Amarin Corporation

REDUCE-IT® Heart Failure Analyses by VASCEPA® (Icosapent Ethyl)-Driven Serum Eicosapentaenoic Acid (EPA) Levels Suggest Potential Benefit in New Heart Failure in Studied At-Risk Patients as Presented at the American College of Cardiology's 70th Annual Sci

May 15, 2021

Post hoc analyses by estimated on-treatment serum EPA levels in the VASCEPA group suggest potentially reduced incidence of new heart failure and new heart failure requiring hospitalization with higher achieved serum EPA levels

Amarin to Webcast Discussion of Data Presented at ACC.21 Monday, May 17, 2021 at 4:30 p.m., Eastern Time

DUBLIN, Ireland and BRIDGEWATER, N.J., May 15, 2021 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced the presentation of REDUCE-IT® HEART FAILURE (HF) at ACC.21, the American College of Cardiology's 70th Annual Scientific Session, being held virtually from May 15 – 17, 2021. These new analyses supported by Amarin were presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

"The REDUCE-IT HF analyses provide interesting data about a potential new approach to addressing heart failure, a condition that continues to challenge patients and cardiologists worldwide," commented Dr. Deepak L. Bhatt, M.D., M.P.H., Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital Heart and Vascular Center, Professor of Medicine at Harvard Medical School, and principal investigator of REDUCE-IT. "The potential benefit of increased serum EPA levels in reducing the composite of cardiovascular death or new heart failure requiring hospitalization in at-risk patients is a novel finding for icosapent ethyl and requires further prospective validation. These results add to the growing body of knowledge regarding icosapent ethyl."

The REDUCE-IT HF analyses examined the effects of icosapent ethyl on the incidence of new heart failure by achieved on-treatment serum EPA levels in REDUCE-IT patients. New heart failure and new heart failure requiring hospitalization were prespecified tertiary endpoints and were not significant in the overall patient population. *Post hoc* analyses were conducted based on estimated average on-treatment EPA levels in patients in the icosapent ethyl group with available EPA measurements, as compared to patients in the placebo group with available EPA measurements; these analyses showed that new heart failure and new heart failure requiring hospitalization may be reduced in patients who achieve serum EPA levels higher than approximately 150 µg/mL, though this needs to be tested prospectively.

As previously reported, the REDUCE-IT cardiovascular outcomes study enrolled 8,179 patients who were required to be treated with statins and other conventional therapies, and all patients had controlled low-density lipoprotein cholesterol, elevated triglyceride levels, and either established cardiovascular disease or diabetes with other cardiovascular risk factors.

Heart failure is a major and often debilitating cardiovascular condition, significantly impacting not only patients and their loved ones, but also healthcare systems globally. In the United States (US), the latest statistical update from the American Heart Association (AHA) shows that approximately 6.0 million people have HF, with the prevalence projected to increase by 46% from 2012 to 2030, affecting >8 million people 18 years of age or older. The overall US cost of HF continues to rise as well; in 2012 the total cost for HF was estimated to be $30.7 billion, primarily attributable to direct medical costs. The trajectory we are on could lead to a 127% (or $69.8 billion) increase by 2030.[1]

"Cardiovascular disease continues to be the leading cause of death worldwide, with the economic and societal burden increasing each year," said Steven Ketchum, Ph.D., senior vice president and president, research & development, and chief scientific officer, Amarin. "Heart failure, in particular, devastates patients, their families and economies with significant direct costs and societal impact. We owe it to at-risk patients to analyze the data from our cardiovascular outcomes study and explore whether therapies such as icosapent ethyl might ease the burden."

The REDUCE-IT HF analyses include both prespecified and *post hoc* analyses. Heart failure was a prespecified tertiary endpoint within REDUCE-IT. Approximately 14% of the patients did not have EPA levels determined at baseline; baseline characteristics and outcomes in those with or without EPA measures were similar. On-treatment EPA values were estimated from available annual serum samples.

Brigham and Women's Hospital receives research funding from Amarin for Dr. Bhatt's work as the REDUCE-IT study Chair.

The REDUCE-IT HF analyses can be found here. Additional REDUCE-IT® and icosapent ethyl (EPA)-related topics will be presented at ACC.21 and can be found here.

Audio Webcast Information

Amarin will host an audio webcast on Monday, May 17, 2021, at 4:30 p.m. ET to further discuss these and other VASCEPA-related findings presented during ACC.21, with replay available for a period of 14 days. The discussion will include various clinicians and scientists and will be moderated by Amarin's chief medical officer, Craig Granowitz, M.D., Ph.D. To listen please register here, listen live on the investor relations section of the company's website at www.amarincorp.com, or via telephone by dialing 877-545-0320 within the United States, 973-528-0016 from outside the United States. A replay of the call will be made available for a period of two weeks following the conference call. To hear a replay of the call, dial 877-481-4010 within the United States, 919-882-2331, PIN: 41266. Any opinions or views expressed by the clinicians and scientists on the audio webcast are theirs alone. They have neither been scripted nor previewed by Amarin. While Amarin respects the scientific opinions of these clinicians and scientists, Amarin takes no responsibility for those opinions. Rather, this audio webcast is intended to provide summaries of recently presented scientific data for consideration by Amarin's investors.

About Amarin

Amarin is an innovative pharmaceutical company leading a new paradigm in cardiovascular disease management. From our scientific research foundation to our focus on clinical trials, and now our commercial expansion, we are evolving and growing rapidly. Amarin has offices in Bridgewater, New Jersey in the United States, Dublin in Ireland, and Zug in Switzerland as well as commercial partners and suppliers around the world. We are committed to rethinking cardiovascular risk through the advancement of scientific understanding of the impact on society of significant residual risk that exists beyond traditional therapies, such as statins for cholesterol management.

About Cardiovascular Risk

Cardiovascular disease is the number one cause of death in the world. In the United States alone, cardiovascular disease results in 859,000 deaths per year.[2] And the number of deaths in the United States attributed to cardiovascular disease continues to rise. In addition, in the United States there are 605,000 new and 200,000 recurrent heart attacks per year (approximately 1 every 40 seconds). Stroke rates are 795,000 per year (approximately 1 every 40 seconds), accounting for 1 of every 19 U.S. deaths. In aggregate, in the United States alone, there are more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, 1 every 13 seconds.

Controlling bad cholesterol, also known as LDL-C, is one way to reduce a patient's risk for cardiovascular events, such as heart attack, stroke or death. However, even with the achievement of target LDL-C levels, millions of patients still have significant and persistent risk of cardiovascular events, especially those patients with elevated triglycerides. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35%.[3] Significant cardiovascular risk remains after statin therapy. People with elevated triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins. [4,5,6]

About REDUCE-IT®

REDUCE-IT was a global cardiovascular outcomes study designed to evaluate the effect of VASCEPA in adult patients with LDL-C controlled to between 41-100 mg/dL (median baseline 75 mg/dL) by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides between 135-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or diabetes mellitus and at least one other cardiovascular risk factor (primary prevention cohort).

REDUCE-IT, conducted over seven years and completed in 2018, followed 8,179 patients at over 400 clinical sites in 11 countries with the largest number of sites located within the United States. REDUCE-IT was conducted based on a special protocol assessment agreement with FDA. The design of the REDUCE-IT study was published in March 2017 in *Clinical Cardiology.*[7] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[8] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[9] These and other publications can be found in the R&D section on the company's website at www.amarincorp.com.

About VASCEPA® (icosapent ethyl) Capsules

VASCEPA (icosapent ethyl) capsules are the first-and-only prescription treatment approved by the U.S. Food and Drug Administration (FDA) comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. VASCEPA was launched in the United States in January 2020 as the first and only drug approved by the U.S. FDA for treatment of the studied high-risk patients with persistent cardiovascular risk after statin therapy. VASCEPA was initially launched in the United States in 2013 based on the drug's initial FDA approved indication for use as an adjunct therapy to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Since launch, VASCEPA has been prescribed over ten million times. VASCEPA is covered by most major medical insurance plans. In addition to the United States, VASCEPA is approved and sold in Canada, Lebanon and the United Arab Emirates. In Europe, in March 2021 marketing authorization was granted to icosapent ethyl in the European Union for the reduction of risk of cardiovascular events in patients at high cardiovascular risk, under the brand name VAZKEPA.

Indications and Limitation of Use (in the United States)
VASCEPA is indicated:

- As an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary 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 two or more additional risk factors for cardiovascular disease.
- As an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Important Safety Information

- VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components.
- VASCEPA was associated with an increased risk (3% vs 2%) of atrial fibrillation or atrial flutter requiring hospitalization in a double-blind, placebo-controlled trial. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter.
- It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Patients with such allergies should discontinue VASCEPA if any reactions occur.
- VASCEPA was associated with an increased risk (12% vs 10%) of bleeding in a double-blind, placebo-controlled trial. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel or warfarin.
- Common adverse reactions in the cardiovascular outcomes trial (incidence ≥3% and ≥1% 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%).

- Common adverse reactions in the hypertriglyceridemia trials (incidence ≥1% more frequent than placebo): arthralgia (2% vs 1%) and oropharyngeal pain (1% vs 0.3%).
- Adverse events may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.
- Patients receiving VASCEPA and concomitant anticoagulants and/or anti-platelet agents should be monitored for bleeding.

Key clinical effects of VASCEPA on major adverse cardiovascular events are included in the Clinical Studies section of the prescribing information for VASCEPA as set forth below:

Effect of VASCEPA on Time to First Occurrence of Cardiovascular Events in Patients with Elevated Triglyceride levels and Other Risk Factors for Cardiovascular Disease in REDUCE-IT

	VASCEPA		Placebo		VASCEPA vs Placebo
	N = 4089 n (%)	Incidence Rate (per 100 patient years)	N = 4090 n (%)	Incidence Rate (per 100 patient years)	Hazard Ratio (95% CI)
Primary composite endpoint					
Cardiovascular death, myocardial infarction, stroke, coronary revascularization, hospitalization for unstable angina (5-point MACE)	705 (17.2)	4.3	901 (22.0)	5.7	0.75 (0.68, 0.83)
Key secondary composite endpoint					
Cardiovascular death, myocardial i nfarction, stroke (3-point MACE)	459 (11.2)	2.7	606 (14.8)	3.7	0.74 (0.65, 0.83)
Other secondary endpoints					
Fatal or non-fatal myocardial infarction	250 (6.1)	1.5	355 (8.7)	2.1	0.69 (0.58, 0.81)
Emergent or urgent coronary revascularization	216 (5.3)	1.3	321 (7.8)	1.9	0.65 (0.55, 0.78)
Cardiovascular death [1]	174 (4.3)	1.0	213 (5.2)	1.2	0.80 (0.66, 0.98)
Hospitalization for unstable angina [2]	108 (2.6)	0.6	157 (3.8)	0.9	0.68 (0.53, 0.87)
Fatal or non-fatal stroke	98 (2.4)	0.6	134 (3.3)	0.8	0.72 (0.55, 0.93)

[1] Includes adjudicated cardiovascular deaths and deaths of undetermined causality.
[2] Determined to be caused by myocardial ischemia by invasive/non-invasive testing and requiring emergent hospitalization.

FULL U.S. FDA-APPROVED VASCEPA PRESCRIBING INFORMATION CAN BE FOUND AT WWW.VASCEPA.COM.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential impact of VASCEPA in various clinical uses. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Among the factors that could cause actual results to differ materially from those described or projected herein include the following: uncertainties associated generally with research and development and clinical trials such as further clinical evaluations failing to confirm earlier findings. A further list and description of these risks, uncertainties and other risks associated with an investment in Amarin can be found in Amarin's filings with the U.S. Securities and Exchange Commission, including its most recent Quarterly Report on Form 10-Q. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Amarin undertakes no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise. Amarin's forward-looking statements do not reflect the potential impact of significant transactions the company may enter into, such as mergers, acquisitions, dispositions, joint ventures or any material agreements that Amarin may enter into, amend or terminate.

Availability of Other Information About Amarin

Investors and others should note that Amarin communicates with its investors and the public using the company website (www.amarincorp.com), the investor relations website (investor.amarincorp.com), including but not limited to investor presentations and investor FAQs, Securities and Exchange Commission filings, press releases, public conference calls and webcasts. The information that Amarin posts on these channels and websites could be deemed to be material information. As a result, Amarin encourages investors, the media, and others interested in Amarin to review the information that is posted on these channels, including the investor relations website, on a regular basis. This list of channels may be updated from time to time on Amarin's investor relations website and may include social media channels. The contents of Amarin's website or these channels, or any other website that may be accessed from its website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

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[7] Bhatt DL, Steg PG, Brinton E, et al., on behalf of the REDUCE-IT Investigators. Rationale and Design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol*. 2017;40:138-148.

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