Amarin Corporation

Amarin Receives FDA Approval of VASCEPA® (icosapent ethyl) to Reduce Cardiovascular Risk

December 13, 2019

VASCEPA *becomes the first and only FDA-approved medication for reducing cardiovascular risk beyond cholesterol lowering therapy in high-risk patients approved for treatment*

- ***Millions of people in the United States qualify as treatment candidates for* VASCEPA**
- ***Cardiovascular disease events, including heart attack, stroke and cardiovascular death, occur in the United States every 14 seconds and are economically, physically and emotionally costly***
- **VASCEPA *has been assessed by independent bodies as priced cost effectively as a cardiovascular risk reduction treatment***
- **VASCEPA *total net revenue guidance increased for 2019 to a range of $410 to $425 million and for 2020 is newly guided to a projected range of $650 to $700 million***

Amarin to host webcast on Monday, December 16 at 7:30 a.m., Eastern Time

DUBLIN, Ireland and BRIDGEWATER, N.J., Dec. 13, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN) today announced that the U.S. Food and Drug Administration (FDA) has approved a new indication and label expansion for VASCEPA® (icosapent ethyl) capsules. After more than a decade of development and testing, VASCEPA is now the first and only drug approved by the FDA "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." It is estimated that millions of high-risk patients in the United States could benefit from this one-of-a-kind prescription therapy.[1]

"We at Amarin are excited and gratified to now have the opportunity to introduce VASCEPA as a new FDA-approved treatment option to reduce the persistent cardiovascular risk that many patients face despite use of statins with other contemporary standard-of-care therapies," said John F. Thero, president and chief executive officer of Amarin. "We aim to help millions of high-risk patients, including statin-treated patients and statin-intolerant patients. For the first time, physicians, patients and payers have an FDA-approved treatment option beyond cholesterol lowering that has been demonstrated to significantly reduce major adverse cardiovascular events when used on top of a statin. We look forward to helping educate physicians and patients on the value of VASCEPA. The expanded indication and related clinical study labeling is broadly worded, informative on the many effects of VASCEPA and will empower physicians with critical information to help them apply their clinical judgment in addressing cardiovascular disease risk for patients in need."

Amarin reaffirmed its intention to promptly launch VASCEPA in the United States for this important new preventative care indication. As previously disclosed, Amarin doubled the size of its sales force near the beginning of 2019 and is on track to double the size of its sales force again to a total of 800 sales representatives near the beginning of 2020.

"The FDA approval of icosapent ethyl as an addition to statin therapy to reduce the risk of cardiovascular events is a major milestone in cardiovascular prevention," said 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 lead investigator of the REDUCE-IT study which served as the basis for the supplemental New Drug Application to the FDA for VASCEPA. "Nothing this significant has happened in the world of cardiovascular prevention since the introduction of statins nearly three decades ago. Many patients stand to benefit from this historic advance in care."

In the global REDUCE-IT® cardiovascular outcomes study, approximately 28 percent of patients in the control arm treated with statins and other contemporary therapy but not treated with VASCEPA experienced a major adverse cardiovascular event (MACE), defined as the first occurrence of either myocardial infarction (heart attack), stroke, coronary revascularization, unstable angina requiring hospitalization or cardiovascular death.[2] As evidenced by this MACE occurrence, there is a group of patients who, despite controlling their cholesterol on statin therapy, continue to have a high need for additional preventative cardiovascular care. For those adult patients in this group who have elevated triglycerides (TG) ≥150 mg/dL and established cardiovascular disease or diabetes and two or more additional risk factors for cardiovascular disease, VASCEPA is the first drug approved to help reduce this persistent cardiovascular risk. In a published exploratory analysis of the REDUCE-IT study, examining total (first and subsequent) cardiovascular events over a period of approximately five years, patients taking VASCEPA on average experienced one fewer MACE per six patients studied, representing a 30 percent risk reduction in total MACE compared to placebo.[3]

The overall rates of adverse events and serious adverse events in the 5-year REDUCE-IT study were similar between VASCEPA-treated patients and placebo-treated patients. As reflected in VASCEPA's expanded label and described below, VASCEPA has been associated with increased risks of bleeding and atrial fibrillation/flutter, the latter being more prevalent in patients with a previous history of atrial fibrillation or flutter. It is recommended that patients taking VASCEPA and concomitant anticoagulants and/or anti-platelet agents for bleeding be monitored. Also noted in the REDUCE-IT study is that patients for whom bleeding and/or atrial fibrillation/flutter were reported appeared to obtain a similar reduction in MACE as patients not reporting such adverse events. Such findings are consistent with published results of the study, which noted that the increased rates of such adverse events were low, notably lower than the reduction in MACE.[3]

Recurrent event analyses were conducted of the total primary endpoint events and total key secondary endpoints in REDUCE-IT using a series of statistical models and published in the *Journal of the American College of Cardiology*. These analyses are not in FDA labeling, were tertiary or exploratory endpoints; most of the models used were prespecified and one was post hoc. Each recurrent event statistical model has inherent strengths and weaknesses, with no single model considered definitive or outperforming the other models, and this is an evolving field of science. Nonetheless, results from these analyses are consistent across the various models; they also are consistent with the original primary and secondary endpoint results. Together, the REDUCE-IT recurrent event analyses and the original primary and key secondary endpoint analyses support the robustness of the clinical benefit of VASCEPA therapy in reducing cardiovascular risk.

Need Is Acute for a Cost-Effective, Preventative-Care Therapy Like VASCEPA
Despite current treatment options, in the United States, there is one stroke and one heart attack each occurring on average every 40 seconds, and one cardiovascular death occurring on average every 38 seconds, or, in aggregate one such cardiovascular event every 14 seconds.[4,5] Cardiovascular disease costs in the United States are in excess of $500 billion each year, making it the nation's most expensive disease. [6] The number of cardiovascular deaths is also increasing, serving as the No. 1 cause of death for men and women in the United States.[7] These facts point to an acute need for more innovation in the cardiovascular disease therapeutic area.

Since statin therapy was introduced nearly three decades ago, healthcare professionals have sought effective preventative care treatment options to reduce persistent cardiovascular risk beyond management of cholesterol. Many potential solutions failed to show favorable effects in cardiovascular outcomes studies. The development of VASCEPA included learnings from these failures and now VASCEPA is the first and only drug to succeed in reducing that risk in the patient group included in the new VASCEPA label.

Recently, a health economics study conducted by an expert group presented at the American Heart Association 2019 Scientific Sessions showed that use of VASCEPA offers potential cost savings for the overall healthcare system (i.e., the cost of VASCEPA is offset by cost savings from reducing the occurrence of high-cost major adverse cardiovascular events).[7] This rare finding follows conclusions from a separate independent drug pricing watchdog group that found VASCEPA cost effective for cardiovascular risk reduction, a result seldom achieved in this organization's analyses. [8]

Based on the unprecedented results of the REDUCE-IT outcomes study, multiple professional societies have updated guidelines or issued advisories to incorporate icosapent ethyl, including the American Diabetes Association,[9] the European Society of Cardiology, The European Atherosclerosis Association,[10] and the National Lipid Association.[11]

Today's announced new indication for VASCEPA is incremental to its indication for which it was initially FDA approved, as an adjunct to diet to reduce triglyceride 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.

"In achieving this expanded indication, Amarin appreciates the FDA's guidance in the design and conduct of multiple clinical trials of VASCEPA across the past decade and for its diligence in reviewing the results of these studies," said Steven Ketchum, Ph.D., senior vice president and president, research & development and chief scientific officer, Amarin. "Moreover, Amarin is grateful to the thousands of patients and clinical sites who participated in the extensive study of VASCEPA, which exceeded 37,000 patient-years of study in the clinical development program. Amarin also thanks its dedicated employees and advisors who overcame many challenges to achieve this important life-saving accomplishment."

Revenue Guidance Updated for 2019 and Provided for 2020
Amarin last updated its revenue guidance for 2019 in its press release dated July 2, 2019. Amarin now makes the following update to that guidance and issues its first guidance for 2020:

With respect to the year ending December 31, 2019, while the year is not yet complete, Amarin increases its guidance for total net revenue to a range of $410 to $425 million. Prior guidance for this period given in July 2019 was total net revenue in a range of $380 to $420 million. The midpoint of this new full-year 2019 guidance, $417.5 million, would represent an increase of approximately 82% over full year 2018 results.

With respect to 2020, Amarin projects that total net revenue will be in a range of $650 to $700 million, mostly from sales of VASCEPA in the United States. Amarin is providing this projected revenue guidance for 2020 and has based its projection on a number of factors, including, but not limited to, expectations on market acceptance of the newly expanded label for VASCEPA and current plans for expanded promotion. VASCEPA revenues are anticipated to continue to increase in 2020, accompanied by quarterly industry variability, including recurring seasonal factors, particularly in the first quarter. Given that it takes time to educate providers and patients, Amarin expects a delayed impact from planned promotional programs either because they are new, such as the impact of new sales representatives, or, in the case of direct-to-consumer promotion, because separate regulatory approval is required and not currently expected until mid-2020. In addition, while multiple studies have concluded that VASCEPA is cost effective, how managed care organizations will react to a cost-effective therapy lacks adequate precedent.

Beyond 2020, Amarin believes that VASCEPA total net revenue will grow to reach multiple billions of dollars. However, the history of other therapies for chronic conditions suggests that growth builds over multiple years. At this time, the company is not providing guidance regarding annual revenue levels beyond 2020.

Conference Call and Webcast Information:
Amarin will host a conference call Monday, December 16, at 7:30 a.m. ET to discuss this information. The conference call can be heard 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, or by using the call back feature at https://bit.ly/35nxY8k. A replay of the call will be made available for a period of two weeks following the conference call. To hear a replay of the call, dial 877-481-4010, PIN: 56897. A replay of the call will also be available through the company's website shortly after the call.

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 and 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 for bleeding should be monitored.

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.

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, Lebanon and the United Arab Emirates. Amarin, together with its commercial partners in select geographies, is pursuing additional regulatory approvals for VASCEPA in Canada, China, the European Union and the Middle East. For more information about Amarin, visit www.amarincorp.com.

Forward-Looking Statements
This press release contains forward-looking statements, including expectations regarding commercial expansion and the use of VASCEPA to potentially help millions of patients, revenue and prescription growth, including updated revenue guidance for 2019 and guidance for 2020 and beyond; sales force expansion and marketing initiatives expected in 2019 and beyond; managed care acceptance; the applicability and reliability of REDUCE-IT results and cost effectiveness data. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. In addition, Amarin's ability to effectively commercialize VASCEPA will depend in part on its ability to continue to effectively finance its business, efforts of third parties, its ability to gain regulatory approvals, create market demand for VASCEPA through education, marketing and sales activities, to achieve market acceptance of VASCEPA, to receive adequate levels of reimbursement from third-party payers, to develop and maintain a consistent source of commercial supply at a competitive price, to comply with legal and regulatory requirements in connection with the sale and promotion of VASCEPA and to maintain patent protection for VASCEPA. Among the factors that could cause actual results to differ materially from those described or projected herein include the following: uncertainties associated generally with acceptance of clinical trial results and related regulatory approvals; the risk that sales may not meet expectations and related cost may increase beyond expectations; the risk that patents may not be upheld in patent litigation and applications may not result in issued patents sufficient to protect the VASCEPA franchise. 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.

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:
Elisabeth Schwartz
Investor Relations
Amarin Corporation plc
In U.S.: +1 (908) 719-1315
investor.relations@amarincorp.com

Lee M. Stern
Solebury Trout
In U.S.: +1 (646) 378-2992
lstern@soleburytrout.com

Media Inquiries:
Gwen Fisher
Corporate Communications
Amarin Corporation plc
In U.S.: +1 (908) 325-0735
pr@amarincorp.com

(Note for reporters: if you require additional assets to accompany your stories, including product photos or b-roll, please contact Gwen Fisher at the above email address.)

References

1 Fan W, Philip S, Toth PP, et al. Prevalence of United States adults with triglycerides ≥ 135 mg/dL: NHANES 2007–2014. Cardiol J. 2019;26(5). DOI: 10.5603/CJ.2019.0000.

2 Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med 2019;380:11-22.

3 Bhatt DL, Steg PG, Miller M, et al. Effects of Icosapent Ethyl on Total Ischemic Events: From REDUCE-IT. J Am Coll Cardiol 2019; 73:2791-2802.

4 American Heart Association: Heart Disease and Stroke Statistics -- 2019 At-a-Glance.

5 American Heart Association. Heart Disease and Stroke Statistics – 2019 Update: A Report from the American Heart Association. Published January 31, 2019.

6 American Heart Association. 2017. Cardiovascular disease: A costly burden for America projections through 2035.

7 Cost-Effectiveness of Icosapent Ethyl in REDUCE-IT. https://www.abstractsonline.com/pp8/#!/7891/presentation/35097.

8 https://icer-review.org/wp-content/uploads/2019/02/ICER_CVD_Final_Evidence_Report_10.17.19.pdf.

9 American Diabetes Association. [web annotation]. Diabetes Care 2019;42(Suppl.1):S103–S123.
10 Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2019; ehz455. doi: 10.1093/eurheartj/ehz455.
11 Orringer CE, Jacobson TA, Maki KC. National Lipid Association scientific statement on the use of icosapent ethyl in statin-treated patients with elevated triglycerides and high- or very-high ASCVD risk. J Clin Lipidol. 2019. doi: 10.1016/j.jacl.2019.10.014.