



Leading a New Paradigm in Cardiovascular Health Management

Investor Presentation October, 2019

NASDAQ: AMRN



## Forward-Looking Statements and Disclaimer



#### Forward-looking statements

This presentation contains forward-looking statements, such as those relating to the commercial potential of Vascepa®, 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-Q filed with the SEC and cautionary statements outlined in recent press releases for more complete descriptions of risks in an investment in Amarin.

#### <u>Presentation is for investors (not drug promotion)</u>

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.

## Amarin Addressing Large Unmet Medical Needs



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

- Unprecedented results published in NEJM in Nov'18 and JACC in Mar'19
- Amarin's sNDA, which pursues expanded label and promotion for Vascepa based on REDUCE-IT™ outcomes study results, approaching PDUFA date Dec 28, 2019
- Landmark global outcomes study results position Vascepa to become first drug to effectively help address residual CV risk beyond cholesterol management

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** 

## Recent Highlights



#### Increased guidance for 2019 total revenue to range of \$380 to \$420 million, 66% to 83% over '18

- Increase based on acceleration in revenue growth YTD and expectations for further growth
- Total net revenue of \$174.1 million in H1 2019, including \$100.8M in Q2, 80% increase over H1 2018

#### International expansion in process

- Canada: Priority review ongoing from Health Canada towards anticipated approval before end of '19
- Europe: Submission of application seeking approval anticipated before end of '19
- Middle East: Approved in Lebanon and UAE. Additional approvals pending

#### 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)

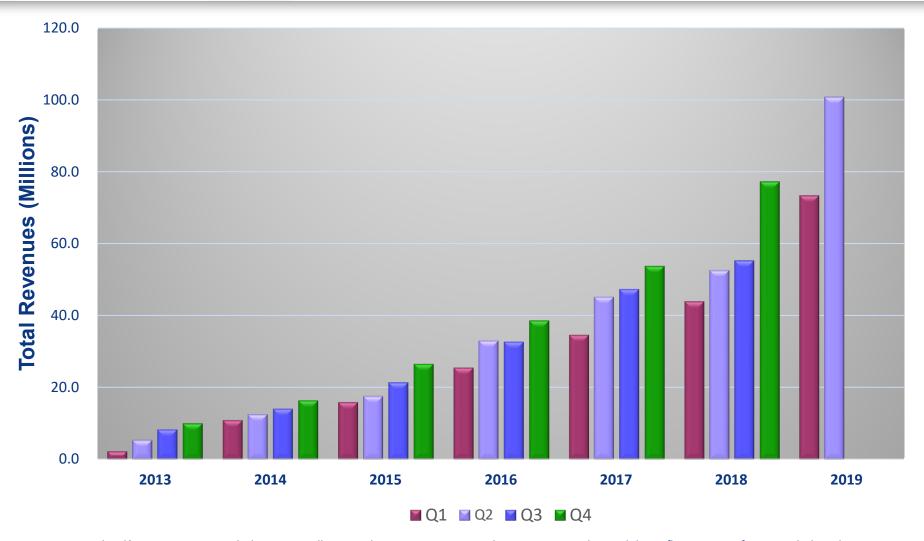
## Upcoming Milestone Targets Pursuing CV Risk Reduction Indication in U.S. Based on REDUCE-IT



Milestone	Date
ICER to issue its final report on Vascepa cost effectiveness	Oct 17 <sup>th</sup>
AdCom regarding sNDA seeking CV risk reduction indication for Vascepa	Nov 14 <sup>th</sup>
<ul> <li>Presentations at American Heart Association Annual Scientific Sessions</li> <li>Cost-effectiveness of Icosapent Ethyl in REDUCE-IT (Nov 16<sup>th</sup>)</li> <li>Effect of Icosapent Ethyl on Progression of Coronary Atherosclerosis in Patients with Elevated Triglycerides (200-499mg/dL) on Statin Therapy (EVAPORATE Study) (Nov 18<sup>th</sup>)</li> </ul>	Nov 16 <sup>th</sup> - 18 <sup>th</sup>
PDUFA date for sNDA	Dec 28 <sup>th</sup>
Launch of Vascepa for CV risk reduction (assuming label expansion)	Early '20

# Quarterly Total Net Revenue Growing from Increased Vascepa TRx in Advance of Expected Label Expansion





- Normalized\* prescription growth driving overall net product revenue increase, however, quarterly variability reflects various factors including changes in inventory levels maintained by independent wholesalers
- 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

### Large Need for CV Risk Reduction Beyond Controlled LDL-C

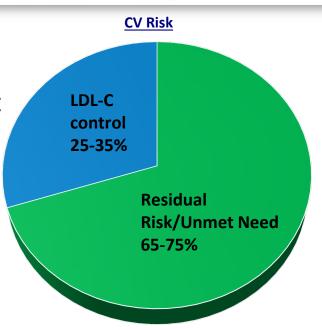


#### ~65%-75% residual CV risk beyond current standard of care<sup>1</sup>

- 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

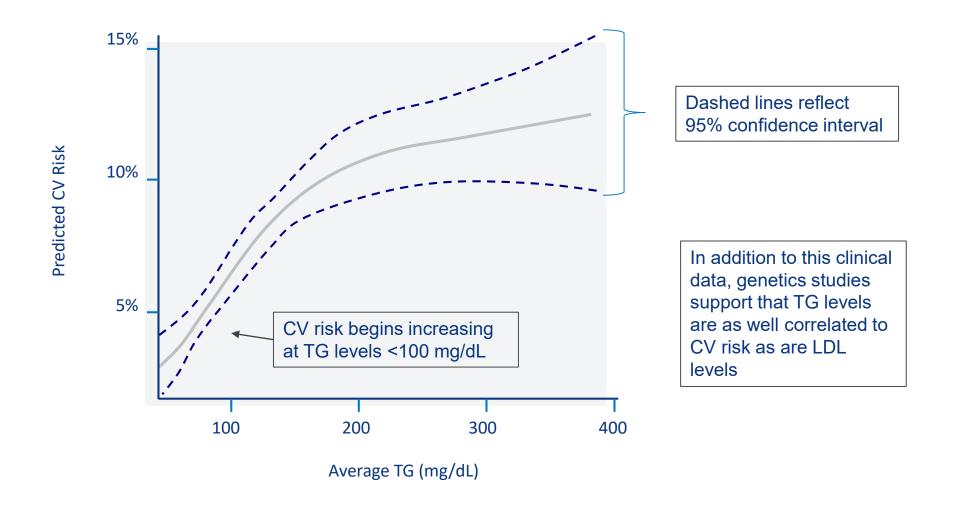


#### No FDA approved therapy exists for treating CV risk in dyslipidemia patients beyond LDL-C

- ~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 >150 mg/dL)
  - ~15M of these patients are already on statin therapy

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





Adapted from Navar AM et al. Poster presented at: 68th Scientific Session of the ACC; March 18, 2019; New Orleans, LA.

### Unprecedented CV Outcomes Position Amarin for Growth



### REDUCE-IT cardiovascular outcomes study was robustly conducted

- Evaluated Vascepa effects on statin-treated patients with residual elevated TG and other CV risks
  - Patients had well-controlled baseline LDL-C (median 75 mg/dL) and remained on statin therapy and other standard of care medications
  - 8,179 patients randomized 1:1 between Vascepa-arm and placebo-arm
- Conducted under a Special Protocol Assessment (SPA) agreement with FDA
- >35,000 patient years of study

### REDUCE-IT results were positive as per peer reviewed presentations and publications

- Primary results based on first occurrence of major adverse cardiovascular events (MACE):
  - Presented at AHA scientific sessions in Nov 2018
  - Published in The New England Journal of Medicine (NEJM); the NEJM Journal Watch Cardiology and the American College of Cardiology recognized REDUCE-IT results as top cardiovascular news for 2018
- Total events based on first and recurrent MACE:
  - Presented at ACC scientific sessions in Mar 2019
  - Published in Journal of American College of Cardiology

## 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)	<b>↓ 25</b> %	0.0000001	
Key Secondary Endpoint (3-point "H	ard" MACE) <b>↓ 26</b> %	0.000006	
CV Death	<b>↓ 20%</b>	0.03	
Heart Attack (Fatal or Nonfatal)	<b>↓ 31%</b>	0.000005	
Stroke (Fatal or Nonfatal)	<b>↓ 28</b> %	0.01	

### "This may be the biggest development in cardiovascular prevention since statins."

- Deepak L. Bhatt, MD, MPH

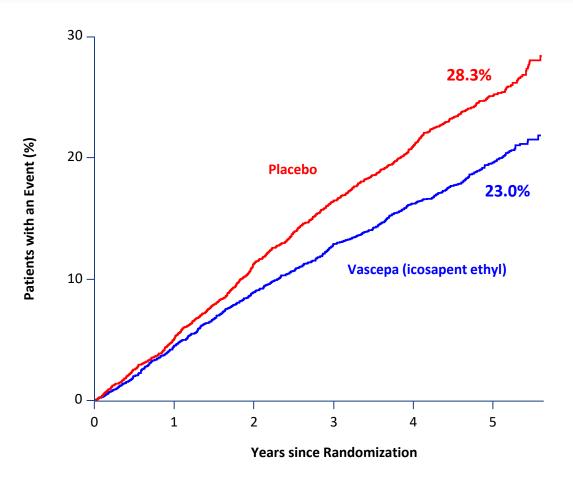
**Professor of Medicine at Harvard Medical School** 

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

# 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%

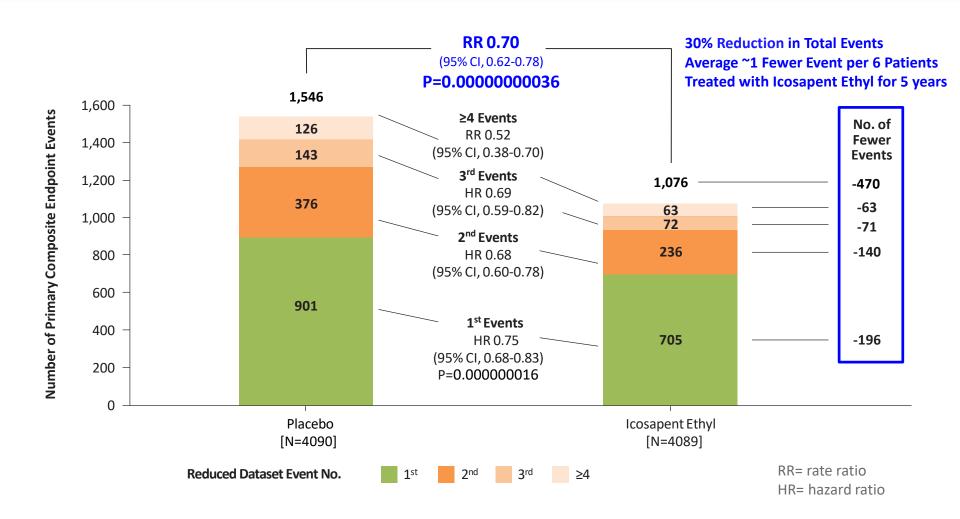
**NNT = 21** (95% CI, 15–33)

P=0.0000001

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)

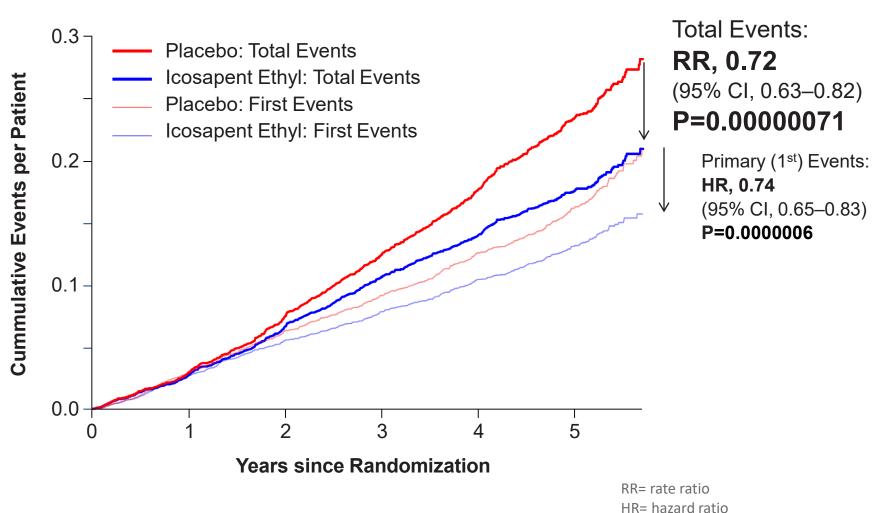




## Total (First and Subsequent) Events Key Secondary Endpoint (3 Point "Hard" MACE: CV Death, MI, Stroke)



#### Key Secondary Composite Endpoint



## Additional Important Results from REDUCE-IT



#### Positive results consistent across multiple subgroups including

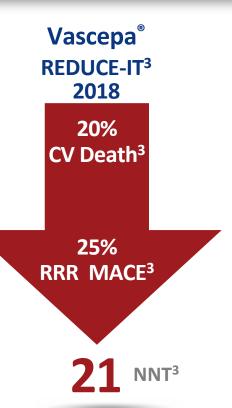
- Male/female
- Diabetes/no diabetes
- Secondary/primary prevention cohorts

#### 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®)¹: 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 analysis4

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://doi.org/10.1016/2019/03/01/j.jacc.2019.02.032

### Robust CV Risk Reduction Independent of TG Levels



#### 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</p>
- At 1 year ~36% of patients on Vascepa had TG levels <150 mg/dL</p>
  - Primary endpoint RRR in such patients were 29% and 30% for TG ≥150 mg/dL and <150 mg/dL</li>

#### 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 effects 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 antithrombotic effects, antioxidant effects, antiplatelet or anticoagulant effects, membrane-stabilizing effects, effects on stabilization and/or regression of coronary plaque and inflammation reduction

## Vascepa Well Tolerated with Safety Profile Consistent with Omega-3 Fatty Acids and Current FDA Labelling



## 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) ≥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	сvот	Relative Risk Reduction (RRR)	Positive CVOT	Peak Net Sales in U.S.	
STATIN THERAPY					
Statins	Various	25-35%	٧	>\$20B - 2016	
OTHER LDL-CHOLESTEROL LOWERIN	NG DRUGS <u>ON T</u>	OP OF STATIN THEF	RAPY		
Cholesterol Absorption Inhibitors	IMPROVE-IT	6%	٧	\$1.8B - 2007	
PCSK9 Inhibitors	FOURIER ODYSSEY	15% 15%	٧	Recently Launched	
OTHER DRUGS ON TOP OF STATIN THERAPY					
Anti-Inflammatory	CANTOS	15%	٧	N/A	
Omega-3 Mixture (Lovaza 1g/d)	ASCEND/VITAL	Not Significant	Χ	\$1.0B - 2013	
EPA (Epadel)	JELIS	19%	٧	N/A (in Japan only)	
EPA (Vascepa)	REDUCE-IT	25%	٧	TBD	

25% RRR with Vascepa <u>is largest of any therapy on top of statins</u>
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)

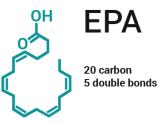
- Unique omega-3 molecule<sup>1</sup> derived from nature
  - New chemical entity designation by FDA for Vascepa as pure EPA
  - Purity achieved while overcoming the fragility and stability issues associated with omega-3s
- Excludes saturated fats, omega-6s and other components in fish oil
- No known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

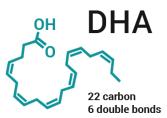
#### EPA is smaller than DHA in length and number of double bonds that influence activities

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

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

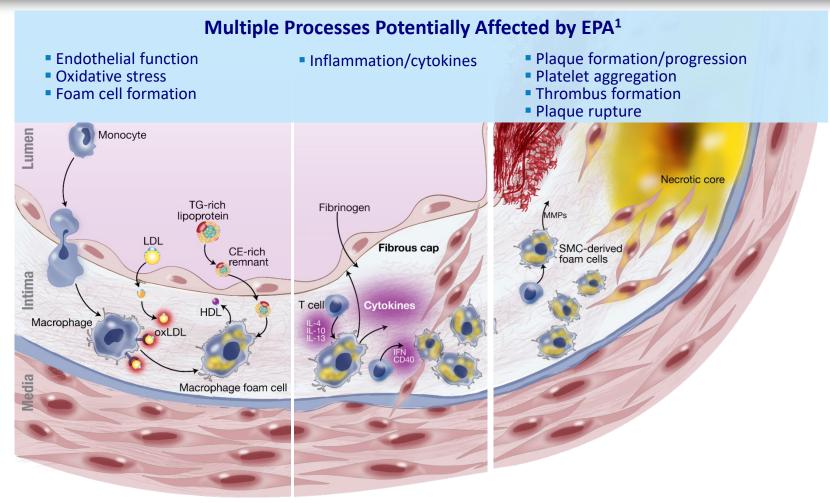
- Vascepa is expertly manufactured and encapsulated
- Demonstrated multi-year stability with consistent reproducibility





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





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

## Commercial Expansion Aligns with Improved Patient Care



#### 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
- Initial feedback from healthcare professionals regarding REDUCE-IT results broadly positive with new prescribers increasing
- Current promotion is qualified and limited, particularly to consumers

## U.S. launch plans for expected upcoming expanded Vascepa label include doubling sales force size

- Recruiting and training commenced to double US sales force size from ~400 to ~800 sales professionals by end of 2019
  - Will increase U.S. physician targets to ~70k-80K from ~50k and increasing sales call frequency
- Other promotional efforts also expanding, including plans for robust DTC promotion assuming OPDP approval





## **Preparing for Growth**



#### **Strengthening relationships**

- Building relationships with KOLs and industry groups
  - 24 scientific publications/posters supported in H1 2019 and >40 in 2018
  - Active in medical education programs and other forms of educational and promotional outreach

#### Supply capacity expanding

- Multiple proven suppliers for Vascepa
  - Evaluating options to expand capacity to support multiple billions of dollars in revenue

#### 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

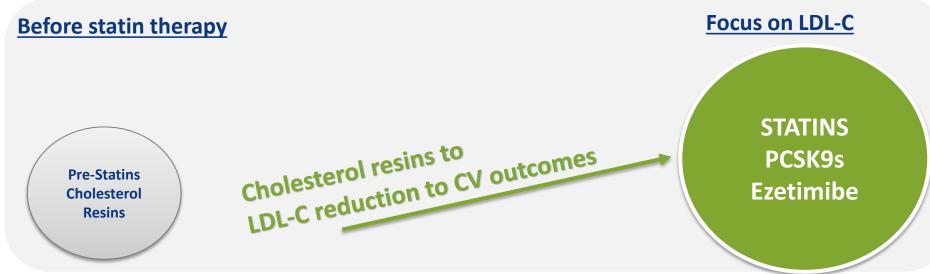
#### **International expansion**

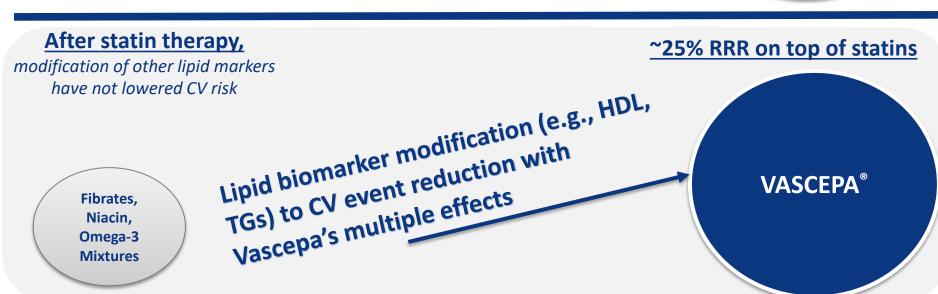
- Middle East: Partner obtained approved for Vascepa sales in Lebanon and United Arab Emirates with applications in other countries under review
- Canada: Partner received priority review designation from Health Canada for Vascepa; anticipate
   Vascepa approval in Canada before end of 2019
- China: Regulatory approval for Vascepa being pursued via ongoing clinical study
- Europe: Aiming before the end of 2019 to submit application seeking approval for Vascepa
- Other geographies: opportunities being pursued



### **Evolution of Preventative Cardiovascular Care**







## Capitalization Summary (Millions)





	As of 6/30/2019	Proforma as of 6/30/2019 for Equity Offering	
Cash and Cash Equivalents	\$222	\$661	Proforma includes ~\$440 million from July 2019 equity offering, including full exercise of the underwriters' option
Debt Obligations			
NOTES	\$ -	\$ -	None
ROYALTY-BEARING INSTRUMENT <sup>1</sup>	\$74	\$74	10% of revenues until fully paid; no maturity date
Common Stock and Equivalent Shares	<b>3</b>		
COMMON/PREFERRED SHARES <sup>2</sup>	360	386	Proforma includes ~25.5 million common shares issued in above referenced July 2019 equity offering
OPTIONS AND RESTRICTED STOCK	26	26	
TOTAL IF ALL EXERCISED	386	412	
Tax Jurisdiction (primary)	Ireland	Ireland	Loss carryforwards of ~\$800

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

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





Leading a New Paradigm in Cardiovascular Health Management

Investor Presentation October, 2019

NASDAQ: AMRN

