



# Leading a New Paradigm in Cardiovascular Disease Management

Investor Presentation
July 1, 2020



## 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 regulatory approvals, patent litigation appeal, generic product launch, intellectual property, cash flow, research and development, 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 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 Forms 10-K and 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.

## 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®

- Doubled U.S. sales force size in 2020 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** 

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



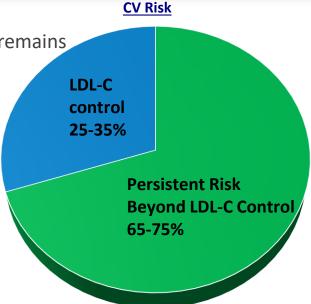
### ~65-75% persistent CV risk beyond historical standard of care<sup>1</sup>

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 13 seconds<sup>2</sup>
- Annual treatment cost \$555 billion; expected to double within twenty years<sup>3</sup>

VASCEPA is first and only FDA-approved therapy for treating persistent CV risk beyond statin therapy with its new indication



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

- ~38M patients are on statin therapy
  - ~12 million of these statin treated patients have TG ≥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>4</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 hypertriglyderidemia management. J Am Coll Cardiol. 2018. 2) American Heart Association. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. Circulation. 2020;141:e139—e596. 3) 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. 4) Newman CB, Preiss D, Tobert JA, et al. Statin Safety and Associated Adverse Events- A Scientific Statement From the American Heart Association. Feb. 2019.

## 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)	<b>↓ 25</b> %	0.0000001	
Key Secondary Endpoint (3-point "H	ard" MACE) <b>↓ 26%</b>	0.0000006	
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	

## "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

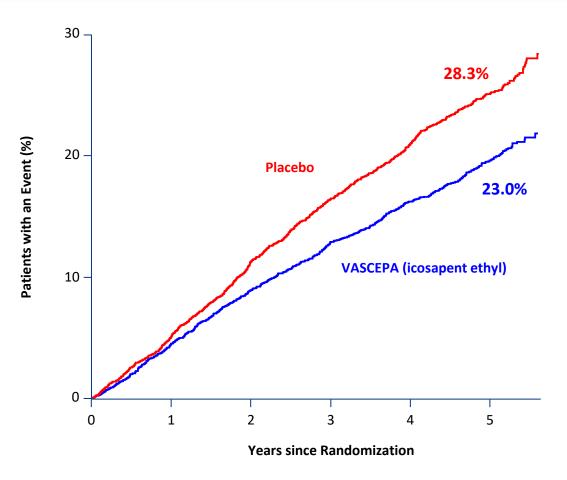
Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital Heart and Vascular Center Global Principal Investigator and Steering Committee Chair for REDUCE-IT

- 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%** 

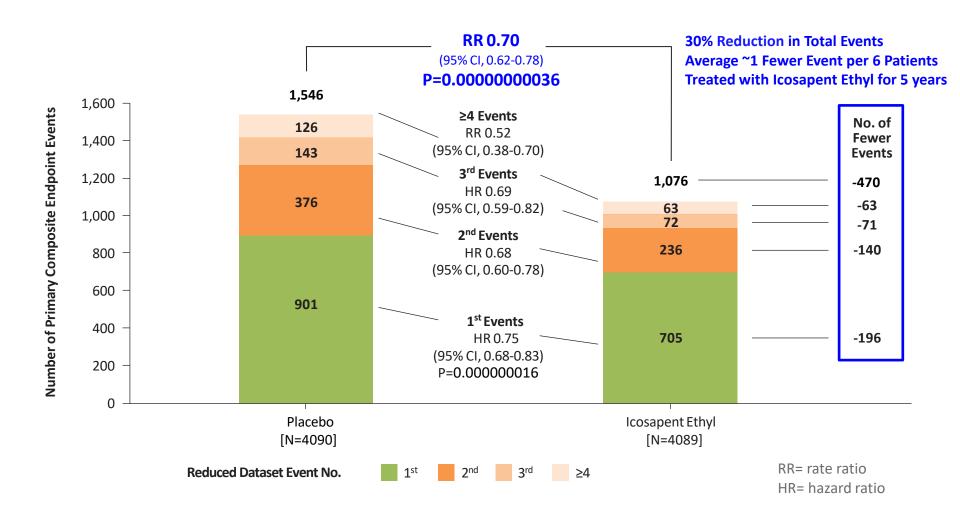
**NNT = 21** (95% CI, 15–33)

P=0.0000001

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)

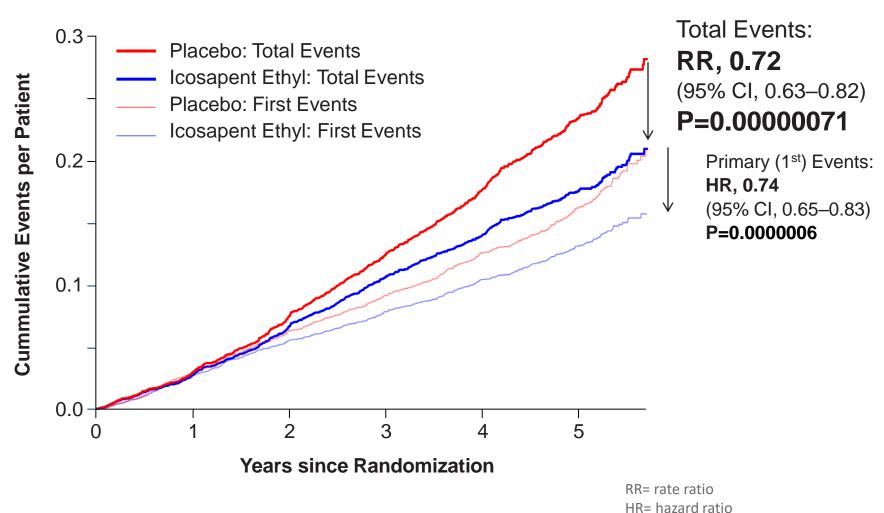




## Total (First and Subsequent) Events Key Secondary Endpoint (3 Point "Hard" MACE: CV Death, MI, Stroke)



#### Key Secondary Composite Endpoint



## VASCEPA Development and New Expanded Indication for Use



### 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
    - STRENGTH study of Epanova discontinued in early 2020

### Approved indications for VASCEPA in U.S.

New cardiovascular 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 (>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 (≥500 mg/dL) hypertriglyceridemia"

## Broadly defined cardiovascular 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

## VASCEPA's Well-Tolerated Safety Profile



#### **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%)
    - Note: MACE reduction in patients with reported bleeding and atrial fibrillation or flutter consistent with overall trial result

### 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
  - Bleeding (12% vs 10%), with a greater incidence in patients on concomitant antithrombotics (e.g., aspirin, clopidogrel or warfarin)
    - Note: the FDA-approved label does not direct physicians to discontinue VASCEPA use in patients with such AEs
- 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 ≥3% and ≥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%)

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

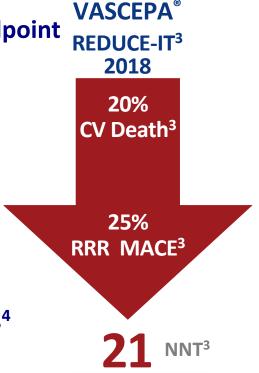


## **VASCEPA** number needed to treat (NNT): 21 for primary endpoint

- 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®)¹: 45
  - Evolocumab (Repatha®)²: 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 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

## Broad Third-Party Support for VASCEPA



#### 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 (TG) (135-499 mg/dL) (Sep'19)
- European Society of Cardiology and European Atherosclerosis Society jointly updated patient treatment guidelines to include icosapent ethyl for high-risk cardiovascular patients with elevated triglycerides (135-499 mg/dL) (Sep'19)
- American Heart Association issued Scientific Advisory recognizing that elevated TG may be a causal factor for CVD; dietary supplements are not recommended, nor FDA approved, to treat medical conditions and 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)
- The American Association of Clinical Endocrinologists, American College of Endocrinology, Brazilian Society of Cardiology, The Japanese Circulation Society and Thrombosis Canada supportively reference REDUCE-IT and icosapent ethyl in recently updated guidelines

#### 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 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
- European Heart Journal
- Circulation

## 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

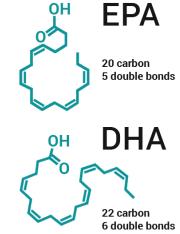
- Small molecule capable of entering and improving function of endothelial cells
- Doesn't inhibit clearance of LDL-C like DHA (docosahexaenoic acid)

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

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

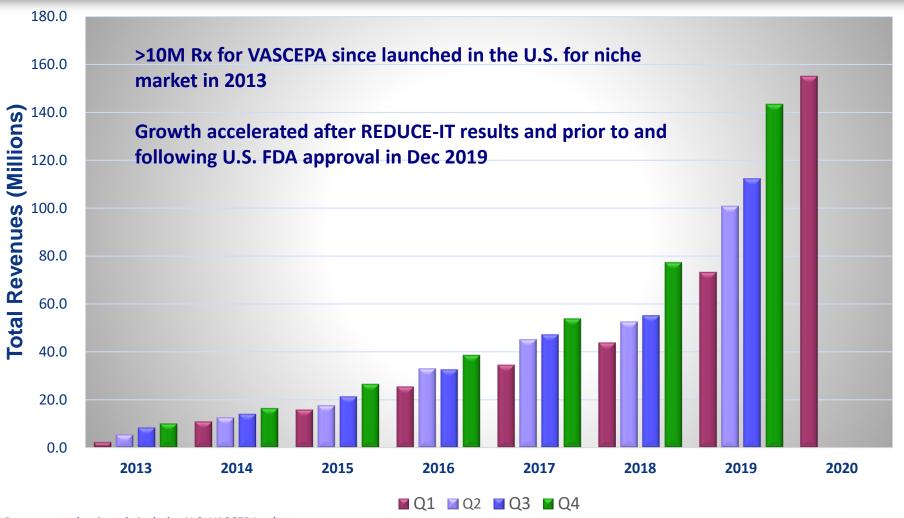


Class	сvот	Relative Risk Reduction (RRR)	Positive CVOT	Peak Net Sales in U.S.			
STATIN THERAPY							
Statins	Various	25-35%	٧	>\$20B - 2016			
OTHER LDL-CHOLESTEROL LOWERING DRUGS <u>ON TOP</u> OF STATIN THERAPY							
Cholesterol Absorption Inhibitors	IMPROVE-IT	6%	٧	\$1.8B - 2007			
PCSK9 Inhibitors	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)			
Omega-3 Mixture (Epanova 4g/d)	STRENGTH	Not Successful	X	N/A			
EPA (VASCEPA)	REDUCE-IT	25%	٧	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) Statins lower CV risk by 25%-35%; REDUCE-IT effect is incremental to statins



## VASCEPA Quarterly Total Net Revenue History



- Revenue predominantly includes U.S. VASCEPA sales revenue
- Normalized\* prescription growth in the U.S. 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 most representative
- \* Normalized = 30-day supply of 4g VASCEPA daily

## Amarin Priority Focus in Mid-2020



VASCEPA

#### Increase VASCEPA use and revenue levels in U.S.

- Increase education of healthcare professionals and patients
  - Plans include ~\$80 million in incremental promotional initiatives and educational support
- Emerge from COVID-19 suspension of in-person meetings with healthcare professionals in a phased manner as patients resume routine physician visits
- Align commercial expansion with improved patient care

### **Expand VASCEPA regulatory approvals and revenue internationally**

- EU: targeting EMA recommendation for regulatory approval near end of 2020; evaluating commercial options (direct or partner or hybrid)
- China: clinical trial anticipated to be completed near end of 2020 via established commercial partner
- Canada: launched in Q1 2020 via commercial partner
- Other: launched in Lebanon and United Arab Emirates and pursuing opportunities for VASCEPA in other countries

### Overcoming threat of generic competition in U.S.

- Appealing district court patent litigation decision
  - Hikma received FDA approval of generic VASCEPA, has not launched at risk
- Use proven, adequate capacity, consistent and cost-effective manufacturing capabilities as established over multiple years to maximize value if VASCEPA goes generic in U.S.

## U.S. Commercialization of VASCEPA in 2020



#### Q1 2020 net total revenue of \$155.0 million

- Represents increase of 112% over Q1 2019
- Revenue increase mostly from U.S. VASCEPA prescription growth
- Due to COVID-19, prescription growth on a year-over-year basis in Q2'20 expected to be considerably slower than in Q1'20

## Healthcare professional targeted education and promotion

- Sponsoring numerous medical education programs and scientific presentations/publications
  - Build on KOL relationships; >100 scientific publications/posters supported in recent years, >25 in YTD 2020
- Doubling size of U.S. sales force to 800 sales representatives completed in March 2020 increasing number of target physicians in U.S. for direct

## Patient/consumer targeted education and promotion

- Planning advertising program in second half of 2020, focused on physician and consumer, as first such advertising of the cardiovascular risk reduction indication of VASCEPA
- As United States is reopening from the COVID-19 pandemic resume field-based face-to-face interactions with healthcare providers on a phased basis
  - Due to COVID-19, field-based face-to-face interactions were suspended on March 15





## Operational Foundation for CV Risk Reduction Launch



## Managed care coverage at beginning of 2020 was good and has improved further

- Seeking volume driven growth supported by affordable product pricing
  - Current pricing comparable to Lipitor® prior to it going generic; VASCEPA net pricing relatively flat for past several years
  - Volume anticipated to grow based on new FDA-approved label, expanded sales force and other promotion
- Managed care coverage historically good for most commercial and Medicare Part D plans
  - While always dynamic, multiple improvements in managed care coverage for VASCEPA witnessed in 2020
  - 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

#### Supply capacity established and further expanding

- Multiple proven suppliers for VASCEPA
- Historically difficult and expensive product to produce
  - Suppliers have facilities dedicated to production of VASCEPA
  - Track-record of consistent, high quality product



## U.S. Patent Litigation and Appeal



#### **District court decision favored generics**

- ANDA litigation argued in court in Q1 2020 with two generics companies; Dr. Reddy's and Hikma
  - Litigation pertained to patents protecting VASCEPA's initial indication (TG  $\geq$ 500 mg/dL)
  - Teva and Apotex settlements permit launch in Aug 2029 or earlier under certain circumstances if other generics launch
- Two issues: 1) infringement of patents and 2) and obviousness (validity) of Amarin's patents
- On March 30, 2020, the court ruled that the generic companies would infringe Amarin's patents if they launched a generic VASCEPA, but also found the patents at issue invalid due to obviousness

#### District court ruling was a surprise

 Amarin together with third-party analysts and advisors providing public commentary believed that Amarin would prevail; ruling was contrary to prior action of U.S. patent office

### Appealing to U.S. Court of Appeals for the Federal Circuit

- Good arguments on appeal
- Proceeding on an expedited schedule
  - Completed briefing in June 2020
  - Oral argument (possibly telephonic) expected in Q3/Q4 2020
  - Ruling expected in Q4 2020 or Q1 2021

## **Europe First in Class Opportunity**



## >80 million people in Europe with CVD<sup>1</sup>

- Prevalence is growing with ~11 million new CVD cases added annually
- ~1.8 million CV deaths per year plus many debilitating events such as stroke and heart attacks

### EMA recommendation for regulatory approval anticipated near end of 2020

- Review of centralized EU regulatory submission underway by European Medicines Agency
- Seeking cardiovascular risk reduction indication consistent with recent new indication for VASCEPA in U.S. and recent approval for VASCEPA in Canada

### Commercialization opportunities

- Leading medical societies in Europe, ESC and EAS, have already added icosapent ethyl (US brand name VASCEPA) to their medical guidelines
- Seeking to become first and only drug in EU with this labeling for large unmet medical need
- Pricing review underway based on cardiovascular risk reduction with unprecedented outcomes study data from REDUCE-IT (not for TG lowering indication for which VASCEPA launched in U.S.)
- Evaluating whether to launch in EU directly, via a partner or in a hybrid form with decision targeted for Q3 2020

## Exclusivity expected for at least ten years

- Regulatory exclusivity expected for 10 to 11 years
- Patent protection could extend into 2033

## China First in Class Opportunity



## Clinical trial ongoing

- Anticipate completion in 2020
- Not anticipating delay in clinical trial due to COVID-19

### If trial is successful VASCEPA could be positioned as First in Class

First approval in China creates high hurdle for competitive product(s)

#### Commercial partner in China, Eddingpharm, preparing for commercial launch

- Successfully promote multiple products in China
- Understand the importance of VASCEPA's high quality manufacturing

Further details regarding regulatory, reimbursement and commercialization plans to be available after results of VASCEPA's clinical trial are available near the end of 2020

## Capitalization Summary (Millions)





Cash, Cash Equivalents and Investments	\$624	
Debt Obligations		
NOTES	\$ -	None
ROYALTY-BEARING INSTRUMENT	\$38	10% of product revenue until fully paid
Common Stock and Equivalent Shares		
COMMON/PREFERRED SHARES <sup>1</sup>	391	
OPTIONS AND RESTRICTED STOCK	24	
TOTAL IF ALL EXERCISED	415	
Tax Jurisdiction (primary)	Ireland	Loss carryforwards of ~\$900

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





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