Icosapent Ethyl Included in the Chinese Society of Cardiology (CSC) Updated Guidelines for Primary Prevention of Cardiovascular Diseases

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DUBLIN, Ireland and BRIDGEWATER, N.J., Jan. 21, 2021 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced that the Chinese Society of Cardiology (CSC) has included icosapent ethyl in its updated Guidelines for Primary Prevention of Cardiovascular Diseases for 2021 as published in the *Chinese Journal of Cardiovascular Diseases*. The guideline authors include "icosapent ethyl 2 grams twice a day (as studied in REDUCE-IT®) as a treatment consideration to further lower atherosclerotic cardiovascular disease (ASCVD) in the appropriate patient population."[1]

"Inclusion of icosapent ethyl in the CSC treatment guidelines further validates the increasing independent support and acceptance of this unique drug to reduce cardiovascular risk," stated Craig B. Granowitz, M.D., Ph.D., senior vice president and chief medical officer of Amarin. "Importantly, these updated guidelines also support that the preventive effect of omega-3 fatty acids on ASCVD is not only related to the dose, but also to the type and formulation of omega-3 fatty acid and incorporates findings from the REDUCE-IT cardiovascular outcomes study of VASCEPA®."

"With this new recommendation, icosapent ethyl is now included in the treatment guidelines or otherwise recommended for use by 13 medical associations internationally, solidifying its role as an important treatment option beyond cholesterol management for millions of patients worldwide at risk for a cardiovascular event," added Dr. Granowitz. Similar to Europe, where the European Society of Cardiology and the European Atherosclerosis Society added icosapent ethyl to their medical treatment guidelines prior to completion of the ongoing regulatory submission and review processes for VASCEPA (icosapent ethyl), CSC inclusion of icosapent ethyl in its updated treatment guidelines has been made separate from and in advance of completion of the analogous regulatory processes for VASCEPA in China.

In November 2020, Amarin shared positive, statistically significant top-line results from a Phase 3 clinical trial of VASCEPA conducted in China by Amarin's partner, Edding. The study, which investigated VASCEPA as a treatment for patients with very high triglycerides (≥500 mg/dL), met its primary efficacy endpoint and demonstrated a safety profile similar to placebo. This pivotal study mirrored Amarin's MARINE study in patients from the United States and other countries and showed consistency across the Chinese and non-Chinese study populations. These findings will provide support as Edding progresses towards and through the next steps of regulatory submission and review of VASCEPA for potential approval in Mainland China.

The CSC recommendation is classified as a Category IIa recommendation denoting that icosapent ethyl is useful and effective and should be considered for treatment of at-risk patients. The classification is an Evidence Level B recommendation which reflects that the evidence comes from a single randomized trial or multiple large non-randomized studies. CSC cited that its recommendations are supported by the results of the REDUCE-IT cardiovascular outcomes study. The CSC does not provide endorsements of any brand name commercial product. Accordingly, CSC Guidelines for Primary Prevention of Cardiovascular Diseases reference icosapent ethyl. The CSC guideline does not reference VASCEPA, the brand name of icosapent ethyl in the United States, and such guideline should not be construed as an endorsement or approval by the CSC of VASCEPA.

Amarin acknowledges the rigor with which the Guidelines for Primary Prevention of Cardiovascular Diseases are crafted and approved by the CSC, which is comprised of leading medical professionals in China who specialize in the care of patients with cardiovascular disease.

The complete 2021 updates to the Guidelines for Primary Prevention of Cardiovascular Diseases from the CSC can be accessed online here.

About Hypertriglyceridemia in China
There were approximately 180.4 million hypertriglyceridemia (HTG) patients in China in 2019, representing approximately 20.2% of the adult population. Among all HTG patients in China, there were approximately 9 million adults who had very high TG levels (≥500 mg/dL). In 2019, there were approximately 36.1 million statin-treated adult patients in China with elevated TG levels (≥150 mg/dL) and either established CVD or diabetes mellitus and two or more additional risk factors for CVD, the addressable patients of the U.S. FDA-approved indication for reducing CV events of VASCEPA in China.

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 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.*[2] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[3] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[4] 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 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 U.S. 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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[1] Cardiovascular Branch of Chinese Medical Association, Cardiac Prevention and Rehabilitation Professional Committee of Chinese Rehabilitation Medicine Association, Chinese Gerontology and Elderly Cardiology Committee of the National Medical Association, et al. Guidelines for Primary Prevention of Cardiovascular Diseases in China. Chinese Journal of Cardiovascular Diseases. 2020;48(12):1000-1038.

[2] 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.

[3] 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.

[4] 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.