Amarin Corporation

VASCEPA® (Icosapent Ethyl) Found to Significantly Reduce Ischemic Events in Patients with Prior Percutaneous Coronary Intervention (PCI) in Post Hoc Subgroup Analyses of Landmark REDUCE-IT® Study Presented at Transcatheter Cardiovascular Therapeutics (TCT

October 15, 2020

VASCEPA®, compared with placebo, significantly reduced primary composite first and total MACE (major adverse cardiovascular events) in post hoc exploratory analyses of patients with a history of PCI by 34% and 39%, respectively, and key secondary composite first hard MACE, comprised of heart attacks, stroke and cardiovascular death, by 34%

Administration of VASCEPA resulted in robust absolute risk reductions of 8.5% and 5.4% and numbers needed to treat (NNT) of 12 and 19, respectively, for both primary and key secondary (hard MACE) composite endpoints in post hoc exploratory subgroup analyses

Consistent and robust benefit seen in post hoc exploratory analyses of patients with a history of PCI across the hierarchy of endpoints prespecified for the full study cohort

DUBLIN, Ireland and BRIDGEWATER, N.J., Oct. 15, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced the presentation of REDUCE-IT® PCI at Transcatheter Cardiovascular Therapeutics (TCT) Connect, the 32nd annual scientific symposium of the Cardiovascular Research Foundation, being held virtually from October 14 – October 18, 2020 adding to the growing body of knowledge on the clinical impact of VASCEPA® (icosapent ethyl). These new analyses supported by Amarin were presented during the *TCT Connect 2020 Best of Abstracts* session by Benjamin E. Peterson, M.D., Brigham and Women's Hospital Heart & Vascular Center and Harvard Medical School.

"The opportunity to further explore REDUCE-IT data and effects in those patients with prior PCI provides additional understanding of the potential benefit of icosapent ethyl in the clinical setting," commented Dr. Deepak L. Bhatt, M.D., M.P.H., Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School, principal investigator of REDUCE-IT and senior author of the REDUCE-IT PCI analyses. "The findings of benefit in at-risk patients with prior PCI are consistent with previously presented data on overall reductions in first and total coronary revascularization events of 34% and 36%, respectively. Moreover, the statistically significant substantial benefit in reduced coronary revascularization procedures seen as early as 11 months provides clinicians with a potential additional intervention in a patient population for whom time is of the essence."

The REDUCE-IT PCI analysis looked at 3,408 (41.7%) of patients enrolled in REDUCE-IT who had undergone a prior PCI. These patients were randomized a median of 2.9 years after PCI. Baseline characteristics were similar among patients randomized to VASCEPA versus placebo. *Post hoc* exploratory analyses of the subgroup of 3,408 patients with a prior PCI showed that, for the primary composite endpoint of 5-point MACE, time to first event was significantly reduced with VASCEPA versus placebo by 34% ($p<0.0001$) and total (first and subsequent) events were also reduced by 39% ($p<0.0001$). For the key secondary composite endpoint of 3-point MACE, time to first event was reduced by 34% ($p<0.0001$) in the subgroup of patients with a prior PCI.

Coronary revascularization procedures, such as stenting, are invasive, carry multiple risks, and can have significant direct and indirect costs. Patients with elevated triglycerides despite statin therapy have increased risk for ischemic events, including coronary revascularizations. These procedures, whether pre-scheduled or performed in an emergency, inevitably result in additional time spent in a healthcare setting. The latest statistical update from the American Heart Association (AHA) shows that, in 2014, an estimated 480,000 inpatient PCI procedures were performed in the United States with a mean inpatient hospital charge for PCI of $84,813.[1]

"Revascularization procedures overall significantly impact the healthcare system, with PCI procedures adding to the burden and driving substantial costs," said Steven Ketchum, Ph.D., senior vice president and president, research & development and chief scientific officer, Amarin. "The subgroup data presented at TCT Connect 2020 reflect new findings demonstrating the substantial impact of VASCEPA on at-risk patients in REDUCE-IT with prior PCI procedures and how the therapy can help avoid subsequent events that could have dire consequences."

REDUCE-IT was not specifically powered to examine individual cardiovascular endpoints or patient subgroups, therefore p-values presented for these revascularization analyses are nominal and exploratory with no adjustment for multiple comparisons. In addition, coronary revascularization as an endpoint can sometimes be considered subjective; however, these endpoints were adjudicated by an independent, blinded clinical endpoint committee. Results from the total coronary revascularization events analyses are consistent across the various recurrent event statistical models and are also consistent with the first coronary revascularization events results. Together, the REDUCE-IT first and total coronary revascularization events results support the robustness and consistency of the clinical benefit of VASCEPA therapy in reducing coronary revascularization.

The presentation as well as additional information on TCT Connect 2020 can be found here.

About Amarin
Amarin Corporation plc is a rapidly growing, innovative pharmaceutical company focused on developing and commercializing therapeutics to cost-effectively improve cardiovascular health. Amarin's lead product, VASCEPA® (icosapent ethyl), is available by prescription in the United States, Canada, Lebanon and the United Arab Emirates. VASCEPA is not yet approved and available in any other countries. Amarin, on its own or together with its commercial partners in select geographies, is pursuing additional regulatory approvals for VASCEPA in China, Europe and the Middle East. For more information about Amarin, visit www.amarincorp.com.

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%.[2] 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.[3,4,5]

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.*[6] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[7] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[8] 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 FDA comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. 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 eight million times. VASCEPA is covered by most major medical insurance plans. The new, cardiovascular risk indication for VASCEPA was approved by the FDA in December 2019.

Indications and Limitation of Use
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 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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