Amarin Corporation

Amarin Reports Encouraging Efficacy and Safety Results from Pilot Study Treating COVID-19 Infected Outpatients with VASCEPA® (Icosapent Ethyl) in Late Breaker Presentation at National Lipid Association (NLA) Scientific Sessions 2020

December 13, 2020

VASCEPA COVID-19 CardioLink-9 Randomized Trial suggests improvement in patient-reported COVID-19 symptoms while achieving its primary endpoint by demonstrating a 25% reduction in high-sensitivity C-reactive protein (hsCRP) with encouraging short-term safety and tolerability data using VASCEPA loading dose

VASCEPA administration resulted in a significant 52% reduction of the total patient-reported symptom outcome prevalence score as compared to a 24% reduction in the usual care group

Larger follow-on clinical studies have commenced of VASCEPA as a therapeutic option in COVID-19 settings, anticipated to be completed in 2021

Amarin to Webcast Discussion of Presented Data on Monday, December 14, 2020 at 8:00 a.m., Eastern Standard Time

DUBLIN, Ireland and BRIDGEWATER, N.J., Dec. 12, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced the presentation of clinical results from the CardioLink-9 Trial, the first results of a study of VASCEPA® (icosapent ethyl) in COVID-19 infected outpatients. The presentation, *"First Human Trial of a Loading Dose of Icosapent Ethyl in Patients with COVID-19: Primary Results of the VASCEPA COVID-19 CardioLink-9 Randomized Trial"*, *was* made virtually as a Late Breaker at the National Lipid Association (NLA) Scientific Sessions 2020, and was 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.

"In the current environment, most COVID-19 positive patients remain outside of the clinical setting, following the advice of their doctor to stay home and quarantine unless absolutely necessary to enter the hospital," commented Subodh Verma, M.D., Ph.D., FRCSC, Professor and Cardiac Surgeon at University of Toronto and co-principal investigator of COVID-19 CardioLink-9 and the encouraging results of this pilot study. "The large and significant improvement in patient-reported symptoms may provide a safe, well-tolerated, and relatively inexpensive option to impact upon COVID-19-related morbidity. The reduction in markers of inflammation with icosapent ethyl is also important given what we know about the pathobiology of COVID-19."

The VASCEPA COVID-19 CardioLink-9 Trial was a randomized, open-label trial enrolling 100 SARS-CoV-2 positive and symptomatic outpatients displaying at least one of the following: fever, cough, sore throat, shortness of breath, myalgia. Patients in the VASCEPA arm received a loading dose of 8 g/day for 3 days followed by 4 g/day for 11 days on top of usual care. Patients randomized to the non-active arm received usual care. Baseline characteristics were comparable between groups.

The primary biomarker endpoint of the study was within-group changes in high-sensitivity C-reactive protein (hsCRP), a measure of inflammation. Within-group changes in D-dimer were also examined. VASCEPA administration resulted in a 25% reduction in hsCRP (p=0.011) as well as a reduction in D-dimer (p=0.048).

In addition to these biomarker changes, assessment was made of COVID-19 symptom changes from baseline to 14 days in the influenza patient-reported outcome (FLU-PRO) score, a validated patient-reported outcome measure designed to evaluate the presence, severity and duration of flu symptoms in clinical trials. VASCEPA administration resulted in a significant 52% reduction of the total FLU-PRO prevalence score as compared to a 24% reduction in the usual care group (p=0.003 between groups), with reductions across individual score domains, including a significantly larger reduction compared to usual care in the body/systemic domain (54% vs. 26%; p=0.003). Significant reductions in the FLU-PRO symptom score compared to usual care were also observed in the total symptom score (p=0.003), as well as in the body/systemic (p=0.0007) and chest/respiratory (p=0.01) domains.

VASCEPA CardioLink-9 Study is an investigator-initiated study supported by Amarin and by HLS Therapeutics, Inc. The principal investigators of the study were Subodh Verma, M.D., Ph.D., FRCSC, Professor and Cardiac Surgeon at University of Toronto and 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.

Limitations of this study include the modest sample size, the unblinded nature of this randomized trial, and that the trial was not powered for clinical events. These results have not yet been published or reviewed by regulatory authorities. Additional study is needed.

This randomized trial represents the first human experience with an 8 g/day loading dose of icosapent ethyl and has suggested short-term safety and tolerability in a modest sample size. Regarding COVID-19, this study provides the first evidence of potential early anti-inflammatory effect of icosapent ethyl in symptomatic, COVID-19 positive outpatients.

Amarin added that the VASCEPA COVID-19 CardioLink-9 trial is the first in a series of ongoing investigator-sponsored studies into the potential role of VASCEPA therapy in COVID-19 settings. Other ongoing trials include *PREPARE-IT: Prevention of COVID19 With EPA in Healthcare Providers at Risk - Intervention Trial* sponsored by Estudios Clínicos Latino América, and *A Pragmatic Randomized Trial of Icosapent Ethyl for High-Cardiovascular Risk Adults (MITIGATE)* sponsored by Kaiser Permanente.

This presentation of CardioLink-9 study results was one of multiple data presentations at the NLA Scientific Sessions supported by Amarin. Additional information on NLA Scientific Sessions 2020 can be found here.

Audio Webcast Information
Amarin will host an audio webcast on Monday, December 14, 2020, at 8:00 a.m. EST to further discuss these and other VASCEPA-related findings

presented during the NLA Scientific Sessions 2020. 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 877-407-8033 within the United States, 201-689-8033 from outside the United States. 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 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 COVID-19
Current understanding of the biology of COVID-19 is that patients that have or are at high risk for developing atherosclerotic cardiovascular disease (ASCVD) are at higher risk of death and severe effects from infection, and that the morbidity and mortality associated with COVID-19 are due both to the direct toxicity of the virus as well as the body's robust inflammatory response leading to 'cytokine storm'. [1,2,3,4]

Scientific Rationale for Study of VASCEPA in COVID-19 Patients
Based on data related to the mechanism of action and effects of VASCEPA, it is hypothesized that VASCEPA may play a potential beneficial role in preventing SARS-CoV-2 infection and to potentially reduce clinical severity in patients infected by the virus.[4,5,6]

The clinical effects of VASCEPA are multi-factorial. Multiple mechanisms of action associated with VASCEPA based on clinical and mechanistic studies support the rationale to test its effects in patients with or at risk for COVID-19 disease. Some of these postulated mechanisms include the following:

- Potential antiviral/antimicrobial effects[7,8]
- Fibrosis and cardiac damage mitigation in animal models[9,10]
- Anti-inflammatory effects (acute) in pulmonary/lung tissue[11,12]

Ongoing preclinical and clinical research may provide further insights into the scientific and clinical understanding of these hypothetical effects of VASCEPA in COVID-19 disease mitigation. Whereas vaccines are intended to help eradicate the virus from proliferating, other therapeutics under development and clinical testing such as antibodies or other medicines may play roles in the treatment of patients in various settings across the infection and recovery continuum.

For more information on studies of VASCEPA in COVID-19 patients, see the frequently asked question entry on Amarin's corporate website, here.

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.[13] 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%.[14] 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.[15,16,17]

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.*[18] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[19] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[20] 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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