Amarin Corporation

VASCEPA® (Icosapent Ethyl) Found to Significantly Reduce Cardiovascular Events in Patients with Compromised Renal Function at Baseline in Prespecified and Post Hoc Subgroup Analyses of Landmark REDUCE-IT® Study Presented at American Society of Nephrology

October 26, 2020

Patients with decreased renal function prior to treatment with VASCEPA or placebo had higher rates of cardiovascular events than the overall population studied in REDUCE-IT

REDUCE-IT patients with decreased renal function prior to treatment showed similarly favorable relative risk reductions and numerically greater absolute risk reductions in cardiovascular events in comparison with the overall patient population

Consistent and robust benefit in cardiovascular outcomes seen in both prespecified and post hoc exploratory analyses across a broad range of baseline eGFR (estimated Glomerular Filtration Rate) categories

DUBLIN, Ireland and BRIDGEWATER, N.J., Oct. 26, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced the first presentation of REDUCE-IT® RENAL results at American Society of Nephrology (ASN) Kidney Week 2020, held virtually from October 22 – October 25. REDUCE-IT RENAL consisted of important prespecified and *post hoc* subgroup analyses of patients from the landmark REDUCE-IT cardiovascular outcomes study who had compromised renal function. The results of these analyses add to the growing body of knowledge on the clinical impact of VASCEPA® (icosapent ethyl) in at-risk patient populations. These new analyses, supported by Amarin, were presented by Arjun Majithia, M.D., Lahey Clinic.

“In the REDUCE-IT RENAL analyses we not only studied outcomes following icosapent ethyl administration, which were greatly improved, but equally importantly, we also examined the event rates in at-risk patients with compromised renal function, which clearly demonstrate that those patients urgently need additional solutions for cardiovascular risk reduction,” 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 RENAL analyses.

The REDUCE-IT RENAL analyses examined the full REDUCE-IT cardiovascular outcomes study patient population in prespecified and *post hoc* analyses across subgroups of eGFR categories. The primary endpoint (5-point major adverse cardiovascular events [MACE] consisting of non-fatal myocardial infarction [MI], stroke, cardiovascular death, unstable angina requiring hospitalization and coronary revascularization) and key secondary endpoint (3-point MACE consisting of non-fatal MI, stroke and cardiovascular death) events were consistently reduced when looking at data cut by prespecified baseline eGFR categories; eGFR <60 mL/min/1.73 m2 (n=1816), eGFR ≥60 to <90 mL/min/1.73 m² (n=4455), and eGFR ≥90 mL/min/1.73 m² (n=1902). Similar consistent cardiovascular risk reduction benefits were observed across *post hoc* analyses by finer cuts of eGFR categories. Primary and key secondary endpoint MACE rates increased with decreasing eGFR compared to the total patient population studied in REDUCE-IT, resulting in similarly favorable relative risk reductions and numerically greater absolute risk reductions with VASCEPA versus placebo in comparison with the overall patient population.

Adverse event rates were higher with decreasing eGFR, but total adverse events occurred at similar rates with VASCEPA versus placebo. A safety profile similar to the full REDUCE-IT study cohort was observed for VASCEPA compared with placebo across eGFR subgroups.

“We continue to see the consistency in benefit and safety of VASCEPA administration across various at-risk patient populations, including across varying degrees of renal function,” said Steven Ketchum, Ph.D., senior vice president and president, research & development and chief scientific officer, Amarin. “It is notable that, despite observing with REDUCE-IT patients the known increase in cardiovascular events with decreased kidney function, all patients experienced similar relative cardiovascular risk reduction benefits, resulting in overall greater absolute risk reductions in patients with compromised kidney function.”

“It is important to provide cardiovascular risk reduction solutions for patients with chronic kidney disease as data continue to highlight cardiovascular disease as an unfortunate and damaging comorbidity,” added Craig Granowitz, M.D., Ph.D., Amarin’s senior vice president and chief medical officer.

REDUCE-IT was not specifically powered to examine individual cardiovascular endpoints or patient subgroups, and urine samples were not collected during the REDUCE-IT study.

In addition to presentation of REDUCE-IT RENAL at ASN Kidney Week 2020, as previously reported, a separate presentation was made of real-world data analysis of U.S. veterans showing that increased triglyceride levels in patients with compromised renal function is a potential predictor of increased risk of cardiovascular events.

Links to above cited data presented at ASN Kidney Week 2020

“Benefits of Icosapent Ethyl Across a Range of Baseline Renal Function in Patients with Established Cardiovascular Disease or Diabetes: Results of REDUCE-IT RENAL” – presented on behalf of all authors by Arjun Majithia, M.D. – available from October 23

“Increased Residual Cardiovascular Risk in US Veterans with Moderately Elevated Baseline Triglycerides, Well-Controlled LDL Cholesterol Levels on Statins, and Decreased Renal Function” – presented on behalf of all authors by Sarah Leatherman, Ph.D. – available from October 22

Additional information on ASN Kidney Week 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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