AMARIN CORP PLC\UK
Form 8-K
November 13, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of the Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): November 10, 2018

Amarin Corporation plc

(Exact name of registrant as specified in its charter)

England and Wales	**0-21392**	**Not applicable**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

2 Pembroke House, Upper Pembroke Street 28-32,
Dublin 2,

Ireland	**Not applicable**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code: +353 1 6699 020

Not Applicable

Former name or former address, if changed since last report

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01. Regulation FD Disclosure.

Investor FAQ Updates

Investors and others should note that from time to time Amarin Corporation plc, or the Company, communicates with its investors and the public using the investor FAQs section within the investor relations website of the company s website (http://investor.amarincorp.com/) without notice through filings with the SEC. The contents of the Company 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, as amended. Between November 10, 2018 and November 13, 2018, the Company has posted the following new FAQ documents, among others:

What is Amarin s perspective on the use of mineral oil in its clinical trials? , detailing the robust regulatory history and independent review of light liquid paraffin oil as used in Vascepa clinical trials and an analysis with figures showing data from the Company s REDUCE-IT cardiovascular outcomes study detailing the similar cardiovascular risk reduction observed in patient groups regardless of whether there was an increase in LDL-C level among the patients in the placebo group.

I heard the Global Principal Investigator for the REDUCE-IT study comment in his late-breaker presentation at AHA that there was no change in hsCRP in the placebo-arm of the study, please explain why that was referenced? , detailing, among other information, that using the log high-sensitivity C-reactive protein, or hsCRP, method, the standard and generally recognized method to avoid a misleadingly skewed result due to the high variability of hsCRP for the population studied in REDUCE-IT, there was no increase in log hsCRP from baseline in the placebo arm and that the between-group change was a 22.5% reduction at Year 2 and was driven by Vascepa therapy (with data using the log hsCRP method as presented within the peer reviewed NEJM publication).

November 10, 2018 Press Release Regarding REDUCE-IT Results

On November 10, 2018, the Company issued a press release announcing the primary results of its REDUCE-IT study. A copy of this press release is furnished as Exhibit 99.1 to this Report and is incorporated herein by reference.

The information contained in, or incorporated into, this Item 7.01 and in Exhibit 99.1 attached hereto is being furnished and shall not be deemed filed for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any registration statement or other filing under the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference to such filing.

Item 8.01. Other Events.

On November 10, 2018, the Company announced primary results from its REDUCE-IT study. REDUCE-IT met its primary endpoint demonstrating a 25% relative risk reduction, or RRR, to a high degree of statistical significance ($p<0.001$), in first occurrence of major adverse CV events, or MACE, in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo. Patients qualified to enroll in REDUCE-IT had LDL-C between 41-100 mg/dL (median baseline LDL-C 75 mg/dL) controlled 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 age 50 or more with diabetes mellitus and at least one other CV risk factor (primary prevention cohort). Approximately 59% of the patients had diabetes at baseline and approximately 71% of the patients had established cardiovascular disease at time of enrollment. REDUCE-IT also

showed a 26% RRR in its key secondary composite endpoint of cardiovascular death, heart attacks and stroke (p<0.001). On November 10, 2018, REDUCE-IT results were published in *The New England Journal of Medicine* and presented as late-breaking clinical results at the 2018 Scientific Sessions of the American Heart Association, or AHA. The Company commenced the REDUCE-IT trial in 2011 and has expended more than $300 million to fund its completion.

Number needed to treat, or NNT, was 21 for the first occurrence of MACE in the 5-point primary composite endpoint. The NNT is a statistical concept intended to provide a measurement of the impact of a medicine or therapy by estimating the number of patients that need to be treated in order to have an impact on one person.

An additional seven secondary endpoints were achieved below the key secondary endpoint, in order of sequential statistical testing within the prespecified hierarchy:

- Cardiovascular death or nonfatal heart attack: 25% RRR (p<0.001)
- Fatal or nonfatal heart attack: 31% RRR (p<0.001)
- Urgent or emergent revascularization: 35% RRR (p<0.001)
- Cardiovascular death: 20% RRR (p=0.03)
- Hospitalization for unstable angina: 32% RRR (p=0.002)
- Fatal or nonfatal stroke: 28% RRR (p=0.01)
- Total mortality, nonfatal heart attack or nonfatal stroke: 23% RRR (p<0.001)

The next prespecified secondary endpoint in the hierarchy was the only such endpoint that did not achieve statistical significance:

- Total mortality, which includes mortality from non-cardiovascular and cardiovascular events: 13% RRR (p=0.09)

Positive REDUCE-IT results were consistent across various patient subgroups, including female/male, diabetic/non-diabetic and secondary/primary prevention. Vascepa was well tolerated with a safety profile generally consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling of such products. Excluding the MACE results described above, overall adverse event rates in REDUCE-IT were similar across the statin plus Vascepa and the statin plus placebo treatment groups. There were no significant differences between treatments in the overall rate of treatment emergent adverse events or serious adverse events leading to withdrawal of study drug. The one serious adverse event occurring at a frequency of >2% was pneumonia which occurred at a numerically higher rate in the statin plus placebo treatment group (2.9%) than in the statin plus Vascepa treatment group (2.6%). Adverse events occurring in 5% or greater of patients and more frequently with Vascepa than placebo were peripheral edema (6.5% Vascepa patients versus 5.0% placebo patients), constipation (5.4% Vascepa

patients versus 3.6% placebo patients), and atrial fibrillation (5.3% Vascepa patients versus 3.9% placebo patients). There were numerically more serious adverse events related to bleeding in the statin plus Vascepa treatment group although overall rates were low with no fatal bleeding observed in either group and no significant difference in adjudicated hemorrhagic stroke or serious central nervous system or gastrointestinal bleeding events between treatments.

In the REDUCE-IT trial, cardiovascular benefits appeared not to be influenced significantly by TG levels at baseline (above or below 150 mg/dL baseline range) or as achieved at one year, potentially suggesting mechanisms at work with use of Vascepa that are independent of baseline TG levels or therapy-driven reduction in TG levels. Mechanisms responsible for the benefit shown in REDUCE-IT were not the focus of REDUCE-IT. As summarized from the primary results of REDUCE-IT in *The New England Journal of Medicine,* potential Vascepa mechanisms of action at work in REDUCE-IT may include TG reduction, anti-thrombotic effects, antiplatelet or anticoagulant effects, membrane-stabilizing effects, effects on stabilization and/or regression of coronary plaque and inflammation reduction, each as supported by earlier stage mechanistic studies. In addition, the median change in LDL cholesterol levels from baseline was higher in the placebo group versus the Vascepa group (difference of 5.0 mg/dL; $p < 0.001$). However, a *post hoc* analysis of REDUCE-IT data published in *The New England Journal of Medicine* showed no material difference in each of the primary and key secondary cardiovascular risk composite endpoint event rates for placebo patients that experienced an increase in LDL-C at one year versus those with no change or a decrease, and also suggested a similar relative risk reduction regardless of whether there was an increase in LDL cholesterol level among the patients in the placebo group. Moreover, as the authors of the paper published in *The New England Journal of Medicine* noted, the relatively small differences in LDL-C levels between the groups would not be likely to explain the 25% lower MACE risk observed with Vascepa and the Japan open-label EPA Lipid Intervention Study (JELIS), an over 18,000 patient cardiovascular outcomes study in Japan of a highly-pure EPA product similar to Vascepa, previously demonstrated a 19% risk reduction without a mineral oil placebo.

Following the announcement of REDUCE-IT topline results, the Company has begun promoting REDUCE-IT results to healthcare professionals in the United States based on what the Company believes is its continuing obligation under its First Amendment settlement to ensure that its promotion of Vascepa remains truthful and non-misleading. This effort continued after November 10, 2018 as more data became available with REDUCE-IT primary results. The Company is also developing Vascepa for FDA approval of additional indications based on REDUCE-IT.

The REDUCE-IT study was designed under a special protocol assessment agreement, or SPA, with the FDA. The Company intends to submit an sNDA to the FDA in early 2019 seeking approval to expand the label for Vascepa based on the cardioprotective effect of Vascepa demonstrated in the REDUCE-IT study. The FDA s determination of standard or priority review will be made when the sNDA is submitted. At this time, the Company is planning for a standard review with potential approval anticipated in late 2019.

Forward-Looking Statements

This report contains forward-looking statements, including expectations regarding planned regulatory filings and the nature of FDA s review and related timing thereof; expectations that REDUCE-IT results could lead to a new treatment paradigm in the patient population studied; and plans for sales force, international and insurance coverage expansion. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. In addition, the Company 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 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 research and development, clinical trials 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 the Company can be found in the Company 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. The Company 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.

Item 9.01. Financial Statements and Exhibits.

Exhibits

Exhibit No.	Description
99.1	Press Release, dated November 10, 2018, furnished herewith

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 13, 2018

AMARIN CORPORATION PLC

By: /s/ John Thero
John Thero
President and Chief Executive Officer