



Leading a New Paradigm in Cardiovascular Health Management

Investor Presentation April 1, 2018 NASDAQ: AMRN



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### 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 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.

## Amarin: Growing Prescriptions and Blockbuster Opportunity

#### Current: net product revenues growing from U.S. sales of Vascepa

- Lead product Vascepa<sup>®</sup> uniquely positioned for statintreated patients with persistent elevated triglycerides
- Focused specialty sales effort in select geographies of U.S.
- 2017 net product revenue \$179.8M
  - Represents increase of \$50.8M versus 2016

## Upcoming: REDUCE-IT outcomes study nearing completion

- Evaluating effect of Vascepa in lowering cardiovascular events as an add-on to statin therapy; larger need than current TG lowering label
- Studying at-risk patients with persistent elevated triglycerides
- Cardiovascular events driven study
  - Final patient study visits started March 2018
  - Top-line results expected before the end of Q3 2018
  - 90% powered per study design to detect a 15% relative risk reduction between Vascepa plus statin arm vs. placebo plus statin arm



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

#### Cardiovascular Disease: #1 cause of death in the United States

- >800,000 people die each year in United States attributable to cardiovascular disease<sup>1</sup>
- #1 cause of death in the United States; average 1 death every 38 seconds
- Heart attacks, stroke and other CV disease are expensive to treat<sup>2</sup>
  - Estimated annual total cost of \$555 billion
  - Costs expected to double to \$1.1 trillion within twenty years

#### Lowering LDL-C reduces CHD risk but not sufficiently alone

- Statins lower CV risk ~25% to 40%
- Remaining residual CV risk of ~60% to 75%

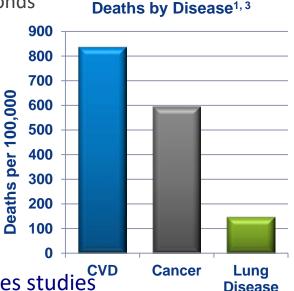
# Raising HDL-C is failed solution demonstrated in multiple outcomes studies

#### Promising remaining targets for lowering CV risk beyond well-controlled LDL-C

- Lowering high triglycerides (fats in the blood) or other atherogenic biomarkers
- Lowering inflammation or other factors contributing to atherosclerosis

#### Sources:

1) AHA: Heart Disease and Stroke Statistics 2018 At-a-Glance 2) AHA: Cardiovascular Disease: A Costly Burden for America — Projections through 2035 <u>http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm\_491543.pdf\_3</u>) Centers for Disease Control and Prevention, https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm, January, 20, 2017



## Elevated TGs Correlated with Increased CV Risk

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# Lipid disorders contribute to pancreatitis, heart disease, atherosclerosis and other health issues

### Triglyceride (TG) levels measured on most lipid panels

- Other measurements of lipids and atherogenic particles to consider in conjunction with TG levels include: LDL-C (addressed by statins and other therapies) and Non-HDL-C; Apo B; Ox-LDL; APO C-III; RLP-C, LDL-P and hsCRP
  - HDL-C might also be considered but not independently
  - Not all such measures are readily available without added tests

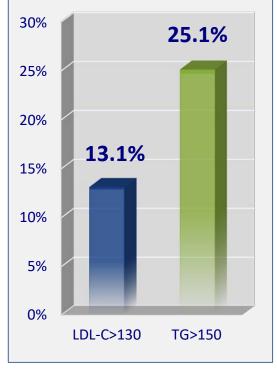
## Correlation between TG level and CV risk broadly established

 Extensive genetic, epidemiological and clinical data suggest that elevated TG levels are associated with increased CV risk

#### Prospective CV outcomes study on persistent elevated TGs

- First study is Amarin's REDUCE-IT, which evaluates broad effects of Vascepa, including TG lowering, on CV risk reduction after statin therapy
- Earlier generation TG lowering therapies have significant limitations (e.g. they raise LDL-C or have tolerability issues)

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



Source: NHANES 2009-2012

## Vascepa is Unique and Pragmatic Prescription Therapy

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

- Unique omega-3 molecule<sup>1</sup> derived from nature
  - New chemical entity designation by FDA for Vascepa as pure EPA
- Small molecule capable of entering and improving function of endothelial cells
- Doesn't inhibit clearance of LDL-C like docosahexaenoic acid (DHA)
- Excludes saturated fats, omega-6s and other ingredients in fish oil
- Expertly manufactured and encapsulated to mitigate oxidation risk of omega-3s

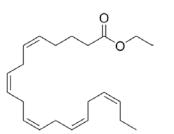
#### Effectiveness demonstrated in two placebo-controlled Phase 3 studies

- Significantly lowers TGs and other atherogenic biomarkers in patients with elevated TGs; does not increase LDL-C (bad cholesterol)
- Significantly lowers markers of inflammation
  - Separate data supports EPA having positive effects on each of the other processes beyond inflammation associated with atherosclerosis
- FDA approved for treating patients with very high TGs (>500 mg/dL)

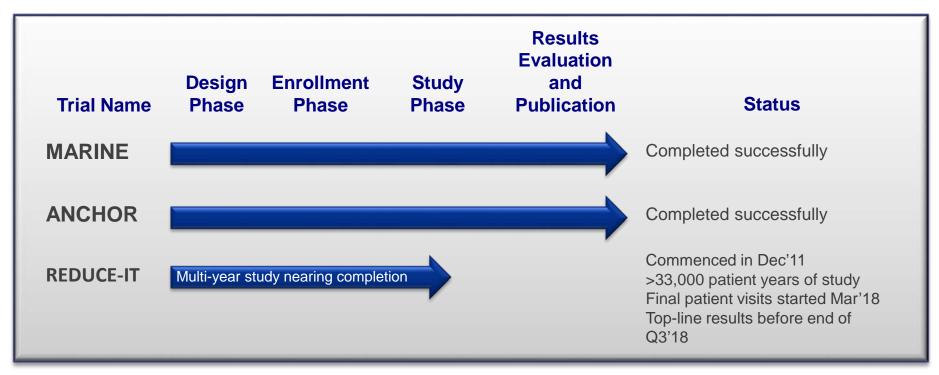
#### Orally administered with safety and tolerability comparable to placebo

No known drug-drug interactions<sup>1</sup>

## Affordably priced (similar to statins) and broadly available in U.S.







- MARINE: Demonstrated efficacy as an adjunct to diet to reduce triglyceride (TG) levels in patients with severe (≥500 mg/dL) hypertriglyceridemia, leading to FDA approval
- ANCHOR: Demonstrated efficacy in patients who, despite statin therapy, have persistent high TG levels (200-499 mg/dL), indication not approved by FDA, promotion permitted
- REDUCE-IT: Ongoing cardiovascular (CV) outcomes study evaluating potential to reduce residual CV events in statintreated patients with persistent elevated triglycerides
- Other: Multiple potential other indications could be advanced further post REDUCE-IT

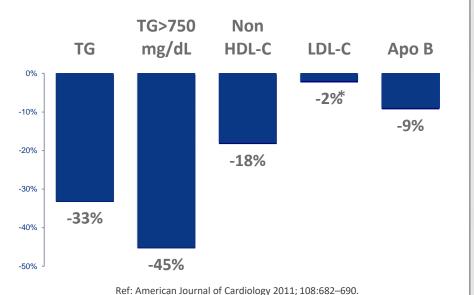
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# Vascepa Phase 3 Results Show Broad Lipid Level Improvement (4g/day dose)

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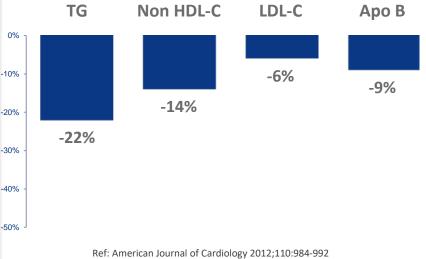
#### **MARINE Trial:**

Phase 3 median placebo-adjusted 12 week results for Vascepa 4g/day dose in patients with very high TGs (≥500 mg/dL)



ANCHOR Trial:

Phase 3 median placebo-adjusted 12 week results for Vascepa 4g/day dose in patients on statin therapy with persistent high TGs (200 to 499 mg/dL)



- Primary TG-lowering endpoint achieved
- Favorable effect on other clinically relevant endpoints

## Favorable safety and tolerability profile

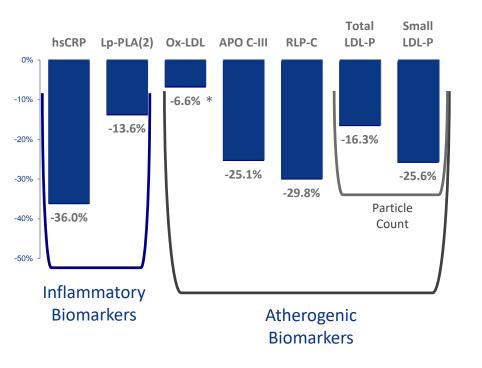
- Use with caution in patients with known hypersensitivity to fish and/or shellfish
- Only reported adverse reaction across the clinical profile for Vascepa with an incidence >2% and greater than placebo in Vascepa-treated patients was arthralgia (2.3% for Vascepa, 1.0% for placebo)

## Vascepa Additional Key Published Findings (4g/day dose)

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#### **MARINE Trial:**

Phase 3 median placebo-adjusted 12 week results for Vascepa 4g/day dose in patients with very high TGs (≥500 mg/dL)



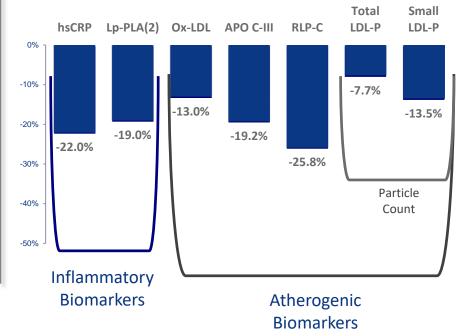
#### Sources:

Bays HE et al. Journal of Clinical Lipidology 2012; 6(6):565-572 Bays HE et al. American Journal of Cardiovascular Drugs 2013; 13(1):37-46 Ballantyne CM et al. Journal of Clinical Lipidology 2014; 8(3):313-314 Ballantyne CM et al. Journal of Clinical Lipidology 2015; 9(3):377-383 Ballantyne CM et al. Atherosclerosis 2016; 253:81-87

\* All statistically significant results, except Ox-LDL reduction in MARINE trial

#### **ANCHOR Trial:**

Phase 3 median placebo-adjusted 12 week results for Vascepa 4g/day dose in patients on statin therapy with persistent high TGs (200 to 499 mg/dL)



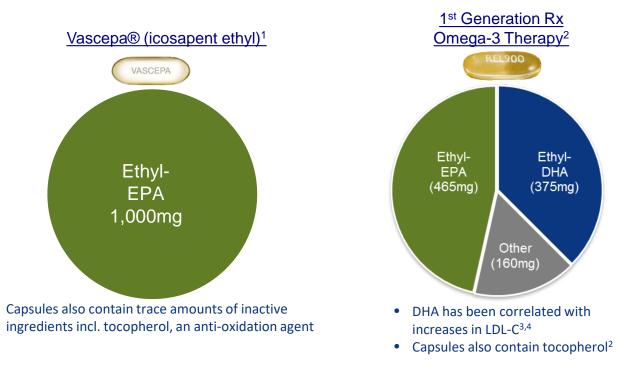
## Both the Amount and Type of Omega-3 Fatty Acid are Important for TG Lowering



Science of lipid management and clinical effects of omega-3 fatty acids are complex

## Both the amount and type of omega-3 fatty acid are important for TG lowering<sup>1</sup>

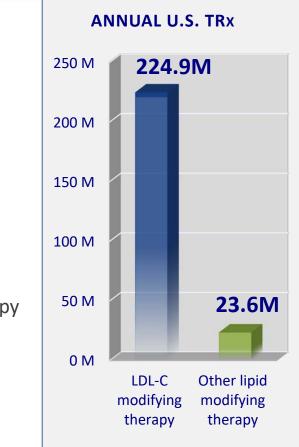
- Fish oil typically contains approximately 18% EPA
- Available prescription omega-3 therapies range from ~47% to nearly 100% EPA
- As evidenced in Phase 3 studies of Vascepa, low doses of omega-3s (<4 grams/day) have limited effects on lipid and other biomarkers in patients with serious medical conditions



1. Vascepa<sup>®</sup> {package insert}. Bedminster, NJ: Amarin Pharma Inc.; 2017; 2. Lovaza<sup>®</sup> {package insert}. Research Triangle Park, NC: GlaxoSmithKline 3. Jacobson TA et al. *J Clin Lipidol*. 2012;6(1):5-18; 4. Wei MY, Jacobson TA. *Curr Atheroscler Rep*. 2011;13(6):474-483 *No head to head studies conducted* 

## Treatment Guidelines for CV Disease Rely on Outcomes Data





Source: Symphony Health, PHAST Monthly, accessed 12/21/17

# Positive outcomes study results for LDL-C lowering therapy supports vast Rx use

- ~38M patients in U.S. are on statin therapy
- Before going generic, statins sold over \$34B/year
  - Lipitor alone sold over \$12B/year globally before going generic
- ~650K physicians in the U.S. prescribe statins annually

# No positive, labeled outcomes data exists for therapy that improves lipid measures on top of well-controlled LDL-C

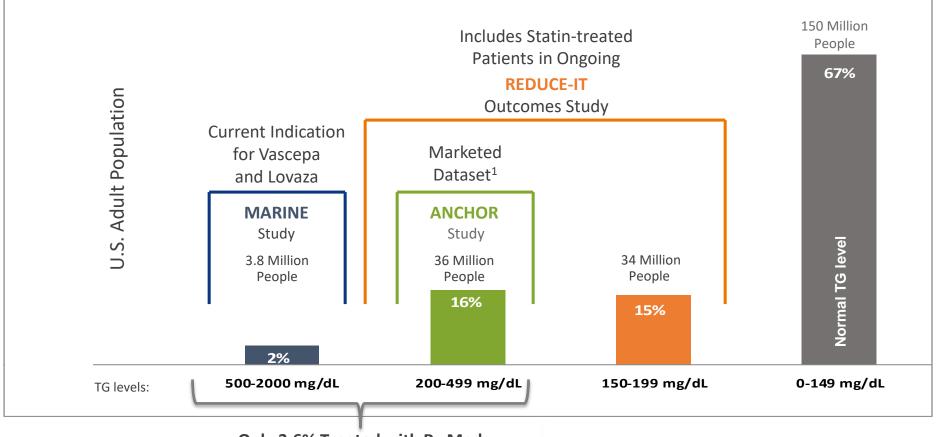
- Fenofibrate and niacin failed in CV outcomes studies after statin therapy
- Recent study, CANTOS, positive results for lowering inflammation

## <4% of patients with elevated TGs treated with Rx therapy

- Physicians want outcomes data to support broad Rx use after statins
- Current use of TG lowering therapy is limited
- Earlier generation TG lowering therapies are fenofibrates (~2M patients on therapy); Lovaza (~600K patients on therapy) and niacin (~240K patients on therapy); none have successful outcomes data



## U.S. Adult Population Stratified Based on TG Levels

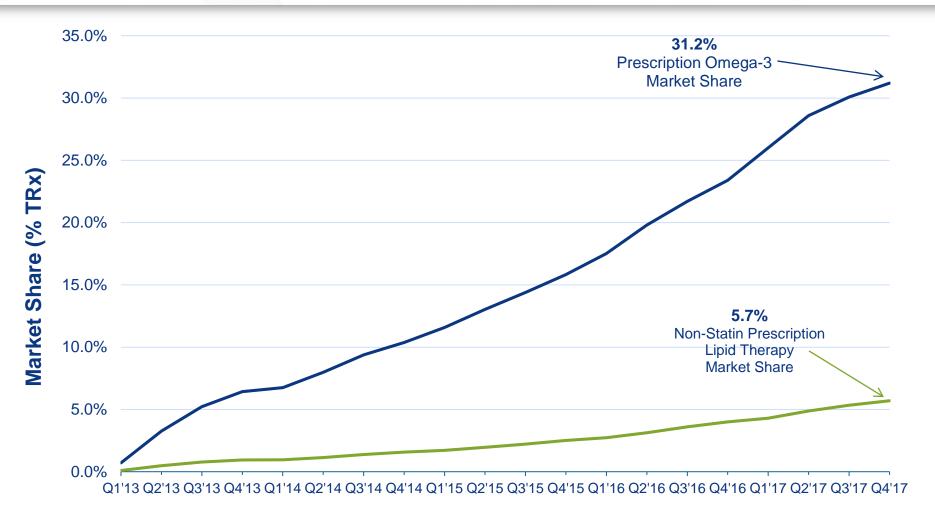


Only 3.6% Treated with Rx Meds

## >100M People in Top 7 Global Markets for Initially-Targeted Indications

1) For use in patients with persistent high (200-499 mg/dL) TGs after statin therapy, as studied in ANCHOR Sources: Journal of Clinical Lipidology 2015; 9:377-383, Datamonitor and Archives of Internal Medicine, 2009;169(6):572-578

## Vascepa Share of Market Is Growing



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

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## Net Product Revenue History (\$Millions)



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## Vascepa Commercialization Vision in the U.S.



	2017 and Prior	2018 Before REDUCE-IT Results	Post REDUCE-IT (assumes trial success followed by label expansion)
# of AMRN sales reps	~135	~150	~400 to 500
# of top target physicians	~20K	~20K	>40K
Consumer promotion	Minimal	Slightly expanded (potential trial DTC programs)	Yes (level tbd post trial results)
Co -promotion partner	Yes	Yes	Unlikely post-2018
Positioning	Improve biomarkers	Improve biomarkers	CV risk reduction
TRx growth focus	Market share	Market share	Expand market and market share
Net pricing to managed care payers and patients	Similar to generic Lovaza <sup>1</sup>	Similar to generic Lovaza <sup>1</sup>	Tbd (unlikely to increase significantly)
Revenue growth	5 yrs. from \$0 to ~\$179.8M	Continue growth via productivity gains	Accelerated growth (aiming for billions)

## REDUCE-IT Cardiovascular Outcomes Study: Results Expected Before End of Q3'18

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First ever prospective, blinded study of therapy which lowers TG levels (and other markers associated with CV risk) in statin-treated patients with elevated TG levels and other CV risk factors

Designed under Special Protocol Assessment (SPA) agreement

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

- Blinded evaluation of CV risk reduction vs. placebo
- 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 for 90% power to detect 15% relative risk reduction

- Assumes 1,612 primary endpoint events across a 4 to 5 year median patient follow-up period
- As with other long-term outcomes trials, actual study power may be higher or lower

#### >33,000 patient years of study since outcomes trial started in Dec 2011

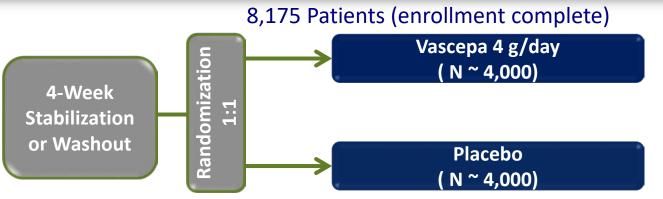
### Nearing completion: topline study results expected before end of Q3 2018

Final patient site visits commenced in March '18



## REDUCE-IT Enrolled Patients All Have Multiple CV Risk Factors Despite Statin Therapy





### Patient criteria for enrollment of high-risk population included

- Men or women age ≥45 years with established CV disease or age ≥50 years with diabetes mellitus and 1 additional CV risk factor
- Fasting triglycerides ≥150 mg/dL and <500 mg/dL</p>
- LDL-C >40 mg/dL and ≤100 mg/dL with stable statin (+/-ezetimibe) ≥4 weeks prior to qualifying measurements

## All patients remain on statin therapy (both arms of the study)

#### Statistical method: compare Vascepa-arm to placebo-arm of study

- Kaplan-Meier analysis based on stratified log-rank test
  - Hazard ratio and its 95% confidence intervals will be estimated using a stratified Cox proportional hazards model
  - Success requires p<0.0436 for primary endpoint</li>
    - p-value subject to potential adjustment to reflect actual number of events (above number based on assumption that the study is completed with exactly 1,612 primary MACE, actual result may differ)

## Data Supporting Potential for Vascepa Outcomes Benefit Goes Well Beyond TG Lowering and Prior Phase 3 Trial Successes

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#### **TG Lowering Data Examples**

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</li>
 <200 mg/dL were associated with 40% lower risk of recurrent CHD events vs. TG> 200 mg/dL

Subset of patients in clinical outcomes studies evaluating therapies that lower TG levels showed benefit in subset populations with baseline elevated TG, despite failed trials

- ACCORD (fenofibrate): Subgroup TG ≥ 204 mg/dL and HDL-C ≤ 34 mg/dL; MACE relative risk reduction 31%
- AIM-HIGH (Niacin ER); Subgroup TG>200 mg/dL and HDL-C <32 mg/dL; MACE relative risk reduction 36%</li>

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

As summarized in recent reviews (e.g. Noordestgaard<sup>3</sup>)

#### **Benefits Beyond TG Lowering Examples**

Mechanistic effects of EPA have shown broad favorable effects on atherosclerotic processes<sup>1</sup>

- Endothelial function
- Oxidative stress
- Foam cell formation
- Inflammation/cytokines

#### Supporting data examples:

- Plaque formation/progression
- Platelet aggregation
- Thrombus formation
- Plaque rupture
- Inflammation: CANTOS study established inflammation as independent marker of CV risk; EPA lowered hsCRP in ANCHOR and MARINE
- Plaque: CHERRY study showed EPA added to high dose statin doubled incidence of plaque regression vs. high dose statin therapy alone
  - U.S. plaque study, EVAPORATE, is ongoing<sup>4</sup>

#### Protective effect of EPA shown post PCI

 Nosaka et al. showed early EPA + statin post PCI resulted in 11% reduction in CV events vs. statin alone; CV death reduced 3.4%<sup>2</sup>

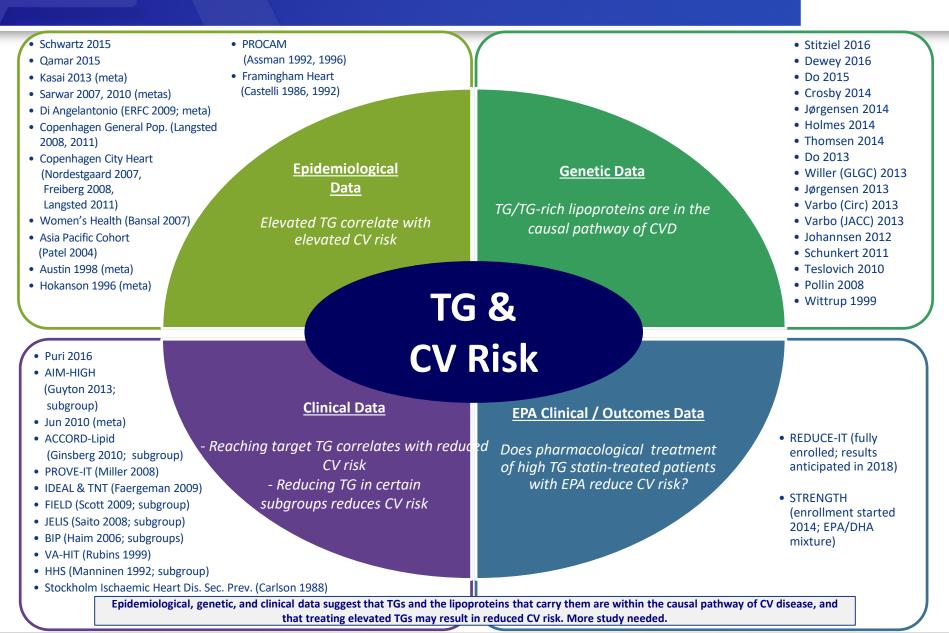
### Hybrid Example of Broad Favorable Effects of EPA from JELIS (large Japanese outcomes study)

- Overall population without high TG levels:
- Subgroup TG >150 mg/dL and HDL-C <40 mg/dL:</p>

**19%** reduction in CV events (p =0.011); little change in TG levels **53%** reduction in CV events (p=0.043)

<sup>1</sup>Borow KM et al. Atherosclerosis. 2015;242(1). <sup>2</sup>Absolute risk reduction at 1 year (9.2% vs 20.2%); absolute reduction in CV related deaths was 3.4%. Nosaka K et al. Int'l Journal Cardiology. 228 (2017); 173-179. <sup>3</sup>Nordestgaard, BG. AHA. *Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease: New Insights From Epidemiology, Genetics, and Biology*. 2016. <sup>4</sup>Budoff M, Effect of Vascepa (icosapent ethyl) on progression of coronary atherosclerosis in patients with elevated triglycerides (200–499 mg/dL) on statin therapy: Rationale and design of the EVAPORATE study. Clin Cardiol. 2018;1–7. https://doi.org/10.1002/clc.22856.

## >40 Papers Support Correlation Between TGs and CV Risk



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Recent RWE studies support correlation that high triglycerides, despite controlled LDL ("bad") cholesterol, result in significantly greater risk for major adverse cardiovascular events (MACE)\*

## Data from the nationwide Optum database showed<sup>1</sup>:

- 35% increased risk for myocardial infarction (heart attacks)
- 51% increased risk for coronary revascularization

### Data from the Kaiser database showed<sup>2</sup>:

- 30% increased risk for myocardial infarction (heart attacks)
- 30% increased risk for coronary revascularization

### Both studies analyzed adults already taking statins and with controlled LDL

- One cohort had people with normal triglycerides (<150 mg/dL)</li>
- One cohort had people with high triglycerides (200-499 mg/dL)

## Optum study also showed

- 15% higher average total health care cost of patients with high TG levels
- 17% higher rate of occurrence of an inpatient stay over time of patients with high TG levels

\* Nonfatal MI, nonfatal stroke, coronary revascularization, unstable angina, and all-cause mortality (Kaiser) or CV-related mortality (Optum)

- Data across multiple genetic studies is consistent
  - Both TG and LDL-C genetic data point to a causal association with CVD
- Data suggest mutations that lower TGs over lifetime correlate with reduced CV risk

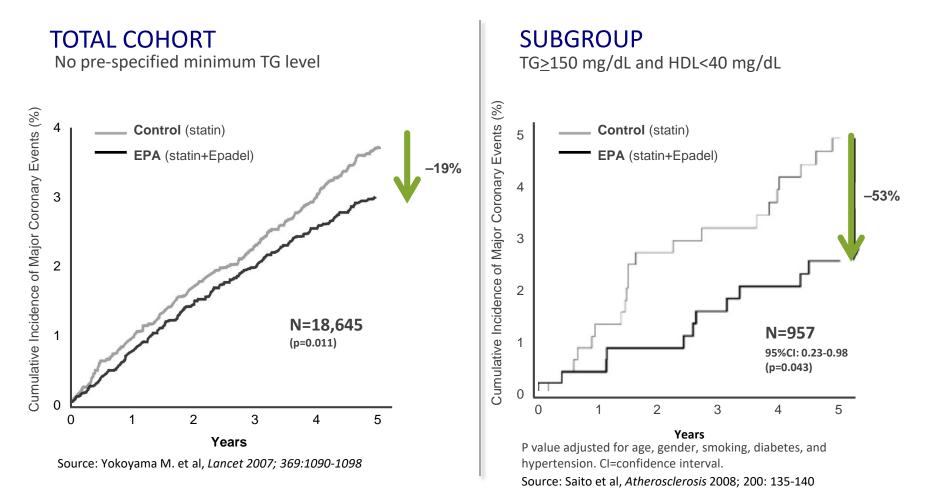
	<u>CHD Risk</u>		
<b>Predictor</b>	Effect Size	<b>Perspective</b>	<u>P-value</u>
TG	0.40	Genes regulating TG and LDL-C levels are	<<<0.0001
LDL-C	0.39	comparably strong predictors of CHD	<<<0.0001
HDL-C	0.04	HDL-C is weak predictor	0.32

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# Japan: Ethyl-EPA Reduced Coronary Events 19% to 53% on Top of Statin Therapy in Outcomes Study (JELIS)



Patients Randomized to Statin Alone or Statin + Ethyl-EPA (Epadel) and Followed for 5 Years with Comparison of Cumulative Incidence of Major Coronary Events



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## "Enriched" patient population in REDUCE-IT

- REDUCE-IT: all patients have elevated TGs and other CV risk factors despite statin therapy
  - Mean and median baseline TGs >200 mg/dL and ~1/2 of patients expected to also have low HDL-C
  - Fewer CV events likely classified as unstable angina in REDUCE-IT due to higher risk patient population. Also, advances in medicine better separate patients with unstable angina, a more subjective endpoint, from patients with myocardial infarction, a hard MACE endpoint
- JELIS: many patients had normal TG levels and a 19% risk reduction was achieved
  - Published subgroup with 53% risk reduction population had TG  $\geq$ 150 mg/dL and low HDL-C

## Higher treatment dose in REDUCE-IT

- REDUCE-IT 4 grams/day of ethyl-EPA (Vascepa); JELIS 1.8 grams/day of ethyl-EPA
- In 12-week Phase 3 ANCHOR study, 4 grams/day of Vascepa increased EPA in the plasma to approximately the same level as achieved with 1.8 grams/day of ethyl-EPA in JELIS
  - Difference likely due to high fish diet in Japan
  - EPA levels in REDUCE-IT control likely lower than JELIS due to dietary differences outside Japan
- Statin therapy targeted to US guidelines in REDUCE-IT, lower statin dose given in JELIS

## **REDUCE-IT** is a global study

- REDUCE-IT: enrollment in 11 countries including strong participation in the United States; randomized double-blinded study
- JELIS: Japan only, mostly women; open label, randomized with blinded endpoint analysis

## **Amarin Preparing for REDUCE-IT Success**

## Strengthening relationships

- Building relationships with KOLs and industry groups
  - 25 scientific publication/posters supported in 2017, including real world evidence data from Kaiser and Optum
- Broad managed care coverage already in place for Vascepa
  - Approval rates for Vascepa similar to earlier generation generic product

## Supply capacity expanding

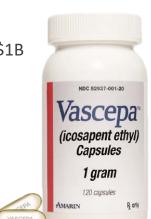
- Multiple proven suppliers for Vascepa
  - Current capacity to support >\$500M in revenue; capacity to expand in 2019 to support >\$1B
  - Gross margin increased to mid-70%'s in 2017

## Sustainable business

- Vascepa patents listed in the FDA's Orange Book expire in 2030
- NCE protection

## International expansion

- Commercial partners pursuing regulatory approvals for Vascepa in Canada, China and Middle East
- Vascepa recently approved for sale in Lebanon





## Capitalization Summary (Millions)



	As of 12/31/2017	Pro Forma as of 12/31/2017 for Q1'18 Financing Only	
Cash	\$73.6 <sup>1</sup>	\$143.9	Net proceeds \$70.3 of financing announced Jan'18
Debt Obligations <sup>2</sup>			
EXCHANGEABLE SENIOR NOTES <sup>3</sup>	\$30.0	\$30.0	First put date Jan'22
ROYALTY-BEARING INSTRUMENT	\$109.1	\$109.1	10% of revenues until fully paid; no maturity date
Common Stock and Equivalent Shares			
COMMON/PREFERRED SHARES <sup>4</sup>	303.9	324.5	Preferred shares mirror common but non-voting
OPTIONS AND RESTRICTED STOCK	36.0	36.0	
TOTAL IF ALL EXERCISED	339.9	360.5	
Tax Jurisdiction (primary)	Ireland	Ireland	Loss carryforwards of ~\$700 million

<sup>1</sup>Net quarterly cash burn history in 2017 of \$15.9, \$10.6, \$6.4 and \$5.5 million, in Q1, Q2, Q3 and Q4, respectively, excluding net proceeds of transactions relating to exchangeable senior notes announced in Q1'17

<sup>2</sup> Full face value of debt shown here; lower carrying value is reported in financial statements for accounting purposes in accordance with U.S. GAAP

<sup>3</sup> \$30 million of 3.5% exchangeable senior notes due 2047; exchange price \$3.89/sh., adjusted under certain circumstances

<sup>4</sup> Includes 32.8 million common share equivalents issuable upon conversion of preferred shares

## Investment Highlights



Large Global Sales Potential	<ul> <li>Multiple underserved patient populations with elevated TG levels</li> <li>Multi-billion dollar potential assuming outcomes study success</li> <li>Significant growth opportunity based on current indication</li> </ul>
Differentiated Product	<ul> <li>TG reduction – decrease or no increase in LDL-C</li> <li>Reductions in Apo B, non-HDL-C, VLDL-C and total cholesterol</li> <li>Safety comparable to placebo</li> </ul>
Positive Execution	<ul> <li>Strong historical annual TRx growth</li> <li>Broad managed care coverage</li> <li>Phase 3 trials successfully completed with all primary endpoints achieved</li> <li>Outcomes study fully enrolled and nearing completion in 2018</li> </ul>
Commercialization Strategy	<ul> <li>Grow revenues through specialty sales focus</li> <li>Prepare for expanded opportunity upon REDUCE-IT success</li> <li>Cost-effectively advance other opportunities</li> </ul>
Experienced Management	<ul> <li>Team with history of product development and commercial successes</li> <li>Recently added CCO with history of creating substantial growth</li> <li>Specialty sales team with history of increasing productivity</li> </ul>

## Leading a New Paradigm in Cardiovascular Health Management





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