORD (Fenofibrate): Subgroup TG  $\geq 204$  mg/dL and HDL-C  $\leq 34$  mg/dL; MACE relative risk reduction 31%
- AIM-HIGH (Niacin ER): Subgroup TG  $\geq 200$  mg/dL and HDL-C  $< 32$  mg/dL; MACE relative risk reduction 36%

## Supportive evidence of EPA's cardio-protective mechanisms beyond TG lowering

- CHERRY study: EPA + high dose statin  $\longrightarrow$  2x plaque regression vs high dose statin alone
- Nosaka et al.: early EPA + statin post PCI  $\longrightarrow$  11% reduction in CV events vs statin alone; CV death reduced 3.4%
- Mechanistic effects of EPA have broad favorable effect on:
  - endothelial function
  - oxidative stress
  - foam cell formation
  - inflammation/cytokines
  - plaque formation/progression
  - platelet aggregation
  - thrombus formation
  - plaque rupture