Amarin Corporation

VASCEPA® (Icosapent Ethyl) Found in Prespecified and Post Hoc Analyses to Significantly Reduce Stroke in At-Risk Patients in Analyses of Landmark REDUCE-IT® Study Presented at International Stroke Conference 2021

March 17, 2021

28% and 32% significant reductions in first and total strokes, respectively, demonstrated with VASCEPA compared to placebo, as well as reductions in first and total ischemic strokes each by 36%, without increasing hemorrhagic stroke, in statin-treated patients with elevated cardiovascular risk

Consistent reductions in overall stroke and in ischemic stroke observed across multiple subgroups

Administration of pure icosapent ethyl, VASCEPA, represents a novel clinical approach to stroke reduction

REDUCE-IT® STROKE abstract receives prestigious Paul Dudley White International Scholar Award to recognize the authors with the highest ranked abstract from the United States at the International Stroke Conference 2021

DUBLIN, Ireland and BRIDGEWATER, N.J., March 17, 2021 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced the presentation of REDUCE-IT® STROKE at the International Stroke Conference 2021, being held virtually from March 17 – March 19, 2021, adding to the growing body of knowledge on the clinical impact of VASCEPA® (icosapent ethyl). 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 STROKE analyses provide important data supporting a new approach to prevent strokes using icosapent ethyl in appropriate patients," commented Dr. Deepak L. Bhatt, M.D., M.P.H., Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital, Professor of Medicine at Harvard Medical School, and principal investigator of REDUCE-IT. "The findings of benefit in at-risk patients include significant reductions in overall strokes and in ischemic strokes. Importantly, with respect to safety, we did not observe any significant increase in hemorrhagic stroke. These results further strengthen the case for pure eicosapentaenoic acid (EPA) in the form of prescription icosapent ethyl as a key intervention beyond statins for stroke prevention in studied patients."

The REDUCE-IT STROKE analyses examined stroke rates across the enrolled patient population (n=8179). Enrolled patients were required to be treated with statins and other conventional therapies, and all patients had either established cardiovascular disease or diabetes and had other cardiovascular risk factors such as elevated triglyceride levels. Event rates for time to first fatal or nonfatal stroke were 2.4% for VASCEPA vs. 3.3% for placebo for a relative risk reduction (RRR) of 28% (p=0.01). Ischemic stroke time to first event rates were 2.0% for VASCEPA vs. 3.0% for placebo for a RRR of 36% (p=0.002). Hemorrhagic stroke occurred at low rates with no significant difference for VASCEPA vs. placebo (0.3% vs 0.2%; p=0.55).

Stroke is a major and often debilitating cardiovascular event significantly impacting not only patients and their loved ones, but also the healthcare system. Patients with elevated triglycerides despite statin therapy have increased risk for stroke-related events. Each year in the United States, about 795,000 people experience a new or recurrent stroke. Approximately 610,000 of these are first strokes, and 185,000 are recurrent strokes, or approximately 1 stroke every 40 seconds.[1] The latest statistical update from the American Heart Association (AHA) shows that in the United States, the annual cost of stroke is $49.8 Billion.[2]

"Strokes significantly impact the healthcare system, driving substantial immediate and long-term costs," said Steven Ketchum, Ph.D., senior vice president and president, research & development and chief scientific officer, Amarin. "The subgroup data presented at ISC 2021 provide new insight into the unique potential benefits of VASCEPA administration on alleviating the societal burden of strokes."

The REDUCE-IT STROKE abstract received the prestigious Paul Dudley White International Scholar Award, recognizing the authors with the highest ranked abstract across the United States at the International Stroke Conference 2021. The esteemed Paul Dudley White Award is named in honor of one of Boston's most revered cardiologists, Dr. Paul Dudley White, who was a founding father of the American Heart Association and an early leader in preventive cardiology.

REDUCE-IT was designed and powered for the primary composite endpoint, of which stroke was one of five prespecified components; it was not powered for subgroup analysis. Stroke was a prespecified secondary endpoint within the testing hierarchy; ischemic stroke was a prespecified tertiary endpoint; stroke subgroup analyses were *post hoc*. No information was collected on stroke related disability, such as Rankin scores.

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

Additional information on ISC 2021 can be found here.

About Amarin

Amarin is a rapidly growing, 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. In 2009, Amarin had fewer than twenty employees. Today, with offices in Bridgewater, New Jersey in the United States, Dublin in Ireland, and Zug in Switzerland, Amarin has approximately 1,000 employees and 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

The number of deaths in the United States attributed to cardiovascular disease continues to rise. There are 605,000 new and 200,000 recurrent heart attacks per year (approximately 1 every 40 seconds), in the United States. Stroke rates are 795,000 per year (approximately 1 every 40 seconds),

accounting for 1 of every 19 U.S. deaths. Cardiovascular disease results in 859,000 deaths per year in the United States.[1] In aggregate, there are more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, one every 13 seconds in the United States alone.

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. 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, approval is anticipated in April 2021 following the January 28, 2021 favorable opinion of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommending that marketing authorisation be 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 infarction, 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 Annual Report on Form 10-K. 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.

Amarin Contact Information
Investor Inquiries:
Investor Relations
In U.S.: +1 (908) 719-1315
Amarin Corporation plc
IR@amarincorp.com (investor inquiries)

Solebury Trout
lstern@soleburytrout.com

Media Inquiries:
Alina Kolomeyer
Communications
Amarin Corporation plc
In U.S.: +1 (908) 892-2028
PR@amarincorp.com (media inquiries)

[1] American Heart Association. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. Circulation. 2020;141:e139–e596.
[2] American Heart Association. Heart Disease and Stroke Statistics—2021 Update: A Report From the American Heart Association*Circulation*. 2021;143:e254–e743.
[3] Ganda OP, Bhatt DL, Mason RP, et al. Unmet need for adjunctive dyslipidemia therapy in hypertriglyceridemia management. *J Am Coll Cardiol*. 2018;72(3):330-343.
[4] Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.
[5] Toth PP, Granowitz C, Hull M, et al. High triglycerides are associated with increased cardiovascular events, medical costs, and resource use: A real-world administrative claims analysis of statin-treated patients with high residual cardiovascular risk. *J Am Heart Assoc*. 2018;7(15):e008740.
[6] Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.
[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.
[8] Bhatt DL, Steg PG, Miller M, et al., on behalf of the REDUCE-IT Investigators. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. *N Engl J Med*. 2019;380:11-22.
[9] Bhatt DL, Steg PG, Miller M, et al., on behalf of the REDUCE-IT Investigators. Reduction in first and total ischemic events with icosapent ethyl across baseline triglyceride tertiles. *J Am Coll Cardiol*. 2019;74:1159-1161.